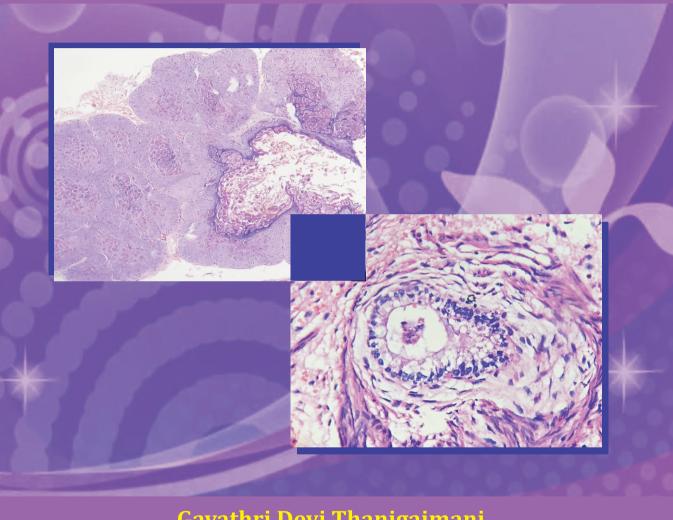
A CONCISE BOOK OF GENERAL PATHOLOGY

Covers Questions of Past 10 years University Question Paper



Gayathri Devi Thanigaimani



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Ph. 044 - 24364303. Cell: 9282134542,

E-mail: murali.aks@gmail.com, Website: aksharaa.co.in

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About the Author



The author Dr. Gayathri Devi Thangaimani is a medical graduate of Kilpauk Medical College. She pursued her higher studies in UK on obstetrics and gynaecology. But her destiny brought her to pathology in India.

She completed her post graduation in India in Sree Balaji Medical College. After obtaining her masters she worked in Medall Histopathology lab. Her passion for teaching brought her back to her home ground of Sree Balaji Medical College as assistant professor in Pathology.

She is also a sought after pathology faculty for post graduate NEET coaching and FMGE examination. This book is her first attempt to simplify pathology for undergraduate medical, dental and allied medical students.

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E-mail: murali.aks@gmail.com, Website: aksharaa.co.in



A CONCISE TEXT BOOK OF MCQ's IN IMMUNOLOGY

FIRST EDITION



Author Dr Priya Santharam



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The Book

- User Friendly and easy to understand
- Text is presented in a simple and clear manner
- Colour diagrams incorporated in appropriate places
- Chapter wise organisation for In depth understanding of subject

The Author



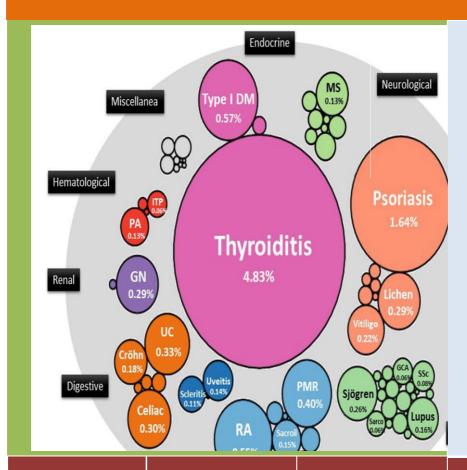
Dr Priya Santharam

Dr Priya Santharam, Associate Professor of Microbiology at Sree Balaji Medical College and Hospital, Chennai has been in teaching for the past 10 years. She has also worked in other places like Annapoorna Medical College and Vinayaka Missions Kirupananda Variyar Medical College, Salem. She has held posts as Academic Coordinator and Member faculty of Medical Education Unit. She has published papers in National and International Journals. Her thesis won the Best paper Award at VINBASIX conference in 2012.

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A CONCISE TEXT BOOK OF MEASURES OF DISEASE FREQUENCY



2018

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Department of Community Medicine

Sree Balaji Medical College and Hospital.

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Medical College and Hospital, to disseminate valuable information targeting the

Medical students, Interns & Postgraduate students regarding the concepts and

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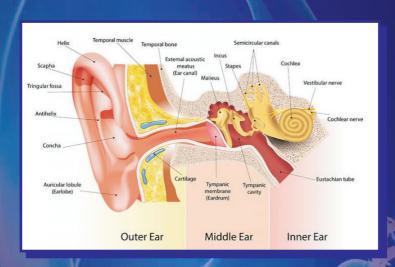
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A Concise Textbook of Syndromes in the Ear



Prof. Dr. M.K. Rajasekar, M.B.B.S, MS ENT, D.L.O
Dr. Shwetha Shashikumar





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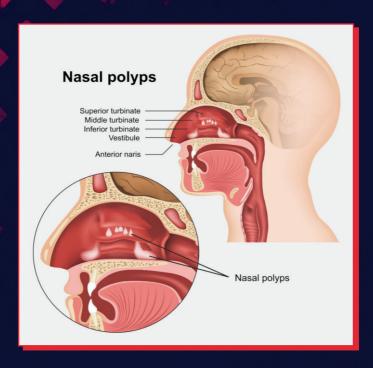
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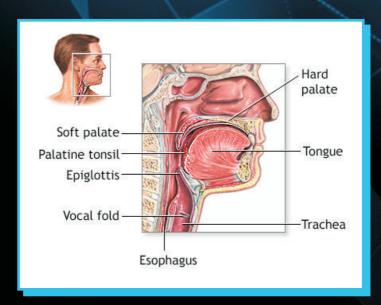
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A Concise Textbook of Syndromes in the Throat



Prof. Dr. M.K. Rajasekar, M.B.B.S, MS ENT, D.L.O Dr. Shwetha Shashikumar Dr. Nithya Balasubramanian











SREE BALAJI MEDICAL COLLEGE HOSPITAL CHROMEPET, CHENNAI.

MEDICAL EDUCATION UNIT DEPARTMENT OF GENERAL MEDICINE

A BOOK ON DEEP VENOUS THROMBOSIS & PULMONARY EMBOLISM

Prof. Dr. N N ANAND | Dr. RAM PRASAANTH P



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- 7. DVT IN PREGNANCY

A CONCISE TEXT BOOK OF ADOLOSCENT HEALTH

Adolescent H

Dr. Gopalrao Jogdand, M.I. Professor & Head, Department of Community Med



Author: Professor. Dr. Rashmi Gour

Department of Community Medicine

Sree Balaji Medical College and Hospital.

PREFACE

We the faculties of Department of Community Medicine started this book

with an intention to disseminate valuable information about adoloscent health,

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A CONCISE TEXTBOOK ON ATOPIC DERMATITIS

Authors:

Prof. Ashok Kumar N

Professor, Department of DVL, Sree Balaji Medical College & Hospital, Chennai, Tamil Nadu, India

Prof.Manoharan.D

Professor, Department of DVL, Sree Balaji Medical College & Hospital, Chennai, Tamil Nadu, India

Co-Authors:

Dr. Geo Danny C

Assistant Professor, Department of DVL, Sree Balaji Medical College & Hospital, Chennai, Tamil Nadu, India

Dr. Sivaramakrishnan.S

Senior Resident, Department of DVL, Sree Balaji Medical College & Hospital, Chennai, Tamil Nadu, India

Prof.K.Manoharan

H.O.D, Department of DVL, Sree Balaji Medical College & Hospital, Chennai, Tamil Nadu, India

Editorial Office

Prof.K.Manoharan

Professor & Head of Department,

Department of Dermatology, Venereology & Leprosy,

Sree Balaji Medical College & Hospital,

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A Concise Text Book on Common ARBO Viral Infections



Author
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A CONCISE TEXTBOOK ON DONOVANOSIS

Authors

Dr. Sane Roja Renuka

Senior Resident, Department of DVL, Sree Balaji Medical College & Hospital, Chennai, Tamil Nadu, India

Prof. Ashok Kumar N

Professor, Department of DVL, Sree Balaji Medical College & Hospital, Chennai, Tamil Nadu, India

Co-Authors

Dr. C. Geo Danny

Assistant Professor, Department of DVL, Sree Balaji Medical College & Hospital, Chennai, Tamil Nadu, India

Prof. D.Manoharan

Professor, Department of Dermatology, Venereology & Leprosy, Sree Balaji Medical College & Hospital, Chennai, Tamil Nadu, India

Prof. K. Manoharan

Professor and Head of Department, Department of DVL, Sree Balaji Medical College & Hospital, Chennai, Tamil Nadu, India

Editorial Office

Prof.K.Manoharan

Professor and Head of Department,

Department of DVL,

Sree Balaji Medical College & Hospital,

7, CLC Works Road, Chromepet, Chennai 600044,

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A CONCISE TEXTBOOK ON LYMPHOGRANULOMA VENEREUM

Authors:

Dr. Sukanya G.

Associate Professor, Department of DVL, Sree Balaji Medical College and Hospital, Chennai, India.

Dr. Sane Roja Renuka

Senior Resident, Department of DVL, Sree Balaji Medical College and Hospital, Chennai, India.

Co-Authors:

Dr. Geo Danny C

Assistant Professor, Department of Dermatology, Venereology & Leprosy, Sree Balaji Medical college & Hospital, Chennai, India

Dr. Vignesh NR

Assistant Professor, Department of DVL, Sree Balaji Medical College & Hospital, Chennai, TN, India

Prof. K. Manoharan

Prof & HOD, Department of DVL, Sree Balaji Medical College & Hospital, Chennai, TN,
India

Editorial Office

Prof.K.Manoharan

Professor and Head of Department,

Department of DVL,

Sree Balaji Medical College & Hospital,

7, CLC Works Road, Chromepet, Chennai 600044,

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Chennai 600077

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Authors

Dr. Vignesh NR

Assistant Professor, Department of DVL, Sree Balaji Medical College & Hospital, Chennai, Tamil Nadu, India

Dr. Sukanya G

Associate Professor, Department of DVL, Sree Balaji Medical College & Hospital, Chennai, Tamil Nadu, India

Co-Authors:

Dr. Ramesh TV

Assistant Professor, Department of DVL, Sree Balaji Medical College & Hospital, Chennai, Tamil Nadu, India

Dr. Sane Roja Renuka

Senior Resident, Department of DVL, Sree Balaji Medical College & Hospital, Chennai, Tamil Nadu, India

Prof. K. Manoharan

Prof & HOD, Department of DVL, Sree Balaji Medical College & Hospital, Chennai, Tamil Nadu, India

Editorial Office

Prof.K.Manoharan

Professor and Head of Department,

Department of DVL,

Sree Balaji Medical College & Hospital,

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Authors

Dr. Sivaramakrishnan.S

Senior Resident, Department of DVL, Sree Balaji Medical College & Hospital, Chennai,
Tamil Nadu,India

Dr. Shreya Srinivasan

Senior Resident, Department of DVL, Sree Balaji Medical College & Hospital, Chennai,
Tamil Nadu,India

Co-Authors

Dr. Sukanya G

Associate Professor, Department of DVL, Sree Balaji Medical College & Hospital, Chennai,
Tamil Nadu, India

Prof. D. Manoharan

Professor, Department of DVL, Sree Balaji Medical College & Hospital, Chennai, Tamil Nadu, India

Prof. K. Manoharan

Professor and H.O.D, Department of DVL, Sree Balaji Medical College & Hospital, Chennai,
Tamil Nadu, India

Editorial Office

Prof.K.Manoharan

Professor & Head of Department,

Department of Dermatology, Venereology & Leprosy,

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A CONCISE TEXTBOOK ON SEBORRHEIC KERATOSES

Authors

Dr. Shreya Srinivasan

Senior Resident, Department of DVL, Sree Balaji Medical College & Hospital, Chennai,
Tamil Nadu, India

Dr. Sivaramakrishnan .S

Senior Resident, Department of DVL, Sree Balaji Medical College & Hospital, Chennai,
Tamil Nadu, India

Co-Authors

Prof.N.Ashok Kumar

Professor, Department of DVL, Sree Balaji Medical College & Hospital, Chennai, Tamil Nadu, India

Dr.Sukanya.G

Associate Professor, Department of DVL, Sree Balaji Medical College & Hospital, Chennai, Tamil Nadu, India

Prof.K.Manoharan

Professor and Head of Department, Department of DVL, Sree Balaji Medical College & Hospital, Chennai, Tamil Nadu, India

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Prof.K.Manoharan

Professor & Head of Department,

Department of Dermatology, Venereology & Leprosy,

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A CONCISE TEXTBOOK ON VOLUNTARY HEALTH AGENCIES

AUTHORS:

DR.G.ANGELINE GRACE, Assistant Professor
DR.P.SUJITHA, Assistant Professor



Department of Community Medicine,
Sree Balaji Medical College and Hospital, BIHER, Chennai600044.

PREFACE

We the faculties of Department of Community Medicine started this book with an

intention to disseminate valuable information about Voluntary Health Agencies, targeting the

Medical students, Interns & Postgraduate students. This topic is salient for health professionals

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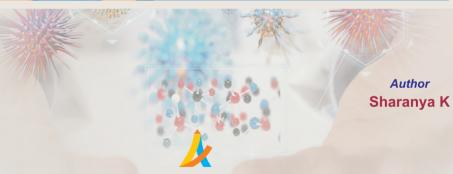
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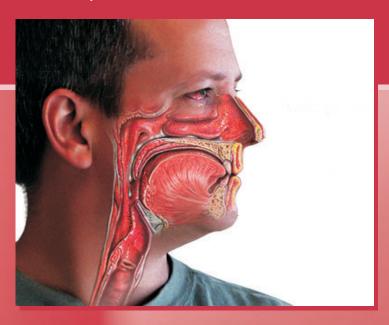
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A REVISION TEXT BOOK OF EAR, NOSE AND THROAT



Author
Prof. Dr. M.K. Rajasekar



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E-mail: murali.aks@gmail.com



A Short Textbook on Child Abuse-A Challenge



AUTHORS: DR RASHMI GOUR PATEL DR S HARIHARAN

DEPARTMENT OF COMMUNITY MEDICINE
SREE BALAJI MEDICAL COLLEGE AND HOSPITAL
Chromepet, Chennai- 600044

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Medical College and Hospital, to disseminate valuable information targeting the

Medical students, Interns & Postgraduate students regarding the concepts and

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A SHORT TEXTBOOK ON NEGLECTED TROPICAL DISEASES



<u>AUTHOR</u> Dr. SHANTHI EDWARD

DEPARTMENT OF COMMUNITY MEDICINE
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SREE BALAJI MEDICAL COLLEGE AND HOSPITAL CHROMEPET, CHENNAI.





A SHORT TEXTBOOK ON VERBAL AUTOPSY IN INDIA

AUTHORS:
DR.P.SUJITHA
DR.G.ANGELINE GRACE

Department of Community Medicine, Sree Balaji Medical College and Hospital, BIHER, Chennai-600044. A SHORT TEXTBOOK ON VERBAL AUTOPSY IN INDIA

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A Study on Reducing Waiting Time in Out Patient Department In A Multispecialty Hospital



Dr. S. Brigida



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Bharath Institute of
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About the Author

The author of this book Dr. Brigida is an allopathy doctor with post graduation in pharmacology and hospital management. Her next talent acquisition is pursuing skills in administration. As a step towards it she focused on Reducing waiting time for patients in hospital acknowledging the time delay happening in patient management. Considering time as a key factor for any excellence this book set fire on reduction of waiting time favoring patient and hospital management using "SIX SIGMATECHNIQUE".

No.441/303, Anna Salai, Teynampet, Chennai-18. Tamilnadu, India

Ph. 044 - 24364303. Cell: 9282134542,

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A TEXT BOOK ON CONCEPTS IN MYCOLOGY



Author Dr. K. Dinesh



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ACUTE POISONING

DR.K SHANMUGANANDAN

DR.KAVURU NAGA SIRI

DEPARTMENT OF GENERAL MEDICINE,

SREE BALAJI MEDICAL SCIENCES AND HOSPITAL.

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Editorial Office

Prof. Dr. (Brig.) Shanmuganandan Krishnan

Professor of Department of General Medicine

Consultant Rheumatologist

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ACUTE RESPIRATORY DISTRESS SYNDROME

(MONOGRAPH)

By

Dr NITHARSHA PRAKASH M

Post-Graduate Resident

Department of General Medicine,

Sree Balaji Medical College and Hospital, Chennai-44

Editorial Office:

Prof. Dr. (Brig.) Shanmuganandan Krishnan

Professor of Department of General Medicine

Consultant Rheumatologist

Sree Balaji Medical College and Hospital

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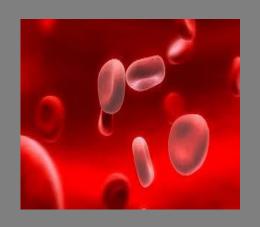
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ANAEMIA IN PREGNANCY –A PUBLIC HEALTH PROBLEM





AUTHOR: Dr.R.UMADEVI,MD

PROFESSOR & HOD
DEPARTMENT OF COMMUNITY MEDICINE
SREE BALAJI MEDICAL COLLEGE AND HOSPITAL
CHROMEPET, CHENNAI- 600044

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Medical College and Hospital, to disseminate valuable information targeting

the Medical students, Interns & Postgraduate students about Anaemia in

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ANAEROBIC CULTURE TECHNIQUES



Author
Dr Sindhu Cugati



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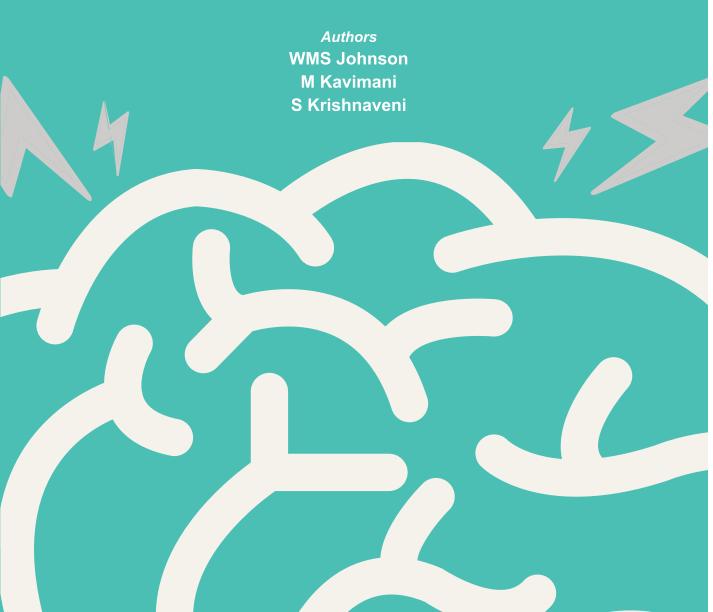
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Ph. 044 - 45080083. Cell: 9282134542

E-mail: murali.aks@gmail.com



ANATOMY FOR TOMORROW





ANATOMY FOR TOMORROW

Authors
WMS Johnson
M Kavimani
S Krishnaveni

Department of Anatomy
Sree Balaji Medical College and Hospital
Chennai - 600044

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National Conference on Anatomy of Yoga, Dance & Plyometrics

04th to 05th April 2019

Organising Committee



Anatomy for Tomorrow

National Conference in Anatomy Sree Balaji Medical College & Hospital Chennai

Yoga has been the subject of research in the past few decades for therapeutic purposes for modern epidemic diseases like mental stress, obesity, diabetes, hypertension coronary heart disease, and chronic obstructive pulmonary disease. Many studies report beneficial effect of yoga in these conditions, indicating that it can be used as non pharmaceutical measure or complement to drug therapy for treatment of these conditions. Dancing can be a way to stay fit for people of all ages, shapes and sizes. It has a wide range of physical and mental benefits including: improved condition of heart, lungs, Increased muscular strength, endurance and motor fitness. There are many strength and conditioning programs, Plyometric training is a specific type of training involving exercises in which the active muscles are stretched prior to shortening and usually requires explosive-strength training commonly used in rehabilitation programs.

This **National Conference** – *Anatomy for tomorrow* focuses on Yoga dance & Plyometry is conducted by the **Department of Anatomy of Sree Balaji Medical College and Hospital** will highlight and enrich the audience the Importance of understanding anatomy in yoga, the anatomical correlation of core muscle activation in different yogic postures, the ascending reticular activation system and yoga. The conference will pave path to individuals and medical faculty to understand the kinematic of joints among dancers, the various range of movements of small joints in different mudras. The conference will also provide the viewer the recent trends in plyometric training and its health benfits.

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SREE BALAJI MEDICAL COLLEGE & HOSPITAL



DEPARTMENT OF ANATOMY

The Management and the Organising Committee cordially invite you to the inaugural function of the

> National Conference on

Anatomy of Yoga Dance and Plyometrics



Presided by **Dr. V. Kanagasabai**Vice-Chancellor of BIHER

Guest of Honour

Kalaimamani K.V. Swarnamukhi

("Dance Laureate" of Govt. of Tamil Nadu)

On 4th April 2019 at 9:30 AM Venue: T.R Raman Hall

Organising Secretary

Dr. WMS Johnson MD PhD

Vice Principal

Organising Chairman
Dr.P.Sai Kumar MD PhD
Dean

Founder Chancellor Message



I am extremely happy that a National Conference on Anatomy of Yoga, Dance & Plyometrics – YODAP - is to be conducted by the Department of Anatomy of Sree Balaji Medical College & Hospital, Chrompet along with the support of Medical Council of India. Yoga & Dance being the ancient knowledge of India is scientifically approved and practiced world over. The importance of plyometrics is being recognized world over. I am happy that such a theme is thought of for a conference by the department of Anatomy. The glorious heritage of India's medical education continues, and today, our medical expertise and quality of our performance in the field of science health have earned us an enviable global recognition.

In this present day national context of a fresh impetus, the Management of Sree Balaji Medical College & Hospital, chooses to express its deep sense of appreciation of your zeal and vision. I hope that deliberation at the conference will shed fresh light on our path towards realization of our cherished goal of service-the noble cause of our people's health.

I wish the Conference every success.

Dr. S Jagathrakshagan, M. A., D. Litt Founder Chancellor, Bharath University

Chairman Message



It is heartening to note that a National conference on Yoga, Dance and Plyometrics – YODAP -19 is to be conducted by the Department of Anatomy of the Sree Balaji Medical College & Hospital.

The enthusiasm shown by the Dean, Vice-Principal and the Staff of the Anatomy department is commendable and this has motivated the management of the institution in supporting them. I am told the conference would be attracting anatomists and medical faculty not from all over Tamil Nadu but also from all over India. I consider it my good fortune and privilege as the Chairperson of the Sree Balaji Medical College and Hospital to be associated with this conference and support it in whatever way I could.

I take this opportunity to congratulate our Dean, Dr. P.Saikumar, Vice-Principal and organizing secretary of the conference Dr.W.M.S.Johnson, for their leadership. I also congratulate all the supporting staff of the Anatomy department and other department for rising up to the occasion and organizing this important event which would be remembered as an important milestone in the life of this young institution.

I wish the Conference every success.

Dr. J. Srinisha

Chairman

Sree Balaji Medical College and Hospital

Advisor's Message



Yoga is Religion...

It is the personal change, adjustment, integration

It is not profession of doctrine

It is the reconditioning of one's nature

It is not intellectual orthodoxy

It is the awakening of the life of spirit in man

- Swami Vivekananda

I wish the National Conference on Anatomy of Yoga, Dance and Plyometrics bring the goal of spiritual realization that can be reached by any one of the different methods and also understand the Anatomy of muscle synergies and various range of movements of the body.

It is heartening to note this conference paves the way of understanding Anatomy in a novel way.

Dr. R. Veerabahu, M.D.,

R Keevahahu

Advisor

Vice Chancellor Message



I am extremely happy to know that the Dept of Anatomy is organizing a National Conference on "Anatomy of Yoga, Dance and Plyometrics"

Non-Communicable diseases is the major cause of death world wide. Physical inactivity is the major cause of non-communicable diseases. Physical inactivity can be overcome by yoga, Dance and Plyometrics. The National Conference will throw light on the benefits of yoga, dance and Plyometrics and they will contribute to reduction in non-communicable diseases. The Conference will not only motivate our young medicos to take active research in these fields but also practice any of these physical activities to keep them safely, away from the non-communicable diseases.

As prevention is better than cure, preventive measures has to be followed by all which would further increase the economy of the country and quality of life of the people.

I wish the national conference a grand success.

Dr. V. KanagasabaiVice Chancellor

Bharath University

Dean Message



It gives me immense pleasure to know that the Department of Anatomy, Sree Balaji Medical College and Hospital is organising a **National Conference on Anatomy of Yoga, Dance, Plyometrics "YODAP 19"** between 4th and 5th APRIL 2019 under the able guidance of Prof. Dr. WMS JOHNSON, Vice principal (Dean additional Incharge) and Head of Anatomy Department, SBMCH.

I take this opportunity to congratulate the organizing committee of this conference who have put in their efforts to make the event a grand success.

I wish the invited lectures and the research paper presentation will enlighten and update the delegates of the recent developments in this field.

My best wishes to one and all.

Dr. P Sai Kumar

Dean

Sree Balaji Medical College and Hospital

Vice-Principal Message



It gives me great pleasure to pen this greeting for the National conference in Anatomy of Yoga, Dance & Plyometry.

The organizing committee has well conceptualized the theme which is of practical importance rather than dealing with routine Anatomy topics. Keeping fit is anyone's desire and staying fit is what matters in maintaining positive health. Hence the combination of deliberations on Yoga, Dance & Muscle training will throw light on this particular aspect.

I wish the organizing committee all the very best & the participants to have enlightment on health.

Best Wishes

Dr. WMS Johnson, MD PhDVice Principal & Dean i/c

HOD Department of Anatomy

Medical Superintendent's Message



At the outset, I congratulate the Department of Anatomy to host the National Conference /International conference every year. Conferences are held to facilitate knowledge & exchange of ideas. By attending conferences, presenting papers, graduate students get trained in research early in their career. I would appreciate the mentors of the students if they can guide the presentations to be made as manuscripts for journals. This will help them learn the next level in their scientific knowledge.

The theme selected for the conference is very interesting and I hope meaningful deliberations will be made during the academic feast. Many professional and Olympic athletes use plyometrics training to improve muscular strength and jumping abilities which therefore increases their power. There are varying levels of intensity to plyometrics. Another benefit of plyometrics are that you can vary your level of intensity which means anyone looking to improve strength and jump training can be involved regardless of fitness.

Sports Medicine is an emerging field & hence am sure young students will choose this as specialization.

I once again congratulate the organizers for conducting the conference and inviting good resource persons as Guest speakers

Best wishes

Dr Sridhara Narayanan MSMedical Superintendent

Guest Speakers



Dr. C. Vasanthi

Asst Professor

Dept of Arthroscopy & Sports Medicine
Sri Ramachandra Institute of Higher
Education & Research, Chennai



Dr. Vidhya C.SAssociate Professor of Anatomy,
JSS Medical college,
Mysore



Dr. Kumar Satish Ravi
Sub Dean (Academics) &
Additional Proctor,
Associate Professor of Anatomy,
AIIMS Rishikesh.



DorairajanClassical Bharathnatiyam Dancer,
Director,
Kalanjali Centre for Performing Arts,
Chennai

Kalaimamani Mrs. Padmini



Varghese
Professor and Vice Principal
Saveetha College of
Physiotherapy, Chennai

Dr. Jibu George



Dr.Kafeel Hussain
Associate Professor,
Dept. of Anatomy, Shri Sathya
Sai Medical College & Research
Institute

Panel Discussion Panellists



Dr.PSL. SaravananProfessor of Physiology
Sivagangai Medical College



Dr. C. Vasanthi

Asst Professor

Dept of Arthroscopy & Sports Medicine
Sri Ramachandra Institute of Higher
Education & Research, Chennai,



Mrs. Bhagyashree.R Certified Zumba Instructor, Chennai



Dr. P. SathyaProfessor of Physiology

Madras Medical College, Chennai

Organising Committee

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(Founder Chancellor, BIHER)

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Dr. R.Rahe

Dr. Krishanveni S

Dr. Sreelekha. D

Dr. Jinu Merlin Koshy

Dr. Shakthi Kumarasami

Dr. Gowtham S

Dr. Dhanalakshmi K

Programme Schedule - Day 1			
4.04.2019	Time		
Registration	9:00 am – 9:30 am		
Inauguration	9:30 am – 10:00am		
"Plyometric Anatomy"	10:00 am – 10:45am		
Dr. C. Vasanthi Asst Professor, Dept of Arthroscopy & Sports Medicine Sri Ramachandra Institute of Higher Education & Research, Chennai,			
"Common muscle synergies for balance and walking" Dr. Kumar Satish Ravi Sub Dean (Academics) & Additional Proctor, Associate Professor of Anatomy, AIIMS Rishikesh.	11:00 am - 11:45 am		
"Role of Anatomy in Yoga" Dr. Vidhya C.S Associate professor of Anatomy JSS Medical college, Mysore	12:00noon - 12:45pm		
Lunch (Venue College Block)	1:00pm – 2.00 pm		
Panel Discussion (Hippocratus Hall) "Staying fit, what helps Best? Yoga/ Dance / Plyometry" Moderator: Dr. P Sathya	2:00pm - 4:00pm		
Professor of Physiology, Madras Medical college.			
Panelists Dr. PSL. Saravanan Professor, Sivagangai Medical College			
Dr. C. Vasanthi, Asst. Professor, SRIHER			
Mrs. Bhagyashree .R Certified, Zumba Instructor.			

Programme Schedule - Day 2				
5.04.2019	Time			
"Kinematic of Joints among dancers; the various range of movements of small joints in different Mudras"	9:30 am- 10:30am			
Kalaimamani Mrs. Padmini Dorairajan				
Classical Bharathnatiyam Dancer				
Director, Kalanjali Centre for Performing Arts, Chennai				
"Plyometric training - Adding explosiveness	10:30 am – 11:15am			
to movements"				
Dr. Jibu George Varghese				
Professor and Vice Principal				
Saveetha College of Physiotherapy				
Saveetha University, Chennai				
"Repetitive Injuries in sports personnel"	11:15 am - 12:00 Noon			
Dr. Kafeel Hussain				
Associate Professor of Anatomy				
Sri Sathya Sai Medical College & Research Institute,				
Tiriporur.				
Paper & Poster Presentations	12 Noon – 1:00 pm			
Lunch (Venue College Block)	1:00pm – 2:00 pm			
Valedictory Function & Prize Distribution	2:00 pm - 3:00 pm			

Guest Speaker's Synopsis

Plyometric Anatomy

Dr. C. Vasanthi MD

Assistant Professor, Department of Arthroscopy and Sports Medicine, Sri Ramachandra Institute of Higher Education and Research, Chennai

Plyometric training is defined as a quick, powerful movement involving an eccentric contraction, followed immediately by an explosive concentric contraction. This is accomplished through the stretch-shortening cycle or an eccentric-concentric coupling phase. Plyometric exercise stimulates the body's proprioceptive and elastic properties to generate maximum force output in a minimum amount of time.

Plyometric training is an effective mode of training as it enhances motor learning and neuromuscular efficiency promoting the excitability, sensitivity, and reactivity of the neuromuscular system to increase the rate of force production (power), motor-unit recruitment, firing frequency (rate coding), and synchronization.

Plyometric training provides the opportunity to train specific movement patterns in a biomechanically correct manner at a more functionally appropriate speed. This provides functional strengthening of the muscle, tendon, and ligaments specific to the demands of everyday activities and sports. The ultimate goal of plyometric training is to improve the reaction time of the muscle action spectrum-eccentric deceleration, isometric stabilization, and concentric acceleration.

Three Phases of Plyometric Exercise

There are three distinct phases involved in plyometric training including the eccentric, or loading, phase; the amortization, or transition, phase; and the concentric, or unloading, phase.

Minimum Requirements for Participation in Plyometric Training Program

Proper technique for each drill

More than three months of resistance training experience

Sufficient strength, speed, and balance for the level of drill used

Over 13 years of age. No current injuries to involved body segment

Plyometric Program Design

After an evaluation of the client's needs, the mode, intensity, frequency, duration, recovery, progression, and a warm-up period must all be included in the design of a sound plyometric training program.

Role of Anatomy in yoga

Dr Vidya CS

Associate Professor, Department of Anatomy JSS Medical College JSS Academy of Higher education and Research, Mysore-15

Abstract:

Yoga is the art and science of resolving the inherent opposition in all things to create a union of body, mind and soul. Meditation is an integral component and the essence of yoga. Yoga is the path, which integrates the body, senses, mind and the intelligence with the self". Understanding of basic anatomy is essential to:

- enhance one's yoga practice
- improve one's ability to increase strength, flexibility, cardiovascular fitness and inner wellbeing
- minimise the risk of injuries as a result of yoga practice
- help to use hatha yoga to recover from a variety of musculoskeletal injuries and medical conditions.

Yoga can be divided into two parts that can be referred to as physical yoga and non-physical yoga. Physical yoga, which consists of physical exercises(Asana) and breath-control (Pranayama), is often thought of as a static or slow-moving type of stretching and relaxation. Physical yoga can manipulate internal organs and modify blood chemistry Non-physical yoga, which consists of ethical disciplines and meditative practices, can help to expand one's mind, explore one's emotions, and develop the relationships between oneself and the rest of the world.

Yoga exercises bring an awareness or sensation to muscles through learning to activate or stretch the muscles of different body parts. In order to safely and effectively stretch both muscles and tissues in hatha yoga one must establish correct positioning (asanas), understand nerves as (physical manifestation of specialized naadis), understand muscle co-oactivation and to create proper physiological environment through a combination of breath control and diet. However, in some cases, incorrect practice or unsafe technique can aggravate a practitioner's pre-existing medical problems or it can actually create new problems.

"Kinematic of Joints among dancers; the various range of movements of small joints in different Mudras"

Kalaimamani Mrs. Padmini Dorairajan

Classical Bharathnatiyam dancer Director, Kalanjali Centre for Performing Arts, Chennai

Bharatanatyam is the classical form of dance originating from Tamil Nadu in the South of India. A highly stylised dance form using body, mind and soul it has won many admirers world over

Dancers in all dance forms engage in aesthetic and challenging movements. Their training, choreography and performances require a great deal of strength, stamina, flexibility, grace, passion, and emotion.

In our presentation today I would like to touch upon the use of the joints in our body in Bharatanatyam - both major and minor to create beauty of movement in our art. The small joints of our fingers create the gestures or "mudras", whereas the larger joints allow the performance of the varied steps and poses.

The "mudras" all used in dance to speak using hand gestures. In visually converge the outer event as well as inner felings. Approximately 55 roof "mudras" are used in Bharatanatyam using one hand of both hands.

Every part of a dancer works in perfect harmony, right from the eyebrows to the toes- the gliding of the neck from side to side and the roll of the eyes creating an expressive, graceful experience.

"Plyometric training - Adding explosiveness to movements"

Dr. Jibu George Varghese

Professor and Vice Principal, Saveetha College of Physiotherapy
Saveetha University, Chennai

Introduction and history of Plyometrics: Plyometric system of training was first formalized in the early 1960's as a scientific training system by Dr. Yuri Verkhoshansky. Verkhoshansky favored the term 'shock method' to distinguish between naturally occurring plyometric actions in sport and the training system he devised to develop speed-strength

The actual term *plyometrics* was first introduced in 1975 by American track coach Fred Wilt, although there is agreement on the benefits of basic plyometric principles, there is controversy regarding an optimal training routine. Today, the chief proponents of plyometrics are still in the track and field community

Plyometrics — plyos for short — is a type of exercise that trains muscles to produce power (strength + speed)

While strength training mostly creates nervous system and muscular adaptations to get stronger, plyometric exercises will help improve explosiveness — our ability to generate maximum force in a minimum time. The gains athletes make from plyometric training can directly translate to better performance on the field. Plyometric training takes advantage of a rapid cyclical muscle action known as the 'stretch-shortening cycle (SSC)', whereby the muscle undergoes an eccentric contraction, followed by a transitional period prior to the concentric contraction

Physiology of Plyometric exercise: The physiological research supporting the effectiveness of plyometrics cites two important factors:

- 1. The serial elastic components of the muscle which includes the tendons and the cross bridging charactyeristics of the act in and the myosin that make up the muscle fibers
- 2. The sensors in the muscle spindles that play the role of presetting muscle tension and relaying sensory input related to rapid muscle stretching for activation of the stretch reflex.

Phases of Plyometric exercises: It is considered to be Triphasic – Loading, Coupling & Unloading

Many neurophysiological mechanisms have been considered to underpin and explain the impact of plyometric training on the SSC. Most of which include:

- Improved storage and utilization of elastic strain energy
- Increased active muscle working range
- Enhanced involuntary nervous reflexes
- Enhanced length-tension characteristics
- Increased muscular pre-activity
- Enhanced motor coordination

Plyometrics are highly-coordinated and skillful movements: Plyometric activities require athletes to produce high levels of force during very fast movements. They also demand the athletes to produce this force during very short timeframes.

As a result, plyometrics are not typically seen as just exercises or drills, but more as complex 'movement skills' due to their high-complexity. Understanding this is vital and highlights how highly-coordinated these movements are, and why they require a large amount of attention and coaching if optimal, yet safe, performance gains are to be made. The intensity of plyometrics is difficult to measure

Criteria for initiating Plyometric exercise: The athlete should maintain sufficient neuromuscular control to generate and attenuate high impulse joint loads. He should also demonstrate good dynamic posture, full range of joint motion, adequate base level strength, endurance and neuromuscular control.

Plyometric Precautions: There are also considerations of precautions to avoid adverse effects:

- Higher risk of injury
- Not for beginners
- It's really hard
- It can lead to overtraining

Repetitive Injuries in sports personnel

Dr. Kafeel Hussain

Associate Professor, Dept. of Anatomy, Shri Sathya Sai Medical college & Research Institute

Abstract

Injury occurs when mechanical energy is transferred to the body in amounts or at rates that exceed the threshold for human tissue damage. Injuries could either be acute or due to over use. Acute Injuries are often caused by a macro traumatic even where extrinsic factors like the opponent, defective equipment or surface play a major role, where as overuse injuries are typically are more complex and there is a greater contribution from intrinsic factors like Age, strength, movement quality, previous injury, fitness, training load and fatigue. Common repetitive injuries include Bursitis, tendinitis / tendonitis, epicondylitis (tennis elbow),ganglion cyst, tenosynovitis and trigger finger. When an athlete gets injured, apart from the physical stress, psychological and emotional responses like sadness, isolation, irritation, lack of motivation, anger, frustration, changes in appetite, sleep disturbance and disengagement occur. Moreover, Sports Injuries take 2 weeks to 6 months or even more to heal. This considerabily affects not only their morale but also their livelihood. Hence, proper counselling and support are as much as important as physical rehabilitation.

Common Muscle Synergies for Balance and Walking

Dr. Kumar Satish Ravi

MBBS, MD (JIPMER), MAMS Sub Dean (Academics), AIIMS RISHIKESH

"Synergy" literally means "working together". Synergistic control of movements is normal but may become abnormal when person can't move out of the synergistic pattern.

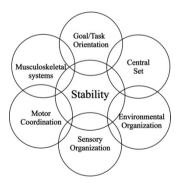
"Muscle synergies" - Coordinated recruitment of a group of muscles with specific activation balances or specific activation waveforms.

''BALANCE'' - Technically defined as the ability to maintain the center-of-gravity (COG) of an object within its base-of-support (BOS).

If this relationship isn't maintained then a system will be unbalanced

Human balance is a complex process involves the integration of sensory information from peripheral end organs to detect body position in relation to environment. Integration of this information by CNS to produce adequate and proper motor output in form of automatic postural responses.

SYSTEMS MODEL OF BALANCE



Model Components of Musculoskeletal System

• ROM of joints, Strength/power, sensation, Pain, Reflexive inhibition, Abnormal muscle tone

Central Set

• CNS may select a motor program to fine-tune a motor experience

Model Components Environmental Organization

• Nature of contact surface, Nature of the "surrounds"

Regulatory features of the environment (Gentile)

Model Components of Motor Coordination

 Movement strategies, Feedback & feed forward control & Adjustment/tuning of strategies

Strategies to Maintain/Restore Balance - Ankle, Hip, Stepping & Suspensory

Model Components of Sensory Organization

• Balance/postural control via three systems: Somatosensory, Visual & Vestibular

Recent research demonstrates the neural control of muscles may be modular, organized in functional groups often referred to as muscle synergies. Each muscle synergy is proposed to specify a fixed pattern of co-activation across multiple muscles at any given time point.

Muscle synergies have been used to describe muscle coordination during a variety of motor behaviours including balance control, walking reaching and grasping. Moreover, common muscle synergies have been identified across different motor behaviours such as frog swimming, kicking, and jumping, forward and backward locomotion, and across reactive balance conditions

Muscle synergies have been used to describe muscle coordination during a variety of motor behaviours including balance control, walking reaching and grasping. Moreover, common muscle synergies have been identified across different motor behaviours such as frog swimming, kicking, and jumping, forward and backward locomotion, and across reactive balance conditions

'Gravity line falls: Forward of ankle, Through or forward of the knee, Through of behind the hip (common hip axis), Behind or through thoracic spine & through acromium

Panel Discussion

Staying Fit, what helps best? Yoga/ Dance/ Plyometry

Physical fitness is a state of health and well-being and, more specifically, the ability to perform aspects of sports, occupations and daily activities. Physical fitness is generally achieved through proper nutrition, moderate-vigorous physical exercise, and sufficient rest

Fitness involves many aspects like – cardiovascular fitness, muscular fitness, flexibility, body composition and also mental stability. Only some of these are measurable physiologically and through lab investigations.

Yoga is a group of physical, mental, and spiritual practices or disciplines which originated in ancient India. It is a system of physical and spiritual practices. There is a broad variety of yoga schools, practices, and goals. For fitness the asana's'usually advocated are "paripurna navasana" or the boat pose, "Chaturanga dhandasana" or the four limbed staff pose, "salabhasana" or the locust pose, the dolphin pose etc. There is no particular age to practice yoga. Yoga poses for health can be light hearted as well as hard core. Yoga ranges from asanas to pranayam. While the asanas involve body movement, the pranayams are mainly calm and for mind relaxation. Practicing yoga by young and old alike regularly will not only improve your physicality but also relax your mental system keeping you composed to handle situations with ease. The advantage of yoga is that it also helps in mental fitness. Yoga is a very effective stress reduction and relaxation tool. Performance of various postures requires the tensing and stretching and then relaxing of muscle groups and joints, which effectively produces relaxation. It also helps in improving quality of life. The disadvantage is if the person enrols in a wrong practioners or wrong type of classes.

Dance is a performing art form consisting of purposefully selected sequences of human movement. This movement has aesthetic and symbolic value, and is acknowledged as dance by performers and observers within a particular culture. Dance can be categorized and described by its choreography, by its repertoire of movements, or by its historical period or place of origin. Aracheological evidence for early dance includes 9,000-year-old paintings in India at the Rock Shelters of Bhimbetka, and Egyptian tomb paintings depicting dancing figures, dated c. 3300 BC. It has been proposed that before the

invention of written languages, dance was an important part of the oral and performance methods of passing stories down from one generation to the next. In India there are about 10 forms of classical dance and many types of folk dance.

Zumba is an exercise fitness program created by Colombian dancer and choreographer Alberto "Beto" Perez during the 1990s. Zumba involves dance and aerobic movements performed to energetic music. The choreography incorporates hiphop, soca, samba, salsa, merengue and mambo. Sqauts and lunges are also included. In one Zumba class, a person can burn up to 600 calories, depending on the energy put forth. There are many forms of Zumba depending on age, sex and physical health of a person. The advantage of Zumba is that it targets lots of different muscle groups at once for total body toning. It helps in boosting heart health. Not only the person get aerobic benefits, but also get anaerobic benefits which helps you maintain a good cardiovascular respiratory system. It greatly helps in de-stress. The disadvantages are that since zumba is an aerobic-based dance and workout routine, so it helps in losing weight, but if it is stopped and not done regularly, it might cause a gain in weight. It is a workout that can be fast in its pace, so there are chances of injury by falling or tripping or a muscle sprain.

Plyometrics, also known as jump training or plyos, are exercises in which muscles exert maximum force in short intervals of time, with the goal of increasing power. Plyometrics are ideal for athletes or people looking to improve muscular power, speed and strength. Plyometric exercises include vertical and broad jumps, where you jump as high and/or as far as possible. Skipping rope, jumping squats, single leg hopping and clapping push-ups are also great examples of plyometric exercises. They also help facilitate weight loss and help tone and define your muscles; however, these exercises are not without risk.

Yoga, Dance in any form and plyometrics all are very useful in staying fit. Depending on the age, sex and physical health of a person appropriate training must be given. The ultimate thing is that fitness is very important for a person.

Abstracts of Oral Presentation

The Neurobiology of Developmental Dyslexia

R. Kavithaa¹, Dr. R. Archana², Dr.WMS. Johnson³

¹Ph.D., Research Scholar, Department of Psychology, Bharath Institute of Higher Education and Research, Chennai. ²Associate Prof. of Anatomy, SBMCH, ³Prof. of HOD of Anatomy, SBMCH ¹Email: kavitharameshrocks@yahoo.com. Mobile: 9840754690.

Introduction

Dyslexia is a learning disorder that involves difficulty reading due to problems identifying speech sounds and learning how they relate to letters and words (decoding). Also called reading disability, dyslexia affects areas of the brain that process language. People with dyslexia have normal intelligence and usually have normal vision. Most children with dyslexia can succeed in school with tutoring or a specialized education program. Emotional support also plays an important role. Though there's no cure for dyslexia, early assessment and intervention result in the best outcome. Sometimes dyslexia goes undiagnosed for years and isn't recognized until adulthood, but it's never too late to seek help.

Keywords: Development, Communication Skills, Early Intervention.

What is dyslexia?

Dyslexia has been around for a long time and has been defined in different ways. For example, in 1968, the World Federation of Neurologists defined dyslexia as "a disorder in children who, despite conventional classroom experience, fail to attain the language skills of reading, writing, and spelling commensurate with their intellectual abilities." The International Dyslexia Association offers the following definition of dyslexia:

"Dyslexia is a specific learning disability that is neurobiological in origin. It is characterized by difficulties with accurate and/or fluent word recognition and by poor spelling and decoding abilities. These difficulties typically result from a deficit in the phonological component of language that is often unexpected in relation to other cognitive abilities and the provision of effective classroom instruction. Secondary consequences may include problems in reading comprehension and reduced reading experience that can impede growth of vocabulary and background knowledge."

Dyslexia is the most common learning disability in children and persists throughout life. The severity of dyslexia can vary from mild to severe. The sooner

dyslexia is treated, the more favorable the outcome. However, it is never too late for people with dyslexia to learn to improve their language skills.

What causes dyslexia?

Children with dyslexia have difficulty in learning to read despite traditional instruction, at least average intelligence, and adequate motivation and opportunity to learn. It is thought to be caused by impairment in the brain's ability to process phonemes (the smallest units of speech that make words different from each other). It does not result from vision or hearing problems. It is not due to mental retardation, brain damage, or a lack of intelligence.

The causes of dyslexia vary with the type. In primary dyslexia, much research focuses on the hereditary factors. Researchers have recently identified specific genes identified as possibly contributing to the signs and symptoms of dyslexia. This research is very important because this may permit the identification of those children at risk for developing dyslexia and allow for earlier educational interventions and better outcomes.

What are the different types of dyslexia?

- Primary dyslexia: This is the most common type of dyslexia, and is a dysfunction of, rather than damage to, the left side of the brain (cerebral cortex) and does not change with age. There is variability in the severity of the disability for Individuals with this type of dyslexia, and most who receive an appropriate educational intervention will be academically successful throughout their lives. Unfortunately there are others who continue to struggle significantly with reading, writing and spelling throughout their adult lives. Primary dyslexia is passed in family lines through genes (hereditary) or through new genetic mutations and it is found more often in boys than in girls.
- Secondary or developmental dyslexia: This type of dyslexia is caused by problems with brain development during the early stages of fetal development.
 Developmental dyslexia diminishes as the child matures. It is also more common in boys.
- Trauma dyslexia: This type of dyslexia usually occurs after some form of brain trauma or injury to the area of the brain that controls reading and writing. It is rarely seen in today's school-age population.

Areas of typical difficulty for all Specific Learning Difficulties

(i) Information Processing

• Difficulties with taking in information efficiently (this could be written or auditory).

• Slow speed of information processing, such as a 'penny dropping' delay between hearing something and understanding and responding to it.

(ii) Memory

- Poor short term memory for facts, events, times, dates.
- Poor working memory; i.e. difficulty holding on to several pieces of information while undertaking a task e.g. taking notes as you listen, coping with compound questions.
- Mistakes with routine information e.g. giving your age or the ages of your children.
- Inability to hold on to information without referring to notes.

(iii) Communication skills

- Lack of verbal fluency and lack of precision in speech.
- Word-finding problems.
- Inability to work out what to say quickly enough.
- Misunderstandings or misinterpretations during oral exchanges.
- Over-loud speech (which may come across as aggressive) or murmuring that cannot be clearly heard.
- Sometimes mispronunciations or a speech impediment may be evident.

(iv) Literacy

- Lateness or difficulty in acquiring reading and writing skills. Some dyslexic adults have severe literacy problems and may be functionally illiterate.
- Where literacy has been mastered, residual problems generally remain such as erratic spelling, difficulty extracting the sense from written material, difficulty with unfamiliar words, an inability to scan or skim text.
- Particular difficulty with unfamiliar types of language such as technical terminology, acronyms. Sequencing,

(v) Organization and Time Management

- Difficulty presenting a sequence of events in a logical, structured way.
- Incorrect sequencing of number and letter strings.
- Tendency to misplace items; chronic disorganization.
- Poor time management: particular difficulties in estimating the passage of time.

(vi) Direction and Navigation

 Difficulty with finding the way to places or navigating the way round an unfamiliar building.

(vii) Concentration

- Weak listening skills, a limited attention span, problems maintaining focus.
- A tendency to be easily distracted, inability to remain focused.

(viii) Sensory Sensitivity

- A heightened sensitivity to noise and visual stimuli.
- Impaired ability to screen out background noise or movement.
- Sensations of mental overload/switching off.

(ix) Lack of awareness

- Failure to realize the consequences of their speech or actions.
- Failure to take account of body language.
- Missing the implications.

Neurobiology of DD

Evidence for a neurobiological basis for DD comes from postmortem examinations and brain imaging of individuals with DD. Postmortem examinations of four male and three female brains with DD made two primary observations; an increase in abnormalities of the left hemisphere concentrated around the perisylvian region and near symmetry of the planum temporal. The abnormalities included neuronal ectopias and focal architectonic dysplasias, specifically micropolygyria, of the left planum temporale. The ectopias, consisting of nest of neurones, and occasionally the dysplasias, were often found in layer I of predominantly the left inferior frontal and superior temporal gyri. An important inference from these studies was that the abnormalities, or lesions, occurred at a time of peak neuronal migration during embryonic development. Subsequently, visual processing experiments indicated problems with rapid visual processing in individuals with DD. This led to the postmortem re-examination of the same DD brains as before. This revealed dis- organisation of the magnocellular, but not the parvocellular, layers of the lateral geniculate nuclei (LGN). This region of the brain forms part of the primate visual system and so these observations were consistent with the visual processing deficiencies observed in DD. The cell bodies comprising the magnocellular layers of the LGN from the DD brains also appeared smaller than in control brains.

Similarly, the results from auditory processing experiments indicated problems with rapid auditory processing in individuals with DD. This again led to the reexamination of same DD brains. This time the medial geniculate nuclei (MGN) were examined as these are involved in the auditory processing system. The DD brains presented greater asymmetry between the left and right MGN than in control brains, and generally the left MGN had more smaller and less larger neurones. Much has been learnt about the processes of reading by functional neuroimaging of brains unaffected with DD. These studies suggest that two posterior pathways exist, namely the dorsal and ventral pathways, along with an anterior component and that generally there is a bias of left side processing. The dorsal pathway is centred on the left temporoparietal regions. It includes the angular and supramarginal gyri, and also the left posterior end of the superior temporal gyrus, and deals with attentionally controlled mapping of graphemes of a visual word onto phonological representation. An underactivation in this pathway is considered as correlate of a phonological deficit. The ventral pathway is centred on the left inferior occipitotemporal region and includes the posterior fusiform gyrus. It may be required for the quick automatic processing of familiar visual words or frequent letter strings within words. The under activation of this pathway in dyslexic subjects was interpreted as correlate of the slow and erroneous word recognition. The anterior component is centred on the left inferior frontal gyrus and mainly cor- relates with the articulation of speech sounds. An over activation in this brain region was seen as compensatory, although ineffective articulatory-based access to phonological word representations in DD.

Many functional neuro imaging studies have demonstrated altered activity of exactly these regions in DD brains. For example, in one study, phonological and lexical tasks resulted in the activation of the left inferior temporal gyrus of most control brains, whereas almost none of the DD brains showed any activation of this region. Several studies have also demonstrated reduced activity of left temporoparietal regions (including the angular and supramarginal gyri) on tasks of word reading, non-word reading and letter rhyming, and left occipitoparietal regions on tasks of letter matching.

A large study comparing 70 DD brains to 74 control brains similarly revealed reduced left inferior frontal, left superior temporal, left occipitotemporal and left temporo- parietal regional activity on several reading-related tasks. In addition, a positive correlation was observed between individual reading skill and activity in left posterior regions, for example, between pseudoword reading and the left occipitotemporal region. A compensatory higher activation pattern in DD subjects was found repeatedly in the left inferior frontal brain area. Imaging studies have also identified greater asymmetry and

less grey matter content of the cerebellum in DD brains, with one study indicating as maller right anterior lobe correlates with phonological deficits.

Finally, it is often observed that the equivalent homo- topic right hemispheres display increased activity in DD brains, perhaps as a compensatory measure. For example, the right temporoparietal regions (including the angular gyrus) displayed greater activation in response to both word and non-word reading, and increased activity in the right relative to the left inferior temporal gyrus during a phonological task.

Genetic studies on dyslexia

Familiarity of DD

Developmental dyslexia does not just occur randomly within the population. In fact, familial clustering of DD was observed well over 100 years ago. It was later observed that an individual's risk of being affected increased, when other family members were already affected. Later, it was observed that 9% of control children had a sibling or parent with some form of reading problem, when compared with 34% of children with DD. Recently, it has been shown that 20–33% of siblings of affected individuals, with unaffected parents, are themselves also affected. This increased to 54–63% if either (but not both) parent was also affected, and to 76–78% if both parents were affected. For spelling disorder, the percentage of affected siblings has been found to be higher (52–62%) than for word reading. The sibling recurrence risk of DD, that is the probability of an individual being affected with DD given a sibling is already affected (regardless of parental affection status), is estimated as 43–60%. With a population prevalence of *10% and a sibling recurrence risk of *50%, the sibling relative risk can be estimated as between 4 and 6, and increases with stricter affection status criteria.

Heritability of DD

With such a strong familial basis for DD, twin studies have been employed to evaluate the contribution of the environmental and genetic components underlying its aetiology. Typically, such studies utilise large sets of monozygotic (MZ) and same sex dizygotic twins. The concordance rate for DD is then compared between the two sets of twins. A higher concordance rate in the MZ twins would be suggestive of a genetic aetiology for DD, and fittingly this has been shown consistently; 1.00 versus 0.52, 0.91 versus 0.45 and 0.68 versus 0.38. Twin studies also enable estimates of the heritability of DD, that is the proportion of phenotypic variation attributable to genetic variation, with figures ranging from 0.30 to 0.70, depending on the diagnostic criteria, age and sample size.

The dyslexic's brain

The seminal anatomical studies of the Boston school

Undoubtedly, the most significant contribution of these last few decades to the neurology of dyslexia was the description by Galaburda and colleagues of the brains of one (Galaburda and Kemper, 1979), then four (Galaburda et al., 1985) brains of male dyslexic subjects. Later on, the same group reported the analysis of three additional female brains (Humphreys et al., 1990). To summarize these studies, two main observations were made. First, at the microscopic level, a meticulous analysis of serial coronal slices of the post-mortem specimens, compared with a similar analysis of nondyslexic brains (Kaufmann and Galaburda, 1989) disclosed specific cortical malformations including ectopias (small neuronal congregations in an abnormal superficial layer location), mainly distributed across both frontal regions and in the left language areas; dysplasia (loss of characteristic architectural organization of the cortical neurons, mainly subjacent to the site of ectopias); and more rarely, vascular micromalformations. In some instances, these cortical malformations took the appearance of a microgyrus (or micropolygyrus), an aspect also found in the subsequent analysis by Cohen and colleagues of the brain of a dysphasic child (Cohen et al., 1989) (It must be noted that, even though the child whose brain was studied by Cohen and colleagues was unequivocally suffering important delays in oral language acquisition, in several of the dyslexics reported by Galaburda et al. (1985), oral language was also reported as being delayed.) No ectopias were found in the study by Cohen and colleagues, but the microgyrus, as reported by Galaburda and Kemper (Galaburda and Kemper, 1979), was located in the left temporal cortex. The main lesson drawn from these microscopic observations is that all the brains studied differed from control brains in a way that suggested abnormal cortical development. Since neuronal migration is thought to take place during the sixth gestational month, the mechanism leading to these cortical lesions was presumed to occur before or during this period of the foetal brain development. Finally, in addition to these neuronal abnormalities, the female brains showed glial scars in the border zones between the arterial territories, suggesting a vascular mechanism, supposedly of immune origin (Humphreys et al., 1990).

Besides these microscopic anomalies, all the dyslexic brains of the Boston studies, as well as that of the dysphasic child studied by Cohen and colleagues (Cohen et al., 1989), displayed a macroscopic peculiarity, namely an absence of the usual left > right asymmetry of the planum temporale. In fact, this small triangular part of the superior surface of the temporal lobe had been reported by earlier anatomists as

asymmetrical in the majority of brains, a fact confirmed in the first such study in the modern area by Geschwind himself (Geschwind and Levistky, 1968; for a review, see Galaburda and Habib, 1987). Since this asymmetry was believed to parallel the functional linguistic preponderance of the left hemisphere, and by reference to the above-mentioned evidence of incomplete lateralization in dyslexics, this region naturally deserved to come under close scrutiny. The prediction was apparently totally confirmed, since all the brains studied displayed this particular symmetrical aspect; however, it is not specific since it is present in roughly one-third of routine brains. In other terms, planum symmetry seemed necessary but not sufficient to define the dyslexic's brain. Although the developmental mechanisms leading to such atypical symmetry still remain a subject of debate (see, for instance, Steinmetz, 1996), these findings, combined with the above-mentioned microscopic features, have been generally considered good evidence of maturational deviance being at the origin of the learning difficulties of dyslexics.

Conclusion

Dyslexia is not some pre-existing brain fault, distinct from normality, which hinders learning to read. Rather, dyslexia is just what happens when a brain is not particularly well suited to learning to read, a "shorthand descriptor [that] summarizes the...major area of deficit" ([3], p. 39). As aptly put by Bishop and Rutter [3], "[a] statement such as 'My child can't read because he's dyslexic' is not an explanation, rather it is a circular redescription of the problem" (p. 39). This is because the term "dyslexia" is merely a label for poor word reading that persists in spite of appropriate educational experiences, rather than referring to an underlying cause for it. Treating difficulty learning to read as some sort of neural disorder, akin to brain damage, is as offensive to the people who struggle with reading as it is misleading for the researchers who try to understand it and for the clinicians and educators who encounter it in their daily practice and will mistakenly come to associate it with pervasively disabling conditions with identifiable pathology and substantially poorer prospects.

Effect of Mahamantra Chanting on Autonomic Functions and Cortisol Levels: Implications for Prevention of Stress Related Metabolic Disorders

Lavanya Sekar¹, Niva.W.J², Mahesh Kumar¹, Ganesan Thangavel⁴, Manikantan⁵, Santhi Silambanan⁶, Padmavathi Ramaswamy⁷

^{1,3,4,7}Department of Physiology, Sri Ramachandra Medical College and Research Institute ^{2,5,6}Department of Biochemistry, Sri Ramachandra Medical College and Research Institute

Introduction

Stress is a known significant, modifiable risk factor for life style disorders like diabetes, obesity, sleep disturbances and various other cardiovascular and neurological disorders. Early interventions can reduce stress induced morbidity and mortality.

Aim: To provide an empirical evidence of the effect of Mahamantra chanting in reducing the stress among women nursing professionals.

Objective: To assess the effect of Mahamantra chanting on Heart Rate Variability and serum cortisol levels

Methodology

Psychological stress levels were analysed (n=149) using Perceived Stress Scale (PSS). Subjects with moderate to severe stress levels (PSS \geq 18) were recruited (n=30) and divided into two groups (with and without intervention). Physiological parameters like Heart Rate Variability and Serum cortisol levels were analyzed. Mahamantra intervention was given (n=15) to one group while the no intervention for the control group (n=15). After 45 days of Mahamantra chanting intervention, study parameters were analyzed in both the groups.

Results

Current study shows increase in parasympathetic tone (LF/HF ratio p<0.01), and decreased serum cortisol levels (p=0.01) among subjects who underwent Mahamantra intervention.

Conclusion

This first ever simple interventional study highlighted the beneficial effects of simple, non-invasive method like chanting reduces stress and also reduces the chance of developing stress related metabolic disorders.

Keywords: Mahamantra chanting, Heart rate variability, cortisol

Assessment of Visual Processing skills among Male Kathakali Dancers

Srihari Ramamoorthy

Demonstrator in Physiology, SRMC & RI

Introduction

The Indian Ministry of Culture has recognized eight forms of Classical dance. Kathakali is one among them and traditional dance form of Kerala. It consists more of eye, facial and fine hand movements than gross body movements. During practice sessions more importance were given to eye movements training which are similar to eye exercises prescribed by ophthalmologists/optometrists as preventive/curative therapy for eye disorders.

Aim : The current study proposes to assess the visual processing skills among male Kathakali dancers.

Methodology

The study is cross sectional study and initiated after obtaining approval from Institutional Ethics Committee. Participants were healthy males (23-35yrs) and divided in to study(dancers) and control group (*n*-50). Kathakali dancers (study group) were selected from Madavoor school of classical dance, Kunnathurmedu, Palakkad. Both the groups were screened by Optometrists for refractive errors and normal subjects were included.

Visual processing skills were assessed by means of Visual acuity, Visual reaction time, Eye-hand coordination and eye-hand motor skills performance (unilateral and bilateral).

Results

The Data were analyzed using SPSS software version 20.0. Visual acuity was 18% better in kathakali dancers than control group. VRT in dancers and normal subjects were 221±16 and 248± 23 respectively. The results show that visual processing skills is better in Kathakali dancers than normal subjects.

Conclusion

The current study suggests that along with other health benefits, Kathakali also improves the visual processing skills among dancers and hence could be taught to children and adults for a healthy life.

Keywords: Kathakali, Vision

Effect of Yoga Training on Pulmonary Function Test

Dr. Shobana R¹, Dr. Bagavad Geetha², Dr. Mahesh Kumar³, Dr. Padmavathi R⁴, Dr. S.T.Venkateswar⁵

^{1,2,4}Department of Physiology, SRMC & RI ^{3,5}Government College of Yoga & Naturopathy, Chennai

Introduction

Yoga, originated in India, is the science of right living that includes postures, breathing exercises, and cleansing practices. Yoga is synchronization of breathing with movement and thereby harmonization of heart, brain and the lung". Studies have proved that significant improvement in vital capacity with training programme of breathing exercise. Very few studies are available on long-term effects of yoga on respiratory functions,

Aim & Objectives

To evaluate the respiratory functions among yoga trained young individuals by the following pulmonary parameters—FVC, FEV1, FEV1/FVC Ratio.

Material and Methods

This cross sectional comparative study was conducted in Physiology department, Sri Ramachandra Medical College, among 30 trained yoga and 30 non-trained yoga individuals Institutional Ethical Committee approval was obtained from SRMC. After obtaining informed consent, procedure was explained and the pulmonary function parameters values were recorded by using Smart PFT Spirometerand best of three values was taken for analysis. Statistical analysis done using software version 2.2.

Results

The values were significantly higher among yoga participants: FVC(L/min)- 3.38 ± 0.24 (control) 3.94 ± 0.56 (yoga), FEV1 (L/min)- 3.21 ± 0.39 (control) 3.57 ± 0.48 (yoga), FEV1/FVC ratio (%) - 88.96 ± 3.64 (control) 92.75±4.80 (yoga). FVC & FEV1/FVC ratio is significant with p value <0.05.

Conclusion

Yoga practice seed strengthening and increased endurance of the respiratory muscles, decrease airflow resistance and increase airway caliber thereby causing improvement in dynamic parameters of the lung function test. Yoga can be implemented among students in early period to reduce the stress levels and to improve the lung function in respiratory disorders.

Keywords: yoga, pulmonary function.

Yoga and its benefits on I Year MBBS Students – A Cross Sectional Study

Dr. Sudakshina Chakrabarti

Associate Professor, Saveetha Medical College, Chennai

Abstract

Yoga has been practiced for over 5000 years, it has only newly gained popularity worldwide. The drill originated in India and has been applied to relieve both mental and physical infirmities. Yoga incorporates postures, breathing techniques, and meditation. From the yogic perspective, the body and the mind are so interconnected that they are essentially inseparable. Whatever affects the body must impact the mind and vice-versa. Psychological stress and yoga are believed to be reciprocally related. Previous studies on medical education have shown that perceived stress is higher in medical students than in other age-controlled students.

Aim and objectives

To study the existing stress and anxiety in medical students

To subject medical students to Yoga and meditation for a period of 6 weeks

To assess the stress in medical students after exposing them to above.

Material and Method

The present study was conducted on 50 medical 1st MBBS students of Saveetha Medical College Chennai, to determine the benefit of Yogic practices on anxiety status during their course. Anxiety was assessed by Hamilton anxiety scale prior and after the 6 weeks YOGA and meditation program

Results

The results showed an overall better score after the 6 weeks program of yogic practices. The feedback collected from the students after subjecting them to a ^ weeks. Yogic program was satisfactory and students wanted yoga to be included in co curricular activities at least once in a week.

Conclusion

The improvement in various parameters such as better sense of well being, feeling of relaxation, improved concentration, self confidence, increased attentiveness were some of the beneficial effect experienced by the students in this study.

Significance of Morphology of Bicipital Groove in the Shoulder Subluxation Injuries during Dance

Dr. Kavitha.M¹, Dr. V.S. Anandha Rani²

PG Student, Dept. of Anatomy, SRMC & RI, Chennai Prof. Dept of Anatomy, SRMC & RI, Chennai

Introduction

The morphology of bicipital groove is associated with pathologies of biceps tendon during dance. Pathologies of biceps tendon are frequent causes of shoulder subluxation during dance. Bicipital Groove or Inter-tubercular groove is a deep groove formed between the greater and lesser tubercle. This groove lodges the biceps tendon which results in shoulder subluxation during dance.

Aim and Objectives

The main aim and objectives is to measure the depth of the bicipital groove measurement related to shoulder subluxation injuries.

Materials and Methods

The study was carried out in 100 adult humerus bone (50 right and 50 left sides) from the Department of Anatomy, Sri Ramachandra Institute of Higher Education and Research, Porur, Chennai. Damaged or bones with deformities were excluded from the study. The depth were accurately measured using digital vernier caliper. The parameters were tabulated and statistically analysed.

Observation and Results

A shallow or deep groove was found on the measurement of depth of the bicipital groove.

Discussion

The measurement of depth of the bicipital groove plays an important rule in shoulder subluxation during dance. The morphological data of the bicipital groove was correlated with subluxation injuries of dance.

Conclusion:

By measuring the depth of the bicipital groove, specimens were grouped into shallow or deep groove. Shallow type indicates the suspicion of shoulder subluxation during dance. The knowledge of bicipital groove is important to anatomists for new data, surgeons in carrying out orthopaedic procedures and physicians in managing a shoulder subluxation during dance.

Effect of Yoga Therapy on Children with Attention Deficit Hyperactivity Disorder (ADHD)

Ms. Apparanjitha V Ramana¹, Dr WMS Johnson², Dr Archana³

¹IIIrd Year MBBS Student, SBMCH, Chennai ²Prof of HOD of Anatomy, (SBMCH, Chennai) ³Associate Prof. Dept. of Anatomy (SBMCH, BIHER, Chennai)

Abstract

Yoga is a physical mental and spiritual practice that originated in ancient India 5000 years ago. Attention Deficit Hyperactivity Disorder (ADHD) is one of the commonest neurodevelopmental disorder in children. Stimulants are frequently used in the management of Attention deficit hyperactivity disorder (ADHD). Due to adverse effects of medication there is a growing interest in complementary treatments. Complementary and alternative medicine therapies including yoga are commonly used in children with Attention deficit hyperactivity disorder (ADHD), but little is known about the efficacy of these therapies. The objective of the present study were to find the role of Yoga in the treatment of children with Attention Deficit Hyperactivity disorder (ADHD). The study was done on 15 Children aged between 5-13 years (10 boys, 5 girls) with Attention deficit hyperactivity disorder (ADHD) in a special school. Attention deficit hyperactivity disorder (ADHD) affects 6-7% of children and occurs 4 times more commonly in boys than girls. The children were given Yoga training daily gradually along with proper diet, medicine, and behavior therapy for 6 months, Attention deficit hyperactivity disorder (ADHD) Rating scale is analysed before and after Yoga. The results showed a significant improvement in ADHD symptoms relating to Attention, anxiety and impulsivity. At present the small number of available investigations renders impossible the drawing of any conclusions regarding the effectiveness of yoga for ADHD in children. Large, well-controlled, randomized trials are needed in order to establish the potential value of yoga as a single treatment or adjunct to standard ADHD therapies.

Common Injuries in Sports

Mr. Samyuktha Thadderina. A

1st Year MBBS Student, SBMCH, Chennai

Strength doesn't come from what you can do. It comes from overcoming the things you once thought you couldn't. Involving in sport and physical activities help to develop confidence, lead more satisfying lives, and secure long-term health by reducing the risk for developing chronic illness like diabetes, obesity, cancer and cardiovascular diseases.

All sports have a risk of injury. In general, the more contact in a sport, the greater the risk of a traumatic injury. However, most injuries in young athletes are due to overuse. Most frequent sports injuries are due to accidents, poor training practices or using the wrong gear or equipment. People can also hurt themselves because they are not in shape or because they don't warm up or stretch enough. If injured stop playing. Continuing to play or exercise can cause more harm. Treatment often begins with the RICE (Rest, Ice, Compression, and Elevation) method to relieve pain, reduce swelling, and speed healing. This paper looks at some of the common injuries in sports and factors that help in speeding up the healing process.

Facial Muscles Involved in the Navarasa

Mr. Saranmani Jyotsna K.

1st Year MBBS Student, SBMCH, Chennai

Rasa is about human state of mind. Its about what the mind feels and the expression of the feeling thereafter. In the Bharatas Natyashastra, Rasa is an emotion experienced by the audience created by the facial expression or the Bhava of the actor. In indian classical dance it is referred to as Rasa-abhinaya. The Navarasas or nine emotions give dance a completeness that allows the dancer and the rasikas (audience) to experience the full beauty and meaning of the lyrics and the movements potrayed. There are Nine Rasas with an equal number of complementary moods. These emotions are expressed in the eyes, the face, subtle muscle shifts and the body as a whole. They are:

- 1. Hasya (Happiness)
- 2. Krodha (Anger)
- 3. Bhibasta (Disgust)
- 4. Bhayanaka (Fear)
- 5. Shringara (Beauty)
- 6. Veera (Courage)
- 7. Karuna (Pity)
- 8. Adbhuta (Wonder)
- 9. Shanta (Serenity)

Facial expression and the muscles involved in each rasas is analysed with respect to the classical dance style of south India is studied in this paper.

Sacral Meningocele- A Case Report

Ms. Abinaya S¹, Dr. S. Jayakumari², Dr. WMS Johnson³

¹1st MBBS Student, SBMCH, Chennai ²Assistant Professor of Dept. of Anatomy, SBMCH, Chennai ³Professor and HOD of Anatomy, SBMCH, Chennai

Abstract

The incidence of spinal dysraphism has significantly decreased over the last few decades, all over the world; however, still the incidence is much higher in developing countries with poor socioeconomic status.

Materials and Methods

The present study new born baby diagnosed with sacralmeningocele- closed neural tube defect closed spinal dyraphis Details including demographics, antenatal care history, site and type of lesion, neurological examination, imaging finding, associated congenital anomalies, management offered, and outcome were recorded.

Results

The baby was operated for spinal dysraphism. The baby was healthy.

Conclusion

Spinal dysraphism is still a major public health problem in developing countries. Management of patients with spinal dysraphism is complex and needs close coordination between paediatrician, neurologist, neurosurgeon, and rehabilitation experts. A large number of factors influences the outcome.

Keywords: Meningocele, myelomeningocele, spinal dysraphism

A Variation in the Formation of Median Nerve -A Case Report

Ms. Asimitha¹, Dr. S. Jayakumari², Dr. Krishnavani S³, Dr. WMS Johnson⁴

¹1st year MBBS Student, SBMCH, Chennai ²Assistant Professor, Dept. of Anatomy, SBMCH, Chennai ³Professor and HOD of Anatomy, SBMCH, Chennai

During routine dissection of undergraduate students in the department of anatomy, in the upper extremity of 63 years old a male cadaver observed a variation in the formation of median nerve. Axillary artery passes between the lateral and medial cords of the plexus. The medial root of median nerve crosses the axillary artery to unite with the lateral root to form the median nerve which is lateral and anterior to the axillaryartery. But in this Axillary artery passes between the lateral and medial cords of the plexus. The medial root of median nerve crosses the axillary artery to unite with the lateral root to form t Axillary artery passes between the lateral and medial cords of the plexus. The medial root of median nerve crosses the axillary artery to unite with the lateral root to form median nerve was formed behind the axillary artery. Instead of encircling the axillary artery it encircles the profunda brachial artery. The separate branches arising from the median nerve supplies the Biceps brachia muscle. However; the distribution of the median nerve was normal in the arm, forearm and palm. The arterial pattern in the arm was also normal. Variations in the anatomy of brachial plexus are common. Knowledge of the variations contributes to the surgeons planning and curative intent during surgical repair of the Median nerve deficiencies.

Keywords: Median nerve, brachial plexus, axillary artery.

Morphometric Analysis of Occipital Condyles of Skull – A Pilot Study

Ms. Habeeb Nathira. M¹, Dr. S. Jayakumari², Dr. Dhanalakshmi³, Dr. WMS. Johnson⁴

¹1st year MBBS Student, SBMCH, Chennai ²Assistant Professor, Dept. of Anatomy, SBMCH, Chennai ³Tutor, Dept. of Anatomy, SBMCH, Chennai ⁴Prof. & HOD of Anatomy, SBMCH, Chennai.

Aim

The two prominent oval shaped occipital condyles of the skull bone articulate with the superior articular facet of atlas vertebra and form Atlanta - occipital joint.

They present eitherside of foreman magnum. This investigation intends to record the different shape and measurements of occipital condyle. These parameters are critical for orthopaedic specialists, biomechanical, anatomical, radiologist and clinical examinations.

Methodology:

The occipital condyle length and breadth was measured and various shapes of occipital condyle was noted done.

Result:

There are 7 different shapes were observed. The mean length of occipital condyle of right were 22.80mms and left side were 22.36 mms breath of right side was 12.49mms and left side was 12.80 mms.

Conclusion:

Occipital condyle is likely to have variations with respect to shapes, length, width and its orientation. Therefore, knowledge of the variations in occipital condyle along with careful radiological analysis may help in safe from skull base surgery.

Keywords: occipital condyle, skull, variations

Yoga Therapy in Diabetes Mellitus Type-2

Ms. Monisha

1st year MBBS Student, SBMCH, Chennai

Background

According to diabetes federation atlas, who records 69.2 million people suffering from DM type-2 of which 85-90% are Indians. urban -9%,rural-3% .yoga has reduced the glycemic index of DM type-2 significantly. Today DM type-2 is most trending metabolic disorder. yoga is real therapy for DM type-2 .So I have choosen the benefits of yoga in DM type-2

Objective

The objective of protocol is to have a comparative study of patient with DM type-2 on medication, and person with regular exercise and yoga.

Materials and method

The study subject consists of 25 male diabetic patient attending diabetic clinic.

27 non diabetic male volunteers constituted control group. Other 30 patients on regular exercise yoga. The patients are in age group of 36 to 55 years .The methods used for this are

- 1. HbA1C
- 2. BP
- 3. BMI
- 4. LIPID PROFILE
- 5. FBS
- 6. PPBS

Observation:

Yoga is effective in reducing the blood glucose level in patient with T2DM.

Duration of medication-6 months

Trial follow up -3 months

Conclusion

Yoga is the best adjuant therapy for DM type 2

Acetabulum: A Morphometric Study

Ms. Shanmuga Priyaa.D¹, Dr. Durga Devi.G^{*2}

¹1st year MBBS Student, SBMCH, Chennai ²Associate Professor, SBMCH, Chennai

Introduction

The hip joint is one of the major weight bearing joints of the body. The knowledge of normal anatomical features and morphometry of the acetabulum are prerequisites for complete understanding of the mechanics of hip joint. This information acts as a basis for the making of hip joint prosthesis.

Aim

To do morphometric study of acetabulum of 50 dry human hip bones in South Indian population in order to evaluate the various parameters of acetabulum.

Material and methods

50 randomly collected Indian adult unpaired dry hip bones (27 right side and 23 left side) of unknown sex was taken from the Department of Anatomy of Sree Balaji Medical college and Hospital, Chennai and analysed to evaluate the depth, diameter of acetabulum and length of acetabulur notch.

Results

The raw data obtained was statistically analysed. Range, mean, standard deviation and standard error of mean were determined for each parameter. All values were compared with series of other workers to draw the conclusions.

Abstracts of Poster Presentation

Anatomical Variations & Surgical Relevance of Infraorbital foramen in Human Dry Adult Skulls

Dr. Evangeline Singh

PG Student, PSG Institute of Medical Sciences & Research, Coimbatore

Introduction:

"Infra Orbital Foramen" being situated in the lower margin of the orbit in the maxillary bone, it serves as a pathway for the transmission of infra orbital nerves and vessels.

This nerve provides sensory innervation to the lower eyelid, upper lip and part of the nasal vestibule after passing through infraorbital foramen of the maxilla. Therefore it is the Nerve which is preferred to anaesthetize during periorbital, dental, plastic and or omaxillofacial surgeries.

This study was designed to document the most easily approachable anatomical landmarks for defining the location of infraorbital foramen and to have knowledge of super numerary foraminae for effective nerve blockade and to decrease its risk of injury during periorbital surgeries.

Aims & Objective of the study:

- 1. To estimate the incidence of accessory infra orbital foramen
- 2. To calculate the mean distance between infraorbital foramen and infra orbital margin
- 3. To calculate the distance between infraorbital foramen and piriform aperture

Methodology:

After Obtaining IHEC approval,60 Dry Adult skulls were obtained from departments of Anatomy and Forensic Medicine. Morphometric analysis was done using Digital Vernier caliper.

Result:

The results were analysed using Microsoft excel.

Conclusion

The Significant side related differences in relation to the position of the infraorbital foramen indicate that precaution should be taken during surgical manipulation and administering regional nerve block. With Increased Incidence of accessory foraminae in the left orbit, there lies risk of damaging the nerve that could lead to sensory deficit.

A Study of Persistent Metopic Suture in Adult Human Dry Skulls in Tamilnadu

Dr.Kesavan V.A¹., Dr.Jamuna M², Dr.Amudha G³

¹Second year Postgraduate, ²Professor ³Professor & HOD, P.S.G.Institute of Medical Sciences & Research, Coimbatore.

Introduction

Metopic suture is a dentate type of suture extending from the nasion to anterior angle of bregma. It is present at birth and is usually obliterated at the age of second year. But it may extend upto the age of 6 to 8 years. Morphology of metopic suture varies. If it extends from bregma to nasion it is complete and if not it is incomplete. This study is useful for radiologists and neurosurgeons while studying skull x-rays and also to avoid misinterpretation of metopic suture as frontal bone fracture.

Objectives

- 1. To observe the prevalence of persistent metopic suture in adult human dry skulls.
- 2. To study its morphology.

Methods

After obtaining IHEC clearance, this study was conducted in 40 adult human dry skulls of unknown sex. All the skulls included in the study were adults as evidenced by the eruption of third molar teeth. The damaged skulls were excluded. The prevalence of metopic suture was observed and the frequency distributions of its morphological variations were studied.

Results:

Persistent metopic suture was found in 7.5 % of adult human dry skulls. Morphological variations like complete persistence metopic suture and Linear type of incomplete metopic suture were observed.

Conclusion

The present study confirms the prevalence of this anatomical entity and its morphological variations in the Tamilnadu population. Awareness of these kind of variations will be helpful for the radio diagnosticians, forensic surgeons and neurosurgeons to avoid misinterpretation of these persistent sutures as midline vertical fracture of the skull.

"Histological Changes in Ovaries of Human Fetuses"

Dr. Mythily.N¹, Dr. Amudha. G²

¹PG Student, Dept. of OBG ²Prof & HOD of OBG, PSG Institute of Medical Science, Coimbatore

Introduction

Ovaries are the female gonads which play a major role in reproduction by producing ova and also female sex hormones which play a significant role in the growth and development after birth.

The ovary has two parts, an outer cortex and an inner medulla. The cortex consists of cellular connective tissue and the medulla is composed of loose connective tissue, which contains blood vessels and nerves.

Objective

- To observe the histological changes in human fetal ovaries.
- To compare the results with the previous studies.

Methods

The study was conducted in thirty fetal ovaries collected from fifteen fetuses from the Department Obsteric & Gynacology, PSG Institute of Medical Science and Research.

The 30 ovaries were processed using routine histological techniques and H&E staining and studied under microscope.

Results

20 weeks ovaries showed lymphoid appearance with actively proliferating oogonia and primordial follicles in early stage differentiation with corticomedullary demarcation.

28 weeks ovaries showed plenty of both developing and degenerating primordial follicles which were lined by flat to cuboidal cells.

30 weeks ovaries showed plenty of encapsulated primary Oocyte giving the appearance of tiny white rings with central dots.

Conclusion

The histological assessment of ovaries will help to estimate the age of the fetus in fetal autopsies and also useful to study the syndrome associated diseases and to estimate the age of the fetus aborted due to unknown causes.

Variation in the Origin and Termination of External Jugular Vein-A Cadaveric Study

Dr.G.Yuvarani¹, Prof. Dr. K.Sujatha²

^{1,2}Department of Anatomy, Govt. Stanley Medical College, Chennai-1

Abstract:

The knowledge of the variations in the venous pattern of head & neck, is very important for the Physicians, General surgeons, Vascular surgeons and radiologists. During routine dissection in the Department of Anatomy, Stanley Medical College, Chennai out of 10 cadavers, variations were noted in the origin and termination of external jugular vein in 65 year old female cadaver. The maxillary vein & superficial temporal vein joins to form retro-mandibular vein, which in turn did not divide into anterior and posterior division but continued as external jugular vein and finally terminated into the internal jugular vein behind the sternocleidomastoid muscle. Facial vein also drained into external jugular vein at the level of hyoid bone. Aim of the study was to create awareness regarding the variations of external jugular vein which is important for cannulation, monitoring central venous pressure, giving intravenous fluids/drugs, and vascular reconstructive surgeries of face. Hence the knowledge of these variations is important during surgical procedures like radical neck dissection and radiological interventions.

Keywords: External jugular vein (EJV), retromandibular vein (RMV), Facial vein (FV), Internal jugular vein (IJV).

Introduction:

The veins of head and neck have a complex developmental pattern which predisposes them to anatomical variations. On either side of the face superficial temporal vein unites with the maxillary vein to form retro mandibular vein within the substance of the parotid gland. The retro mandibular vein divides into anterior and posterior divisions. The anterior division joins with facial vein to form common facial vein inferior to the angle of mandible which drains into internal jugular vein. The posterior division joins with the posterior auricular vein to form the external jugular vein which drains into subclavian vein (**Grays Anatomy, T.S.Ranganathan**)^{1,2}. The external jugular vein shows anatomical variation in its origin and termination. The knowledge of these variations is of utmost importance during interpretation of raised JVP in right heart failure and during surgical and radiological interventions.

Aim of the Study

To create awareness regarding the variations of origin and termination of External jugular vein which is important in surgical procedures like radical neck

dissection, flap reconstructive surgeries of face, and in radiological interventions for embolism & catheterization procedures.

Materials & Methods

In 10 unclaimed embalmed human cadavers meant for routine dissection in the Department of Anatomy, Government Stanley Medical College superficial veins of head and neck was studied on both sides. The variations were noted, carefully dissected and photograph taken.

Case Discussion

During routine dissection in the Department of Anatomy, Stanley Medical College, out of 10 cadavers, in one female cadaver of 65 years variations in the origin and termination of external jugular vein was found on the left side. In this cadaver, The left maxillary vein & left superficial temporal vein joins to form left retro-mandibular vein, which in turn did not divide into anterior and posterior division but continued as external jugular vein. Facial vein also drained into external jugular vein at the level of hyoid bone, below the angle of mandible. The external jugular vein runs superficially over sternocleidomastoid muscle upto middle 1/3rd. At the level of lower border of thyroid cartilage, it passes deep to sternocleidomastoid muscle and terminated into left internal jugular vein (fig 1,3). The normal origin and termination of external jugular vein is shown in figure no 2. (Holinshed 1974, B Deslaugiers 1994)^{3,4} said that external jugular vein draining into internal jugular vein was seen in 4% of cases. (Gupta et al 2003 & D'Silva SS 2008)^{5, 6} said that facial vein draining into external jugular vein in humans.

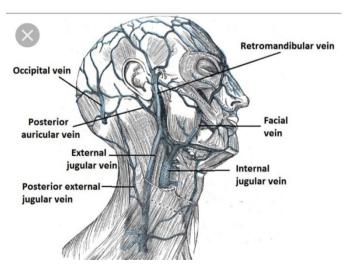


Fig 1: Normal venous pattern of head and Neck.

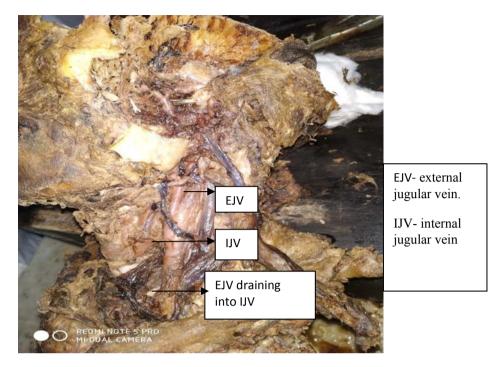


Fig 2: External jugular vein draining into Internal jugular vein

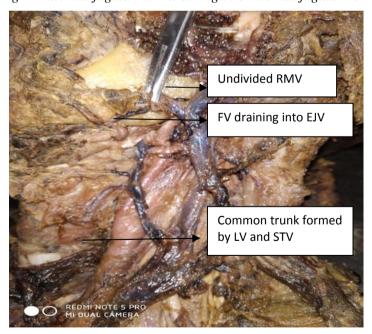


Fig 3: Common trunk formed by lingual vein and superior thyroid vein draining into Internal Jugular vein. (RMV-Retromandibular vein, FV-Facial vein, LV-Lingual vein, STV-Superior thyroid vein.)

Conclusion:

The knowledge on these variation of external jugular vein is important as they are often used for cannulation, monitoring central venous pressure, giving intravenous fluids/drugs in comatose and burns patients when other superficial veins are not accessible (Choudhry.R et al 1997)⁷.Permanent catheterization for hemodialysis is done via external jugular vein. This variations is important for interventional radiologists who perform Transjugular procedures like port implantations and Transjugular intra hepatic Porto systemic shunts.It is also used as patches for carotid endarterectomies and for oral reconstruction.

Variations in Branching Pattern of Maxillary Artery-A Cadaveric Study

Dr. Nasrin Taj.S¹, Prof Dr. K. Sujatha²

^{1,2}Department of Anatomy, Government Stanley Medical College, Chennai.

Abstract

Variation in the course and branches of the Maxillary artery is well documented. Out of ten embalmed cadavers meant for dissection purpose for the first year MBBS students in the Department of Anatomy, Stanley Medical college, Chennai In one male cadaver variation in the branching pattern of Maxillary artery was found. In that cadaver Deep temporal artery had a common origin along with the Inferior alveolar artery. Such variations are of clinical importance for the Plastic surgeons for the reconstructions of facial flap and also for interventional radiologists during arterial embolization in uncontrolled epistaxis, to prevent inadvertent haemorrhage during the resection of tumorin the infratemporal region.

Keywords: Maxillary artery, Deep temporal artery, Inferior alveolar artery, Infratemporal fossa

Aim

The aim of the study is to know about the variations in the branching pattern of Maxillary artery

Introduction

Variation in the arterial system has been well documented in literature. The Maxillary artery is the largest terminal branch of External Carotid artery (T.S.Ranganathan)¹. It arises behind the neck of mandible, runs horizontally forward up to the lower border of lateral pterygoidmuscle superficially (sometimes deep). After emerging between the two heads of lateral pterygoid, it enters into the pterygopalatine fossa by passing through the pterygomaxillary fissure. Here it ends by giving terminal branches. The maxillary artery is divided in to three parts by lower head of lateral pterygoid muscle into Mandibular part, Pterygoid part and Pterygopalatine part. The branches of 1st part (Mandibular part) are deep auricular artery, anterior tympanic artery, middle meningeal artery, accessory meningeal artery and inferior alveolar artery. The branches of 2nd part (Pterygoid part) are deep temporal artery, masseteric artery, buccal artery and pterygoid artery and the branches of 3rd part (Pterygopalatine part) are posterior superior alveolar artery, infra orbital artery, greater palatine artery, pharyngeal artery, artery to pterygoid canal and sphenopalatine artery (Gray)².

The maxillary artery in the infratemporal fossa has been well explored by the oncologists for performing super selective intraarterial chemotherapy for the head and

neck cancers. Due to the close proximity to the cranial base maxillary artery is directly used as the arterial donor in the repair of internal carotid artery dissection and aneurysms (**Buyukmumcu et al 2003**)³. Maxillary artery should be taken care of during dental anaesthesia to prevent intraarterial injection.

Materials:

10 adult unclaimed embalmed cadaver [8 males and 2 females] meant for dissection purpose for the first MBBS students in Department of Anatomy, Stanley Medical College, Chennai.

Methods:

Conventional dissection method

Case study:

During routine dissection out of 10 adult embalmed cadavers, in one 58 year old male cadaver variations in the branching pattern of Maxillary artery was found. The deep temporal artery usually arises from the 2nd part of maxillary artery but in this cadaver it had a common origin along with inferior alveolar artery from the 1st part of maxillary artery (fig 1). The Masseteric artery also arises from the 1st part. The other arteries namely Deep auricular, Anterior tympanic, Middle meningeal and Accessory meningeal had a normal course.

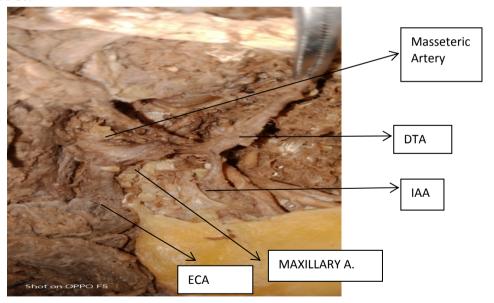


Fig 1: Deep temporal artery arising from 1st part of Maxillary artery with Deep temporal artery. (ECA-External carotid artery, IAA-Inferior Alveolar artery, DTA-Deep temporal artery, Masseteric artery)

Discussion

Several reports of variations in the course of Maxillary artery have been documented. Variations are not common in the origin of deep temporal arteries, however in a study published by (**Suwa et al 1990**)⁴, Deep temporal artery and inferior alveolar artery took origin as a common trunk in (48/278)17.26% hemicraniums. (**Quadros Lydia s et al 2013**)⁵, has also reported the common origin of deep temporal artery along with the inferior alveolar artery which in turn coincides with my study.

Result

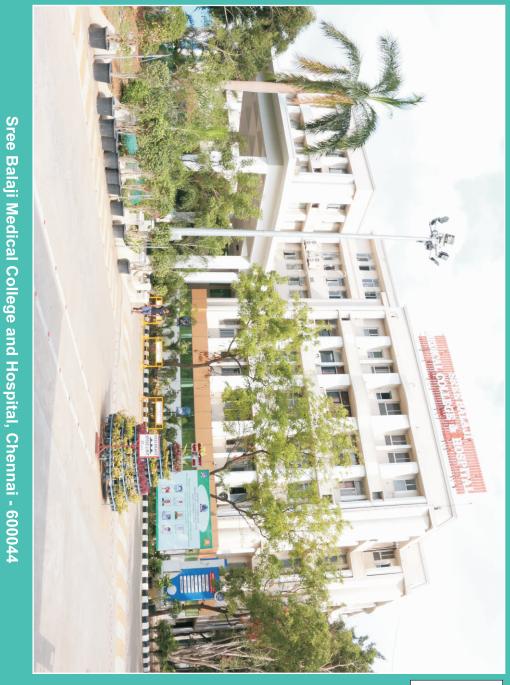
Out of 10 embalmed cadaver in one adult male cadaver deep temporal artery had a common origin along with inferior alveolar artery. Masseteric artery also had its origin from the 1st part.

Conclusion

The above study reveals the possibility of variations in the branching pattern of Maxillary artery. A good knowledge about the existing variations should be known to the plastic surgeon for facial flapreconstructive surgery, radiologist for arterial embolization and for oncologist for superselective intraarterial chemotherapy (Bergmann RA et al)⁶ & (Correa MB et al)⁷.

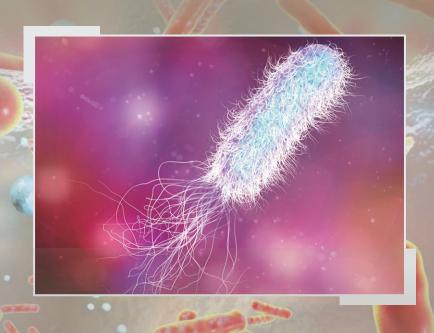


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Antibiotic Resistance in Bacteria



Dr. D. Bindu

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ANTI- PHOSPHOLIPID SYNDROME - REVIEW

DR.SHANMUGANADAN K DR.SURESH KANNA DR.LOHITHA MALLIPEDDI

DEPARTMENT OF GENERAL MEDICINE,

SREE BALAJI MEDICAL SCIENCES AND HOSPITAL.

#7,WORKS ROAD,NEW COLONY, CHROMEPET, CHENNAI-600044

Editorial Office

Prof. Dr. (Brig.) Shanmuganandan Krishnan

Professor of Department of General Medicine

Consultant Rheumatologist

Sree Balaji Medical College and Hospital

7, CLC Works Road, Chromepet, Chennai - 600044, Tamil Nadu, India.

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Dr. S. Sundari Professor and Head

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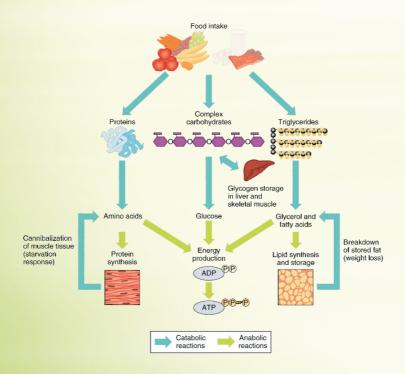
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CARBOHYDRATE METABOLISM - MADE EASY



Dr. B. Shanthi, MD

Co Authors

Dr. V.S. Kalai Selvi, MD. Dr. A. Mary Chandrika Dr. Chaganti Sridevi Dr. Jyothi Elizabeth Roy



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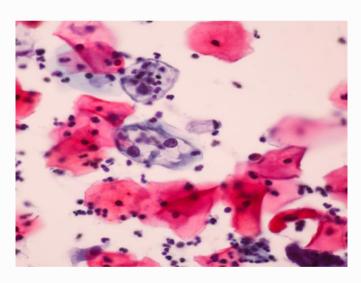




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DEPARTMENT OF PATHOLOGY

CHANGES IN CONVENTIONAL AND LIQUID BASED CYTOLOGY PAP SMEAR IN VARIOUS CERVICAL LESIONS



Dr. Vinutha Gali

Assistant Professor

Department Of Pathology

Dr. Gayathri

2nd yr PostGraduate

Department Of Pathology

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COMMUNITY BASED REHABILITATION-AN OVERVIEW



DR. SWETHA N B DEPARTMENT OF COMMUNITY MEDICINE SREE BALAJI MEDICAL COLLEGE AND HOSPITAL

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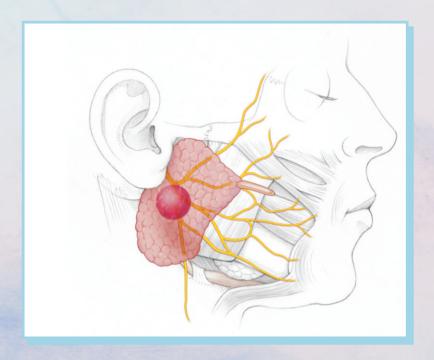
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Comparison of Recent WHO Classification of Salivary Gland Neoplasms with the Previous Classification



Dr. M. Aswin Manikandan, MBBS, MD Dr. Shobana, MBBS, MD



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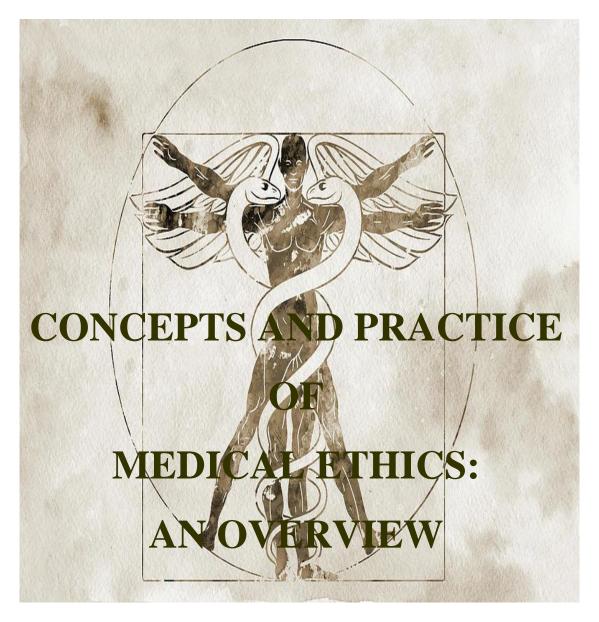
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AUTHOR

DR. R. UMADEVI,

Professor&Head of the Department.

DEPARTMENT OF COMMUNITY MEDICINE SREE BALAJI MEDICAL COLLEGE AND HOSPITAL

Chrompet, Chennai- 600044.

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DEPARTMENT OF COMMUNITY MEDICINE SREE BALAJI MEDICAL COLLEGE AND HOSPITAL CHROMPET, CHENNAI- 600044

Concise Textbook of Skin Biopsy Study in Leprosy



Dr. Subhashini, MBBS, MD
Dr. M. Naga Meena Lochini, MBBS





Publisher

©Dr. Subhashini, MBBS, MD

Associate Professor

Department of Pathology, Sree Balaji Medical College and Hospital

Chromepet, Chennai - 600044

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DR.K SHANMUGANANDAN DR.KAVURU NAGA SIRI

DEPARTMENT OF GENERAL MEDICINE,

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CYTOKINE STORM IN COVID-19

 \mathbf{BY}

Dr. (Brig.) Shanmuganandan Krishnan

Dr. Kavuru Naga Siri

Dr. P Sanjeevi Krishnan

Dr. Sreelatha Nalabothu

Dr. Naveen Kumar M

Editorial Office:

Prof. Dr. (Brig.) Shanmuganandan Krishnan

Professor of Department of General Medicine

Consultant Rheumatologist

Sree Balaji Medical College and Hospital

7, CLC Works Road,

Chromepet,

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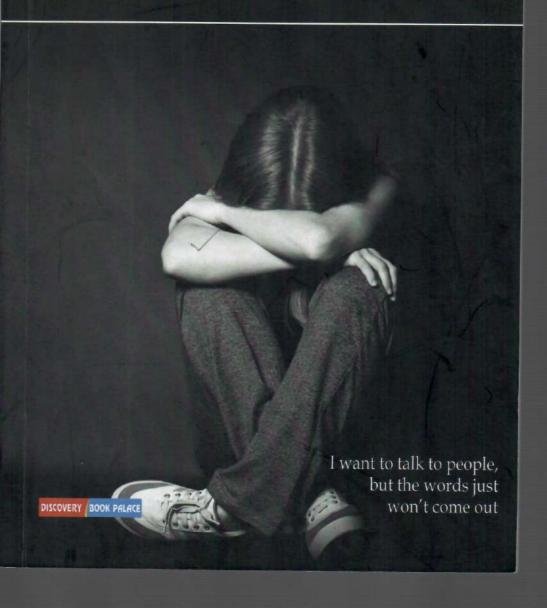
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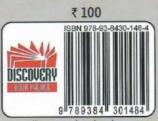
DEPRESSION LET'S TALK

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Dermatology Inter-Collegiate Meet DICM

Editor

Prof. K. Manoharan MBBS, MD, DD

Professor &HOD - Department of Dermatology, Venereology &Leprosy, Sree Balaji Medical College &Hospital, Chennai.

Co-Editors

Prof. D.Manoharan MBBS, MD

Professor - Department of Dermatology, Venereology &Leprosy, Sree Balaji Medical College &Hospital, Chennai.

Prof. N.Ashok Kumar MBBS, MD-DVL

Professor - Department of Dermatology, Venereology &Leprosy, Sree Balaji Medical College &Hospital, Chennai.

Dr.C.Geo Danny MBBS, MD-DVL

Assistant Professor-Department of Dermatology, Venereology &Leprosy, Sree Balaji Medical College & Hospital, Chennai.

Editorial Office

Prof.K.Manoharan

Editor-in-Chief

Professor & Head of Department,

Department of Dermatology, Venereology & Leprosy,

Sree Balaji Medical College & Hospital,

7, CLC Works Road, Chromepet, Chennai 600044,

Tamil Nadu, India.

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Diagnostic Atlas of Pediatric Imaging Chest and Mediastinum

This book is a collection of plain skiagram, USG, CT and MR images with salient key points

Both authors have a long experience in Pediatric Radiology. The book is meant for practicing radiologists, radiology residents, consultant pediatricians, pediatric surgeons and residents in the same specialty and others who have special interest in pediatric imaging.

The text in this book is very crisp and they emphasis on the images. This book deserves a place in your home, office and in library.

M Prabakaran did MBBS from the Government Stanley Medical College, Chennai. He completed his MD (Radiodiagnosis) at the Barnard Institute of Radiology and Oncology, Madras Medical College and Government General Hospital, Chennai. He served as Assistant Professor, Reader, and Additional Professor of Radiodiagnosis in various medical college hospitals in Tamil Nadu. Then, he became a Professor and Head, Department of Radiology and Imageology, Institute of Child Health and Hospital for Children, Egmore, Chennai, the biggest and premier pediatric institute in South Asia.



Presently. He is the Director and Professor, Barnard Institute of Radiology and Oncology, Chennai, which is the first Institution in India, took X-rays for patients. He has presented a number of papers and invited talks in National Conferences. He is a PG Examiner in many Indian Universities.

B Natrajan did MBBS from the Government Madras Medical College, Chennai and completed his DMRD at the Government Stanley Medical College. Presently, he is working as Assistant Professor, Department of Radiology and Imageology, Institute of Child Health and Hospital for Children, Egmore, Chennai, the biggest and premier pediatric institute in South Asia.



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Diagnostic Atlas of Pediatric Imaging

Chest and Mediastinum



M Prabakaran B Natrajan

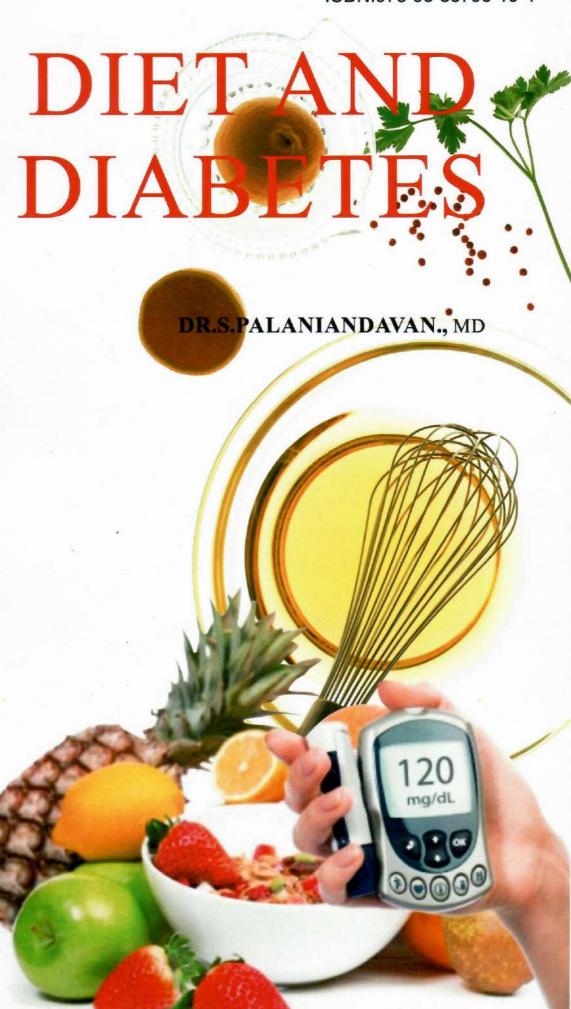
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Foreword
Saradha Suresh



Prof.S.Palaniandavan is a senior physician, PROF and HOD of SreeBalaji Medical College and Hospital, Bharath University, Chennai. He is a former professor of medicine stanely medical college and hospital Chennai, and is a distinguished teacher and clinician. He has a long clinical career during which he has held several positions. He has 27yrs of experience in under graduates and post graduates. He has been examiner for both undergraduates and post graduates. He has 12 papers to his credits.





DISCUSSIONS IN ANATOMY



Authors
Dr. M. Kavimani
Dr. K. Prabhu



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Discussions in Anatomy

 $\mathbf{B}\mathbf{y}$ Dr. M. Kavimani Dr. K. Prabhu

Dedicated to our Parents



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Preface

This text book has been carefully planned for first year students. It follows the revised anatomy curriculum of the Indian medical council. To help students to score high marks in examination, this text book is written in simple language. The text provides essential and relevant information to all the MBBS students. This would prove useful in theory, practical and viva voce examinations. As teachers we have tried our best to make the book easy to understand and interesting to read.

Our special thanks to Dr.W.M.S. Johnson who encouraged us to write this text book.

I am welcome comments and suggestions from students.

Dr. M. Kavimani & Dr. K. Prabhu.

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The Upper Limb

The upper limb is related to the lateral aspect of the lower portion of the neck and with the thoracic wall. It's suspended from the trunk by muscles and a small skeletal articulation between the clavicle and the sternum – the sternoclavicular joint. Based upon the position of it's major joints and component bones, the upper limb is split into shoulder, arm, forearm, and hand.

The shoulder is the area of upper limb connection to the trunk. The arm is the part of the upper limb between the shoulder and the elbow joint; the forearm is between the elbow joint and the wrist joint; and the hand is distal to the wrist joint.

The axilla, cubital fossa, and carpal tunnel are significant regions of transition between the different parts of the limb. Essential structures go through, or are related to, every of these regions.

The axilla is an irregularly shaped pyramidal area created by muscles and bones of the shoulder and the lateral surface of the thoracic wall. The apex or inlet opens directly into the lower portion of the neck. The skin of the armpit creates the floor. All major structures that pass between the neck and arm go through the axilla.

The cubital fossa is a triangularly shaped depression created by muscles anterior to the elbow joint. The major artery, the brachial artery, going from the arm to the forearm goes through this fossa, so does one of the major nerves of the upper limb, the median nerve.

The carpal tunnel is the entrance to the palm of the hand. Its posterior, lateral, and medial walls create an arch, that is created from small carpal bones in the proximal region of the hand. A thick band of connective tissue, the flexor retinaculum, covers the distance between every side of the arch and creates the anterior wall of the tunnel. The median nerve and all the long flexor tendons going from the forearm to the digits of the hand go through the carpal tunnel.

Positioning the Hand

Unlike the lower limb, that is utilized for support, stability, and locomotion, the upper limb is highly mobile for positioning the hand in space.

The shoulder is suspended from the trunk predominantly by muscles and hence moves relative to the body. Sliding (protraction and retraction) and rotating the scapula on the thoracic wall changes the position of the glenohumeral joint (shoulder joint) and extends the reach of the hand. The glenohumeral joint enables the arm to move around three axes with a broad range of motion. Movements of the arm at this joint are of the radius over the ulna. This movement called pronation, takes place solely in the forearm. Supination returns the hand to the anatomical position.

At the wrist joint, the hand can be abducted, adducted, flexed, extended, and circumducted. These movements, combined with those of the shoulder, arm, and forearm, allow the hand to put in a broad range of positions relative to the body.

One of the major functions of the hand is to grip and manipulate objects. Gripping objects usually involves flexing the fingers against the thumb. Depending on the type of grip, muscles in the hand act to:

- Modify the actions of long tendons that emerge from the forearm and insert into the digits of the hand.
- Produce combinations of joint movements inside every digit that can't be generated by the long flexor and extensor tendons alone coming from the forearm.

The hand is utilized to discriminate between objects on the basis of touch. The pads on the palmar aspect of the fingers. Include a high density of somatic sensory receptors. Also, the sensory cortex of the brain devoted to interpreting info from the hand, particularly from the thumb, is disproportionately large relative to that for many other regions of skin.

Component Parts

Bones and Joints

- The bones of the shoulder contain the <u>scapula</u>, <u>clavicle</u>, and proximal end of the <u>humerus</u>.
- The clavicle articulates medially with the manubrium of the <u>sternum</u> and laterally with the acromion of the scapula, which arches over the joint between the <u>glenoid cavity</u> of the scapula and the <u>head</u> of the <u>humerus</u> (the glenohumeral joint).
- The humerus is the bone of the arm. The distal end of the humerus articulates with the bones of the forearm in the elbow joint, that is a hinge joint that enables flexion and extension of the forearm.

- The forearm includes two bones:
 - The lateral bone is the radius.
 - The medial bone is the ulna.
- At the elbow joint, the proximal ends of the radius and ulna articulate with every other as well as with the humerus.
- Along with flexing and extending the forearm, the elbow joint enables the radius to spin on the humerus while sliding against the head of the ulna during pronation and supination of the hand.
- The distal portions of the radius and the ulna also articulate with each other. This joint enables the end of the radius to flip from the lateral side to the medial side of the ulna during pronation of the hand.
- The wrist joint is composed between the radius and carpal bones of the hand and between an articular disc, distal to the ulna, and carpal bones.
- The bones of the hand contain the carpal bones, the metacarpals, and the phalanges.
- The 5 digits in the hand are the thumb and the index, middle, ring, and little fingers.
- Joints between the 8 small carpal bones enable only limited amounts of movement; as a result, the bones work together as a unit.
- The 5 metacarpals, 1 for every digit, are the primary skeletal foundation of the palm.
- The joint between the metacarpal of the thumb (metacarpal I) and one of the carpal bones enables greater mobility than the limited sliding movement that takes place at the carpometacarpal joints of the fingers.
- Distally, the heads of metacarpals II to V (i.e., with the exception of that of the thumb) are interconnected by strong ligaments.
- Lack of the ligamentous connection between the metacarpal bones of the thumb and index finger along with the biaxial saddle joint between the metacarpal bone of the thumb and the carpus supply the thumb with greater freedom of movement in relation to the other digits of the hand.
- The bones of the digits are the phalanges. The thumb has 2 phalanges, while every of the other digits has 3.
- The metacarpophalangeal joints are biaxial condylar joints (ellipsoid joints) that enable abduction, adduction, flexion, extension, and circumduction. Abduction and adduction of the fingers is defined in reference to an axis going through the center of the middle finger in the anatomical position. The

middle finger hence abduct both medially and laterally and adduct back to the central axis from either side. The interphalangeal joints are primarily hinge joints that enable only flexion and extension.

Muscles

Some muscles of the shoulder, like the <u>trapezius</u>, levator scapulae, and rhomboids, attach the scapula and clavicle to the trunk. Other muscles attach the clavicle, scapula, and body wall to the proximal end of the humerus. These contain the pectoralis major, pectoralis minor, latissimus dorsi, teres major, and deltoid. The most significant of these muscles are the 4 rotator cuff muscles—the subscapularis, supraspinatus, infraspinatus, and teres minor muscles, which attach the scapula to the humerus and give support for the glenohumeral joint.

- Muscles in the arm and forearm are divided into anterior (flexor) and posterior (extensor) compartments by layers of fascia, bones, and ligaments.
- The anterior compartment of the arm is located anteriorly in position and is divided from muscles of the posterior compartment by the humerus and by medial and lateral intermuscular septa. These intermuscular septa are continuous with the deep fascia enclosing the arm and connect to the sides of the humerus.
- In the forearm, the anterior and posterior compartments are divided by a lateral intermuscular septum, the radius, the ulna, and an interosseous membrane, which joins adjacent sides of the radius and ulna.
- Muscles in the arm act primarily to move the forearm in the elbow joint, while those in the forearm function predominantly to move the hand in the wrist joint and the fingers and thumb.
- Muscles seen entirely in the hand, the intrinsic muscles, generate delicate movements of the digits of the hand and modify the forces produced by tendons entering the fingers and thumb from the forearm. Included among the intrinsic muscles of the hand are 3 small thenar muscles, which create a soft tissue mound, termed the thenar eminence, over the palmar aspect of metacarpal I. The thenar muscles enable the thumb to move freely relative to the other fingers.

Relationship to other regions

Neck

The upper limb is directly related to the neck. Being located on every side of the superior thoracic aperture in the base of the neck is an axillary inlet, that is created by:

- the lateral margin of rib 1,
- the posterior surface of the clavicle,
- the superior margin of the scapula, and.
- the medial surface of the coracoid process of the scapula.

The major artery and vein of the upper limb pass between the <u>thorax</u> and the limb by passing over rib 1 and via the axillary inlet. Nerves, predominantly originated from the cervical portion of the <u>spinal cord</u>, also go through the axillary inlet and the axilla to supply the upper limb.

Back and Thoracic Wall

Muscles that connect the bones of the shoulder to the trunk are related to the back and the thoracic wall and contain the trapezius, levator scapulae, rhomboid major, rhomboid minor, and latissimus dorsi.

The breast on the anterior thoracic wall has a number of significant relationships with the axilla and upper limb. It overlies the pectoralis major muscle, which creates majority of the anterior wall of the axilla and attaches the humerus to the chest wall. Frequently, part of the breast called the axillary process extends around the lateral margin of the pectoralis major into the axilla.

Lymphatic drainage from lateral and superior parts of the breast is predominantly into lymph nodes in the axilla. Several arteries and veins that supply or drain the gland also starts from, or drain into, major axillary vessels.

Innervation by Cervical and Upper Thoracic Nerves

Innervation of the upper limb is by the <u>brachial plexus</u>, that is created by the anterior rami of cervical <u>spinal nerves</u> C5 to C8, and T1. This plexus is initially created in the neck and after that continues via the axillary inlet into the axilla. Major nerves that ultimately innervate the arm, forearm, and hand starts from the <u>brachial plexus</u> in the axilla.

As a consequence of the innervation pattern, clinical testing of lower cervical and T1 nerves is performed by examining dermatomes, myotomes, and tendon reflexes in the upper limb. Another consequence is that the clinical signs of problems related to lower cervical nerves-pain; pins-and-needles sensations, or paresthesia; and muscle twitching—appear in the upper limb.

Dermatomes of the upper limb are frequently tested for sensation. Regions where overlap of dermatomes is minimal, contains:

- upper lateral region of the arm for spinal cord level C5,
- palmar pad of the thumb for spinal cord level C6,
- pad of the index finger for spinal cord level C7,
- pad of the little finger for spinal cord level C8, and.
- skin on the medial aspect of the elbow for spinal cord level Tl.

Selected joint movements are utilized to test myotomes:

- Abduction of the arm a t the glenohumeral joint is controlled predominantly by C5.
- Flexion of the forearm in the elbow joint is controlled primarily by C6.
- Extension of the forearm in the elbow joint is controlled primarily by C7.
- Flexion of the fingers is controlled primarily by C8.
- Abduction and adduction of the index, middle, and ring fingers is controlled predominantly by Tl.

In an unconscious patient, both somatic sensory and motor functions of spinal cord levels can be tested using tendon reflexes:

- A tap on the tendon of the biceps in the cubital fossa tests primarily for spinal cord level C6.
- A tap on the tendon of the triceps posterior to the elbow tests primarily for C7.

The major spinal cord level related to innervation of the diaphragm, C4, is immediately above the spinal cord levels related to the upper limb.

Evaluation of dermatomes and myotomes in the upper limb can give essential info about potential breathing problems that may develop as complications of damage to the spinal cord in regions just below the C4 spinal level.

Every of the major muscle compartments in the arm and forearm and every of the <u>intrinsic muscles of the hand</u> is innervated predominantly by one of the major nerves that starts from the brachial plexus in the axilla:

All muscles in the anterior compartment of the arm are innervated by the musculocutaneous nerve.

- The <u>median nerve</u> innervates the muscles in the anterior compartment of the forearm, with two exceptions one flexor of the wrist (the <u>flexor carpi ulnaris muscle</u>) and part of one flexor of the fingers (the medial half of the flexor digitorum profundus muscle) are innervated by the <u>ulnar nerve</u>.
- Most intrinsic muscles of the hand are innervated by the <u>ulnar nerve</u>, with the exception of the thenar muscles and 2 lateral lumbrical muscles, that are innervated by the median nerve.
- All muscles in the posterior compartments of the arm and forearm are innervated by the <u>radial nerve</u>.
- In addition to innervating major muscle groups, every of the major peripheral nerves originating from the brachial plexus carries somatic sensory info from patches of skin quite different from dermatomes. Sensation in these type of regions can be utilized to test for peripheral nerve lesions.
- The <u>musculocutaneous nerve</u> innervates skin on the anterolateral side of the forearm.
- The median nerve innervates the palmar surface of the lateral three and one
 -half digits, and the ulnar nerve innervates the medial one and one-half
 digits.
- The radial nerve supplies skin on the posterior surface of the forearm and the dorsolateral surface of the hand.

Nerves Linked to Bone

Three essential nerves are directly related to parts of the humerus:

- The <u>axillary nerve</u>, which supplies the deltoid muscle, a major abductor of the humerus in the glenohumeral joint, enters around the posterior aspect of the upper part of the humerus (the surgical neck).
- The radial nerve, which supplies all of the extensor muscles of the upper limb, enters diagonally around the posterior surface of the middle of the humerus in the radial groove.
- The ulnar nerve, that is ultimately destined for the hand, enters posteriorly
 to a bony protrusion, the medial epicondyle, on the medial side of the distal
 end of the humerus.

<u>Fractures</u> of the humerus in any one of these three regions can endanger the related nerve.

Superficial Veins

Large veins embedded in the <u>superficial fascia</u> of the upper limb are frequently utilized to access a patient's vascular system and to withdraw blood. The most significant of these veins are the cephalic, basilic, and median cubital veins.

The cephalic and basilic veins starts from the dorsal venous network on the back of the hand.

The cephalic vein comes from over the <u>anatomical snuffbox</u> at the base of the thumb, enters laterally around the distal forearm to reach the anterolateral surface of the limb, and after that continues proximally. It crosses the elbow, then enters up the arm into a triangular depression—the clavipectoral triangle.

Clavipectoral Triangle (Deltopectoral Triangle)

Between the pectoralis major muscle, deltoid muscle, and clavicle. In this depression, the vein enters into the axilla by penetrating deep fascia just inferior to the clavicle.

The basilic vein comes from the medial side of the dorsal venous network of the hand and enters proximally up the posteromedial surface of the forearm. It enters into the anterior surface of the limb just inferior to the elbow and after that continues proximally to enter deep fascia about midway up the arm.

At the elbow, the cephalic and basilic veins are connected by the median cubital vein, which crosses the roof of the cubital fossa.

Joints of the Upper Limb

- Sternoclavicular only bony union of upper limb to axial skeleton multiaxial
 - a. Bones manubrium, clavicle
 - b. Cartilages articular cartilage, articular disc, costal cartilage
 - c. Ligaments capsule
 - d. Weakness, etc. none clavicle usually breaks before dislocation occurs
- 2. Acromioclavicular slightly movable planar
 - a. Bones lateral end of clavicle articular surface of acromion
 - b. Cartilages articular, articular disc, disc often incomplete

- c. Ligaments -
 - capsular acromioclavicular
 - accessory coracoclavicular actually a syndesmosis
- d. Weakness "shoulder separation," disruption of acromioclavicular joint and coracoclavicular ligament
- 3. Shoulder glenohumeral scapulohumeral -freely movable, multiaxial ball and socket
 - a. Bones glenoid fossa of scapula, head of humerus
 - b. Cartilages articular, glenoid labrum
 - c. Ligaments -
 - capsular glenohumeral bands (superior, middle, inferior),
 coracohumeral
 - accessory coracoacromial, transverse humeral
 - accessory structures long head of biceps, subscapular bursa, rotator cuff
 - d. Weakness anterior dislocation most common inferior often in children, rotator cuff tear usually the supraspinatus which often deteriorates with age wear and tear
- 4. Elbow humeroulnar & humeroradial (proximal radioulnar is included in capsule) uniaxial hinge
 - a. Bones trochlea and capitulum of humerus, head of radius, trochlear notch of ulna
 - b. Cartilages articular
 - c. Ligaments capsular only ulnar and radial collateral, anular (forms proximal attachment of radial)
 - d. Weakness ulna most commonly dislocated post., epicondylitis, "pitcher's elbow", "pulled elbow"
- 5. Radioulnar pivot joint, allows rotation (pronation and supination), about 135 degrees of rotation
 - a. Proximal radioulnar
 - bones head of radius, radial notch of ulna
 - ligaments anular ligament (lined by cartilage)

- b. Interosseous membrane a syndesmosis between the interosseous margins of radius and ulna
- c. Distal radioulnar
 - bones head of ulna, styloid of ulna and ulnar notch of radius
 - ligaments capsular only, none to name
 - accessory structure articular disc acts as a ligament between ulnar styloid and ulnar notch of radius
- 6. Wrist complex joint, condyloid, planar, and ball and socket; multiaxial with limited movements
 - a. Radiocarpal "Wrist joint" between radius and ulnar disc proximally and proximal row of carpals distally
 - bones radius, scaphoid, lunate, triquetrum (carpals act as a unit)
 - cartilages ulnar disc, articular cartilages of participating bones
 - ligaments dorsal and palmar radiocarpal, radial and ulnar collateral, and interosseous
 - b. Midcarpal between proximal and distal row of carpals
 - bones scaphoid, lunate, triquetrum (prox. unit); trapezium, trapezoid, capitate, hamate (dist. unit)
 - cartilages articular of participating bones
 - ligaments dorsal and palmar, collateral, and interosseous
 - c. Carpo-metacarpal between distal row of carpals and combined metacarpals 2-5
 - bones trapezium, trapezoid, capitate, hamate (prox. unit);
 metacarpals 2-5 (dist. unit)
 - cartilages articular of participating bones
 - ligaments dorsal and palmar, collateral, and interosseous
 - d. Thumb trapezial-metacarpal, multiaxial saddle joint
 - bones trapezium, first metacarpal
 - cartilages articular of participating bones

- ligaments dorsal and palmar, collateral, and interosseous
- e. Piso-triquetral separate joint, but found at wrist, closely associated with tendon of flexor carpi ulnaris muscle; the pisiform is a sesamoid bone in its tendon; a plane joint with triquetrum
- f. Weaknesses: scaphoid fractures, lunate dislocation is common
- 7. Intermetacarpal between metacarpals 2-5 (act as a functional unit) deep transverse metacarpal lig. binds together
- 8. Metacarpophalangeal (MP joints) between distal ends of metacarpals and bases of proximal phalanges
- 9. Interphalangeal (PIP and DIP joints) between adjacent phalanges of same digit

Note: Both MP and IP joints are held together by palmar ligaments, and the extensor expansion, the I-P joints have collateral ligaments as well

Tonsils

- Simplest lymphoid organs; form a ring of lymphatic tissue around the pharynx
- Location of the tonsils
- Palatine tonsils either side of the posterior end of the oral cavity
- Lingual tonsil lies at the base of the tongue
- Pharyngeal tonsil posterior wall of the nasopharynx
- Tubal tonsils surround the openings of the auditory tubes into the pharynx
- Lymphoid tissue of tonsils contains follicles with germinal centers
- Tonsil masses are not fully encapsulated
- Epithelial tissue overlying tonsil masses invaginates, forming blind-ended crypts
- Crypts trap and destroy bacteria and particulate matter

Lungs

The thoracic wall or chest wall is the boundary of the thoracic cavity.

The bony skeletal part of the thoracic wall is the rib cage, and the rest is made up of muscle, skin, and fasciae.

The chest wall has 10 layers, namely skin, superficial fascia, deep fascia, serratus anterior, layer for ribs (containing intercostal muscles), and endothoracic fascia from superficial to deep. However, the muscular layers vary according to the region of the chest wall. For example, they may include muscles like pectoralis major or latissimus dorsi.

The **lungs** are the primary organs of the respiratory system in humans and the lungs also provide airflow that makes vocal sounds including human speech possible.

Humans have two lungs, a right lung and a left lung.

They are situated within the thoracic cavity of the chest.

The right lung is bigger than the left, which shares space in the chest with the heart.

The lungs together weigh approximately 1.3 kilograms (2.9 lb), and the right is heavier.

The lungs are part of the lower respiratory tract that begins at the trachea and branches into the bronchi and bronchioles, and which receive air breathed in via the conducting zone.

The conducting zone ends at the terminal bronchioles. These divide into the respiratory bronchioles of the respiratory zone which divide into alveolar ducts that give rise to the microscopic alveoli, where gas exchange takes place.

Each lung is enclosed within a pleural sac which allows the inner and outer walls to slide over each other whilst breathing takes place, without much friction.

This sac also divides each lung into sections called lobes.

The right lung has three lobes and the left has two. The lobes are further divided into bronchopulmonary segments and lobules. The lungs have a unique blood supply, receiving deoxygenated blood from the heart in the pulmonary circulation for the purposes of receiving oxygen and releasing carbon dioxide, and a separate supply of oxygenated blood to the tissue of the lungs, in the bronchial circulation.

Anatomy

The lungs are located in the chest on either side of the heart in the rib cage. They are conical in shape with a narrow rounded apex at the top, and a broad concave base that rests on the convex surface of the diaphragm.

The apex of the lung extends into the root of the neck, reaching shortly above the level of the sternal end of the first rib. The lungs stretch from close to the backbone in the rib cage to the front of the chest and downwards from the lower part of the trachea to the diaphragm. The left lung shares space with the heart, and has an indentation in its border called the **cardiac notch of the left lung** to accommodate this. The front and outer sides of the lungs face the ribs, which make light indentations on their surfaces. The medial surfaces of the lungs face towards the centre of the chest, and lie against the heart, great vessels, and the carina where the trachea divides into the two main bronchi.

The **cardiac impression** is an indentation formed on the surfaces of the lungs where they rest against the heart.

Both lungs have a central recession called the hilum at the root of the lung, where the blood vessels and airways pass into the lungs.

There are also bronchopulmonary lymph nodes on the hilum.

The lungs are surrounded by the pulmonary pleurae. The pleurae are two serous membranes; the outer parietal pleura lines the inner wall of the rib cage and the inner visceral pleura directly lines the surface of the lungs. Between the pleurae is a potential space called the pleural cavity containing a thin layer of lubricating pleural fluid. Each lung is divided into lobes by the infoldings of the pleura as fissures. The fissures are double folds of pleura that section the lungs and help in their expansion.

The main or primary bronchi enter the lungs at the hilum and initially branch into secondary bronchi also known as lobar bronchi that supply air to each lobe of the lung. The lobar bronchi branch into tertiary bronchi also known as segmental bronchi and these supply air to the further divisions of the lobes known as bronchopulmonary segments. Each bronchopulmonary segment has its own (segmental) bronchus and arterial supply. Segments for the left and right lung are shown in the table. The segmental anatomy is useful clinically for localising disease

processes in the lungs. A segment is a discrete unit that can be surgically removed without seriously affecting surrounding tissue.

Right lung

The right lung has both more lobes and segments than the left. It is divided into three lobes, an upper, middle, and a lower, by two fissures, one oblique and one horizontal. The upper, horizontal fissure, separates the upper from the middle lobe. It begins in the lower oblique fissure near the posterior border of the lung, and, running horizontally forward, cuts the anterior border on a level with the sternal end of the fourth costal cartilage; on the mediastinal surface it may be traced backward to the hilum.

The lower, oblique fissure, separates the lower from the middle and upper lobes, and is closely aligned with the oblique fissure in the left lung.

The mediastinal surface of the right lung is indented by a number of nearby structures. The heart sits in an impression called the cardiac impression. Above the hilum of the lung is an arched groove for the azygos vein, and above this is a wide groove for the superior vena cava and right brachiocephalic vein; behind this, and close to the top of the lung is a groove for the brachiocephalic artery. There is a groove for the esophagus behind the hilum and the pulmonary ligament, and near the lower part of the esophageal groove is a deeper groove for the inferior vena cava before it enters the heart.

Left lung

The left lung is divided into two lobes, an upper and a lower, by the oblique fissure, which extends from the costal to the mediastinal surface of the lung both above and below the hilum. The left lung, unlike the right, does not have a middle lobe, though it does have a homologous feature, a projection of the upper lobe termed the "lingula".

Its name means "little tongue". The lingula on the left serves as an anatomic parallel to the right middle lobe, with both areas being predisposed to similar infections and anatomic complications.

There are two bronchopulmonary segments of the lingula: superior and inferior.

The mediastinal surface of the left lung has a large *cardiac impression* where the heart sits. This is deeper and larger than that on the right lung, at which level the heart projects to the left.

On the same surface, immediately above the hilum, is a well-marked curved groove for the aortic arch, and a groove below it for the descending aorta. The left subclavian artery, a branch off the aortic arch, sits in a groove from the arch to near the apex of the lung. A shallower groove in front of the artery and near the edge of the lung, lodges the left brachiocephalic vein. The esophagus may sit in a wider shallow impression at the base of the lung.

The left lung (left) and right lung (right). The lobes of the lungs can be seen, and the central root of the lung is also present.

High-resolution CT scans of a normal thorax, taken in the axial, coronal and sagittal planes, respectively.

Click here to scroll through the image stacks.

Microanatomy

A respiratory lobule, the functional unit of the lung

The lungs are part of the lower respiratory tract, and accommodate the bronchial airways when they branch from the trachea. The lungs include the bronchial airways that terminate in alveoli, the lung tissue in between, and veins, arteries, nerves and lymphatic vessels. The trachea and bronchi have plexuses of lymph capillaries in their mucosa and submucosa. The smaller bronchi have a single layer and they are absent in the alveoli. All of the lower respiratory tract including the trachea, bronchi, and bronchioles is lined with respiratory epithelium. This is a ciliated epithelium interspersed with goblet cellswhich produce mucus, and club cells with actions similar to macrophages. Incomplete rings of cartilage in the trachea and smaller plates of cartilage in the bronchi, keep these airways open. Bronchioles are too narrow to support cartilage and their walls are of smooth muscle, and this is largely absent in the narrower respiratory bronchioles which are mainly just of epithelium. The respiratory tract ends in lobules. Each lobule consists of a respiratory bronchiole, which branches into alveolar ducts and alveolar sacs, which in turn divide into alveoli.

The epithelial cells throughout the respiratory tract secrete epithelial lining fluid (ELF), the composition of which is tightly regulated and determines how well mucociliary clearanceword.

Alveoli consist of two types of alveolar cell and an alveolar macrophage. The two types of cell are known as type I and type II alveolar cells (also known as pneumocytes). Types I and II make up the walls and alveolar septa. Type I cells provide 95% of the surface area of each alveoli and are flat ("squamous"), and Type II cells generally cluster in the corners of the alveoli and have a cuboidal shape. Despite this, cells occur in a roughly equal ratio of 1:1 or 6:4.

Type I are squamous epithelial cells that make up the alveolar wall structure. They have extremely thin walls that enable an easy gas exchange. These type I cells also make up the alveolar septa which separate each alveolus. The septa consist of an epithelial lining and associated basement membranes. Type I cells are not able to divide, and consequently rely on differentiation from Type II cells.

Type II are larger and they line the alveoli and produce and secrete epithelial lining fluid, and lung surfactant. Type II cells are able to divide and differentiate to Type 1 cells.

The alveolar macrophages have an important immunological role. They remove substances which deposit in the alveoli including loose red blood cells that have been forced out from blood vesels.

The lung is surrounded by a serous membrane of visceral pleura, which has an underlying layer of loose connective tissueattached to the substance of the lung.

Respiratory tract

The lungs as main part of respiratory tract

The lower respiratory tract is part of the respiratory system, and consists of the trachea and the structures below this including the lungs. The trachea receives air from the pharynx and travels down to a place where it splits (the carina) into a right and left bronchus. These supply air to the right and left lungs, splitting progressively into the secondary and tertiary bronchi for the lobes of the lungs, and into smaller and smaller bronchioles until they become the respiratory bronchioles. These in turn supply air through alveolar ducts into the alveoli, where the exchange of gases take place. Oxygen breathed in, diffuses through the walls of the alveoli into

the enveloping capillaries and into the circulation, and carbon dioxide diffuses from the blood into the lungs to be breathed out.

Estimates of the total surface area of lungs vary from 50 to 75 square metres (540 to 810 sq ft); roughly the same area as one side of a tennis court.

The bronchi in the conducting zone are reinforced with hyaline cartilage in order to hold open the airways. The bronchioles have no cartilage and are surrounded instead by smooth muscle. Air is warmed to 37 °C (99 °F), humidified and cleansed by the conducting zone; particles from the air being removed by the cilia on the respiratory epitheliumlining the passageways.

Pulmonary stretch receptors in the smooth muscle of the airways initiate a reflex known as the Hering-Breuer reflex that prevents the lungs from over-inflation, during forceful inspiration.

Blood supply

3D rendering of a high resolution computed tomography of the thorax. The anterior thoracic wall, the airways and the pulmonary vessels anterior to the root of the lung have been digitally removed in order to visualize the different levels of the pulmonary circulation.

The lungs have a dual blood supply provided by a bronchial and a pulmonary circulation. The bronchial circulation supplies oxygenated blood to the airways of the lungs, through the bronchial arteries that leave the aorta. There are usually three arteries, two to the left lung and one to the right, and they branch alongside the bronchi and bronchioles. The pulmonary circulation carries deoxygenated blood from the heart to the lungs and returns the oxygenated blood to the heart to supply the rest of the body.

The blood volume of the lungs, is about 450 millilitres on average, about 9 per cent of the total blood volume of the entire circulatory system.

This quantity can easily fluctuate from between one-half and twice the normal volume.

Nerve supply

The lungs are supplied by nerves of the autonomic nervous system. Input from the parasympathetic nervous system occurs via the vagus nerve. When stimulated by acetylcholine, this causes constriction of the smooth muscle lining the bronchus and bronchioles, and increases the secretions from glands. The lungs also have a sympathetic tone from norepinephrine acting on the beta 2 receptors in the respiratory tract, which causes bronchodilation.

The action of breathing takes place because of nerve signals sent by the respiratory centres in the brainstem, along the phrenic nerve to the diaphragm.

Heart

The **heart** is a <u>muscular organ</u> in most animals, which pumps <u>blood</u> through the <u>blood vessels</u> of the <u>circulatory system</u>. Blood provides the body with <u>oxygen</u> and <u>nutrients</u>, as well as assists in the removal of <u>metabolic wastes</u>. In humans, the heart is located between the lungs, in the <u>middle compartment</u> of the <u>chest</u>.

In humans, other mammals, and birds, the heart is divided into four chambers: upper left and right <u>atria</u>; and lower left and right <u>ventricles</u>. Commonly the right atrium and ventricle are referred together as the *right heart* and their left counterparts as the *left heart*. Fish, in contrast, have two chambers, an atrium and a ventricle, while reptiles have three chambers.

In a healthy heart blood flows one way through the heart due to <u>heart valves</u>, which prevent <u>backflow</u>. The heart is enclosed in a protective sac, the <u>pericardium</u>, which also contains a small amount of <u>fluid</u>.

The wall of the heart is made up of three layers: <u>epicardium</u>, <u>myocardium</u>, and endocardium.

The heart pumps blood with a rhythm determined by a group of pacemaking cells in the <u>sinoatrial node</u>. These generate a current that causes contraction of the heart, traveling through the <u>atrioventricular node</u> and along the <u>conduction system of the heart</u>. The heart receives blood low in oxygen from the <u>systemic circulation</u>, which enters the right atrium from the <u>superior</u> and <u>inferior venae cavae</u> and passes to the right ventricle.

From here it is pumped into the <u>pulmonary circulation</u>, through the lungs where it receives oxygen and gives off carbon dioxide.

Oxygenated blood then returns to the left atrium, passes through the left ventricle and is pumped out through the <u>aorta</u> to the systemic circulation—where the oxygen is used and <u>metabolized</u> to <u>carbon dioxide</u>.

The heart beats at a resting <u>rate</u> close to 72 beats per minute.

<u>Exercise</u> temporarily increases the rate, but lowers <u>resting heart rate</u> in the long term, and is good for heart health.

<u>Cardiovascular diseases</u> (CVD) are the most common cause of death globally as of 2008, accounting for 30% of deaths.

Of these more than three quarters are a result of <u>coronary artery</u> disease and stroke.

Risk factors include: <u>smoking</u>, being <u>overweight</u>, little exercise, <u>high</u> <u>cholesterol</u>, <u>high blood pressure</u>, and poorly controlled <u>diabetes</u>, among others.

Cardiovascular diseases frequently do not have symptoms or may cause <u>chest</u> pain or <u>shortness of breath</u>.

Diagnosis of heart disease is often done by the taking of a <u>medical</u> <u>history</u>, <u>listening</u> to the <u>heart-sounds</u> with a <u>stethoscope</u>, <u>ECG</u>, and <u>ultrasound</u>.

Specialists who focus on diseases of the heart are called <u>cardiologists</u>, although many specialties of medicine may be involved in treatment.

human heart

The human heart is in the middle of the thorax, with its apex pointing to the left.

The human heart is situated in the <u>middle mediastinum</u>, at the level of <u>thoracic</u> <u>vertebrae T5-T8</u>.

A double-membraned sac called the <u>pericardium</u> surrounds the heartand attaches to the mediastinum.

The back surface of the heart lies near the <u>vertebral column</u>, and the front surface sits behind the sternum and rib cartilages.

The upper part of the heart is the attachment point for several large blood vessels – the <u>venae cavae</u>, <u>aorta</u> and <u>pulmonary trunk</u>.

The upper part of the heart is located at the level of the third costal cartilage.

The lower tip of the heart, the apex, lies to the left of the sternum (8 to 9 cm from the <u>midsternal line</u>) between the junction of the fourth and fifth ribs near their <u>articulation</u> with the costal cartilages.

The largest part of the heart is usually slightly offset to the left side of the chest (though occasionally it may be <u>offset to the right</u>) and is felt to be on the left because the <u>left heart</u> is stronger and larger, since it pumps to all body parts. Because the heart is between the <u>lungs</u>, the left lung is smaller than the right lung and has a cardiac notch in its border to accommodate the heart.

The heart is cone-shaped, with its base positioned upwards and tapering down to the apex. An adult heart has a mass of 250–350 grams (9–12 oz).

The heart is often described as the size of a fist: 12 cm (5 in) in length, 8 cm (3.5 in) wide, and 6 cm (2.5 in) in thickness, ma lthough this description is disputed, as the heart is likely to be slightly larger. Well-trained <u>athletes</u> can have much larger hearts due to the effects of exercise on the heart muscle, similar to the response of skeletal muscle.

The heart has four chambers, two upper <u>atria</u>, the receiving chambers, and two lower <u>ventricles</u>, the discharging chambers. The atria open into the ventricles via the atrioventricular valves, present in the <u>atrioventricular septum</u>. This distinction is visible also on the surface of the heart as the coronary sulcus.

There is an ear-shaped structure in the upper right atrium called the right atrial appendage, or auricle, and another in the upper left atrium, the left atrial appendage.

The right atrium and the right ventricle together are sometimes referred to as the *right heart*. Similarly, the left atrium and the left ventricle together are sometimes referred to as the *left heart*. The ventricles are separated from each other

by the <u>interventricular septum</u>, visible on the surface of the heart as the <u>anterior longitudinal sulcus</u> and the <u>posterior interventricular sulcus</u>.

The <u>cardiac skeleton</u> is made of <u>dense connective tissue</u> and this gives structure to the heart. It forms the <u>atrioventricular septum</u> which separates the atria from the ventricles, and the fibrous rings which serve as bases for the four heart valves.

The cardiac skeleton also provides an important boundary in the heart's electrical conduction system since collagen cannot conduct electricity.

The interatrial septum separates the atria and the interventricular septum separates the ventricles.

The interventricular septum is much thicker than the interatrial septum, since the ventricles need to generate greater pressure when they contract.

Cubital fossa

The **cubital fossa** or **elbow pit** is the triangular area on the anterior view of the <u>elbow</u> of a human or other hominid animal. It is also called the **antecubital fossa** because it lies <u>anteriorly</u> to the <u>elbow</u> (Latin *cubitus*) when in <u>standard anatomical position</u>.

Boundaries

- superior (proximal) boundary an imaginary horizontal line connecting the medial epicondyle of the humerus to the lateral epicondyle of the humerus
- medial (ulnar) boundary lateral border of <u>Pronator Teres</u> muscle originating from the medial epicondyle of the humerus.
- lateral (radial) boundary medial border of <u>Brachioradialis</u> muscle originating from the lateral supraepicondylar ridge of the humerus.
- apex- it is directed inferiorly, and is formed by the meeting point of the lateral and medial boundaries
- superficial boundary (roof)- skin, superficial fascia containing the median cubital vein, the lateral cutaneous nerve of the forearm and the medial cutaneous nerve of the forearm, deep fascia reinforced by the bicipital aponeurosis (a sheet o a sheet of tendon-like material that arises from the tendon of the biceps brachii)
- deep boundary (floor)- <u>brachialis</u> and <u>supinator</u> muscles

Contents

The cubital fossa contains four main vertical structures (from lateral to medial):

- The <u>radial nerve</u> is in the vicinity of the cubital fossa, located between <u>brachioradialis</u> and <u>brachialis</u> muscles. It is often <u>ldubious discuss</u> but not always considered part of the cubital fossa.
- The <u>biceps brachii</u> tendon
- The <u>brachial artery</u>. The artery usually bifurcates near the apex (inferior part) of the cubital fossa into the radial artery (superficial) and ulnar artery (deeper)
- The median nerve
- The <u>ulnar nerve</u> is also in the area, but is not in the cubital fossa; it occupies a groove on the posterior aspect of the <u>medial epicondyle of the humerus</u>.
- Several veins are also in the area (for example, the <u>median cubital</u> <u>vein</u>, <u>cephalic vein</u>, and <u>basilic vein</u>) but these are usually considered superficial to the cubital fossa, and not part of its contents.

Clinical aspects

During <u>blood pressure measurements</u>, the <u>stethoscope</u> is placed over the brachial artery in the cubital fossa. The artery runs medial to the biceps tendon. The brachial pulse may be palpated in the cubital fossa just medial to the tendon.

The area just superficial to the cubital fossa is often used for <u>venous</u> access (<u>phlebotomy</u>). A number of superficial veins can cross this region. It may also be used for the insertion of a peripherally inserted central catheter.

Historically, when (venous) blood-letting was practiced, the <u>bicipital</u> <u>aponeurosis</u> (the ceiling of the cubital fossa) was known as the "grace of God" tendon because it protected the more important contents of the fossa (i.e. the brachial artery and the median nerve). Statiscally, the antecubital fossa is the least tender region for peripheral intravenous access, although it provides a greater risk for venous thrombosis.

Brachial plexus

The **brachial plexus** is a <u>network of nerves</u> formed by the <u>ventral rami</u> of the lower four <u>cervical nerves</u> and first <u>thoracic nerve</u> (<u>C5</u>, <u>C6</u>, <u>C7</u>, <u>C8</u>, and <u>T1</u>). This plexus extends fro Structure

The brachial plexus is divided into five *roots*, three *trunks*, six *divisions* (three anterior and three posterior), three *cords*, and five *branches*. There are five "terminal" branches and numerous other "pre-terminal" or "collateral" branches, such as the subscapular nerve, the thoracodorsal nerve, and the long thoracic nerve, that leave the plexus at various points along its length. A common structure used to identify part of the brachial plexus in cadaver dissections is the M or W shape made by the <u>musculocutaneous nerve</u>, lateral cord, <u>median nerve</u>, medial cord, and ulnar nerve.

Roots

The five **roots** are the five <u>anterior rami</u> of the <u>spinal nerves</u>, after they have given off their segmental supply to the muscles of the <u>neck</u>. The brachial plexus emerges at five different levels; C5, C6, C7, C8, and T1. C5 and C6 merge to establish the upper trunk, C7 continuously forms the middle trunk, and C8 and T1 merge to establish the lower trunk. Prefixed or postfixed formations in some cases involve C4 or T2, respectively. The dorsal scapular nerve comes from the superior trunk and innervates the rhomboid muscles which retract the scapula. The subclavian nerve originates in both C5 and C6 and innervates the subclavius, a muscle that involves lifting the first ribs during respiration. The long thoracic nerve arises from C5, C6, and C7. This nerve innervates the serratus anterior, which draws the scapula laterally and is the prime mover in all forward-reaching and pushing actions.

Trunks

These roots merge to form the **trunks**:

- "superior" or "upper" (C5-C6)
- "middle" (C7)
- "inferior" or "lower" (C8, T1)

Division

Each trunk then splits in two, to form six **divisions**:

- anterior divisions of the upper, middle, and lower trunks
- posterior divisions of the upper, middle, and lower trunks
- when observing the body in the anatomical position, the anterior divisions are superficial to the posterior divisions

Cords

These six divisions regroup to become the three **cords** or large fiber bundles. The cords are named by their position with respect to the axillary artery.

- The <u>posterior cord</u> is formed from the three posterior divisions of the trunks (C5-C8, T1)
- The <u>lateral cord</u> is formed from the anterior divisions of the upper and middle trunks (C5-C7)
- The <u>medial cord</u> is simply a continuation of the anterior division of the lower trunk (C8, T1)

Branches

The **branches** are listed below. Most branch from the cords, but a few branch (indicated in italics) directly from earlier structures. The five on the left are considered "terminal branches". These terminal branches are the <u>musculocutaneous nerve</u>, the <u>axillary nerve</u>, the <u>radial nerve</u>, the <u>median nerve</u>, and the <u>ulnar nerve</u>. Due to both emerging from the lateral cord the <u>musculocutaneous nerve</u> and the <u>median nerve</u> are well connected. The <u>musculocutaneous nerve</u> has even been shown to send a branch to the <u>median nerve</u> further connecting them. There have been several variations reported in the branching pattern but these are very rare.

The brachial <u>plexus</u> is responsible for <u>cutaneous</u> and muscular innervation of the entire upper limb, with two exceptions: the <u>trapezius</u> muscle innervated by the <u>spinal accessory nerve (CN XI)</u> and an area of skin near the axilla innervated by the <u>intercostobrachial nerve</u>. The brachial plexus communicates through the sympathetic trunk via gray rami communicantes that join the plexus roots.

The terminal branches of the brachial plexus (musculocutaneous n., axillary n., radial n., median n., and ulnar n.) all have specific sensory, motor and proprioceptive functions. Lesions can lead to severe functional impairment

Brachial Plexus Injury

Brachial plexus injury affects cutaneous sensations and movements in the upper limb. They can be caused by stretching, diseases, and wounds to the lateral cervical region (posterior triangle) of the neck or the axilla. Depending on the location of the injury, the signs and symptoms can range from complete paralysis to anesthesia. Testing the patient's ability to perform movements and comparing it to their normal side is a method to assess the degree of paralysis. A common brachial plexus injury is from a hard landing where the shoulder widely separates from the neck (such as in the case of motorcycle accidents or falling from a tree). These stretches can cause ruptures to the superior portions of the brachial plexus or avulse the roots from the spinal cord. Upper brachial plexus injuries are frequent in newborns when excessive stretching of the neck occurs during delivery. Studies have shown a relationship between birth weight and brachial plexus injuries; however, the number of cesarean deliveries necessary to prevent a single injury is high at most birth weights. For the upper brachial plexus injuries, paralysis occurs in those muscles supplied by C5 and C6 like the deltoid, biceps, brachialis, and brachioradialis. A loss of sensation in the lateral aspect of the upper limb is also common with such injuries. An inferior brachial plexus injury is far less common, but can occur when a person grasps something to break a fall or a baby's upper limb is pulled excessively during delivery. In this case, the short muscles of the hand would be affected and cause the inability to form a full fist position.

To differentiate between pre ganglionic and post ganglionic injury, clinical examination requires that the physician keep the following points in mind. Pre ganglionic injuries cause loss of sensation above the level of the clavicle, pain in an otherwise insensate hand, ipsilateral Horner's syndrome, and loss of function of muscles supplied by branches arising directly from roots—i.e., long thoracic nerve palsy leading to winging of scapula and elevation of ipsilateral diaphragm due to phrenic nerve palsy.

Acute brachial plexus neuritis is a neurological m the spinal cord, through the cervicoaxillary canal in the neck, over the first rib, and into the armpit. It supplies afferent and efferent nerve fibers to the chest, shoulder, arm and hand.

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E-mail: murali.aks@gmail.com









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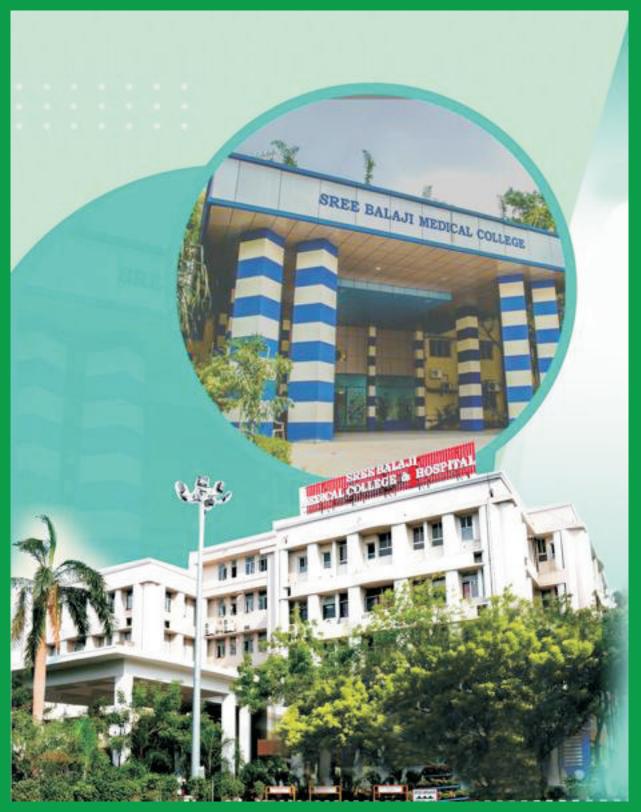
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Ph. 044 - 45080083. Cell: 9282134542,

E-mail: murali.aks@gmail.com



Sree Balaji Medical College & Hospital

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Aksharaa Muthra Aalayam Pvt., Ltd.

No.441/303, Anna Salai, Teynampet, Chennai-18. Tamilnadu, India Ph. 044 - 24364303. Cell: 9282134542,

E-mail: murali.aks@gmail.com, Website: aksharaa.co.in





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Dr. (Brig.) SHANMUGANANDAN KRISHNAN
Dr. P SANJEEVI KRISHNAN
DEPT. OF GENERAL MEDICINE
SREE BALAJI MEDICAL COLLEGE
AND HOSPITAL, CHENNAI

Editorial Office

Prof. Dr. (Brig.) Shanmuganandan Krishnan

Professor of Department of General Medicine

Consultant Rheumatologist

Sree Balaji Medical College and Hospital

7, CLC Works Road, Chromepet, Chennai - 600044, Tamil Nadu, India.

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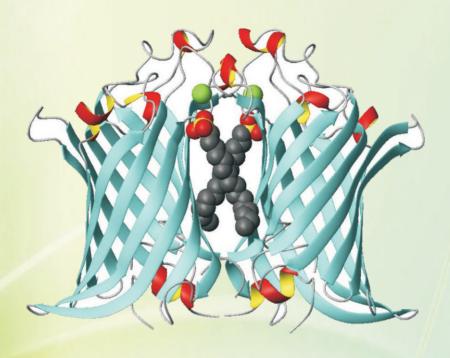
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EMERGENCIES IN RENAL DISORDERS



DR SHANMUGANANDAN KRISHNAN
DR NALABOTHU SREELATHA
DEPARTMENT OF GENERAL MEDICINE,
SREE BALAJI MEDICAL COLLEGE AND HOSPITAL, CHENNAI.

ENZYMOLOGY - A QUICK REVIEW



Dr. V.S. Kalaiselvi, MD

Co Authors

Dr. B. Shanthi, MD

Dr. K. Sumathi

Dr. A. Jamuna Rani

Dr. S. Shenbaga Lalitha



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Essentials of Nephrology

Second Edition

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Assistant Editor

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Associate Professor & Chief

Paediatric Nephrology Division

Department of Paediatrics

SAT Hospital, Govt. Medical College,

Thiruvananthapuram



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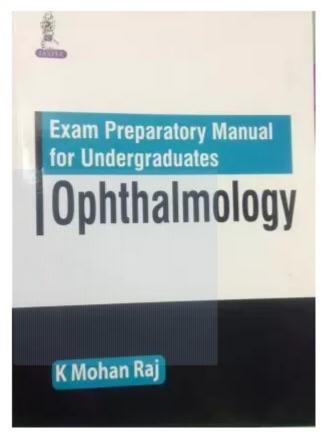
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E-mail: murali.aks@gmail.com



GENERAL PHYSIOLOGY QUICK REVIEW



Dr. S. Mahila







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Aksharaa Muthra Aalayam, Anna Salai, Teynampet, Chennai - 600 018, India

Ph. 044 - 24364303. Cell: 9282134542,

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About the Author

The author Dr. S. Mahila is presently working as assistant professor of physiology, Department of Physiology at Sree Balaji Medical College & Hospital, Chennai.

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- Comprehensive, latest, and in-depth coverage of all the issues related to genital dermatoses in an easy understandable format
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- Expanded coverage of topics like sexually transmitted infection affecting the genitals, genital infections other than sexually transmitted diseases, bullous dermatoses, Inflammatory conditions, premalignant dermatoses, malignant diseases of genitalia, and genital pain syndromes
- · Written by experts in the field of dermatology with an enormous knowledge- and skill-base
- The book is of great interest for derinatologists, physicians, family physicians, and post graduate students in these specialties.

Jayakar Thomas MD DD MNAMS PhD FRCP (Edin, Glasg, Lond, Irel) FRCPCH FAAD FIAD FIAP Professor and Head Department of Dermatology ee Balaji Medical College and Hospital, Bharath University Chennai, Tamil Nadu, India



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Chief Editor

Dr. B.SHANTHI

Professor & Hod Department Of Biochemistry Sree Balaji Medical College & Hospital Chromepet, Chennai, India

DEPARTMENT OF BIOCHEMISTRY
SREE BALAJI MEDICAL COLLEGE AND HOSPITAL, CHENNAI, INDIA



6, Mahaveer Complex, Munusamy Salai, K.K.Nagar West, Chennai-600 078. Ph: +91 - 44-6515 7525, Mobile: +91 87545 07070



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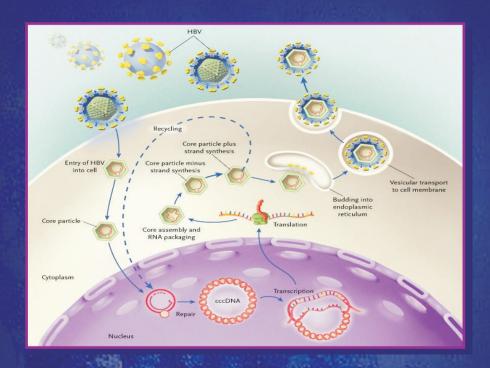
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SREE BALAJI MEDICAL COLLEGE AND HOSPITAL

HANDBOOK ON HEPATITIS B VIRAL INFECTIONS



Author

Dr. B. Kiran Madhusudhan



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E-mail: murali.aks@gmail.com

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Hand Book on Interpretation of Urine Analysis for General Practitioner







Authors
Dr. S. Mary Lilly
Dr. M. Preethi



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Dr. S. Mary Lilly

Dr.S.Mary Lilly is currently working as professor and Head, Dept. of pathology at Sree Balaji Medical College and Hospital. She has 30 years of working experience as diagnostic pathologist as well as undergraduate and postgraduate teacher. Contributed as Oncopathologist at Cancer Wing of Government Royapettah Hospital for 8 years which enabled to enrich her diagnostic skills. She as published 30 papers in reputed journals.

Among them one of her paper on Inflammatory Myofibroblastic Tumour of Thyroid with prominent Spindle Cell Pattern a case report was presented at 10th World Cancer Congress at Spain 2017. Her immense knowledge and interest in field of diagnostic pathology made her to write the book.



Dr. M. Preethi

Dr.M.Preethi is currently working as Assistant Professor, department of Pathology at Sree Balaji Medical College and Hospital. She has 2 years of working experience as diagnostic pathologist and undergraduate and postgraduate teacher in pathology. She has 3 patents and 10 paper publication in reputed journals, her interest and knowledge in the field of clinical pathology made her to write this book.

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E-mail: murali.aks@gmail.com





Dr. G. Durga Devi & Dr. R. Rahe



Sree Balaji Medical College & Hospital
Bharath Institute of Higher Education & Research (BIHER)
Chromepet, Chennai - 600 044, Tamilnadu, India



Hand Book on Radiological Anatomy

Dr. G. Durga Devi & Dr. R. Rahe





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Foreword

The knowledge of gross anatomy and its scope in image interpretation is invaluable for understanding Radiological Anatomy. Recent advances in the field of Radio diagnosis are overwhelming. The students get a glimpse of modern imaging techniques in addition to conventional radiography, so that they are aware of the importance of Cross-sectional Anatomy in Radio diagnosis well before they enter into clinical side. It is a simple handbook providing an overview of the subject for quick recall, which fulfils the needs of the present generation of student

Preface

Medicine is more an art than science in the hands of a skilled physician. But the fact is that the art is fast vanishing with the advent of evolving technology, which has put more diagnostic tools into the physicians' bags. Bedside medicine needs revival so that the patient does not have to go through unnecessary tests and also waste time and money. The need of the hour is to bring back these clinical skills in our students. Gross Anatomy is the most basic and relatively constant of all basic medical sciences. The basic human structure remains the same, though many normal variations have been studied. Hence, thorough knowledge of anatomy is very important to build up our clinical skills and knowledge further. Thus this handbook will be essessenially helpful for 1st year MBBS students. A sincere effort has been made towards promoting the art of medicine. Suggestions from our readers regarding any improvements are always welcome.

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We sincerely acknowledge, S. Jagathrakshagan Founder Chancellor of Sree Balaji Medical |College and Hospital Chrompet Chennai, for all our professional achievements and thank him for giving us this platform to think of such a textbook. We are extremely indebted to Dr J.Sri Nisha Chairman, SBMCH, and DEAN, SBMCH Dr.P.Sai Kumar for their constant guidance and support to do this work. We are extremely thankful to Dr.WMS Johnson Professor Head of Anatomy and Vice principal of SBMCH for his constant support and timely assistance which paved way for the successful completion of this Handbook. We deeply extend our gratitude to our fellow colleagues for the their support and ideas during the course of this work

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Principles of Radiology

Introduction

It is a branch of medical science that deals with the use of radiant energy in the diagnosis and treatment of disease.

The radiant energy, called X-ray, was discovered by Wilhelm Conrad Roentgen in 1895.

X-rays are a form of energy waves compared to visible light rays, but they are shorter in length and travel in straight line.







These rays can penetrate through the tissues of the body and also are partially absorbed by the tissues. Some X-rays which pass through the body without being absorbed. All the above can be recorded on X-ray fim in varying densities. The X-rays are produced in a glass tube which has vacuum and contains a wire filament at one end and a target of tungsten wire at the other end. The filament releases electrons when heated by an electric current to become luminous (white heat). These electrons are made to accelerate toward the target by applying a very high voltage between the filament and the target. The high velocity electrons lose their kinetic energy after striking the target and release X-rays as a form of energy. The X-ray tube made of glass, has to be covered by lead tube except a small hole for the passage of X-rays.

Radiology: Upper Limb

Usually the limb radiographs are taken as plane radiographs to either assess the age by looking at the un ossified parts, ossification centers and non fused epiphyses or to note the fractures of the bones. The contrast radiographs of the limbs are usually the angiograms. The age assessment is done by taking the radiographs at the joints which involve more than one bone.

Shoulder Region (Fig. 1.)

- This is usually a plane radiograph to study the shoulder joint. In this
 radiograph the head of humerus, glenoid cavity and parts of processes of
 scapula are visualized.
- The view selected is anteroposterior or posteroanterior.
- The acromion process, coracoid process and part of the lateral border of scapula are visible.
- The ends of the bones and their level of ossification help in assessing age.



Fig. 1 Plane radiogram of the shoulder region antero posterior view. Fully ossified scapula, upper end of humerus, lateral part of clavicle, parts of ribs, acromioclavicular joint and glen humeral joint are visualized.

Elbow

The plain radiographs with antero posterior and lateral views are taken to study the lower end of humerus and upper ends of radius and ulna. Radiograph shows the lower end of humerus and upper ends of radius and ulna the center for the medial epicondyle appears at the age of 6th year and fuses separately with the shaft at 20th year.

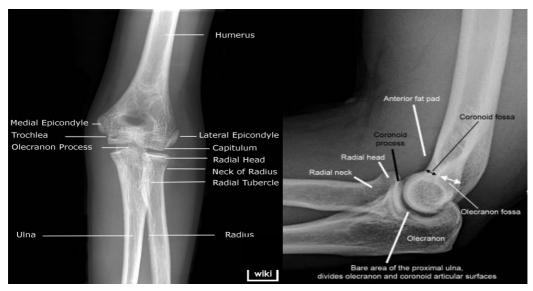


Fig. 2.1. Plane radiogram of the elbow region posteroanterior view.

The elbow joint and superiorradioulnar joint are visualized.

Fig 2.1b Plane radiogram of the elbow region lateral view

Wrist And Hand (Fig.3.)

For the plane radiographs of the wrist, anteroposterior view, lateral view and semi-prone view are usually taken. This is used to study the lower ends of radius, ulna, carpal bones, metacarpals and phalanges.



Fig.3. Plane radiograph of a hand showing the shadows of lower ends of radius and ulna, carpals, metacarpals, and phalanges.

Radiology of Lower Limb

Hip Region (Fig,4)

- Normally viewed in antero posterior view.
- The position of the lower limb should be in such a way that there is separation of lower limb at heels and all the toes are directed antero medially.
- This position of lower limb allows the femur to rotate slightly medially and femoral
 neck lies parallel to the radiographic film.
- In this position the shadows of upper end of the femur and acetabular region are visualized better. The borders of acetabular cavity and head of femur appear as curved lines indicating the radiodense cortical tissue (compact part) of the bone.
- The shadow of the thick corticaltissue of the medial edge of the acetabulum can be traced above which becomes continuous with pelvic brim shadow and below it ends just above and lateral to the Obturator foramen margin.

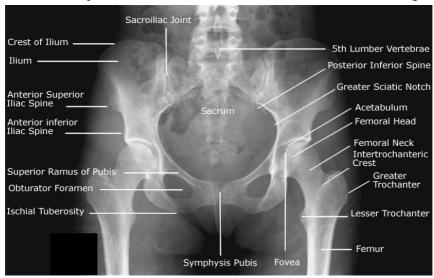


Fig.4. Plane radiogram of pelvis, lower lumbar region and hip joint, antero posterior view \
In normal antero posterior view, two curved lines can be appreciated.

1. Shenton's line (Fig4.1.): Line at the upper margin of obturator foramen that becomes

continuous with the shadow of inferior surface of the neck of femur and the medial border of shaft of the femur till lesser trochanter shadow. This lineis not altered on change of the posture but discontinuity in the curved lines is seen in fractures of neck of femur or in dislocations of hip joint. The neck shaft angle can be visualized when the foot is slightly turned medially. Its measurement varies between 120° and 135°. It is less than 120 degrees in coxa vara and more than 135 degrees in coxa valga depending upon the age, pelvic width and stature. The shadows of trabeculae caused due to pressure present a peculiar patterns and help in assessing the amount of calcifiation of the bone.

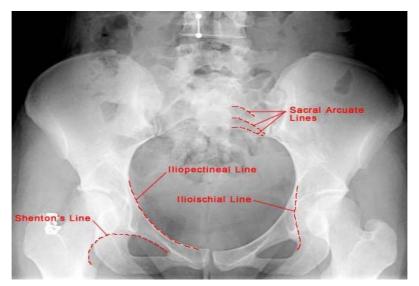


Fig.4.1Plane radiograph of the pelvis and hip region, posteroanterior view, showing the Shenton's line.

Knee Joint

Normally antero posterior and lateral views are taken.

Antero posterior View (Fig.5.)

The borders of the bones taking part in the joint formation present a smooth, white line (radio opaque line) which is due to the presence of thin cortical bone tissue.

- The joint space appears as radiolucent area—about 3 to 5 mm vertically, superimposed patellar shadow is seen on the shadow of lower end of femur the medial lateral condylar shadows of femur are seen on either side of the lower part of patellar shadow.
- The lateral border of the lateral condyle of the femur presents a notch which represents the groove for the popliteus muscle.

- The intercondylar area of tibia presents shadows of intercondylar spines between medial and lateral semilunar areas which are covered by menisci (semilunar firocartilages).
- Sometimes a small shadow of sesamoid bone is seen close to the origin of lateral head of gastrocnemius (close to lateral condyle of femur) and is called **FABELLA**. It usually measures about 5 mm in diameter.
- Shadow of upper end of fibula is seen close to the lower part of the lateral condyle of tibia.

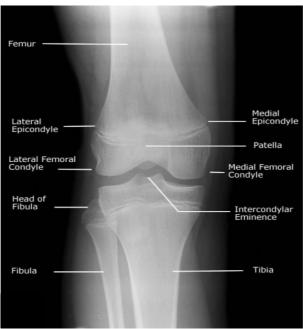


Fig.5.Plane radiograph of the adult knee anteroposterior view. Shadows of lower end of femur and upper ends of tibia and fiula. Rounded radiopaque shadow at the lower end of the femur superimposing the lower end of the femur is that of patella.

Lateral view: Fig.5.1

- The patellar shadow can be seen anterior to the lower end of femur.
 In complete flexion of knee joint the patellar shadow comes to lie distal to the condylar shadows of femur.
- The shadows of medial and lateral condyles of femur are superimposed and the same with the condyles of tibia.
- The shadow of upper end of fibula and condylar shadows of tibia are also superimposed.
 - The shadows of the shafts of tibia and fibula show shades of grey and white.

- The white shadows are of outer border of cortical tissue.
- The spongy part appears greyish and the marrow cavity appears radiolucent. In lateral view of leg, the shadow of fibular shaft appears posterior to the shadow of tibial shaft.



Fig.5.1: Plane radiograph of the knee in the lateral view. Shows shadows of lower end of femur and upper ends of tibia and fiula.

Ankle Joint

- In anteroposterior view, the shadows of lower ends of tibia, fiula, talus, calcaneum, navicular, cuboid and cuneiforms are seen.
- The shadow of ankle joint with lower ends of tibia, fibula (medial and lateral malleoli) and upper end of talus are seen. Joint cavity appears radiolucent.
- The lateral malleolar shadow extends slightly beyond the medial malleolar shadow.
 - In lateral view, the lower ends of tibia and fibula are superimposed.
- The shadow of subtler joint (talocalcaneonavicular joint) can be seen clearly. The shadows of cuboid overlapping the shadows of cuneiform are seen.

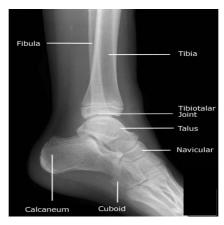


Fig.6 Plane radiograph of adult foot in lateral view showing the lateral aspect of the ankle joint, tarsals, metatarsals and phalanges.

Foot

- In this the shadows of tarsal bones, metatarsals and phalanges are seen.
- The fith metatarsal bone presents a projection called styloid process. Calcaneocuboid joint, talonavicular joint can be well appreciated.
- Shadows of sesamoid bones are seen near the plantar surface of distal end of fist metatarsal bone.



Fig 7. Plane radiograph of adult right foot viewed from above.

Radiology of Thorax

- Radiographic examination of thorax is done to see the thoracic cage, the lungs, bronchial tree, hilum and roots of lungs, heart, great vessels, and the mammary glands.
- The radiologic study of thorax includes, plane radiograph and contrast radiograph.
- The plane radiograph of chest (thorax) is taken with a normal distance of 2 meters
- between the X-ray tube and the film which prevents scattering of the rays and distortion of the shadow.
 - o In plane radiography of chest there are various views in which the radiographs can be taken.
 - They are—anteroposterior (AP) view, posteroanterior (PA) view, right lateral view, left lateral view, right oblique view, and left oblique view.

In posteroanterior view (PA view or anterior view—the person is usually standing or can be sitting with straight back. Th fim is kept on the anterior aspect of the chest and the X-ray tube is behind. The distance between X-ray tube and the fim is 2 meters (6 feet) to avoid distortion of the shadow. The center of the X-ray beam is directed to the tip of the spine of the 4th thoracic vertebra. The exposure time is calculated to be 1/10th of a second to prevent blurring of the shadow due to the movements of heart and lungs. Th position of the person whose radiogram is to be taken is as follows:

- 1. Overhead abduction at shoulder with both hands on the back of the head or both dorsums of hands kept on the upper gluteal regions.
- 2. In both cases the elbows should be directed anteriorly. This prevents the overlapping of the shadows of scapulae on the lung fields.
- 3. The shoulders should be symmetrically placed.
- 4. At the time of exposure to the X-rays the person is instructed to take a deep breath and hold the breath for few seconds to cause immobility of lungs during respiration.

In such radiographs the lung fields, cardiac shadow, shadows of trachea and great vessels, skeletal shadows and soft tissue shadows are seen which include mediastinum, diaphragm, sub-diaphragmatic area, mammary glands, etc.

Lung Shadow

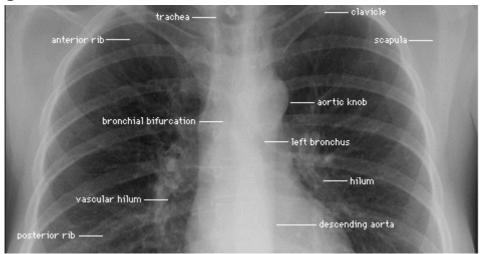


Fig. 8: Plain radiograph of thorax, posteroanterior view

- The lung fields contain shadows of pulmonary vessels, bronchial vessels, bronchopulmonary lymph nodes which are arranged from the hila of the lungs to the peripheral parts of the lung fields.
- The costodiaphragmatic and cardiophenic angles can be seen in this view.
- The costodiaphragmatic angles contain costodiaphragmatic recesses of the pleurae.
- The right cardiophrenic angle is acute and contains terminal part of inferior venacaval shadow. On the left side it is the apex of the heart and is again acute normally.
- The lung fields are crossed obliquely by shadows of ribs.

Cardiac Shadow

- Cardiac shadow is caused by pericardium, heart, and adjacent great vessels of heart.
- All ofthese are together called mediastinal shadow. In the cardiac shadow the right, left and the inferior borders of heart can be appreciated.
- The pericardial shadow cannot be appreciated due to its close proximity to the heart and the shadow merges with that of heart. The right border is

- made up of right atrium, which becomes continuous with the right border of superior vena cava and right brachiocephalic vein present in the mediastinal shadow.
- The left border of the cardiac shadow consists of left ventricle, left atrium, which becomes continuous with pulmonary artery or its left branch, left subclavian artery and arch of a rta of the left border of mediastinal shadow.
- The shadow of arch of aorta is convex to left and is called **aortic knuckle**.

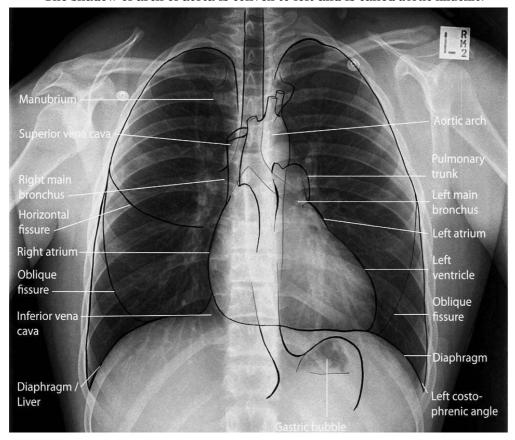


Fig. 8.1: Plain radiograph of thorax. The cardiac area, aortic knuckle (shadow of arch of aorta) and shadows of domes of diaphragm have been marked.

Cardio Thoracic Ratio

In the PA view the size of the heart can be calculated and is as follows:

- 1. Mid-sagittal line is drawn.
- 2. 2. A horizontal line is drawn from the most convex border on the right side to the midline.

- 3. 3. Another horizontal line is drawn from the most convex part of the left border of cardiac shadow to the midline.
- 4. The distances of both the horizontal lines are added.
- 5. The total maximum width of the thorax is taken and compared with the width of the heart. If it is more than 50% of the transthoracic diameter, then cardiomegaly is diagnosed.

This is radiological diagnosis of Cardiomegaly (Fig. 8.3).

Normal cardiac shadow = < 50%

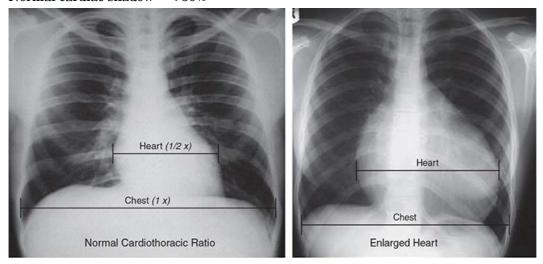


Fig.8.2,8.3: Plain radiograph of thorax in PA view. Estimation of the cardiac size in he radiogram of thethorax (Refer text).

Lateral view (Figs.12.7):

- In this view the person is in standing or sitting position. Arms are raised above the head.
- The X-ray tube emits rays which are directed to the 6th thoracic vertebra at the level of mid-axillary line.
- In **right lateral view**, the tube is on the left side and the fim is on the right side.
- In **left lateral view** the tube is on the right side and the fim is on the left side. In these views the shadows to be looked for—lung filds, heart and great vessels, trachea, skeletal shadows, and the diaphragm.

 The lung fields appear as radiolucent shadows which are overlapped by the shadows of ribs, blood vessels, and hilar shadows. In well-exposed radiograms the fisures of the lungs can be appreciated specially the oblique fisure.

In right lateral view the horizontal fissure is visualised

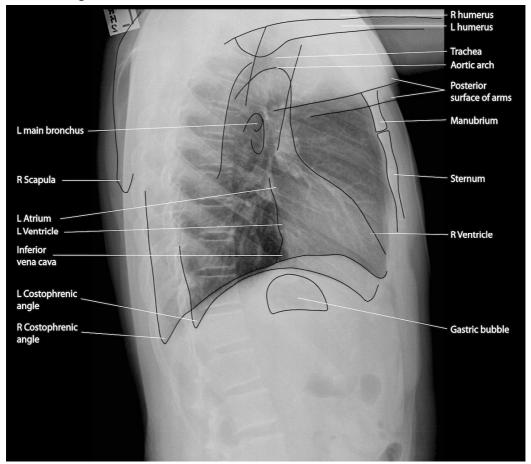


Fig. 12.7: Plain radiograph of the thorax, lateral view.

Contrast Radiographs of Thoracic Region

To visualize bronchial tree: Procedure called Bronchography is done.

To visualize cardiac parts: Transesophageal echo—the anterior wall of esophagus lies in close proximity with left atrium (base of heart).

- 1. This relation helps to carryout transesophageal echo through oesophagus.
- 2. To visualize coronary arteries: Coronary angiogram.

- 3. To see the larger vessels: Angiograms—consisting of arteriogram, venogram, and lymphangiogram.
- 4. To visualize the esophagus: Barium swallow.

Bronchography

To visualize lower respiratory tract (which includes larynx, trachea, and bronchi) a procedure called Bronchography is done. After the invention of CT scans, MRI and bronchoscopy the Bronchography has become obsolete and is done only when it is recommended.

It is a procedure where in a contrast medium is introduced into the bronchial tree and radiography is done.

The radiograph is taken as soon as the trachea and bronchi are filed with contrast medium. This procedure is done to see the interior of the respiratory tract, growths inside if any and to locate foreign bodies if trapped and the obstruction by the growth or abnormal dilatation of bronchial tree and lungs. It is also done in case of tracheoesophageal fistula. The patient is explained about the procedure. The effiency of the respiration is assessed.

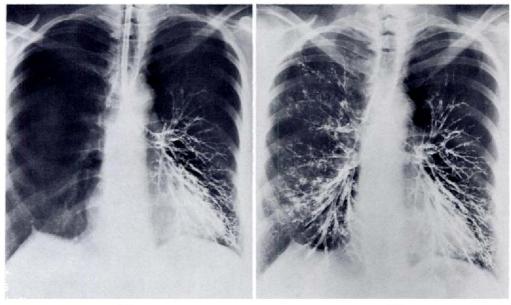
Before the procedure—patient is to be explained about the procedure and written consent is to be taken by the patient.

- If any medications are taken by the patient specifially the blood thinners like aspirin or any anticoagulants, allergies to medicines containing iodine, latex, local anesthetics, or any other medicines.
- In case of young females menstrual history is to be taken to rule out pregnancy.

Procedure

- A course of antibiotics are administered to the patient for few days before the procedure.
- Sensitivity test for the contrast medium which is going to be used is carried out.
- Nil orally from the night before the procedure.
- Sedative is administered a night before the procedure to avoid anxiety. Intramuscular injection of Atropine is administered to prevent secretion.

- This prevents secretion of glands in the bronchial tree which may cause dilution of the dye and also may induce cough.
- The throat (which includes palate, fauces, posterior part of tongue, posterior pharyngeal wall, all the pillars in the throat, epiglottis, and trachea till carina) is sprayed with 2% local anesthetic 3 to 4 times with an interval of 5–7 minutes.
- This prevents the pharyngeal (gag) reflux and palatal reflux. The patient also complains about inability to swallow.
- A catheter or a bronchoscope is introduced into the throat and passed till the bifurcation of trachea and the radio opaque dye is instilled into the bronchial tree as the catheter is being advanced. There will be discomfort but there will not be any blockage to the airways.
- Thin radiographs are taken in various positions. The catheter is removed once all the required radiographs are taken.
- During the procedure, the respiratory rate, blood pressure and the pulse are to be monitored throughout.
- After the procedure the patient is advised not to eat or drink anything till the gag reflux returns to normal.
- Forceful coughing and posture will help in early drainage of the contrast dye.



1A 1B

Radiology of Abdomen and Pelvis

In the plain radiograph of abdomen (FIG 14) the shadows of lower ribs, lower thoracic vertebrae, lumbar vertebrae, sacrum and coccyx, hip bones, pubic symphysis are seen.

The softtissue shadows of kidneys, liver, spleen are also visualized as opaque shadows. Gas shadows in the fundus of stomach and in the large intestine appear radiolucent.

Plain anteroposterior and lateral views are taken to study the bones, in particular, the lower part of vertebral column from lower thoracic to coccygeal part.

The shadows of domes of diaphragm appear as partition between thorax and abdomen. The gas in the fundus of stomach is seen just below the left dome of diaphragm (Fig. 14).

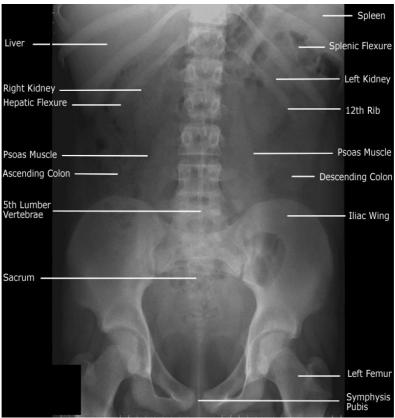


Fig. 14: Plain radiograph of the abdomen in anteroposterior view.

The outlines of the viscera are marked

Contrast Radiograph of Abdomen and Pelvis

Barium meal

This procedure is done to study the stomach and the duodenum. Procedure is as follows:

- About 250–300 mL of 50% barium sulfate emulsion is given to the patient to swallow after 6–8 hours of fasting to ensure that the stomach is empty at the time of the procedure.
- As the emulsion reaches the stomach it comes in contact with the mucous membrane and the rugae become visible as radio opaque shadow.
- The ulcers in the gastric mucosa are seen as craters in the shadow.



Fig. 15: Contrast radiograph of stomach—barium meal, anteroposterior view.

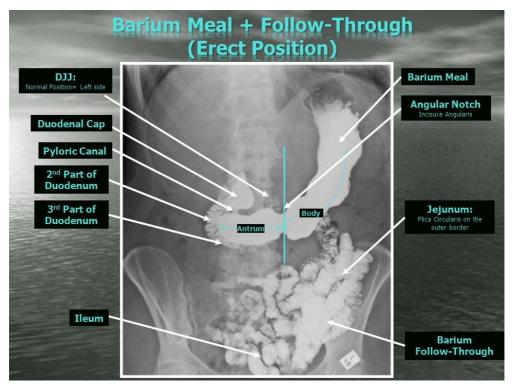


Fig. 16 Contrast radiograph of stomach—barium follow through l, anteroposterior view.

- The shape of the stomach can be appreciated by the shadow and are classified into "J" shaped, steer horn stomach, etc.
 - The shadow of stomach depends on shape of the stomach, number of rugae and the size of the stomach. In case of normal tone of the musculature of stomach the right and the left walls of the shadow of stomach appear parallel to each other. If the tone of the musculature of stomach is reduced there is sagging of the greater curvature shadow.
 - o The peristaltic waves appear as soon as the emulsion reaches the stomach and they appear as indentations which are seen within a minute or less. Within few minutes the emulsion reaches the duodenum.
 - As the emulsion reaches the first part of duodenum it produces a cap like shadow called duodenal cap. The size of the duodenal cap appears smaller than the size of the first part of the duodenum because of its obliquity. If the atmospheric temperature is reduced or person dislikes the taste of emulsion

- or fears the procedure for the examination will delay the emptying of the stomach.
- After few hours if a normal meal is given to the subject, the gastrocolic reflex is initiated and the barium meal reaches the beginning of colon. Otherwise it takes as early as
- 2–3 hours for stomach emptying or as late as 5–6 hours for emptying of the stomach.
- The duodenal cap appears as a triangular shadow with its base directed to the pyloric part of the stomach.
 - o The duodenum empties the emulsion fast and the 2nd, 3rd, and 4th parts of duodenum get filled with the contrast medium gradually. The shadows of mucosal folds can be appreciated.



Fig. 17. Excretory urogram (descending pyelogram). Done to visualize the shadows of kidney, ureter, and urinary bladder.

Pyelography

It is a procedure in which the contrast material is introduced into the urinary system to study the urinary organs—kidneys (K), ureters (U), and urinary bladder (B). It consists of two methods:

- 1. Intravenous pyelography or descending pyelography or excretory urography (Fig.17).
- 2. Retrograde/ascending pyelography (Fig. 17.2).
- 1. Intravenous pyelography: Also called descending pyelography or excretory urography.

In this procedure the dye is injected into any superficial vein of the limbs and the dye is excreted via the urinary tract. Thus the excreted dye appears in the urinary system and causes the shadow.

Procedure

- A radio opaque dye (urograffin) is injected into the median cubital vein.
- The radio opaque substance enters the blood stream and reaches the heart, pulmonary circulation, back to heart and then to kidney for excretion.
- Radiographs are taken at intervals to assess the level of dye with urine and its filling into the hollow part of the urinary system.
- Immediately after the contrast medium is administered the dye appears in the cortex of the kidneys as "renal blush".
- The radiographs are taken at 3 min, 5–6 min, at 9 min and 15 min after the dye has been introduced into the superficial veins of the arm.
- Between 3 and 5 min the dye appears in the calyces. Around 9–14 min the dye starts entering into the ureters and into the urinary bladder.
- After the emptying of urinary bladder another radiograph is taken to visualize the urinary bladder for residual urine.
- The contour of kidneys are appreciated, shadows of calyces—both major and minor—are seen as cup like shadows. Routine excretory urogram (Fig. 17):

It is a procedure done when there is an unexplained microscopic hematuria or in case of tumor of kidney. This should be done after the plain radiograph of abdomen is done to visualize the renal area. Sometimes a compression is applied to the lower abdomen which increases the distension in the upper renal part. But compression is contra indicated in case of obstruction.

Pyelography is done in cases of emergency like the renal colic or macroscopic hematuria or renal calculi without any obstruction. Patients have to be admitted in case of renal calculi or in case of obstruction for further treatment. In this emergency procedure a plain radiograph of abdomen is taken. About 50 mL of the contrast medium is injected intravenously. A delayed abdominal radiograph is taken after about 15 min after the dye has been injected. Then radiographs are taken 30 min, 1 hr, 2 hrs, 4 hrs after micturition. This will help the radiologist to see the level of obstruction.

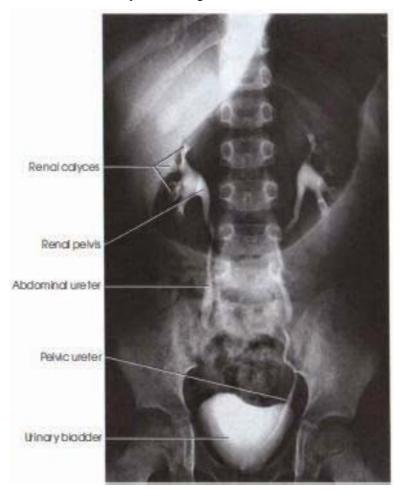


Fig. 17.1: Excretory urogram (descending pyelogram). Done to visualize the shadows of kidney, ureter, and urinary bladder



Fig. 17.2: Ascending pyelography. Note the catheter in the urinary bladder directed toward the ureter.

The procedure: A small tube is introduced via the urethra into the urinary bladder.

Then dye is introduced into the ureters by passing the tube into the ureteric opening. Dynamic radiography or fluoroscopy is done to visualize the kidney, ureter, and urinary bladder (KUB). This procedure has to be done safely under general anesthesia of local anesthesia.

- Pyelography detects pelvi ureteric and vesicoureteric constrictions.
- It is also diagnostic in hydronephrosis where there is dilatation of the conducting pathway of the kidney (calyces to ureters). Here the calyces appear dumbbell shaped (Fig. 13.9).
- Polycystic kidney can also detected.
- Filling defects in the urinary bladder may suggest ulcers/polyps/carcinomas.

Radiology of Head and Neck

The plain radiographs of head and neck show the radiopaque shadows of skull bones, mandible, hyoid and ossified laryngeal cartilages if any and cervical vertebrae. Radiolucent shadows of air filled cavities and tubes are seen, e.g. paranasal air sinuses, mastoid air cells, oral cavity, pharynx, laryngeal cavity, and trachea. The greyish shadows indicate soft tissues which include muscles, tendons, ligaments, vessels, and nerves. The soft tissue shadows cannot be differentiated in plain radiographs. The skulls is made up of many small, flat, and irregular bones which articulate with one another at various types of fibrous joints especially at the sutures. In young skulls the sutures can be appreciated as zigzag dark lines.

Views The radiographs of head and neck are taken in anteroposterior, posteroanterior, lateral (right lateral or left lateral), superior (submentovertical), anterior oblique, posterior oblique, and lateral oblique views.

Posteroanterior View (FIG. 18) In this view, the forehead of the individual to be radiographed should face the film with orbitomeatal plane lying perpendicular to the film. The coronal suture, sagittal suture and part of lambdoid suture can be seen in the calvaria shadow. The inner and outer tables and the diploe are also visualized. Depressions of 6 to 8 mm diameter can be seen in a few radiographs which are caused by arachnoid granulations. The other features which can be seen are as follows: a. Shadows of orbits. b. The frontal, ethmoid, sphenoid, and maxillary air sinuses. c. The opaque shadows of greater and lesser wings of sphenoid. d. Inferolaterally, the shadows of mastoid process and air cells. e. Dense triangular radiopaque shadow of petrous part of temporal bone. f. The mandibular condyles make a shadow close to the petrous part of temporal bone. g. The upper and lower teeth produce dense radiopaque shadow. h. The shadows of nasal septum, conchae, and nasal cavities. i. In a slightly tilted view, the odontoid process of axis vertebra can be visualized. j. In children between 1½ and 2 years the anterior fontanelle makes radiolucent shadow.



Fig. 18: Plain radiograph of head, PA view. (I and OT: Inner and outer tables of skull vault; FAS: Frontal air sinus; EAS: Ethmoidal air sinus; NS: Nasal septum; INC: Inferior nasal concha; MAS: Maxillary air sinus).

Anteroposterior View

It is taken with back of the head facing the radiographic film and the orbitomeatal plane lying perpendicular to the film.

The features which are visualized clearly are as follows:

- a. The lambdoid suture, occipital bone foramen magnum, dorsum sellae, posterior clinoid processes, mastoid air cells, petrous part of temporal bone.
- b. Calcified choroid plexus, pineal gland with brain sand may be seen in radiographs of old age group.
- c. The shadows of emissary vein foramina and arachnoid granulations.
- d. The condyles of mandible.

Lateral view (figs. 18.1 and 18.2)

In this view, one side of the head is toward the film and the other side to the tube.

The orbito- meatal plane lying parallel to the film and interpupillary line horizontal and perpendicular to the orbitomeatal plane.

For visualization of the entire skull the X-ray beam should be 1 cm above the orbitomeatal line and 2 to 2.5 cm anterior to the external acoustic meatus.

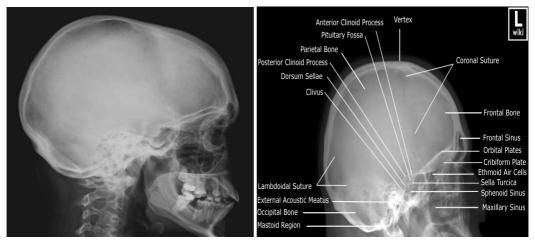
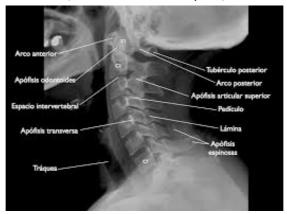


Fig. 18.1 18.2: Plain radiograph of head and neck, lateral view. (AC: Anterior cranial fossa; B: Sella turcica; MC: Middle cranial fossa; P: Petrous part of temporal bones; EAM: External accoustic meatus; PC: Posterior cranial fossa; SC: Skull cap).



Figs. 18.3: Plain radiograph of head and neck in lateral view with neck extended. (A) Labeled diagram and also Dens has been outlined; (B) Unlabeled and without markings. (EAM:

External accoustic meatus).

The skull cap presents outer and inner tables [compact part of flat bones (Fig. 18.3)] with diploe (spongy or cancellous part of flat skull bones).

The shadows of tables appear radiopaque and the diploe appears trabeculated. The sutures appear as serrated or zigzag radiolucent lines.

Parts of coronal and lambdoid sutures can be seen clearly in youngskulls and lambdoid suture can be seen in old age also. Vascular impressions can be appreciated on the inner table which is caused by the middle meningeal vessels which are seen extending toward the coronal and lambdoid sutures in upward direction.

Close to the lambdoid suture, horizontally curved radiolucent shadow is seen which is caused by transverse dural venous sinus.

- In sharp images of young skulls the radiolucent shadows of cerebral gyri can be seen.
- The arachnoid granulations produce shadows which are seen as notches or indentations on the inner table of skull vault, more prominent in older skulls.
- External ear produces a dense shadow in the posterior part of skull.
- The frontal air sinus of one side is seen as triangular or conical radiolucent shadow in the anterior part of the skull with its apex upwards. Here the shadows of inner and outer tables are separated by the shadow of the frontal air sinus.
- Base of the skull:
- The floor of the cranial fossae which are arranged like steps. The anterior part is at a higher position and separates the anterior cranial fossa with that of the orbit.
- The posterior end of the floor of the anterior cranial fossa is pointed and this is caused by the anterior clinoid process.
- When traced posteriorly the middle cranial fossa is seen which presents a concavity called shadow of sella turcica (Figs. 14.3A and B). The posterior wall of sella turcica is the dorsum sellae. The upper border of dorsum sellae presents posterior clinoid process, one on each side.
- The anterior and posterior clinoid processes are sometimes connected by ossified interclinoid ligament that appears as a bridge on sella turcica.
- The anterior and posterior walls of dorsum sellae meet at posterior clinoid process. Sometimes both walls fuse and form a single, thin layer. Absence of clear line of the anterior wall of dorsum sellae near the base is the first sign of pathological rise in the intracranial pressure caused by a tumor.

- The direct pressure from the tumor causes the erosion of dorsum sellae and posterior clinoid processes and compression of posterior clinoid processes can occur in case of 3rd ventricular dilatation as in hydrocephalus
- Posterior to the dorsum sellae there is a triangular, dense, radiopaque shadow of petrous part of temporal bone. In the middle of the petrous temporal shadow
- there is a small, circular, radiolucent shadow caused by air in the external acoustic meatus.
- Behind the posterior vertical border of petrous temporal shadow there is a honey comb like shadow caused by the mastoid air cells.
- Below the mastoid air cells shadow and posterior cranial fossa there is a superimposed radiopaque shadow of first cervical vertebra. In the old age skulls the shadow of external occipital protuberance is seen.
- SUPERIOR VIEW In this view the film is facing the top of the head, with orbitomeatal line lying parallel to the film. Rays pass horizontally anteroposteriorly below the level of chin. In this view, the following shadows are seen:
- Mandibular shadow with teeth, maxillary air sinuses. Mandibular shadow
 with teeth, maxillary air sinuses with prominent posterior walls, nasal
 septum, nasal cavities, sphenoidal air sinuses, ethmoidal air sinuses,
 foramina ovale and spinosum, basisphenoid, petrous temporal bones,
 condyles of mandible are seen.
- In the midline, behind basisphenoid, the anterior arch of atlas, odontoid process of axis vertebra, foramen magnum which is limited posteriorly by posterior arch of atlas.
- Behind the shadow of petrous temporal bone, lateral to odontoid process of axis the mastoid air cells are seen. Lateral oblique view and anterior or posterior oblique views are taken to visualize the shadows of paranasal air sinuses, mastoid air ells, mastoid antrum, temporomandibular joint, some dural venous sinuses, orbital margins, etc.

Waters View (FIG. 18.4) It is also called occipitomeatal view.

In this view the beam is transmitted at 45° angulation to the orbitomeatal plane. The rays pass at right angles to the radiographic plate. This view is taken to visualize the paranasal air sinuses especially the maxillary air sinus. Shadows of other paranasal air sinuses, orbits, odontoid process of axis vertebra just below the

symphysis menti, mandible, upper and lower teeth, nasal cavities, nasal septum, zygomatic bones, zygomatic arches and petrous temporal bone are seen.

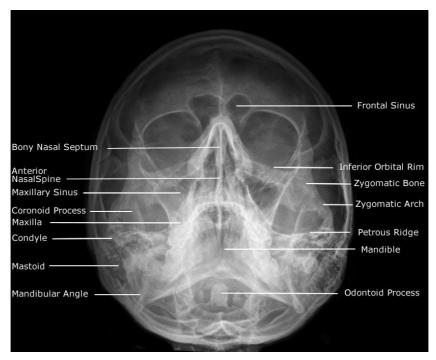


Fig. 18.4: Plain radiograph of head region in Waters view or orbitomeatal view. This is taken for the para nasal air sinuses. (FAS: Anterior cranial fossa; EAS: Sella turcica; MAS: Middle cranial fossa).

Radiology of Neck

Posterior view:

This view is taken to study the cervical part of vertebral column, atlanto occipital joint, atlanto axial joint, intervertebral disk spaces, air-filled spaces like oral cavity, pharynx, larynx, trachea, etc. Hyoid bone and ossified laryngeal cartilages also are seen in this view. The shadows of bones appear as radiopaque and that of air-filled spaces appear radiolucent. Lateral view (Fig. 18.3):

It is the better view to see cervical part of vertebral column, atlanto occipital joint, atlanto axial joint, intervertebral disk spaces, air-filled spaces like oral cavity, pharynx, larynx, trachea, hyoid bone and ossified laryngeal cartilages.

The anterior and posterior arches of atlas vertebra can be appreciated well. The shadow of anterior arch is superimposed on the odontoid process of axis vertebra.

The shadow of posterior arch of atlas vertebra lies immediately below that of occipital bone.

The posterior part of axis vertebral shadow appears prominent. The bodies of 2nd to 7th cervical vertebrae with the disk spaces between them, the spinous processes of 2nd to 7th cervical vertebrae are visualized. The shadow of spine of the 7th cervical vertebra appears longer and distinct when the neck is flexed. In the upper part of the neck shadow the lower jaw (body of mandible), temporomandibular joint (in some radiographs), teeth are visualized.

Air present in the mouth, pharynx, larynx, and trachea are seen as radiolucent shadows. Between the shadows of trachea and vertebral bodies the soft tissue shadow of esophagus and prevertebral muscles and fascia are seen. Ossified laryngeal cartilages and calcified tracheal rings are seen below the hyoid bone shadow. Hyoid bone is seen just below the mandibular shadow.

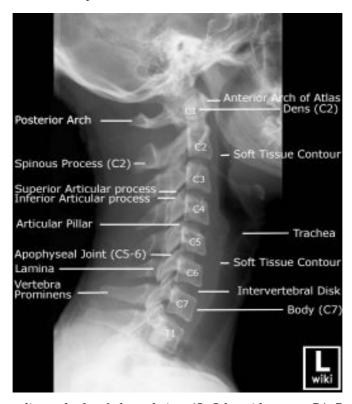


Fig. 19: Plain radiograph of neck, lateral view. (O: Odontoid process; PA: Posterior arch of atlas; Ax: Body of axis vertebra; S: Spinous process of axis vertebra; C3–C5: Bodies of C3, C4, and C5 vertebrae; T: Teeth; M: Mandible; H: Hyoid bone).

Recent Advances in Radiology

Computed Tomography(CT)

- First demonstrated in 1973 by Godfrey Hounsfield
- X-ray computed tomography (x-ray CT) is a technology that uses computerprocessed x-rays to produce tomographic images (virtual 'slices') of specific areas of the scanned object, allowing the user to see what is inside it without cutting it open.
- Medical imaging is the most common application of x-ray CT.
- Its cross-sectional images are used for <u>diagnostic</u> and therapeutic purposes in various medical disciplines.

Significance

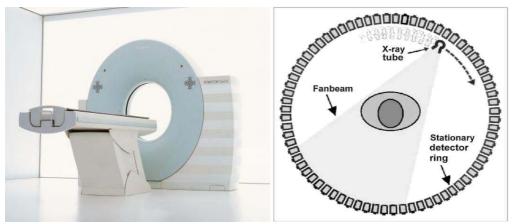
- Overcame difficulties of conventional radiographs
- Made dangerous invasive techniques unnecessary

Construction

Gantry:

- It employs an **x** ray tube on a yoke that allows a 360 degrees rotation around the body
- Stationary X ray detector ring(crystal chips)

Patient Table



Principle of CT

• A thin **fan shaped** x-ray beam penetrates the body and produces a cross sectional view of the tissues within

- By revolving the x-ray tube around the body, CT machines view thin slices of tissue
- Hundreds of crystal chip <u>detectors records what the scanner sees</u> and delivers the information to a digital computer
- The computer forms a image which is displayed on the screen

Sensors

- The earliest sensors were scintillation detectors, with photomultiplier tubes excited by (typically) cesium iodide crystals.
- Cesium iodide was replaced during the 1980s by ion chambers containing high-pressure Xenon gas.
- These systems were in turn replaced by scintillation systems based on photodiodes instead of photomultipliers
- modern scintillation materials (for example rare earth garnet or rare earth oxide ceramics) with more desirable characteristics.
- Two-dimensional CT images are conventionally rendered so that the view is as though looking up at it from the patient's feet.
- Hence, the left side of the image is to the patient's right and vice versa, while anterior in the image also is the patient's anterior and vice versa.

Hounsfield Units

- Water has an attenuation of 0 Hounsfield units (HU
- air is -1000 HU
- cancellous bone is +400 HU, cranial bone can reach 2000 HU or more (os temporale) and can cause artifacts.
- The attenuation of metallic implants depends on atomic number of the element used:
- Titanium usually has an amount of +1000 HU, iron steel can completely extinguish the X-ray and is, therefore, responsible for well-known lineartifacts in computed tomograms.

Developments In Recent Years

- Initial machines would rotate the X-ray source and detectors around a stationary object. Following a complete rotation, the object would be moved along its axis, and the next rotation started.
- Newer machines permitted continuous rotation with the object to be imaged slowly and smoothly slid through the X-ray ring. <u>These are called helical</u> or [[Helical cone beam computed tomography|spiral CT]] machines.

- A subsequent development of helical CT was <u>multi-slice</u> (or <u>multi-detector</u>) <u>CT</u>; instead of a single row of detectors, multiple rows of detectors are used effectively capturing <u>multiple cross-sections simultaneously</u>.
- CT angiography avoids the invasive insertion of a catheter.

Virtual CT

 CT Colonography (also known as Virtual Colonoscopy or VC for short) may be as useful as a barium enema for detection of tumors, but may use a lower radiation dose.

Contrast -CT

- Sometimes contrast materials such as intravenous iodinated contrast are used. This is useful to highlight structures such as blood vessels that otherwise would be difficult to delineate from their surroundings. Using contrast material can also help to obtain functional information about tissues.
- Often, images are taken both with and without radiocontrast. CT images are called precontrast or native-phase images before any radiocontrast has been administrated, and postcontrast after radiocontrast administration

Indications

Brain: Hematomas, Infective lesions of the brain, Cerebro vascular accidents (infact or hemorrhage), Mass lesions, Ventricles.

Spinal Cord: tumors, disc prolapse, congenital anomalies etc

Lesions In Abdominal Cavity: liver, gall bladder, pancreas, peritoneum

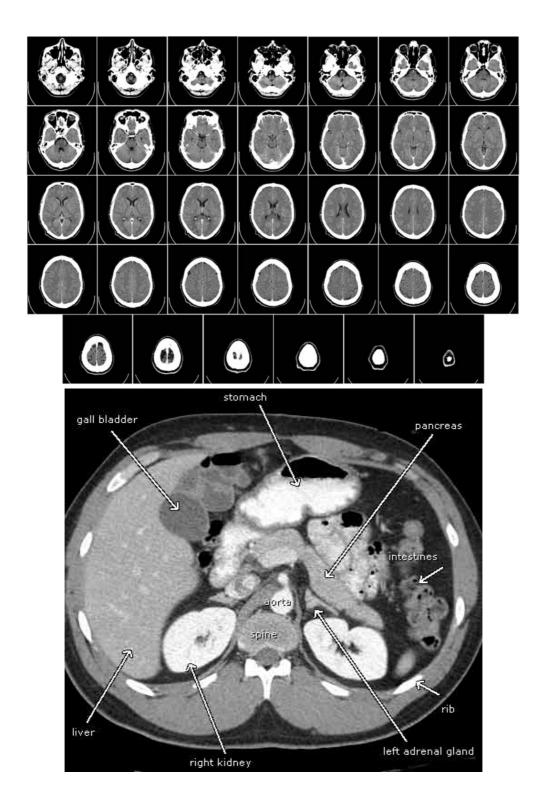
Urinary Tract Anomalies

Advantages:

- Absence of confusing superimposition of structures
- high-contrast resolution of CT(diff in tissue density less than 1% can be distinguished)
- Non invasive and quick
- More accurate results

Disadvantages:

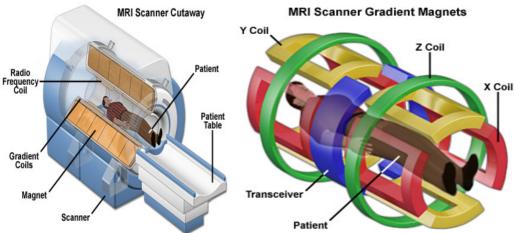
- Expensive
- Risk of Radiation exposure (LUKEMIA, BRAIN CA)
- Limited role in cardiology(movements of heart makes the image blurred)



Magnetic Resonance Imaging

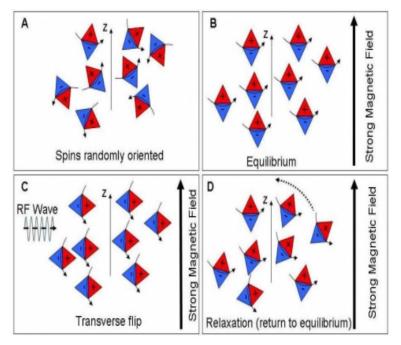
- Introduced In 1973 By Paul Lauterbur.
- In MRI instead of X-rays, radio waves and magnetic field is used for imaging





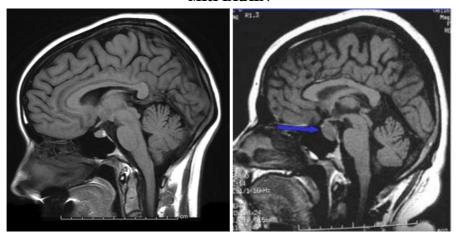
Principle of MRI

- Hydrogen atoms line up when subjected to an oscillating magnetic field
- When radiofrequency is aimed at these atoms the alignment is changed
- When the radiofrequency is turned off they realign in a line emmitimg small electric pulses
- Images are generated from the returning pulses

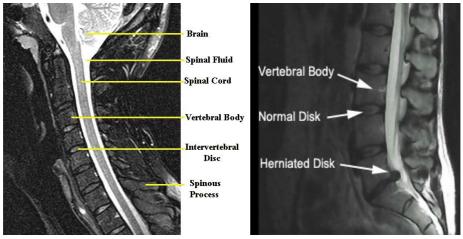


- Human body is primarily composed of hydrogen ions
- Tissues having higher water density will appear brightest on MRI
- Bone and teeth having less water molecules do not appear bright on MRI
- The contrast between various tissues is determined by the rate at which excited atoms return to equilibrium
- Preferred for soft tissue scanning

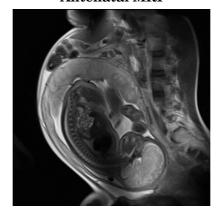
MRI BRAIN



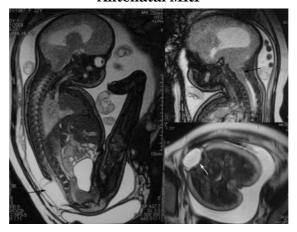
Spinal cord MRI



Antenatal MRI



Antenatal MRI



ADVANTAGES:

- No radiation hazards
- Contrast resolution is superior to CT
- Cross sectional images can be **obtained in any plane**
- Can be used in heart and great vessels where there is moving blood
- Very effective in spinal cord lesions

DISADVANTAGES:

- Expensive
- Longer duration (upto 30 min)
- Not suited for calcified lesions
- Cannot be used in patients with metallic implants
- Cant be used in claustrophobics

T1 AND T2 WEIGHTED IMAGES

- Image contrast may be weighted to demonstrate different anatomical structures or pathologies.
- Each tissue returns to its equilibrium state after excitation by the independent processes of T1 (spin-lattice) and T2 (spin-spin) relaxation.

T1-weighted image

- To create a T1-weighted image, we wait for different amounts of magnetization to recover before measuring the MR signal by changing the repetition time (TR).
- This image weighting is useful for assessing the cerebral cortex, identifying fatty tissue, characterizing focal liver lesions and for post-contrast imaging.

T2-weighted image

- To create a T2-weighted image, we wait for different amounts of magnetization to decay before measuring the MR signal by changing **the echo time** (TE).
- This image weighting is useful for detecting edema, revealing white matter lesions and assessing zonal anatomy in the prostate and uterus.
- To create a T2-weighted image, we wait for different amounts of magnetization to decay before measuring the MR signal by changing **the echo time** (TE).

• This image weighting is useful for detecting edema, revealing white matter lesions and assessing zonal anatomy in the prostate and uterus.

Contraindications to MRI

- cochlear implants
- cardiac pacemakers
- shrapnel
- metallic foreign bodies in the orbits
- some ferromagnetic surgical implants.

Contrast agents

- Gadolinium is used as contrast
- Anaphylaxix is less low nephrotoxicity

Diffusion MRI

- Diffusion MRI measures the diffusion of water molecules in biological tissues.
- Clinically, diffusion MRI is useful for the diagnoses of conditions (e.g., stroke) or neurological disorders (e.g., multiple sclerosis), and helps better understand the connectivity of white matter axons in the central nervous system

Magnetic resonance angiography (MRA)

- Magnetic resonance angiography (MRA) generates pictures of the arteries to evaluate them for stenosis (abnormal narrowing) or aneurysms (vessel wall dilatations, at risk of rupture).
- MRA is often used to evaluate the arteries of the neck and brain, the thoracic and abdominal aorta, the renal arteries, and the legs (called a "run-off").
- Magnetic resonance spectroscopy (MRS) is used to measure the levels of different metabolites in body tissues. The MR signal produces a spectrum of resonances that corresponds to different molecular arrangements of the isotope being "excited".
- This signature is used to diagnose certain metabolic disorders, especially those affecting the brain, and to provide information on tumour metabolism.

Functional MRI (fMRI)

• Functional MRI (fMRI) measures signal changes in the brain that are due to changing neural activity.

- Compared to anatomical T1W imaging, the brain is scanned at lower spatial resolution but at a higher temporal resolution (typically once every 2–3 seconds).
- Increases in neural activity cause changes in the MR signal via T2 changes; this mechanism is referred to as the BOLD (blood-oxygen-level dependent) effect.
- Increased neural activity causes an increased demand for oxygen, and the vascular system actually overcompensates for this, increasing the amount of oxygenated hemoglobin relative to deoxygenated hemoglobin.
- Because deoxygenated hemoglobin attenuates the MR signal, the vascular response leads to a signal increase that is related to the neural activity.
- The precise nature of the relationship between neural activity and the BOLD signal is a subject of current research
- The BOLD effect also allows for the generation of high resolution 3D maps of the venous vasculature within neural tissue.

Real-time MRI

- Real-time MRI refers to the continuous monitoring ("filming") of moving objects in real time
- Temporal resolution is more

INTERVENTIONAL MRI

- The lack of harmful effects on the patient and the operator make MRI well-suited for "interventional radiology", where the images produced by an MRI scanner are used to guide minimally invasive procedures.
- Of course, such procedures must be done without any ferromagnetic instruments.

ULTRASOUND

- It is a dynamic imaging technique
- First used medically by Austrian physician Karl Dussik in 1942.
- However professor Ian Donald of Glasgow was first person to use it in clinical practice to diagnose gravid uterus and hence is known as father of modern ultrasound.



PRINCIPLE OF USG

- A small transducer/transmitter receiver is placed on the surface of the area to be scanned
- High frequency sound waves penetrate the body and strike various tissues within.
- These waves are reflected back to the transducer
- The **time delays** will be sketched and the structural details are processed and displayed on the screen
- Solid and cystic structures transmit ultrasound waves
- Gas filled structures dissipate the sound waves
- hyper echoic.
- hypo echoic.

Uses

• Gall bladder disease, renal diseases (gives good details of renal parenchyma)

- Imaging during pregnancy, to detect congenital anomalies, placental and uterine anomalies.
- Bladder and prostate disorders.
- Diseases of breast, thyroid, parathyroids, scrotum
- Heart diseases

Advantages:

- Clear visualization of tissue movements
- No radiation hazards
- Non invasive, rapid and safe technique
- Accuracy is almost 90%
- Only diagnostic modality absolutely safe and efficient in pregnancy
- Cheaper than CT or MRI

Disadvantages

- Gives 2 dimensional image
- Gas containing bowels and structures below it are not visualized
- Does not give extent of lesion with precision

Antenatal USG



Pet Scan

Positron emission tomography (PET) is a nuclear medicine, functional imaging technique that produces a three-dimensional image of functional processes in the body

Principle

- The system detects pairs of gamma rays emitted indirectly by a positronemitting radionuclide (tracer), which is introduced into the body on a biologically active molecule.
- Three-dimensional images of tracer concentration within the body are then constructed by computer analysis
- In modern PET-CT scanners, three dimensional imaging is often accomplished with the aid of a CT X-ray scan performed on the patient during the same session, in the same machine.
- If the biologically active molecule chosen for PET is fludeoxyglucose (FDG), an analogue of glucose, the concentrations of tracer imaged will indicate tissue metabolic activity by virtue of the regional glucose uptake.

Use of this tracer to explore the possibility of cancer metastasis (i.e., spreading to other sites) is the most common type of PET scan in standard medical ca

Process of Scanning

- To conduct the scan, <u>a short-lived radioactive tracer isotope</u> is injected into the living subject (usually into blood circulation).
- The tracer is chemically incorporated into a **biologically active molecule**.
- There is a waiting period while the active molecule becomes concentrated in tissues of interest; then the subject is placed in the imaging scanner.
- The molecule most commonly used for this purpose is **fluorodeoxyglucose** (**FDG**), a sugar, for which the waiting period is typically an hour.
- Radionuclides used in PET scanning are typically isotopes with short half-lives such as carbon-11 (~20 min), nitrogen-13 (~10 min), oxygen-15 (~2 min), fluorine-18 (~110 min)., or rubidium-82(~1.27 min).
- During the scan a record of tissue concentration is made as the tracer decays

• As the radioisotope undergoes positron emission decay (also known as positive beta decay), it emits a positron, an antiparticle of the electron with opposite charge.

The emitted positron travels in tissue for a short distance (typically less than 1 mm, but dependent on the isotope), during which time it loses kinetic energy, until it decelerates to a point where it can interact with an electron

- The encounter annihilates both electron and positron, producing a pair of annihilation (gamma) photons moving in approximately opposite directions.
- These are detected when they reach a scintillator in the scanning device, creating a burst of light which is detected by photomultiplier tubes or silicon avalanche photodiodes (Si APD).
- The technique depends on simultaneous or coincident detection of the pair of photons moving in approximately opposite direction (it would be exactly opposite in their center of mass frame, but the scanner has no way to know this, and so has a built-in slight direction-error tolerance).
- Photons that do not arrive in temporal "pairs" (i.e. within a timing-window of a few nanoseconds) are ignored

Spect

• Single-photon emission computed tomography (SPECT, or less commonly, SPET) is a nuclear medicine tomographic[1] imaging technique using gamma rays.

It is very similar to conventional nuclear medicine planar imaging using a gamma camera.[2] However, it is able to provide true 3D information

- The basic technique requires delivery of a gamma-emitting radioisotope (called radionuclide) into the patient, normally through injection into the bloodstream.
- On occasion, the radioisotope is a simple soluble dissolved ion, such as a
 radioisotope of *gallium(III)*, which happens to also have chemical
 properties that allow it to be concentrated in ways of medical interest for
 disease detection.
- However, most of the time in SPECT, a marker radioisotope, which is of
 interest only for its radioactive properties, has been attached to a specific

- <u>ligand to create a radioligand</u>, which is of interest for its chemical binding properties to certain types of tissues.
- SPECT is similar to PET in its use of radioactive tracer material and detection of gamma rays.
- In contrast with PET, however, the tracer used in SPECT emits gamma radiation that is measured directly, whereas PET tracer emits positrons that annihilate with electrons up to a few millimeters A PET scanner detects these emissions "coincident" in time, which provides more radiation event localization information and, thus, higher spatial resolution images than SPECT (which has about 1 cm resolution).
- SPECT scans, however, are significantly less expensive than PET scans, in part because they are able to use longer-lived more easily-obtained radioisotopes than PET.
- away, causing two gamma A PET scanner detects these emissions "coincident" in time, which provides more radiation event localization information and, thus, higher spatial resolution images than SPECT (which has about 1 cm resolution).
- SPECT scans, however, are significantly less expensive than PET scans, in part because they are able to use longer-lived more easily-obtained radioisotopes than PET.
- photons to be emitted in opposite directions.

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No.441/303, Anna Salai, Teynampet, Chennai-18. Tamilnadu, India Ph. 044 - 24364303. Cell: 9282134542,

E-mail: murali.aks@gmail.com, Website: aksharaa.co.in



Hand Book on Staining Techniques in Microbiology



Dr. K. Dinesh



Sree Balaji Medical College & Hospital Bharath Institute of Higher Education & Research (BIHER) Chromepet, Chennai - 600 044, Tamilnadu, India



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Dr. K. Dinesh

Associate Professor
Department of Microbiology
Sree Balaji Medical College and Hospital
Chromepet, Chennai-44, Tamilnadu, India



Sree Balaji Medical College & Hospital Bharath Institute of Higher Education & Research (BIHER) Chromepet, Chennai - 600044, Tamilnadu, India



Published in Association with

Aksharaa Muthra Aalayam, Anna Salai, Teynampet, Chennai. 600 018. India

Ph. 044 - 24364303. Cell: 9282134542, E-mail: murali.aks@gmail.com,

Website: aksharaa.co.in

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No.441, Anna Salai, Teynampet, Chennai - 600 018,

Ph. 044 - 24364303. Cell: 9282134542.

E-mail: murali.aks@gmail.com, Website: aksharaa.co.in

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Dedication

Dedicated to My Parents

Dr. S. Kaliyamoorthi & Mrs.Vasanthi

My Wife

Dr. S.Ramapraba

My Son

Mast. D.Varun Krishna

My Daughter

Baby. D.Rutva

They have always been my Constant encouragement and have always been with me throughout my Endeavour.



Preface to First Edition



Teaching as always been my dream and I always relish teaching Microbiology for the past 5 years. My Professors and students have always been my constant inspiration that made me Come up with this Hand Book on Staining Techniques in Microbiology.

The salient features of this book are:

- 1. What are the different methods in staining
- 2. Staining technique
- 3. Modifications
- 4. Interpretation
- 5. Correlation clinically

This book is written keeping in mind both undergraduate, postgraduates and, persons working in health related professions.

It was tough to come out with this textbook on Hand Book on Staining Technique in Microbiology, I have tried my best to keep the textbook easily readable and in understandable language which makes it easy for the readers.

I could have not come out with this book without the help and encouragement of our Dean Dr.P.Saikumar., Vice-Principal Dr.W.M.S Johnson.

This book could not have been possible without Dr.Chitraleka Saikumar, Professor and Head Department of Microbiology for the invaluable advice and suggestions, from time to time.

I extend my heartfelt thanks to My Professor, Associate Professor, Assistant Professor and Tutors of department of Microbiology.

I am immersely grateful to my family members, especially my wife and childerns who have always been my strength and for supporting throughout my book.

Chennai

Dated:08/11/2018

Dr.K.Dinesh

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I. Introduction

Bacteria are microscopic organisms. They are also colourless for the most part. In order to visualize them to study their structure, shape and other structural characteristics, it becomes necessary to make them more easily visible.

This means that the structures have to be **contrasted** from their environment so that they can be seen easily visualised through the Microscope.

II. Types of Staining

- **ACIDIC**: Negatively charged acid radicals imparts color in eosin, acid fuchsine, malachite green, nigrosin, Indian ink.
- **BASIC**: Positively charged basic radicals combines with negatively charged particles in cytoplasm and gives color.

Ex: Haematoxillin, methylene blue, crystal violet, gention violet.

• **NEUTRAL**: Both positively and negatively charged imparts different colors to different components.

Ex: Geimsa's stain, Leishman's stain, Wright's stain.

III. Staining Methods

POSITIVE STAINING: - where the actual cells are themselves coloured and appear in a clear background.

a) **Simple staining**: A stain which provides color contrast but gives same color to all bacteria and cells.

Ex: Loeffler's methylene blue, Polychrome methylene blue, Diluted carbol fuchsin

(b) Differential Staining: A stain which imparts different colors to different bacteria is called differential stain (which contains more than one stain).

Ex: Gram's stain, Acid fast staining, Special stains.

Negative staining:

Where the cells remain clear (uncolored) and the background is colored to Create a contrast to aid in the better visualization of the image.

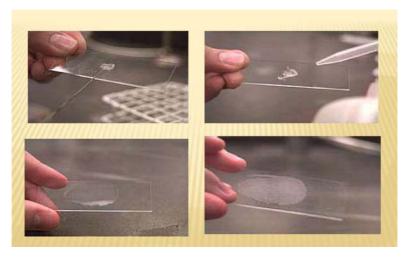
- a) Indian ink
- b) Nigrosin

IV. Bacterial Smear Preparation

Smear - is a distribution of bacterial cells on a slide for the purpose of viewing them under the microscope.

Method:

- Aseptically a small sample of the culture is spread over a slide surface.
- This is then allowed to air dry.
- The next step is heat fixation to help the cells adhere to the slide surface.
- The smear is now ready for staining.



V. Tissue Section:

- The sections being embedded in paraffin.
- It is necessary to remove the paraffin so that the watery stain may penetrate.
- The paraffin is first removed with xylene, the xylene is then removed with Alcohol and the alcohol are replaced with water.
- The staining is then done.

VI. Smear Fixation:

1) Heat fixation

- a) Pass air-dried smears through a flame two or three times. Do not overheat.
- b) Allow slide to cool before staining.

2) Methanol fixation

- a) Place air-dried smears in a coplin jar with methanol for one minute. Alternatively, flood smear with methanol for 1 minute.
- b) Drain slides and allow drying before staining.

VII. Simple Staining

Loeffler's methylene blue:

It is generally the most useful, it shows the characteristic morphology of polymorphs, lymphocytes and other cells more clearly than do stronger stains such as the Gram stain or dilute carbol fuchsin.

Polychrome methylene blue:

This is made by allowing Loeffler's methylene blue to 'ripen' slowly.

The slow oxidation of the methylene blue forms a violet compound that gives the stain its polychrome properties.

The ripening takes 12 months or more to complete, or it may be ripened quickly by the addition of 1.0% potassium carbonate (K2co3) to the stain.

It is also employed in McFadyean's reaction.

In contrast to the blue staining of most structures by the methylene blue, the violet component stains acidic cell structures red-purple, e.g. the acid capsular material of the anthrax bacillus in the McFadyean reaction.

Dilute Carbol Fuchsin

Made by diluting Ziehl-Neelsen's stain with 10-20 times its volume of water. Stain for 10-25 seconds and wash well with water. Over-staining must be avoided, as this is an intense stain, and prolonged application colours the cell protoplasm in addition to nuclei and bacteria.

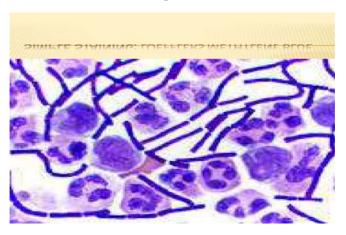
Requirement

- 1. Loefflers Methylene blue
- 2. Dil. Carbol Fuchsin
- 3. Distilled Water
- 4. Compound Microscope
- 5. Cedar Wood oil
- 6. Fixed smear

Procedure

- Make a thin smear on a slide.
- Heat fixes the smear by passing the slide 2-3 times gently over the Bunsen flame with the smear side up

- Pour Loeffler's methylene blue over the smear and allow it to stand for 3 minutes.
- Wash the stained smear with water and air dry it.
- Observe the smear first under low power (10x) objective, and then under oil immersion (100x) objective.
- Observe the presence of organisms and also the cellular content of sample.



VIII. Gram Staining

- Gram staining is most widely used differential staining in Microbiology.
- Gram staining differentiates the bacteria into 2 groups:
 - o Gram positive.
 - o Gram negative

Hans Christian Gram

The Gram stain was devised by the Danish physician, **Hans Christian Joachim Gram**, while working in Berlin in 1883. He later **published this procedure** in 1884. At the

time, Dr. Gram was studying lung tissue sections from patients who had died of **pneumonia**.

Original Formulation of Program consist of

- Aniline Gentian violet,
- Lugol's Iodine,
- Absolute Alcohol,
- Bismarck Brown

Carl Weigert (1845- 1904)

German pathologist Carl Weigert (1845-1904) from Frankfurt, added a final step of staining with safranin. In his paper, Dr. Gram described how he was able to visualize what we now call *Staphylococcus*, *Streptococcus*, *Bacillus*, and *Clostridia* in various histological sections. Interestingly, Dr. Gram did not actually use safranin as a counter stain in the original procedure (Gram negative cells would be colorless). He instead recommended using Bismarck brown as a counter stain to enable tissue cell nuclei to be visualized.

Principle:

- The Gram Reaction is dependent on permeability of the bacterial cell wall and cytoplasmic membrane, to the dye-iodine complex.
- In Gram positive bacteria, the crystal violet dye iodine complex combines to form a larger molecule which precipitates within the cell. Also the alcohol/acetone mixture which act as decolorizing agent, cause dehydration of the multi-layared peptidoglycan of the cell wall. This causes decreasing of the space between the molecules causing the cell wall to trap the crystal violet iodine complex within the cell.

Hence the Gram positive bacteria do not get decolorized and retain primary dye appearing violet. Also, Gram positive bacteria have more acidic protoplasm and hence bind to the basic dye more firmly.

• In the case of Gram negative bacteria, the alcohol, being a lipid solvent, dissolves the outer lipopolysaccharide membrane of the cell wall and also damage the cytoplasmic membrane to which the peptidoglycan is attached. As a result, the dye-iodine complex is not retained within the cell and permeates out of it during the process of decolourisation. Hence when a counter stain is added, they take up the colour of the stain and appear pink.

Methods consist of four components

- Primary stain—Crystal violet, Methyl violet & Gentian violet.
- Mordant—Gram Iodine, Rarely Lugol's Iodine.
- Decolourizer—Alcohol, Acetone, Alcohol: Acetone (1:1) mixture.
- Counter stain—Dilute Carbol fuchsin, Safranin, Neutral red, Sandi ford stain for Gonococci.

Procedure:

- Primary staining: The smear is covered with gentian violet, for 1 minute and washed with water.
- Mordanting: It is then covered with Gram's iodine, Kept for 1 minute, and washed with water.
- Decolourisation: The smear is covered with alcohol and is washed with water immediately.

- Counter staining: The smear is then covered with safranine, kept for 30 seconds and washed with water.
- Using filter paper the slide is gently blotted to dry.
 Place a drop of cedar wood oil/Liquid paraffin on the smear.
- Adjust the microscope for increased light by raising the condenser, and the slide is examined under the oil immersion objectives using the plane mirror.

Result:

- Organism which mange to maintain there original colour will be purple in colour and are called as Gram Positive organism.
- Organism which lose the primary dye take up the secondary dye and look pink in colour and are called as Gram Negative organism.

Quick Gram Staining:

- By this method fairly good results may be obtained with very short staining times, which are convenient when only one slide has to be stained.
- Flood the slide with crystal or methyl violet stain and allow to act for about 5 seconds.
- Tip off the stain and flood the tilted slide with iodine solution and allow to act for about 5 seconds.
- Tip off the iodine and flood the tilted slide
- With acetone and allow this to act for only 2 seconds before washing it off with water from the tap.
- Flood the slide with basic fuchsin counter stain and allow it to act for about 5 seconds. Wash off with water, blot and dry.

Quality Control:

Daily and when a new lot is used, prepare a smear of *Escherichia coli* (ATCC 25922) and *Staphylococcus epidermidis* (ATCC 12228)or *Staphylococcus aureus* (ATCC 25923). Fix and stain as described.

Modifications of Gram Staining:

1. Kopeloff & Beerman's Modification:

Primary stain is Methyl violet.

Decolourizer is Acetone/ Acetone-Alcohol mixture.

2. Jensen's Modification:

Primary stain is Methyl violet.

Decolourizer is Absolute Alcohol.

Counter stain is Neutral Red.

3. Preston & Morrell's Modification:

Primary stain is crystal Violet

Decolouriser is Iodine-Acetone

4. Weigert's Modification:

Primary stain is Carbol Gentian violet.

Decolouriser is Aniline-Xylol

Used in tissues section

Common Errors in Gram staining:

- Excessive heat during fixation
- Excessive washing between steps
- Insufficient iodine exposure
- Prolonged decolourization
- Excessive counterstaining

IX. Ziel Nehlson Staining for AFB

The acid fast staining method is a modification of Ehrlich's (1882) method.

The Ziehl-Neelsen acid fast staining method has proved to be most useful for staining acid fast bacilli belonging to the genus Mycobacterium especially Mycobacterium tuberculosis and Mycobacterium leprae, and also for Nocardia.

Principle:

- Acid fastness of acid-fast bacilli is attributed to the presence of large quantities of unsaponifiable wax fraction called mycolic acid in their cell wall and also the intactness of the cell wall. The degree of acid fastness varies in different bacteria.
- In this staining method, application of heat helps the dye to penetrate the tubercle bacillus.
- Once stained, the stain cannot be easily removed. The tubercle bacilli resist the decolorizing action of acidalcohol which confers acid fastness to the bacteria.
- The other microorganisms, which are easily decolorized by acid-alcohol, are considered non-acid fast. The non-acid fast bacilli readily absorb the colour of the counter stain appearing blue, while the acid fast cells retain the red colour of primary stain.

Methods:

- Zeihl Neelsen's- hot stain
- Kinyoun's-cold stain

Requirement:

1. Primary And Mordant Staining with Strong Carbol fuchsin (Red)

- 2. Decolourization with Acid Alcohol: The acid alcohol contains 3% HCl and 95% ethanol or 20% H2 SO4.
- 3. Counterstain with Methylene Blue.
- Acid Fast Cells Red
 - o Non Acid Fast Blue

Procedure:

- 1. Make a smear, Air Dry, Heat Fix.
- 2. Flood smear with Carbol Fuchsin stain
- 3. Steam for 5 minutes. Add more Carbol Fuchsin stain as needed
- 4. Cool slide for 5 minutes
- 5. Wash with Distilled water
- 6. Flood slide with acid alcohol (leave 15 seconds).
- 7. Tilt slide 45 degrees over the sink and add acid alcohol drop wise (drop by drop) until the red colour stops streaming from the smear
- 8. Rinse with Distilled water
- 9. Add Loeffler's Methylene Blue stain (counter stain). Leave Loeffler's Blue stain on smear for 15-20 seconds.
- 10. Rinse slide and let it dry.
- 11. Use oil immersion objective to view.

Microscopic Reading:

The stained smear are contains pink coloured slender rod shaped structures are seen with curved ends acid fast bacilli seen among the blue coloured multilobed pus cells. The smear is positive for acid fast bacilli.

Modifications:

- 1. 5% Sulphuric acid is used as a decolourizing agent for staining Mycobacterium leprae.
- 1% Sulphuric acid is used as a decolourizing agent for staining Nocardia species, Cryptosporidium and Isospora oocysts (Kinyoun's modification of acid fast stain).
- 3. 0.25% Sulphuric acid is used as a decolourizing agent for staining spores.

X. Flourescent Staining

- Fluorochrome stained smears require a fluorescent microscope
- Generally read at 250X-450X magnification which allows rapid scanning of the smear
- Auramine-rhodamine is an example of such a stain where the AFB appear yellow against a black background

Procedure:

Place the dried, heat-fixed smear on a staining rack over the sink. Smears of sputum should be thin.

Cover the smear with auramine phenol and leave to stain at room temperature for 10 minutes.

Wash off stain with water from the tap.

Cover the slide with an excess of 1% acid-alcohol and leave to decolorize for 5 minute.

Wash off decolourizer with water from the tap.

Cover the smear with the 0.1% potassium permanganate counter stain and leave for 15 seconds.

Wash off counter stain with water from the tap.

Dry on heated drier or dry in air. Do not use blotting paper.

Examine the film dry by fluorescence microscopy with a 4 mm objective. Tubercle bacilli are seen as yellow luminous rods in a dark field. When detected under low power, the morphology of the bacilli is confirmed with an oil-immersion objective.

Flurochrome AFB Microscopy:

More rapid and sensitive

- * Specificity: same with sufficient expérience Equipment cost, bulbs, technical demands for busy labs
- * External quality assessment should be done if this method is performed

Advantages:

- More accurate: 10% more sensitive than light microscopy, with specificity comparable to ZN staining
- Faster to examine = less technician time

Disadvantages:

• Higher cost and technical complexity, less feasible in many areas.

XI. Staining of Volutin Granules:

Well developed granules of volutin (polyphosphate) may be seen in unstained wet preparation as round refractile bodies within the bacterial cytoplasm.

Principle:

With basic dyes they tend to stain more strongly than the rest of the bacterium, and with toluidine blue or methylene blue they stain metachromatically, a reddish-purple colour.

They are demonstrated most clearly by special methods, such as Albert's and Neisser's

which stain them dark purple but the remainder of the bacterium with a contrasting counter stain.

The diphtheria bacillus gives its characteristic volutinstaining reactions best in a young culture on a blood or serum medium.

Procedure:

Make film, dry in air, and fix by heat.

Cover slide with Albert's stain and allow to act for 3-5 min.

Wash in water and blot dry.

Cover slide with Albert's iodine and allow to act for 1 minute.

Wash and blot dry.

By this method the granules stain bluish black, the protoplasm green and other

Organisms mostly light green.

XII. Albert Staining

Corynebacterium diphtheriae Stained by Albert's stain Green colored bacilli showing "Chinese-letter"arrangement at angles to each other containing bluish-black metachromatic granules of cells.

XIII. Capsule Staining

The capsules serves as protective material by slowing down or preventing penetration of chemicals and body juices.

Principle:

Chemically, the capsular material is a polysaccharide, a glycoprotein or a polypeptide.

Capsule staining is more difficult than other types of differential staining procedures because the capsular materials are water soluble and may be dislodged and removed with vigorous washing.

Bacterial smears should not be heated, because the resultant cell shrinkage may create a clear zone around the organism, an artifact that can be mistake for capsule.

The capsule is non-ionic, so that the dyes commonly used will not bind to it. Two dyes, one acidic and one basic, are used to stain the background and the cell wall, respectively.

Methods:

- 1. Negative staining.
- 2. Positive staining.
- 3. Mc Fdyean reaction: which uses the Loefflers polychrome methylene blue to demonstrate the capsule of the Bacillus anthracis.

Capsulated Bacteria:

Polysacchride capsule: Streptococcus pneumoniae,

Haemophillus influenzae, Anaerobic GNB.

Polypeptide capsule: Bacillus anthracis.

Procedure:

For positive staining of smears:

Make a smear from colony of S.pneumoniae on a clean grease free glass slide, and allow it to air dry.

Note: The smear should not be heat fixed.

Put the smear on a slide rack and flood smear with crystal violet. Allow it to stain for 5-7 minutes.

Wash the smear with 20% copper sulphate solution and blot it dry.

Observe the smear first under low power (10x) objective, and then under oil immersion(100x) objective.

In the culture smear, the capsule is seen as a light blue in contrast to the deep purple colour of the cell.

For negative staining of smears:

Take a clean grease free glass slide.

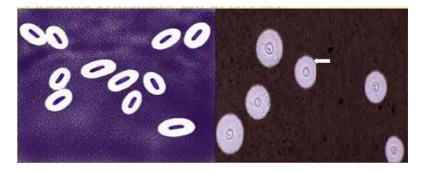
Put a large loopful of undiluted India ink on the slide.

Then add a small loopful of liquid bacterial culture to the India ink and emulsify.

Take a clean, grease free cover slip and place on the ink drop and press it down, so that the film becomes very thin and thus pale in colour.

Observe the wet film under high power (40x) objective.

The capsule in negative staining method is seen as clear retractile, halo around the organism against a black background.



XIV. Lactophenol Cotton Blue

It is used to demonstrate fungi and fungal elements under the microscope in LPCB wet mount preparation.

Prepare lactophenol cotton blue wet mount of fungal colony.

The fungi identified by characteristic microscopic morphology such as shape, size, arrangements of spores and hyphae.

Procedure:

Scotch tape preparation:

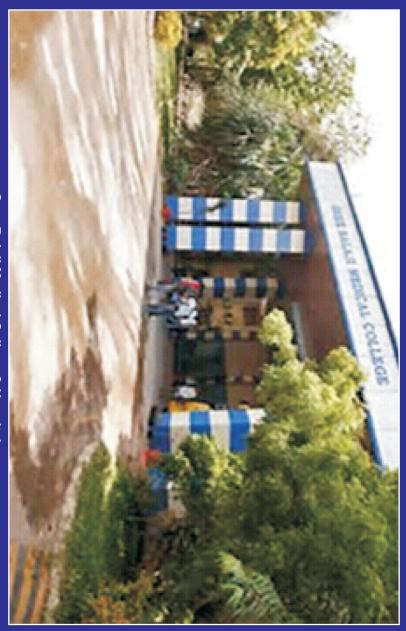
On a clean glass slide, place one drop of LPCB.

Touch the adhesive side of the tape of transparent scotch tapes on the surface of the colony at a point intermediate between its centre and periphery. Fix the adhesive side of the tape over an area on the glass slide containing the LPCB. Examine the preparation under 10x and 40x of a light microscope.

Tease mount preparation:

Place a drop of LPCB on a clean glass slide. Remove a small portion of the colony and the supporting agar at a point between the centre and periphery and place it in the drop of LPCB. With a needle, tease the fungal culture first and spread in the LPCB. Examine microscopically after giving sufficient time for the structures to take up the stain usually 30 mins.





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HANDBOOK ON VACCINES



Author
Dr. Aishwarya J Ramalingam



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Hand Book on Vaginal Infections



Author
Dr. Lakshmi Krishnasamy



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E-mail: murali.aks@gmail.com







HEALTH MANAGEMENT



DEPARTMENT OF COMMUNITY
MEDICINE,
SREE BALAJI MEDICAL COLLEGE AND HOSPITAL,
CHROMEPET, CHENNAI-44.

HEALTH MANAGEMENT

By Dr. G. ANGELINE GRACE

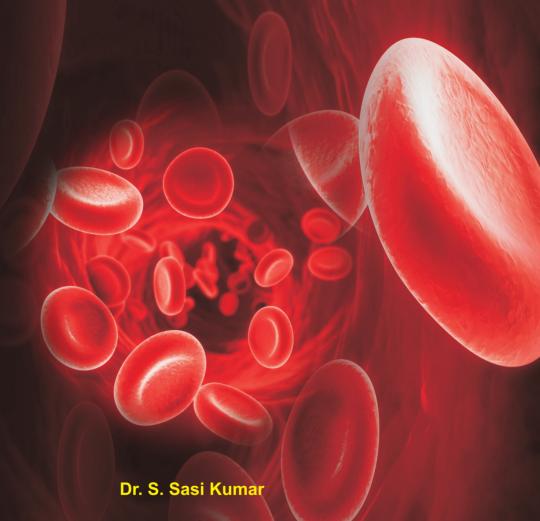
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About the author

Author is an assistant professor working at SBMCH. He has teaching experience of almost two years and is interested in medical education technologies. Author has identified the need of the students and has accordingly formed the questions in hematology which is very important in practical point of view.

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HER 2 NEU MUTATION IN VISCERAL ORGANS



DR.JOSEPHINE
ASSOCIATE PROFESSOR
DEPARTMENT OF PATHOLOGY
SREE BALAJI MEDICAL COLLEGE & HOSPITAL

SARIKA
SECOND YEAR RESIDENT
DEPARTMENT OF PATHOLOGY
SREE BALAJI MEDICAL COLLEGE

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HYPERTENSIVE DISORDERS IN PREGNANCY



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ILLUSTRATED LECTURE NOTES ON LIPID METABOLISM



Author

Dr. V.S. Kalaiselvi

Co-Authors

Dr. C. Sridevi
Dr. A. Mary Chandrika
Dr. B. Shanthi
Dr. K. Sumathi
Dr. S. Shenbaga Lalitha



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ILLUSTRATED LECTURE NOTES ON PROTEIN METABOLISM



Author Dr. K. Sumathi

Co-Authors

Dr. B. Shanthi Dr. V.S. Kalaiselvi Dr. S. Shenbaga Lalitha Dr. C. Sridevi Dr. A. Mary Chandrika



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Instant Notes in Laboratory Diagnosis of Fungi



Author Dr. Lakshmi Krishnasamy



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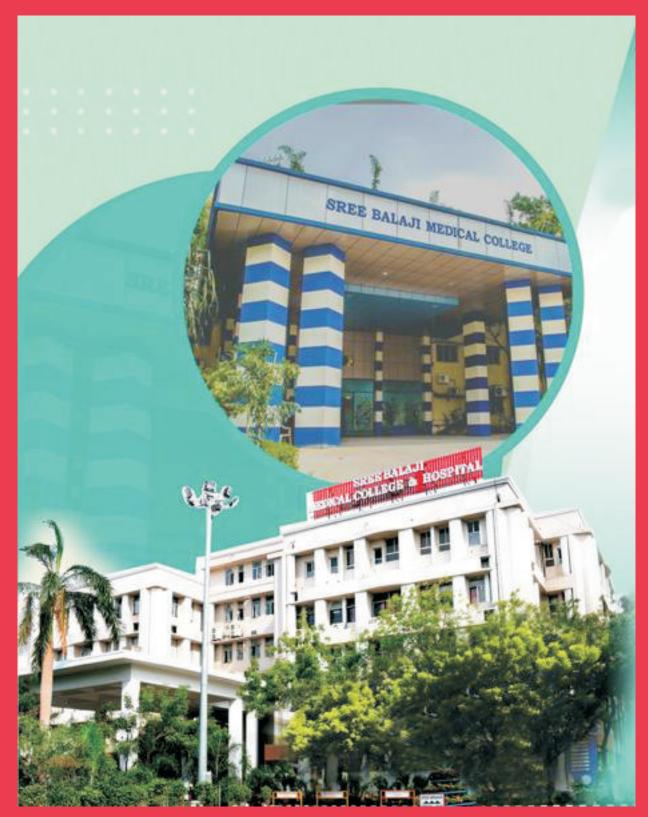
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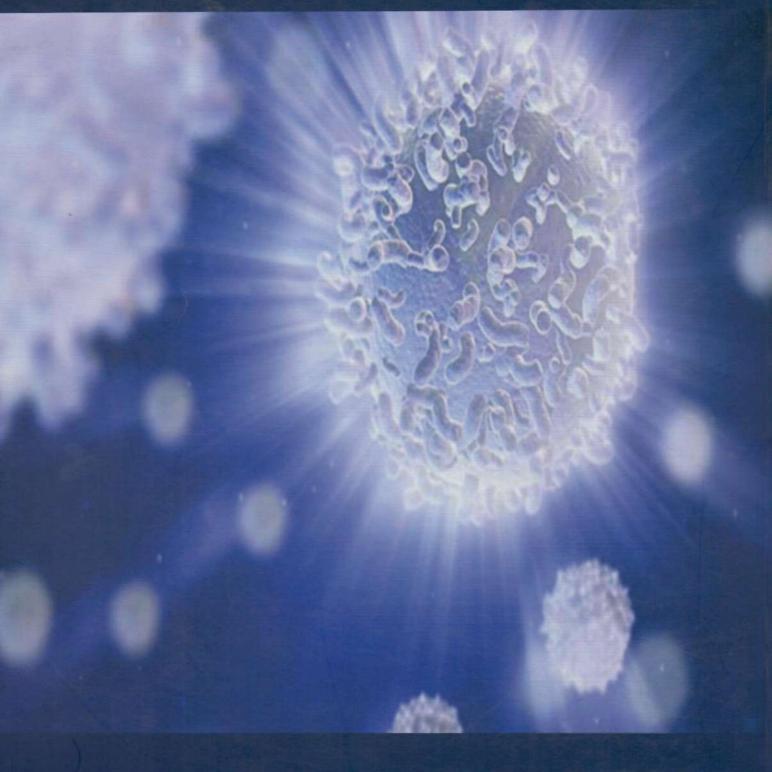
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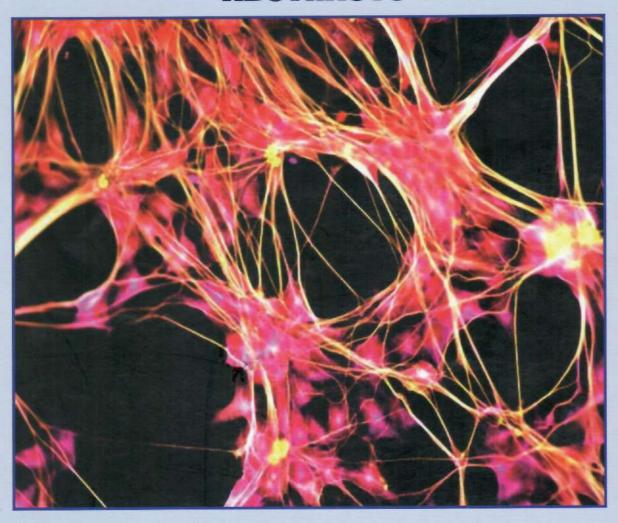
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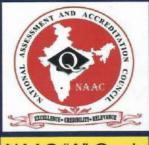
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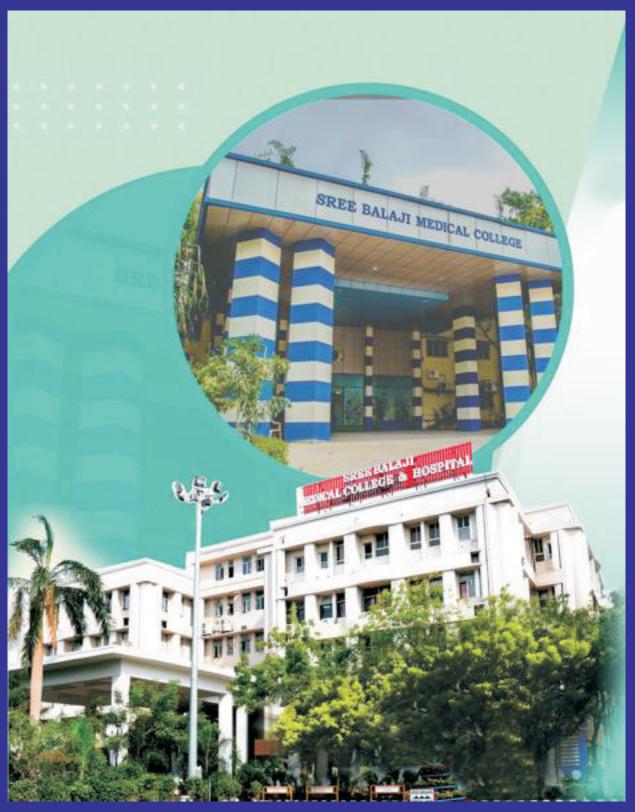
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MEDICAL EDUCATION UNIT DEPARTMENT OF GENERAL MEDICINE

LIVER FUNCTION TEST AT A GLANCE

DR. MANIMEKALAI PERIYASAMY
DR. PON DIVYA BHARATHI

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- 1.2 FUNCTION OF LIVER
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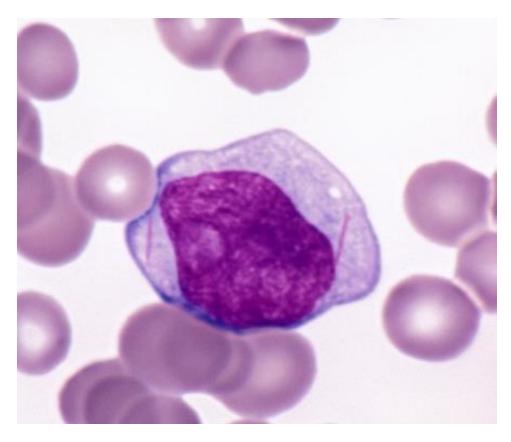
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by

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MBBS, DCH, M.D (Ped), FRCPCH (London), M. Med. Sc. Haematology (U.K), FUICC (Geneva), M.A, D. Litt

Professor & Director of Pediatrics, Sree Balaji Medical College and Hospital, Chennai – 600044.



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Chennai, Tamil Nadu, India

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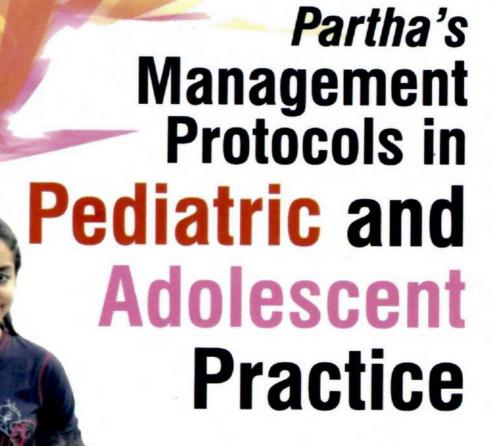
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MCQs IN BACTERIOLOGY



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MCQs in Gross Anatomy - I A Guide to Undergraduate Exam Preparation

Dr. Archana Rajasundaram Dr. WMS Johnson Dr. Rahe Ramachandran



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- Multiple choice questions have been framed from clinically important topics.
- This book will be very useful for I MBBS University examination.
- Further it would act as a perfect guide, helping the students who are aspiring to excel in their competitive exams, like the PG NEET examination.
- The questions in this book have been organized region wise, so that on completion of a region in Anatomy the student can take a test and self assess his level of understanding.
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Multiple Choice Questions In Neuroanatomy



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About the author

Dr. D. Sreelekha is an alumni of the Government Medical College, Guntur, She is presently Assistant professor in Anatomy at Sree Balaji Medical College. She has a good academic record of presenting scientific papers in several state and national conference from her undergraduate years. She was awarded the gold medal in the subject of Anatomy in her undergraduate training and she stood university second in her post graduate training. Her passion for Anatomy fuelled by her quench to improvise herself constantly has culminated in conceiving this book.

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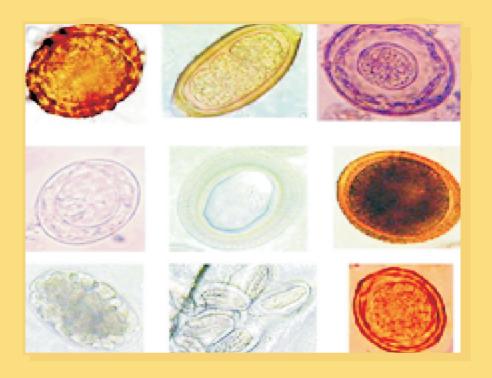
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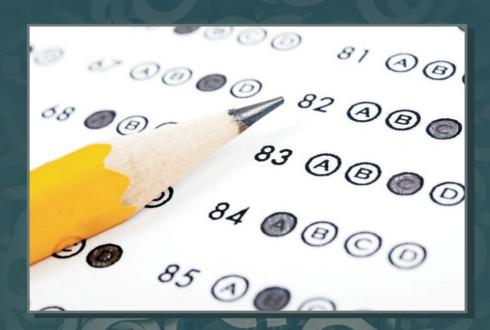
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MULTIPLE CHOICE QUESTIONS IN VIROLOGY



Author
Dr. B. Kiran Madhusudhan



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MEDICAL AUDIT: AN OVERVIEW



DR. SWETHA N B DEPARTMENT OF COMMUNITY MEDICINE SREE BALAJI MEDICAL COLLEGE AND HOSPITAL

Chromepet, Chennai- 600044

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MOLECULAR METHODS IN MICROBIOLOGY



Author

Dr Sindhu Cugati



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MOLECULAR PATHWAY OF CARCINOMA BREAST

Dr.Vindu Professor of pathology Dr. Hemnath 2nd year pathology PG

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Dr. Nikath Nasreen, MS (OG)
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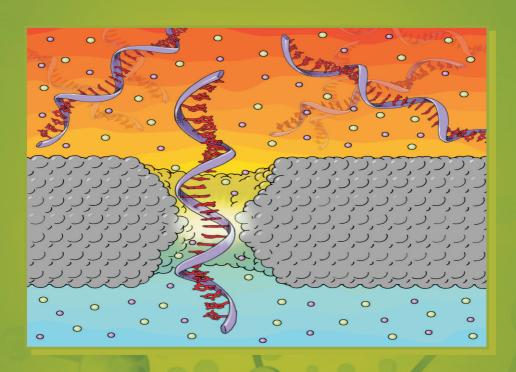
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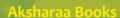
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NANOTECHNOLOGY IN PHARMACOLOGY - AN OVERVIEW



Author Dr. S. Brigida



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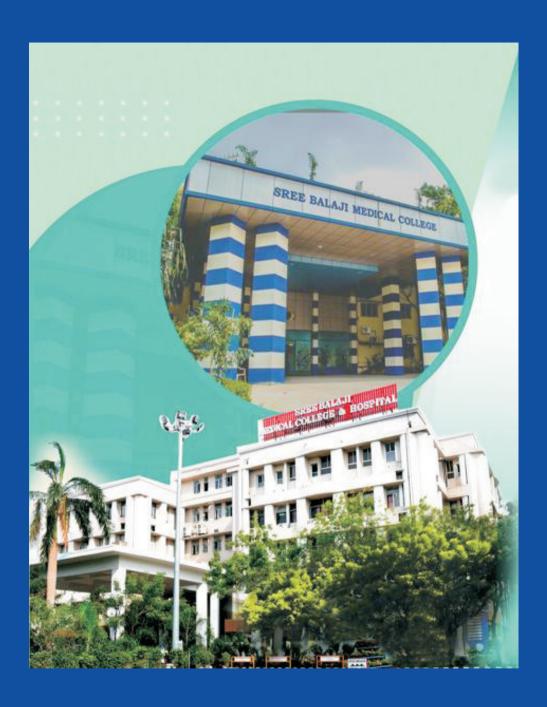
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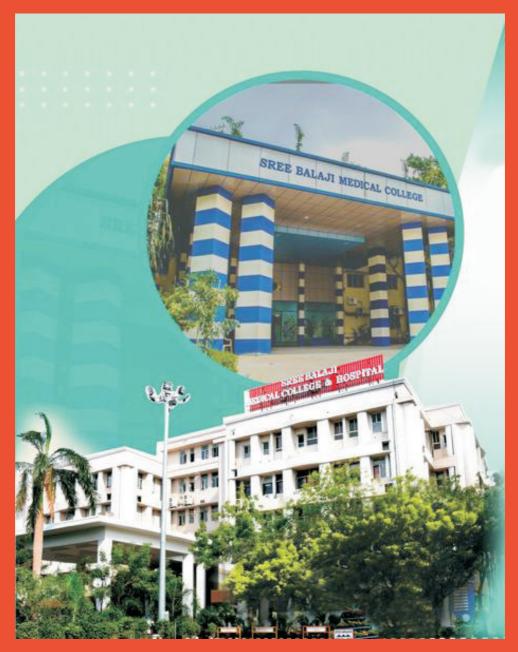
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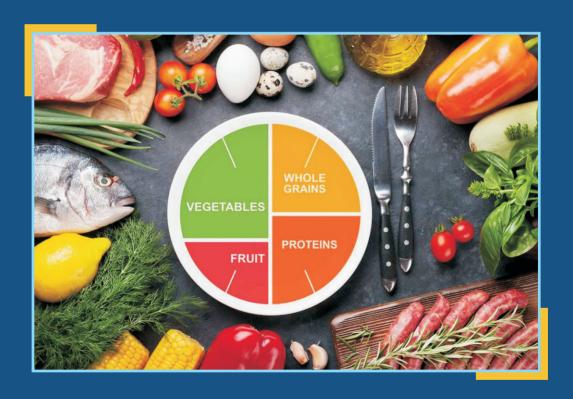




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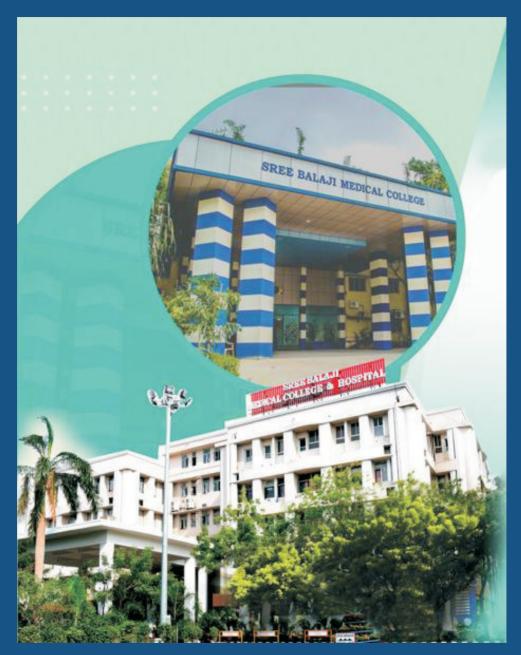
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- 4. MANAGEMENT OF BP IN ACUTE ISCHEMIC STROKE
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Dr. Sabarinath Ravichandar



Department of Pulmonology

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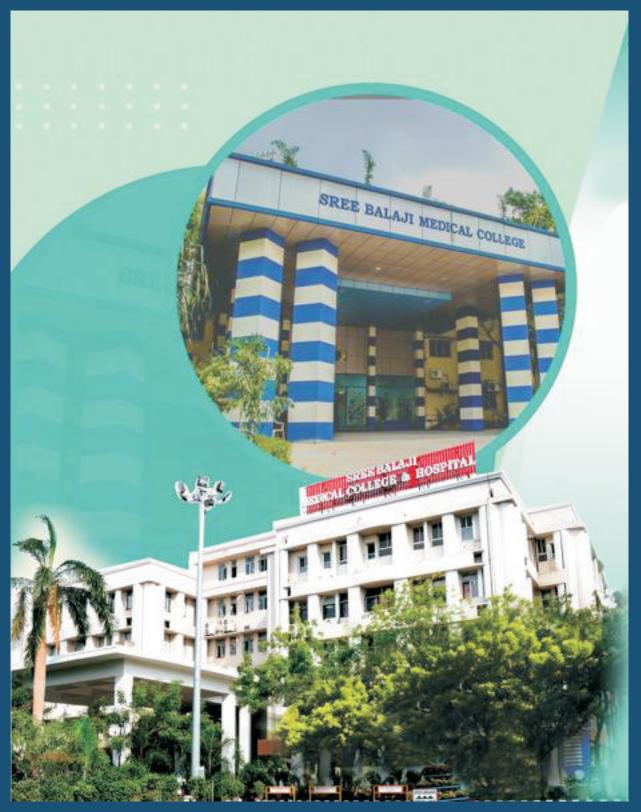
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Book Chapter "Phage therapy for control of bacterial diseases"

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Palaniappan Ramasamy, Research and Development Wing, Sree Balaji Medical College and Hospital, Bharath Institute of Higher Education and Research (BIHER), Chennai-600044, Tamilnadu, India.

Address for communication: Prof. Palaniappan Ramasamy, Director-Research, Research and Development Wing, Central Research Lab, Sree Balaji Medical College & Hospital, BIHER, Chromepet Chennai-600044, Tamilnadu, India. Email id: researchsbmch@gmail.com; ramasamypalaniappan@hotmail.com

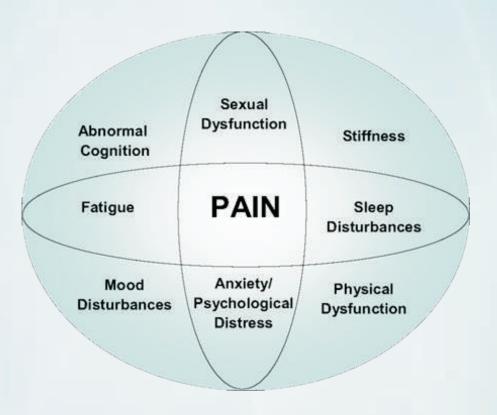
Abstract

Phage therapy is one of the most important control strategies envisaged for the management of bacterial diseases in the aquatic environment. There are no other effective alternative approaches for the natural control of bacterial diseases while phage therapy remains the best method which has not yet been exploited. The occurrence, infectivity, lytic activities, therapeutic potentials and efficacy of the bacteriophages of Bacillus spp / Vibrio spp for control of pathogenic bacteria diseases such as Vibrio vulnificus, V. damsela, and V. furnissi in the cultures of crustaceans are presented. An ideal method for long term storage and recovery of the lytic bateriophages and validation of the usefulness of phage therapy are reviewed. The application and efficacy of the phages of Bacillus / Vibrio against the bacterial pathogens Vibrios in the aquaculture of crustaceans are considered. Agar bioassay method and one-step growth experiments of the lytic phages infected Vibrio spp and Bacillus spp., in vivo and in vitro experiments to determine the efficacy of phage therapy on the host bacterial population are described. The review highlight the occurrences of plagues of lytic phages of Vibrio sp and Bacillus spp and their control effects of vibriosis both in vivo and in vitro in the crustaceans, thus established the application and efficacy of the phages of Vibrio/ Bacillus against the pathogenic Vibrio spp. Development of specific phage therapy or a cocktail of phages to a wide variety of systems is considered to represent an interesting emerging alternative to antibiotic therapy and vaccination.

Keywords: phage therapy, bacterial diseases, Vibriosis, probiotics, bacteriophages, antimicrobials, antibiotic resistance, crustaceans, shrimp, lobster, crab, artemia.



PHARMACOTHERAPY OF FIBROMYALGIA



Dr. Anitha. E

Tutor
Department of Pharmacology
Sree Balaji Medical College & Hospital



Sree Balaji Medical College & Hospital Bharath Institute of Higher Education & Research (BIHER) Chromepet, Chennai - 600 044, Tamilnadu, India



Pharmacotherapy of Fibromyalgia

Dr. Anitha. E

 $(Tutor,\, Department\ of\ Pharmacology,\, SBMCH)$







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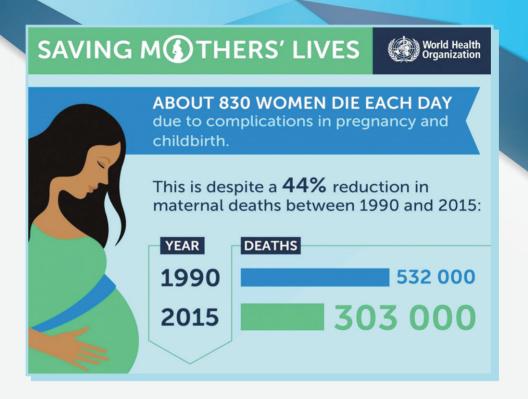
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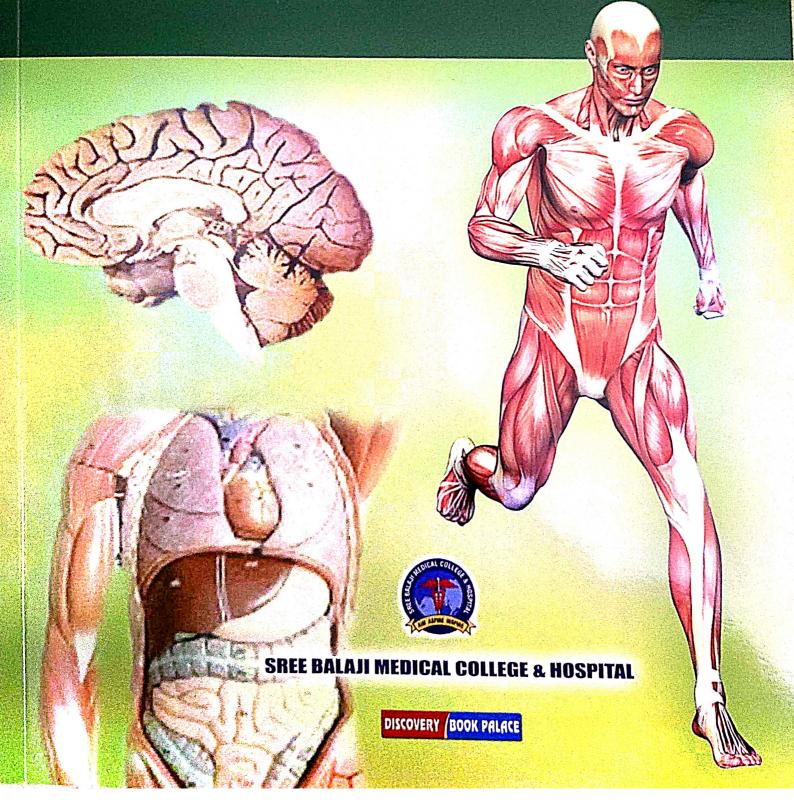
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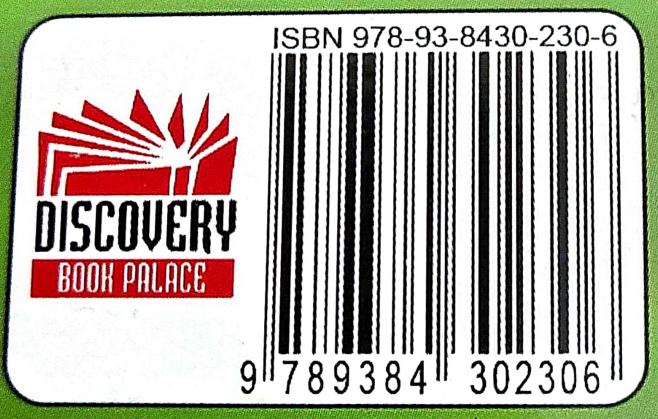
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Prof. Dr. R. Somasekar, MD, DCH, FIAP, was born in Thegamputhur, Sasthankoilvilai, a small hamlet near Nagercoil, Kanyakumari District. He completed his MBBS and DCH from Kilpauk Medical College, Chennai and MD (Paediatrics) from Madras Medical College, Chennai. He joined the Tamil Nadu Medical

Prof. Dr. R. Somasekar Service in 1989. Dr. Somasekar has recevied many awards for his meritorius services and has got several publications both national and International to his Credentials. He was honored with Raiiv Gandhi Award at New Delhi for conducting medical camps for the urban poor in Chennai. He received the Best Doctor Award from Friends Cultural Academy. He is the recipient of Active Pediatrician Award from IAP - TNSC 2003. He received the Best Doctor Award from IMA Tambaram in 2015. He has undergone the "Training for specialist of Health Care Associated Infection Control and Prevention" at National Center for Global Health and Medicine, Government of Japan in 2015. He received Lifetime Achievement Award from Lions Club of Madras in 2017 and Best Performance and Appreciation Award by the Government of Tamil Nadu, Ministry of Health and Family Welfare in 2018. He is the life member of Breastfeeding Promotion Network of India, Indian Academy of Paediatrics IAP-IYCF, Disaster Management Group, Indian Medical Association, Human Milk Bank Association of India, He is also a member of professional bodies namely, Indian Council of Child Welfare, International Union of Health Education Bureau. He is the WHO Consultant on Clinical Case Management of Dengue Fever and A H1N1. Presently he is the Professor of Paediatrics at Sree Balaji Medical College & Hospital and Visiting Consultant, Dr. Rela Institute & Medical Centre, Chennai.

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Health, Chennai. He is a practising psychiatrist in Chennai for more than three decades. He is the past president of the Indian Psychiatric Society, National Body. He is also the Past Honorary General Secretary and Past Chairperson of the Forensic Psychiatry, Speciality Section of Indian Psychiatric Society. He is the Past Secretary of the State Mental Health Authority and Chief Nodal Officer at District Mental Health Program in Tamil Nadu. He has been the principal investigator for two Indian Council of Medical Research (ICMR) projects on Mental Health. He twice won the coveted Marfatia Award of the Indian Psychiatric Society. He has presented scientific papers mostly in the area of forensic psychiatry in the state, regional, national and international psychiatric conferences. He has authored four books on mental health. His area of interest is forensic psychiatry.

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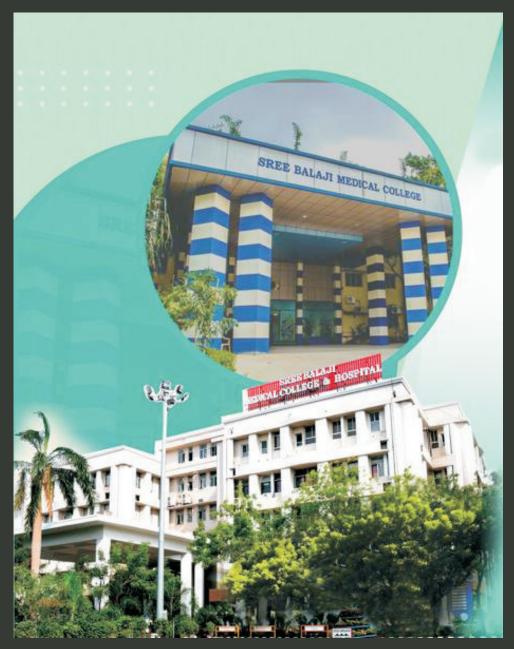
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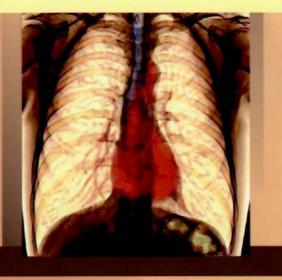
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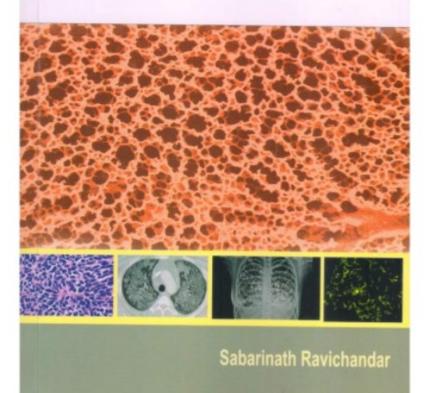
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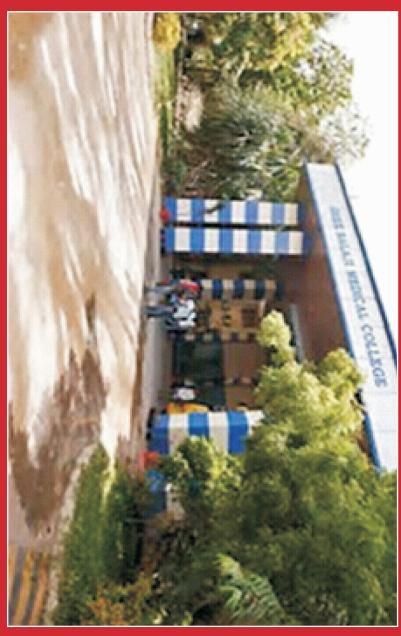
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FRCPCH FAAD FIAD FIAP
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Editors

Parimalam Kumar MD DD DNB FRCP FIAD

Professor and Head Department of Dermatology Government Villupuram Medical College Villupuram, Tamil Nadu, India

Sindhu Ragavi Balaji MBBS MD

Consultant Dermatologist Carves Skin Clinic Chennai, Tamil Nadu, India Dinesh Kumar Devaraj MBBS MD

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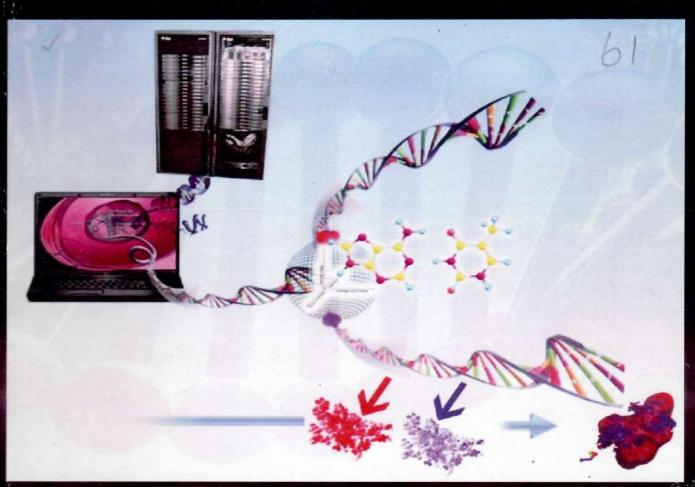
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Editorial Office

Prof. Dr V Padma

Professor

Department of Internal Medicine

Sree Balaji Medical College and Hospital,

7, CLC Works Road, Chromepet, Chennai 600044,

Tamil Nadu, India

Email Id: padma.v@bharathuniv.ac.in

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Contributing Authors:

Dr Sandhya P C MD

Dr SatyaPriya S V MD

Dr Sarath Bhaskar S MBBS

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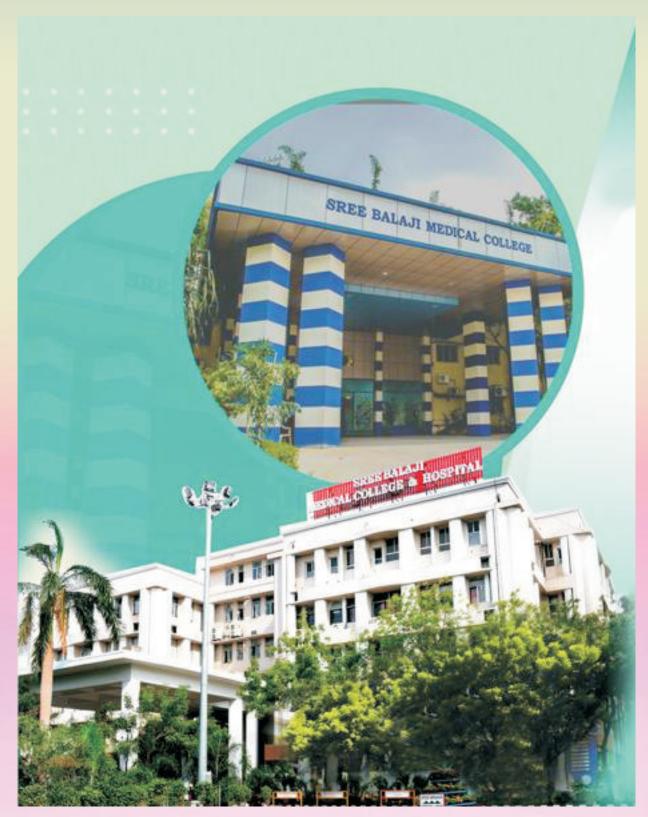
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HYPERTENSIVE OPHTHALMIC THREAT	8:30 AM – 9:15 AM
INAUGURATION	9:15 AM – 9:45 AM
FOOTPRINTS OF HYPERTENSION ON PREGNANCY	9:45 AM -10:30 AM
THE DIAD OF DIABETES AND HYPERTENSION	10:30 AM – 11:15 AM
THERAPEUTIC ADVANCEMENTS IN THE MANAGEMENT OF HYPERTENSION	11:15 AM – 12:00 NOON
LUNCH BREAK	12:00 – 1:00 PM
ORAL PRESENTATION AND POSTER PRESENTATION	1:00 PM – 4:00 PM
VOTE OF THANKS	4:00 PM – 4:10 PM







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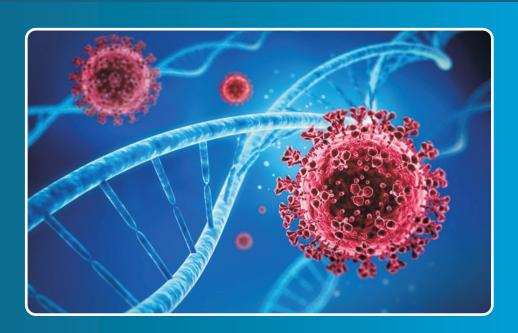
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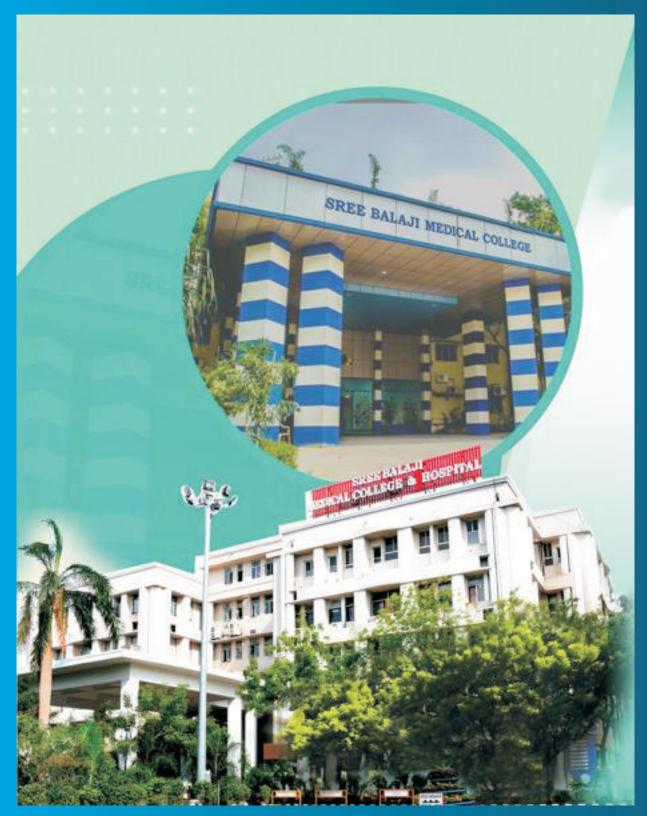
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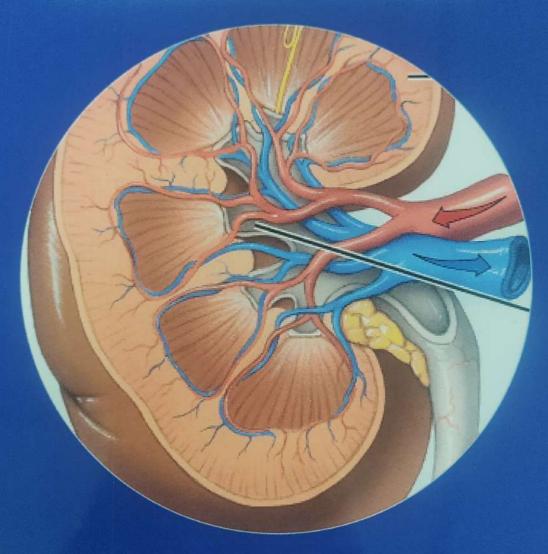


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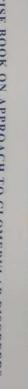
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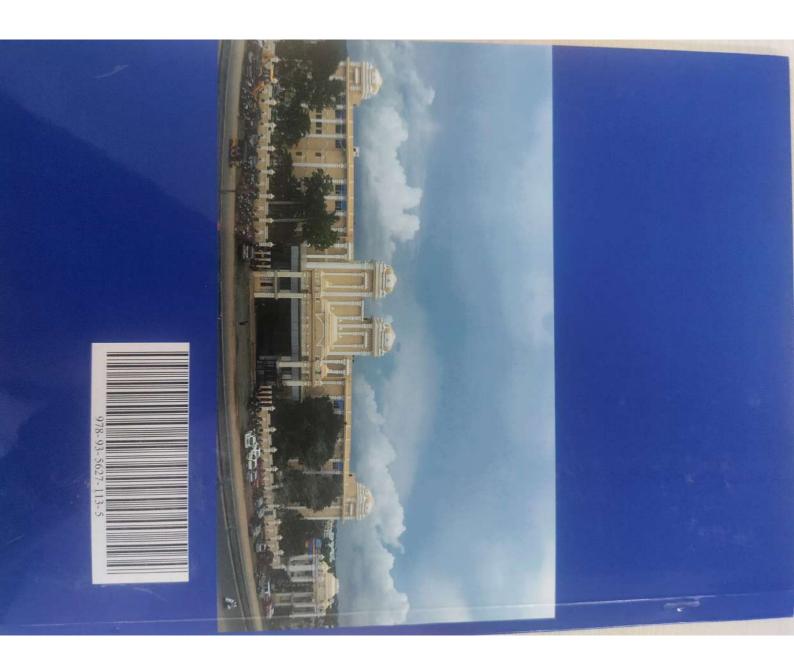
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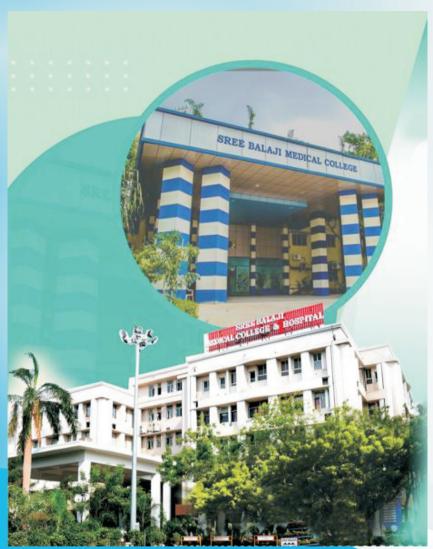
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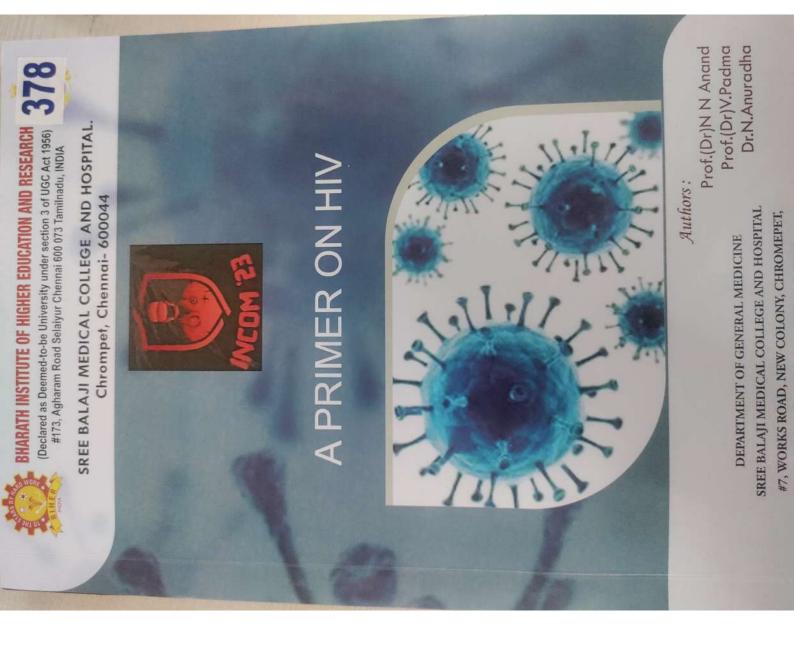
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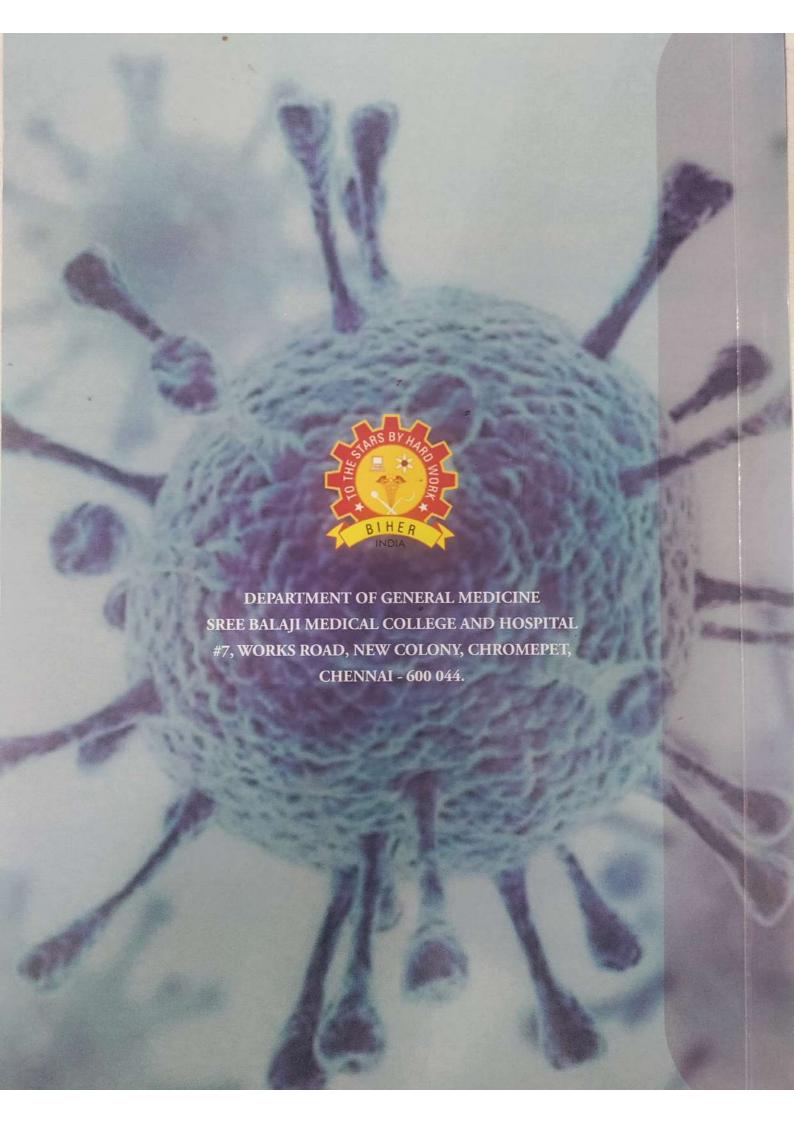
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Authors Dr. Yuvarani

Dr. Ayushi

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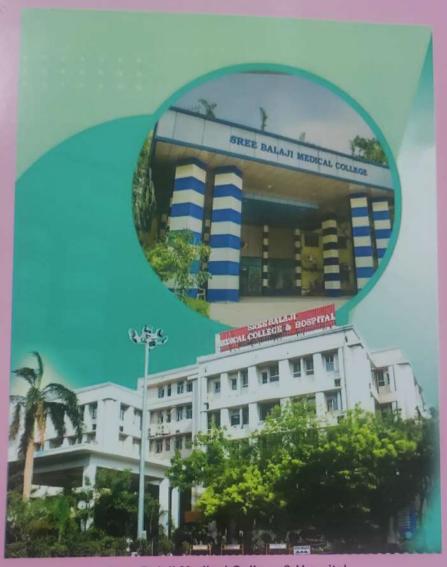
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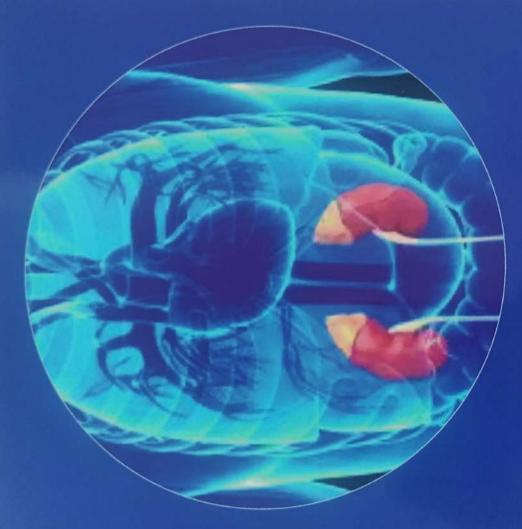








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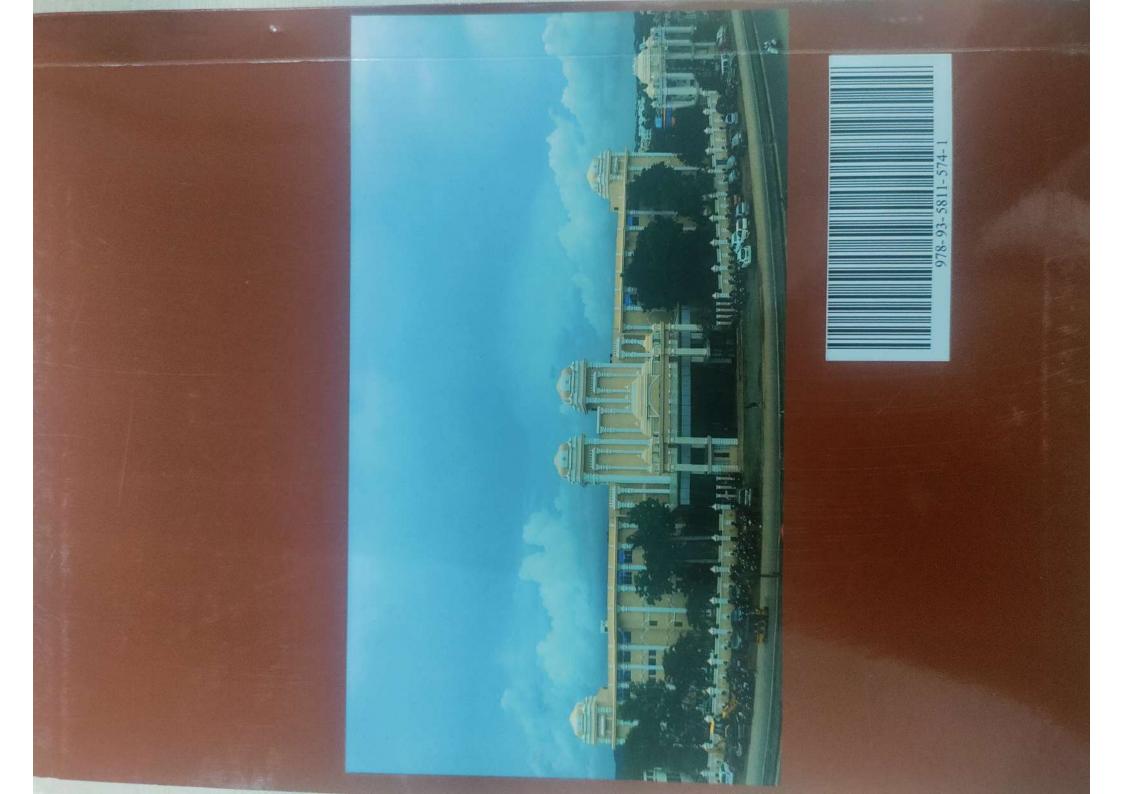
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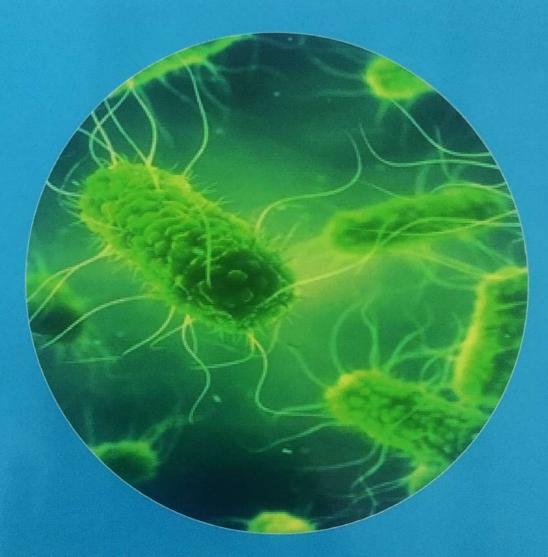


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Authors:

Dr. DEVIKA ANILKUMAR

Dr. MANIMEKALAI P

Dr. VINATHA MC

DEPARTMENT OF GENERAL MEDICINE SREE BALAJI MEDICAL COLLEGE AND HOSPITAL #7, WORKS ROAD, NEW COLONY, CHROMEPET, CHENNAI - 600 044.

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Author: DR. DEVIKA ANILKUMAR

Junior Resident General Medicine

Guide: DR. P MANIMEKALAI

Associate professor General Medicine

Co-Guide: DR M C VINATHA

Assistant Professor General Medicine

Sree Balaji Medical College and Hospital

Bharath Institute of Higher Education and Research (Declared as Deemed-to-be University under Section 3 of UGC Act 1956) Chennai- 600 100

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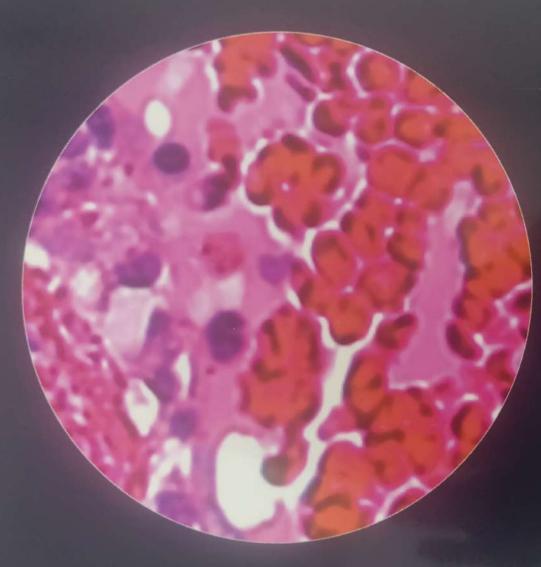




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Dr. Shangmuganandhan.K. Dr. Sujana. P. Reddy

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Author:

By:
Dr. Shanmuganandhan.K.
Professor
Dept of General Medicine
Sree Balaji Medical College and Hospital

Co- author: Dr. Sujana. P. Reddy 2nd year Post graduate Dept of General Medicine Sree Balaji Medical College and Hospital

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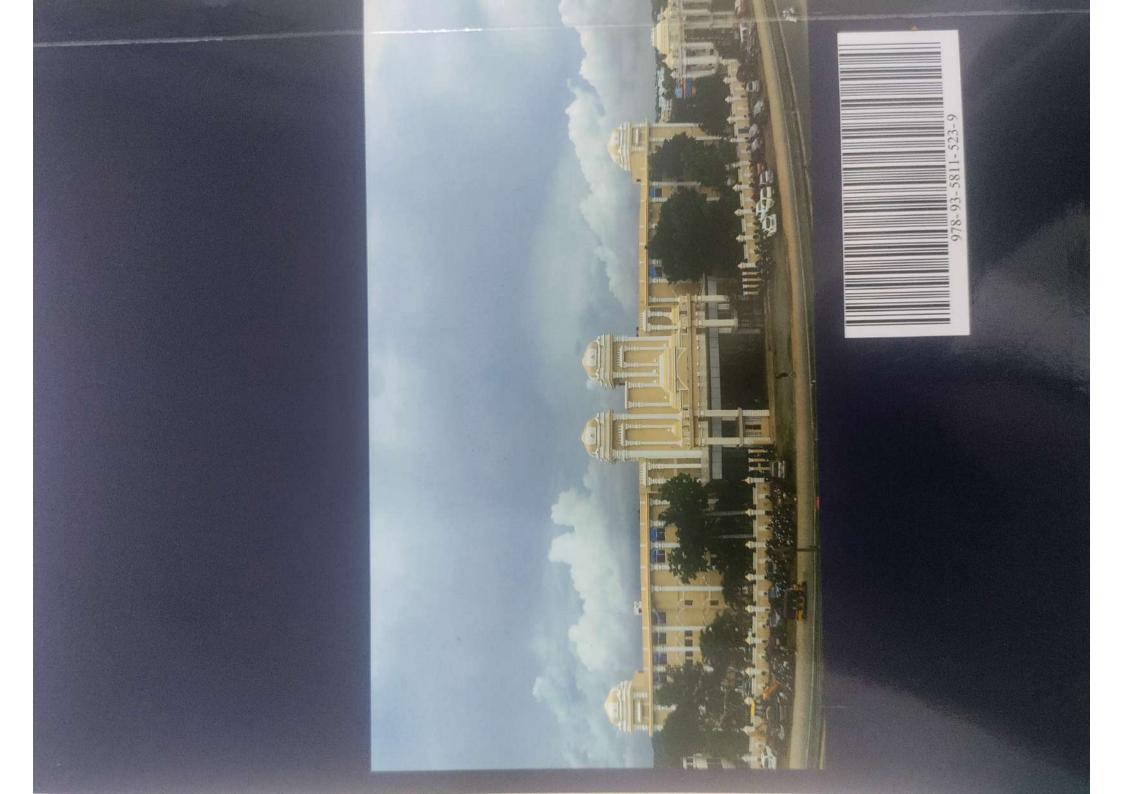
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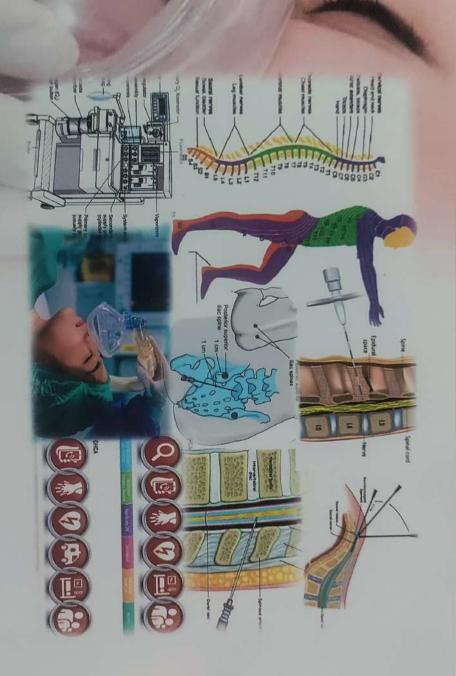
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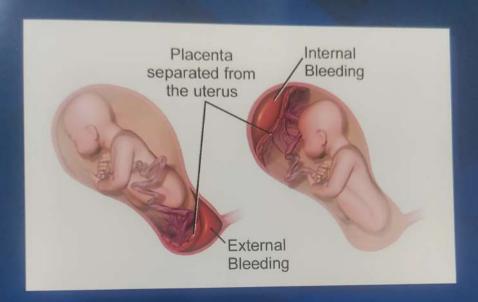
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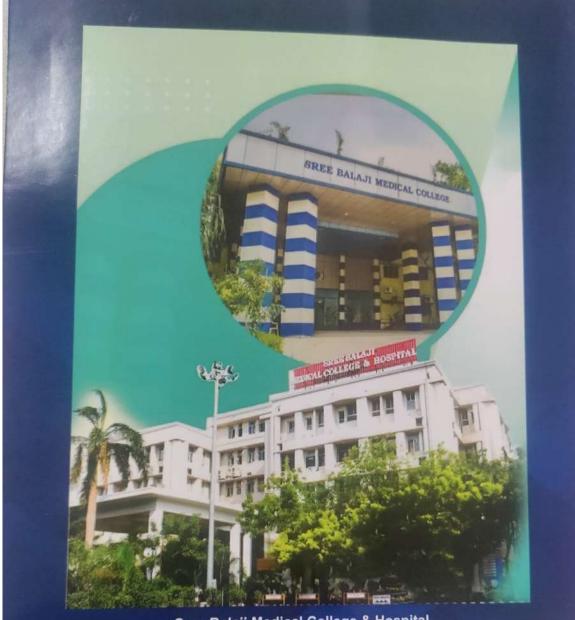
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AUTHOR:

Dr. KALAICHEZIAN., MDRD
DR.POONAM.C., MDRD RESIDENT
DR.SYEDHA FARIHEEN., MDRD RESIDENT.
DR.K.S.ESWAR., MDRD RESIDENT.
DR.MONIKA.R., MDRD RESIDENT.

Department of Radiology Sree Balaji Medical College and Hospital, BIHER, Chennai



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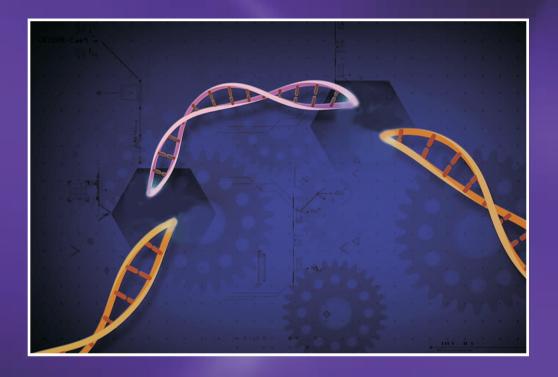
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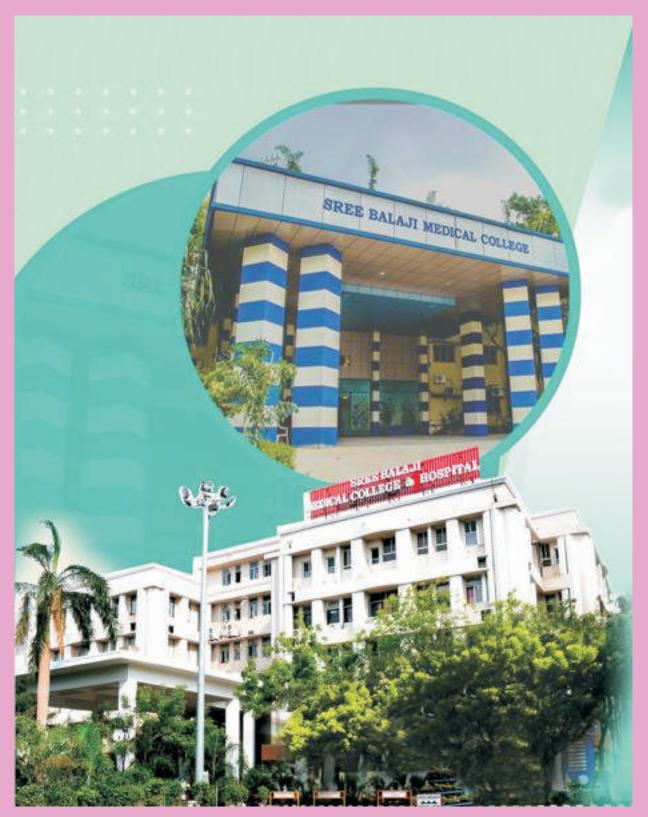
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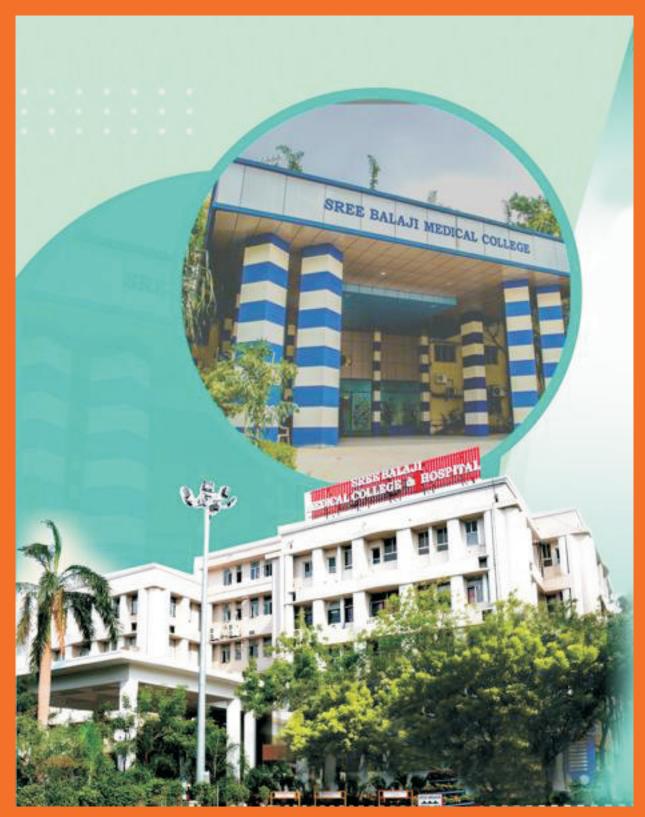
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Department of R & D Wing Sree Balaji medical college and Hospital chromepet-600044



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DR MYLA VIJAY KRISHNA YADAV DR ANANDAN P DR KARTHIKEYA T M

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A CONCISED BOOK ON CARDIOMYOPATHY



authors:

DR.BODDEPALLI MADHURI DR.A.SANKAR DR.UMASHANKAR

SREE BALAJI MEDICAL COLLEGE AND HOSPITAL #7, WORKS ROAD, NEW COLONY, CHROMEPET, DEPARTMENT OF GENERAL MEDICINE CHENNAI - 600 044.

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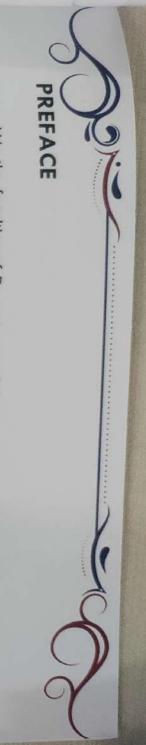


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Dr.P.Sujitha

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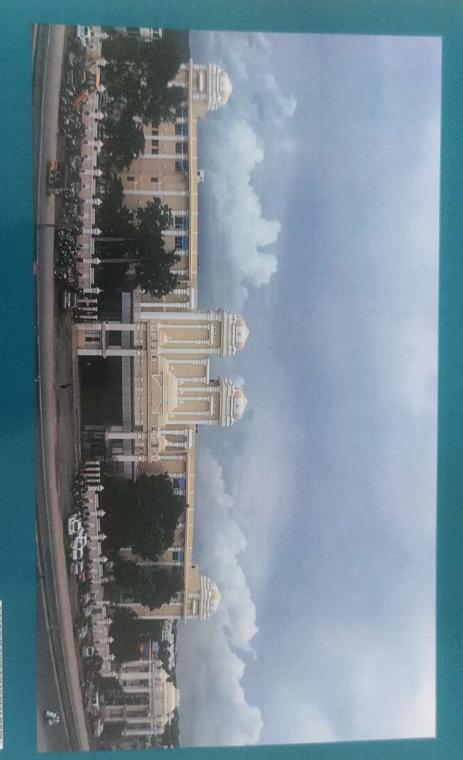
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Authors

Dr M.R. Renuka Devi, M.D.
Dr P.R. Devaki, M.D.
Dr S. Rajam Krishna, M.D.
Dr S. Parijatham, M.D.
Dr S. Sasikumar, M.D.
Dr J. Danti, M.D.



Department of Physiology Sree Balaji Medical College & Hospital Chromepet, Chennai - 600044.



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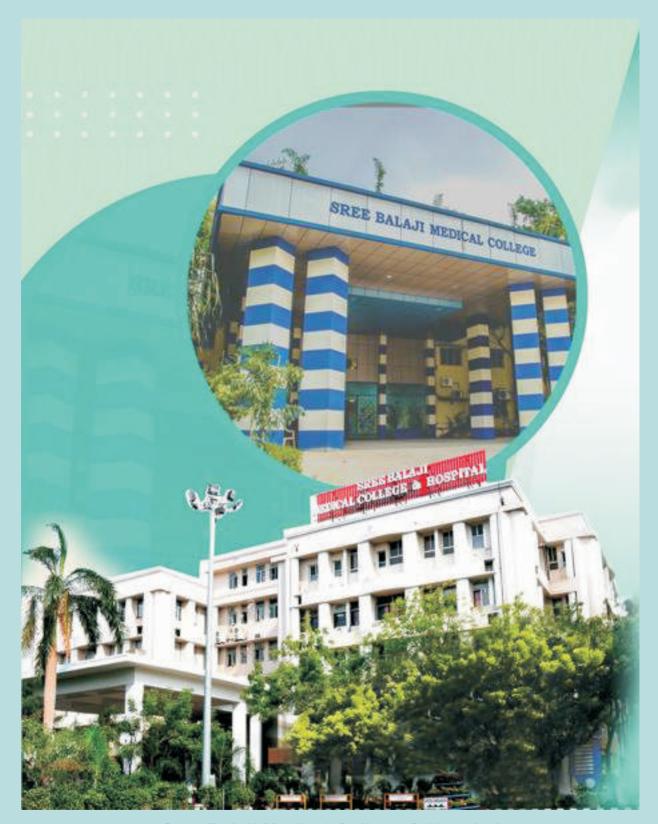
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SREE BALAJI MEDICAL COLLEGE AND HOSPITAL CHROMEPET, CHENNAI.



CHRONIC KIDNEY DISEASE

Author

Dr. Manimekalai P

Dr. Vinatha M C

Dr. Vishnuvarthan R S

Dr. NANDHYALA DURGA VENKATA SAINADH

DEPARTMENT OF GENERAL MEDICINE,
SREE BALAJI MEDICAL SCIENCES AND HOSPITAL,
CHROMEPET, CHENNAI-600044

CHRONIC KIDNEY DISEASE

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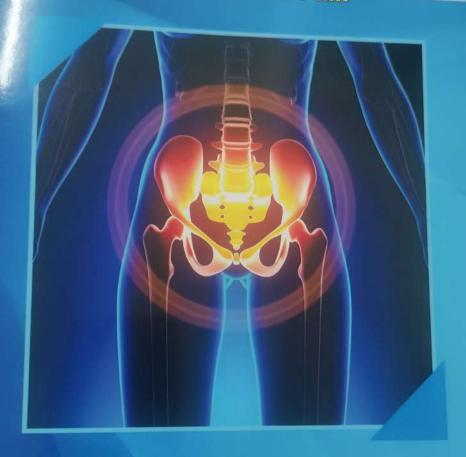
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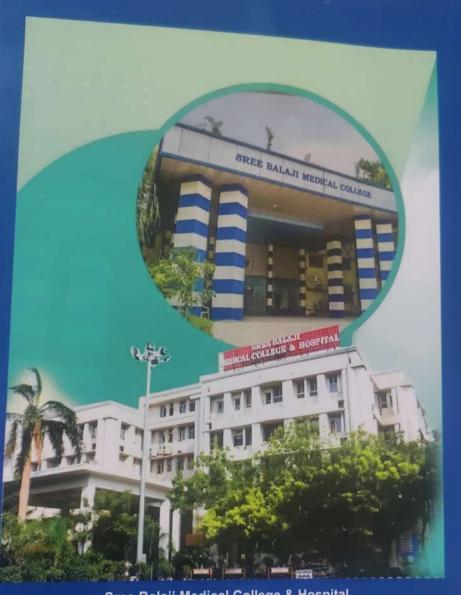
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Clinical Manual of ENT



Author

Dr. MK Rajasekar MS, DLO

Professor and Head Department of ENT, Head and Neck Surgery Sree Balaji Medical College and Hospital Bharath University, Chennai, Tamil Nadu

Co-Author

Dr. K.R Muralidharan

Junior Resident Department of ENT Sree Balaji Medical College and Hospital Bharath University, Chennai, Tamil Nadu

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Dr. MK Rajasekar MS, DLO

Professor and Head

Department of ENT, Head and Neck Surgery

Sree Balaji Medical College and Hospital

Bharath University, Chennai, Tamil Nadu

Co-Author

Dr. K.R Muralidharan

Junior Resident
Department of ENT
Sree Balaji Medical College and Hospital
Bharath University, Chennai, Tamil Nadu



Department of ENT

Sree Balaji Medical College & Hospital

Bharath Institute of Higher Education & Research (BIHER)

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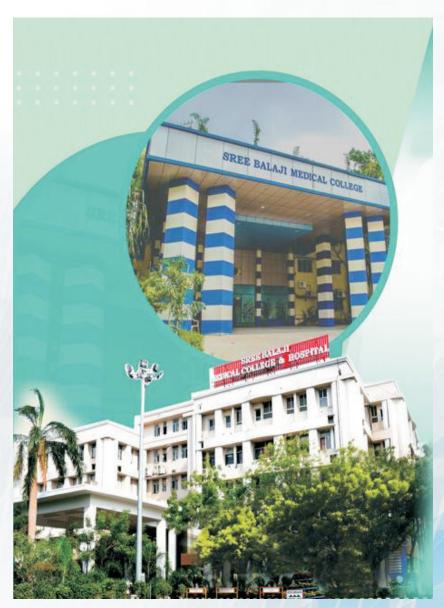
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E-mail: murali.aks@gmail.com





SREE BALAJI MEDICAL COLLEGE AND HOSPITAL CHROMEPET, CHENNAI.



CLINICAL PEARLS ON SEIZURE

Author

Dr. Manimekalai P

Dr. Vinatha M C

Dr. Vishnuvarthan R S

Dr. Arvindh Manohar

DEPARTMENT OF GENERAL MEDICINE,
SREE BALAJI MEDICAL SCIENCES AND HOSPITAL,
CHROMEPET, CHENNAI-600044

Clinical pearls on seizure

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Dr. Vinod M.D., Professor

Department of Anaesthesiology, Sree Balaji Medical College and Hospital, Chennai-45



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Competency Curriculum Based Biochemistry Practical Manual



Authors

Dr. B. Shanthi MD

Dr. V.S. Kalai Selvi MD

Dr. K. Sumathi MD

Dr. A. Mary Chandrika MD

Dr. S. Shenbagalalitha

Dr. Chaganti Sridevi MD

Dr. A. Jamuna Rani

Ms. Nivedhini.V.P

Mr. E. Vasudevan

Mrs. M Mahalakshmi

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Dr. B. Shanthi MD

Dr. V.S. Kalai Selvi MD

Dr. K. Sumathi MD

Dr. A. Mary Chandrika MD

Dr. S. Shenbagalalitha

Dr. Chaganti Sridevi MD

Dr. A. Jamuna Rani

Ms. Nivedhini.V.P

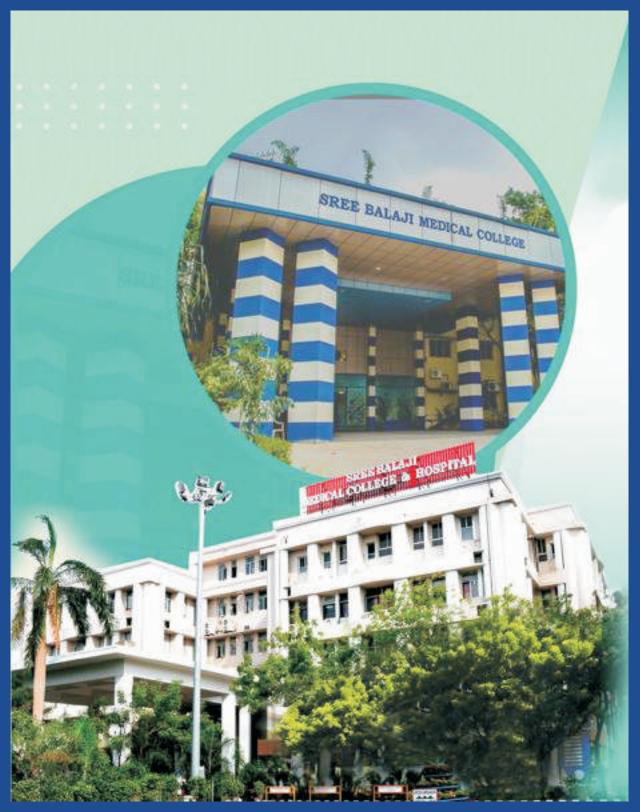
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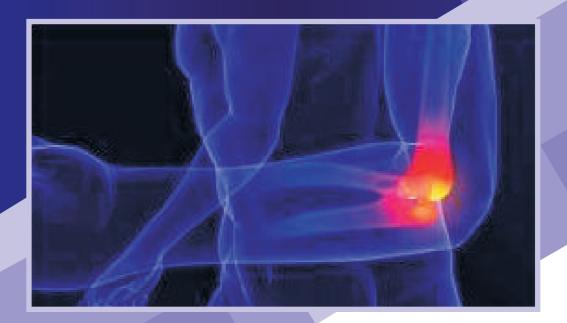
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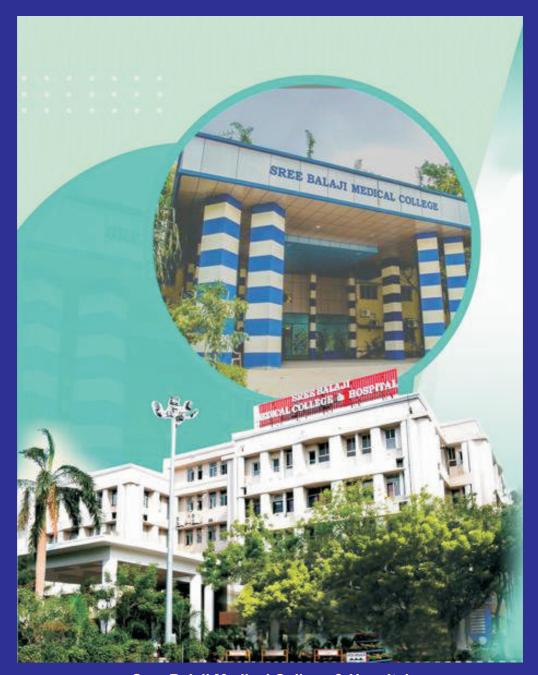
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CONCISE BOOK OF PRINCIPLES OF SHOULDER EXAMINATION

By
DR .VIJAY NARASIMMAN REDDY
DR . POOJA PRADEEP SURATWALA
DR . MERVINROSARIO

Department of Ortho, Sree Balaji Medical College and Hospital, Chennai



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- 7. Special Test



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A CONCISE MANUAL ON BIOMEDICAL WASTE MANAGEMENT



AUTHORS:

DR.R.UMADEVI

DR. V. NITHYA

DR. S.ABIRAMI

DR. S.SUSHMITHA SARAN

DR. S.G.SHOBANA PRIYA

DEPARTMENT OF COMMUNITY MEDICINE

SREE BALAJI MEDICAL COLLEGE AND HOSPITAL

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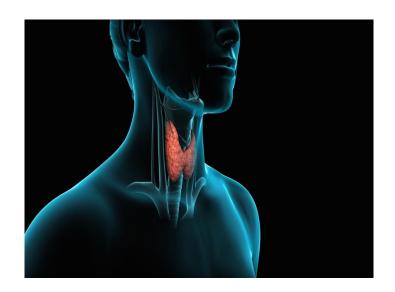
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Concise Note on HYPOTHYROIDISM &

HYPERTHYROIDISM

Dr.N.Anuradha

Dr A. Viknesh Prabhu.

Dr. Harshvardhan Patel

PREFACE

I am delighted to welcome you to my effort on one of my favorite topic from Endocrinology Thyroid Disorders. This Notes is geared toward providing a cogent navigation through the Thyroid Anatomy, Physiology, Thyroid hormone & Thyroid disorders. My challenge remains to be both concise and didactic, while still covering all relevant to Thyroid gland in an accessible and comprehensive fashion. For this book, I have added new images of symptoms of both Hypo & Hyperthyroidism, Thyroid gland scans of Grave's disease, MNG. These new contributions reflect the changing emphasis of endocrine practice today. Each section has undergone significant deep information and to bring the most attractive way to present information to readers.

There are so many Endocrine disorder for which the treatment algorithm is also getting evolved. Though the method of treatment might change, the basic modality or the first test that is done when any Thyroid disorder is suspected, is the Thyroid function test. By having a thorough knowledge of components of Thyroid gland anatomy, Thyroid hormone & it's function, Thyroid disorder, Thyroid test and its interpretation, diagnosis of early Thyroid disorder becomes possible. Early diagnosis and early treatment can prevent morbidity and mortality due to Thyroid disorder.

The main aim of this book is providing concise, accurate and up to date information on each components of the Hypothyroidism and Hyperthyroidism, making it easy for the budding practitioners and students to diagnose certain Thyroid disorders by enabling the practitioners to assess the Thyroid function test. This book mainly aims at the clinical aspect of each component of the Hypothyroidism and Hyperthyroidism separately and not aimed for academic purpose.

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DR V. VIJAY NARASIMMAN REDDY
DR LIONEL JOHN. J
DR MURALIDHARAN.R
DR M. KARTHIKEYAN

Department of Ortho, Sree Balaji Medical College and Hospital, Chennai



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DR LIONEL JOHN. J
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SREE BALAJI MEDICAL COLLEGE AND HOSPITAL CHROMEPET, CHENNAI.



CONCISE TEXT ON

SECONDARY HYPERTENSION

P. ANANDAN DEVANG J. BARAD

DEPARTMENT OF GENERAL MEDICINE,
SREE BALAJI MEDICAL SCIENCES AND HOSPITAL,
CHROMEPET, CHENNAI-600044

Concise Text on SECONDARY HYPERTENSION

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ABOUT THE BOOK

This book provides a broad overview of secondary hypertension for clinicians including physicians and general practitioners.

A large proportion of patients suffer from high blood pressure and it is currently thought that only 5-10% of all cases of hypertension are accounted by Secondary Hypertension. However, as our understanding in the field of secondary hypertension is growing due to the advent of new diagnostic tools and due to new research studies, it is being increasingly recognised that the proportion of secondary hypertension is higher than that thought previously. Still, secondary forms of hypertension are often overlooked or forgotten by clinicians in many fields of medicine. Unlike primary hypertension, the diagnosis and management of secondary hypertension involves other super-specialities also. This book allows the readers to have overview on secondary hypertension.



SREE BALAJI MEDICAL COLLEGE AND HOSPITAL CHROMEPET, CHENNAI.



Concise Text Book on HEART FAILURE

Author
Dr. Sankar
Dr. Umashankar
Dr. Alex

DEPARTMENT OF GENERAL MEDICINE,
SREE BALAJI MEDICAL SCIENCES AND HOSPITAL,
CHROMEPET, CHENNAI-600044

Concise text book on HEART FAILURE

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PREFACE

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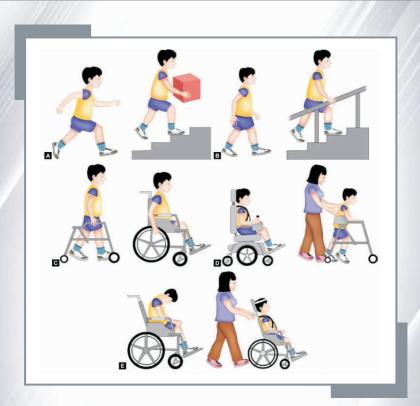
This book is written for healthcare professionals to gain depth of knowledge on heart failure in healthcare. It is suitable as a guide textbook for undergraduate and postgraduate training in the clinical aspects of informatics, and as an informative text book for professionals.

The text is designed to be used by all healthcare professionals, including nurses and allied health professionals, and not just medical practitioners. This book will guide you throughout all aspect on clinical judgement and challenges of heart failure. The book also gives you the latest updates which we believe will be fruitful for professionals.

DR SANKAR
DR UMASHANKAR
DR ALEX

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Professor & Head

Department of Paediatrics

Sree Balaji Medical College and Hospital

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Dr. S. Sundari. MBBS., DCH., MD (Paed)

Professor & Head

Department of Paediatrics

Sree Balaji Medical College and Hospital







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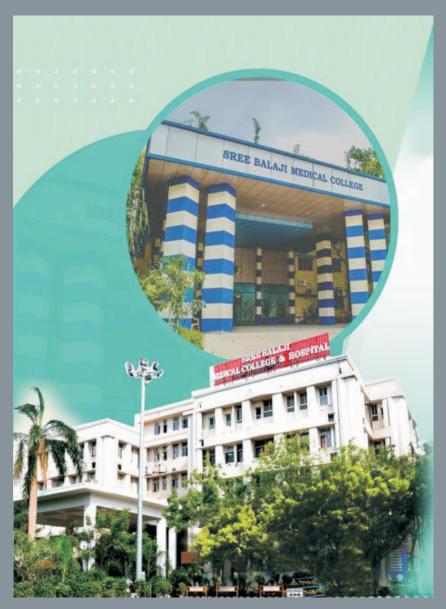
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E-mail: murali.aks@gmail.com



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E-mail: murali.aks@gmail.com





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CHROMEPET, CHENNAI.

CONCISE TEXTBOOK OF COVID – 19

Dr. N. ANURADHA
Dr. A. VIKNESH PRABU
Dr. K.M. VIGNESH

DEPARTMENT OF GENERAL MEDICINE,

SREE BALAJI MEDICAL SCIENCES AND HOSPITAL,

CHROMEPET, CHENNAI-600044

CONCISE TEXTBOOK OF

COVID - 19

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PREFACE

The world is fighting against the COVID-19 outbreak, which is now spread to more than 200 countries worldwide. There has been a huge loss of life, drastic changes in our way of life, disrupted plans due to travel restrictions and social distancing. Emerging and reemerging infectious diseases have plagued mankind and have been potential killers since historic times. The current pandemic of COVID-19 is the latest crisis that has challenged leadership and health infrastructures globally.

The COVID-19 pandemic has posted major challenges around the globe. The COVID-19 pandemic has taken us unprecedented, and management of comorbidities has become challenging as a consequence. With ever increasing case load, lack of efficient treatment and vaccine for prevention, there is increased demand on health-care workers, in terms of work hours, and also, they are faced by, increased risk of infection, physical stress, and associated physical illness due to use of personal protection equipment, mental health issues, and social issues. Thorough understanding of the impact of the ongoing pandemic on health-care work force is pivotal in appropriate management of the pandemic, as well as in ensuring the physical and mental well-being of health-care workers and prevent attrition of health-care work force.

Combating this malevolent virus requires sifting of facts from myths by means of worldwide available accurate scientific information that takes high moral ground and conveys research driven narratives. Strategies to enhance the antiviral potency of antiviral agents, vaccine, and ways to mitigate immunopathological host responses contributing to COVID-19 severity require further research in patients of COVID-19. Even after development of a specific drug/vaccine, this new disease is here to stay. Past experiences have taught us to learn to live with it and adjust our lifestyle accordingly.

We hope everyone to navigate the maze, learn the finer facts, which can help us stand united in the management of the Pandemic.

SYNOPSIS:

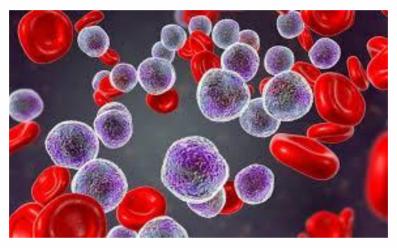
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CONCISE TEXTBOOK OF LEUKEMIAS



Authors:

Dr. N. Anuradha M.D

Dr. Harshvardhan Patel M.B.B.S

DEPARTMENT OF GENERAL MEDICINE, SREE BALAJI MEDICAL COLLEGE, CHROMEPET, CHENNAI-600044.

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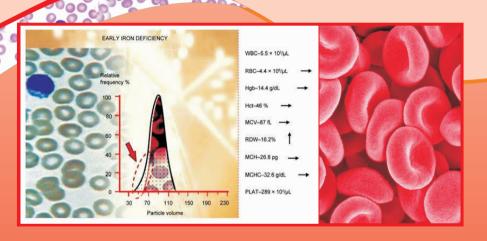
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Concise Text Book of RBC Disorder and Interpretation with Clinical Relevance



Authors

Dr. M. Preethi MBBS, MD. Dr. Kaushika MBBS



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Concise text book of RBC Disorder and Interpretation with Clinical Relevance

Dr. M. Preethi, MBBS, MD

Assistant Professor

Department of Pathology

Sree Balaji Medical College and Hospital

Bharath Institute of Higher Education and Research

Dr. Kaushika, MBBS

Postgraduate
Department of Pathology
Sree Balaji Medical College and Hospital
Bharath Institute of Higher Education and Research



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E-mail: murali.aks@gmail.com



Dr. M. Preethi

Dr.M.Preethi is currently working as Assistant Professor, department of Pathology at Sree Balaji Medical College and Hospital. She has 4½ years of working experience as diagnostic pathologist and teaching experience for undergraduate and postgraduate students. She has 3 patents and 15 paper publications in reputed journals to her credit. Her first book on 'Hand Book on Interpretation of Urine Analysis for General Practitioner' was well received by the Medical Community. Her interest and knowledge in the field of clinical pathology made her to write this book.



Dr. Kaushika

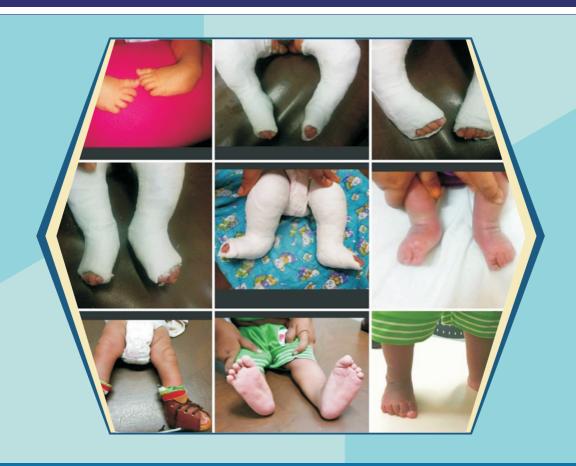
Dr.Kaushika is a senior resident in Pathology, Sree Balaji Medical College. She has authored two publications. She won the best poster award for '*Drug Profile and Management in Dengue*' in MAHER national summit on current research in science 2015. She presented a case study of an unimmunized child at the 56th Annual national conference of Indian Public Health Association in Kochi, in the year 2012.

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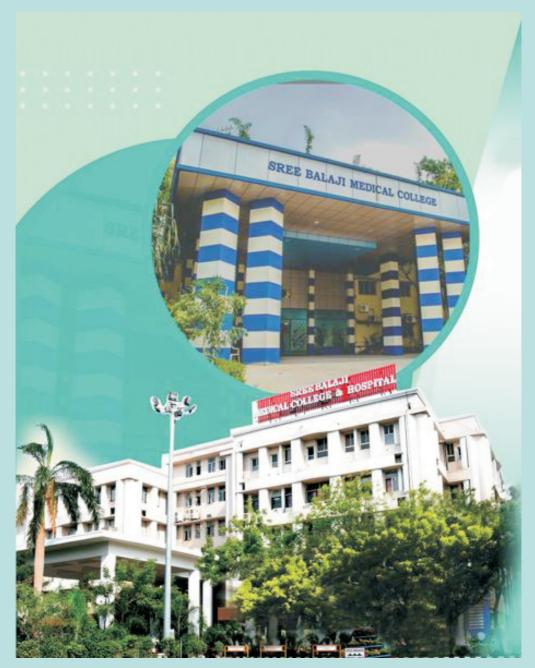
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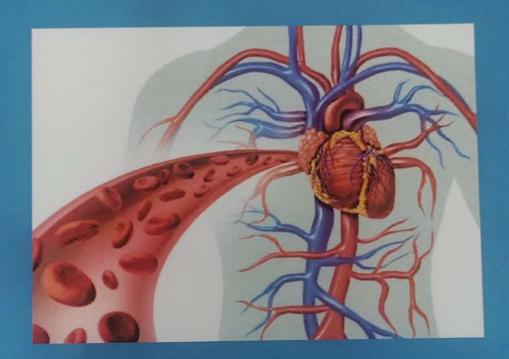


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ELECTRIFYING RESILIENCE: CONQUERING SHOCK DISEASE THROUGH EFFECTIVE MANAGEMENT



Authors:

DR.J.VISHALAKSHI DR.P.ANANDAN DR.KARTHIKEYA

DEPARTMENT OF GENERAL MEDICINE

SREE BALAJI MEDICAL COLLEGE AND HOSPITAL

#7, WORKS ROAD, NEW COLONY, CHROMEPET,

CHENNAI - 600 044.

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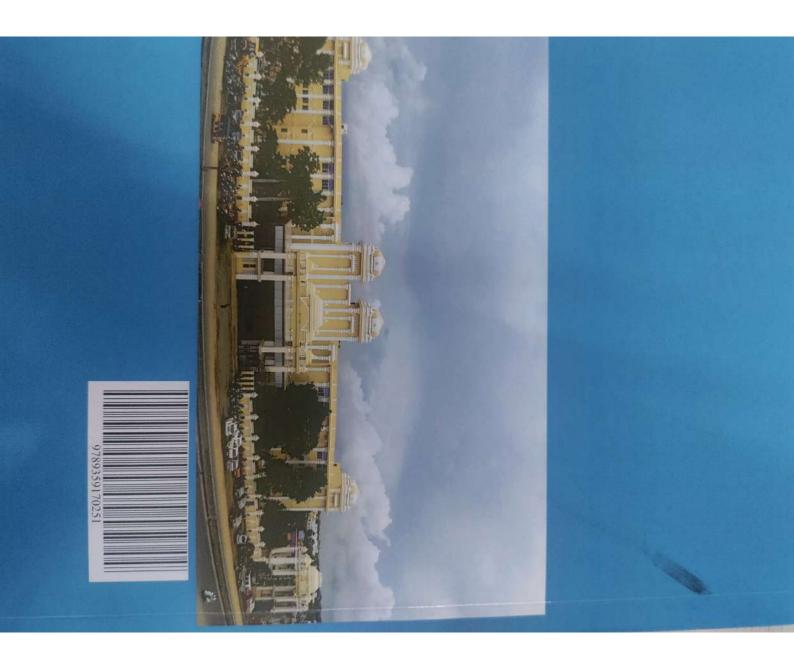
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CURRENT CONCEPTS IN MANAGEMENT OF GOUT

DR.K.SHANMUGANADAN
DR. NN ANAND
DR.SHWETHA SURESHBABU
DR.LOHITHA MALLIPEDDI
DR.KAVURU NAGA SIRI

DEPARTMENT OF GENERAL MEDICINE, SREE BALAJI MEDICAL SCIENCES AND HOSPITAL, CHENNAI

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INTRODUCTION

Gout is characterized by accumulation in the synovial fluid and other tissues of monosodiumurate monohydrate (MSU). It is the most common form of inflammatory arthritis. Its prevalence is about 3.9% in the United States, 0.9% in France, 1.4-2.5% in the United Kingdom, 1.4% in Germany, and 3.2% in New Zealand.

Gout production involves three distinct steps: long-standing hyperuricaemia Formation of crystals of monosodium urate monohydrate (MSU) Interaction between MSU crystals and the inflammatory process. The clinical signs of gout may include:

- Recurring inflammatory inflammation episodes (gout flare)
- A Chronic Disease
- Urate crystal deposition in the form of tophaceous deposits
- Nephrolithiasis of the uric acid
- A chronic nephropathy

that is most often caused by comorbid conditions in gouty patients, hyperuricemia is a necessary but not sufficient cause for developing urate crystal deposition disease and should be differentiated from gout, the medical disorder. Many people with hyperuricemia rarely undergo a medical occurrence arising from deposition of crystals.

Down Syndrome



Editors Dr. Shanthi Ramesh Professor

Dr. S. Sundari

Professor and Head Department of Paediatrics Sree Balaji Medical College & Hospital



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Professor

Dr. S. Sundari

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Department of Pediatrics Sree Balaji Medical College & Hospital Bharath Institute of Higher Education & Research (BIHER)



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ELECTROLYTE ABNORMALITIES AN OVERVIEW



Authors:

DR.KEERTHANA.I DR.SURESH KANNA.S DR.NAGASIRI

SREE BALAJI MEDICAL COLLEGE AND HOSPITAL #7, WORKS ROAD, NEW COLONY, CHROMEPET, DEPARTMENT OF GENERAL MEDICINE CHENNAI - 600 044.

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Author: DR.KEERTHANA!

Junior Resident General Medicine Guide: DR.SURESH KANNA S

Associate professor

General Medicine

Co-Guide: DR NAGASIRI NEELENDRA

Senior Resident General Medicine

(Declared as Deemed-to be University under section 3 go UGC Act 1956) Bharath Institute of Higher Education And Research Sree Balaji Medical College And Hospital

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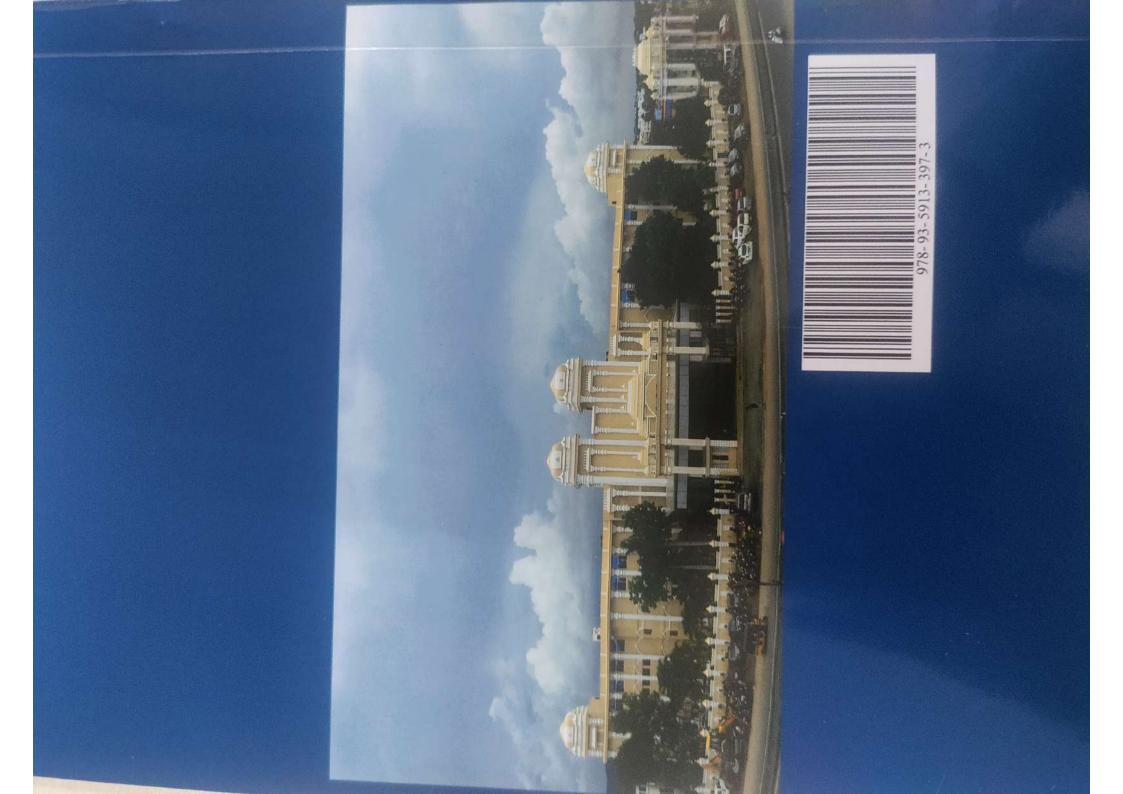
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EMPORIATRICS: An Overview

By Dr. Amritha Lekha. A. K

DEPARTMENT OF COMMUNITY MEDICINE SREE BALAJI MEDICAL COLLEGE AND HOSPITAL

Chrompet, Chennai- 600044



Discovery Publications

No. 9, Plot,1080A, Rohini Flats, Munusamy Salai, K.K.Nagar West, Chennai - 78. Tamilnadu, India.

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"ENDOCRINE FUNCTION TESTS"



Department of Biochemistry SREE BALAJI MEDICAL COLLEGE AND HOSPITAL #7, WORKS ROAD, NEW COLONY, CHROMEPET, CHENNAI - 600 044.

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Chennai-77

Editors

Dr.B.Shanthi

Dr.V.S.Kalai Selvi

Dr.K.Sumathi

Dr.A.MaryChandrika

Dr. A. Jamuna Rani

Dr.S.Shenbagalalitha

Dr.ChagantiSridevi

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Mr.E.Vasudevan

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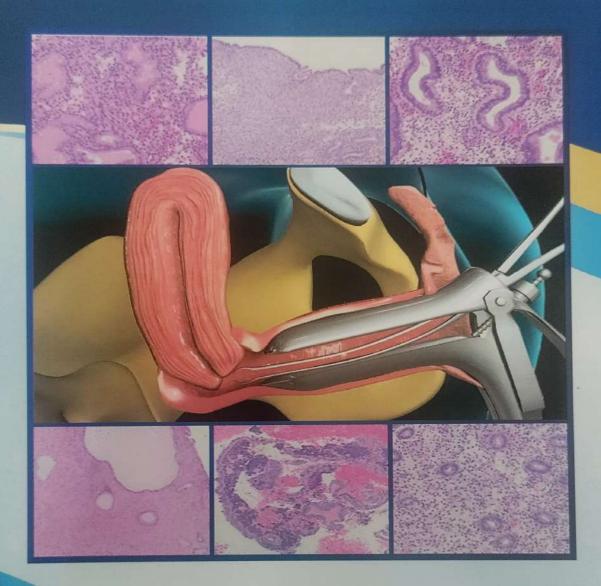
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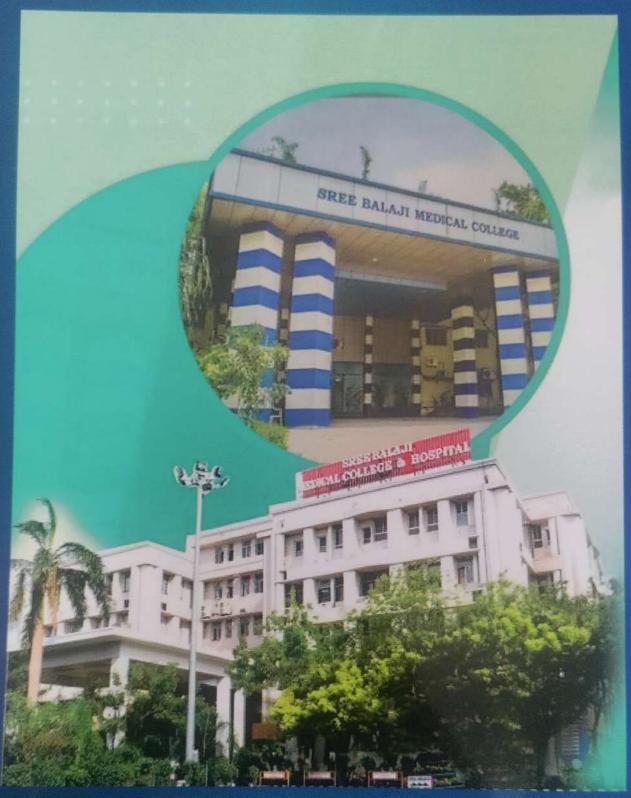
Authors
Dr. Veni
Dr. C. Mahalakshmi

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ESSENTIAL & RATIONAL USE OF MEDICINES IN PRIMARY HEALTH CENTRES

A MONOGRAPH

Dr.S.Gopalakrishnan. MD, DPH Professor, H.O.D

DEPARTMENT OF COMMUNITY MEDICINE SREE BALAJI MEDICAL COLLEGE AND HOSPITAL CHROMPET, CHENNAI. 600044

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ESSENTIAL NEWBORN CARE



Dr. S. Jagadeeswari, M.D D.CH,
Professor
Department of Pediatrics
SBMCH

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Essential Newborn Care

Dr. S. Jagadeeswari, M.D D.CH,

Professor
Department of Pediatrics
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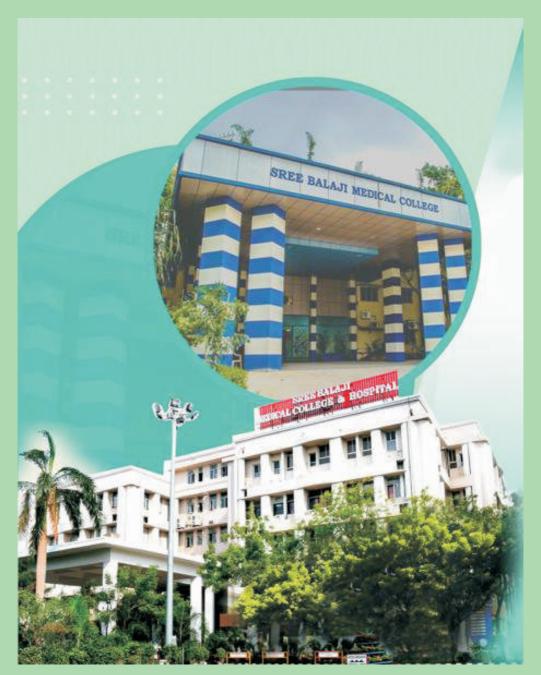
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ESSENTIALS OF BREASTFEEDING



Author Dr. SWETHA N B

SREE BALAJI MEDICAL COLLEGE AND HOSPITAL DEPARTMENT OF COMMUNITY MEDICINE #7, WORKS ROAD, NEW COLONY, CHROMEPET, **CHENNAI - 600 044.**

PREFACE

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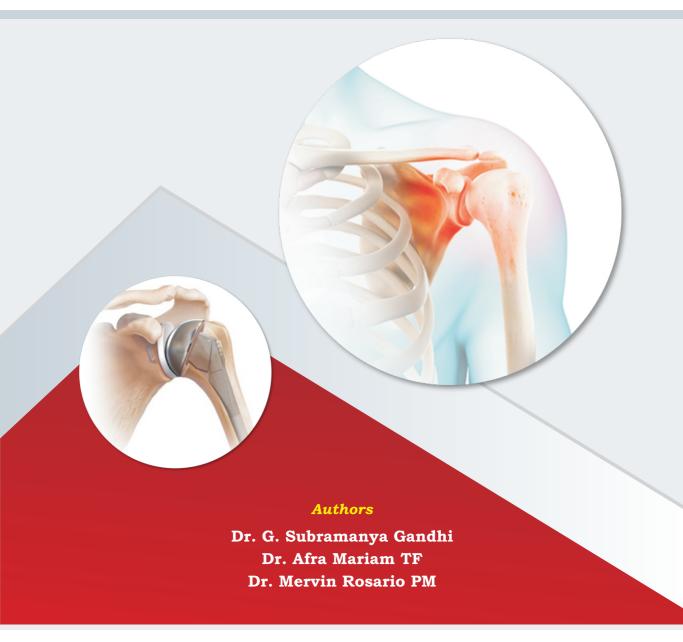
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Authors

Dr. G. Subramanya Gandhi Dr. Afra Mariam TF

Dr. Mervin Rosario PM







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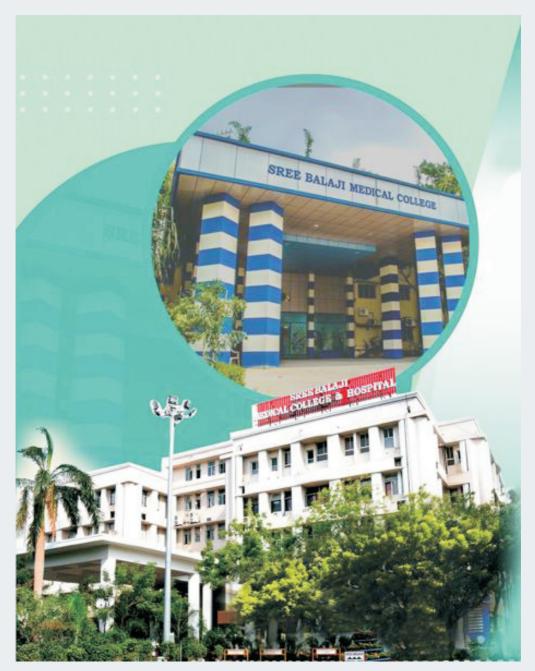
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E-mail: murali.aks@gmail.com



Experimental Studies On Antimicrobial Peptides By DR. SOFI BEAULA.W Assistant Professor

Research and Development Wing, Sree Balaji Medical College and Hospital (SBMCH), Bharath Institute of Higher Education and Research (BIHER), Chennai-600 044, India



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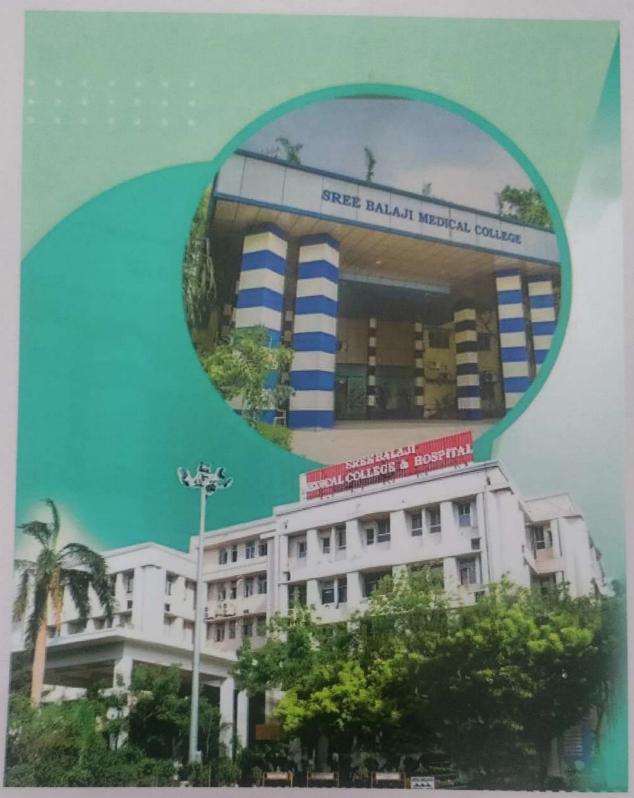
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Dr. Vidhya Selvam Dr. Sailekshmi

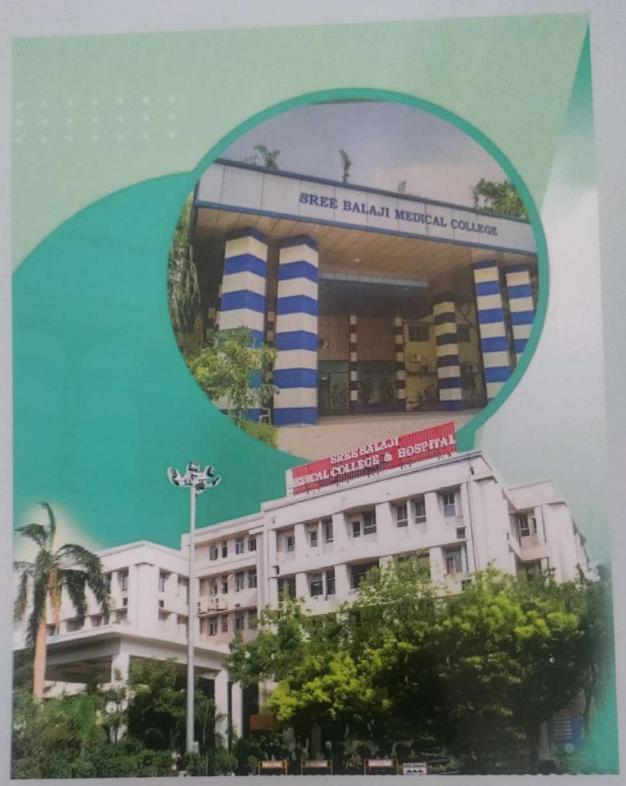
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E-mail: murali.aks@gmail.com





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Department of General Medicine
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Prof. Dr.V.Padma MD, PG Dip in Diabetology, CCEBDM, FIMSA, FACP, FRCP (Glasgow)

Prof. Dr.Brig.K.Shanmuganandan MD, DNB, EULARCC (Rheumatology)

Prof. Dr.Suresh Kanna MD, CCEBDM

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AUTHORS AND CONTRIBUTORS

- 1. Prof.Dr. P. Manimekalai MD
- 2. Prof.Dr. A. Sankar MD
- 3. Prof.Dr. N. Anuradha MD
- 4. Prof.Dr. P. Anandan MD
- 5. Prof.Dr. Vijay Edward MD
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- 23. Dr. Ram Prasaanth P MD Junior resident
- 24. Dr. R.Arvindraj MD Junior resident
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- 27. Dr.S. Sarath Bhaskar MD Junior resident
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- 34. Dr. Nandhyala Durga Venkata Sainadh MD Junior resident
- 35. Dr. Kalluru Padmalatha MD Junior resident
- 36. Dr. P. Kanmani MD Junior resident
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- 38. Dr. Patel Harshvardhan Anilbhai MD Junior resident
- 39. Dr. Srinivasa Rao Gopisetty MD Junior resident
- 40. Dr. R.Mathisha Ebby Perin MD Junior resident
- 41. Dr.A.P Goutham Kumar MD Junior resident
- 42. Dr. Devang Jivabhai Barad CTCCM, MD Junior resident
- 43. Dr. P. Benish Pius MD Junior resident

PREFACE

This textbook will function as a comprehensive guide for a physician - to dealing with the ailments, challenges facing the elderly and the disorders that prevail among the geriatric population.

In this book, we have dealt with educating the elders about insights into ageing, the ethical and legal challenges, atypical presentations of diseases, various disorders among the elderly, while throwing some light on the abuse faced by the elders. This book also gives an insight into palliative care of the elderly as well as public health awareness and vaccination of the elderly.

As there are limitations in evidence-based literature on geriatric medicine, so recommendations on medical care are often opinion and experience based.

The satisfaction of good geriatric care is often lost to many physicians, who become overwhelmed by the complexity of seemingly insurmountable problems in the elderly. This book aims to provide a structured, logical, and flexible approach to problem solving which we hope will give practical help for the physician, to improve the care given to older patients in various situations.

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Chapter 2: ETHICAL AND LEGAL CHALLENGES IN ELDERLY

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Chapter 6: ABUSE OF OLDER PEOPLE

Chapter 7: PALLIATIVE AND END OF LIFE CARE

Chapter 8: PREVENTION - PUBLIC HEALTHCARE, VACCINATION

GLOBAL PUBLIC HEALTH THREATS

By

Dr.S.Gopalakrishnan, Dr.M.Arunkumar, Dr.G.Angeline Grace, Dr.K.Renuka

Department of Community Medicine, Sree Balaji Medical College and Hospital, BIHER, Chennai-600044





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Published by:

Dr.S.ANBALAGAN Author:

Junior Resident

General Medicine

Dr.A.SANKAR Guide:

Associate professor

General Medicine

Dr. UMASHANKAR Co-Guide:

Assistant Professor

General Medicine

Sree Balaji Medical College And Hospital

Bharath Institute of Higher Education And Research

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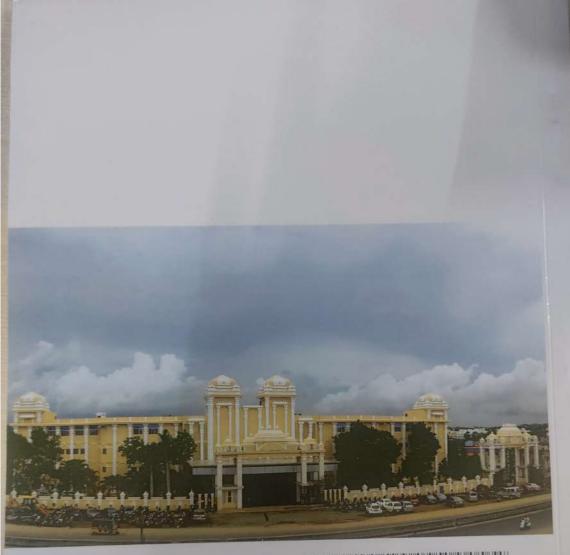
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HANDBOOK ON IV FLUID THERAPY



Dr. SURESH KANNA
Dr. MATHISHA EBBY PERIN.R

DEPARTMENT OF GENERAL MEDICINE
SREE BALAJI MEDICAL COLLEGE,
CHROMEPET, CHENNAI-600044.

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Authors

Dr. A. Mary Chandrika MD
Dr. B. Shanthi MD
Dr. K.Sumathi MD
Dr. Chaganti Sridevi MD

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Authors

Dr. A. Mary Chandrika MD, PhD Dr. B. Shanthi MD Dr. K. Sumathi MD Dr. Chaganti Sridevi MD, PhD Mr. E. Vasudevan MSc, PhD



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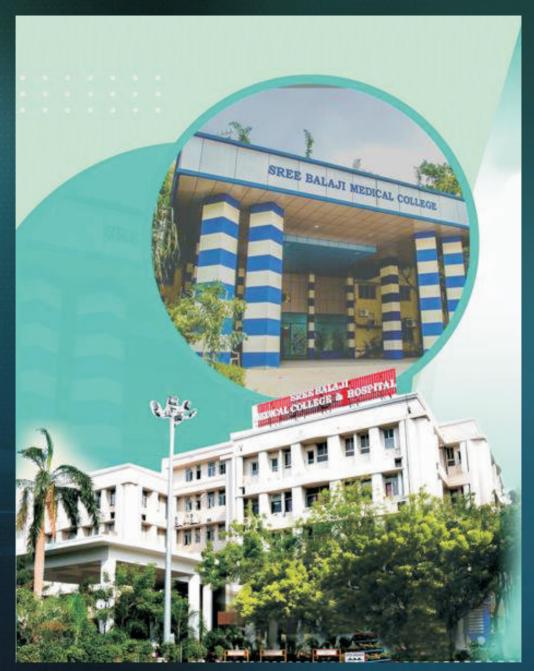
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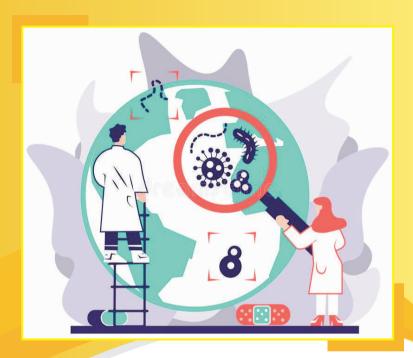


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A HANDBOOK ON OUTBREAK INVESTIGATION



Dr. V. Priya

Department of Microbiology Sree Balaji Medical College and Hospital

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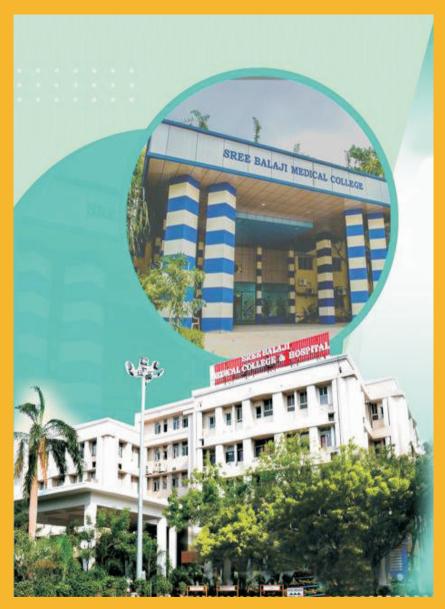
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E-mail: murali.aks@gmail.com



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E-mail: murali.aks@gmail.com



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By

Dr.S.Gopalakrishnan, Dr.M.Arunkumar, Dr.G.Angeline Grace, Dr.K.Renuka





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HEATH EDUCATION METHODS & MATERIALS

By

Dr. S. GOPALAKRISHNAN Dr. M. ARUNKUMAR Dr. G. ANGELINE GRACE

DEPARTMENT OF COMMUNITY MEDICINE, SREE BALAJI MEDICAL COLLEGE AND HOSPITAL, CHROMEPET, CHENNAI-44.



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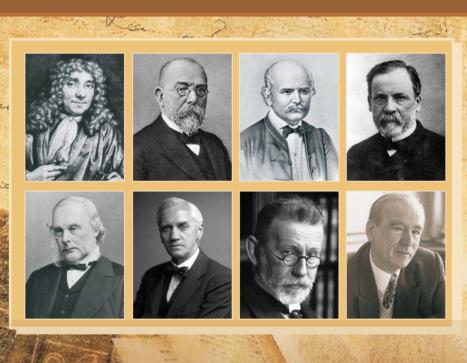
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Dr. R. Praveena



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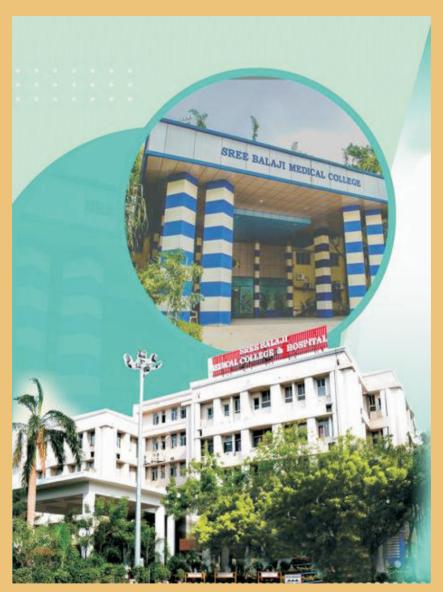
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HOMOCYSTEINE AND HYPERHOMOCYSTEINEMIA

V PADMA MD, FRCP, FACP, FIMSA

Professor, Department of Internal Medicine Sree Balaji Medical College and Hospital, Chennai, Tamil Nadu, India

SAKETH RAMINENI, MBBS

Junior Resident, Department of Internal Medicine Sree Balaji Medical College and Hospital, Chennai, Tamil Nadu, India

Editorial Office

Prof. Dr V Padma

Professor Department of Internal Medicine

Sree Balaji Medical College and Hospital,

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Contributing Authors:

Dr Sandhya P C MD

Dr SatyaPriya S V MD

Dr Abhilash B Nair MBBS

Dr Sarath Bhaskar S MBBS

Dr Kannan Meera Devi MBBS

PREFACE



Homocysteine is a grossly underated topic. "Homocysteine and hyperhomocysteinemia" is a small step in assimilating all the important information that an clinician may need in their day to day practise and also help young budding doctors in their quest for knowledge and hopefully help them in achieving their quest.

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DR.NIRANJAN.K., MDRD RESIDENT.

Department of Radiology, Sree Balaji Medical College and Hospital, Chennai



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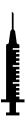


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An overview of

HYPER-COAGULABLE STATES

Prof.Dr.PADMA V | Dr SARATH BHASKAR.S



PREFACE

Hypercoagulability is a state when a fluid becomes congealed from a liquid to semisolid state called coagulum. When this hypercoagulability happens to the blood it leads to the formation of thrombus, the process is termed as coagulation. In a normal healthy individual maintaining hemostatsis coagulation is physiological manifestation in response to any trauma or bleeding. The absence of this coagulation cascade in the individual will cause bleeding manifestations like haemophilia and other platelet disorders. The over-exaggerated coagulation or coagulation in lack of bleeding is a pathology of hypercoagulability. The interaction of aberrant blood constituents forms the thrombus. Thrombophilic diseases and different hypercoagulable states will cause hypercoagulability. Arterial manifestations like myocardial infarction, stroke; venous manifestations like deep vein thrombosis, pulmonary embolism differs in pathophysiology and treatment with overlapping risk factors.

The aim of this book is to furnish our knowledge about the hypercoagulability and to ameliorate our algorithm of approach to various disorders in the line. It helps to segregate the abundant topics comes under this condition. It will be useful for better understanding of the topics in a precise manner.

I sincerely thank my Prof.Dr.Padma V for guiding me throughout the journey to complete this book. And I am very grateful for the support from the Head of the Department - Prof.Dr.Anand.N.N. and other faculties of General Medicine for their insight in this handbook.

ABOUT THE BOOK

Hypercoagulability is an increased tendency to cause thrombosis. The aetiology can be in acquired and inherited factors. It predisposes to arterial, venous and micro vascular complications. Hypercoagulability itself is a risk factor for venous thrombotic and atherothrombotic events. Some prevalent inherited hypercoagulable states are factor v Leiden mutation and prothrombin G20210A which is due to factor v and prothrombin gene mutation. The other inherited hypercoagulable states are due to deficient of antithrombin, protein C and protein S. Mutation in methyl tetrahydrofolate reductase cause raised homocysteine which is a misconception of inherited hypercoagulable state. Antiphospholipid syndrome is a significant factor for acquired hypercoagulability. It's a secondary response to rheumatological and Other acquired conditions lymphoproliferative conditions. are heparin thrombocytopenia, paroxysmal nocturnal hemoglobinuria, myeloproliferative malignancies etc,.Malignancy associated venous thromboembolism differs with type of malignancy and management.

Hypercoagulability can be suspected, when the patient presents with

- A. Idiopathic thrombotic events at any age
- B. Family history of venous thromboembolism
- C. Thrombosis at unusual sites
- D. Recurrent unprovoked thrombosis
- E. Recurrent unexplained foetal loss
- F. Warfarin induced skin necrosis
- G. Purpurin fulminans
- H. Recurrent superficial thrombophlebitis

This book focus on the overview of hypercoagulable conditions and its manifestations in a precise manner. It is to fetch the knowledge among the medical practitioners and students for preventing the cascade of thrombotic events and to get better prognosis in management.



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"AN OVERVIEW OF HYPERMOBILITY SYNDROMES".



Authors:

Dr.(Brig) k SHANMUGANANDAN Dr MANOJ KUMAR RAVILLA.

DEPARTMENT OF GENERAL MEDICINE

SREE BALAJI MEDICAL COLLEGE AND HOSPITAL

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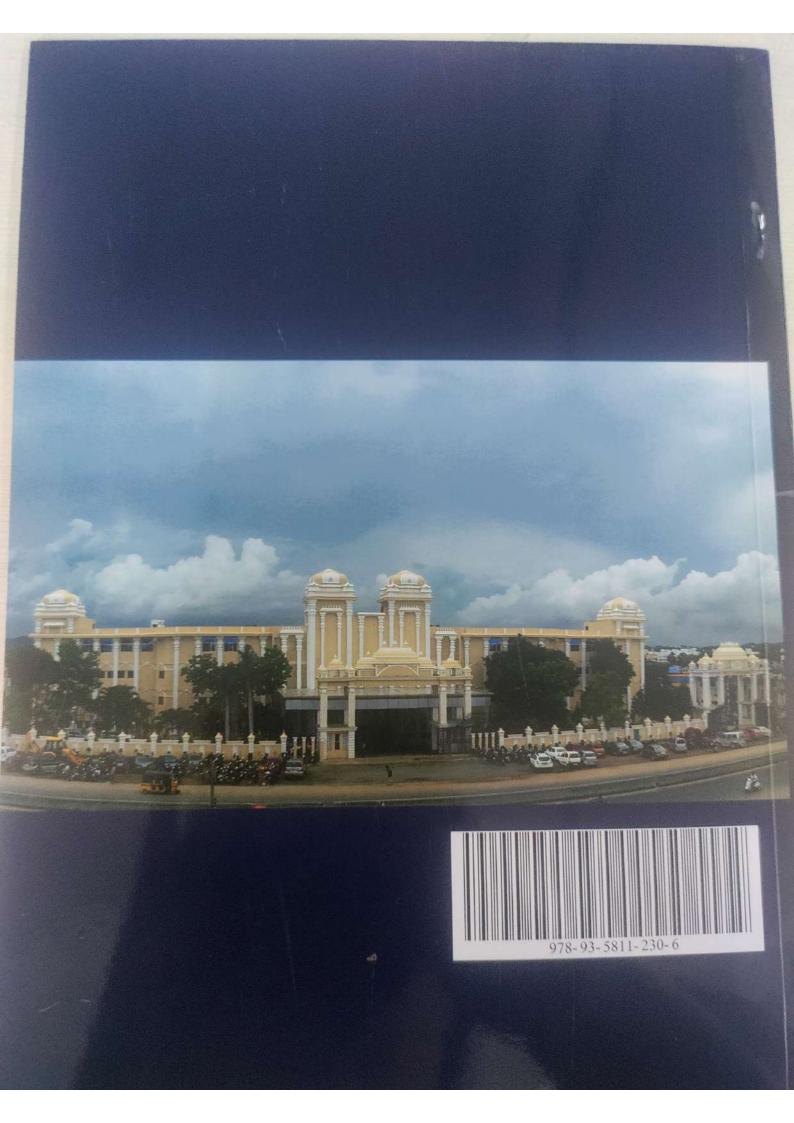
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Imaging And Intervention In Gastrointestinal Hemorrhage

AUTHOR:

Dr. Naveen.p., Mdrd Dr.poonam.c., Mdrd Resident Dr.jatin.v.k., Mdrd Resident. Dr.manpreet Singh., Mdrd Resident.

Department of Radiology, Sree Balaji Medical College and Hospital, Chennai



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Department of Radiology, Sree Balaji Medical College and Hospital, Chennai



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Dr. NAVEEN.P., MDRD DR.POONAM.C.,
MDRD RESIDENT DR.JATIN.V.K.,
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Department of Radiology, Sree Balaji Medical College and Hospital, Chennai



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Imaging signs in brain, head, neck and spine - Newer and the lesser known ones

Venkatraman Indiran MD, DNB

Professor, Department of Radio-diagnosis, Sree Balaji Medical College and Hospital,

Bharath Institute of Higher Education and Research (BIHER),

Chennai, Tamilnadu, India

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Preface

Signs are always a pleasant way to know and remember things in radiology. Sometimes classic

Auntminnie signs help in directly clinching the diagnosis. Sometimes the knowledge of newer signs help

us in putting our money on one of the two close differentials. Though the classic signs are well known

among the radiology residents, I have tried to focus on the newer and lesser known ones, so that the book

could be helpful for the practicing radiologists and clinicians (brain and spine surgeons, neurologists,

ENT surgeons) as well as the residents and medical students. The drawback of this book is the absence of

the images, but I hope the appropriate references mentioned with the signs is helpful in pointing the

readers to the relevant published articles. I hope every reader of the book learns find at least 10 percent of

the signs new and find them helpful in their day-to-day practice.

Venkatraman Indiran MD,DNB

Professor, Department of Radio-diagnosis, Sree Balaji Medical College and Hospital,

Bharath Institute of Higher Education and Research (BIHER),

Chennai, Tamilnadu, India

Email: ivraman31@gmail.com

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INFLAMMATORY BOWEL DISEASES



Authors:

DR BOPPANA VENKATA PURNESH DR MANIMEKALAI P DR VINATHA MC

DEPARTMENT OF GENERAL MEDICINE

SREE BALAJI MEDICAL COLLEGE AND HOSPITAL

#7, WORKS ROAD, NEW COLONY, CHROMEPET,

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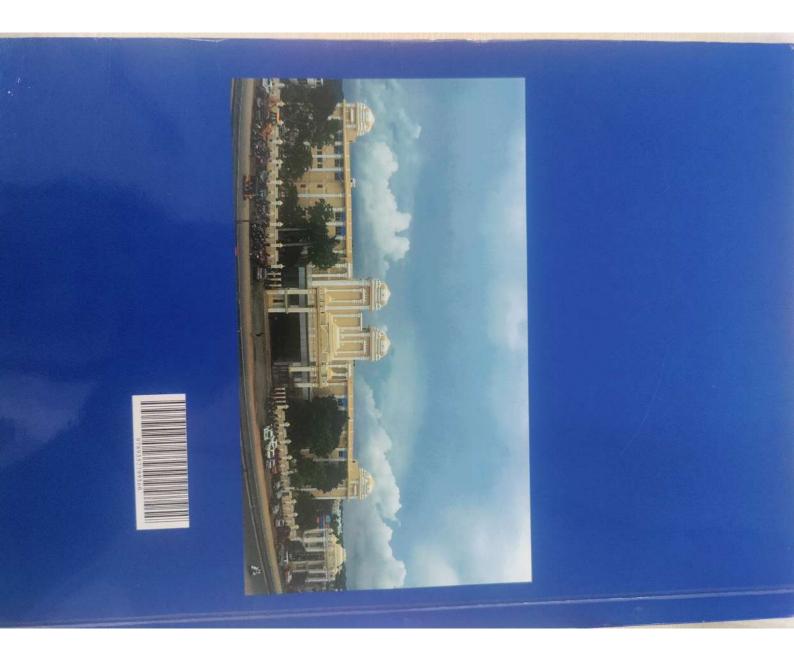
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INSTRUMENTS IN ENT



Author Dr. M K Rajasekar MS, DLO

Professor and Head Department of ENT, Head and Neck Surgery Sree Balaji Medical College and Hospital Bharath University, Chennai, Tamil Nadu

Co-Author

Dr. K.S Sarenya

Junior Resident Department of ENT Sree Balaji Medical College and Hospital Bharath University, Chennai, Tamil Nadu



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Author

Dr. M K Rajasekar MS, DLO

Professor and Head
Department of ENT, Head and Neck Surgery
Sree Balaji Medical College and Hospital
Bharath University, Chennai, Tamil Nadu

Co-Author

Dr. K.S Sarenya

Department of ENT Sree Balaji Medical College and Hospital Bharath University, Chennai, Tamil Nadu







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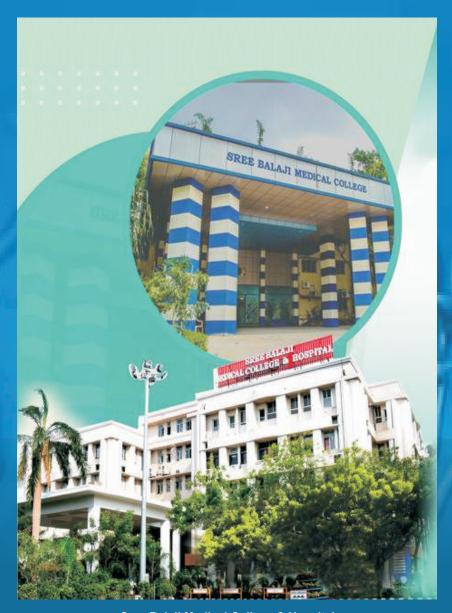
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Mrs Ashni Bhandari

Statistician, Department of Community Medicine, SBMCH



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DR A SANKAR

DR UMASHANKAR R

DR K PADMALATHA

DEPARTMENT OF GENERAL MEDICINE, SREE BALAJI MEDICAL COLLEGE, CHROMEPET, CHENNAI-600044.





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Dr. S.Selvamani M.D., D.A., Professor Dr. Bhagya vardhan.B MBBS., M.D., Assistant Professor

Department of Anaesthesiology Sree Balaji Medical College and Hospital, BIHER, Chennai-600044



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Authors:

-Dr. Dinesh Reddy.

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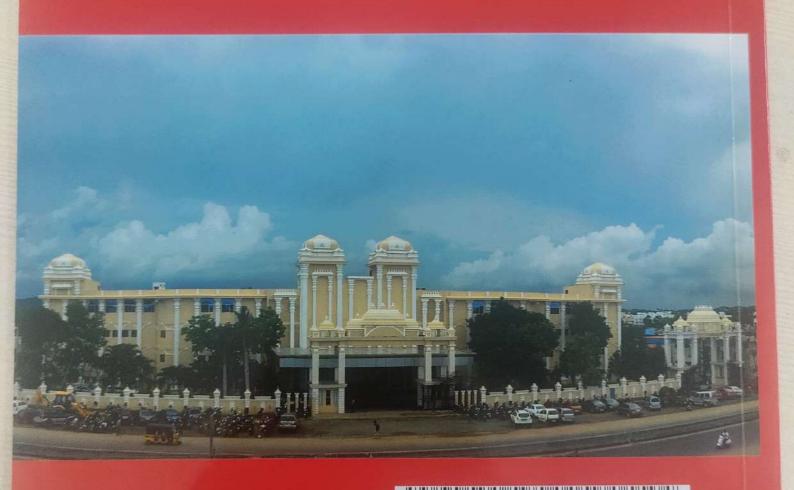
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Authors:

DR RANGEELA P DR ANANDAN P DR KARTHIKEYA T M

DEPARTMENT OF GENERAL MEDICINE

SREE BALAJI MEDICAL COLLEGE AND HOSPITAL

#7, WORKS ROAD, NEW COLONY, CHROMEPET,

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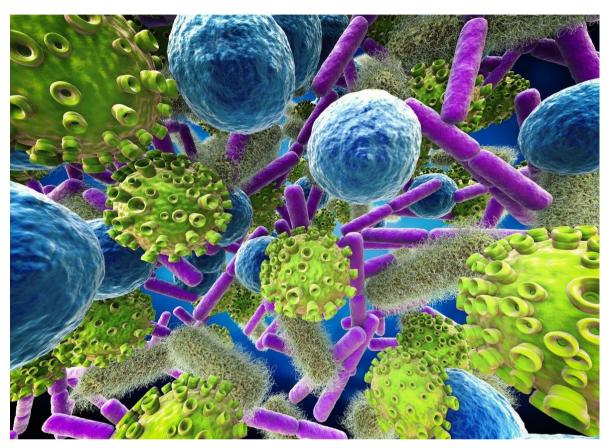
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Department of Physiology,
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VOLUME 1

AUTHORS

DR. SURESH KANNA S

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ABOUT THE BOOK

The myopathies are among the most fascinating group of disorders both to treat and to study. However, although symptoms relating to the muscles such as myalgia, fatigue and cramps are extremely common, most of the myopathies are very rare indeed. It is therefore difficult for a clinician with an average practice to gain much experience in the recognition of different types of muscle disease, let alone their optimum management. Myopathies in Clinical Practice brings together the latest knowledge of the subject, and provides the general clinician with a concise yet comprehensive manual for their encounters with myopathies. The content is biased towards clinical assessment and those disorders that are commonest or of particular importance.

PREFACE

Textbook on Myopathy Evaluation and Treatment covers the approach to a patient suspected to have myopathy it also comprise the different types of myopathy which include muscular dystrophy, congenital myopathy, metabolic myopathy, endocrine myopathy, myositis, and those associated with general medical conditions, including critical illness myopathy. advent of gene analysis, the Despite the diagnostic use electrophysiologic technique still has its place as a screening test. Needle studies contribute not only in differentiating myogenic from neurogenic in delineating the distribution of paresis but also myopathic abnormalities. The patterns classically associated with myopathy may occasionally result from neurogenic involvement in late stages. Nerve conduction studies may mimic a neuropathic process of the motor axons with a reduction of compound muscle action potentials and preservation of sensory nerve potentials. This chapter describes a simplified overview of the major disorders commonly encountered in an electrophysiologic laboratory with emphasis on clinical and physiologic features rather than the molecular mechanism.



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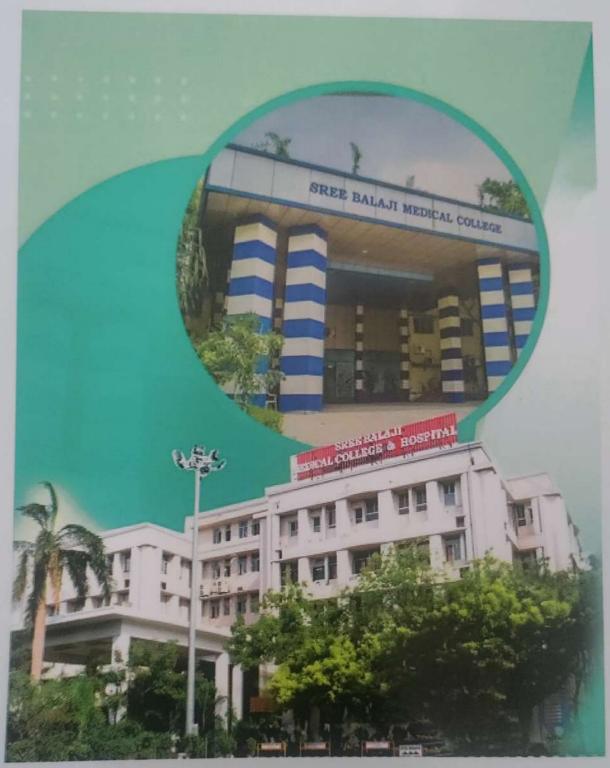
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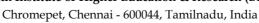
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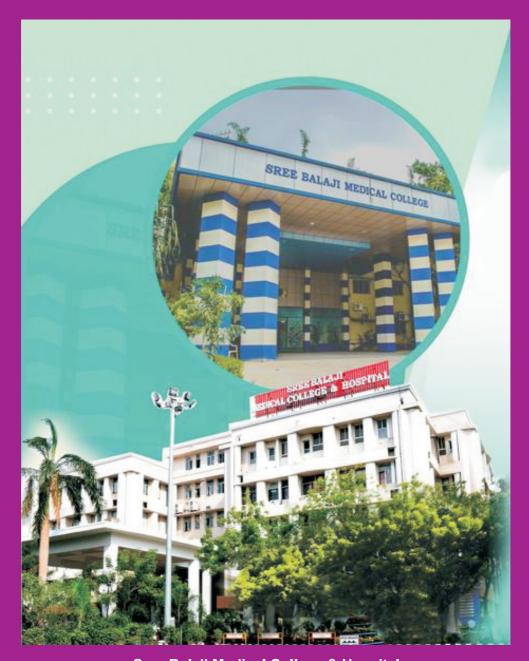
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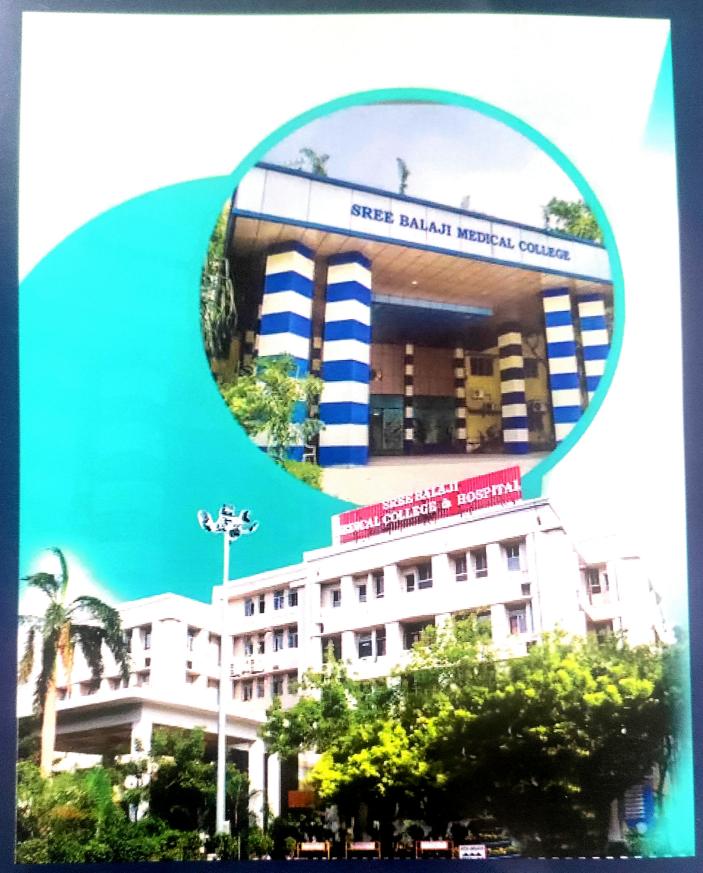
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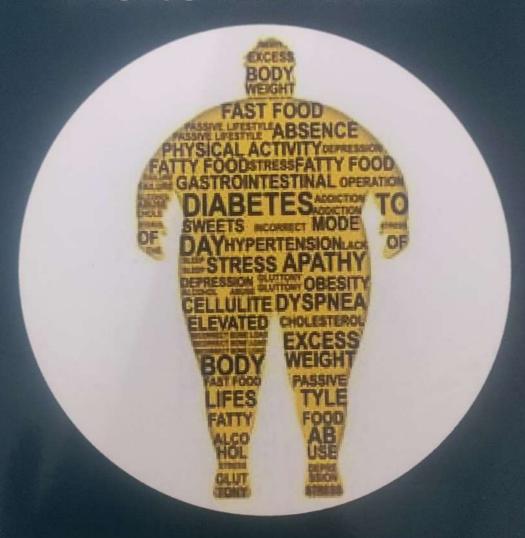


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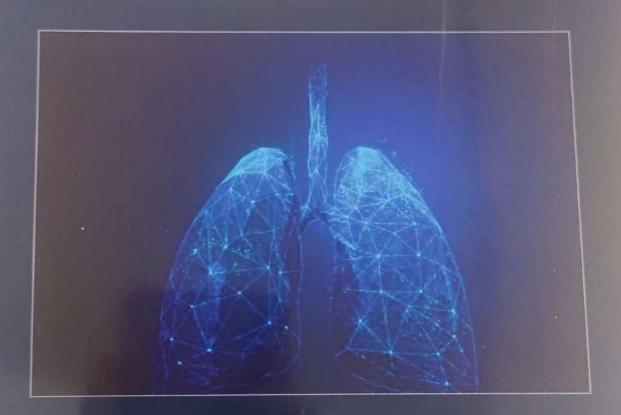


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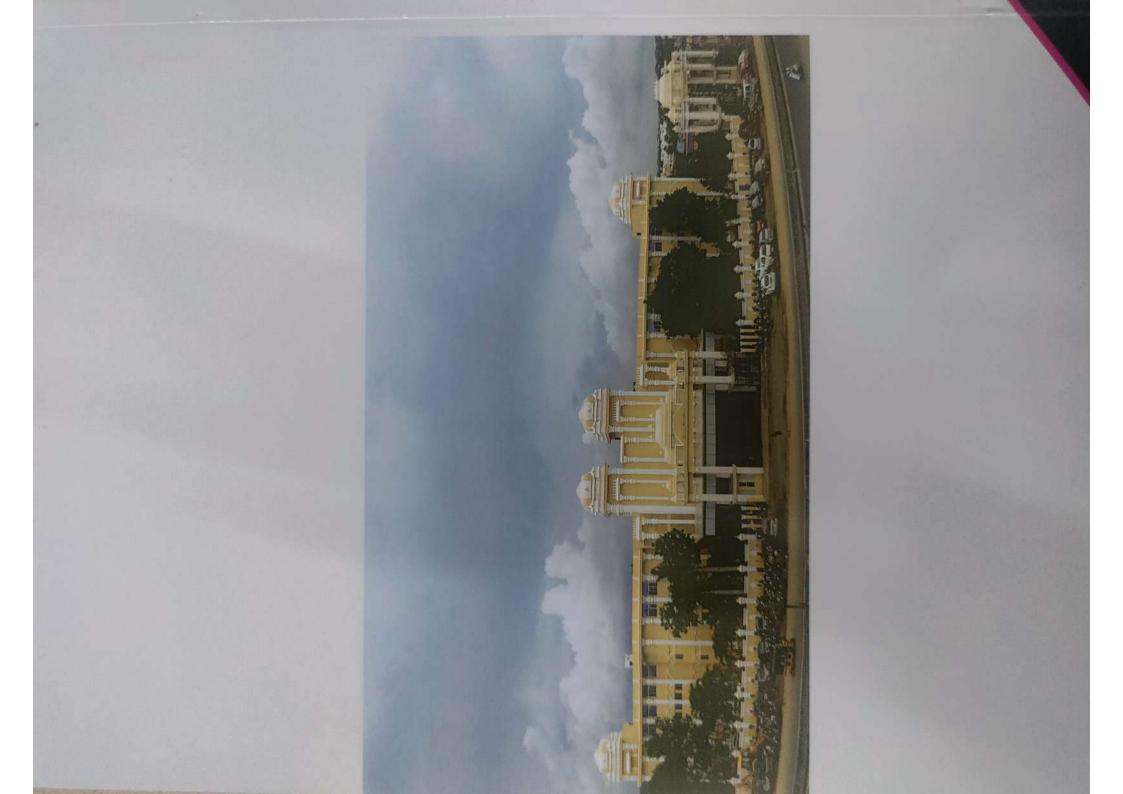
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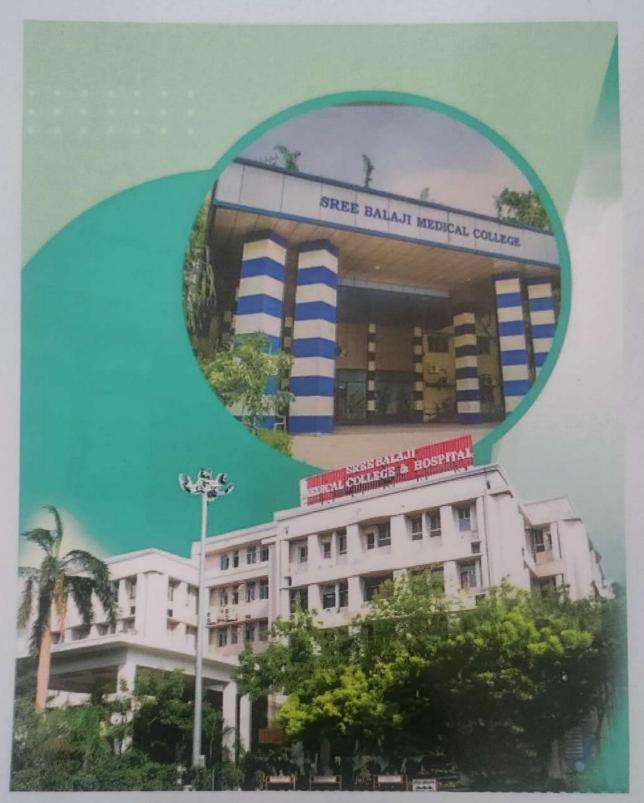
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Pediatric Radiology: Chest, Head, Abdomen

AUTHOR:

Dr. VENKATRAMAN.I., MDRD, ASSOCIATE PRO-FESSOR DR.POONAM.C., MDRD RESIDENT DR.SYEDHA FARIHEEN., MDRD RESIDENT. DR.NIRANJAN.K., MDRD RESIDENT.

Department of Radiology, Sree Balaji Medical College and Hospital, Chennai



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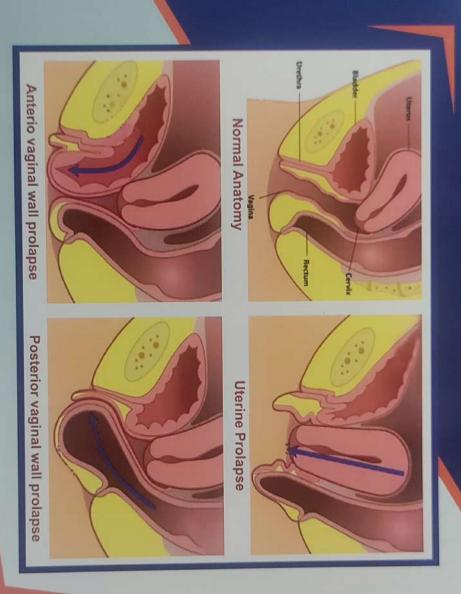
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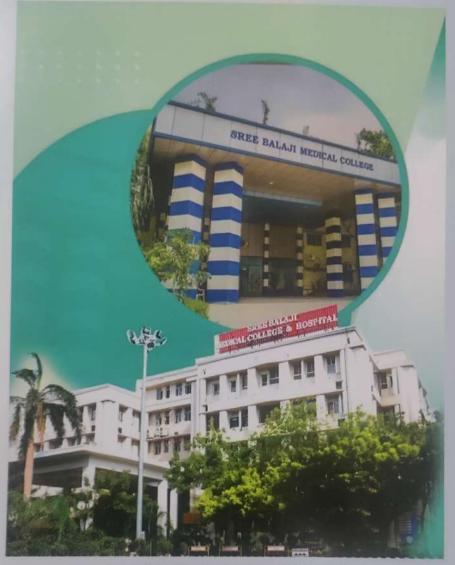
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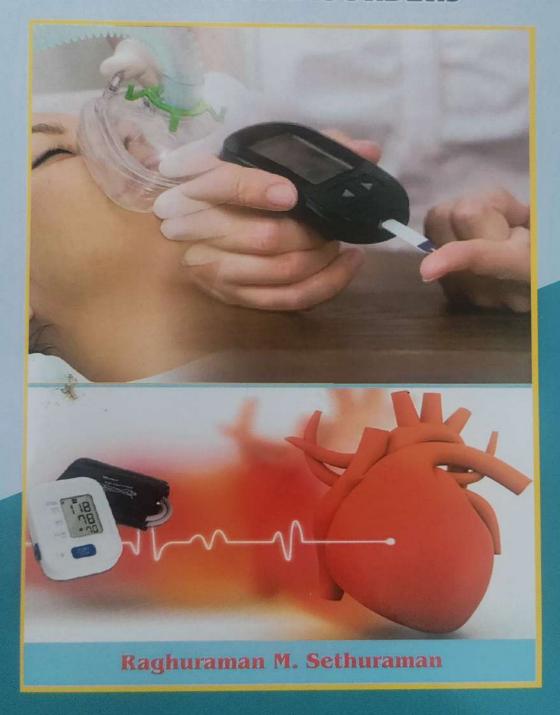
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PERIOPERATIVE MANAGEMENT OF COMMON DISORDERS





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About the Book



Diabetes and hypertension are the two most common diseases prevailing in the world currently.

Once considered as "lifestyle diseases" pertaining mainly to the western part of the world is no

Raghuraman M. Sethuraman longer true as these disorders have become very common in developing countries too. It is imperative that the anesthesiologists, also known as "Perioperative physicians", should be well-versed with these conditions and the drugs used for controlling them because they do have a major impact on anesthetic management. Yet, the guidelines to manage these two conditions during the perioperative phase are lacking in our country. Hope this book would be very helpful in guiding the perioperative team of physicians while managing these common medical conditions during surgeries.

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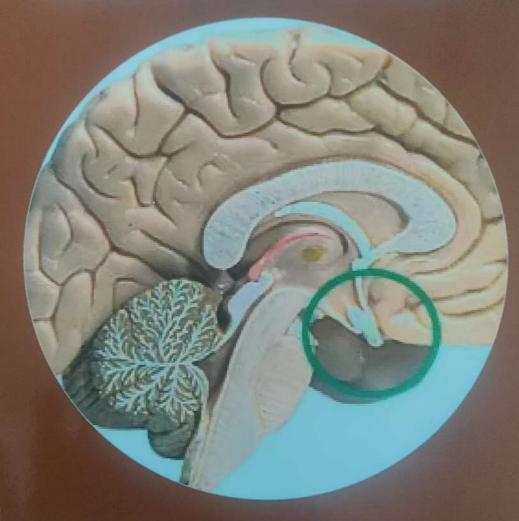


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A CONSICE BOOK ON PITUITARY GLAND AND ITS DISORDERS



Authors:

DR.N ANURADHA DR.VIKNESH PRABU DR. KONDA SANJITH

DEPARTMENT OF GENERAL MEDICINE

SREE BALAJI MEDICAL COLLEGE AND HOSPITAL

#7, WORKS ROAD, NEW COLONY, CHROMEPET,

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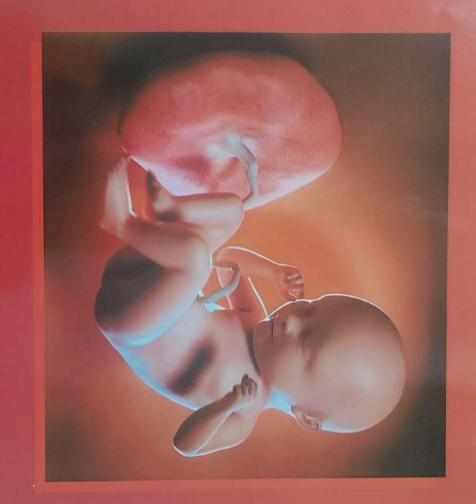
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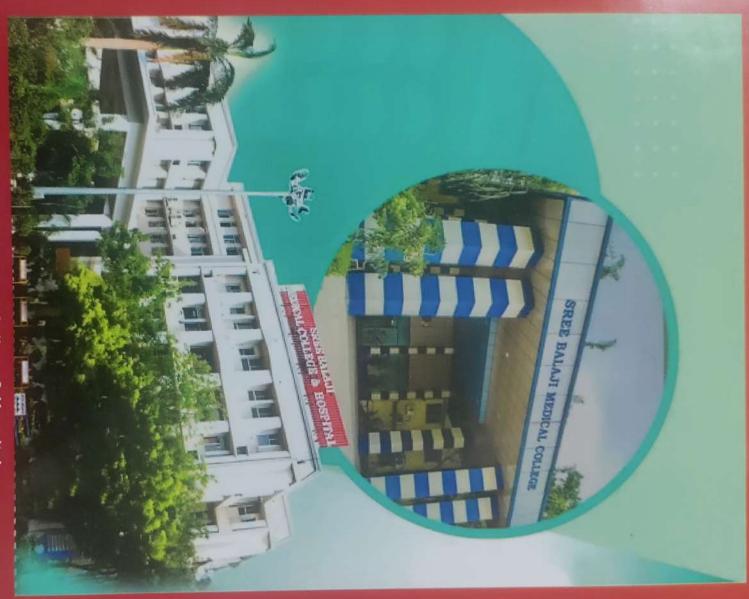
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Dr. K. Sharanya Dr. Aishwarya J Ramalingam

Department of Microbiology
Sree Balaji Medical College and Hospital, Chrompet, Chennai



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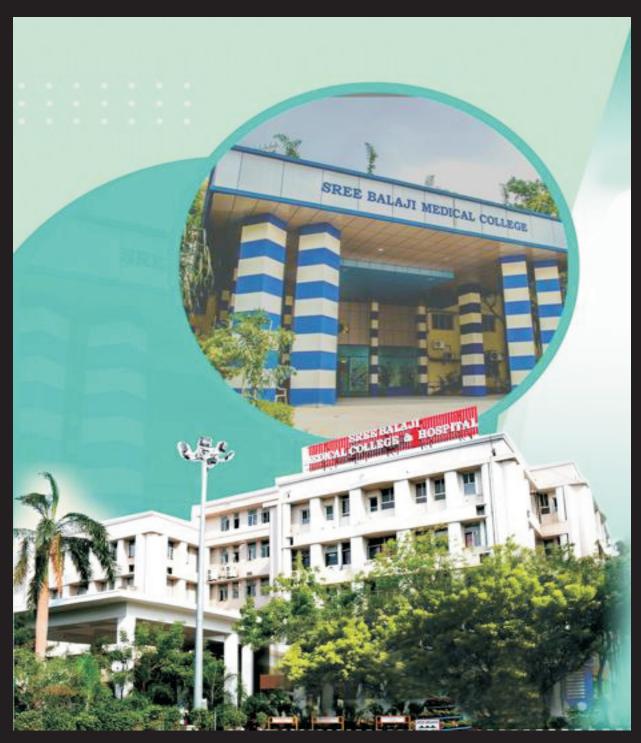
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Protein Functional Annotation Of Drug Targets

By Dr. D. Prabhu Dr. S. Rajamanikandan

Research and Development Wing
Sree Balaji Medical College and
Hospital (SBMCH)
Bharath Institute of Higher Education
and Research (BIHER)
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QUALITY OF FUNCTIONING AND DRUG USAGE PATTERN IN PRIMARY HEALTH CARE

A MONOGRAPH

Dr.S.Gopalakrishnan.MD, DPH Professor, H.O.D

Department of Community Medicine, Sree Balaji Medical College and Hospital, BIHER, Chennai-600044



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2	The drug usage pattern in Primary Health Care	Dr S. Gopalakrishnan



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Questions in radiology and imaging which

budding radiologists want to ask

but are afraid to ask

Venkatraman Indiran MD,DNB

Professor, Department of Radio-diagnosis, Sree Balaji Medical College and Hospital,

Bharath Institute of Higher Education and Research (BIHER),

Chennai, Tamilnadu, India

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Preface

I have always wondered about the need for additional books on radiology when there is already a

plethora of excellent radiology textbooks and journals. But I have also been amused about the moments

when we need to review some basic or important data or measurements or literature while we are

actively doing an ultrasound scan or reporting a CT or MRI; or when we have to answer a seemingly

basic question from our non-medical or non-radiology friends or acquaintances. This is just a small

attempt where I have tried to assemble and answer these queries at the back of my mind into a small

book in question and answer format. Though it might not be very useful to a specialist radiologist in

their own sub speciality, I hope that the radiology residents, young radiologists and interested medical

students find it quite useful.

Venkatraman Indiran MD,DNB

Professor, Department of Radio-diagnosis, Sree Balaji Medical College and Hospital,

Bharath Institute of Higher Education and Research (BIHER),

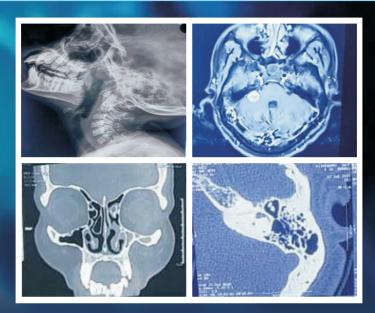
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- VI. Thorax
- VII. Vascular imaging
- VIII. Spine
- IX. Musculoskeletal Imaging
- X. Miscellaneous

RADIOLOGY IN ENT



Author Dr. M K Rajasekar MS, DLO

Professor and Head Department of ENT, Head and Neck Surgery Sree Balaji Medical College and Hospital Bharath University, Chennai, Tamil Nadu

Co-Author

Dr. R.P Jayapreetha

Junior Resident

Department of ENT

Sree Balaji Medical College and Hospital Bharath University, Chennai, Tamil Nadu



Department of ENT Sree Balaji Medical College & Hospital Bharath Institute of Higher Education & Research (BIHER) Chromepet, Chennai - 600044, Tamilnadu, India





Radiology in ENT

Author

Dr. M K Rajasekar MS,DLO

Professor and Head

Department of ENT, Head and Neck Surgery

Sree Balaji Medical College and Hospital

Bharath University, Chennai, Tamil Nadu

Co-Author

Dr. R.P Jayapreetha

Junior Resident
Department of ENT
Sree Balaji Medical College and Hospital
Bharath University, Chennai, Tamil Nadu



Department of ENT

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AUTHOR:

Dr. PRABHAKARAN.M., B.SC, MD, DMRD DR.BENO JEFFERSON., MDRD RESIDENT DR.REVATHY., MDRD RESIDENT DR.ANISH., MDRD RESIDENT

Department of Radiology, Sree Balaji Medical College and Hospital, Chennai



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Department of Community Medicine, Sree Balaji Medical College and Hospital, BIHER, Chennai-600044



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1.	Epidemiology of Research: Why we need to do Re- search?	Dr.Krishna Prasanth Assistant Professor Dept. of Community Medicine	10 to 10.45 am
2.	Study designs and Review of Litera- ture	Dr.N.B.Swetha Assistant Professor Dept. of Community Medicine	10.45 to 11.30 am
3.	Role of Biostatistics in Medical Re- search	Ashni. B Lecturer in Biosta- tistics Dept. of Community Medicine	11.30 to 12.15 pm
4.	How to write a Research Report. Concluding Ses- sion: Take Home mes- sage	Dr. Hariharan. S Assistant Professor Dept. of Community Medicine	12.15 to 1 pm

Sports Medicine & Health Sciences Research Process in



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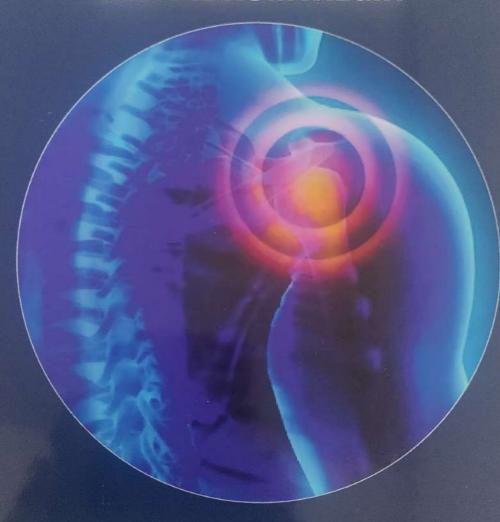


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OVERVIEW OF SOFT TISSUE RHEUMATISM AND FIBROMYALGIA



Authors:

Dr. (Brig.) K SHANMUGANANDAN Dr. SANJEEVI KRISHNAN P

DEPARTMENT OF GENERAL MEDICINE

SREE BALAJI MEDICAL COLLEGE AND HOSPITAL

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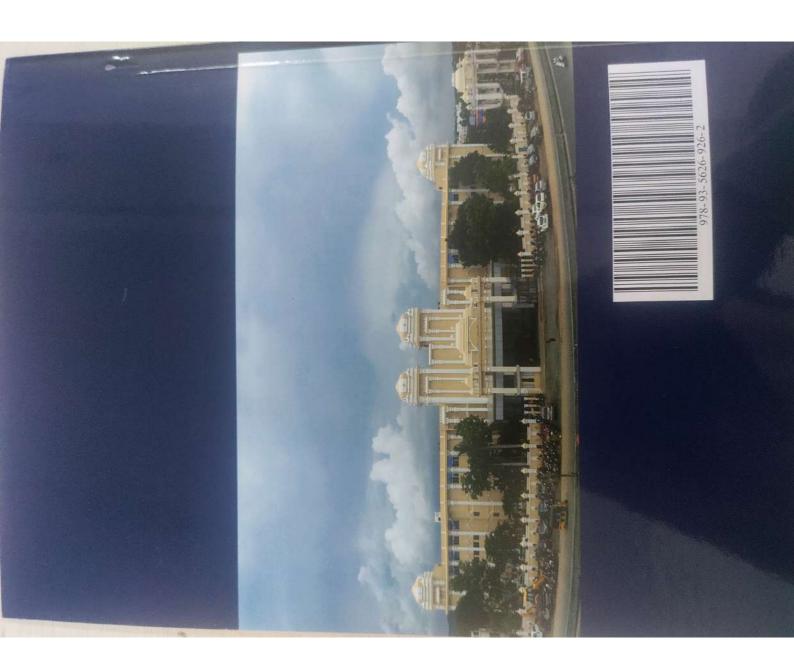
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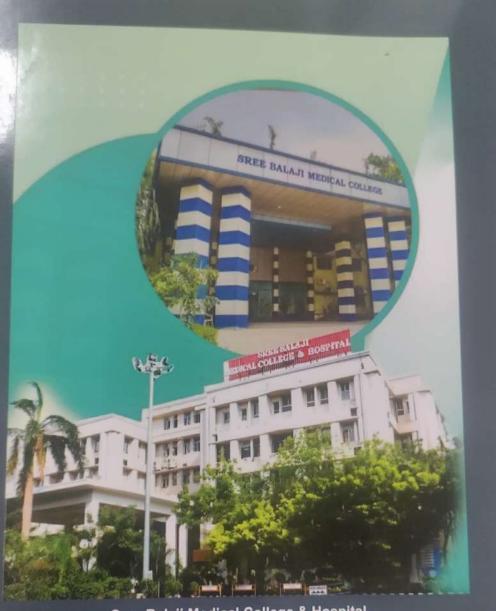


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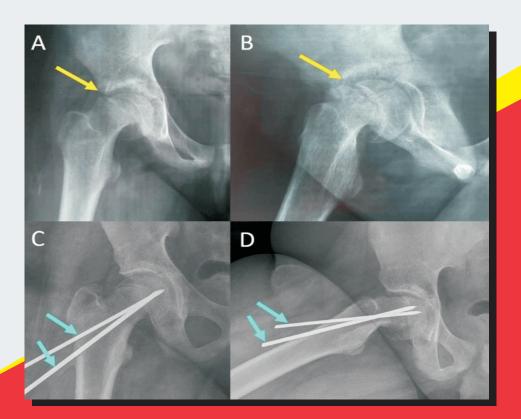
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Ph. 044 - 45080083. Cell: 9282134542

E-mail: murali.aks@gmail.com



Slipped Capital Femoral Epiphysis



Authors

Dr. Vijay Narasimman Reddy
Dr. Mervin Rosario P.M

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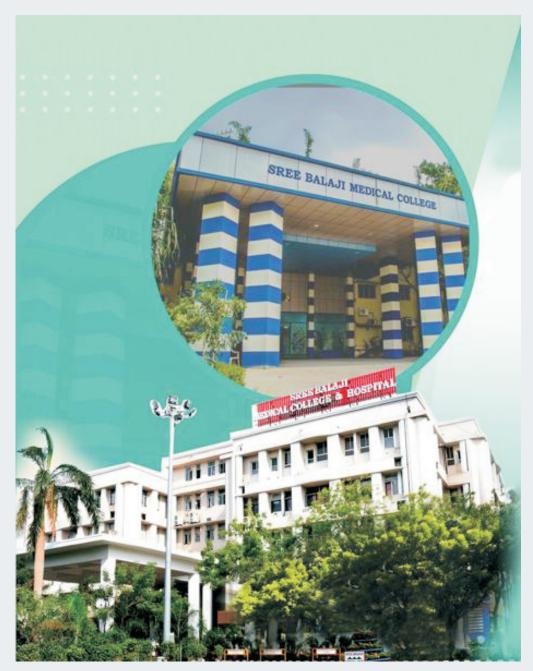
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By Palaniyandi Velusamy

Department of R & D Wing Sree Balaji medical college and Hospital chromepet-600044



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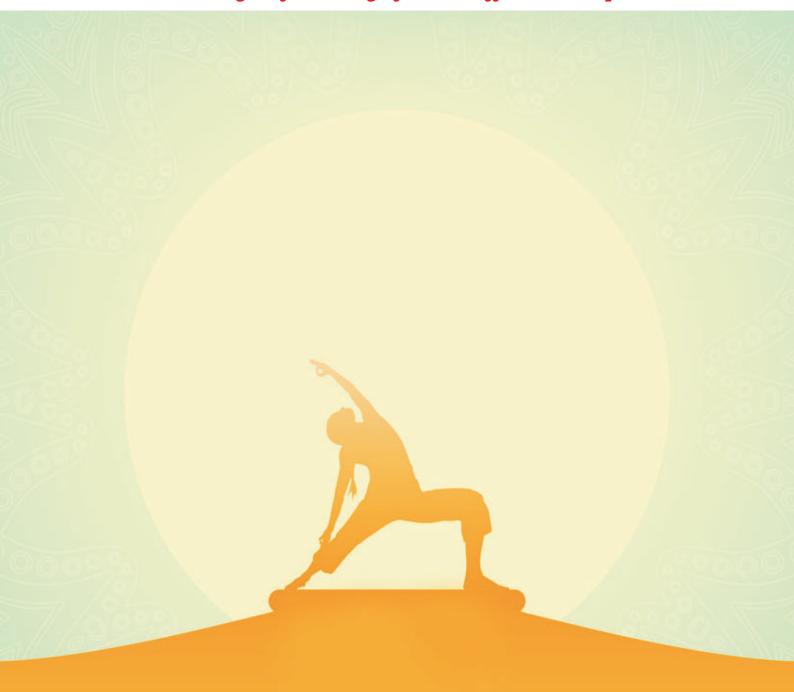






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Under the Aegis of Ministry of Youth Affairs and Sports



Department of Sports Medicine & Yoga Sree Balaji Medical College and Hospital (SBMCH)

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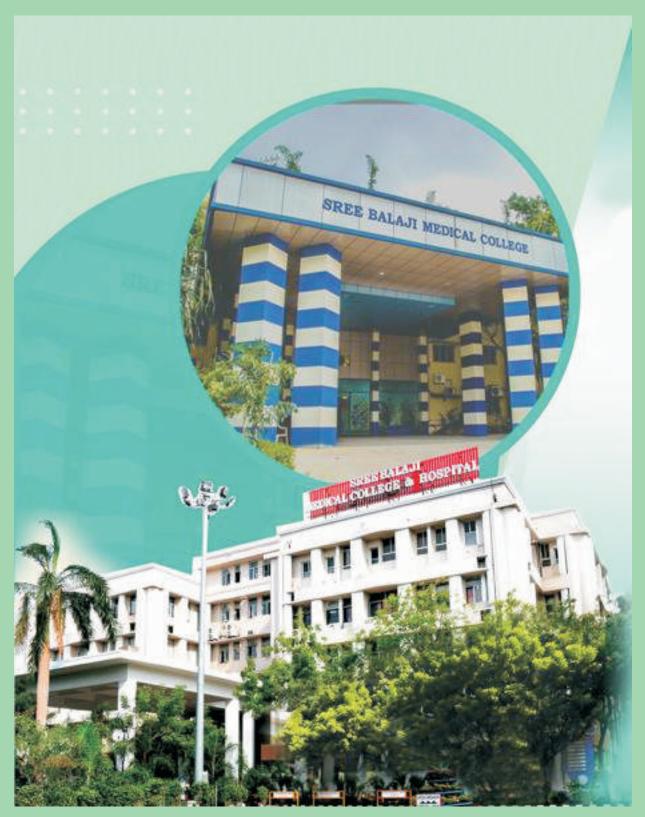
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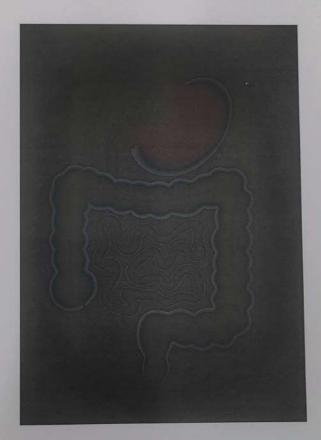


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DR. Anuhya adusumilli DR. P. Anandan DR. T.M. Karthikeya

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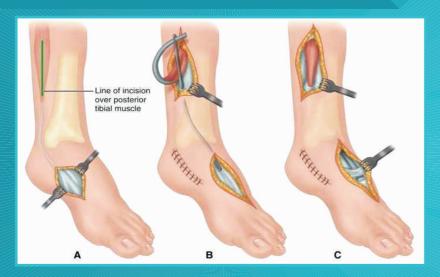
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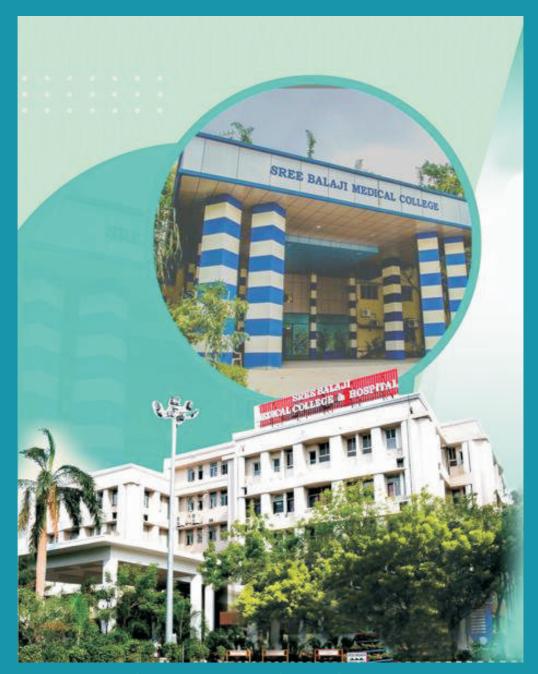
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Dr. S. Rajamanikandan Dr. D. Prabhu

Research and Development Wing, Sree Balaji Medical College and Hospital (SBMCH), Bharath Institute of Higher Education and Research (BIHER), Chennai-600 044, India



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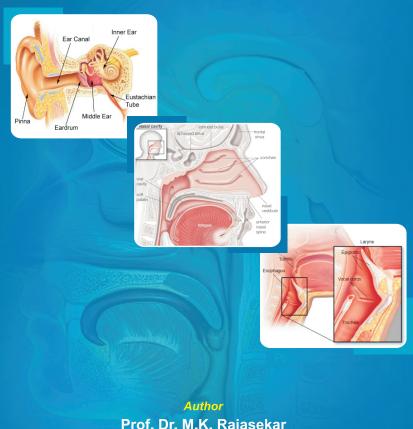
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Prof. Dr. M.K. Rajasekar



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Dr. M K Rajasekar MS, DLO

Professor and Head

Department of ENT, Head and Neck Surgery

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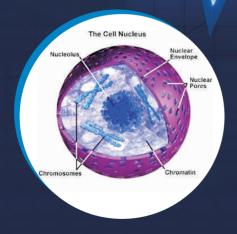
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I Semester





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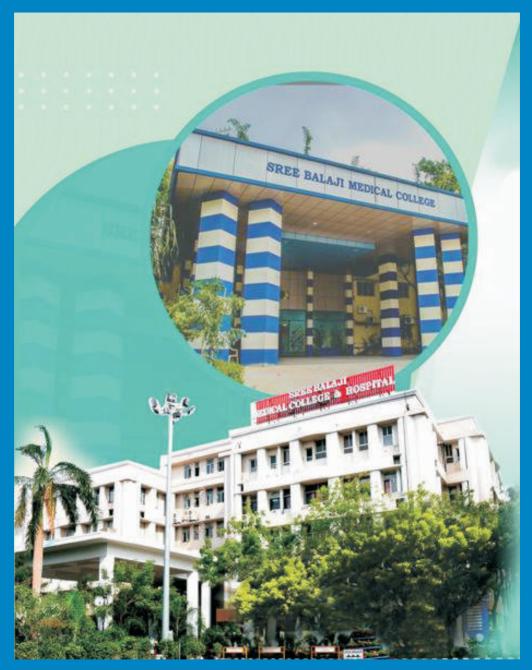
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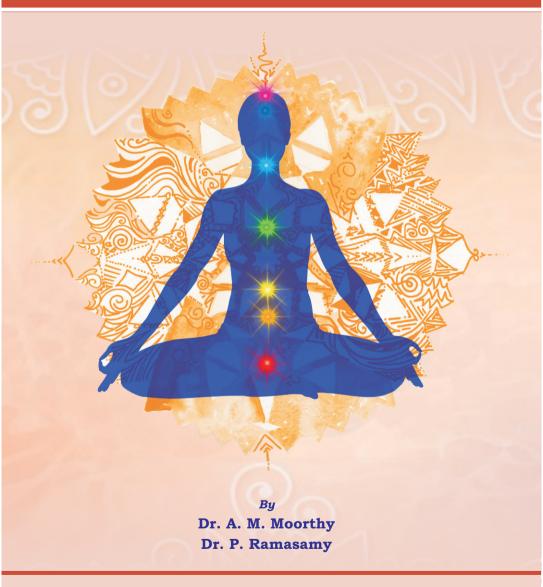
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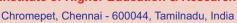
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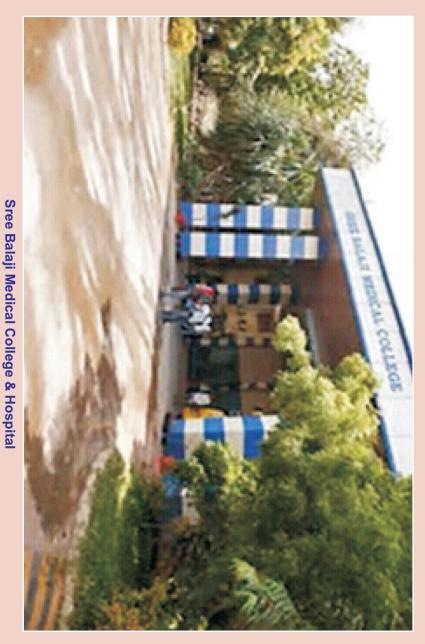
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Author:

Dr. Sumitha Ramanathan Department of ENT

DEPARTMENT OF ENT

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DEPARTMENT OF COMMUNITY MEDICINE, SREE BALAJI MEDICAL COLLEGE AND HOSPITAL, BIHER, CHENNAI-600044



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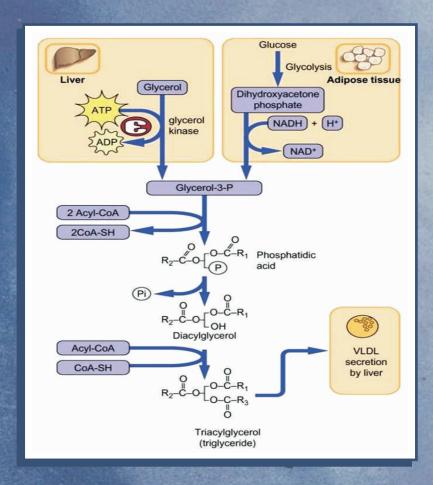
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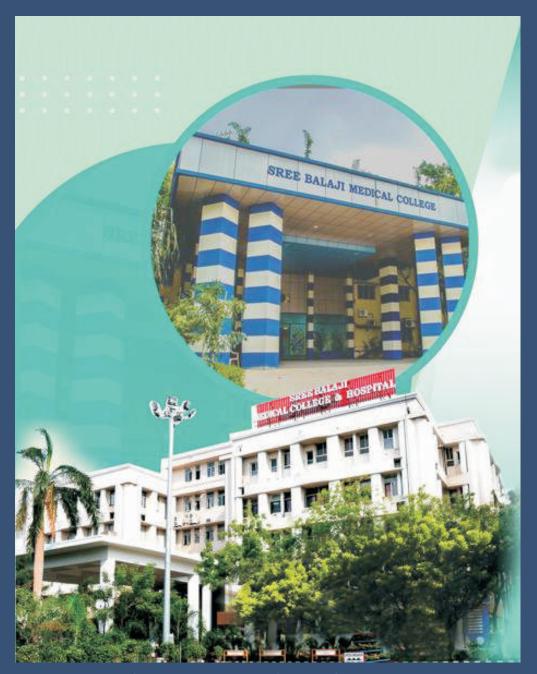
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Ph. 044 - 45080083. Cell: 9282134542,

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PREFACE

intention to disseminate valuable information about Innovative methods in Community medical students and Interns. This topic is salient for health professionals working in medical colleges. The contents, photos / pictures used in this book are solely for educational purpose. No copyright infringement is intended while using the content, photos / pictures used here and we acknowledge and thank the owners of the same. This book We the faculties of Department of Community Medicine started this book with an the targeting is not for sale. Medicine

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their inputs and contributions in drafting and proof-reading to make this book as informative I greatly appreciate and acknowledge other Faculty members and Post Graduates for as possible.

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Vaginal Candidiasis: An Overview



Author

Dr. Lakshmi Krishnasamy

Professor of Microbiology Sree Balaji Medical College and Hospital Chennai, Tamilnadu







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Dr. Lakshmi Krishnasamy

Professor of Microbiology Sree Balaji Medical College and Hospital Chennai, Tamilnadu



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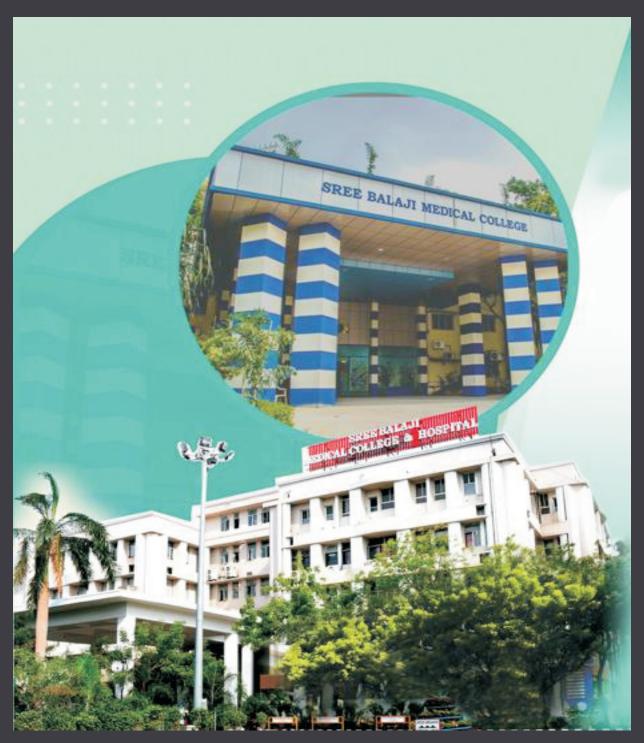
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E-mail: murali.aks@gmail.com, Website: aksharaa.co.in





SREE BALAJI MEDICAL COLLEGE HOSPITAL CHROMEPET, CHENNAI.



VIRAL HEMORRHAGIC FEVER

DR.N.N.ANAND DR.R.ARVINDRAJ

PREFACE

Infectious diseases plays a major role in our society, affecting our development, the way we relate ourselves to our surroundings. In spite of the technological development around us, some of us escape from the hold of the infectious disease, whether it is as mild but discomforting as common cold, to a serious life-threatening influenza. There are many new emerging infections and organisms causing different diseases.

> The main reason to write a monograph on Viral Haemorrhagic Fevers is because of the constant fear that these virus can cause high mortality and also because of my personal interest in these diseases. There is so much to learn and understand from these diseases, on how these viruses contain these pandemics and the end result of these diseases.

> Viral haemorrhagic fever consist of a variety of human illness and animal illness that is caused by viruses belonging to the RNA family such as Arenaviridae, Filoviridae, Bunyaviridae, and Flaviviridae. Basically viral haemorrhagic fever denotes multi organ dysfunction involving damage of the vascular system, leading to the impairment of the body's ability to regenerate. Most of the Viral haemorrhagic fever presents with bleeding manifestations and fever, and in severe cases can progress to shock and demise. There are few exceptions in Viral haemorrhagic fever viruses which will only cause mild illness. Viral haemorrhagic fever can present as an isolated case due to local causes or it can also present as an epidemic.

This book is primarily targeted at the front line warriors, virologists, biomedical researchers, and students of medicine wanting to acquire a rapid overview of these viruses linked only by their propensity of causing diseases with haemorrhagic manifestation. We hope that this monograph will serve its purpose and be a useful source for the ones who are interested in viral haemorrhagic fevers.

VIRAL HEMORRHAGIC FEVER

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Dr. B. Shanthi

Dr. V.S. Kalai Selvi

Dr. K. Sumathi

Dr. S. Shenbagalalitha

Dr. Chaganti Sridevi

Dr. A. Mary Chandrika

Dr. B. Gautham

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Mr. E. Vasudevan

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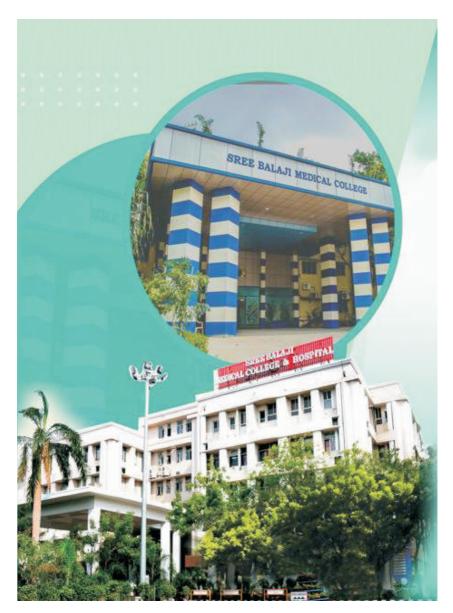
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Er. N. இளமாறன்

Dr. A.M. மூர்த்தி

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5. ULUSLARARASI ANKARA MULTIDISIPLINER BİLİMSEL ÇALIŞMALAR KONGRESİ

A CALL TO CONSIDER FOOD CULTURE IN PUBLIC HEALTH INITIATIVES: WHY WE EAT THE WAY WE DO

K.R.Don

Reader, Department of Oral Pathology and Microbiology, Sree Balaji Dental College and Hospital, Bharath Institute of Higher Education and Research (BIHER) Bharath University, Chennai, Tamil Nadu, India

ORCID ID: 0000-0003-3110-8076.

K.R.Padma

Assistant Professor, Department of Biotechnology, Sri Padmavati Mahila Visvavidyalayam (Women's)
University, Tirupati, AP

ORCID ID: 0000-0002-6783-3248

P. Josthna

Professor, Department of Biotechnology, Sri Padmavati Mahila Visvavidyalayam (Women's) University, Tirupati, AP.

ABSTRACT

Eating habits are among the most complex facets of human behavior since they are impacted by a number of variables and are controlled and directed by a number of stimuli. Food acceptance is a complex response that is influenced by biochemical, physiological, psychological, social, and educational factors. The metabolism's condition must be considered. Important factors to take into account include age, sexual orientation, and mental health. People react to food in different ways on a sensory level depending on who they are based on race, tradition, economic status, and environmental factors all influences on a person's culinary preferences and dislikes. Our food habits have drastically changed in just a few decades. Although the term "food culture" has been defined before and there isn't a clear explanation of how modern food culture may be used to advance health. In this article, we propose a concept of food culture for use in public health, list advantageous elements of food culture as opposed to those that have dominated in industrialised countries, and talk about the consequences for both physical and mental health and wellbeing. We appreciate the requests for reform in eating habits made by the international community. Macro (policy & systems) and meso (community) level environmental components from all corners of society must work together to create a culture of healthy food. The ultimate goal is to work together to promote persistent changes in how people as a whole consume, see food, and act.

Keywords: Nutrition, Dietary habits, Public health, Physical and Mental health, Health awareness.

Introduction

Food selection and consumption habits, food meanings and significance, and what people eat are all common features of all communities. These concepts are also referred to as food culture. Although there isn't a singular definition of food culture, the idea has been described by several academics.



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DISRUPTION OF EDUCATIONAL SYSTEM AND SUSTAINABILITY MANAGEMENT DURING COVID-19 PANDEMIC

K.R.Padma

Assistant Professor, Department of Biotechnology, Sri Padmavati Mahila Visvavidyalayam (Women's) University, Tirupati, AP

Orcid no: 0000-0002-6783-3248

K.R.Don

Reader, Department of Oral Pathology and Microbiology, Sree Balaji Dental College and Hospital, Bharath Institute of Higher Education and Research (BIHER) Bharath University, Chennai, Tamil Nadu, India Orcid No: 0000-0003-3110-8076.

P.Josthna

Professor, Department of Biotechnology, Sri Padmavati Mahila Visvavidyalayam (Women's) University, Tirupati, AP.

B.Kishori

Professor, Department of Biotechnology, Sri Padmavati Mahila Visvavidyalayam (Women's) University,

Tirupati, AP.

Abstract

What has to be done to recover from COVID-19 pandemic? This remains the main concern for all domains globally. The early lockdowns has devastated the educational system, which in turn led to psychological trauma in populace. Although, restrictions were implemented to stop the spread of the disease but entire country lost their freedom through social distancing activity. However, main domains affected mostly are educational system,





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BIODEGRADABLE AND MEDICALLY BENEFICIAL HYDROGEL BASED BANDAGES MADE WITH DURIAN HUSK

K.R.Padma

Assistant Professor, Department of Biotechnology, Sri Padmavati Mahila Visvavidyalayam (Women's) University,
Tirupati, AP.

Orcid no: 0000-0002-6783-3248

K.R.Don

Reader, Department of Oral Pathology and Microbiology, Sree Balaji Dental College and Hospital, Bharath Institute of Higher Education and Research (BIHER) Bharath University, Chennai, Tamil Nadu, India Orcid No: 0000-0003-3110-8076.

P.V.Jahnavi

Department of Biotechnology, Sri Padmavati Mahila Visvavidyalayam (Women's) University, Tirupati, AP.

Abstract

Durio zibethinus, usually called as Durian, is a foreign Southeast Asian tropical fruit. This fruit is good for health, because of the presence of antioxidants and bioactive compounds that has discrete health promoting benefits. Generally for the treatment of blister we put a loose bandage or use padding. In addition to this; these bandages are made from plastic which is more harmful to the environment and takes years to degrade. Our main focus is to create a band-aid from fruit waste. As cellulose is a strong sugar molecule that exists naturally in plants and once extracted it can be molded into everyday products. These eco-friendly bandages can be made

Junaid Ahmad Malik Mohamed Jaffer Sadiq Mohamed *Editors*

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Mohamed Jaffer Sadiq Mohamed Department of Physics King Fahd University of Petroleum and Minerals Dhahran, Saudi Arabia

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Chapter 26 Artificial Photosynthesis with Gold Nanostructures Incorporation in Non-photosynthetic Bacteria



K. R. Padma (6) and K. R. Don

Abstract The most extensive, necessary, and abundant solar energy conversion mechanism on our planet, natural photosynthesis is a time-consuming process. The majority of species inhabiting the biosphere obtain their energy from bacteria and photosynthetic plants. The existence of photosynthetic pigments, which in turn produce assimilative power for converting atmospheric carbon into carbohydrates, is a characteristic that distinguishes plants from other living things. Several scientists intend to add gold nanoclusters of different sizes to the non-photosynthetic bacteria M. thermoacetica to increase energy production. The light from the sun causes photogenerated electrons to leave the bacterium, interact with several enzymes, and then start a series of reactions that convert CO₂ into acetic acid, a useful byproduct for the production of solar energy. Artificial photosynthesis, which imitates the natural phenomenon of photosynthesis, is the technique of creating solar energy through a natural process with the assistance of biological organisms and nanotechnology. The information in our chapter, however, focuses on how gold nanoparticle clusters prevent reactive oxygen species while maintaining bacterial viability. Through our research, we have also demonstrated the development of photosynthetic biohybrid systems and electron transfer systems. This review's goal is to offer suggestions for improving artificial photosynthesis system design and optimization in order to meet upcoming energy and environmental issues on a worldwide scale.

Keywords Photosynthetic biohybrid system (PBS) · M. thermoacetica · Nanotechnology · Natural photosynthesis · Artificial Photosynthesis System (APS)

Department of Biotechnology, Sri Padmavati Mahila Visvavidyalayam (Women's) University, Tirupati, India

K. R. Don

Department of Oral Pathology and Microbiology, Sree Balaji Dental College and Hospital, Bharath Institute of Higher Education and Research (BIHER), Bharath University, Chennai, Tamil Nadu, India

K. R. Padma (M)

"Research Franka: A Step Towards Interdisciplinary Research" is not meant to be a definitive account of all cross-disciplinary endeavours, but rather a catalyst for inspiration and exploration. It is our hope that this book will ignite a spark in researchers, educators, students, and policymakers alike, encouraging them to embrace the power of collaboration and to venture into uncharted territories of knowledge.



RESEARCH FRANKA: A STEP TOWARDS INTERDISCIPLINARY RESEARCH

RESEARCH FRANKA: A STEP TOWARDS INTERDISCIPLINARY RESEARCH



Editors Rima Kumari Saxena Dr. Nitivant Kumar Dr. S S Ramajayam Wakil Kumar Yadav

8. AN OVERVIEW OF STUDIES ON URBANIZATION AND ITS IMPACT ON SUSTAINABLE DEVELOPMENT ¹K.R. Padma

Assistant Professor, Department of Biotechnology, Sri Padmavati Mahila Visvavidyalayam (Women's) University, Tirupati, AP. email id: thulasipadi@gmail.com

Orcid no: 0000-0002-6783-3248.

2K.R. Don

Reader, Department of Oral Pathology and Microbiology, Sree Balaji Dental College and Hospital, Bharath Institute of Higher Education and Research (BIHER) Bharath University, Chennai, Tamil Nadu, India email id drkrdon@gmail.com.

Orcid No: 0000-0003-3110-8076.

Abstract

A multitude of social, economic, and environmental variables all contribute to urbanization, one of the largest social changes of the modern era. Global, regional, and local effects of urbanization's multifarious effects on the environment are all evident. The six primary factors that this article addresses are air pollution, ecosystems, utilization of land, water pollution from biogeochemical cycles, solid waste management, and the effects of climate change. It also discusses current developments in conceptual and empirical knowledge relating to urbanization and the environment. Research on sustainability and urban transformation are hot topics in the building profession right now. With a focus on the themes that these studies address and an identification of the primary topics covered within these themes, this study attempts to understand the historical and contemporary trends in the relationship between urban transformation and

Nanotechnology in the Life Sciences

Anand Krishnan ·
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Emerging Nanomaterials for Advanced Technologies



Nanonutraceuticals in Chemotherapy of Infectious Diseases and Cancer

C. Sumathi Jones, V. Uma Maheshwari Nallal & M. Razia

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Abstract

Nanotechnology, an upcoming field of science dealing with nanoparticles (10⁹), has a wide range of biomedical applications in prophylaxis, diagnosis, and therapy of infectious diseases and cancer. Similarly, nutraceuticals (nutritional and pharmaceutical hybrid) play a key role as immunomodulators, thereby acting as a defense mechanism to fight against microbial pathogens and cancer. Owing to nonspecificity and major adverse reactions of the conventional antimicrobial and anticancer drugs, there exists a pertinent search for novel naturally occurring nutraceuticals that are target specific and devoid of toxicity. Hence, recent research focus is on the combination of nutraceutical with nanotechnology to produce nanonutraceuticals. This chapter deals with nanonutraceutical classification, formulations in

Abhijit Bandyopadhyay Tamalika Das Sabina Yeasmin

Nanoparticles in Lung Cancer Therapy - Recent Trends







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Abstract

Cancer is regarded as a deadly disease and characterized as one of largest problems among the universal population. Worldwide, the population insists on a positive approach for curing the disease. However, plant resources are found to possess multiple phytochemicals which revealed promising effects for various cancer maladies. Over 60% of drugs are obtained from natural source only. Therapy for common cancer involves radiotherapy or chemotherapy, which alters the physical condition of the individual with diverse side effects and ultimately drains the immunity of the individual. Several available drugs are also unable to cure cancer completely, but recent advancement in utilization of plant-based compounds revealed greater beneficial efficacy in management of cancerous cell growth. Therefore, this chapter portrays the bioactive compounds obtained from natural sources and how these traditional medicines act as drug candidates against cancer.

Chapter Preview



Chapter 7

Natural Products Possess Bioactive Agents Investigated for Their Anticancer Potential: Medicinal Importance of Natural Products

Kanchi Ravi Padma

https://orcid.org/0000-0002-6783-3248 Sri Padmavati Mahila Visva Vidyalayam (Women's) University, India

Kanchi Ravi Don

Shree Balaji Dental College and Hospital, Bharath Institute of Higher Education and Research, India

ABSTRACT

Cancer is regarded as a deadly disease and characterized as one of largest problems among the universal population. Worldwide, the population insists on a positive approach for curing the disease. However, plant resources are found to possess multiple phytochemicals which revealed promising effects for various cancer maladies. Over 60% of drugs are obtained from natural source only. Therapy for common cancer involves radiotherapy or chemotherapy, which alters the physical condition of the individual with diverse side effects and ultimately drains the immunity of the individual. Several available drugs are also unable to cure cancer completely, but recent advancement in utilization of plant-based compounds revealed greater beneficial efficacy in management of cancerous cell growth. Therefore, this chapter portrays the bioactive compounds obtained from natural sources and how these traditional medicines act as drug candidates against cancer.

1. INTRODUCTION

Natural products obtained from diverse plant resources have contributed a dominant function in therapy for various maladies. Among them, cancer is in second place and regarded as the most deadliest devastating malady in both developing as well as developed countries. (Lin et al., 2019; Siegel et al., 2020).

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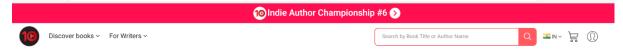
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MULTI-DISCIPLINARY RESEARCH FOR SAVING FUTURE



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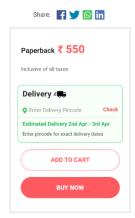
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MULTI-DISCIPLINARY RESEARCH FOR SAVING

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This book contains Multi-Disciplinary Research that will help research scholars, academicians and various research agencies to sort out human problems and save the future. Currently India is facing a lot of issues in various fields like social, cultural, political and economic. These issues are hurdle for overall development of India. Academicians have tried to solve these problems by their possible ideas. It is expected that readers will get a plethora of kno



26. GREEN HOUSE GASES INFLUENCES CLIMATIC CHANGES AND ENHANCES GLOBAL WARMING

K.R. PADMA, K.R. DON

Assistant Professor, Department of Biotechnology, Sri Padmavati Mahila VisvaVidyalayam (Women's) University, Tirupati, AP. email id: thulasipadi@gmail.com

> Mobile no: 8897146167, Orcid no:0000-0002-6783-3248 K.R.Don

Reader, Department of Oral Pathology and Microbiology, Sree Balaji Dental College and Hospital, Bharath Institute of Higher Education and Research (BIHER) Bharath University, Chennai, Tamil Nadu, India email id drkrdon@gmail.com

Abstract

Due to enhanced greenhouse gases as the outcome of human actions poses possible threat to human kind. Our Earth maintains equilibrium between the absorption and radiation of solar energy. Nevertheless, with the expansion of industries there is steady increase in the concentrations of green house gases such as methane, carbon dioxide (CO2), nitrous oxide, carbon monoxide and chlorofluorocarbons. If the greenhouse effect not present it would directly reveal its impact by altering the global temperature and life on our earth would have become impossible as change to colder condition. Thus, our article shows the relationship of greenhouse effects and its influence on global warming. Howev stability on the Earth is sustained between the net inbound solution from top of the atmosphere.

The edited book titled "Cognitive Load: A Learning-Teaching Perspective" has introduced the dimensions of cognitive load related to pedagogical process which may conduct learning in an ease way. The contributions of this book from India, Nigeria, Burzai and other places protein the collaborated idea on the various aspects of cognitive load. These all aspects converge to learning and teaching processes. Classroom instruction as well as online pedagogy and new nonal educational system in 21" century have been discussed in this edited book. Learning teaching regarding the age groups of students has been clarified under the consequences of cognitive load. Especially the chapterisation of each them e related to the research papers and articles has done with experies. En his book may fulfill the academic and research needs of every teacher, research scholar, planner and educationist.



Ranjini Ghosh, Lecturer, Katwa Government Primary Teachers Training Institute, Bardhaman, West Bengal. She has done her MA in Education, B Lid. and M Ed. University of Calculat, and Certificate Course in Counseling (International TEFL Canada), She is also NET (Education) qualified She is pursuing Ph.D. in Education and POIDEMA.

Liducation and PGDEMA.

She is Former Research Fellow in Ginnbir Fellowship (Rajasthan), Former Research Assistant in Major Project of ICSSR. She has worked as assistant professor in GTT College and ARPP Institution, Murahadabad, West Bengal. She has taken part as guest faculty in Calcuta Curis College and ISSRT Belur, West Bengal. She has published Books (with ISSRS) on Education, Book College and ISSRST Belur, West Bengal. She has published Books (with ISSRS) on Education, Book College and ISSRST Belur, West Bengal. She has published Books (with ISSRS) on Education She and research papers in Northwall International Journals and UCC CARE. Instet attended Workshops, Teacher Trainings, and Faculty Development Pupprans as participant and speaker. She works as the Education wave official guide on. She is a life time professional member of InSe and her ORCID id is 0000-0002-8899-7102.



Dr. Kedar Nath Dey, Assistant Professor & H.O.D., Department of Education, Swami D.D.K. Mahavidyalaya, affiliated to Bankura University, Bankura, West Hengal, India.

He is also a member of UGHS in Bankura University. He has worked as lecturer in Landau and Company of the Com



Manasseh Ternenge Adi, Senior Information and Protocol Officer, Federal University Wukari, Taraba State - Nigeria. English Education PLD billed for exit with Joseph Sarwan Tarab University (femerity University of Agriculture), Makurdi. Have flar for humanlarian and voluntary services. Editorial member of somany international journals and has also published in language learning research works in see Imagi mentalorial journals too. A member of Teachers Registration Council of Nigeria (TRCN) and IFIAA Nigeria.





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Cognitive Load: A Learning-Teaching Perspective

By: Ranjini Ghosh Dr. Kedar Nath Dey Manasseh Ternenge Adi

Cognitive Load Theory Plays A Major Role in Teaching-Learning Process

K.R. Padma*

K.R. Don**

B. V. Sai Chandana***

P. Josthna****

Introduction

ognitive load theory was explained by psychologist John Sweller in the late 1980s. Cognitive load refers to the activities that acting on working memory of a learner. It explains how a student's short-term memory (working memory) and long-term memory operates with respect to instructional design and the functioning of working

^{*}Assistant Professor, Department of Biotechnology, Sri Padmavati Mahila Visvavidyalayam (Women's) University, Tirupati, Andhra Pradesh, India.

^{**}Reader, Department of Oral Pathology and Microbiology, Research (BIHER) Bharath University, Chennai, Tamil Nadu, India.

^{***}Student, Department of Biotechnology, Sri Padmavati Mahila Visvavidyalayam (Women's) University, Tirupati, Andhra Pradesh, India.

^{****}Associate Professor, Department of Biotechnology, Sri Padmavati Mahila Visvavidyalayam (Women's) University, Tirupati, Andhra Pradesh, India.

BOOK OF FULL TEXT



CUMHURİYET 6. ULUSLARARASI SOSYAL BİLİMLER KONGRESİ



CUMHURIYET 6th INTERNATIONAL CONGRESS ON SOCIAL SCIENCES

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IMPACT OF COVID-19 RESULTED IN GLOBAL MIGRATION OF IMMIGRANTS

K.R.Padma

Assistant Professor, Department of Biotechnology, SriPadmavatiMahilaVisvaVidyalayam
(Women's) University, Tirupati,AP.email id: thulasipadi@gmail.com
mobile no:8897146167 Orcid no:0000-0002-6783-3248

K.R.Don

Reader, Department of Oral Pathology and Microbiology, Sree Balaji Dental College and Hospital, Bharath Institute of Higher Education and Research (BIHER) Bharath University, Chennai, Tamil Nadu, India email id drkrdon@gmail.com

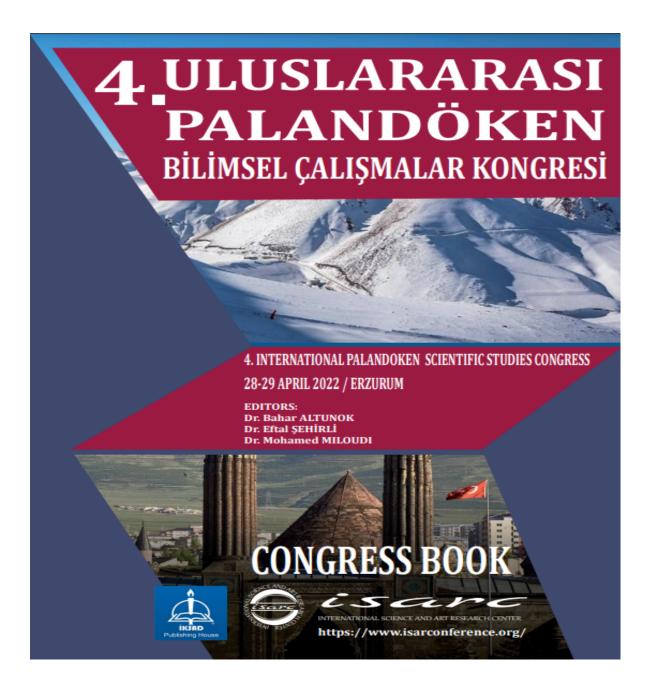
Abstract

Immigrants faced significant issues during the covid-19 crisis. COVID-19 outbreak has caused strict lockdown globally which showed significant impact on the mobility of immigrants and what role the government organizations played. The outburst of covid-19began form December 2019 but increase in number of cases was acknowledged by WHO around March 20 which globally shook all population and led to severe economic crisis. Amongst, most affected were the immigrants who lost their jobs and unable to reach back to their hometown. Because of pandemic they had no alternative way to earn income and even lost security as well as safety. However, India is occupied with more number of migrant workers who were left unemployed due to lockdown globally. This poses great challenge among workers and increase in malnutrition among children as there was disruption in food supply chain. Nevertheless, the humanitarian organizations has instigated to reconsider the matter at the national migration policies, for offering support as well as security to migrants arriving from diverse parts of country. Therefore, our article primary aim is to concentrate on sufferings of immigrants and what social outcomes to mitigate their food insecurity existence and reduction of stress, pressure among migrants.

Key words: Immigrants, Pandemic, Malnutrition, Food supply chain, Food insecurity.

Introduction

The pandemic disease currently devastating whole world is COVID-19 and has shattered the





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METHODS OF TEACHING HOME SCIENCE: A NEW PERSPECTIVE

K. R. Padma

Assistant Professor, Department of Biotechnology, Sri Padmavati Mahila VisvaVidyalayam (Women's) University, Tirupati, AP.

Orcid no:0000-0002-6783-3248.\

K. R. Do

Reader, Department of Oral Pathology and Microbiology, Sree Balaji Dental College and Hospital, Bharath Institute of Higher Education and Research (BIHER) Bharath University, Chennai, Tamil Nadu, India Orcid No: 0000-0003-3110-8076.

V.Bindu

Associate Professor, Department of Home Science, Sri Padmavati Mahila Visvavidyalayam (Women's) University, Tirupati, AP.

ABSTRACT

The aim of research in science was to explore innovative ideas from young minds. Home Science is a prevocational subject in the higher secondary education. Although, home science is a vast subject and many have misconception that it is related to food preparation/cooking alone. The Home Science education in curriculum helps students to develop domestic skills, home decoration, new pattern of cookery, stitching etc. The method employed in teaching students must be high lightened. Best teaching practices need to be followed to improve the quality of education. Our current review article objective was to examine the effective teaching methodology for success in the students academics at all phases of their lifetime. Nevertheless, what best teaching aids followed to improve the quality of educational system. Thus, our article provides broad window on fruitfulness techniques followed with advancements in science and technology.

Keywords: Higher secondary education, curriculum, Quality of education, Home decoration

I Introduction

The progression in Science in the United States as well as globally in innovations, creative development widely improved the economic advancement. Well trained researchers with subjective knowledge are most vital teachers to produce a better scientist, nurse, dietician plus effective community management resource along with a good homemaker. The National Research Council (NRC) highlighted the importance of well trained teachers in stream of productivity as well as technical innovations (NRC, 2007). Several literature reports have highlighted about science education, ideas to promote scientific knowledge, innovative teaching methods, usage of digital platforms inculcated interest and excitement to learn science. This aided to students to determine the value of evidence-based reasoning along with acquiring higher-order cognitive skills to solve problems (DeHaan, 2005 andDiamond, 2007).

The higher educational institutions must stresson student learning outcomes along with the skill acquired during their learning process to achieve success. Every single teacher with good academic qualifications along with efficient skills based on creative thinking plus able to include innovative teaching strategies must be appointed in schools, colleges and universities (Morris & Hudson, 1995). However, U.S. tertiary education experts have been following certain strict policies implementation which can provide best learning

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provision for the different kinds of students (Gurin, Dey, Hurtado, &Gurin, 2002). Sticking to syllabus curriculum is not considered as teaching methodology for efficient outcome of students. Nevertheless, the basic strategy of any kind of teaching methodology must be outside/exteriorto ourdetailed curriculum utilizing several digital technology for easy comprehensionwith advanced teaching process along with imaginativethoughts to attract the attention of students and inculcate knowledge. Earlier methods for teaching was preparation of lesson plans based on each and every student of his classroom but this has shown failure in outcomes. The resourceful technology with latest advancements other than a chalk and board creates creative

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KIWIFRUIT A NUTRIENT-DENSE FRUIT ON REGULAR CONSUMPTION IMPROVE NUTRITIONAL STATUS AMONG COVID-19 DISEASE

K R Padma

Assistant Professor, Department of Biotechnology, Sri Padmavati MahilaVisvavidyalayam (Women's) University, Tirupati, AP.

K.R.Don

Reader, Department of Oral Pathology and Microbiology, Sree Balaji Dental College and Hospital, Bharath Institute of Higher Education and Research (BIHER) Bharath University, Chennai, Tamil Nadu, India

S. Sowjanya

Student, Department of Biotechnology, Sri Padmavati MahilaVisvavidyalayam (Women's)
University, Tirupati,AP.

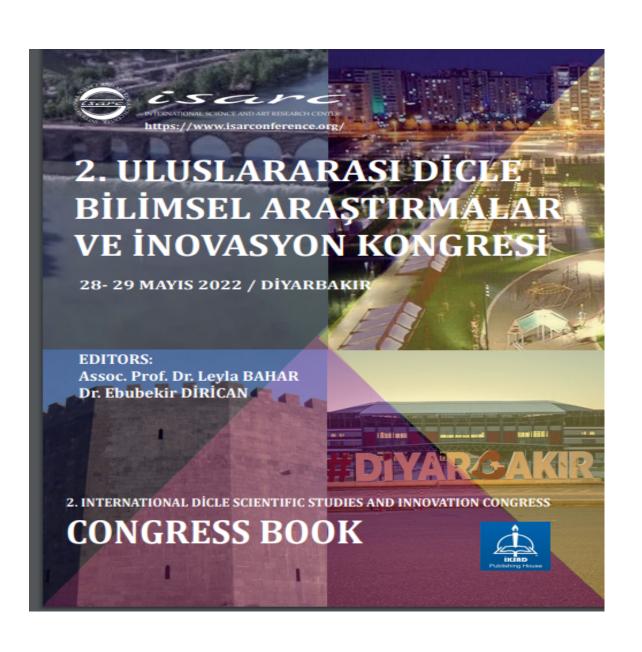
M. Vaishnavi

Student, Department of Biotechnology, Sri Padmavati MahilaVisvavidyalayam (Women's)
University, Tirupati, AP.

Abstract

Irrespective of age in some people, there is so diminution function of immune system which might result to serious menace of respiratory tract infections (RTI) mainly upper respiratory tract infections (URTI) chiefly during these pandemic circumstances. To prevent the attack from corona virus consumption of the miraculous fruit i.e, kiwi fruit (Actinidia chinesis) indirectly boosts immune function. The kiwi fruit contains abundant vitamin C, E, Folate, Polyphenols and carotenoids which helps in diminution from symptoms of corona virus infection. Furthermore, several literature studies has revealed its antioxidant, antimicrobial, antiviral and anticancer properties. The whole fruit without any exception of peel has many

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LATEST METHOD FOR REDUCING PLASTIC POLLUTION ACCUMULATION ON EARTH

K. R. Padma

Assistant Professor, Department of Biotechnology, Sri Padmavati Mahila Visvavidyalayam (Women's) University,
Tirupati, AP.

ORCID: 0000-0002-6783-3248

K. R. Don

Reader, Department of Oral Pathology and Microbiology, Sree Balaji Dental College and Hospital, Bharath Institute of Higher Education and Research (BIHER) Bharath University, Chennai, Tamil Nadu, India

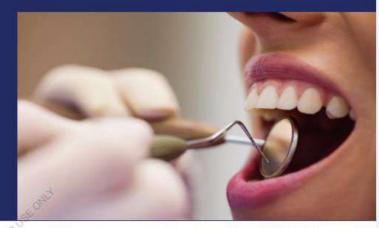
ORCID: 0000-0003-3110-8076.

ABSTRACT

Generally, plastics are complex polymers consisting of long and repeating chains of molecules. Although it is transparent, durable and light it creates detrimental problems for environment. Among the plastics, most commonly used thermoplastic polymer is polyethylene terephthalate (PET) which is used to produce plastic products such as plastic bottles and food container. Now a days, it has become a major problem and it is very tough to break down plastic bottles into their building block to produce new ones from old ones. To reduce this, scientists have found bacteria that can utilize plastic as their vital energy and carbon source for growth known as plastic -eating bacteria. The specific bacteria termed as Ideonella sakaiensis have shown its potential in PET contaminated environment. It is a gram-negative, rod shaped and the cells are motile with a polar flagellum. Ideonella sakaiensis produces an enzyme called PETase which is capable of hydrolyzing polyethylene terephthalate can be melted and rapidly cooled to make amorphous plastic that supports bacterial growth. This strain gives two enzymes able of hydrolyzing PET and the reaction intermediate, mono(2-hydroxyethyl) terephthalic acid during its growth on PET. The entire degradation of PET is the final goal, either to CO₂ or recovered monomers for making fresh PET.

Keywords: Plastic, Polyethylene terephthalate (PET), Ideonella sakaiensis, Thermoplastic polymer

Dental trauma is one of the important oral health problems in childhood which is expected to exceed the prevalence of dental caries and periodontal diseases in foreseeable future posing a significant threat among young people in terms of aesthetics, psychological aspects, social and therapeutic aspects. It causes pain and distress not only to children but also to their parents, Traumatic injuries are on the rise and are the third largest cause of the mortality of teeth in children. As pediatric dentists dental trauma in children is of prime importance for us, because here not only the teeth will be involved, but the child's entire self-image and self-esteem is at stake. Traumatic injuries are caused by many external factors such as violence, accidents, fall etc., the extension, intensity and gravity of which may reach both dental element and its supporting structures and good prognosis of traumatized teeth depends on how quickly and efficiently the tooth has been treated not only by dental professionals but also by the lay persons who are present at the scene of the accident. Traumatic injuries constitute unfortunate, painful, and distressing events.



Tavleen Kour Sajid Hussain

Management of dental trauma

Management Strategies



Dr. T. Kour, B.D.S., M.D.S did her UG from Jammu University, from Institute of Dental Sciences, and her PG in Pedodontics & Preventive Dentistry, from Guru Nanak Dev Dental College, Sunam, Dr. S. Hussain, B.Sc, M.D.S is a Periodontist & Associate Professor in the Department of Periodontics at Sree Balaji Dental College and Hospital, Chennai.

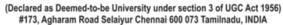




Tayleen Kour, Sajid Hussain



BHARATH INSTITUTE OF HIGHER EDUCATION AND RESEARCH





A HAND BOOK ON APHTHOUS ULCERS

AUTHORS:

DR. T.SARUMATHI

DR. B.SARAVANAKUMAR

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INTRODUCTION

A plethora of pathologic conditions may affect the normal morphologic characteristics and intactness of the oral mucosa, presenting as surface alterations. These changes on the surface of the oral mucosa can be divided into 3 major groups:

1) ulcerative, 2) vesiculobullous, and 3) papillary, papular or polypoid lesions.

While *both* ulcerative and vesiculobullous eventually manifest similar clinical a appearance, consisting of mucosal ulcerations and/or erosions, their difference lies in their initial presentation: the loss of tissue in vesiculobullous lesions is preceded by the formation of blisters which eventually rupture to form ulcers and erosions; in contrast, the so-called ulcerative lesions appear as ulcers from the outset in the absence of a previously identifiable clinical stage. On the other hand, papillary, papular or polypoid lesions encompass lesions caused by pathologic changes that distort the normal involving the mucosa appearance of the mucosal surface and assume an

exophytic presentation, without significant extension to the deeper submucosal tissues (Scully.C 2002)²⁰¹.

Ulcers and erosions can be the final common manifestation of a spectrum of conditions ranging from the simplest traumatic breach of the epithelium, to epithelial damage resulting from an immunological attack as in pemphigus, pemphigoid, lichen planus and aphthae; to damage because of an immune defect as in human immunodeficiency virus (HIV) disease and leukemia; to infections as in herpes viruses, tuberculosis and syphilis; to nutritional defects such as in vitamin deficiencies and some intestinal disease; or to neoplasia. The term 'ulcer' is used usually where there is damage to both epithelium and lamina propria, and a crater, sometimes made more obvious clinically by swelling caused bvedema proliferation in the surrounding tissue. The term 'erosion' is often used for breaches of the epithelium in which there is little damage to the underlying lamina propria. Such lesions, if penetrating the epithelium only partially, usually have a red or red and yellow appearance. If they penetrate the full thickness of the epithelium, however, they are

typically covered by a fibrinous exudate and may then have a yellowish appearance (Scully.C and Felix.D.H-2005)²⁰².

Histological examination is important in the of erosions and ulcerations. Early. diagnosis uncomplicated lesions are often easily identified histologically. However, contamination with saliva and super infection with oral flora may change a stillundiagnosed defect (e.g., herpetic blister) into a nonspecific lesion that can no longer be separated from other defects of different origin. With detailed inspection based on several factors it is possible in many cases to narrow the diagnostic possibilities. Important factors are (among others): shape, size, and distribution of the lesions, age of the patient, and involvement of other organs. In some cases there may still be areas in which the original diagnostic features are preserved. Small and large blisters are transitory findings in the oral cavity, since the constantly moist epithelium is very fragile. Vesicular and bullous dermatoses therefore fall under the main symptom tissue defect classification, since in these dermatoses the defect is the long lasting clinical finding (Wolfgang Bengel, Gunther Veltman – 1989)
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According to **Wood and Goaz** – 1980 ²⁵³ oral erosions and ulcerations can be subdivided into transitory and persistent forms. **Transitory** forms do not last longer than 3 weeks and heal spontaneously; **persistent** lesions remain for longer than 3 weeks and should be considered of possible malignant nature until the contrary can be demonstrated.

Erosive-ulcerative changes of the oral mucosa may be divided into three subgroups

- 1. Aphthous-aphthoid lesions (transitory): includes the aphthous as well as the vesiculoerosive mucosal changes of many viral dermatoses.
- 2. Bullous-erosive lesions (transitory): includes the primary bullous dermatoses, often still recognizable because of blister rests found on the periphery of the lesion.
- 3. Ulcerative lesions (persistent): includes the deep tissue defects, which remain for longer than 3 weeks

lesions of the oral mucosa. The morphological similarity of the defects of different origins, however, creates a major diagnostic problem for dentists (Johnson, R, L-1972) 105. Under superficial examination, lesions initially appear relatively monomorphic: after loss of the epithelial covering there is a superficial inflammation. This creates roundish erosion or ulceration, which is covered with a yellowish fibrinoid deposit encircled by a red halo (Chole, R. A.; G.H.Domb – 1979) 31 and the most common among them, is the recurrent aphthous stomatitis. This library dissertation reviews in detail about the very common but poorly understood mucosal disorder "Recurrent Aphthous Stomatitis".

Classification of Oral Ulcers

Ulceration is a breach in the oral epithelium, which typically exposes nerve endings in the underlying lamina propria, resulting in pain or soreness, especially when eating spicy foods or citrus fruits. Patients vary enormously in the degree to which they suffer and complain of soreness in relation

to oral ulceration. It is always important to exclude serious disorders such as oral cancer or other serious disease, but not all patients who complain of soreness have discernible organic disease. Conversely, some with serious disease have no pain. Even in those with detectable lesions, the level of complaint can vary enormously. Some patients with large ulcers complain little; others with minimal ulceration complain bitterly of discomfort. Sometimes there is a psychogenic influence.

Ulcers and erosions can also be the final common manifestation of a spectrum of conditions.

1. Oral Ulcers (Lawrence C. Schneider et al – 1998) 118

Acute	Multiple Ulcers Recurrent	Chronic	Solitary Ulcers
1. Acute necrotizing ulcerative gingivitis 2. Allergies* 3. Chemotherapy 4. Erythema multiforme* 5. Herpangina* 6. Herpes simplex virus, primary* 7. Herpes zoster virus* 8. Mucous patches 9. Radiotherapy	1. Aphthae 2. Herpes simplex virus, secondary*	1. Allergies* 2. Bullous pemphigoid* ' 3. Epidermolysis bullosa* 4. Lichen planus* 5. Lupus erythematosus 6. Mucous membrane pemphigoid* 7. Paraneoplastic pemphigus*	1. Aphthae 2. Chancre 3. Fungi (deep) 4. Gumma 5.Necrotizing sialometaplasia 6. Squamous cell carcinoma 7. Trauma 8. Tuberculosis

8. Pemphigus vulgaris*

- * Vesicles or bullae may occur in these conditions
- 2. Systemic and iatrogenic causes of oral ulcers (Crispian Scully, Rosemary Shotts-2000) 39

Microbial disease

- 1. Herpetic stomatitis
- 2. Chickenpox
- 3. Herpes zoster
- 4. Hand, foot, and mouth disease
- 5. Herpangina
- 6. Infectious mononucleosis
- 7. HIV infection
- 8. Acute necrotizing gingivitis
- 9. Tuberculosis
- 10. Syphilis
- 11. Fungal infections

Cutaneous disease

- 1. Lichen planus
- 2. Pemphigus
- 3. Pemphigoid
- 4. Erythema multiforme

- 5. Dermatitis herpetiformis
- 6. Linear IgA disease
- 7. Epidermolysis bullosa
- 8. Chronic ulcerative stomatitis
- 9. Other dermatoses

Malignant neoplasms

Blood disorders

- 1. Anaemia
- 2. Leukemia
- 3. Neutropenia
- 4. Other white cell dyscrasias

Gastrointestinal disease

- 1. Coeliac disease
- 2. Crohn's disease
- 3. Ulcerative colitis

Rheumatoid diseases

- 1. Lupus erythematosus
- 2. Behcet's syndrome
- 3. Sweet's syndrome
- 4. Reiter's disease

Drugs

- 1. Cytotoxic agents
- 2. Nicorandil

3. Others

Radiotherapy

3. According to Martin S. Greenberg 2003 133

I. Acute Multiple Ulcers

- 1. Herpes simplex virus infection
- 2. Coxsackie virus infection
- 3. Varicella zoster infection
- 4. Erythema Multiforme
- 5. Allergic Stomatitis
- 6. ANUG

II. Recurring Oral Ulcers

- 1. RAS
- 2. Behcet's Disease
- 3. Recurrent Intraoral Herpes
- 4. Cyclic Neutropenia

III. Chronic Multiple Ulcers

- 1. Pemphigus
- 2. Bullous Pemphigoid
- 3. Mucous Membrane Pemphigoid
- 4. Erosive Lichenplanus

IV. Single Ulcers

- 1. Histoplasmosis
- 2. Blastomycosis
- 3. Mucormycosis
- 4. Tuberculosis
- 5. Syphilis
- 6. Necrotising Sialometaplasia
- 4. According to Joseph A. Regezi et al 2003 107

A. I. Reactive Lesions

- A. Bacterial Conditions
- (i) Syphilis
- (ii) Actinomycosis
- (iii) NOMA
- B. Fungal Diseases
- (i) Mucormycosis
- (ii) Sporotrichosis
- II. Conditions associated with Immunologic Dysfunction
- (i) Aphthous ulcer
- (ii) Behcet's syndrome
- (iii) Erythema Multiforme
- (iv) Drug Reactions
- (v) Contact Allergy
- (vi) Wegener's Granulomatosis

- (vii) Cyclic neutropenia
- (viii) Midline Granuloma

III. NEOPLASMS

(i) Squamous cell carcinoma

(B) I. Short Term Ulcers

- 1. Traumatic Ulcer
- Recurrent aphthous, Recurrent herpes simplex
 & Herpetiform ulcers
- 3. Ulcer occurring as a result of odontogenic infection
- 4. Ulcer secondary to non infectious systemic disease

II. Persistent Ulcers

- 1. Traumatic ulcer
- 2. Major Aphthous ulcer
- 3. Squamous cell carcinoma
- 4. Low grade mucoepidermoid carcinoma
- 5. Metastatic Tumor
- 6. Keratoacanthoma
- 7. Necrotising sialometaplasia
- 8. Chancre
- 9. Gumma
- 10. Ulcer secondary to systemic disease.

5. Etiology of mouth ulcers (C. Scully and D. H. Felix – 2005)

Local causes

Trauma

- 1. Appliances
- 2. Iatrogenic
- 3. Non-accidental injury
- 4. Self-inflicted
- 5. Sharp teeth or restorations

Burns

- 1. Chemical
- 2. Cold
- 3. Electric
- 4. Heat
- 5. Radiation

Recurrent aphthae

Infections

- 1. Acute necrotising gingivitis
- 2. Chickenpox
- 3. Deep mycoses
- 4. Hand, foot and mouth disease
- 5. Herpangina
- 6. Herpetic stomatitis
- 7. *HIV*

- 8. Infectious mononucleosis
- 9. Syphilis
- 10. Tuberculosis

Drugs

- 1. Cytotoxic drugs,
- 2. Nicorandil, NSAIDs
- 3. Many others

Malignant neoplasms

- 1. Oral
- 2. Encroaching from antrum

Systemic disease

a. Mucocutaneous disease

- 1. Behcet's syndrome
- 2. Chronic ulcerative stomatitis
- 3. Epidermolysis bullosa
- 4. Erythema multiforme
- 5. Lichen planus
- 6. Pemphigus vulgaris
- 7. Sub-epithelial immune blistering diseases
- 8. (Pemphigoid and variants, dermatitis herpetiformis, linear IgA disease)

b. Haematological disorders

- 1. Anaemia
- 2. Gammopathies
- 3. Haematinic deficiencies
- 4. Leukaemia and myelodysplastic syndrome
- 5. Neutropenia and other white cell dyscrasias

c. Gastrointestinal disease

- 1. Coeliac disease
- 2. Crohn's disease
- 3. Ulcerative colitis

Miscellaneous uncommon diseases

- 1. Eosinophilic ulcer
- 2. Giant cell arteritis
- 3. Hypereosinophilic syndrome
- 4. Lupus erythematosus
- 5. Necrotising sialometaplasia
- 6. Periarteritis nodosa
- 7. Reiters syndrome
- 8. Sweet's syndrome
- 9. Wegener's granulomatosis

Recurrent Aphthous Stomatitis (RAS)

Definition of RAS

An inflammatory condition of unknown etiology characterized by painful, recurrent (single or multiple) ulcerations of the oral mucosa (Graykowski et al. 1966) 80.

Synonyms

Chronic-recurring aphthae; habitual aphthae; benign aphthosis; recurrent stomatitis; canker sore.

Recurrent aphthous stomatitis is a common oral mucosal disorder that, despite detailed investigation, has an unknown cause and poor effective management in general and specialty dental practice. RAS is an ulcerative disease that most often occurs in otherwise healthy individuals and presents as a painful lesion of the buccal and labial mucosa and tongue (Martin S. Greenberg – 2005) 133.

Historical Perspective

Recurrent aphthous ulcer (RAS) seems to be as old as humanity itself. The Father of Medicine, Hippocrates (460 to 370 BC) is credited with the first use of the term "aphthai" in relation to focal painful inflammation of the oral mucosa, although valid clinical description of RAS only appeared in 1898 in

a paper published by Mikulicz and Kummel (Sircus et al. 1957²¹⁸). RAS is one of the most common and poorly understood mucosal disorders. It is found in men and women of all ages, races, and geographic regions (Embil et al. 1975) 55. It occurs more frequently in times of stress (Sibley 1899 215, Andrews and Hall 1990 6), and it is estimated that at least 1 in 5 individuals is afflicted with RAS (Axell and Henricsson 1985)9. Much progress has been made over the last four decades on the epidemiology, clinical description, predisposing factors, and symptomatic treatment of RAS. Considerable research attention has been devoted to elucidating the etiology of RAS. Local and systemic conditions, genetic, immunologic, and microbial factors all may play a role in the pathogenesis of RAS. However, to date, no principal cause has been discovered (Ship 1996 211, Porter et al. 1998¹⁷⁰).

Since the etiology is unknown, the diagnosis is entirely based on history and clinical criteria and no laboratory procedures exist to confirm the diagnosis (Ship 1996)²¹¹. There is no curative therapy to prevent the recurrence of ulcers, and all available treatment modalities can only reduce the frequency or

severity of the lesions. Although RAS may be a marker of an underlying systemic illness such as coeliac disease (Meini et al. 1993) 139, or may be present as one of the features of Behcet's disease (International Study Group for Behcet's Disease 1990)102, in most cases no additional body systems are affected, and remain otherwise fit patients and well. Theetiopathogenesis of RAS is not fully understood. Different etiologies and different mechanisms might be operative in the aetiopathogenesis of aphthous ulceration, however, pain, recurrence, self-limitation of the condition, and destruction of the epithelium seem to be the ultimate outcomes. For better understanding of RAS, it is important to study the inflammatory cytokines network and the cells involved in the initiation and progression of inflammation. This information should provide clues to the cause(s) of RAS and may lead to the development of effective and rational treatment for the control of this condition. The findings of an expansion of the dendritic cell system, high density and hyperactive mast cells, prominent expression of pro-inflammatory cytokine tumor necrosis factor (TNF), marked cell proliferation insitu. and high counts of intraepithelial (T lymphocytes) in RAS lesions are not the end of the RAS story, but the beginning of an exciting new chapter in attempts to understand the etiopathogenesis of this fascinating, periodical and painful- and still enigmatic- condition.

Epidemiology

Race affected

Epidemiologic studies have shown that the prevalence of RAS is influenced by the population studied, diagnostic criteria, and environmental factors. RAS seems to be infrequent in Bedouin Arabs and is more common in Western countries (Embil et al. 1975 55, Fahmy 197661).

In cross sectional study RAS lesions were found only in about 2% of Swedish adults (Axell and Henricsson 1985) 9.

Approximately 20% of the general population is affected by RAS, but incidence varies from 5% to 50% depending on the ethnic, and socioeconomic groups studied (Rogers RS - 1997) ¹⁸⁶.

Sex predilection

Activities of daily living affect the prevalence of RAS. RAS prevalence was higher (male, 48.3%; female, 57.2%) among professional-school students than in the same subjects 12 years later when they had become practicing professionals. This finding led some investigators to theorize that stress during student life is a major factor in RAS, although the difference in age groups should also be considered (Martin S. Greenberg – 2005) 133.

Age of onset

The peak age of onset is the second decade (Sircus et al. 1957 218, Lehner 1969¹¹⁹).

The onset of RAS seems to peak between the ages of 10 and 19 years before becoming less frequent with advancing age and does not seem to depend on geographic influences, age, gender, or race (Ship JA et al -2000) 212 .

RAS beginning or worsening well into adult life should increase suspicion that the oral ulcers are being caused by an underlying medical disorder such as hematologic, immunologic, or connective tissue disease or Behcet's syndrome (Martin S. Greenberg – 2005) 133.

Children

Children with RAS-positive parents have a 90% chance of developing RAS compared with 20% in those with RAS-negative parents (Ship II – 1972) 207 .

In children, prevalence of RAS may be as high as 39% and is influenced by the presence of RAS in one or both parents (Miller MF et al -1980) ¹⁴⁵.

In childhood, RAS is the most common form of oral ulceration (Field et al. 1992)⁷⁰.

In children of high socioeconomic status, RAS is five times more prevalent and represents 50% of oral mucosal lesions in this cohort (Crivelli MR – 1988) 40.

Studies of self-reported prevalence of recurrent aphthous ulcers (RAS)

Author(s) Year Country		Study population		Prevalence (%)		
Hathor(s)	1007	GOWNING.	N	Age (yr)	Characteristics	RAS
Sircus et al ²¹⁸	1957		1738	All ages	Hospital & medical patients	19.3
Ship et al ²⁰⁹	1960	U.K	1788	X=19.1	Health science students	55
Ship et al ²⁰⁸ Shapiro et al	1967	U.S	343	X = 21.7	Medical/dental students	66.2
Donatsky et al	1970 1973	U.S U.S	78 88 31 512	n.r n.r n.r	Smokers Non smokers Past smokers Dental students	26.9 46.6 38.7
Embil et al ⁵⁵	1975	Denmark	10531	n.r	Health science students	56.4 43.1
Fahmy 61	1976 1976	21 countries Sweden Kuwait	20333 9000	15+ all ages	Country residents Kuwait Arabs	17.7 18.0 35.0
Miller et al ¹⁴⁶	19/0	U.S	11000	x=31	Non Kuwait Arabs	50.7
Ferguson et al	1977 a	U.K	704 217	25-30	Health professionals Women	25.4 6.1
	1984			46- 56	Women	

n.r - not reported

Etiologic factors associated with recurrent aphthous stomatitis:

(Sunday O. Akintoye 2005) 225

Environmental factors

- Stress / psychological imbalance
- Trauma
- Tobacco
- Dysregulated saliva composition

Microbiological agents

- Bacterial
- Viral

RAS and Hormonal changes

Nutritional

- Gluten sensitive enteropathy
- Iron, folic acid, zinc deficiencies
- Vitamin B1, B2, B6 and B12 deficiencies

Genetic

- Ethnicity
- HLA haplotypes

Allergic / immunologic

- Local T-lymphocytes cytotoxicity
- Abnormal; CD4: CD8 ratio

- Dysregulated cytokine levels
- Microbe induced hypersensitivity
- Sodium lauryl sulfate sensitivity
- Food sensitivity
- Drugs and RAS

Systemic diseases associated with RAS

- Behcets disease
- MAGIC syndrome
- Marshalls syndrome
- Sweet's syndrome
- Crohns diseases
- Ulcerative colitis
- Cyclic neutropenia
- HIV infection

Environmental factors

Stress

Earlier studies by Sircus et al. 1957 ²¹⁸, Ship et al. 1960 ²⁰⁹, 1967 ²¹⁰, Miller et al. 1977a¹⁴⁶ have documented an association between RAS and a variety of psychological factors including anxiety, repressed hostility, as well as job related and other stress factors.

Conversely, other studies have failed to reveal any association between anxiety (Heft and Wray 1982) 95, depression (Ferguson et al. 1984) 68, psychological life stress (Pedersen 1989) 160 and recurrences of RAS.

A study by Andrews and Hall 1990 ⁶, in which the relaxation/imagery treatment program was used found a significant decrease in the frequency of ulcer recurrence for all treated subjects.

According to **Robert W. Barrons 2001** ¹⁸¹ emotional and environmental stresses may precede 60% of first time aphthous ulcer cases and involve 21% of recurrent episodes. A frequency of RAS of 31-66% has been reported among medical and dental students, compared with 10-20% in the general population.

Stress of student life may be the precipitating factor for the higher prevalence of RAS in a cohort of professional students (Sunday O.Akintoye 2005) 225.

Although the majority of studies have been unable to validate the concept that stress plays an important role in the development of RAS, the literature continues to report that stress may play a role in precipitating RAS. (Natah.S.S 2005)¹⁵⁰

Psychological imbalance

Psychological illness has been proposed to initiate some episodes of RAS (Ship et al., 1961²¹⁰; Miller et al., 1977 a¹⁴⁶), and there are sparse data to suggest that some patients may benefit from antidepressant therapy (Yaacob and Hamid, 1985) ²⁶¹. Nevertheless, no significant objective neurosis has been observed in two further studies (Pedersen, 1989 ¹⁶⁰; Buajeeb et al., 1990) ²⁵.

Trauma:

According to **Ross et al. 1958** ¹⁹⁰, **Wray et al. 1981** ²⁵⁹ a subset of patients with RAS are predisposed to develop aphthae at sites of trauma. Local, physical trauma may initiate ulcers in susceptible people.

Sallay and Banoczy, 1968 ¹⁹¹ have stated that RAS is uncommon where mucosal keratinization is present.

The reason why local trauma such as anesthetic injections, sharp foods, tooth brushing, and dental treatment (**Kvam et al. 1987**) ¹¹⁵ can trigger aphthous ulceration in these patients is still unknown.

In a trial by **Robert W. Barrons 2001** ¹⁸¹ involving 128 patients 16% claimed that a traumatic incident was associated with their RAS

Trauma predisposes to RAS by inducing edema, early cellular inflammation associated with an increased viscosity of the oral submucosal extracellular matrix. Not all oral trauma lead to RAS, because denture wearers are usually three times more susceptible to oral mucosal ulceration, but RAS is not the most prevalent ulceration in this cohort. (Sunday O.Akintoye 2005) 225

Tobacco:

In the early 1960s it was reported that aphthous ulceration was relieved by the resumption of cigarette smoking by **Brookman 1960²²**; **Dorsey 1963** ⁵¹.

RAS is uncommon where mucosal keratinization is present especially in patients who smoke tobacco (Sallay and Banoczy, 1968) 191.

In a population study, **Shapiro et al** (1970)²⁰⁵ showed a negative correlation between self reported smoking histories and RAS.

This was further confirmed by a study by Axell in 1985 (Axell and Hericsson 1985) 9.

According to **Rennie et al. 1985** ¹⁷⁶ the majority of patients with RAS are nonsmokers.

Nicotine has been found to be beneficial in RAS (Bittoun 1991) ¹⁸ and its effects may result from influences on nerve function, although these agents may also exert direct anti-inflammatory effects.

According to **Grady et al 1992** 79 smokeless tobacco has also been noted to have a negative correlation with RAS.

These studies relying on self reporting of tobacco habits have shown that there appears to be a negative epidemiological correlation between smoking and aphthous stomatitis. A single plasma cotine level determination has been shown to give an accurate indication of cotine long term levels and therefore a sensitive and specific marker for determination of smoking status (Kemmeren et al 1994 111, Perez – Stable et al 1995 163)

In a recent study by **Tuzun et al. 2000** ²³⁶ only 9% of RAS patients were found to be active smokers compared with 25% among the control subjects.

Using cotine levels to estimate the smoking status Atkin PA et al 2002 8 found that a significantly smaller population of RAS patients (2.38%) were smokers compared with an age and sex matched control population (14.81%), confirming the findings of earlier studies using other methods of assessing smoking status.

Nicotine containing tablets also appear to control the frequency of RAS. (Crispian Scully et al 2003) 38.

However, the mechanism by which cigarette smoking protects against RAS is still unknown. $(Natah.S.S~2004)^{150}$

Dysregulated saliva composition:

Some changes in the saliva composition, such as pH, that affect the local properties of saliva and a stress induced rise in salivary cortisol have been correlated with RAS. Quantitative or qualitative changes in salivary gland function have been hypothesized to play a role in the pathogenesis of RAS, however most studies have not found a definite relationship. (Ship JA - 1996) 211 . Although direct association of salivary gland dysfunction with RAS has not been demonstrated, patients with a combination of RAS and xerostomia may experience increased symptoms. (Sunday O.Akintoye 2005) 225

Microbial agents

Bacterial:

Oral streptoccocci

Some studies have disclosed elevated serum antibody titers to viridans streptococci among RAS patients; other investigations have yielded contradictory results (Barile et al., 1968¹²; Donatsky, 1976⁵⁰).

Studies by (Donatsky 1976) ⁵⁰ have found raised levels of antibodies against certain oral streptococcal strains in patients with RAS when compared with controls.

Oral streptoccocci were previously suggested as important in the pathogenesis of RAS, either as direct pathogens or as an antigenic stimulus culminating in the genesis of antibodies that may conceivably cross-react with keratinocyte antigenic determinants (Martin et al., 1979¹³⁴; Lindemann et al., 1985 ¹²³).

The initial L-form isolate from RAS patients was typed as S. sanguis, but later analysis disclosed that this organism was actually a strain of S. mitis (Hoover and Greenspan, 1983) 100.

Furthermore, lymphocyte mitogenic responses to S. sanguis and S. mitis in RAS patients are not significantly different from those in control subjects (Gadol et al., 1985⁷⁴; Greenspan et al., 1985⁸²).

Cross-reaction of antibacterial antibodies with oral mucosa has been postulated as an immunopathogenic mechanism in RAS. Later studies, however, have not confirmed these observations (Hoover et al. 1983 100, Greenspan et al. 1985 82).

Cross - reactivity between mycobacteria 65 kDa heat shock protein and Streptococcus oralis has been demonstrated, and significantly elevated levels of serum antibodies to recombinant 65 - K Da mycobacterial heat shock protein have been observed in RAS. Lymphocytes of RAS patients have a significantly increased lymphoproliferative response to peptide epitope 91 - 105 of the 65 - k Da mycobactria heat shock protein in the ulcerative stage as opposed to the period of remission. There is a cross reactivity between the microbial 65 - k Da heat shock protein and the 60 k DA human mitochondrial heat shock protein. Thus RAS may be a T cell mediated responses to antigens of S.oralis that cross react with the mitochondrial heat shock proteins and induce oral mucosal damage. Conversely other investigators have suggested that immediate up regulation of heat shock proteins in any cell type,

anywhere in the body, as a consequence of stress may trigger T cells with a regulatory phenotype. This would provide the immune system with an immunoregulatory mechanism which acts to monitor and control dangerous or potentially deleterious inflammatory responses. However heat shock proteins in RAS are protective or destructive or have a dual role is still unclear. (Natah.S.S 2004) 150.

Helicobacter pylori (H. pylori)

Helicobacter pylori (H. pylori) is a Gram negative, spiral bacteria which has several pili and grows in anaerobic or semi-aerobic environments. By secreting urease and other proteinase, this germ can grow and duplicate on the surface of gastric mucosa and the space of its villi (Jordan RC et al 1997 106, Greenwood D et al 2002 84).

In 1989 the bacteria were isolated from dental plaques; therefore, the oral cavity is considered as a secondary resource of infection (Thomas E et al 1997) 233 .

Because of the important role of H. pylori in peptic ulcers, the histological similarities between RAS and peptic ulcers, and the response of RAS to the broad-spectrum antibiotics such as tetracycline used to eradicate H. pylori infection in some gastrointestinal (GI) disorders, some articles suggest that H. pylori has a probable role in RAS development. However, there is limited documentation of the colonization and probable role of H. pylori in the induction of oral aphthous ulcers (Birek C 1999)¹⁷.

PCR is a complex molecular method that has a sensitivity of about 95% and specificity of about 100% for the presence of H. pylori DNA in stomach specimens (Reeves G 2000) ¹⁷⁵.

The germ was isolated from a human gastric biopsy specimen in 1983 for the first time. It lives very well in the acidic medium of the host stomach and forms a clone there. Then it causes active chronic gastritis, acute gastritis, and peptic and duodenal ulcers. It is also related to peptic ulcer complications, gastric carcinoma and primary B-cell

lymphoma, food allergy in chronic gastritis, exacerbation of hyperemesis gravidarum, and ischemic cerebral stroke risk factors (Bobrzynski A et al 2002) 19.

Fariborz Mansour-Ghanaei et al 2005 65 used this molecular method, and found only one positive case of H. pylori among the 50 cases examined. This can show that in spite of histological similarity between gastric ulcer and RAS, a lack of H. Pylori in recurrent aphthous stomatitis is possible. These results are similar to those of Porter and Champan using other diagnosis methods. Porter and colleagues expressed the opinion that H. pylori possesses no etiological importance in RAS development because the frequency of anti-H. pylori seropositivity in patients with RAS (30.6%) was not significantly different from that of patients with other oral ulcerative lesions (33%) and a control group (24%). In a study, no H. pylori was found in their patients' ulcers using the Campylobacter-like aphthous organisms (CLO) test on biopsy specimens. Riggio et al (2000) 179 could isolate H. pylori DNA in 11% of oral aphthous biopsy specimens using PCR, but they

stated that the obtained results could not defend an etiological role for H. pylori in RAS development. Also, Fritscher et al (2004)⁷², using PCR, concluded that there was not any association between RAS lesions and H. pylori infection of the oral cavity in children and adolescents. In contrast to these studies, Birek and colleagues (1999)¹⁷ could isolate H. pylori DNA from 71.9% of oral aphthous swab specimens using the PCR method. They concluded that mostly H. pylori can be related to RAS. Therefore it is necessary in doing another study with a control group and a greater sample volume to verify the absence of this relation. (Fariborz Mansour-Ghanaei et al 2005)

Viral:

An association of RAS with adenoviruses has been suggested by Sallay et al., 1971 ¹⁹², 1973 ¹⁹³, but adenoviruses are ubiquitous organisms, and these results need confirmation. It has been suggested that viruses may play a role in RAS and Behcet's syndrome (Hooks, 1978) ⁹⁸.

Given the common and recurrent nature of RAS. an association with viral infection has long been postulated. In particular, the human herpes viruses (HHVs) have been commonly implicated in the pathogenesis of RAS. The HHV family now includes 8 members: herpes simplex virus 1 (HSV.I), herpes simplex virus 2 (HSV-Z), varicella zoster virus (VZV), Epstein-Barr virus (EB V), cytomegalovirus (CMV), human herpesvirus-6 (HHV-6), human herpesvirus-7 (HHV-7), and human herpesvirus-8 (HHV-8). Previous studies have demonstrated HHV in the oral mucosa and/or peripheral blood of subjects with RAS. However, because of the small number of subjects examined, no definitive conclusions regarding the association of HHV with RAS have been possible (Jester JD et al 1990) 104.

Previous studies in which viral cultures, electron microscopy, and histopathologic and immunohistochemical techniques were used have failed to document a causal association between RAS and viral infection. With the development of highly sensitive laboratory techniques such as PCR and in situ hybridization, the concept of a viral pathogenesis

of RAS has received renewed support as HHV nucleic acids have been detected in the oral mucosa and peripheral blood of patients with RAS (Jester JD et al 1990) 104.

Pedersen et al 1993b ¹⁶¹ demonstrated VZV DNA in 20/20 RAS lesions; this compared with 2/10 controls. However, the VZV DNA was identified with only 1 of 5 PCR primer pairs, creating doubt that what was detected was specifically VZV. In addition the presence of VZV in the oropharynx appears to be limited to the period of acute varicella or temporarily after exposure to household contacts with varicella.

Sun et al 1996 ²²² reported the presence of CMV in 3/9 RAS lesions in comparison with 0/5 controls; again. However, these findings were not supported when larger numbers of patients were examined.

One could speculate that in patients with RAS. HHVs or other incidental infectious agents in the oropharynx stimulate an abnormal inflammatory reaction, resulting in mucosal damage and ulceration.

Recent studies examining T cell epitopes of the 65-kD microbial heat shock protein in patients with RAS and Behcet's disease provide further support for such an infection induced autoimmune phenomenon. Viruses can stimulate the production of human heat shock protein, enhancing this immunologic event. In addition, certain human herpes viruses have been identified as having superantigen actively which has been linked to the induction of autoimmunity (Renno T, Acha-Orbea H 1996) 177.

Ghodratnama et al 1997 77 detected HHV-6 in 6/12 RAS lesions.

If HHVs are important in the pathogenesis of RAS either directly or indirectly (eg, viral induced alteration of local immunity), it is hypothesized that one or more of these viruses should be routinely detected in lesions of RAS and/or peripheral blood leukocytes of a subject with RAS if he or she is examined early during an acute episode (Sylvia L. Brice et al 2000) 227.

PCR analysis of oral biopsies or swabs from patients with RAS must be interpreted with caution. Viral DNA in saliva, exfoliated salivary gland epithelial cells, desquamated oral mucosal cells from sites distant to the active ulcer, and peripheral blood could all contribute to a positive result. The problem is further compounded by the fact that most HHVs may be routinely detected in the oropharynx, saliva, and peripheral blood cells of the normal population, although the frequency with which this is observed varies among studies (Sylvia L. Brice et al 2000) 227.

RAS and hormonal changes

Sircus and co-workers (1957) ²¹⁸ had reported that almost no men developed RAS after the age of 50, whereas 10% of women had their first episode between 50-59.

A complete remission during pregnancy have been reported (Sircus et al. 1957²¹⁸, Vincent and Lilly 1992 ²⁴²) but with exacerbations occurring in the puerperium (Dolby 1968) ⁴⁷.

It appears from different conflicting studies (Ship et al. 1961 ²¹⁰, Dolby 1968 ⁴⁷, Segal et al. 1974 ²⁰⁴, Boggess et al. 1990 ²⁰, McCartan and Sullivan 1992 ¹³⁶) that minor subsets of women with RAS have cyclical oral ulceration related to the onset of menstruation or the luteal phase of menstrual period.

However, the association between RAS and menopause (McCartan and Sullivan 1992)¹³⁶ has not been established.

The menstrual cycle, an event that punctuates the lives of most women, may be associated with diverse physical, psychological, and behavioral changes. Exacerbation of certain medical conditions specific menstrual cycle phases is a wellrecognized phenomenon. Accurate documentation of menstrual calendar allows symptoms ona identification of women with cyclic alterations in disease activity. The majority of these effects occur during the luteal and menstrual phases of the cycle. Several theories have been proposed to explain these menstrual cycle-related effects on existing disease processes, including fluctuations in levels of sex

steroids, cyclic alterations in the immune system, and changing perceptions of disease severity brought about by premenstrual alterations in mood, as seen in premenstrual syndrome. Disorders exacerbated by the postovulatory and premenstrual phases of the menstrual cycle include acne, endocrine allergy and anaphylaxis, hereditary angioedema, erythema multiforme, urticaria, aphthous ulcers, Behcet's syndrome, acute intermittent porphyria, paroxysmal supraventricular tachycardia, glaucoma, and multiple sclerosis(Allison M 1998)⁵.

Hematological deficiencies

Hematological deficiencies have been found in about (20%) of patients with RAS. In several studies, deficiencies of iron, vitamin B12, and folate have been reported although in many cases the deficiencies were marginally low (Wray et al. 1975 ²⁵⁷, Ferguson et al. 1976 ⁶⁷, 1980 ⁶⁹, Tyldesley 1981 ²³⁷, Challacombe et al. 1983 ²⁹, Porter et al. 1986 ¹⁶⁸, Field et al. 1987 ⁷¹).

However, Olson and colleagues (Olson et al. 1982) 154 found that vitamin B12, folate and iron

deficiencies were not significantly different between the patients with RAS and controls.

Low serum ferritin levels were found in 8-12% of patients with RAS, compared with 3-5% in controls, and the level did not differ in different subtypes of RAS (Challacombe et al. 1983) ²⁹.

Another pilot study on 22 HIV-infected patients with RAS suggested that vitamin B12 or folate deficiencies were not risk factors for HIV-associated RAS (MacPhail and Greenspan 1997) 127.

Masayuki Ogura et al's (2001) ¹³⁵results based on the aspect of food frequency intake were partially consistent with the hematologic studies, showing iron and vitamin B deficiencies in patients with RAS. Because food intake is one of the treatable factors for RAS, the results of the study might be helpful as a daily preventive measure in patients with RAS. The study suggested the hypothesis that not only iron and vitamin BI but also calcium and vitamin Care deficient in patients with RAS. This hypothesis was supported by the studies demonstrating inhibited

keratinization of hamster cheek pouch epithelium in the media with lower calcium concentration. In addition, vitamin C is required for the synthesis of collagen, and vitamin C deficiency might lead to the breakdown already healed wounds.

However, in the majority of cases, there was no identifiable underlying cause for those RAS patients who had a ferritin deficiency. In a Scottish study, Nolan and co-workers (1991)¹⁵² found that 28.2% of patients with RAS had deficiencies of vitamins B1, B2, and/or B6. They showed also that patients who have both RAS and a vitamin B deficiency could benefit from vitamin replacement therapy. It appears from the above-mentioned literature that the wide variations in the findings may be due to differences in genetic background and dietary habits of examined patients, or the multi-factorial etiology of RAS. (Natah.S.S 2004) 150

Zinc deficiency

The improvement of RAS with zinc sulphate supplementation were described in an open trial and in a case report of aphthous ulcers with zinc

deficiency and immunodeficiency (Merchant et al. 1977 141, Endre 1991 56).

But such improvement could not be confirmed in later studies (Merchant et al. 1981 ¹⁴², Wray 1982²⁵⁵).

In a Chinese study (Pang 1992) ¹⁵⁸, the level of serum zinc of 75 cases of RAS was found to be on a lower level within normal range, and serum copper was also normal. So far no information exists on the association of RAS and other trace elements.

Antioxidants

There is an increased oxidative stress and antioxidant vitamins (A, E and C) levels are significantly decreased in patients with aphthous ulceration. Serum and saliva vitamin A levels in patients with RAS were significantly lower when compared to the controls (p < 0.005). Vitamin A functions as catalyzer of removal of singlet oxygen and as a result vitamin A inhibits singlet oxygen dependent reactions (Jound 1986) 108 .

In normal conditions, mucous membranes are protected from damage caused by harmful molecules as well as from free radicals by protective surface phenomena, general host defenses and specific immune responses. The human body has its own natural free radical scavengers, which include the antioxidant vitamins, vitamin A and beta-carotene, B-complex vitamins, vitamin C and vitamin E, the mineral selenium and superoxide dismutase, glutathione peroxidase, reductase and catalase (Arthur 1988 7; Halliwell 1994) 86.

Nonenzymatic antioxidant system, which consists of vitamins A, E, and C and Se, has been shown to react with organic free radicals and protect biomembranes from free radical-induced damage (Cohen 1994 33; Halliwell 1994 86).

Malondialdehyde (MDA) is a stable end product of peroxidation of membrane lipids by reactive oxygen species, and is widely used as an indicator of increased lipid peroxidation. It is well established that interactions between MDA and membrane components result in disturbed structure and function of cell membranes (Nielsen et al. 1997) ¹⁵¹.

Serum and saliva vitamin E levels in patients with RAS were also significantly lower when compared to the controls (p < 0.005). Serum vitamin C levels in the patients with RAS were significantly lower when compared to the controls (p < 0.05). Vitamin C also has a role in activating vitamin E when it loses its antioxidant capacity by turning into tocopherol (Levine 1997) 122 .

As a free radical scavenger, ascorbate works directly in the watery environment of the cells and in the lipid rich areas of the cell, interacting with vitamin E in the later medium. The same property of vitamin C also prevents the formation of nitrosamines from nitrites and nitrates. Vitamin C inhibits division and growth of cell through the production of hydrogen peroxide, which damages the cells probably through an unidentified free radical(s) generation (Maramag et al. 1997) 131.

There have been studies linking increased oxidative stress and impaired antioxidant capacity in patients with RAS. Cimen et al. (2003) 32 reported increased oxidative stress and decreased antioxidant defenses in mucosa of patients with RAS. Since free reactive oxygen radicals cause destruction of biomembranes by oxidizing unsaturated fatty acids, and oxidative stress suppresses the immune system's ability to protect and restore affected cells, antioxidative status of patients suffering from RAS is among to the potential determinants of susceptibility to this disorder. In the study by Yunus Saral et al (2005) ²⁶⁴, they observed that serum and saliva levels of some non-enzymatic indicators of antioxidant protective system (vitamins A, C and E) and levels of MDA (an indicator of lipid peroxidation) was higher in patients with RAS than in a matched group of healthy control subjects. Cimen et al. (2003) 32 reported that plasma MDA levels in patients with RAS was higher than that in the control group (p < 0.01). Consistently, in the study by Yunus Saral et al (2005) ²⁶⁴ serum and saliva MDA levels in patients with RAS were significantly higher than in the controls (p < 0.005).

Furthermore, an increased level of lipid peroxidation and a decreased level of tocopherols in experimental gastric mucosalinjury and also in plasma of patients with gastric ulcer has been reported (Tandon et al. 2004) 228.

Genetic

In some individuals, RAS may have a familial basis. Possibly more than 40% of patients may have a familial history of RAS (Sircus et al. 1957) ²¹⁸.

Patients with a positive family history of RAS develop oral ulcers at an earlier age and have more severe symptoms than individuals with no family history of RAS (Ship 1965 ²⁰⁶, Miller et al. 1977a ¹⁴⁶, Miller et al. 1980 ¹⁴⁵).

The probability of a sibling developing RAS is influenced by the parents' RAS status with increased risk in children of two affected parents (67-90%), as well as there being a high correlation of RAS in identical twins (Ship 1972 ²⁰⁷, Miller et al. 1977b¹⁴⁴).

Nevertheless, there is a clear variability in host susceptibility, which can be explained by a polygenic inheritance, with the penetrance being dependent on environmental factors (Ship 1972)²⁰⁷.

Genetic factors have been implicated numerous studies on the association of RAS and the genetically determined human leukocyte antigen (HLA) subtypes. An increase in the frequency of HLA2 (Challacombe et al. 1977(b)) 28, B12 (Lehner et al. 1982 120, Malmstrom et al. 1983 130), B51 and Cw7 in Jewish patients (Shohat-Zabarski et al. 1992) 213, DR2 (Lehner et al. 1982 120, Ozbakir et al. 1987 156), DR4 in Turkish RAS patients (Ozbakir et al. 1987) 156, DR5 and A28 in Greeks (Albanidou-Farmaki et al. 1988) 3, DR7 and MT3 (Gallina et al. 1985) 76 in Sicilians and DRw9 in Chinese patients (Sun et al. 1991 224) have been noted in patients with RAS. There may be a negative association with HLA-B5 in Sicilians (Gallina et al. 1985) 76 and DR4 in the Greek population (Albanidou-Farmaki et al. 1988)³.

Many studies have reported a variety of associations or absence of associations (Platz et al.

1976 ¹⁶⁷, Dolby et al. 1977 ⁴⁹, Gallina et al. 1985 ⁷⁶, Ozbakir et al. 1987¹⁵⁶) between RAS and a particular HLA antigen. This could be explained by the variable ethnic backgrounds of studied patients, or more likely the multiple etiologic basis for RAS. The above mentioned literature, however, suggests that RAS, at least in certain persons, has a genetic basis.

Allergic / immunologic

Allergic factors:

Allergy has been suspected as a cause of RAS, and hypersensitivity to certain food substances, oral microbes such as Streptococcus sanguis causative factors, although there remains no strong evidence that allergy is a major cause of this disorder. Although some studies have reported that RAS patients tend to have a higher hypersensitivity to environmental allergens, other reports did not find significant correlation between hypersensitivity and RAS (Sunday O.Akintoye 2005²²⁵, Martin S. Greenbrg 2005 133).

Sodium lauryl sulfate (SLS) is an anionic detergent that has been used as the major or sole surfactant in most dentifrices for more than 20 years. It solubilises flavour oils and lipid-soluble antibacterial agents such as triclosan in dentifrice, and it has a direct anti-microbial effect. Searls and Berg (1986) 204 demonstrated the ability of SLS to increase the epithelial desquamation rate when they reported increased salivary epithelial cell counts in healthy volunteers during 1 week's use of SLS-containing dentifrice when compared to those obtained during 1 week's use of SLS-free dentifrice. Subsequent studies investigating the effect or SLS on oral desquamation have involved exaggerated use models, either using mouthwashes with higher SLS concentrations than are available on the market or using capsplints for the direct application of toothpaste to the oral mucosa.

It is well established that SLS is an irritant to skin at high concentrations and that it's repeated application results in a dose-dependent contact dermatitis. It causes an increase in trans-epidermal water loss and increased penetration of molecules

through the epithelium into the underlying connective tissue. Thus, it is possible that SLS in dentifrice could influence the barrier function of oral mucosa causing enhanced penetration of exogenous antigens. This raises the possibility that SLS could play a role in the pathogenesis of RAS and it was thus of interest to investigate the possibility that SLS could exacerbate ulcer pattern in RAS sufferers (Serup and Staberg, 1987²⁰⁵, Wilhelm et al, 1991).

Barkvolland Rolla (1991)¹³ was the first to report a possible association between the use of an SLS-containing dentifrice and RAS. They reported a mean decrease in ulcer incidence of 71.5% in a group of 10 RAS patients during a 3 month period using an SLS-free dentifrice when compared to the incidence experienced during a period of the same duration when an SLS paste was used. The authors attributed this reduction in ulcer incidence to a denaturing effect of SLS on the oral mucin layer although there was no evidence to support this hypothesis.

In a study of the effect of an SLS-containing mouthwash on plaque formation, it was reported a

protracted burning sensation after 4 days in almost all of 16 volunteers who rinsed twice daily for I min with a 1% SLS mouthwash. Additionally, mucosal erosions were observed in seven of the volunteers. The concentration of SLS in dentifrices in Europe and North America ranges from approximately 0.5-2.0%. In another study II subjects rinsed with a 1.5% SLS mouthwash using the same regime as in the previous study. SLS induced painful desquamations in seven subjects, with two additional subjects having soreness without desquamation (Waaler et al, 1993)²⁴⁵.

Herlofson and Barkvoll (1993) ⁹⁶ investigated the effect of SLS-containing dentifrices when applied in capsplints for 2 min twice daily for 4 days to the attached gingivae and alveolar mucosa of 10 volunteers. Six volunteers developed abnormal desquamation (epithelial sheet sloughing) following application of a 1.5% SLS paste. 'In a further study they demonstrated that pre-menopausal women were more susceptible than post-menopausal women to SLS-induced desquamation (Herlofson and Barkvoll, 1996) ⁹⁷.

Reports of side effects attributable to the surfactant content of dentifrice have been reported leading to speculation that it may exacerbate some oral mucosal conditions (Healy CM 1999) 91.

Food hypersensitivity

Some studies have noted an increased prevalence of atopy among RAS patients (Tuft and Ettleson 1956 ²³⁵, Wilson 1980 ²⁵⁰), whereas Wray and co-workers (1982)²⁵⁹ found no significant difference in the incidence of atopy in RAS patients compared with normal population.

Some studies correlate the onset of ulcers with exposure to certain foods,

Cow's milk -Thomas et al. 1973 232.

Chocolate, nuts -Wray et al. 1982 259.

Cheese -Hay and Reade 1984 88.

Gluten -Wray 1981 254, O'Farrelly et al. 1991 153.

Azo dyes, flavoring agents and preservatives - Wright et al. 1986 260, Nolan et al. 1991 152.

Eversole and co-workers (1982) 60 did not find any significant association of RAS with 3 specific food items (tomatoes, strawberries and walnuts).

Drugs

Drugs such as non-steroidal anti-inflammatory drugs (NSAIDS) (the proprionic acid and phenylacetic acid, diclofenac) rarely give rise to oral ulcers similar to those of RAS, along with genital ulceration or only oral ulcers in case of piroxicam (Healy and Thornhill 1995 92, Siegel and Balciunas 1991 216). However, such types of ulcers usually occurs as an adverse side effect and disappear with discontinued usage of the drug. A recent French study (Boulinguez, et al. 2000) 21 has found that typical clinical description of aphthous ulcer and/or clinical presentation suggesting the diagnosis of aphthous ulcers were noted for 8 drugs, along with another group of 20 drugs where the diagnosis of aphthous ulcers remained to be confirmed.

List of drugs for which a complete clinical description of RAS or indicative photograph was available.

Drug-induced RAS	Reference
Phenobarbital	Kennet 1968 ¹¹²
Niflumic acid	Kuffer et al. 1976 114
Phenindione	Kuffer et al. 1976 114
Gold salts	Kuffer et al. 1976 114
Captopril	Corone et al. 1987 ³⁷
Sodium hypochloride	Menni et al. 1988 ¹⁴⁰
Piroxicam	Siegel and Balciunas
	1991 216
Nicorandil	Shotts et al. 1999 ²¹⁴

Immunologic Factors:

For the past 30 years, much of the research on the cause of RAS focused on detecting an abnormality in the immunologic response. Early work suggested a relationship between several immune- mediated reactions and development of RAS. These reactions include cytotoxicity of T lymphocytes toantibody dependent epithelium, cellmediated cytotoxicity, and defects inlymphocyte subpopulations. One theory is that multiple immune reactions cause damage induced by deposition of immune complexes within the oral epithelium. More

recent studies have shown an association between RAS severity and abnormal proportions of CD4+ and CD8+ cells, alterations of the CD4+: CD8+ ratio, and elevated levels pf interleukin 2, interferon gamma, and tumor necrosing factor a, mRNA in RAS lesions. Immunohistochemical studies of RAS biopsy tissues have demonstrated numerous inflammatory cells with variable ratios of CD4+:CD8+ lymphocytes depending on the ulcer duation. CD4+ cells were more numerous during the preulcerative and healing stags, whereas CD8+ cells tended to be more numerous during the ulcerative state of the ulcer. Similar studies on non affected sites were negative, making researchers focus more on the theory that RAS may be caused by an antigen triggering effect (Sunday O.Akintove 2005 225, Martin S. Greenbrg 2005 133).

Systemic diseases associated with RAS

Behcet's disease (Al-Otaibi L.M.2005)4

Behcet's disease (BD) is a multi-system inflammatory disorder dominated clinically by recurrent oral and genital ulceration, uveitis, and erythema nodosum. The disease tends to wax and wane, the frequency and duration of exacerbations being unpredictable. Behcet's disease is a vasculitis, affecting vessels of different types, sizes, and localizations.

Diagnostic criteria

Prior to 1990, five different criteria for the diagnosis of Behcet's disease had been suggested. Such a diversity in diagnostic criteria limited comparisons between relevant studies and hampered collaborative research. There are now internationally agreed diagnostic criteria for Behcet's disease, derived from a collaborative study of 914 patients in 12 centers from seven countries. (International Study Group for Behçet's Disease, 1990) 102

International Study Group Criteria for Behcet's Disease (1990) ¹⁰²

Recurrent oral ulceration	Minor aphthous, major aphthous or herpetiform ulceration observed by physician or patient, which recurred at least 3 times in one 12-month period.
Plus 2 of:	
Recurrent genital ulceration	Aphthous ulceration or scarring, observed by physician or patient.
Eye lesions	Anterior uveitis, posterior uveitis, or cells in vitreous on slit lamp examination; or retinal vasculitis observed by ophthalmologist.
Skin lesions	Erythema nodosum observed by physician or patient, pseudofolliculitis or papulo-pustular lesions; or acneiform nodules observed by physician in post- adolescent patients not on corticosteroid treatment.
Positive pathergy test	Read by physician at 24-48 hrs, performed with oblique insertion of a 20-gauge or smaller needle under sterile conditions.

Clinical features

Behcet's disease gives rise to a wide spectrum of clinical features characterized by unpredictable exacerbations and remissions (Uzun et al., 2003) 238.

Principal Clinical Features of Behcet's Disease

System	Features
Gastrointestinal	Aphthous mouth ulcers
	Isolated multifocal ulcer
	Particularly in ileo-cecal region
Urogenital	Scrotal and/or penile ulcers
•	Vulval and/or vaginal ulcers
	Peri-anal ulcers
	Epidiclymo-orchitis in men
Dermatological	Papules and pustules
·	Erythema nodosum
	Ulcers
	Cutaneous pathergy response
Ocular	Anterior or posterior uveitis
	Retinal vasculitis
Musculoskeletal	Arthralgias
	Arthritis
	Fatigue
Neural	Headaches
	Dural sinus thrombosis
	Parenchymal inflammatory lesions
	Meningo-encephalitis
Vascular system	Superficial thrombosis
	Deep vein thrombosis
	Arterial occlusion and/or aneurysms

Recurrent Oral (Aphthous-like) Ulcerations

Ulceration akin to recurrent aphthous stomatitis (RAS) occurs in all patients diagnosed with Behcet's disease. The oral ulceration is the initial clinical feature of up to 86.5% of adults and children with BD. All three types of RAS-like ulcers can arise in BD, although minor ulcers seem to be the most common presentation in BD. One study suggested that major RAS-like ulcers may be more common in BD patients than in those with RAS. The oral ulcers of BD have the same periodicity as those of RAS and can

affect any oral mucosal surface, although they may be more common on the soft palate and pharynx than in RAS. Some patients have almost continuous episodes of oral ulceration. Recurrent oral ulceration is often reported in other family members of patients with BD. As in RAS, tobacco smoking may reduce the severity of ulceration of BD. (Silveira and McGrath, 1992 217; Ayata et al., 2002¹⁰; Kaklamani et al., 2003) 109.

Etiopathogenesis

Theof BD isbut cause notknown. autoimmune reaction triggered by an infectious or environmental agent (possibly local to a geographic region) in a genetically predisposed individual seems most likely. However, if BD has an autoimmune basis, it is unusual, since there is no female preponderance, no association with other autoimmune diseases or HLA antigens typically associated (A1, B8, DR3, DR4) with such disease, and no associated specific auto antibodies. There are, however, scattered reports of neonatal BD in the children of mothers with BD, possibly caused by transplacental transfer of an as-yet unidentified antibody (Fam et al., 198163; Eglin et al., 1982 54).

Therapies for Behcet's Disease (Porter and Scully, 2002) 169.

Agent	Comment
(1) Topical corticosteroids	Typically for oral*, genital (Yazici and Ozyazgan, 1999; Porter and Scully, 2002), and ocular disease (Yazici and Barnes, 1991)
(2) Systemic corticosteroids	Short-term benefit, unlikely to improve long-term prognosis (Russell et al., 2001)
(3) Corticosteroid-sparing immuno	suppressants:
Colchine	Commonly prescribed for mucocutaneous disease, arthritis, and genital ulcers (Mizushima et al., 1977; Aktulga et al., 1980; Yurdakul et al., 2001)
Azathioprine	as., 1740; Infratani et al., 2001. May improve leng term outcome (Akoglu et al., 1990; Hamuryudan et al., 1997) Mycophenolate mofetilFewer achierse side-effects than azathioprine, but little data of efficacy in BD (Kilmartin et al., 1998; Larkin and Lidshiman. 1999)
Thalidomide	May be treatment of choice, but adverse side-effects, particularly risk of peripheral neuropathy and teratogenicity (Russell et al., 2001; Shek and Lim, 2002)
Ciclosporin Tacrolimus	May be beneficial for ocular disease of BD (Binder et al., 1987; Masuda et al., 1989) More potent than cyclosporin, may have a role in the management of ocular disease recalcitrant to cyclosporin (Sloper et al., 1999)
Methotrexate	Pulsed therapy may reduce ocular and neuropsychotic complications of BD (Shah et al., 1992; Hirohata et al., 1998; Kari et al., 2001) Cyclophosphamide/chlorambucilReserved for disease unresponsive to other therapies. Bone marrow suppression is a significant adverse side-effect (O'Duffy et al., 1984; Tessler and Jennings, 1990; Russell et al., 2001)
(4) Antimicrobials:	
Antibacterials	Penicillin may reduce arthritis (Saenz <i>et al.</i> , 2004), and minocycline may reduce mucocutaneous and oral disease (Kaneko F <i>et al.</i> , 1997).
Antivirals	Acyclovir is not effective (Davies et al., 1988). Little data on efficacy of famcyclovir (Sohn et al., 2001)
(5) Retinoids	Isotretinoin may improve arthritis and nodulocystic acne (Akyol et al., 2002).
(6) Dapsone	Useful for the management of mucocutaneous disease (Sharquie et al., 2002). Regular monitoring for possible side-effects required.
(7) Anticoagulation	Short-term therapy for known thrombotic disease. Little data on the need for long-term anticoagulant therapy (Russell et al., 2001).
(8) Non-steroidal anti-inflammatory agents	Important for symptomatic arthritis (Simsek et al., 1991)
(9) Biological agents:	
Interferon α-2a (IFN-α-2a)	May improve mucocutaneous, ocular, and joint disease of BD (Hamuryudan <i>et al.</i> , 1994; Demiroglu <i>et al.</i> , 2000; Stuebiaer <i>et al.</i> , 2000; Alpsoy <i>et al.</i> , 2002). Therapy is expensive.
Anti-TNF alpha	Utilide data and a few controlled studies (Melikoglu et al., 2002; Sfikakis et al., 2004), but efficacy might be expected in view of the known benefits of thalidomide. Some clinical observations reporting dramatic responses on clinical signs and symptoms (Goossens et al., 2001; Robertson and Hickling, 2001; Sfikakis et al., 2001; Estrach et al., 2002; Sfikakis, 2002; Haugeberg et al., 2004), while others do not report such findings (Yucel et al., 2004).

The Marshall's syndrome (Berlucchi M 2004)¹⁶

Diagnosis criteria / Definition

The Marshall's/The PFAPA syndrome is a chronic disease of unknown etiology characterized by **P**eriodic episodes of high **F**ever accompanied by

Aphthous stomatitis, Pharyngitis, and cervical Adenitis, often associated with headache and/or abdominal or joint pain. This syndrome belongs to the group of recurrent fever syndromes, which includes systemic onset juvenile rheumatoid arthritis, cyclic neutropenia, and the group of hereditary fevers. PFAPA however differs from these hereditary autoimmune fevers as it is a sporadic syndrome and second cases in siblings are not found.

In 1948, Raimann ¹⁷⁴ coined the term "periodic disease" to identify a heterogeneous group of disorders of unknown cause, characterized by short episodes of illness that regularly recur for several years alternated with healthy periods. Many periodic diseases have been subsequently described with well-defined clinical and laboratory characteristics.

In 1987, Marshall et al. ¹³² described a new periodic fever that was initially indicated as Marshall's syndrome and subsequently given the acronym FAPA (fever, aphthous stomatitis, pharyngitis, cervical adenitis). This was later changed to PFAPA (periodic fever, aphthous

stomatitis, pharyngitis, cervical adenitis) syndrome in order to emphasize the presence of periodic fever, which is considered a main characteristic of the illness.

The Marshall's/PFAPA syndrome is defined clinically and diagnosis is made by exclusion. The dramatic resolution of febrile attacks by single oral administration of corticosteroids can also be used as diagnostic criterion. Nevertheless, in order to facilitate recognition of the disease, in 1989 diagnostic criteria were proposed, which were modified 10 years later.

Diagnostic criteria for Marshall's/PFAPA syndrome

Thomas, Feder, Lawton &Edwards [68]	Padeh [46]
I. Regularly recurring fevers with an early age of onset (<5 years of age)	Monthly fevers – cyclic fever at any age groups
II. Constitutional symptoms in the absence of upper respiratory infection with at least 1 of the following clinical signs: a) Aphthous stomatitis b) Cervical lymphadenitis c) Pharyngitis	II. Possibly aphthous stomatitis III. Cervical lymphadenitis IV. Exudative tonsilitis + negative throat culture
III. Exclusion of cyclic neutropenia IV. Completely asymptomatic interval between episodes	V. Completely asymptomatic interval between episodes
V. Normal growth and development	VI .Rapid response to a single dose of corticosteroids

Etiology

At present, the cause of Marshall's or PFAPA syndrome remains unknown. The ability of steroids to resolve febrile episodes in PFAPA-patients seems to that theorigin of illness suggest may inflammatory. Elevated levels of cytokines observed during attacks could support this hypothesis. Finally, since Marshall's/PFAPA syndrome does not recur in most children after tonsillectomy, it is postulated that the disease can be elicited by an immunologic process beginning at the level of the tonsillar parenchyma. Studies on the tonsillar immunologic profile could provide additional information on the pathogenesis of this rare disease (Thomas et al. 1999) 231.

Clinical description

In 1987, Marshall et al. 132 reported a previously undescribed periodic fever syndrome of unknown cause in 12 children. These patients presented febrile episodes that recurred every 2 to 12 weeks (mean cycle = 4.5 weeks). In all cases, the onset of symptoms started before 5 years of age and the fever reached high temperatures (40 to 41°C) lasting approximately 5 days. Fever was associated

with pharyngitis and stomatitis in 9 of the 12 cases (75%), cervical reactive adenopathies in 8 of the 12 (66.6%), and other minor symptoms such as headache, abdominal pain, nausea, vomiting, chills and malaise. None of these children were immunodeficient. Bacterial, viral, and fungal studies were all negative. Only patients had group A B-hemolytic Streptococcus isolated from the pharynx. Acute episodes were often associated with leukocytosis and mild elevation of the erythrocyte sedimentation rate, but no patient showed atypical lymphocytosis or neutropenia. During asymptomatic intervals, children were in good health and growth was normal. On the assumption of streptococcal pharyngitis, all underwent unsuccessful therapy with patients antibiotics and nonsteroid anti-inflammatory drugs. The use of oral prednisone dramatically controlled symptoms, although subsequent relapses were not prevented.

Thomas et al. (1999) ²³¹ and Padeh et al. (1999) ¹⁵⁷ reported respectively 94 and 28 patients affected by Marshall's/PFAPA syndrome. Both

authors confirm the clinical picture observed by Marshall in 1980s.

Therefore, a patient who complains of periodic fever (during asymptomatic periods growth is normal) associated with aphthous stomatitis, pharyngitis, and cervical adenitis can be considered to be affected by Marshall's/PFAPA syndrome. In these patients, anti-inflammatory and antibiotic therapy is ineffective, whereas one or 2 oral doses (1 to 2 mg/Kg) of corticosteroid (i.e. prednisone) temporarily resolved symptoms within 24-36 hours, although it did not avert the next cycle.

Thomas et al. [46]	Padeh et al. [68]
(%)	(%)
100	100
72*	100
NA	100
88	100
70	68
60	18
49	18
79	11
80	$NA^{@}$
13	NA
32	NA
16	NA
9	NA
	(%) 100 72* NA 88 70 60 49 79 80 13 32 16

Laboratory investigation

Laboratory investigation at onset of the fever showed a normal hemoglobin level, mild leukocytosis of 13×10 -9 /mm3, moderate elevation of the sedimentation rate 41-56 mm/1st h, and normal platelet count. Serum IgD levels were elevated in 12

of the 18 patients (66%) in whom we measured. The levels were >100 U/mL, which is the cutoff level for HIDS. The serum IgD levels (140.2 \pm 62.4 U/mL) were significantly higher than those found in healthy children in an age-matched control group (16.5 ± 15.8 U/mL) or children with juvenile rheumatoid arthritis (85.9 \pm 47.4 U/mL). Serum IgD levels were normal in the European and US reports. Immunologic and serologic studies were uniformly nondiagnostic. Distributions of T-lymphocyte subsets were normal in all 12 patients studied. IgE levels were elevated in 8 of 16 patients. Imaging studies included chest films, sinus films, gastrointestinal series, computed tomography scans of the head and abdomen, gallium scans, and bone scans, all of which were negative.

Management

The treatment of PFAPA syndrome is still a matter of debate. Administration of antibiotics (penicillins, cephalosporins, macrolides, and sulfonamides), nonsteroidal anti-inflammatory drugs (acetaminophen, ibuprofen), acyclovir, acetylsalicylic acid and colchicine has been shown to be ineffective.

On the contrary, the use of oral steroids (prednisone or prednisolone) causes a dramatic resolution of febrile episodes, although it does not prevent their recurrence.

To date, data regarding the long-term efficacy and possible rebound phenomena associated with steroids are not available. Furthermore, an increased frequency of the febrile cycles and persistence of fever and other symptoms have been observed in some children after steroid therapy. Finally, Marshall's/PFAPA syndrome resolves spontaneously after several years in about 40% of patients, and, in some cases, neurobehavioral and social effects such as difficulties with peer relations and absenteeism fromschool have been observed(Abramson al.19891; Thomas et al. 1999231; Padeh et al. 1999¹⁵⁷; Dahn et al. 2000 ⁴²; Galanakis et al. 2002 ⁷⁵; Berlucchi et al. 2003¹⁵).

In 2000 Dahn et al ⁴² emphasized the role of tonsillectomy with or without adenoidectomy in the management of PFAPA, reporting successful results in 5 children. More recently, observed similar results

in a cohort of 15 patients. Thus to our knowledge, a total of 43 patients with PFAPA have undergone surgical procedures, including our series (5 children). Overall, tonsillectomy was successful in 90.6% of children and improved symptoms in 4.6% of cases.

In conclusion, that tonsillectomy (with or without adenoidectomy) can be currently considered the ideal treatment for patients with Marshall's/PFAPA syndrome.

Sweet's syndrome (Cohen PR 2003) 34

The syndrome was originally described by Dr Robert Douglas Sweet as an "acute febrile neutrophilic dermatosis" in 1964.

Definition

Classical Sweet's syndrome

Sweet's syndrome is characterized by pyrexia, elevated neutrophil count, tender erythematous skin lesions (papules, nodules, and plaques) and a diffuse

infiltrate consisting predominantly of mature neutrophils typically located in the upper dermis.

Diagnostic criteria

The diagnostic criteria for classical (or idiopathic) Sweet's syndrome were modified by von den Driesch in 1994 243. Although these criteria include malignancy-associated Sweet's syndrome as a subset of classical Sweet's syndrome, several authors choose to distinguish between the classical form and the malignancy-associated form since many of the cases of Sweet's syndrome are cancer-related. Diagnostic criteria for drug-induced Sweet's syndrome were proposed by Walker and Cohen in 1996.

Diagnostic criteria for classical Sweet's syndrome

Major criteria	Abrupt onset of painful erythematous plaques or nodules Histopathologic evidence of a dense neutrophilic infiltrate without evidence of primary leukocytoclastic vasculitis
Minor criteria	Pyrexia (greater than 38°C) Association with an underlying hematological or visceral malignancy, inflammatory disease, or pregnancy or preceded by an upper respiratory or gastrointestinal infection or vaccination Excellent response to treatment with systemic corticosteroids, potassium iodide, or colchicines
	 Abnormal laboratory values at presentation (3 of the following 4): erythrocyte sedimentation rate greater than 20 mm/hr, positive C-reactive protein, greater than 8000 leukocytes, and greater than 70% neutrophils

Clinical description (Cohen PR 2003) 34

Fever

Fever is the most frequent symptom in patients with Sweet's syndrome. The cutaneous manifestations may be preceded by fever; alternatively, pyrexia can concurrently be present throughout the duration of the dermatosis. However, in some patients with biopsy-confirmed malignancy-associated Sweet's syndrome, fever may be absent. Arthralgia, general malaise, headache, and myalgia are other Sweet's syndrome-associated symptoms that may also be present. Indeed, patients with this condition may appear dramatically ill.

Skin lesions

Sweet's syndrome skin lesions are typically tender and often painful. They appear as red or purple-red papules and nodules. The pronounced edema in the upper dermis of the lesions results in their transparent, vesicle-like appearance; in patients with malignancy-associated Sweet's syndrome, the lesions may appear bullous, become ulcerated, and/or mimic the morphologic features of pyoderma gangrenosum. Over a period of days to weeks, the individual lesions enlarge and may coalesce to form irregular, sharply border plaques. The upper extremities, face and neck are the most frequent lesion locations.

Cutaneous lesions of Sweet's syndrome may appear at sites of trauma to the skin, such as locations where procedures have been performed (biopsies, intravenous catheter placement, or venipuncture), sites where either bites (insect) or scratches (cat) have occurred, areas that have received radiation therapy, or places that have been contacted by sensitizing antigens; this dermatosis-

associated feature is referred to a skin hypersensitivity or cutaneous pathergy. Occasionally, the distribution of the skin lesions has been noted to occur in sun-exposed areas or the location of prior sunburn (phototoxic reaction).

Less commonly, the lesions of Sweet's syndrome present as a pustular dermatosis—either as tiny pustules on the tops of the red papules or as eythematous-based pustules. Many investigators consider those patients who have previously been reported to have either "neutrophilic dermatosis of the dorsal hands" or "pustular vasculitis of the dorsal hands" to be included in this clinical variant of Sweet's syndrome. In addition, it is likely that some of the patients who were described as having "pustular eruption of ulcerative colitis" also should be included as patients with the pustular variant of Sweet's syndrome.

Extracutaneous manifestations

Extracutaneous manifestations of Sweet's syndrome may involve the following sites: bone, central nervous system, eyes, kidneys, intestines,

liver, heart, lung, mouth, muscles, and spleen. Dermatosis-related sterile osteomyelitis has been reported in children. Mucosal involvement of the mouth, presenting as oral ulcers, is uncommon in classical Sweet's syndrome; however, this is more frequently noted in patients with Sweet's syndrome and hematological disorders.

The reported incidence of ocular involvement (such as conjunctivitis) is variable in classical Sweet's syndrome and uncommon in the malignancy-associated and drug-induced forms of the dermatosis; however, in some patients with Sweet's syndrome, ocular manifestations have been observed to be the presenting feature of the condition.

Associated diseases

Several conditions have been observed to occur either before, concurrent with or following the diagnosis. Hence it is reasonable to conclude that the occurrence of Sweet's syndrome may be associated with the development of some of these conditions.

Specifically, a bonafide association between Sweet's syndrome and the following conditions probably exists :cancer (both hematological malignancies—most commonly acute myelogenous leukemia—and solid tumors—most commonly carcinomas of the genitourinary organs, breasts, and gastrointestinal tract), infections (most commonly of the upper respiratory tract—streptococcosis—and the gastrointestinal tract—salmonellosis and versiniosis), inflammatory bowel disease (Crohn's disease and ulcerative colitis), medications (with granulocytecolony stimulating factor being the most commonly reported drug), and pregnancy. In addition, it is also possible that a bonafied association exists between Sweet's syndrome and the following conditions: Behcet's disease. ervthema nodosum. relapsing polychondritis, rheumatoid arthritis, sarcoidosis, and thyroid disease (Grave's disease and Hashimoto's thyroiditis). However, for many of the conditions that been observed in patients with syndrome, the presence of that disorder in a patient with Sweet's syndrome is likely to represent a coincidental occurrence. However, for many of the conditions that have been observed in patients with

Sweet's syndrome, the presence of that disorder is likely to be coincidental.

Management

Sweet's syndrome lesions may persist for weeks to months. However, in some patients with classical Sweet's syndrome, the dermatosis-related symptoms and cutaneous lesions eventually resolved without any therapeutic intervention. Successful management of dermatosis-related cancer in patients themalignancy-associated Sweet's syndrome occasionally resulted in clearing of the condition. And, in patients with drug-induced Sweet's syndrome, discontinuation of the associated medication was typically followed bvspontaneous improvement andsubsequent resolution of the syndrome. Some of the patients with Sweet's syndrome associated tonsillitis, solid tumors, or renal failure experienced resolution of the following dermatosis appropriate surgical intervention (Von den Driesch P, Steffan C, Zobe A, et al.1994 ²⁴⁴)

Reported associations in Sweet's syndrome (Cohen PR, Kurzrock R.2000) 35

Cancer (21%)	Hematological malignancies		
	(15%)		
	most commonly acute		
	myelogenous leukemia		
	Solid tumors (6%)		
	most commonly carcinomas of		
	the genitourinary organs,		
	breast and gastrointestinal		
	tract		
Infections	Mostly of the upper		
	respiratory tract		
	(75 to 90% in patients with		
	classical or idiopathic Sweet's		
	syndrome) Streptococcosis		
	Gastrointestinal tract		
	Salmonellosis and Yersiniosis		
Inflammatory bowel	Crohn's disease and ulcerative		
disease	colitis		
Pregnancy	1		

Other conditions
for which there is a
possible association

Relapsing polychondritis,
Rheumatoid arthritis,
Sarcoidosis,
Thyroid disease
(Grave's disease and
Hashimoto's thyroiditis)

MAGIC syndrome

MAGIC is an acronym for mouth and genital ulcers with inflamed cartilage. Either sex may be affected with onset typically in the 4th or 5th decades. It is unclear whether it is a variant of Behcet's diseases, but is sometimes termed Behcet's disease with relapsing polychondritis.

Oral ulceration is less frequent than in Behcet's disease and the prominent feature is episodic painful inflammation of cartilage, especially in the nose, auricles, larynx and trachea with non erosive, seronegative polyarthritis and ocular lesions similar to those of Behcet's disease.

Oral aphthae in MAGIC syndrome have to be managed by conventional means. Dapsone and prednisolone may be effective in controlling the cutaneous lesions secondary to chondritis (Roderich A et al 2001) 183.

Coeliac disease

Coeliac disease is an inflammatory disease of the upper small intestine and results from gluten ingestion in genetically susceptible individuals. (Cooke WT – 1984) ³⁶ Inflammation may lead to the malabsorption of several important nutrients. Clinical and mucosal recovery after institution of a gluten free diet is objective evidence that the enteropathy is gluten induced. In 1950, Dicke ⁴⁶ observed the central role of gluten in the pathogenesis of celiac disease.

Symptoms (and related signs) of coeliac disease (Robinson.NA 2004) 182 Infancy (< 2 years)

• Diarrhoea (miserable, pale)

- Abdominal distension (enlarged abdomen)
- Failure to thrive (low weight, lack of fat, hair thinning)
- Anorexia, vomiting
- Psychomotor impairment (muscle wasting)

Childhood

- Diarrhoea or constipation
- Anaemia
- Loss of appetite (short stature, osteoporosis)

Adulthood

- Diarrhoea or constipation
- Anaemia
- Aphthous ulcers, sore tongue and mouth (mouth ulcers, glossitis, stomatitis)
- Dyspepsia, abdominal pain, bloating (weight loss)
- Fatigue, infertility, neuropsychiatric symptoms (anxiety, depression)
- Bone pain (osteoporosis)
- Weakness (myopathy, neuropathy)

An association between RAS and glutensensitive enteropathy/coeliac disease (CD) has been
proposed for the last 20 years as some RAS patients
showed evidence of small bowel changes suggestive of
CD; nevertheless, there is still considerable dispute
concerning the actual prevalence of CD in RAS
patients, CD being still present in 4% to 25% of
examined RAS patients.

This association was suggested in 1976 when Ferguson and co-workers⁶⁷ found 8 (24%) of 33 English patients with RAS to show histological evidence of CD on jejunal biopsy. Haemoglobin indices and serum folate levels were significantly lower in the RAS patients with CD than those without. The 8 patients with RAS and CD had complete clinical and haematological remission when given a glutentree diet. In contrast, only 1 of 26 Scottish patients with RAS was found to show histopathological evidence of jejunal CD, and did not have any notable resolution of oral ulcers with a gluten-tree diet.

A study of 50 Scottish patients with RAS reported 2 females with CD. These 2 patients

presented with typical features of minor RAS and were folate-deficient. A gluten free diet produced a marked reduction in oral ulceration. Likewise, 6.2% of 97 English patients with RAS were found to have CD. The affected patients had no signs of systemic illness except for a lowered serum folate, but did have an improvement in oral ulceration when given a gluten-free diet.

Merchant and co-workers 1977 ¹⁴¹ in Glasgow found 3 of 100 dental patients with RAS to have CD. Three patients were found to have IgA reticulin antibodies; only 1 of whom had histopathological evidence of CD. Four of a group of 24 RAS patients (16%) were found to have subtotal jejunal villous atrophy and significantly higher intra-epithelial lymphocyte counts than healthy control subjects. Furthermore, a significantly higher intra-epithelial lymphocyte count was reported in the remaining 20 patients with normal intestinal morphology when compared with healthy controls.

Prevalence of Coeliac Disease in Patients with Recurrent Aphthous Stomatitis

References	No. of RAS patients	No. of RAS patients with CD	Improvement of RAS on a gluten-free dies
Wray et al ²	130	5 (3.8%)	Not recorded
Ferguson et al24	33	8 (24%)	Yes
Rose et ai-1	26	1 (3.8%)	No
Ferguson et al ¹⁶	50	2 (4%)	Yes
Tyldesley"	97	6 (6.2%)	Yes
Merchant et alis	100	3 (3%)	Not recorded
Veloso and Saleirob	24	4 (16%)	Yes

CD: coeliac disease; RAS: recurrent aphthous stomatitis

Liability to oral ulceration in CD may be immunogenetically based as the frequencies of HLA DRWIO and DQWI may be significantly higher in some groups of CD patients with oral ulceration than those without oral ulcers.

Identification of RAS patients with underlying CD is important for effective management as CD is eminently treatable with a gluten-free diet. In relation to this, 25% of a group of RAS patients known to have no jejunal disease had resolution of RAS with a gluten-free diet. Similarly, in another study, 10

patients with RAS and a normal jejunal biopsy were divided into 2 groups based on their anti-gliadin antibody levels. Four patients had raised levels of the antibody while the remaining 6 had normal levels. Three of the 4 patients with elevated anti-gliadin antibodies responded to a gluten-free diet with resolution of oral ulcers and had relapse with gluten challenge. None of the 6 anti-gliadin antibodynegative patients had remission of the ulceration during the period of gluten withdrawal.

However, a gluten-free diet is not always effective in the management of RAS. Hunter and coworkers (1993) 101 conducted a well-designed double-blind study of a gluten-free diet in patients with RAS but who had no detectable gluten enteropathy. Out of 23 patients with RAS who completed the trial, 11 were given a gluten-free diet; the other 12 served as controls and received a gluten-free diet supplemented by gluten given blind. Four out of the 11 patients on the gluten-free diet and 7 out of the 12 on the control diet reported significant benefit in terms of the RAS, but there were no significant statistical differences between the responses. Thus, there is equivocal

evidence of an association between RAS and CD. This may in part reflect low numbers of study patients or possibly the lack of a genuine association (Robinson NA 2004) ¹⁸².

Tests for anti-gliadin antibodies have moderate sensitivity but poor specificity and positive predictive value for CD. IgA anti-gliadin antibodies are present in up to 90% of untreated coeliac patients while the IgG class is seen in about 82% of cases and up to 3.4% of healthy controls. However, nearly 25% of patients with Crohn's disease and 10% of patients with ulcerative colitis can have anti-gliadin antibodies. The presence of anti-reticulin antibodies is both more sensitive and specific for untreated CD. IgA antireticulin antibodies have been reported in 97% of untreated CD patients and in 2% of control subjects, although 2 large studies failed to detect the antibodies in healthy subjects. The detection of IgG anti-reticulin antibodies is not as useful as that for IgA antibodies as one third of patients with coeliac disease may not have IgG antireticulin antibodies. The presence of IgA anti-endomysial antibodies is currently considered a better serological marker for

untreated CD. Sensitivity and specificity, as well as positive predictive values of the antibody have approached almost 100% in several studies.

Tissue transglutaminase has recently been identified as the target antigen recognised by antiendomysial antibodies. A reliable enzyme-linked immunosorbent assay (ELISA) has been developed to detect IgA tissue transglutaminase antibodies. The sensitivity and specificity of this test has been shown to correlate highly with anti-endomysial antibodies in the detection of CD. In future, the detection of antibodies to tissue transglutaminase may prove to be the superior serological marker for screening CD55.

In the study by NA Robinson et al, they have specifically examined the frequency of anti-reticular and anti-endomysium antibodies in patients with RAS. While perioral intestinal biopsy together with clinical improvement on a gluten-free diet remains the "gold standard" for the diagnosis of CD, the detection of anti-gliadin, anti-reticulin and anti-endomysium antibodies are more acceptable in the screening and subsequent progress of CD. The serological study

confirms previous studies suggesting that there is little association between RAS and CD. It is concluded that detailed screening of patients with clinical features and a history typical of RAS for CD is unlikely to be of clinical value. (Robinson.NA 2004) 182

HIV-associated RAS

Severe episodes of RAS have been observed in patients infected with HIV. Although the lesions are mainly oral, HIV-associated aphthae have been reported in the esophagus and more distal gastrointestinal tract (Bach et al. 1990) 11.

The ulcers are of the minor, major and herpetiform types and are often located on the soft palate, tonsils or tongue, where they hinder eating and speaking. Macphail et al. (1991) 128 showed that 66% of HIV patients affected by RAS had the usually uncommon herpetiform or major types and that patients with Major RAS were significantly more immuno-suppressed than those with Minor RAS in that they had fewer CD4 and CD8 lymphocytes. The role played by the marked neutropenia seen in most of the

HIV patients with Major RAS is unclear, but the healing of the ulcers without resolution of the neutropenia argues for the ulcers being Major RAS rather than neutropenic ulcers. About half (44%) of the patients denied or could not recall having had RAS during their childhood, which was presumably before they became infected with HIV. The rest (56%) gave a definite history of childhood RAS and described the ulcers as Minor RAS (Macphail et al. 1991) 128.

Patients with HIV infection have an overall prevalence rate of recurrent aphthae ranging from 1% to 4% (Phelan et al. 1991 ¹⁶⁵, Muzyka and Glick 1994 ¹⁴⁹).

As progress in the treatment of HIV disease results in more patients living longer in a state of significant immuno-suppression, managing severe RAS may become an increasing challenge (Macphail et al. 1991) 128.

Although it has not yet been definitely accepted that RAS-like lesions found in association with HIV

infection are indeed RAS, they meet the diagnostic criteria for RAS, they respond to treatment like RAS, and therefore, until proven otherwise, they must be considered RAS (MacPhail et al. 1992) 129.

HIV-associated RAS lesions tended to be more severe and longer lasting, and may cause debilitating pain with associated alteration of important oral functions such as speaking, chewing and swallowing which ultimately lead to malnutrition and weight loss, compromise a patient's ability to take medications and seriously interfere with the patients' quality of life (Muzyka and Glick 1994 149).

Although HIV DNA has been identified in buccal mucosal scrapings from apparently healthy mucosa of (18/45) HIV-seropositive subjects, to my knowledge no studies have demonstrated the presence of HIV in oral ulcers. It is unknown whether such lesions represent a localized auto-immune reaction, developing in response to an undefined antigen which triggers a normal immunologic response or represent an overactive HIV in the mucosa of a T cell deficient host (Oureshi et al. 1997) 173.

Description and clinical forms of RAS

The clinical features of RAS consist of recurrent bouts of one or several rounded, shallow, painful oral ulcers at intervals of a few months to a few days (Porter.S.R Scully.C-1998) 170. RAS has 3 main presentations-

According to the classification of Stanley (1972) 220.

- 1. minor (MiRAS)
- 2. major (MaRAS)
- 3. herpetiform (HU) ulcers

The frequency of outbreaks of the aphthae varies remarkably between patients. Some persons will have only one or two attacks a year, while others will have one or two attacks a month every month for prolonged periods sometimes years. Occasional patients have continual, repeated outbreaks and are never free of lesions for extended intervals.

The onset of the disease may occur with a variety of manifestations, which are not invariably present in all cases. These include the occurrence of one or more small nodules; generalized edema of the

oral cavity, especially the tongue; paresthesia; malaise; low – grade fever; localized lymphadenopathy; and vesicle – like lesions containing mucus.

The apthous ulcer begins as a single or multiple superficial erosions covered by a gray membrane. It generally has a well circumscribed margin surrounded by an erythematous halo. The lesion is typically very painful so that it commonly interferes with eating for several days.

The number of lesions present in any one patient during a single outbreak may vary from one to over 100. However, according to Graykowski and his associates 1966⁸⁰, over 90 per cent of patients have six lesions or less during a single outbreak. They vary in size from 2-3 mm. to over 10 mm in diameter. The most common sites of occurrence are the buccal and lingual sulci, tongue, soft palate, pharynx and gingival, all locations of labial mucosa not bound to periosteum.

The most frequent type of aphthae affecting about 80% of RAS patients (Porter et al.1998) ¹⁷¹. They appear as single discrete ulcers or in groups of two or more. They are characteristically found on the free movable oral mucosa rather than the attached mucosa. The formed ulcers are discrete with a white yellow base, which is a fibrinous slough, and a distinct irregular border with a red halo. When the lesions are extensive, trismus or edema of the cheek can develop. Often there is painful swelling of regional lymph nodes.

They may appear in the form of "attacks" of single or multiple lesions but can clearly be distinguished from primary or secondary viral infections, bacterial infections (necrotizing ulcerative gingivitis), dermatologic conditions (lichen planus, cicatricial pemphigoid, pemphigus), and traumatic episodes (contusions, lacerations, burns) by the healthy appearance of adjacent tissues and the lack of distinguishing systemic features. Diagnosis is generally made on the basis of history and clinical presentation; there are no known laboratory

procedures available for definitive diagnosis, and histopathologic examination of biopsy specimens will not provide a definitive diagnosis.

Clinically it can be subdivided into three stages according to **Djawari et al 1980** 53.

- 1. **Prodromal stage:** seldom observed, of very short duration. In a matter of hours a reddish spot with a diameter of 1 to 5 mm (infiltrate of lymphocytes, monocytes, plasma cells) develops in the healthy epithelium.
- 2. **Preulcerous stage:** the spot becomes a nodule. Initiation of epithelial necrosis.
- 3. Ulcerous stage: after loss of the necrotic epithelium a flat ulceration with a whitish, fibrinoid bottom usually develops. The border is not undermined. Characteristic is severe pain, while during the preceding phases there is burning hyperesthesia.

According to **Robert E. Marx and Diane Stern 2003**180 the lesions emerge in four stages

- 1. **Prodromal stage** the individual will experience a tingling or burning pain in a clinically normal appearing site.
- 2. **Preulcerative stage** red oval papules appear and the pain intensifies
- 3. Ulcerative stage- the classic ulcer appears; it will measure between 3 and 10 mm and may last 7 to 14 days
- 4. **Healing stage** granulation tissue followed by epithelial migration incurs healing without scar.

Minor recurrent aphthous stomatitis



Major type

Synonyms: Sutton's aphthae, periadenitis mucosae necroticans, stomatitis neurological chronica.

Major recurrent aphthous stomatitis (MaRAS) a rare, severe form of RAS, also known as periadenitis mucosa necrotica recurrens. According to the review of this disease by Hjorting - Hansen and Siemssen, there is no predilection for occurrence in any particular age group, although females are frequently affected than males more (Sivapathasundharam B 2006) 219. These lesions are oval and may exceed 1 cm in diameter; indeed, they may approach 3 cm. Major RAS has a predilection for the lips, soft palate, and fauces, but can affect any site and cause significant pain and dysphagia. The ulcers of Major RAS persist for up to 6 weeks and often heal with scarring. The depth of the involvement is also responsible for the chronicity and scaring of these ulcers Major RAS usually has its onset after puberty and is chronic, persisting for up to 20 or more years (Scully and Porter, 1989) 203. They are frequently found in patients infected with human

immunodeficiency virus perhaps because of the amplification of local immune imbalance secondary to HIV disease.

Extreme pain, fever, associated edema, jaw trismus, and lymphadenitis are characteristic. Because Major RAS often involves underlying mucous glands, at one time major aphthae were thought to be associated with salivary glands hence the term periadenitis mucosae necroticans recurrens.

Major recurrent aphthous stomatitis





Herpetiforme type (Cook's aphthae)

The third and least common variety of RAS is herpetiform (HU), characterized by multiple recurrent crops of small, painful ulcers that are widespread and may be distributed throughout the oral cavity. They were first described by Cooke in 1960 ³⁶. It occurs in less than 10% of patients with RAS. As many as 100 ulcers may be present at a given time, each measuring 2-3 mm in diameter, although they tend to fuse, producing large irregular ulcers. HU may have a predisposition for women and have a later age of onset than other types of RAS (Lehner, 1976 ¹²¹; Scully and Porter, 1989) ²⁰³ or may represent a spectrum of oral disorders manifesting as recurring

ulcers (Porter and Scully, 1998) ¹⁷⁰. They last for 7 to 30 days and have the potential to scar.

The characteristic clinical features of this uncommon condition were listed by Brooke and Saap as follows:

- Numerous, small lesions may be found on any intraoral mucosal surface
- Lesions begin as small pinhead sized erosions that gradually enlarge and coalese
- Lesions are more painful than would be suspected by their size
- Lesions are present almost continuously for one to three years, with relatively short remissions
- The patient receives immediate but temproray relief from symptoms with a 2 percent tetracycline mouth wash

While these clinical features are very reminiscent of herpes simplex infection, Brooke and Saap pointed out that laboratory tests show that:

• The herpes simplex virus cannot be cultured from the lesions or demonstrated by lectron microscopy, although Saap and Brooke have

- demonstrated nonviral intranuclear bodies in adjacent epithelial cells
- Cytologic smears fail to reveal the typical multinucleated epithelial giant cells found in herpetic lesions.
- The microscopic findings are nearly identical with those described for the recurrent apthous ulcer
- Immunofluorescent and serologic techniques are negative for antibodies to herpes virus as well as to oral epithelium.

Herpetiforme recurrent aphthous stomatitis



Characteristics of the Different Types of Recurrent Aphthous Stomatitis

	Minor	Major	Herpetiform
Sex ratio	M = F	M = F	F>M (?)
Age of onset	5-19	10-19	20-29
(yrs)	1-5	1-10	10-100
No. of	< 10	> 10	1- 2
ulcers	4-14	> 30	< 30
Size of	1-4	< monthly	< monthly
ulcers(mm)			
Duration	lips,	lips, cheek,	lips, cheek,
(days)	cheeks,	tongue,	tongue,
Rate of	tongue,	palate,	palate,
recurrence	floor of the	pharynx.	pharynx,
(months)	mouth		gingiva, floor
Sites			of mouth
Permanent	uncommon	common	uncommon
scarring			

Differential diagnosis:

The diagnosis of RAS is typically established from the careful history and clinical presentation. However, it is important to differentiate aphthous

ulcers from other stomatologic mucocutaneous, diseases that have ulcerative manifestations. Elucidation of the timeline, provocative and palliative factors, and association with other symptoms such as ocular, musculoskeletal, or urogenital symptoms is important. Usually these conditions can be differentiated from RAS by the location of the lesion and/or the presence of an additional symptom (Ship JA-2000) ²¹².

The physical exam should focus on the location and nature of the lesions, in addition to assessing other organ systems for relevant findings. In such patients, the physician must evaluate and rule out other conditions with similar features. Aphthous stomatitis ulcers involve the non-keratinized oral mucosa such as the tongue, floor of mouth, soft palate, and buccal and labial mucosa. (Rodu B-1992 184, Petersen MJ-1996 164, Schneider LC-1998 197)

Diagnostic evaluation is usually fruitless, unless vitamin deficiencies are highly suspect. Most diagnostic tests are useful in ruling out other

etiologies, rather than being specific to aphthous stomatitis (Farhad Melamed-2001) ⁶⁴.

Herpes simplex virus infections may have similar-appearing lesions; however, primary HSV infections present with a diffuse gingival erythema and fever preceding oral mucosal vesicles and ulcers. Also, recurrent, HSV lesions are found primarily on attached keratinized mucosa, such as the hard palate or gingiva. Ulcers of RAS are not preceded by fever or vesicles and they occur almost exclusively on movable oral mucosa, such as the buccal and labial mucosa, tongue, and soft palate (Rodu B et al - 1992) Such lesions usually respond to acyclovir, especially inimmunocompromized patients (Schneider LC-1998. 197)

Recurrent aphthous lesions can be differentiated from varicella zoster virus (VZV) infections (shingles) based on clinical presentation (VZV lesions have a unilateral extraoral and intraoral distribution pattern following the trigeminal nerve) and symptoms (VZV infections have a

prodrome of pain and burning prior to lesion eruption) (Ship JA-2000) 212 .

Less common oral viral infections such as herpangina and hand-foot-and-mouth disease. should also be included in the differential diagnosis of RAS when initial symptoms occur(Fenton SJ- 1997) ⁶⁶. However, coxsackie virus-related oral ulcers present with other symptoms, such as a low-grade fever or malaise, and will resolve within 1 to 2 weeks (Ship JA-2000) ²¹².

Erythema multiforme presents with painful oral ulcers, but unlike RAS, erythema multiforme lesions occur on both attached and movable mucosa and usually involve crusting of the lips with skin macules and papules (Lozada F-1978) 125 . Approximately two thirds of patients with oral lichen planus show ulcerative lesions, which primarily occur on the buccal mucosa (Brown RS -1993) 23 . However, secondary sites on the gingiva and hard palate will distinguish oral lichen planus from RAS. In addition oral lichen planus is not always painful, whereas pain is usually the chief complaint in RAS. Vesiculobullous

oral lesions that tend to rupture within hours of occurrence, resulting in painful erosions or ulcerations, are characteristic of cicatricial pemphigoid and pemphigus vulgaris (Weinberg MA – 1997) ²⁴⁹. These lesions may occur on both attached and unattached oral mucosa, and a biopsy will reveal a characteristic histomorphometric pattern (Ship JA-2000) ²¹².

Quite often, systemic disorders will present with oral ulcers that are similar to those of RAS. These include systemic lupus erythematosus, (Yell JA – 1996) ²⁶² ulcerative colitis, Crohn's disease, Behcet's disease (Rogers RS – 1997) ¹⁸⁶ Reiter's syndrome, and acquired immunodeficiency syndrome (AIDS) or HIV infection(Macphail LA -1992)¹²⁹. A detailed medical history and thorough clinical examination are required to establish an accurate diagnosis.

Behcet's syndrome is characterized by similar ulcerations as discussed above, but also includes uveitis, urethritis, and arthralgia, in addition to skin, vascular, and neurological involvement. These

findings usually are not present simultaneously, thus a careful history is integral to the evaluation ($Rodu\ B$ et al -1992) 184 .

Crohn's disease is an idiopathic chronic inflammatory disease that can involve any part of the gastrointestinal tract. Oral ulcers can be seen, but biopsy reveals characteristic chronic granulomatous inflammation ($Rodu\ B\ et\ al-1992$) ¹⁸⁴.

Squamous cell carcinoma should be entertained in the initial presentation of a solitary ulcer that does not resolve in a timely manner. This is of higher concern in the patient with a history of tobacco use and/or alcohol consumption (Schneider LC-1998)¹⁹⁷.

Mouth and genital ulcers with inflamed cartilage characterize MAGIC syndrome. As part of this syndrome, patients can also have fever, pharyngitis, and aphthous ulcers (Porter SR-1998) 171

PFAPA syndrome was described by Marshall and colleagues based on a group of 12 pediatric patients with periodic fever, aphthous stomatitis,

pharyngitis, and adenitis (Marshall GS -1987) ¹³². Several possible cases have been described in adults, but no definitive tests exist for the diagnosis of this condition, further research is necessary (Farhad Melamed-2001) ⁶⁴.

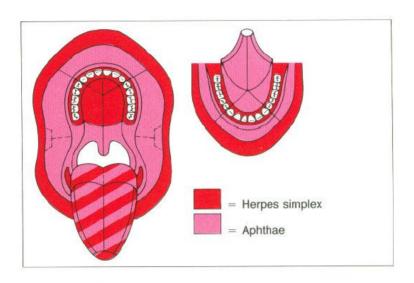
Hypersensitivity reactions in the oral cavity can be induced by a variety of allergens (eg, foods, gums, mints, dental materials, metals, and medications) but are often difficult to diagnose. In allergic contact stomatitis, common manifestations. are burning sensations, erythema, and edema (Van Loon LA-1992) ²⁴⁰; aphthous like ulcers do not usually occur. If an allergy is suspected, a more detailed patient history will be required, and allergy testing should be considered (Ship JA-2000) ²⁰¹.

Differential	Oral signs	Other signs and
Diagnosis		symptoms
Recurrent	Single or multiple	May be
aphthous	ulcers	associated with,
Stomatitis	on unattached mucosa	Oropharyngeal
	Single or multiple	or

Herpes	ulcers	gastrointestinal	
simplex virus	on attached mucosa	ulcers	
	Diffuse gingival	Preceding fever	
	erythema	and mucosal	
Varicella	Extraoral and	vesicles	
zoster, virus	intraoral ulcers		
	Unilateral	Prodrome of	
Herpangina,	distribution	pain and	
	Multiple ulcers in	burning may	
Hand foot	hard palate, soft	cause scarring	
and mouth	palate, and	and neuralgia	
disease	oropharynx		
Erythema Ulcers preceded by		Fever and	
multiforme	vesicles	malaise	
	Lesions on attached		
	and	Skin lesions,	
	unattached mucosa;	low grade fever	
	lip crusting	and malaise	
Oral lichen	May be preceded by	Sudden onset of	
planus	herpes	skin macules	
	infection	and papules	
	Erosive and reticular	Target iris	
	lesions	lesions on skin	

Cicatrical	on buccal mucosa,	May be
phemphigoid	gingiva,	asymptomatic
	palate, and tongue	Lesions may
	White (Whikham's)	occur on skin
	striae	
Pemphigus	Vesicuiobullous	
vulgaris	lesions on	Can affect eyes
	attached and	and genitalia
	unattached	Lesions may
	mucosa	scar
	Positive Nikolsky's	
	sign	
	Vesiculobullous	Lesions can
	lesions on	occur on skin
	attached and	
	unattached	
	mucosa	
	Positive Nikolsky's	
	sign	

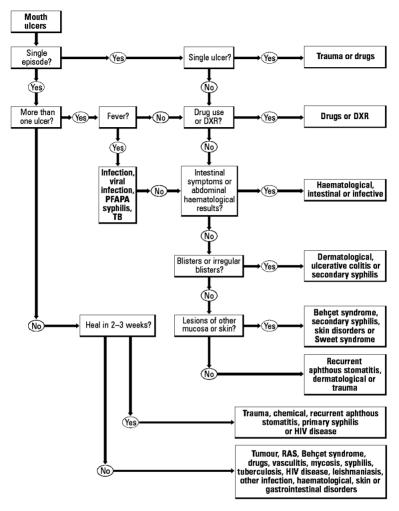
Chronic-recurring aphthae (Cook's)	Herpes simplex
 Primary efflorescence: erosion Chronic-recurring appearance 	• Primary efflorescence: blisters, fast transformation to erosions
 Localization: usually non keratinized Unknown cause 	 Recurrences only in herpes simplex recidivans Localization: predominantly on keratinized mucosa Demonstration of cause possible



Preferred areas of development of chronic-recurring aphthae and of recurrent herpes simplex

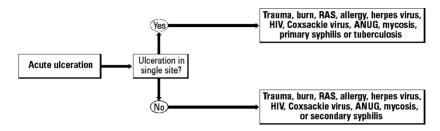
Chronic recurrent aphthae	Aphthae in Behcets syndrome
 Aphthae are the only symptom Superficial ulcerations Aphthae mostly in the anterior region of the mouth 	 Mouth aphthae are part of a systemic disease Deep ulcerations Aphthae also in posterior region of the mouth
Chronic recurrent aphthae Roundish oval form	Bite wound after local anesthesia Irregular jagged margin

 Erythematous halo Very painful Recurrent appearance at different locations Typical localizations nonkeratinized mucosa Cause unknown 	 Inflammatory erythema is ill defined Moderately painful Lesions occurs only once Typical localization – lower lip off median Self induced damage during local anesthesia
Chronic-recurring aphthae (on the salivary papilla)	Salivary papilla coated with fibrin
 Coated erosion Very painful Chronic – recurring appearance 	 Pseudomembranous coating without significant epithelial defect Little or no pain No aphthae history

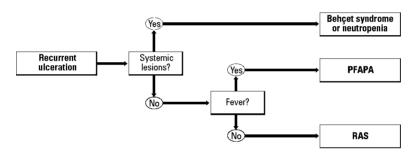


Algorithm for Oral Ulceration. (DXR, irradiation; PFAPA, periodic fever, aphthae, pharyngitis, adenitis; RAS, recurrent aphthous stomatitis; TB, tuberculosis)

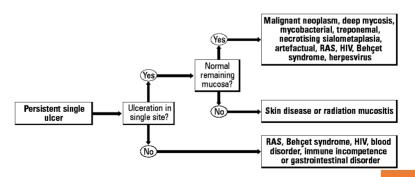
Algorithm for Acute Ulceration



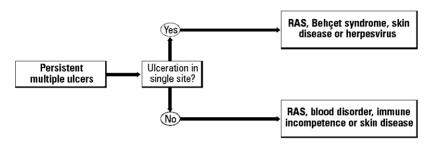
Algorithm for Recurrent Ulcers



Algorithm for Persistent Single Ulcers



Algorithm for Persistent Multiple Ulcers



Investigations

Serologic, chemical, and hematologic findings

Full hematologic screening of patients with RAS has been proposed to reveal deficiency states of serum ferritin, iron, folate, and vitamin B12 (Rogers RS – 1986)¹⁸⁷. Deficient levels of serum ferritin or iron are the most common findings occurring in 11% to 36% of patients with RAS. Hemoglobin levels and red blood cell indexes are generally within normal range in patients with RAS (Challacombe SJ – 1977(a)) ²⁷ and are similar to levels in control patients. However, underlying anemic states are sometimes discovered on screening and replacement therapy maybe attempted to resolve the ulcers. Hematologic screening of children with RAS is also recommended, because it has been reported that 21%

of patients have some type of hematologic abnormality, most notably latent iron deficiency without anemia (Field EA - 1987)⁷¹.

Histopathology of recurrent aphthous ulcer

I. The ulcer area

Superficial tissue necrosis with fibrinopurulent exudate consisting of clotted fibrin, numerous red blood cells forming hemorrhagic foci, neutrophils and cellular debris covers the necrotic area. Theepithelium is infiltrated with variable numbers of intraepithelial lymphocytes and some neutrophils (Stanley 1972) 220. Neutrophils predominate in the immediate ulcerated area, although peripheral areas surrounding the ulcer remain mononuclear in nature (Lehner 1969 119; Mills et al. 1980148; Schroeder et al. 1983 198; Hayrinen-Immonen et al. 1991 90). Granulation tissue may be noted near the base of the lesion. Epithelial proliferation is present at the margins of the lesions, similar to that found in any non specific ulcer.

Accessory salivary gland tissue, commonly present in areas of apthae, will typically exhibit focal periductal and perialveolar fibrosis, ductal ectasia and mild chronic inflammation. Theses features may be present in even clinically normal mucosa of the aphthous patients. It has also been found that the aphthous ulcer itself, atleast in some cases, begins immediately above the excretory duct of one of these minor glands where there is disruption of this ductal epithelium. The tissue involvement is generally superficial.

Lehner has shown that the histologic findings by light microscopy of the severe oral ulcers in recurrent aphthous major are identical with those described under the recurrent aphthous minor. Electron microscope studies have confirmed this similarity.

Wood and his associates have described characteristic changes in the nuclei of epithelial cells taken by cytologic smears from around recurrent aphthous ulcers. These have been referred to as Anitschkow cells and consist of cells with elongated

nuclei containing a linear bar of chromatin with radiating processes of chromatin extending towards the nuclear membrane. They are quite abundant in patients with recurrent aphthous Stomatitis but are not pathognomic of the disease, since they are also inpatients with sickle cell disease. found Megaloblastic anemias and iron deficiency anemias, in children receiving chemotherapy for cancer, and even in normal people. Their ultrastructure has been described by Haley and their associates, who found the nuclear chromatin was madepleomorphic masses forming an irregular band along the long axis of the nucleus rather than being randomly dispersed.

II. The area lateral to the ulcer

Defined as the epithelium covered area from the edge of the ulcer and sideway to the periphery of the biopsy. An intense leukocytic infiltration with predominance of lymphocytes in non-ulcer regions, where they outnumbered neutrophils (Mills et al. 1980¹⁴⁸; Hayrinen-Immonen et al. 1991 ⁹⁰). Monocyte macrophages are also numerous in the tissue adjacent and lateral to the ulcer. The density of

MCs is increased in the lamina propria (Lehner 1969 ¹¹⁹, Schroeder et al. 1984 ¹⁹⁹). The lymphocytes in RAS lesion are primarily T cells, and only 5-12% of all cells in the lesion are B cells (Hayrinen-Immonen et al. 1991 ⁹⁰). A small proportion of plasma cells and eosinophils can be found and more often in the older lesion (Lehner 1969¹¹⁹). Dilatation of blood vessels is a constant and prominent feature of RAS lesions as are foci of perivascular mononuclear cell infiltrates (Lehner 1969 ¹¹⁹; Schroeder et al. 1984 ¹⁹⁹).

The microscopic picture is non-specific, and without a careful clinical history and description, does not permit the specific diagnosis of the disease.

Immunohistopathology of RAS

Immunological aberrations involving both cell-mediated and humoral immunity have been reported in previous studies of RAS (Porter et al. 1998) ¹⁷¹. Both class I and II MHC antigens were found to be expressed on the epithelial basal cells in preulcerative RAS lesions and more diffusely within the epithelium at the ulcer stage, consistent with active cell mediated inflammation (Savage et al. 1986)

196, Poulter and Lehner 1989 ¹⁷²). In vitro studies have shown that peripheral lymphocytes from patients suffering from RAS were found to be directly cytotoxic against oral epithelial cells (Dolby 1969 ⁴⁸, Rogers et al. 1976) ¹⁸⁸, which, however, 32 has not been confirmed by others (Peavy et al. 1982¹⁵⁹, Gadol et al. 1985 ⁷⁴, Burnett and Wray 1985 ²⁶). RAS patients have significantly increased antibody-dependent cellular cytotoxic (ADCC) activity in the early stage of the disease (Greenspan et al. 1981) ⁸³.

Immunofluorescence studies demonstrated deposits of IgG, IgM, IgA, and C3 in and along mucosal blood vessels and in the cytoplasm of stratum spinosum cells in aphthous ulcers lesions from patients with RAS and Behcet's disease (Lehner 1969¹¹⁹, VanHale et al. 1981 ²³⁹, Malmstrom et al. 1983 ¹³⁰). Previous studies on peripheral NK-cells in patients with RAS have been contradictory as their percentages have been reported to be either increased (Greenspan et al. 1982) ⁸¹ or similar to that of controls (Savage et al. 1988 ¹⁹⁵, Pedersen and Pedersen 1993¹⁶²). Furthermore, Thomas et al. (1990) ²³⁰ found that depletion of CD-16 positive cells

(Natural Killer cells) produced no change in cytotoxicity towards the oral epithelial target cells. Another report demonstrated that among patients with major RAS, Natural Killer cell activity is increased when active oral lesions are seen depressed during periods of resolution and normal in patients in remission (Sun et al. 1991 ²²⁴).

of perivascular Formation lymphocyte infiltrates are probably in part mediated by endothelial intercellular adhesion molecule-1 (ICAM-1) and lymphocyte function- antigen-3 (LFA-3)binding to their counterpart ligands lymphocyte function-antigen-1 (LFA-1) and CD-2 on lymphocytes, respectively (Hayrinen-Immonen et al. 1992 89. Verdickt et al. 1992 241). ICAM-1 is expressed on the epithelium and submucosal capillaries and venules, suggesting that it may support T-cell adhesion and control the trafficking of leukocytes into submucosa and epithelium (Savage et al. 1986 196, Hayrinen-Immonen et al. 199289, Eversole 1994 58, Healy and Thornhill 1999 93), while LFA-3 and its counterpart ligand CD-2 are likely to be involved in T-cell activation in RAS (Hayrinen-Immonen et al.

1992 ⁸⁹). Increased numbers of CD1+ Langerhans 33 cells were found in the epithelium and lamina propria in BD and RAS (Poulter and Lehner 1989 ¹⁷², Hayrinen-Immonen 1992 ⁸⁹). It is thus evident that there is no unifying theory of the immunopathogenesis of RAS.

Diagnostic criteria

Due to the absence of a definitive aetiology or diagnostic test for RAS, the identification of RAS in clinical practice usually, relies on the combination of history, clinical features and historathology. A set of diagnostic criteria for Minor RAS which are meant to distinguish the condition from other diseases, and to be practical, all based on working knowledge of aphthous ulcers and clinical experience have been reviewed by S.S Natah et al. They have not been tested for sensitivity and specificity and further studies might be required before widespread use of these criteria. The diagnosis of primary RAS minor (idiopathic) or secondary RAS minor (that occurs in association with systemic diseases) can be made if the condition fulfils the four major criteria (which are necessary to establish the diagnosis of Minor RAS)

plus at least one of the minor (supportive) criteria (Natah S.S -2004) 150.

Major criteria for recognizing and diagnosing the condition as RAS minor

Major criteria	Description
1. External	Single or multiple round / oval
appearance	shaped ulcers, never preceded by vesicles. The ulcers are shallow and have regular margins and a yellow grey base surrounded by thin erythematous halos. Variable in size, but less than 1cm in diameter.
2. Recurrence	At least three attacks of RAS within the past 3 years and the recurrences do not affect the same focal site.
3. Mechanical hyperalgesia	The lesion is painful and the pain is exacerbated by movement of the area affected by the ulcer.
4. Self –	The ulcer heals spontaneously

limitation of	without	sequelae	either	with	or
the	without t	reatment.			
condition					

Minor criteria for recognizing and diagnosing RAS minor

Minor criteria	Description
l. Family history of	A positive family history of
RAS	RAS is present.
2. Age at onset	The first RAS attack started
	before the age of 40 years
3. Location of ulcers	Occur on non-keratinized oral
	mucosa
4. Duration of the	Each bout of ulceration lasts
lesion	from a few days to two weeks
5. Pattern of	Irregular
recurrence	
6. Histological	Shows non-specific

examination inflammation 7. Presence of a The attacks are triggered by precipitating factor hormonal changes, exposure to certain foods or drugs, intercurrent infections, stress and local trauma. investigations 8. Presence of Laboratory haematinic reveal an accompanying deficiencies deficiency. haematinic Inparticular, ferritin, folate, iron, vitamin B and zinc 9. Negative RAS patients is a non-smoker association with or develops the ulcer after smoking stopping smoking 10. Therapeutic trial Positive response to treatment with glucocorticoids with localorsystemic steroids.

Treatment

Goals of treatment

Treatment of RAS has 4 major goals:

- (1) Ulcer management (to promote healing and reduce duration),
- (2) Pain management (to reduce morbidity and enhance function),
- (3) Nutritional management (to ensure adequate food and fluid intake), and
- (4) Disease control (to prevent recurrence or reduce frequency).

The relative importance and priority of each goal depends on the severity of the condition.

Minor and infrequent RAS may only require brief pain management. Alternatively, major RAS, frequent minor RAS, and herpetiform RAS are all associated with greater discomfort, severity, and duration of symptoms that require intervention and nutritional management. Furthermore, because several systemic conditions are associated with RAS, possible underlying causes must be ruled out before a treatment strategy is selected. (Rogers RS 1997) 186

According to Crispian Scully et al 2003 ³⁸ to help determine management strategies, the practitioner may find it useful to classify RAS in three clinical presentations:

Type A

Type B and

Type C.

Type A: RAS episodes lasting for only a few days, occurring only a few times a year, are classified as "type A." In this scenario, pain is tolerable. The clinician should try to identify what precipitates the ulcers, what the patient uses to treat them, and how effective that treatment is. If it is effective and safe, the health care provider, or HCP, should encourage the patient to continue it. If a precipitating factor(s) is identified, the HCP should try eliminating it first. For example, if trauma-induced RAS is suspected, the HCP can suggest a softer toothbrush and gentler brushing. Medication may not be indicated.

Type B: Painful RAS each month, lasting between three and 10 days, is type B. In this scenario, the patient may have changed diet and oral hygiene habits because of the pain. If a precipitating factor can be identified-for example, oral hygiene, stress, trauma or diet-alternatives or remedies should be discussed with the patient. It is imperative to identify patients who experience prodromal symptoms, such as tingling or swelling, because the patient can use corticosteroids at the prodromal stage to abort the attacks. Treatment often includes the use of a chlorhexidine mouthwash (without alcohol base), and a short course of topical corticosteroids as soon as the ulcers appear. Because of the consistent recurrent pattern, these patients may need a maintenance treatment protocol.

Alternative regimens include dexamethasone 0.05 milligrams/ 5 ml (rinse and spit three times per day) or a high-potency topical corticosteroid such as clobetasol ointment 0.05 percent in Orabase (1:1) (Colgate Oral Pharmaceuticals, Canton, Mass.) or fluocinonide ointment 0.05 percent in Orabase (1:1) if the ulcer(s) recur on the same site, used three times daily. If corticosteroids are used, patients should be monitored for yeast superinfection. In patients with poor oral hygiene, professional help from a dental hygienist should be considered once ulcers heal.

In patients with recalcitrant RAS, a short course of systemic corticosteroid therapy may be required, never exceeding more than 50 mg per day (preferably in the morning) for five days. This course of treatment is best left to a physician or oral medicine specialist.

Type C: Type C RAS involves painful, chronic courses of RAS in which by the time one ulcer heals, another develops. These patients are best treated by an oral medicine specialist, who often will use potent topical corticosteroids (such betamethasone. asbeclomethasone. clobetasol. fluticasone fluocinonide), systemic corticosteroids, azathioprine or other immunosuppressants such as dansone. and sometimes thalidomide. pentoxifylline Inaddition, oral medicine specialists may administer intralesional injections of a corticosteroid such as betamethasone, dexamathasone or triamcinolone to enhance or boost the local response, thus allowing for shorter systemic treatment. In patients with poor oral hygiene, professional help from a dental hygienist should be considered.

Management/Treatment (Cynthia Hodgins et al 2003)⁴¹

1. Non-pharmacological therapy

Oral hygiene, tRASma prevention, avoidance of certain foods/drinks, use of straws, relaxation techniques

2. Pharmacological therapy for minor to major recurrent aphthous stomatitis:

Over-the-counter conservative treatment

• liquid antacids or 3% hydrogen peroxide/water solution

Covering agents/topical analgesics/anesthetics /numbing agents/ antiinflammatory

- Orabase, Benzydamine hydrochloride (HCL) mouthwash
- Diphenhydramine EMLA alone or mixed with Kaopectate or aluminum hydroxide, or Maalox
- Viscous Lidocaine 1:1 with Benadryl plus Maalox
- $\bullet \quad Aphthasol~5\%~(amlexanox)\\$

Antiseptic mouthwashes

- Benzydamine hydrochloride (Difflam)
- Chlorhexadine gluconate [Peridex/Corsodyl]
- Carboxymethylcellulose paste (Orabase)

Low potency topical steroid pellets and ointments

- Triamcinolone 0.1% in carboxymethylcellulose paste (Adcortyl in Orabase) & Triamcinolone acetonide (Kenalog in Orabase)
- Hydrocortisone sodium succinate (Corlan)

Aerosols

Beclomethasone dipropionate aerosol (Beconase spray)

Steroid mouthwashes

- Betamethasone sodium phosphate (Betnesol mouthwash/Diprolene)
- Fluocinonide (Lidex), clobetasol (Temovate)

3. Pharmacological therapy for severe aphthous stomatitis

Systemic drugs

- Oral prednisolone
- Thalidomide
- Colchicines or Pentoxifylline
- Azathioprine
- Tetracycline (capsules and/or topical)

Topical immunomodulatory agents (azelastine, human alpha-2 interferon cream, topical cyclosporine, deglycyrrhizinated licorice, topical 5-aminosalicylic acid [5-ASA], amlexanox 5% paste, prostaglandin E2 [PGE2])

4. Pharmacologic therapy for children under age 12 First line treatment

- Benzydamine and local anesthetics
- Lidocaine gel preps [Calgel teething gel])

In more severe cases

• Triamcinolone 0.1% in carboxymethylcellulose paste (Adcortyl in Orabase)

• Hydrocortisone sodium succinate (Corlan)

5. Treatment for HIV-associated ulcers

• Antifungal treatment in conjunction with steroids

Management of RAS

Lifestyle modifications may aid in prevention, decreased frequency of sores, or minimizing discomfort. Modifications include practicing good oral hygiene, preventing trauma by using adequate sized toothbrush, instituting relaxation techniques to minimize stress, drinking through straw, and avoiding acidic beverages and spicy or sharp/crispy foods, such as chips

Non-pharmacological treatments include good oral hygiene, prevention of trauma (adequate sized toothbrush), avoidance of spicy foods and acidic fruit juices or carbonated drinks, drinking through a straw to bypass the mouth, avoiding sharp foods such as crisps, avoiding stress if possible which may exacerbate ulcers or trigger a series of ulcers, and orthodontist referral. In addition, if vitamin deficiency has been diagnosed, this should be treated

and corrected; if food allergies have been determined, these foods should be avoided.

Pharmacological therapy for minor and major recurrent aphthous stomatitis

- Pharmacological treatment options include vitamins and nutritional supplements, topical glucocorticoids, topical anesthetics, and systemic medications.
- Follow up in 1 to 2 days for infants and elderly persons not taking fluids

Treatment regimens minor to major recurrent aphthous ulcers

Type of	Preparations	Particularly
treatment		suitable for
Over-the-	Liquid antacids	Minor recurrent
counter	or 3% hydrogen	aphthous ulcer
conservative	peroxide/water	
treatment	solution, 1:1 as	
	a gargle	

Type of treatment	Preparations	Particularly
		suitable for
Covering	1. Orabase,	Single,
agents/topical	Benzydamine	sporadic,
analgesics/anesthetics	hydrochloride	infrequent
/numbing	(HCL)	minor or
agents/anti-	mouthwash	major ulcers.
inflammatory	2.	Accelerate
	Diphenhydram	resolution of
	ine EMLA, or	pain and
	mixed 1:1 with	healing, have
	Kaopectate or	not been
	aluminum	shown to
	hydroxide, or	reduce the
	Maalox	rate of
	3. Viscous	occurrence
	lidocaine 1:1	
	with Benadryl	
	plus	
	Maalox	
	4. Aphthasol	
	5%(amlexanox	
) paste,	

apply over
canker sore,
forms a film
which
protects
canker sore
and delivers
medication,
four times
daily (QID),
after meals
and at
bedtime (HS).

Type of treatment	Preparations	Particularly suitable for
Antiseptic	1. Benzydamine	Antibacterial
mouthwashes	hydrochloride	mouthwashes.
	(Difflam), at least	Primarily for
	three times daily (TID)	reduction of
	2. Chlorhexadine	pain and with
	gluconate	wide range of
	(Peridex/Corsodyl) at	oral sites not

least TID	accessible to
3.	covering
Carboxymethylcellulose	pastes, also
paste (Orabase)	speed up
	healing

Type of	Preparations	Particularly
treatment		suitable for
Low potency	1. Triamcinolone 0.1%	Anti
topical	in	inflammatory
steroid	carboxymethylcellulose	agents.
pellets and	paste (Adcortyl in	Frequently
Ointments	Orabase) &	recurring
	Triamcinolone	mild ulcers
	acetonide (Kenalog in	or major
	Orabase), qid to dried	ulcers.
	areas around ulcers	Steroids may
	with moistened finger.	be used to
	Allow film to hydrate	reduce the
	before allowing contact	frequency of
	with	attacks. Most
	uninvolved mucosa, one	successful

application last thing with ulcers located in the atHS (minor AU). sulci where pellet can be 2. Hydrocortisone left to dissolve. sodium succinate 2.5mg (Corlan) qid during attack, bid between attacks for at least 6 weeks before reducing to use during attacks only (minor AU) (use of steroids is consensus effective treatment from almost all sources).

Type of	Preparations	Particularly
treatment		suitable for
Aerosols	1. Beclomethasone	Most useful
	dipropionate aerosol	when more
	(Beconase spray) 2	potent steroid
	puffs (100	needed and for
	micrograms) spray	inaccessible
	onto affected	sites (i.e., soft
	mucosa to a max of	palate or
	8 puffs/day. Reduced	oropharynx).
	risks of adverse	
	effects over	
	Betamethasone	
	mouthwash but	
	slightly less	
	effective. Useful if	
	only one or two	
	ulcers are present	
	(moderately severe).	

Type of	Preparations	Particularly
treatment		suitable for
Steroid	1. Betamethasone	Useful with
mouthwashes	sodium phosphate	wide range of
	(Betnesol	ulcer sites
	mouthwash/Diprolene)	and of
	one 0.5mg tablet	sufficient
	dissolved in 5 to 10 ml	severity to
	of water used as a	merit
	mouthwash qid during	therapeutic
	ulcer attack. Must be	treatment.
	held in mouth for a	Monitoring
	minimum of 3 minutes	for side
	for maximum	effects of
	effectiveness; spit out	steroids is
	after use. Can be used	essential as
	6 times a day under	some
	strict supervision	medication
		always gets
	2. Fluocinonide	swallowed
	(Lidex), clobetasol	inadvertently.
	(Temovate) same as	
	Betamethasone	

Pharmacological therapy for severe, recurrent aphthous ulcers

Type of treatment	Preparations	Particularly
		suitable for
Systemic drugs	1. Oral	Reserved for
	prednisolone 40	severe
	mg for 5 days,	recurrent
	reduce by 5 mg	aphthous
	every 2 days to 5	ulcers
	mg, reduce by 1	interfering
	mg/day until	with
	complete. Monitor	nutrition.
	severity closely at	
	15 mg dos; select	
	maintenance dose	
	to maintain	
	remission before	
	ulcers reappear	
	2. Thalidomide	
	200 mg qd or bid	
	3 to 8 weeks for	
	HIV or Behcet's	

	disease severe AU	
	3. Colchicines 500	
	micrograms/day	
	or	
	Pentoxifylline 400	
	mg tid	
	4. Azathioprine 50	
	to 100mg daily	
	primarily as a	
	steroid sparing	
	agent during	
	maintenance	
	phase of	
	treatment	
Tetracycline	1. Tetracycline	Herpetiform
	250-mg capsules	ulcers. Often
	dissolved in 10 ml	unresponsive
	of water and used	to steroids,
	as a mouthwash.	which form a
	Gargle for 3	second line
	minutes then spit	of
	out	treatment.

	2. Topical	
	tetracycline	
	(aureomycin,	
	chlortetracycline,	
	and tetracycline)	
Topical	Azelastine, human	Suggested to
immunomodulatory	alpha-2 interferon	be of some
agents	cream, topical	benefit in
	cyclosporine,	the
	deglycyrrhizinated	management
	licorice, topical	of
	5-aminosalicylic	recurrent
	acid (5-ASA),	aphthous
	amlexanox 5%	stomatitis
	paste, and	may
	prostaglandin E2	significantly
	(PGE2) gel.	reduce
		the pain and
		healing time
		to RAS
		ulceration.

Recommendations for Recurrent Aphthous Stomatitis in children under age 12

First Line	 Benzydamine and local anesthetics Lidocaine gel preps (Calgel teething gel) may be applied several times a day in small quantities and before meals to improve eating
In more severe cases	 Triamcinolone 0.1% in carboxymethylcellulose paste (Adcortyl in Orabase) can be managed only by older children. Hydrocortisone sodium succinate 2.5mg tablets (Corlan) are safe in children because of their low steroid potency

Principles of treatment for HIV-associated ulcers

- Antifungal treatment may be required in conjunction with steroids.
- Biopsy may be indicated to ensure treatable infection (i.e., herpes simplex, cytomegalovirus [CMV]).

- A further immunosuppression with new infections may arise.
- Steroids should be used with caution: prednisolone 40 mg for 4 days, reducing by 5 mg every 2 days until 5 mg, then reducing by 1 mg per day to 0 mg provide rapid relief.
- Intralesional injection delivers high doses of steroids directly to the lesion and avoids long-term systemic adverse effects.

Recently Researched Treatments for Recurrent Aphthous Stomatitis (Crispian Scully et al 2003) 38

- Acyclovir
- Amelexanox
- Azelastlne
- Chlorhexidine
- Colchicine
- Corticosteroids
- Dapsone
- Diclofenac in Hyaluronan
- Doxymycine cyanoacrylate
- Eupatorium Laevigatum
- Helium Neon Lasers

- Interferon-Alpha
- Irsogladine Maleate
- Levamisole
- Nicotine
- Pentoxifylline
- Photophoresis of Oxolin Ointment
- Relaxation/Imagery
- Shark Liver Oil
- Sucralfate
- Tetracyclines
- Thalidomide
- Triclosan
- Ultrasound

Management of RAS based on type of treatment Primary line of treatment Topical gels, creams, and ointments:

The primary treatment of RAS lesions utilizes topical anti-inflammatory agents. The problem with topical gels, creams, and ointments, however is establishing effective drug delivery, because substances applied to mucosal surfaces are inevitably rubbed or rinsed away (Macphail L.1997) 126. This

problem is addressed by using strong topical corticosteroids which, when compounded with mucosal adherents (eg, Orabase, Bristol-Myers Squibb; isobutyl cyanoacrylate or Iso-Dent, Ellman International) are effective despite limited contact time (Lozada- Nur F et al 1991) 124.

The efficacy of topical agents can be increased markedly if they are administered during the early phase of ulceration (ie, when lymphocyte activity is at its maximum): Clinicians should be cognizant of the potential of topical glucocorticoids to cause acute pseudomembranous candidiasis (Kay LW. 1976) 110. However the use of topical glucocorticoids will diminish the risk of suppressing the hypothalamic pituitary adrenal system, a frequent complication of systemic glucocorticoids.

The topical glucocorticoids that have demonstrated efficacy for RAS are fluocinonide, triamcinolone, and clobetasol. Triamcinolone acetonide with Orabase (a mucosal adherent), however, may not be as effective as stronger glucocorticoids, such as fluocinonide and, clobetasol.

Therefore fluocinonide or clobetasol, used alone or mixed with Orabase, may be preferable for the treatment of recurrent RAS. Another topical paste with anti-inflammatory and antiallergic properties is 5% amlexanox which has demonstrated clinical safety and efficacy in several vehicle-controlled multicenter clinical studies. Application of paste directly to ulcers, 4 times daily resulted in enhanced resolution of pain and healing of ulcers with minimal adverse experiences. Several other topical medicaments have been used with encouraging research results. although additional investigations are required to establish reliable safely and efficacy data. Topical prostaglandin E2 may have useful prophylactic activity, and oral human interferon-a may assist in ulcer remission. A single topical treatment with doxymycine-cyanoacrylate was reported to relieve the intensity of pain for 6 days after a 1 day latency period.

Hydroxypropylcellulose film, or Zilactin (Zila Pharmaceuticals), is a topical medication with mucosal adherence properties; it has been demonstrated to adhere to mucosa significantly

longerthan Orabase and may protect the existing ulcer and provide pain relief (Ship JA et al 2000) 212.

Corticosteroids

Topical corticosteroid use in patients with RAS is intended to limit the inflammatory process associated with theformation of aphthae. Corticosteroids may act directly on T lymphocytes or alter the response of effector cells to precipitants of immunopathogenesis (e.g., food allergies, trauma, microorganisms) (Vincent SD et al 1992) 242. two double-blind, placebo-controlled trials have evaluated the efficacy of topical corticosteroids for RAS (Thompson Ac, et al 1989) 234. The patients enrolled in one trial had minor RAS. Classification of ulcers was not available for the other trial. Both trials assessed patients for immunocompetence through laboratory studies. One trial excluded other medications used in RAS. In both trials there were significant reductions, compared with placebo in ulcer duration and pain severity and no changes in the frequency of RAS in patients who applied betamethasone gel or beclomethasone aerosol spray

to ulcers four times daily for six days to four weeks(Vincent SD et al 1992) 242.

Two non-placebo controlled trials found no differences triamcinolone significant between ointment or betamethasone tablets and adhesive vehicles and Orabase [Colgate-Hoyt] in the frequency and duration of severe RAS (Browne RM 1968) 24. Subjective improvement tended to be greater with corticosterolds than with adhesive vehicle (Orabase) although thedifference statistically was notsignificant. A single blind placebo-controlled trial involving fluocinonide ointment was performed in patients with minor and major RAS. Fluocinonide ointment significantly reduced ulcer duration but ulcer frequency and subjective improvement were the same as for adhesive vehicle (Orabase). In the latter three trials study design ulcer severity and vehicle activity may have contributed to findings inconsistent with those in the doubleblind placebo-controlled studies (Robert W. Barrons 2001) 181.

Amlexanox

A tablet formulation of amlexanox has been marketed in Japan since 1981 for the long term treatment of asthma. In the United States amlexanox is available only as a 5% topical paste (Aphthasol) for use in the treatment of RAS. Amlexanox is a potent inhibitor of the formation and release of inflammatory cells, neutrophils, mediators from mast mononuclear cells. Given topically amlexanox could be expected to facilitate the healing of aphthous ulcers but not to reduce the frequency of RAS episodes. Four vehicle-controlled randomized doubleblind. multicenter trials assessed the efficacy of amlexanox with respect to ulcer healing and pain resolution in 1335 patients with minor RAS. As the trials excluded patients using concurrent medications to treat RAS patients with medical conditions posing a risk for study involvement and patients alternative causes of RAS including irritable-bowel disease Behcet's syndrome and anemia. The patients applied small dabs of amlexanox oral paste four times daily directly to the ulcers for 4-10 days. The first trial established the efficacy of 5% amlexanox paste relative to either 1% amlexanox paste or the paste

The5% amlexanox paste vehicle. produced significantly greater reductions in ulcer size than the vehicle and greater improvement in the rate of healing and erythema than either the vehicle or 1% amlexanox paste. The results of the remaining three trials comparing 5% amlexanox paste with the paste vehicle were presented as a meta-analysis examining rates of complete healing of ulcers and resolution of pain. After six days of therapy 14% of the patients receiving amlexanox paste had complete healing of ulcers, versus 54% of those using the vehicle (p < 0.001). Similarly 83% of the patients treated with amlexanox paste had complete resolution of pain compared with 13% of those receiving the vehicle (p < 0.001). The self-limiting nature of aphthous ulcers combined with the protective effects of the paste vehicle produced high rates of healing and pain resolution independent of amlexanox. Patients may benefit from earlier application of amlexanox during the prodromal stage of an RAS episode. In a review of clinical trials and premarketing studies involving 991 subjects only 2.1% of those using 5% amlexanox paste reported adverse events. Almost 10% of these events were associated with the topical application of

amlexanox and included stinging, dryness, bumps on the lips, and mucositis. All of the adverse events were transient and none resulted in early discontinuation of amlexanox therapy (Khandwala A et al 1997) 113.

Topical rinses:

Topical rinses can also effectively provide symptomatic, relief for minor aphthous ulcers. These rinses may be used alone or in combination with other topical drugs. A decrease in the severity or number of ulcers may be observed during treatment with these rinses; however, none provides prevention or a cure.

Sucralfate, which acts by locally binding to proteins at the base of an ulcer, providing a protective covering, may be useful for the relief of pain resulting from minor RAS. Dexamethasone elixir(0.5 mg/5 mL), used as a mouthwash or gargle, can be helpful for multiple minor, major, or herpetiform ulcers that are difficult to treat with topical gels (Macphail LA et al 1992) 129.

Tetracycline can reduce ulcer duration, size, and pain because of its ability to reduce collagenase

activity. Patients should be instructed to swish for up to 5 minutes and spit several times a day.

Other oral rinses, such as chlorhexidine gluconate, benzydamine hydrochloride, Listerine (Warner-Lambert), triclosan (Earnest John Group), aqueous hydrocortisone, and Triamcinolone aqueous suspension, have been reported to provide some relief (Vincent SD et al 1992) 242.

Antimicrobial mouthwash use in RAS is intended to control microbial contamination and secondary infection. Both antibiotic (e.g., tetracycline) and antiseptic (e.g., chlorhexidine) mouth washes have been studied. The time required for healing of aphthous ulcers has been correlated with the ability of antimicrobial mouthwashes to reduce the population of oral mucosal flora (Robert W. Barrons 2001) 181.

Four double-blind, placebo-controlled trials of antiseptic mouthwashes were identified. In these studies, 197 patients were treated for at least five weeks. In three of the studies, the patients had a

history of minor RAS, with maximum ulcer free periods of three to four weeks. Concurrent therapy for RAS was prohibited in these three trials. Patients whose immune function might be compromised because of drugs or diseases were excluded from two of the trials. In three of the four studies, no significant differences in ulcer duration or pain severity were evident between patients treated with antiseptic mouthwash and patients given placebo. In two studies, the total number of ulcers significantly lower with antiseptic mouthwash than with placebo. Three trials demonstrated significant benefits in both the active therapy and the placebo groups throughout the treatment course. While placebo therapy with quinine sulfate may have some antimicrobial properties, the remaining vehicles were without known activity. Enhanced patient awareness and improved oral hygiene from study involvement may have contributed to these findings. Adverse drug reactions were reported for only two trials. These events included nausea in one patient, inflammation of the gums in one patient and discoloration of the teeth and gums in an unspecified number of patients.

Chlorhexidine caused brown staining of the teeth and tongue after two weeks of therapy.

Although frequency and severity were recorded, the potential for staining during prolonged treatment may limit the use of chlorhexidine. In three involving 81 patients, tetracycline studies chlortetracycline mouthwash significantly reduced the duration and pain of RAS compared with placebo; however, the frequency of ulceration was unchanged. The patients received 250-mg doses of antibiotic mouthwash four times daily and were instructed to hold the solution in the mouth for one to two minutes. Aphthous ulcers were treated for 4 days to 2 weeks, and follow up lasted 2.5-8 weeks. Adverse effects were reported only in patients using the mouthwash in excess of five days and included dysgeusia, skin reactions, thrush, angular cheilosis, and burning and soreness of the throat. (Hooter L et al 198199, Guggenheimer J et al 1968 85, Meiller TF 1991 138)

(Robert W. Barrons 2001) 181

Summary of Double-Blind, Placebo-Controlled Trials of Topical Antibiotics, Antiseptics, and Corticosteroids for Treatment of Aphthous Ulcers^a

Reference	No. Patients	Dosage Regimen	Duration of Uicers (Days)	Frequency of New Ulcors ^b	No. Ulcers	Subjective Improvement (Score or %9
Antiseptics						
17	20	1% chlorhexidine gel Li.d. after meals × 35 days	Mean: $T = 4.8$, PC = 7.7 (ρ < 0.05)	NA	T = 104, PC = 1404 (NS*)	Score: 1 = 0.93, PC = 1.21 (p < 0.05)
18	40	0.1% hexetidine mouth rinse 15 mL for 1 min t.i.d. after meals × 6 wk	NA (p > 0.05')	NA	NA (ρ > 0.05')	NA (ρ > 0.05°)
19	41	0.2% chlorhexidine mouthwash 10 mL for 1 min t.i.d. × 6 wk	Mean: J < 5.02, PC = 5.78 (ρ > 0.05)	NA	Mean: T = 7.54, PC = 8.329	NA (NS')
16	96	Listenne mouth rinse (unspecified volume) for 30 sec b.i.d. × 6 mo	NA (NS')	NA	NA (NS')	NA (NS')
Antibiotics						
20	7	0.5% chlortetracycline 50 mL held in mouth 1 min g.i.d.	NA (ρ < 0.01°)	NA	NA	T = 58%, PC = 62% (NS*)
21	49	2.5% chlortetracycline 10 mL held in mouth 1 min q.r.d.	NA (p < 0.01")	NA	NA	NA (p < 0.01")
22	25	5% tetracycline 1 tsp held in mouth 1 min q.i.d.	Mean: T = 5.46, PC = 8.21 (ρ < 0.05)	T = 1.07, PC = 0.20' (NS')	NA	Score: T = 1.11, PC = 1.78 (p < 0.05)
Corticosteroids		T				
23	57	0.025% betametha- sone benzoate gel 1 drop over lesion t.i.d. and h.s.	T < 6, PC > 6 (p < 0.05)	NA	NA	1 = 88%, PC = 60% (p < 0.05)
24	15	Beclomethasone dipropionate spray 2 puffs (800 µg) directly to ulcer g.i.d.	NA (p < 0.001 ^h)	NA	NA	NA (ρ < 0.05°)

Other approaches to therapy.

Another approach to treatment is to convert the ulcer into a wound by using chemical cautery, electrocautery, or lasers, ultrasound has been suggested to provide a beneficial effect, on RAS.

Stress management, relaxation, and imagery training are additional therapeutic approaches that have demonstrated some clinical benefits. Conversely;

no associations have been established between RAS and the premenstrual period, pregnancy, or menopause, and there are no consistent data to suggest that ovarian hormones can be used as an effective therapeutic modality (Ship JA et al 2000) 201.

Low-intensity ultrasound in the treatment of recurrent aphthous stomatitis

Low-intensity ultrasound has been shown to provide a therapeutic benefit in a number of clinical settings, primarily to accelerate wound healing (Enwemeka CS 1989⁵⁷, Heckman JD et al 1994 ⁹⁴). The mechanism underlying the therapeutic response to this form of ultrasound has not been confirmed, although evidence supports a modification of the inflammatory response (Wang SJ et al 1994) 247. It was hypothesized that ultrasound might provide some RAS. a chronic. recurrent. benefit ininflammatory process. One safe and convenient mode of providing ultrasound of the appropriate low intensity to the oral mucosa is through the use of an ultrasonic toothbrush (Terezhalmy GT et al 1994) 229.

Ultrasound is composed of high-frequency mechanical vibrations resulting from the conversion of electrical energy into sound waves. ultrasonic waves are applied to soft tissue, absorption of this energy by the tissue initiates a variety of physiologic responses. Low-intensity ultrasound, such as is emitted by the ultrasonic toothbrush in this study, avoids excessive tissue heating and the physiologic responses noted in tissue exposed to these ultrasonic waves are the result of non thermal effects. One such response is a change in cellular membrane permeability. Other effects of low-intensity ultrasound comparable to that emitted by ultrasonic toothbrush include stimulation fibroblasts and macrophages, increased angiogenesis, promotion of granulation tissue formation (el-Batouty MF et al 1986) 53, accelerated healing of tendon and bone, enhanced healing of full-thickness excised skin lesions (Young SR, Dyson M 1990) ²⁶³, augmentation of leukocyte adhesion to endothelium, a transient increase in RNA production in amniocytes, and alteration of oral microflora. Which, of these physiologic responses plays a role in the improvement of RAS cannot be determined, although improved oral

hygiene, modulation of the inflammatory response, and enhanced wound healing would logically be important factors.

Twice daily application of low-intensity ultrasound has a modest beneficial effect on RAS, both from the standpoint of decreasing the duration of RAS lesions as well as of decreasing the number of lesions that develop. This therapeutic modality is a well-tolerated and safe addition to the treatment armamentarium for RAS (Sylvia L 1997) ²²⁶.

Treatment of underlying systemic disease:

Several svstemic disorders have associated with RAS and identification and treatment of these conditions is an important step in the treatment of RAS. Oral aphthous ulcers may be the first clinical sign of a systemic disorder, making clinical judgment difficult. Treatment of numerous systemic conditions (including Crohn's disease; Behcet's disease; cyclic neutropenia; a syndrome of periodic fever that resembles human cvclic neutropenia; autoimmune neutropenia; pernicious anemia; systemic lupus erythematosus; HIV infection;

periodic fever, aphthosis, pharyngitis, and adenitis [PFAPA] syndrome; and mouth and genital ulcers with inflamed cartilage [MAGIC] syndrome) has been associated with improved RAS lesions. Because resolution of oral symptoms commonly follows effective systemic therapy, multidisciplinary care is recommended for patients with oral manifestations of these systemic conditions (Ship JA et al 2000) 201.

Treatment of nutritional and hematologic deficiencies:

Several deficiencies have been reported at higher rates among patients with RAS compared to non-RAS and healthy controls, providing a rationale for the evaluation of nutritional and hematologic deficiencies (Porter SR 1998 170, Wray D 1978 256). Vitamin B deficiencies have been reported to be associated with RAS and may, occasionally, be the primary cause of RAS: deficiencies in vitamin B1, deficiency) vitamin B2(riboflavin (thiamine deficiency) B6 (pyridoxine deficiency) and vitamin B12 (pernicious anemia). Deficiencies in zinc, folic acid, iron and selenium have also been associated with RAS like ulcers. These deficiency states may all

have an adverse influence on the immune system, which may explain, in part, their possible connection to RAS. Regardless of etiology replacement therapy is given when a deficiency is identified (Wray D 1975) 257.

Treatment with Systemic Zinc Sulfate

Previous reports indicate that systemic zinc treatment causes an improvement or remission in selected patient with RAS (Merchant HW et al 1977 141, Merchant HW et al 1981 142). Among these Battistone and associates (Battistone GC et al 1972)14, McCray and co-workers (McCray LA et al 1972) 137, and Mesrobian and Shklar (Mesrobian AZ, Shklar G 1969) 143 have shown improvement in oral wound healing rates in hamster and guineapigs following administration of zinc sulfate or zinc cysteamine-Nacetic acid. Merchant and associates have reported a marked reduction in number of ulcers and of their sizes, activity periods and especially of pain usually a total of 660 mg of Zinc sulfate per day in a series of 32 patients with recurrent aphthous ulceration. They suggested that RAS may be due to several causes, one of which may be local or general

deficiency of zinc or a defect in its metabolism, perhaps at the cellular level (Merchant HW et al 1977) ¹⁴¹. In their series, the most notable improvement was a reduction in the recurrence rate. Seventeen patients, 8 with initial serum zinc level above 110 µg/dl and 9 below, were provided zinc sulfate supplementation up to a total of 660 mg/day. All patients with initial serum zinc levels <110 µg/dl showed improvement. Three reported complete remission with however recurrences few weeks after cessation of treatment (Merchant HW et al 1977) ¹⁴¹. Serum copper levels of these patients were not reported.

Wray and his group observed no therapeutic effects with systemic zinc sulfate over a 3-month period in a double-blind crossover trial involving 20 patients. Their lack of success was considered secondary to selection of patients whose pretreatment serum zinc levels were not reduced. They apparently did not measure their zinc levels while under therapy (Wray D 1982)²⁵⁵.

Avoidance of allergy-causing foods:

Food sensitivity and allergies to other substances should be considered as an etiologic factor in hematologically normal patients recurrent oral ulceration (Nolan A et al 1991) 152. For example, gluten enteropathy may be a causative factor in RAS, and withdrawal of gluten from the diet has been reported to eliminate aphthous ulcers in some studies, but not in others. One potential etiologic mechanism of RAS is delayed-type hypersensitivity, or cell-mediated response to an antigenic stimulus. Therefore, any material (food, beverage, medication, toothpaste, chewing gum, mint, etc) that comes in contact with the oral mucosa must be considered and evaluated as a potential causative agent (Eversole LR 1997) 59.

Sodium lauryl sulfate (SLS), a detergent commonly used in toothpastes, has been reported to increase the recurrence rate of RAS in several studies. This effect may be related to destabilization of cell membranes by SLS and its denaturing capacity, which increases oral mucosal permeability and may cause epithelial desquamation of oral soft tissues.

Patients with SLS-related adverse reactions should use toothpastes that do not contain SLS (eg, Biotene antibacterial dry-mouth toothpaste, Rembrandt whitening toothpaste for canker sore prevention, Den-Mat) (Fakhry – Smith S et al 1999) 62.

Elimination of possible allergens (eg, glutens, nuts, strawberries, and tomatoes) may have no benefit unless the restricted item has been demonstrated to cause hypersensitivity or allergic reactions. Available data on the role of food allergies and sensitivities in RAS are inconsistent. Several studies have reported a relationship (Nolan A et al 1991) 152, while others have not established food allergies in the etiopathogenesis of RAS.

Alternatively, elimination diets, not diet diaries, have been used successfully-in identification of particular offending foods in a small subgroup of RAS patients. Elimination diets require motivation and strict compliance, and the offending agents found vary from patient to patient (Ship JA et al 2000) ²¹².

Secondary line of treatment:

For the patient whose symptoms are not relieved by the primary line of treatment or whose signs and symptoms warrant a more aggressive treatment modality, prednisone should be considered for both HIV-negative and HIV positive patients. Prednisone, an anti-inflammatory and an immunosuppressive agent, can be used in combination with topical gels and rinses.

Systemic prednisone therapy should be started at 1.0 mg/kg a day as a single dose in patients with severe RAS and should be tapered after 1 to 2 weeks. Prednisone use has potentially serious side effects, including insomnia, nervousness, increased appetite, indigestion, diabetes mellitus, hirsutism, joint pain, and glaucoma. Importantly, however, several studies have found the side effects to be minimal, especially when prednisone is combined with azathioprine and not used for extended periods of time in the treatment of RAS. Most adverse drug effects are related to treatment that persists for more than 2 weeks and can be minimized by reducing drug dosages, when appropriate, alternate day therapy and prednisone

intake as a single dose in the morning will help to reduce drug-related complications. Alternate-day dosing allows cell-mediated immunity, white blood cell subset levels, and potassium excretion to become normalized on the off day and the anti-inflammatory benefits of prednisone will persist longer than the hypothalamic-pituitary-adrenal axis suppression (Wolverton SE 1991) 252.

Prednisone can be combined with another immunosuppressive agent, azathioprine, to reduce the dosage of prednisone required to provide effective treatment. The potentially serious side effects of azathioprine include thrombocytopenia, leukopenia, secondary infections, anemia, nausea, vomiting, anorexia, diarrhea, and lymphoreticular and other malignancies after long-term therapy.

Immunosuppressive drugs (eg, azathioprine) have been associated with the development of cancers such as non-Hodgkins's lymphoma. Short- to mediumterm therapy probably results in a slightly increased risk of malignancy; whereascontinuous therapy for

more than 2 years is poorly documented and should be used cautiously.

Drug related safety and efficacy have been demonstrated when azathioprine is given as an, initial dose of 50 mg per day for 1 week and then increased to no more than 2.5 mg/kg daily with careful monitoring of the complete blood count and platelet count.

Azathioprine, used alone in topical form or taken systemically with topical dexamethasone, has also been reported to help to resolve RAS lesions. Use of prednisone and azathioprine requires careful patient monitoring to identify potential side effects as early as possible as well as to evaluate the effectiveness of the treatment. Consultation with other medical specialists is recommended for patients who are prescribed long term immunosuppressive therapy (Ship JA et al 2000) ²¹².

Tertiary line of treatment:

Thalidomide, an inhibitor of tumor necrosis factor-a, has been shown to be an effective treatment

for severe RAS, despite the potential for significant side effects, use of thalidomide in children has been documented with some success, but long-term effects have not been established. Thalidomide therapy has been thoroughly researched with HIV positive patients. One study reported that HIV infected RASpatients with experienced significant improvement, diminished pain, and an increased ability to eat after a 4 week course of 200 mg of thalidomide daily when compared to placebo. However, the dose was reduced or completely terminated in approximately 20% of patients because of toxicity (eg, rash, somnolence, or peripheral sensory neuropathy), Initial treatment in either HIVpositive or HIV-negative patients should be 100 to 200 mg or thalidomide daily, depending on the severity of lesions and the patient's tolerance. Once remission has been accomplished, therapy may be stopped until ulcers recur. If there is recurrence, the initial regimen should be repeated until remission, and then a maintenance dosage of 50 to 100 mg daily or 50 mg every other day should be attempted. The maintenance dosage should be tapered as much as possible to minimize side effects. Because of the

established teratogenic capacity, of thalidomide strict precautions must be taken in women of child-bearing ages

Levamisole (150 mg daily), an immunotherapeutic drug, may also be an effective treatment for RAS. A recent open label study and several randomized, double-blind studies reported significant reduction in pain, number, and duration of aphthae and frequency of episodes after a course of levamisole. However, at least 3 similar studies did not report any significant differences in symptoms between treatment and placebo groups (Ship JA et al 2000)²¹².

Several other immunomodulating and antiinflammatory drugs, including colchicines,
cyclosporine, pentoxyfylline, azelastine and dapsone
have shown some effectiveness for treatment of RAS in
case studies and open trials. Lysine an amino acid
required for protein synthesis was reported to have
effective prophylactic and healing characteristics
Most of these drugs require further research to

demonstrate safe and effective use in patients with RAS (Ship JA et al 2000) 212 .

Thalidomide

First introduced into the European market in 1957 as a sedative and thalidomide's use was stopped in 1961 after it was linked to a rare congenital birth defect known as phocomelia. Interest in thalidomide was renewed in 1980 after it was used successfully to treat erythema nodosum leprosum. This finding led to the study of thalidomide for various dermatologic disorders and exploration of thalidomide's antiinflammatory and immunomodulatory properties. In a study of healthy male volunteers, thalidomide demonstrated the ability to decrease the ratio of circulating helper T cells to suppressor T cells. Thalidomide has also been found to inhibit the production of various cytokines as a result of its effects onTlymphocytes, monocytes, polymorphonuclear cells. In vitro studies showed that thalidomide selectively inhibits the production of tumor necrosis factor a (TNF-a), a cytokine that plays a central role in regulating immune and inflammatory responses to infection. Patients with erythema

nodosum leprosum have elevated TNF-a levels, which are highest during the lepra reactions. Elevated TNF-a has also been observed both locally and systemically in patients with RAS (Stirling DJ 1998²²¹, Gad SM et al 1985 ⁷³). However, a recent study found that thalidomide actually increased circulating TNF-a levels in HIV-seropositive patients with aphthous ulcers (Jacobson JM 1997) ¹⁰³. Whether it involves a generalized or specific cytokine regulatory pathway, thalidomide's exact mechanism of action in treating RAS remains unknown.

Three double-blind, placebo-controlled trials investigated the use of thalidomide for oral aphthous ulcers in patients with advanced HIV disease, Behcet'ssyndrome, or a history of severe RAS. All the trials excluded patients taking medications that may alter immunocompetency, and one trial excluded Behcet's's syndrome and inflammatory bowel disease as alternative causes of RAS (Revuz J et al 1990) 178. In HIV -seropositive patients, aphthous ulcers were completely or partially resolved in 55% and 34%, respectively; of thalidomide-treated patients (Jacobson JM 1997) 103. Complete and partial

resolution rates for the placebo recipients were 7% and 18%, respectively. The thalidomide-treated patients had diminished pain, an improved ability to eat, and an average weight gain of four pounds in four weeks (compared with no weight gain in the group). In patients with severe RAS. placebo thalidomide treatment resulted in complete resolution of aphthae in 48% of patients (versus 9% of placebo recipients), significant reductions in the number of buccal aphthae, and improved function. A total of 22% of patients with Behcet's syndrome who received thalidomide had complete resolution of oral ulcers, compared with none of the placebo recipients. Thalidomide also reduced the number of minor oral and genital ulcers and the frequency of uveitis episodes that are commonly associated with Behcet's syndrome. Thalidomide was effective at dosages of 100 and 300 mg/day. Complete responses were seen as early as 3.5-6 week safter the start of therapy. The effects of thalidomide are suppressive, not disease modifying. Once thalidomide was discontinued the average duration of remission was 20 days. In the three trials, adverse effects of thalidomide resulted in the discontinuation or interruption of therapy in 6-

26% of patients. The adverse events most frequently associated with thalidomide were neurosensory, gastrointestinal (GI), and cutaneous. Rash occurred in 24% and 32% of patients with Behcet's syndrome and HIV disease, respectively. 40. Constipation was the most common GI event, occurring in up to 65% of thalidomide-treated patients. Neurosensory effects included somnolence (24-87% of patients), headaches (up to 39%), and polyneuropathy (0-6%). In a recent review of thalidomide use for dermatologic conditions, the frequency of peripheral neuropathy ranged from 21% to 50%:13The frequency may vary with the patient population studied, ranging from less than 1% in patients with erythema nodosum leprosum to greater than 70% in patients with prurlgonoduiaris (Revuz J et al 1990 178, Hamuryudan V et al 1998 87, Stirling DJ 1998 221).

Levamisole

An increase in T-helper cells (CD4+ cells) and a decrease in T-suppressor cells (CD8+ cells) may accompany RAS during periods of disease exacerbation and normalize during remission (Sun A et al 1994) ²²³. Levamisole is an immunopotentiating

agent that has demonstrated the ability to normalize the CD4+ celllCD8+ cell ratio and improve symptoms in RAS patients (Sun A et al 1994) 223. Correction of T-suppressor cell deficiency may reduce inflammatory response resulting from cellular immunity and promote resolution of aphthae. Seven placebo-controlled clinical trials assessed the efficacy and safety of levamisole in patients with RAS (De Meyer J et al 1977) 44. More than 68% of the patients in these trials were diagnosed with minor RAS. The remaining studies did not categorize RAS but required at least one RAS episode per month. Use of concurrent drug therapies for RAS was prohibited in three trials. Only two studies excluded drugs or diseases that might compromise immune function. Levamisole was given either at the first sign of ulceration or prophylactically every one to two weeks. The trials lasted from six weeks to more than six months. Four of the studies showed a reduction in the frequency and duration of aphthous ulcers during with ulcer recurrences levamisole treatment. decreasing by half in up to 43% of patients (De Cree J et al 1978⁴³, Lehner T et al 1976 ¹²¹, Zissis NP et al 1983 ²⁶⁵). Efficacy did not differ whether

levamisole was given routinely or started at the first sign of ulcers. In six trials a complete absence of ulcers was found at the conclusion of the study in 16 of 144 patients receiving levamisole(Olson JA et al 1978 ¹⁵⁵, Miller MF et al 1978 ¹⁴⁷, Drinnan N et al 1978 ⁵²). Follow-up of three of these studies showed that 20 levamisole-treated patients were without ulcers for at least 103 days and that 4 patients were ulcer free for six months. In five trials, subjective improvement in a majority of patients taking levamisole was reported.

Levamisole was well tolerated in a majority of the patients. Among 128 patients receiving levamisole, 2 withdrew as result of adverse effects (nausea and flu-like symptoms). The most frequent adverse effects were dysgeusia (21%) and nausea (16%). The other adverse effects occurred in fewer than 10% of the patients and included dysosmia, headaches, diarrhea, influenza-like symptoms, and rash. Some of these events occurred only on the days of treatment and many may not have been attributable to levamisole (Robert W. Barrons 2001) 181.

Summary of Double-Blind, Placebo-Controlled Trials of Levamisole and Thalidomide for Treatment of Aphthous Ulcers*

Reference	No. Patients	Dosage Regimen	Complete Response (%) ^b	Partial Response (%) ^c	Ulcer Duration (Days)	Subjective Improvement ^d
Levamisole						
33	71	150 mg/day × 3 days every 2 wk for 4 mo	Levamisole = 19, PC = 10 $(p < 0.05)$	NA	NA°	Levamisole = 65, PC = 33 (ρ < 0.05)
	20	Above regimen × 2 mo, then 50 mg t.i.d. × 3 days every 2 wk if ulcers present	Levamisole = 10, PC = 0 (p < 0.05)	NA*	NA°	Levamisole > PC (p < 0.001)
35	20	150 mg/day × 3 days every 2 wk	NA	NA	Mean: levamisole = 8.43, PC = 7.40 (p > 0.05)	Levamisole = 90, PC = 30 ^r
37	18	50 mg t.i.d. × 3 days every 2 wk if ulcers present	Levamisole = 30, PC = 0f	NA	Median: levamisole = 4, PC = 8 (p < 0.05)	Levamisole = 66, PC = 11 ¹
34	48	150 mg/day × 3 days every week at first sign of ulcers	NA	NA	Median: levamisole = 7, PC = 6 ¹	Levamisole = 65, PC = 28 (ρ < 0.05)
36	33	150 mg/day × 3 days every week at first sign of ulcers	NA	NA	Mean: levamisole = 8.0, PC = 5.9	Levamisole = 55, PC = 38 (ρ > 0.10)
38	47	150 mg/day × 2 days every week at first sign of ulcers	Levamisole = 13, PC = NA ^e	Levamisole = 51, PC = NA*	NA	NAs
39	33	150 mg/day × 1 or 2 days/wk	NA	NA*	Median: levamisole = 0, PC = 8.5 (p < 0.05)	NA*
Thalidomide					,	
40	57	200 mg h.s. × 4 wk	Thalidomide = 55, PC = 7 (p < 0.05)	Thalidomide = 34, PC = 18 (p < 0.05)	NA	Thalidomide > PC (p < 0.03)
41	96	100 or 300 mg q.d. × 24 wk	Thalidomide 100 mg = 6, thalidomide 300 mg = 16, PC = 0 (p < 0.05 ^h)	NA	NA	NA
42	73	100 mg h.s. × 8 wk	Thalidomide = 48, PC = 9 $(p < 0.05)$	NA	NA	NA

Oxypentifylline in the management of recurrent aphthous ulcers

Oxypentifylline, also known as Trental or pentoxifylline, is an orally active methylxanthine derivative. It is popularly used in the management of peripheral vascular disease and is known to influence regional microcirculation as well as the chemical and cellular mediators of inflammation (Ward A, Clissold SP 1987) ²⁴⁸.

In 1987, oxypentifylline, a potent hemorrhagic drug commonly used in the treatment or intermittent claudication, was exhaustively reviewed by Ward and, Clissold²⁴⁸. In 1994, the established and potential clinical applications of the medication were described by Samlaska and Winfield (Samlaska CP, Winfield EA*1994*) ¹⁹⁴: these applications include the management of vaso-occlusive disorders, infectious diseases, immune deficiency states, hypercoagulable diseases. skin disorders, and some oncologic diseases. The drug is said to have the property of: suppressing leucocyte function while altering fibroblast physiology and stimulating fibrinolysis. Its immunomodulating actions include increasing leukocyte adhesion. It also causes neutrophil degranulation and the release of peroxides, promotes natural killer cell activity and the production of tumor necrosis factor, and inhibits T and B cell activation (Samlaska CP, Winfield EA 1994)194. These properties of oxypentifylline have encouraged clinicians to use it in trials for the management of RAS. 266

Pizarro et al used oxypentifylline for 6 months in 5 patients known to have RAS and reported an absence of ulcers in 4 of the patients. Only 1 patient had gastrointestinal side effects, which were minor (Pizarro A et al 1993) ¹⁶⁶.

Wahba- Yahavll 1995 conducted a 3-month trial in 6 patients with severe RAS. The first month served as a run-in period, during which the patients recorded their ulcers; the second month was the treatment period, during which oxypentifylline was administered at a dose of 400 mg 3 times daily; final assessment was, done at the end of the third month. Three of the 6 patients were followed for 9 months to 2 years. Encouraging results were obtained, all of the patients being ulcer-free at the end of 3 months. One patient followed for 2 years had no recurrence (Wahba- Yahav AV 1995)²⁴⁶.

These results suggest that oxypentifylline could be considered in cases of refractory RAS because it may obviate the need for immune suppressive therapy with potentially toxic drugs (Chandrasekhar. J et al 1999) 30.

Penicillin G in the management of RAS

A number of studies have reported efficacy of topical antibiotics (in terms of a reduction in duration of ulcers and/or pain relief), primarily various tetracycline preparations (Denman AM, Schiff AA 1979) 45, chlorhexidine gluconate preparations (Addy MCR, Roberts WR 1976)2, and Listerine antiseptic mouthrinse (Warner-Lambert Co. Morris Plains, NJ) (Meiller TF 1991) 138. Prevention of secondary bacterial infection of the ulcer site was thought to explain this efficacy, although the non antimicrobial properties of tetracyclines showing efficacy in the treatment of periodontal disease suggest alternative anti-inflammatory mechanisms which have yet to be tested in the treatment of RAS (Golub LM et al 1998) 78. Interestingly there has been reported efficacy of intramuscular injections of benzathine penicillin in the treatment of patients with mucocutaneous signs of Behcet's disease.

Although the exact mechanism of using antibiotic agents in the treatment of RAS remains unclear, it is hypothesized that a concentration of antibiotics high enough to inhibit bacterial flora at

the site of the ulcer may be beneficial in accelerating ulcer healing and pain relief. Unlike tetracycline, penicillin G is a narrow spectrum antibiotic with known bacteriocidal effects against oral bacteria, and has previously been demonstrated to reduce ulcer size and pain compared to placebo in patients with RAS in China (unpublished data) (Ross Kerr A et al 2003) 189

In vitro and in vivo studies (unpublished) demonstrated that a minimum initial application concentration of 10 mg/ml penicillin G resulted in a low valley (trough) concentration greater than the minimum bacterial inhibitory concentration of 2 mg/ml through the end of 1 hour despite the continuous dilution, of the drug by saliva. Given that a 50-mg application of penicillin G is more than adequate to exert an inhibition of bacteria in the area of the ulcer, the results of the study suggest that local bacteria may playa role in the pathogenesis of minor aphthous ulceration, perhaps by modifying the host's immunological response to secondary infection by such bacteria following early ulcer development. An alternative hypothesis is that a local tissue reaction possibly due to the hypertonicity of penicillin G,

causing a chemical "burn," explains the efficacy. This is supported by the fact that more subjects in the penicillin G group experienced symptoms of pain and mucosal changes at the site of application than those in the placebo group.267 However, given that the mucosal changes were mild and occurred in less than half of the subjects, this hypothesis is weak. Interestingly, theanimal invitro (unpublished) demonstrated no such effects following the equivalent application of penicillin G either to intact mucosa or iatrogenic mucosal wounds (Ross Kerr A et al 2003) 189.

Obvious shortcomings to the use of penicillin for the treatment of minor RAS are the risk for allergic reactions and bacterial resistance. Immunoglobulin E-mediated sensitization following repeated use of topical penicillin remains possibility and could lead to an allergic reaction, although parenteral administration of penicillin is more likely to trigger a serious anaphylactic reaction compared to topical application. The increase in methicillin-resistant Staphylococcus aureus and penicillin-resistant Streptococcus pneumoniae

associated with injudicious use of β -lactam antibiotics also questions the use of topical penicillin for the treatment of a RAS²⁶⁸.

Topical penicillin G, by mechanisms which remain unclear, reduces the time of healing and pain relief of minor RAS with minimal safety concerns. Larger phase 3 studies are necessary to confirm these findings (Ross Kerr A et al 2003) ¹⁸⁹.

Adjunctive therapy

Supportive therapy for persistent and painful RAS lesions includes topical analgesics, fluids, and proteins, vitamin, and mineral supplements. For many aphthous lesions individuals. painful impair mastication and deglutition, and therefore patients should be encouraged to maintain fluid and nutritional intake. Dietary supplements such as Ensure (Abbott Laboratories) or Sustacal (Mead Johnson Nutritionals), may be indicated for severe cases. Foods and beverages that exacerbate pain should be avoided: acidic foods; crusty, hard, and difficult to chew foods; spicy or salty foods; citrus fruits and liquids; and alcoholic beverages.

Patients should be encouraged to maintain daily oral hygiene If dentifrices or mouthwashes precipitate or exacerbate RAS lesions, patients should use less irritating agents and those that do not contain sodium lauryl sulfate (eg.Biotene antibacterial dry-mouth toothpaste or Rembrandt whitening toothpaste for canker sore prevention). Topical anesthetics are widely used to treat the painful symptoms of RAS. Oral discomfort may be relieved with topical anesthetics, such as 2% viscous lidocaine hydrochloride, diphenhydramine elixir (Benadryl, Parke-Davis), dyclonine hydrochloride (Dyclone), and sucralfate (Ship JA et al 2000)²¹².

Home remedies in the treatment of aphthous ulcers

Eat plenty of salad with raw onions. Onions contain sulfur and have healing properties. Include in the diet yogurt and other soured products, such as cottage cheese, and buttermilk.

Sodium bicarbonate powder mixed with water is a very effective first aid remedy. This mixture can be used as a mouth rinse as well as swallowed to help make the body more alkaline. Use a toothpaste containing sodium bicarbonate instead of the standard toothpastes high in fluoride and other chemicals.

Cover the ulcer with a wet tea bag; the tannin will help dry up the sore

Apply 1 open capsule of Lactobacillus acidophilus, onto sore twice daily.

Aromatherapy

Apply antiseptic oils of myrrh (Commiphora molmol), tea tree (Metaleuca spp.), and geranium (Pelargonium adoratissimum) on the sores. Also rinse mouth four times a day with 1/2 cup water mixed with 1 drop each of the oils of geranium and lavender (Lavandula officinalis).

Ayurveda

Topical Remedies

1. Honey and Turmeric: Mix together 1 teaspoon honey with 1/4 teaspoon turmeric, and rub it on

- the sore. It will burn a little at first, but the sore area will heal quickly.
- 2. Aloe Vera Juice: Rinse mouth several times a day with a little aloe vera juice.
- 3. Aloe Vera Gel: Apply aloe vera gel, 2 tablespoons at the canker sore. Repeat the application 3 times a day.
- 4. Aloe Vera Gel and Neem: Use a mix of aloe vera gel and neem powder (Indian herb). Mix 1 teaspoon of aloe vera gel with a pinch of neem powder, and apply directly to the canker sore.
- 5. Tea Tree Oil: Add 10 drops of tea tree oil to 1/3 cup of water. Mix it well. Swish the liquid in your mouth. The mild solution will act as an antiseptic to help prevent secondary infection, and it will also help to heal the sore.
- 6. Ayurvedic herb Kama Dudha: Mix 1/4 teaspoon of kama dudha with 1 teaspoon fresh cream.

 Mix together and rub it on the sore.

Herbal Therapy

Several herbs are useful in the treatment of cranker sores. Most of them contain tannins and have other wound healing properties. Tannin, the common name for tannic acid, is a constituent of many plants and gives foods an astringent taste. An antiseptic with broad-spectrum antibacterial and antiviral action, it's especially helpful for treating mouth sores, which could be caused by a bacterium, a fungus, a virus or an allergy.

- 1. Gargle with calendula tea or goldenseal tea to help canker sores heal.

 To make the tea: Pour a cup of boiling water over one to two teaspoons of the dried herb.

 Let this mixture steep for ten minutes. Strain it so that there is no herb left in the liquid. Use this tea as a mouthwash three or four times daily.
- 2. Myrrh: Myrrh contains high amounts of tannins. Powdered myrrh is useful for the treatment of mild inflammations of the mouth. Some herbalists suggest mixing 200-300 mg of herbal extract or 4 ml of myrrh tincture with warm water and swishing it in the mouth two to three times per day. Alternately, you can open a capsule and dab a little directly on the sore.
- 3. **Tea:** Regular beverage tea also has a rich supply of tannins. Or make tea from some of the

- other herbs that are high in tannin, such as bearberry, eucalyptus, St.-John's-wort, sage, raspberry, peppermint and licorice.
- 4. Cankerroot (Coptis groenlandica) or goldthread. This plant got its name because of its traditional use as a treatment for canker sores. American Indians and early settlers alike used cankerroot as a tea to treat both sore throat and canker sores. They chewed raw root for canker sores and fever blisters.
- 5. Goldenseal: This herb was an American Indian favorite for treating all sorts of wounds. Goldenseal contains astringent, antiseptic chemicals that help treat wounds infections. Add teaspoons of dried two goldenseal to a cup of boiling water and steep until cool. Use it as a mouth rinse three or four times a day. Barberry and Oregon grape have similar constituents and healing effects.
- 6. Licorice. Licorice contains tannin, and the compounds glycyrrhetinic-acid and glycyrrhizin. All of these help speed the healing of sores. Licorice that has had the glycyrrhizic acid removed is called deglycyrrhizinated

licorice (DGL). Glycyrrhizic acid is the portion of licorice root that can increase blood pressure and cause water retention in some people. The wound-healing and soothing components of the root remain in DGL.

A mixture of DGL and warm water obtained by combining 200 mg of powdered DGL and 200 ml of warm water may be applied to the inside of the mouth. This is found to shorten the healing time for mouth ulcers. It can then be swished in the mouth for two to three minutes and then spit out. Continue this on each morning and evening for one week.

- 7. Sage: Many herbalists suggest making a strong sage tea to treat inflammations of the mouth and throat. To make this tea, use two teaspoons of dried herb per cup of boiling water. Let it steep until cool and then gargle with it.
- 8. Wild geranium (Geranium maculatum). The Cherokee Indians used wild geranium as an astringent to stop the bleeding of open wounds and as a wash to treat canker sores. It is widely used in folk medicine to treat mouth sores.

- 9. Echinacea: The antiviral, immune-enhancing, and wound-healing properties of echinacea make it a reasonable choice for mouth ulcers. Liquid echinacea in the amount of 4 ml can be swished in the mouth for two to three minutes, then swallowed. This can be repeated three times per day. Tablets and capsules containing echinacea may also be helpful.
- 10. Chamomile: Chamomile has a soothing effect on mucous membranes (including the lining of the mouth). It also has healing properties. A strong tea made from chamomile tincture can be swished in the mouth three to four times per day.
- 11. Aloe Vera: Aloe Vera is used in Ayurvedic medicine to treat cranker sore. An extract from aloe vera has been shown to be beneficial in one preliminary study. Some doctors of natural medicine recommend 1-3 tablespoons of aloe vera juice be used as a mouthwash then swallowed three times daily.
- 12. **Tea tree oil** helps prevent infection and control parasites and candida. Rinse the mouth with 3 drops of tea tree oil diluted in a glass of water.

Twice daily, after brushing the teeth, apply a few drops of oil with a cotton swab directly to infected area.

13. Kamillosan sparay or paste

Nutritional Therapy

If your sores are caused by a vitamin or mineral deficiency, supplements of vitamins C and B complex, as well as folic acid, iron, and zinc, may help.

Several studies have found a high incidence of iron and B vitamin deficiency among people with recurrent mouth ulcers. Supplementing with B vitamins-300 mg vitamin B1, 20 mg vitamin B2, and 150 mg vitamin B6-has been reported to provide some people with relief. Thiamine (B1) deficiency, specifically, has been linked to an increased risk.

Some people with recurrent mouth ulcers have been reported to respond to lactobacillus acidophilus. Chewing four lactobacillus tablets three times per day may reduce soreness in some people with recurrent mouth ulcers.

Take 1,000 milligrams of the amino acid lysine at each meal during an outbreak and then 500 milligrams at each meal for a week afterward.

Rub the liquid from a vitamin E capsule directly on the sore. Apply it three times a day during an outbreak until the sore heals.

Take 4,000 - 5,000 milligrams of vitamin C daily during outbreaks of canker sores and at least 500 milligrams daily as a way of preventing them.

Zinc lozenges help resolves canker sores by supporting the immune system.

Calcium supplements help counteract the over acidity. (Holistic-online.com) ^{269, 270}

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About the Book

Most dantal numerals are recented by a set of physical, chemical and beological tree and a create of these train, of the new being tends to control the quality of the extension. First approach has led to gradual augmontunes in the materials available to the prelimine. Therefore, as improvements in the properties of materials level occurred, references as techniques of tenting have become necessary. This book details the yetteen tenting tentholologies available till date to evaluate the properties of the commonly tending theretoologies available till date to evaluate the properties of the commonly tending tenthologies available till date to evaluate the properties of the commonly tending identical extension.

Testing of Dental Materials





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About Author

Professor D. A. Versialesn, M.D.S., is a recovered scadensician and expert chrician in the field of Conservative dentating and Endodomics for the past 14 years. As an ecodomican, he to serving as a professor in Swee Salisi Dental College and Hospital, Chemisi. As a closidan, he to the director of Jaywei Dental Centre, Chemisi.



He has 80 publications in national and international indexed purhase to his most. He is currently a no lever for many indexed purhase. He has to smooth at being a Asymptic speaker in malconal and international conferences. He has enginited various conferences in national and international level. He has several prestigious Awards to his credit risk has been adocating and serving the society by organising thes dental motion.

He has been elected occasionatively for the accord time as an EC member of Indian Association of Conservative distillant and Excluding (IACDE), in addition he is also deriving as an EC member of CSAT [Conservative demitter) and Endocretical Addition he is also deriving as an EC member of CSAT [Conservative design of a case of the first of the first of the first of the first of the first of the first of the first of the first of the first occurs of the first occupant of the first occupant of the first occupant of the first occupant of the first occupant of the first occupant of the first occupant of the first occupant



Regenerative Endodontics



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Regenerative Endodontics

Regenerative Endodontics-Clinical Procedure and Tooth Discolouration: A Review.

- Source: Indian Journal of Public Health Research & Development . Aug2019, Vol. 10 Issue 8, p1648-1653. 6p.
 Author(s): Karthick, Arumugam; Sangavi, Tamizharasan; Prakash, Venkatachalam; Pearlin Mary, Newbegin Selvakumar Gold
- Abstract: Regenerative endodontics in discoloured tooth involves introduction of stem cells into the disinfected canal space followed by medications and sealing of the dentinal tubules. Discolouration is more an important factor.
- Abstract: Regenerative endodontics in discolorate tooth involves introduction of stem cells into the disinfected canal space followed by endodontic material is one major concern in dentistry. The three main factors that affect discoloration are intracanal medicament, coronal barrier and dentin bonding agent. Recent studies show that sealing dentinal walls of access cavity with dentin bonding agent helps to avoid discoloration of tooth.
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Efficacy and Safety of Oral Premedication on Pain after Nonsurgical Root Canal Treatment—A Review.

- Source: Indian Journal of Public Health Research & Development . Dec 2019, Vol. 10 Issue 12, p2172-2176. 5p.
 Author(s): Sophreniaa, Wesly; Karthick, Arumugam; Geethapriya, Nagarajan; Subbiya, Arunajatesan
- Abstract: Postoperative pain is more likely to arise within a few hours following root canal treatment. Patients who have postoperative pain need analgesics that have fewer side effects for relieving the pain. Postoperative discomfort reduction by various preoperative means is a tried and tested method. Here, we predict symptoms that arise after treatment and try to deal with them before they begin. For those patients presenting with preoperative pain, it has been reported that up to 80% of this population will continue to report pain of different degrees even after endodontic treatment. A number of factors concerning the etiology of postoperative pain have been evaluated. The main contributing factors of pain during root canal treatment comprises of mechanical, chemical, and microbial injuries to the pulp or periradicular tissues which are induced or exacerbated during treatment. Pretreatment analgesia is providing analgesia to patients before initiation of endodontic treatment, which can decrease the establishment of central and peripheral sensitization and has the potential to reduce postoperative pain and postoperative
- analgesic intake. Administration of a nonsteroidal anti-inflammatory drug before root canal therapy will interfere with the inflammatory process before it begins; therefore, presumably decreasing postoperative pain.

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Endodontic Instruments and Canal Preparation Techniques

Laurence Jordan, Francois Bronnec, Pierre Machtou

Book Editor(s):Josette Camilleri

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Summary

Endodontics is both a science and an art. The scientific goal of root canal treatment (RCT) is to prevent or cure apical periodontitis when present. To achieve this objective — whatever the condition of the pulp tissue — the root canal must be shaped, a procedure generally considered the most important phase of the well-accepted endodontic triad: shaping, disinfection, and obturation. The aim of shaping is to create space for irrigant delivery in order to clean and disinfect the root canal system, and then for the placement of filling materials. Shaping is an art, requiring a light touch, attention to detail, and skill. Dedicated endodontic instruments are subject to continuous improvement, whilst the introduction of nickel—titanium (NiTi) alloy and mechanized instrumentation have made the procedure much more straightforward. Numerous good-quality shaping systems are available on the market, and selecting between them involves several criteria, including cost_number of instruments_and the dentist's individual shaping objectives. The goal of

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MORINGA OLEIFERA LAM (DRUMSTICK TREE) WITH ABUNDANT PHARMACOLOGICAL ACTIVITY: AN UPDATE

K.R.Padma

Assistant Professor, Department of Biotechnology, Sri Padmavati Mahila Visva Vidyalayam (Women's) University, Tirupati, AP (Corresponding Author)

ORCID ID: 0000-0002-6783-3248

K.R.Don

²Reader, Department of Oral Pathology and Microbiology, Sree Balaji Dental College and Hospital, Bharath Institute of Higher Education and Research (BIHER) Bharath University, Chennai, Tamil Nadu, India.

ORCID ID: 0000-0003-3110-8076

Abstract

Moringa oleifera Lam (drumstick tree) belonging to the family Moringaceae is a medicinally valued plant as well as nutritional herb. This plant contains various pharmacological actions and has revealed the ability to exhibit anticancer, anti-inflammatory, antipyretic, antimicrobial, antioxidant, antiulcer, hepatoprotective, cardiovascular, gastroprotective, anti-obesity, antiepileptic, anti-allergic, antidiabetic, local anesthetic, wound healing, anthelmintic, immunomodulatory, and antidiarrheal properties. The genus is broadly cultivated throughout South East Asia and Africa for various purposes. The plant has abundant secondary metabolites and often used in African folk medicine against HIV, HBV, EBV and currently, it was acknowledged that the bioactive components present in Moringa include kaempferol, pterygospermin, quercetin, morphine, and apigenin-7-O-rutinoside. Amongst, Apigenin has revealed greater activity against SARS-Cov-2-especially MPro (the main protease of COVID 19). Therefore, our review main objective is to update information on Moringa biological actions, toxicological research, phytochemistry along with exploration of their therapeutic potential. We have conducted search on M.oleifera databases from Web of Science, Scopus, Science Direct, Mendeley and PubMed from 1990-2021. All review articles data was analysed based on the ascending time period and were documented. Our primary aim was to provide researchers, scientist to examine the bioactive compounds as this plant is a nutritional herb and further clinical trials need to be investigated for future research opportunities.

Keywords: Moringa oleifera Lam (drumstick tree), Moringaceae, Corona virus, quercetin, apigenin-7-O-rutinoside

Introduction

Several plants are enriched with secondary metabolites and utilized for therapeutic purposes from ancient days of human civilization. Moreover, from earlier time period till today plant based natural moieties have revealed phenomenal contribution in the field of science for treating various diseases. The M.oleifera from ancient era has remarkable pharmaceutical potential (Vaidya 2007). The genus Moringa oleifera Lam belongs to the family Moringaceae and order Brassicales generally termed as "drumstick tree," is a perennial soft wood plant. The plant is cultivated throughout the tropical and subtropical regions of South Asia with impressive medicinal uses and abundant nutritional value. Amongst various medicinal plant Moringa oleifera is one plant used in folk medicine from ancient time (Flora and Pachauri, 2011). From ancient time of Ayurveda, the plant compounds are utilized for pain relief and robust expulsion of worms (Khan and Balick, 2001). This nutritional soft wood plant's leaves, seeds, pods as

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A MINI REVIEW ON FUNCTIONAL FOODS AND THEIR ROLE IN CHEMOPREVENTION

Assist. Prof. K.R.Padma

Department of Biotechnology, Sri Padmavati Mahila VisvaVidyalayam (Women's) University, Orcid no:0000-0002-6783-3248 Nunna Venkata Mrunalini

Student, Department of Biotechnology, Sri Padmavati Mahila VisvaVidyalayam (Women's) University, K.R.Don

Reader, Department of Oral Pathology and Microbiology, Sree Balaji Dental College and Hospital, Bharath Institute of Higher Education and Research (BIHER) Bharath University, Orcid No: 0000-0003-3110-8076.

Abstract

The whole world is facing the deadly disease termed as 'Cancer'. It is the 2nd prime cause of fatality in the world, after coronary infarction. According to the Global Burden of Disease, about 10 million people die prematurely as a result of cancer every year. Because of increase in death rate, cancer is accounting for one out of every six fatalities. There are many gene alterations for conversion of normal cell to cancerous cell. These unwanted shifts occur for a variety of causes. Environmental exposure to cancer-causing substances, as well as lifestyle decisions and genes acquired from our parents all plays a key role in resulting cancer. Frequently, there is no obvious cause. One of the world's most critical health problems is occurrence of cancer. The majority of patients are diagnosed late in life, with a dismal prognosis. Consequently, identifying modifiable risk factors for primary cancer prevention is critical. However, various health practices in low & middle-income nations are incapable to handle cope with this load, further a huge percentage of cancer patients all-around the globe lack timely approach for exclusive diagnosis as well as therapy. Several kinds of cancer survivability rates are progressing in countries with sturdy health practices, recognition to initial identification, quality treatment, and survivorship care. By altering or avoiding important risk factors and following existing evidence-based preventative methods, between 30 & 50 percent of cancer fatalities could be avoided. Initial recognition of cancer and therapy of patients who acquire cancer also assist to reduce the cancer problem. In the long run, avoidance is also the most cost-effective technique for control of cancer. We summarized and assessed observational studies linking diet, including specific functional food groups, and dietary patterns, which helps in mitigation of emerging cancer in this review. Although there are

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8th INTERNATIONAL ZEUGMA CONFERENCE ON SCIENTIFIC RESEARCH



UKRAINE CRISIS COUPLED WITH COVID-19 PANDEMIC CONSIDERED AS END TO GLOBALIZATION: AN UPDATE ON ASIAN CRISIS

K.R.Padma

Assistant Professor, Department of Biotechnology, Sri Padmavati Mahila Visvavidyalayam (Women's) University,
Tirupati, AP.
Orcid no: 0000-0002-6783-3248

K.R.Don

Reader, Department of Oral Pathology and Microbiology, Sree Balaji Dental College and Hospital, Bharath Institute of Higher Education and Research (BIHER) Bharath University, Chennai, Tamil Nadu, India
Orcid No: 0000-0003-3110-8076.

ABSTRACT

The continuing war between Russia & Ukraine has disclosed global markets into a turmoil. At the beginning of COVID-19 mass transmission led to shut down of schools, colleges, international airports, shipments, export as well as import duties completely shattered Indian economy and just as other countries, Indian banks, central banks are attempting to recuperate from the influence of Covid-19 crisis. The combat has shown adverse impact on India by rising their oil prices. In addition, has shown tremendous drift to 10% increase in oil prices. If war continues it will permanently rise 10% rise of 1.2% in Wholesale Price Index (WPI) and 0.3-0.4% in Consumer Price Index (CPI). The Russia-Ukraine war unreasonably started on 24 February 2022. Several millions of populaces were victims of this war. On increase in new strains of coronavirus such as omicron reached peak during the war. However, war chaos with concomitant psychological factors have removed the COVID-19 problem out of the minds among Ukraine population. Nonetheless, armed tasks along with philanthropical aspects drive people to live in unhygienic conditions without following corona virus reduction strategies. During period of Russia-Ukraine war no top priority given to healthcare system. Thus, our article primary aim to highlight the global issues aroused and change in educational system during Ukraine crisis coupled with COVID-19 pandemic.

Keywords: Wholesale Price Index, Russia-Ukraine war, COVID-19, Consumer Price Index, International airports, Global Markets.

DITECTION





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NEW INSIGHTS ON ALLIUM SATIVUM ANTIVIRAL ACTIONS AGAINST CORONA VIRUS: A SHORT REVIEW

K.R.Padma

Assistant Professor, Department of Biotechnology, Sri Padmavati Mahila Visvavidyalayam (Women's) University, Tirupati, AP. Orcid no: 0000-0002-6783-3248

K.R.Don

Reader, Department of Oral Pathology and Microbiology, Sree Balaji Dental College and Hospital, Bharath Institute of Higher Education and Research (BIHER) Bharath University, Chennai, Tamil Nadu, India. Orcid No: 0000-0003-3110-8076.

B. V. Sai Chandana

Student, Department of Biotechnology, Sri Padmavati Mahila Visvavidyalayam (Women's)

University, Tirupati, AP.

P.Josthna

Associate Professor, Department of Biotechnology, Sri Padmavati Mahila Visvavidyalayam (Women's) University, Tirupati, AP.

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Abstract

Currently, our earth is enthralled with effect of the corona virus disease (COVID-19) pandemic resulting in major health crisis. Although, various kinds of vaccines have been developed but was not found to be long term effective and further in few cases after vaccination also affected with SARS-CoV-2. Moreover, there is no proper medication or effectual drugs to treat or cure the patients affected with corona virus. Nevertheless, several literature reports on medicinal plants revealed few plant sources to possess antiviral actions. Amongst diverse herbal flora, Garlic or Allium sativum was found to be one of the most effectual or capable antibiotics against the wide spread of viruses & bacteria. Nonetheless, sulphur containing phytochemicals in garlic can provide important activities such as immunomodulatory, anti-inflammatory, cardio-protective, anti-cancer. In the active regions, garlic bioactives can prevent the COVID-19 outbreak by the formation of hydrogen bonds. The current review provides insights on the important functions of Allium sativum, its pharmacological actions and how it decreases viral load or viral infections of SARS-CoV-2 in patients affected with COVID-19.

Keywords: Allium sativum, Immunomodulatory, Antiviral actions, SARS-CoV-2, Garlic

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E mail: iksadyayinevi@gmail.com

www.iksadyayinevi.com

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MITIGATION STRATEGIES OF ACRYLAMIDE IN FRIED SNACKS TO PROTECT YOUNG CONSUMERS

K.R.Padma

Assistant Professor, Department of Biotechnology, Sri Padmavati Mahila VisvaVidyalayam (Women's)
University, Tirupati, AP.

Orcid no:0000-0002-6783-3248

K.R.Don

Reader, Department of Oral Pathology and Microbiology, Sree Balaji Dental College and Hospital, Bharath Institute of Higher Education and Research (BIHER) Bharath University, Chennai, Tamil Nadu, India Orcid No: 0000-0003-3110-8076.

P.Josthna

Associate Professor, Department of Biotechnology, Sri Padmavati Mahila VisvaVidyalayam (Women's)
University, Tirupati, AP.

ABSTRACT

Recently, consumers have tended to prefer reduced-fat products due to health concerns, necessitating the need to design reduced-fat items by altering the recipes or the manufacturing procedures. Baking was implemented in the last ten years to produce low-fat potato chips, however, because it requires more processing time, it may result in more acrylamide formation. In this study, new baking procedures to reduce acrylamide in baked reformed potato chips were presented, including vacuum baking and combined conventional and vacuum baking processes.

Biofluid Markers Unveiling Cancer Diagnosis and Prognosis: With Special Reference to Oxidative Stress

Sonaa Elango¹, Karpagam Veerappan² and Usha Subbiah³

- (1)Department of Life Sciences, School of Natural Sciences, University of Suwon, Hwaseong-si, Republic of Korea
- (2) Graduate School of Biotechnology, College of Life Sciences, Kyung Hee University, Yongin, South Korea
- (3)Human Genetics Research Centre, Sree Balaji Dental College and Hospital, Bharath Institute of Higher Education & Research, Chennai, India

Sonaa Elango (Corresponding author)

Karpagam Veerappan

Usha Subbiah

Abstract

Cancer cells have an inherent elevated reactive oxygen species level. Cancer biomarkers include macromolecules such as DNA, RNA, proteins, and certain metabolites; gene; microRNA; immunological, epigenetic biomarkers; and trace elements. This chapter briefly covers up certain biofluids used to analyze cancer biomarkers related to oxidative stress. Oxidative boots can be studied over wide range of biofluids like blood, urine, breath, cerebrospinal fluid, pleural effusions, saliva, tears, and sweat. Biofluids clarify the mechanisms of biological flow and their interrelationships with physiological processes, in health and disease. Biofluid analyses of clinical relevance offer more chances to conduct studies on a large scale as biofluid sample collections are easily accessible, noninvasive, and of easy storage.

Biofluid miRNA profiling, high-precision quantitation using direct mass spectrometry, microfluidic devices, organotypic culture models, cell culture effluent methods employed in biomarker analyses, and the advancements in proteomic/genomic/transcriptomic technologies are highly fruitful. It reflects normal biological functioning, extent of the pathogenic processes, or therapeutic outcomes. Biofluidic diagnostics are scientifically credible. Owing to the biomarker capability in cancer diagnosis and prognosis, necessity for further research is felt.

KeywordsROS -Oxidative stress -Cancer biomarkers -Salivary biomarkers -Biofluids -Cancer diagnostics

Introduction

Oxidative Stress as Biomarkers

Reactive oxygen products get accumulated in all biomatrices, such as blood, urine, saliva, sweat, cerebrospinal fluid, tears, breath, etc. (Hakim et al. 2012). A biomarker is highly beneficial as it can detect a disease at an early stage and can help monitoring the progression of the disease, and it involves noninvasive approaches to acquire patient samples. Biomarkers of oxidative stress have been investigated for their association with the development and progression of several cancers as high level of oxidative and nitrosative stress caused by carcinogens disturbs the antioxidant defense system to a greater extent (Kurutas 2015). Oxidative stress related altered regulation of biological molecules like DNA (microsatellite instabilities), RNA (expression of oncogene, microRNAs), proteins (abnormal cancer specific secretory proteins), lipids, and metabolites were observed in cancer and these can be utilized as cancer biomarkers. Altogether the effect of carcinogens, profound heat generation during smoking, pH changes while chewing (Hoffmann et al. 1994), expression of histocompatibility complex in biofluids all act as biomarkers for tumor immune surveillance and inflammation which turn out to be a promising prognostic cancer biomarkers. Similar wise, ROS-mediated modification of several signaling cascades resulting in initiation of neoplastic transformation can be an effective biomarker (Fig. 1).

Fig. 1
Reactive oxygen species influencing various factors

Biomarkers in Various Human Biospecimens

Biomarkers are being explored for uniformity and accuracy in various biofluids like saliva, sweat, tears, breath, etc. (Figure 2). The diverse techniques include tests for oxidized lipids in blood, hydrocarbons in breath which are volatile, and urinary oxidized DNA bases, employed to analyze various types of cancers. Biofluid miRNA profiling, high-precision mass spectrometry, microfluidic devices, organotypic culture models, cell culture effluent methods employed in biomarker analyses and the advancements in proteomic/genomic/transcriptomic technologies all are collectively very fruitful.

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Fig. 2

Screening and monitoring the response and resistance in various biofluids

Urinary Oxidative Stress Biomarkers

The advantage of stable redox potential of a biomarker present in urine than in the blood makes it more precise in predicting extent of disease. Urinary F2-isoprostanes, the main biomarker of oxidative catalysis of arachidonic acid in vivo (Basu 2007), act as indicator of oxidative stress in lung and prostate cancers. Other biomarkers, such as 4-HNE and n-tetradecanoic acid, are linked with oral squamous cell carcinoma and colorectal patients (Barbosa et al. 2019).

Urinary malondialdehyde (MDA) has been accounted as a significant biomarker of oxidative status which is found to be unstable and nonspecific. Urinary 8-OHdG, a prominent form seen in urine and also in human organs and leukocyte DNA, has been (Valavanidis et al. 2009) used as a biomarker for the development of lung cancer. 8-oxodG and thymidine glycol validated as biomarkers in the biofluids of oral, colorectal, and breast cancer patients were of various concentrations (Al-Mahmood et al. 2018).

Urinary allantoin, evaluated as an oxidative stress biomarker, has profound storage stability at various conditions. Gastric tumor patients eliminate *p*-hydroxybenzoic acid and *p*-cresol in traces which have been developed as novel markers for gastric tumor. Additionally, there are few understudied oxidative markers of protein damage such as acrolein-lysine and dityrosine (Novaković et al. 2013).

Oxidative Stress-Related Salivary Biomarkers

Saliva contains oxidation biomarkers akin to those in blood, which are sensitive neoplastic biomarkers aiding detection at early stage and prognosis of neoplastic changes (Arantes et al. 2018). Since saliva and oral cancer lesions are directly contacting each other, measuring the tumor markers in saliva becomes a potential alternative to serum. Eight oxidative stress biomarkers in saliva include carbonyls, 8-oxoguanine DNA glycosylase, mammary serine protease inhibitor, Ki67, phospho-Src, cyclin D1, metalloproteinase-9, and lactate dehydrogenase (Podzimek et al. 2016) are also associated with DNA repair, carcinogenesis, metastasis, and cellular proliferation. Isoprostane, homologues from arachidonic acid (iso-prostaglandin), docosahexaenoic acid product (neuroprostanes), hydroxyoctadecadienoic acid from linoleic acid, and oxysterols (from cholesterol) are potential lipid peroxidation biomarkers under oxidative stress. Elevated level of dodecanoic acid were found in saliva of OSCC colorectal and melanoma patients (Niki 2008).

DNA Biomarkers

8-oxo-7,8-dihydro-2'-deoxyguanosine (8-oxodG) is one of the biomarkers formed by the addition of hydroxyl group to guanine, the most susceptible among purine and pyrimidine bases. Along with the salivary pattern of 8-oxodG, the total antioxidant capacity and malondialdehyde approximate the degree of DNA oxidation through a measurable index (Roszkowski et al. 2011). Also, studies reported the diurnal variation of 8-oxodG at the time of awakening, relatively stable in the daytime, representing the individual oxidative stress status.

RNA Biomarkers: Salivary MicroRNA

MicroRNAs (miRNAs), associated with cell growth, apoptosis, differentiation, motility, and immunity, are validated for diagnosis of multiple cancers because of the resistance rendered by exosomal miRNAs to RNase-mediated degradation. Oral carcinoma can be diagnosed through analyzing the increased level of six salivary mRNA's namely, DUSP1, H3F3A, IL 1B, IL 8, SAT, and S100. Especially, DUSP mRNA which is associated with protein modification, oxidative stress, and signal transduction does also involve with MAPK pathway. The hypermethylation of DUSP1 gene (Koga et al. 2011) and H3F3A nuclear proteins act as significant markers in oral cancer subjects where these are involved with the structural integrity of chromosomal nucleosome.

Protein Biomarkers

Protein biomolecules are often targeted at varying stresses and could be used as effective biomarkers for evaluation of the normal and diseased conditions. One among the protein biomarkers is heat shock proteins (HSPs), which are molecular chaperons offering protection to cells from denatured proteins getting misfolded during heat-induced stress (Mori et al. 2017).

Several protein cancer biomarkers are present in saliva include: tumor cells proliferation – squamous cell carcinoma antigen, Ki-67 antigen and, inflammation – interleukin-6 (IL-6), extracellular matrix collagen degradation – tissue inhibitor of metalloproteinases 2, matrix metallo-proteinase-9 (MMP-9), oxidative stress – total antioxidant capacity and uric acid. Both uric acid and total antioxidant capacity showed low levels in the saliva of oral cancer patients while IL-6, Ki- 67, SCCA, and MMP-9 showed enhanced levels. Salivary TIMP-2 levels were also found to decline. The level of IL-6 in saliva reflects that of blood (Casares et al. 2019).

Lysozyme

Lysozyme is a prominent antibacterial peptide which hydrolyzes bacterial cell walls and (peptidoglycan) is found in the external secretory fluids of humans (Allgrove et al. <u>2008</u>). It is also related to circulating RNA, extracellular vesicles, and chronic stress. Recently, lysozyme has found usage in cancer metastasis as diagnostic biomarker (Brzozowski et al. <u>2018</u>).

Alpha Amylase

A potent salivary biomarker α -amylase concentration increases drastically during stress conditions, hence a diagnostic in oral disease (Lorenzo-Pouso et al. <u>2018</u>).

Isoprostanes

F2-isoprostanes (F2-IsoPs), produced by the polyunsaturated fatty acids in membrane phospholipids and ROS, are the prostaglandin-like isomers, chemically stable. This becomes another promising marker, and being the most stable, its concentration denotes the oxidative burden over vital organs, such as kidney or liver (Musiek et al. 2005).

Secretory IgA

IgA, involved in gut health, microbiota regulation, and immunity, has a diagnostic role in gastrointestinal diseases (Celi et al. <u>2019</u>). Thus, higher salivary IgA is associated with certain potentially pathogenic bacteria and improved immunity in the oral cavity (Lamb et al. <u>2017</u>).

Oxidative Stress Biomarkers in Blood

Plasma MDA levels have been a good tumor marker for malignancies as the elevated levels of MDA in carcinoma could be used as an important parameter in patients mainly due to its dual role as a mutagen and a tumor promoter (Bitla et al. 2011).

Blood MicroRNAs

Gastric malignancy risk and severity are analyzed by circulating pro-angiogenic miRNAs, such as miR-17-5p, miR-18a, miR-19b-1, miR-20a, miR-210, miR-296, and let-7f (Peng et al. <u>2018</u>). Similarly, different exosomal miRNAs in serum like miR-638 are employed for diagnosis and prognosis of hepatocellular carcinoma (Xue et al. <u>2019</u>). Abnormally expressed miRNAs in the blood helps to diagnose the status of hepatocellular carcinoma and brain tumor (Shen et al. <u>2016</u>).

Heat Shock Proteins

Heat shock proteins (HSP) are stress-related proteins involved in apoptosis, oxidative stress, inflammatory diseases, and cancer. HSP role is crucial in mitochondrial mediated apoptotic pathway. HSP 27 interacts with Bax (apoptotic regulator protein), cytochrome c, and caspase, influencing mitochondrial apoptotic pathways (Calderwood et al. <u>2006</u>). Enhanced levels of HSP90 and HSP70, and glucose-related protein 78 (GRP78), in medullary thyroid carcinoma will be a putative biomarker here after (Soudry et al. <u>2017</u>).

Enzymatic Antioxidants

Oxidative stress-mediated free radicals get eliminated by antioxidant enzymes such as superoxide dismutase (SOD), catalase, and glutathione peroxidase (GPx). The serum GPx is employed in diagnostics of various cancers (Gheita and Kenawy 2014). While decline in the activities of catalase and SOD is attributed to high amount of superoxide anion or reduction in enzymatic scavenging activity in oral cancer (Sonaa et al. 2018). Another important selenium-containing antioxidant enzyme system is thioredoxin reductase that plays a crucial role in eliminating ROS, preventing thioredoxin oxidant action (Trigona et al. 2006).

Nonenzymatic Antioxidants

Structural modifications due to oxidative damage will interfere with the function of proteins tremendously and thus hamper cellular processes that depend on these proteins' function. The nonenzymatic antioxidants (vitamin C and E, carotenes, flavonoids, GSH, and uric acid) protects protein from such damages were declined in many malignancies.

Cerebrospinal Fluid Biomarkers Related to Oxidative Stress

Another important biofluid is cerebrospinal fluid (CSF) which provides information over the pathological state of central nervous system malignancies. Comparatively the brain is highly vulnerable to stress from oxidants. Consequently, a genomic instability (mutation or DNA strand breaks) is created which contributes to carcinogenesis. In brain tumor genesis, oxidative radicals initiated transduction pathways which involve the transcription factors like NF-kappa B, Nrf2, or HIF-1 were analyzed (Papacocea et al. *2011*).

Vast studies on cerebrospinal fluid biomarkers related to oxidative stress and inflammation have been carried out. Galasko and Montine (2010) findings support that oxidative stress is a mechanism of neurologic injury related to CNS-directed treatment for all. The significant increase in F2-isoprostanes gives collective proof for aerobic stress as a mechanism related to endovenous and thecal therapy. Increase in aerobic stress was measured as macromolecule peroxidation in humor throughout treatment for childhood acute lymphocytic leukemia. CSF-derived exosomes are a promising supply of biomarkers with capability to mirror the genetic diversity of neoplasm. Meta-analysis of various studies over the mi RNAs, such as miR-9, miR-15a, miR-16, miR-21, miR-23a, and miR-124, were very accurate to contemplate as potential biomarker for gliomas (Santangelo et al. 2017).

Oxidative Stress Levels in Pleural Effusion

The physiological role of DJ-1, a multifunctional supermolecule, seems to be variably utilized in cancer pathophysiology. It modulates cellular functions as a response to enhanced intracellular aerobic stress burden. Malignant serous membrane effusion (MPF) levels of DJ-1 are inflated in older carcinoma patients (George Vavougios et al. <u>2015</u>) and gonad carcinomas. DJ-1 overexpressing in non-small carcinoma tissue correlates with the cisplatin resistance in cancer cells.

The correlations of DJ-1 with SOD and 8-isoprostane in PF levels that are identified as inhibitor enzymes give insight into the oxidoreduction surroundings of malignant PEs. Oxidative stress levels are higher in exudative serous membrane effusions compared to transdative effusions in all probability thanks to reactive O species created within the former. The native generation of free radicals and also the role of aerobic stress within the pathological process of MPF are verified through their levels of MDA, SOD, total proteins, and bottle-feed dehydrogenase, conjointly to use them as potential markers for MPF. Concentration of reactive O species modulator, a unique supermolecule overexpressed in numerous human tumors, were considerably higher in patients with malignant serous membrane effusion (Chen et al. 2017). Whereas the usage of CEA and CYFRA 21-1 assay together within the malignant effusion is predicted with the possibility of increased diagnostic yield in comparison to CEA and CYFRA used individually (Lai et al. 1999). MMP-9 and MMP-3, CycD1, Ki-67, carbonyls, and p27 were particularly lower in serous membrane effusion of carcinoma patients, acting as economical biological markers. Though carcinoma is that the most predominant reason behind MPE (Neragi-Miandoab 2006), the majority kinds of cancers like ovary, stomach, Hodgkin's and non-Hodgkin's lymphoma can be caused by MPE too (Sahn 1998). In the case of MPE formation, during the primary or pathological process, the tumors could spread to the pleura poignant the traditional resorptive flow of fluid from the membrane, bone to the pleura (DeCamp 1997).

Oxidative Stress Markers in Exhaled Breath Condensate

The methodology of collecting exhaled breath condensate (EBC) has currently acquired importance as it is a noninvasive method of sampling and further a real-time analysis and evaluation of cancer with much accuracy. EBC is the cooling of exhaled gas to gain insight into the composition of extracellular lining fluid and soluble exhaled gases (Lim and Thomas 2013). Sampling breath is very cheap, easy to collect, and repeatable without causing inflammation in the airway. Condensate formed from water too has droplets carrying solute from the lower respiratory tract, which allows transportation of nonvolatile compounds, though in a small amount, such as proteins that are volatile aerosol particles. It does not induce any discomfort in patient and can be used in sensitive humans like children, elders, and mechanically assisted patients. EBC may be implicated in the carcinogenesis process especially greater insight into the pathogenesis of lung cancer. On the other hand, smell fingerprint enables longitudinal studies aiming to monitor environmental influence. Higher oxygen concentrations in the lungs when compared with other organs render it more vulnerable to enhanced oxidative stress (Hiang Chan et al. 2009).

Cancer patients showing significantly elevated levels of hydrogen peroxide and lower levels of antioxidant capacity and pH indicate the pathogenesis of lung cancer and disequilibrium between levels of oxidants and antioxidants. Employing EBC to measure antioxidant capacity in the lung could be helpful in tracking the biomarkers of oxidative stress in the air passage of lower respiratory tract. Thus the oxidative stress biomarkers including F2-isoprostanes, 44-hydroxy-2-nonenal, antioxidants, glutathione, LPO, MDA, nitrogen oxide products, hydrogen peroxide, cytokines, proteins, and DNA were validated successfully (Rahman and Biswas 2004). Cancer-associated inflammation marker like endothelin-1 was found to be elevated in the EBC of cancer cases. The levels of angiogenic markers such as VEGF, bFGF, and angiogenin in the EBC of lung cancer patients vary remarkably. Significant correlation between IL-6 levels and various stages of disease, higher levels of IL-2, leptin, and tumor necrosis factor alpha in the EBC of lung cancer cases were

observed (Gessner et al. <u>2010</u>). Eventually all of the aforementioned reports collectively confirm the usage of EBC sample to testify oxidative stress markers in relation to cancer.

Expression of Oxidative Stress Biomarkers in Tears

The protective secretion of lachrymal gland of eye is tears which are composed of various macromolecules like lipids, proteins, peptides, and certain metabolites and electrolytes. In comparison to blood, tears have less complexity owing to the blood – tear barrier. Thus utility of tear screening for different types of cancer becomes reasonable. Most reports relating cancer and tear biomarkers are from breast and prostate cancer research. Expression of hexanoyl-lysine, an oxidative stress biomarker, is used to countermeasure LPO and 8-OHdG for measuring DNA oxidation (Haworth and Chandler 2017).

Lacryglobin identified in tears is a protein having high sequence homology to the protein mammaglobin and is found to be upregulated in breast and prostate cancers, suggesting lacryglobin a potential marker for these cancer types. Typically, lipocalin-1, expressed mainly in secretory glands such as lachrymal and lingual gland, encodes tear protein lipocalin also called as von Ebner's gland protein. It is said to be the main lipid-binding protein in tears. While another protein lipocalin-2 was promoting breast cancer progression and reported to be highly associated with ER-negative breast tumors. Considerable focus has been levied upon the high-level expression of lipocalin, since it is found to be an independent prognosticator of a poor prognosis in breast cancer condition (Depowski et al. 2001). To add with, advantages of tears as a biomarker source extend on to tear-based wearable devices for medical purpose and health management.

Expression of Oxidative Stress Biomarkers in Sweat

Though there are records stating that sweat lacks protein biomarkers, yet there are observations that eccrine sweat contains diverse proteins and peptides existing in abundance. On close observation, it was noted that most of sweat proteins were different from serum proteins, indicating eccrine sweat not merely a plasma transudate and may be a source of unique disease-associated biomolecules, therefore a valid factor in cancer diagnosis and prognosis (Raiszadeh et al. 2012). Multifunctional and theranostic strategies involving tears and sweat would further broaden their clinical use in the future if in-depth studies were done on these biomatrices.

Trace Elements Dyshomeostasis in Cancer Biofluids

Disruption of trace element homeostasis lead to oxidative stress (Jomova and Valko <u>2011</u>). Cancer onset and progression involve disruption of metals observed as biomarkers in various biofluids like blood, urine, pleural effusion, or tears. The abnormal levels of metals were evidenced in the cancer condition (Table <u>1</u>). Paradoxically, metal containing two major antioxidant enzymes, SOD and catalase, curb the toxic effects of metal-induced oxidative stress. This is evidenced in the serum, whole blood, erythrocytes of radiation treated oral cancer patients where the radiation-mediated elevation in oxidative stress is observed in addition to cancer (Sonaa et al. <u>2018</u>). Alteration in the

serum biomarkers considered important (V/Mn, V/Pb, V/Zn, Cr/Pb), urine (Cr/Cd, Mn/Cd, V/Cd, Co/Cd, Cd/Pb), and BALF (V/Cu) mirrors the metal dyshomeostasis in lung cancer (Callejón-Leblic et al. 2018).**Table 1**

Biomarkers of metals in biofluids of cancer patients

Sample	Elements
Urine:	Al, Cd, Co, Cr, Cu, Fe, Mn, Mo, Ni, Pb, Se, V, Zn
Plasma:	As, B, Cr, Cu, Fe, Mn, Ni, Pb, Sb, Se, Sr, Ti, V, Zn
Serum:	Ca, Cd, Co, Cr, Cu, Fe, Mg, Mn, Mo, P, Pb, Se, Sr, V, Zn
Saliva:	Zn, Fe Mn, Co, Ni, Cu, Fe, Mg
Pleural Effusion:	Cu, Zn, Fe

Studies on Zn metallobiomolecules in childhood brain tumors have been emphasized much. Depletion of Zn impair DNA repair mechanisms; impact on the immune system. Redox-inert zinc (Zn) is crucial for the effective function of various defense-related proteins in the brain against oxidative stress (Jomova and Valko <u>2011</u>). Other important elements include arsenic and cadmium, stress-induced intoxication of which cause metabolic alterations of redox-active copper and iron, resulting in enhanced formation of ROS/RNS (Valko et al. <u>2016</u>).

Therapeutic Outcomes

Because of shorter lifetime, direct detection of ROS is difficult clinically, so there is need for reliable method to quantify oxidative stress. Developing stress detection technologies in is not just crucial for tumor characterization and continuous monitoring of the disease, but also as a basis for creating novel therapies for cancer management. Biofluids can offer to be a better diagnostic, prognostic, and therapeutic biomarkers. Measurement of clinical significance of biomarkers of oxidative stress in various body fluids has certain limitations, yet, considering its potential advantages for the diagnosis of various disease types, further studies are warranted. In addition to conventional biomarkers and sampling procedures of blood, urine, saliva, and other body fluids, the advancements in proteomic/genomic/transcriptomic technologies employed were highly fruitful.

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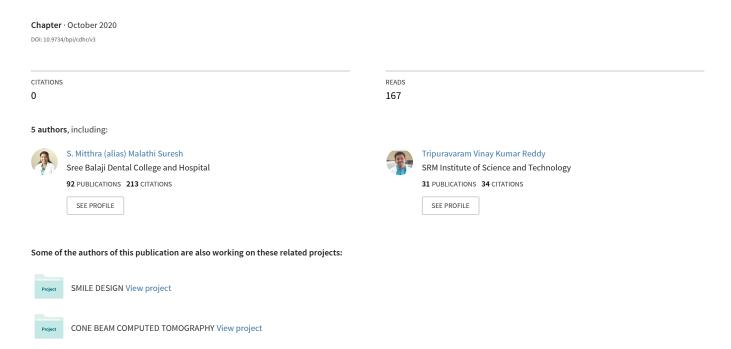
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Emphasizing the Applications of Cone Beam Computed Tomography in Endodontics



Emphasizing the Applications of Cone Beam Computed Tomography in Endodontics

Suresh Mitthra^{1*}, Sekar Sangeetha¹, Ragupathy Shakila¹ and Tripuravaram Vinay Kumar Reddy²

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ABSTRACT

Cone Beam Computed Tomography (CBCT) designed for imaging of the dento facial region is a true shift from 2D to 3D imaging. The word tomography is derived from two Greek words tomos (slices) and graphien (write). CBCT was developed as an alternative to conventional CT to provide rapid acquisition of data of the entire FOV and there is comparatively less radiation exposure. It produces high resolution 3D images in thin, thick or curved slices in axial, saggital and coronal planes. CBCT is a valuable tool for endodontic diagnosis and treatment planning as well as for assessing apical periodontitis, resorption, root fractures, root canal anatomy, perforations and the nature of the alveolar bone around the teeth.

Keywords: Cone beam computed tomography; endodontic diagnosis; endodontic applications.

1. INTRODUCTION

Cone Beam Computed Tomography (CBCT) is a new digital imaging technology to dentistry that produces three dimensional images of the maxillofacial region in thin, thick or curved slices in axial, sagittal and coronal planes. The word tomography is derived from two Greek words tomos (slices) and graphien (write). In CBCT imaging, a divergent pyramidal or cone shaped sources of ionizing radiation is directed through the area of interest to acquire individual image slices of the Field of View(FOV) and then the slices are stacked to obtain a 3D representation[1]

CBCT was developed as an alternative to conventional CT to provide rapid acquisition of data of the entire FOV and there is comparatively less radiation exposure. Intraoral and extraoral radiographs are 2D images captured on plain films and digital sensors. CBCT is superior as it produces 3D imaging of the maxillofacial structures.[1]

2. HISTORICAL BACKGROUND

- 1875 discovery of x-rays emanating from Crookes tubes by Johann Hittorf.
- 1887 Nikola Tesla- Bremsstrahlung emission.
- 1895 Wilhelm Roentgen- discovery of x-rays.
- 1896 Edmond Kells-1st diagnostic dental x-ray.
- 1904 John Ambrose Fleming invented the thermo-ionic diode valve (vacuum tube)
- 1920 replacement of the cold cathode x-ray tubes by Coolidge tubes.
- 1928 Major John Hall-Edwards-use of x-rays for medical purposes.
- 1972 Sir Godfrey Hounsefield CT scanner.
- 1974 SIRETOM first CT system developed by a medical equipment manufacturer.

¹Department of Conservative Dentistry and Endodontics, Sree Balaji Dental College and Hospital, Bharath Institute of Higher Education and Research, Narayanapuram, Pallikaranai, Chennai - 600 100, Tamil Nadu, India.

²Department of Conservative Dentistry and Endodontics, SRM Kattankulathur Dental College & Hospital, SRM University of Science and Technology, Potheri, SRM nagar, Kattankulathur, Tamilnadu – 603 203, India.

^{*}Corresponding author: E-mail: malu.dr2008@yahoo.com;

- 1979 G.N.Hounsefield and A.M.Cormack were awarded the noble prize in medicine.
- 1987 SOMATOM plus- continuous rotation of the tube and detector, selection of five slices thickness (1 to 10mm).
- 1989 first spiral CT scanner in routine operation, continuous volume measurement with high resolution 2mm- SOMATOM AR. Solid state imaging using indirect exposure of CCD became commercially available in Europe.
- 1992 Integrated CT- angiography.
- 1994 SOMATOM plus 4 (0.75 sec scan time for 360⁰ rotation).
- 1998 & 1999 SOMATOM volume zoom with Syngo software(fastest rotation time 0.5 sec), AAMOR- 19th principle developed by Feb 2009.
- 2000 SOMATOM smile (dose modulation and reduced radiation).
- 2002 SOMATOM sensation 16 (multi-slice scanning with 16 slices/ rotation. Resolution upto 0.6mm. (16 X 0.75 mm sub-millimetre slices).[2]

3. RADIOLOGICAL ASPECTS OF CBCT

Cone beam computed tomography is a modified concept of the computed tomography (CT) involving the single rotation of an x-ray source around the dental subject. To create a volume of data, the data are analysed and reconstructed using a CT- based algorithm, which can be viewed in three conventional planes(axial, sagittal and coronal) and multiple alternative planes on manipulation of the data set. A three dimensional visualization of the region of interest is obtained with sufficient detail to localize the teeth and adjacent anatomy, which is not achievable with conventional, 2D, plain dental film imaging.[3]

3.1 Parts of the CBCT Machine

- 1. The scanning unit gantry with tube and detector system.
- 2. The patient chair or table.
- 3. The image processor for image reconstruction.[4]

3.2 Principles of CBCT

The basic principle is tomography (movement of the x-ray source and detector during the exposure). Unlike the conventional CT which have fan shaped beam of x-ray, while CBCT projects a cone shaped x-ray beam. The x ray source and the detector are fixed to a rotating gantry. Patient positioning varies during imaging, it can be standing, sitting or supine. CBCT units can be divided into two types – one type of unit has charged coupled device (CCD) and the other utilizes flat panel imager (FPD). Basically, the x-ray sources and the scanner detector make a full rotation (360°) or half rotation (180°) around the patient head. The rotation occurs within 30secs to 1min. While doing so, hundreds of planar images of the field of view is captured. This data is then analysed by sophisticated software to display images in various planes. Hard copies of the images can be obtained. These images can be transferred to a portable memory devices and also be mailed to clinicians for purposes of diagnosis and treatment plan.[5]

4. EFFECTIVE RADIATION DOSE

The major advantage of CBCT is a low effective radiation dose. The operator should stand at least 8m away from the machine. The effective dose of CBCT may vary, but it almost as low as than the conventional panoramic dental x-ray.[6] The dose depends upon the regions to be scanned, the exposure settings of CBCT scanner, size of the FOV, the exposure time(S), the tube current(mA) and the energy or potential (KV).[7] The radiation dose can be reduced using a smaller FOV, fewer projections (180 degree) and a bigger voxel size. For endodontic applications, the FOV should be limited to region of interest; which is the most effective way to reduce the radiation dose. The radiation dose of a small volume CBCT is comparable to that of 2 to 7 standard periapical radiographs, whereas the radiation dose of a large volume scanner is similar to that of a full mouth series of periapical radiographs.[6]

The effective dose for -

- 1. Full FOV CBCT 29 to 477 μ Sv.
- 2. Spiral CT 474 to 1160 μSv.
- 3. Panoramic radiographs –3 to 24 µSv.[8]

5. ACCURACY OF CBCT

Smaller the field of view more accurate is the image resolution. CBCT is more accurate than radiography in imaging anatomic as well as pathologic dento-maxillofacial structures. CBCT can be accurate in detecting vertical root fracture, apical periodontitis, resorptive defects. When compared to radiography, CBCT provides a better view of root and pulp canal anatomy. For example, buccolingual curvature in a root is most often missed by radiographs, but it can be easily detected in CBCT image. Most radiographs provide little or no information about the presence of additional canals, their shape and curvature, whereas CBCT imaging reveals the same findings with high accuracy. [5] The accuracy level of the nominal voxel resolution varies from 0.076 mm to 0.125 mm.

6. APPLICATIONS

6.1 Apical Periodontitis (AP)

Periapical lesion is defined as periapical radiolucency connected to the root at the apical part that exceeds at least twice the width of the periodontal ligament space. Bender and Shelter; Schwarz and Roster showed that in periapical radiographs we underestimate the size of the periapical lesion.

CBCT detects the radiolucent endodontic lesions before the lingual or buccal plate is demineralised. It eliminates the superimposition of anatomical structures and is useful in identifying pathological changes occurring within the cancellous bone. Both in vitro and in vivo studies have shown that periapical lesions are more effectively detected in CBCT than periapical radiographs.[6]This is especially useful in multirooted teeth, to differentiate between the affected roots and unaffected roots. In non endodontically treated teeth, the diagnostic accuracy of CBCT is high in detection of AP when compared to endodontically treated teeth.

6.2 Assessment of Root Canal Anatomy and Morphology

Conventional radiographs frequently failed to detect the number of canals in teeth undergoing nonsurgical endodontic treatment. Failure to identify and treat accessory canals can negatively influence the treatment outcome using an ex vivo human model was demonstrated by Matherne at al 2008. Hence the superiority of CBCT over conventional radiography in detecting the presence of supplemental canals was confirmed. Conventional radiographs failed to identify at least one root canal in 4 out of 10 of the examined teeth.[9]

The detection of presence or absence of supplemental canals and root prior to the treatment will lead to higher detection rate in the former and more conservative access cavity preparations in the latter.

If the canal morphology is undetermined, it increases the possibility of preoperative mishaps such as ledge formation, canal transportation or even perforation, potentially compromising the outcome of the treatment. CBCT is a reliable tool to accurately assess the degree of curvatures associated with the roots of teeth with normal anatomical forms.

CBCT, in addition is useful in assessment of anatomical and morphological anomalies, such as dens invaginatus and fused teeth that require endodontic treatment. [10]

6.3 Surgical Endodontics

CBCT is an extremely useful tool in planning of surgical endodontic treatment. The spatial relationship of the specific roots undergoing the surgical procedure can be related to the adjacent anatomical structures such as maxillary sinuses, the inferior alveolar nerve canal and the mental foramen. With this information, clinicians can assess the appropriate size of the lesion in individual cases for treatment planning. Identifying and excluding unsuitable cases for surgical treatment can reduce the

morbidity rate.[10] Surgical endodontics without 3D- CBCT – there is an increased risk of iatrogenic damage.

6.4 Dental Trauma

The exact extent of the injuries to the teeth and the alveolar bone can be accurately assessed by eliminating anatomical noise and image compression, thereby the treatment can be confidently implemented. The degree and direction of displacement associated with luxation injuries is evaluated easily by CBCT.

Failure to identity the presence of root fracture can result in poor prognosis. Periapical radiographs have low sensitivity for detection of minimal tooth displacements, root and alveolar fractures. Small volume CBCT scanners, is used for the assessment of endodontic problems, that capture all teeth and surrounding anatomy in 4cm X 4cm slices.

Patient comfort is enhanced during the imaging process, with the use of CBCT extra orally. This is particularly pertinent in the assessment of dental trauma were the patient has difficulty in accommodating bulky film holders and image receptors for conventional imaging is exacerbated by potentially mobile teeth and painful intraoral tissues [11]. CBCT enables accurate diagnosis of the extent and location of crown or root fractures, concussion, subluxation, luxation injuries and injuries to the supporting bone. It is especially useful when multiple teeth are affected.

6.5 Root Resorption

The true extent of inflammatory and external cervical root resorption (ECR) in the early stages, cannot be determined by conventional radiographs. CBCT is a useful diagnostic tool for early detection of the bucco-palatal extent of the lesion and management of root resorption.

Kamburoglu et al., assessed the ability of the examiner to identify and differentiate between simulated internal root resorption (IRR) and simulated ECR of the root canal at the cervical region, using CBCT, conventional and periapical radiographs. It was concluded that CBCT was statistically better than the periapical radiographs in the detection of simulated resorption cavities [12]. The true nature of ECR (fibrovascular and bone-like tissue) is more clearly discernible with CBCT.

6.6 Vertical Root Fracture

Identifying the vertical root fractures (VRF) is an endodontic challenge. A deep, isolated, thin periodontal pocket is suggestive of VRF, whereas difficulty in aligning the periodontal probe across the periodontal defects sometimes means this sign is missed.

Radiographically VRF appears as a J shaped or halo shaped radiolucency, which does not appear until significant bone destruction has occurred.

The 2D nature of periapical radiographs obscures the visibility of the fracture line due to superimposition artefact. 3D nature of CBCT visualizes the fracture line from multiple angulations and different orientations in thin slices at high contrast. The reported sensitivity and specificity of CBCT in detected VRF is 0.92 and 0.85, respectively [13]. In cases where signs and symptoms of VRF are absent, CBCT reveals signs of peri-radicular bone loss indicating the presence of VRF in the adjacent root.

6.7 Endodontic Retreatment

Friedman considered that post – treatment endodontic disease (treatment failure) is commonly associated with root canal intra-radicular infection than the extra-radicular infection [14]. In such cases endodontic treatment is the best option, if there is persistent extra-radicular infection-apical surgery is considered.

CBCT demonstrates the location of inaccessible, unfilled, calcified canals and invagination areas of complex canal morphology.

7. INTRA-OPERATIVE CONSIDERATIONS

CBCT is a useful diagnostic tool for:

- 1. Implant placement
- 2. Impacted third molar removal
- 3. Accessing the palatal root of maxillary molars using a vestibular or trans-antral approach root end surgery.

8. ADVANTAGES

- > CBCT units reconstruct the projection data to provide inter-relation images in three orthogonal planes (axial, sagittal and coronal).
- The presence of collimation of the primary x-ray beam in CBCT reduces the radiation dose at the area of interest.[15]
- It determines the extent of non-endodontic lesion and its effect on surrounding structures.
- It is useful for diagnosis of the periapical pathosis in patients who are having no specific clinical signs and symptoms, poorly localised symptoms associated with an untreated or previously endodontically treated tooth with no evidence of pathosis identified by conventional imaging [15]
- > It is accurate, non invasive, reliable to detect osseous lesion size and volume.
- > Beam limitation focussed on the FOV increased information content.
- > Cone beam computed tomography voxels are isotropic, the images produced are geometrically accurate and image measurements in any planes, are free from distortion. [10]

9. LIMITATIONS

- > CBCT is expensive when compared to conventional radiographs.
- CBCT is not suitable for soft tissue assessment.
- Scanner related artifacts.
- Endodontic sealers also produce artifacts that mimic fracture line [5].
- > Images quality is affected by scatter and beam hardening, that are caused by metal posts and restorations.
- ➤ The scan time of CBCT devices (1- 20 min) which is significantly longer compared to intraoral radiographs. Therefore, during the scan, the slight change in the movement of the patient may render the resulting reconstructed images of minimal diagnostic use. So, this poses a problem with children, elder patients and patients with neurological disturbances for example Parkinson disease. [16]
- ➤ Image noise: Due to large volume being irradiated during CBCT scanning results in heavy interaction with the tissues producing scattered radiation, which in turn leads to non-linear attenuation by the detectors. This x-ray detection is called noise, contributes to image degradation. [17]
- X-ray photon intensities may vary with the density of the tissues, anatomical number and thickness. There is a scattering of x-ray beam and that contribute to poor tissue contrast. [18]

10. CONCLUSION

CBCT is a three-dimensional imaging technique which overcomes the limitations of conventional radiography and is a beneficial adjunct to the endodontic armamentarium. CBCT is a key tool for the diagnosis and management of endodontic disease. It helps in improved decision making thus improves the outcome of endodontic treatment.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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Biography of author(s)



Dr. Suresh Mitthra, M.D.S

Department of Conservative Dentistry and Endodontics, Sree Balaji Dental College and Hospital, Bharath Institute of Higher Education and Research, Narayanapuram, Pallikaranai, Chennai-600 100, Tamil nadu, India.

She is a Reader, Department of Conservative Dentistry and Endodontics, Sree Balaji Dental college and Hospital, completed her B.D.S (2001-2006) from Meenakshi Ammal Dental college & Hospital, Chennai under the Tamilnadu Dr. M.G.R Medical

University and her M.D.S (2008-2011) from SRM Dental college & Hospital, Ramapuram, Chennai. She has over 50 publications to her credit in various indexed international and national journals with 14 years of clinical experience in Dentistry and 9 years of teaching experience in the speciality of Conservative Dentistry and Endodontics.



Dr. Sekar Sangeetha

Department of Conservative Dentistry and Endodontics, Sree Balaji Dental College and Hospital, Bharath Institute of Higher Education and Research, Narayanapuram, Pallikaranai, Chennai-600 100, Tamil nadu, India.

She completed her B.D.S in Sree Balaji Dental College and Hospital, Chennai in November 2019 and is currently into clinical practice.



Dr. Ragupathy Shakila, B.D.S

Department of Conservative Dentistry and Endodontics, Sree Balaji Dental College and Hospital, Bharath Institute of Higher Education and Research, Narayanapuram, Pallikaranai, Chennai-600 100, Tamil nadu, India.

She completed her Under-graduation from Sree Balaji Dental College and Hospital, Chennai in 2019. Currently she is pursuing her clinical practice.



Dr. Tripuravaram Vinay Kumar Reddy, M.D.S

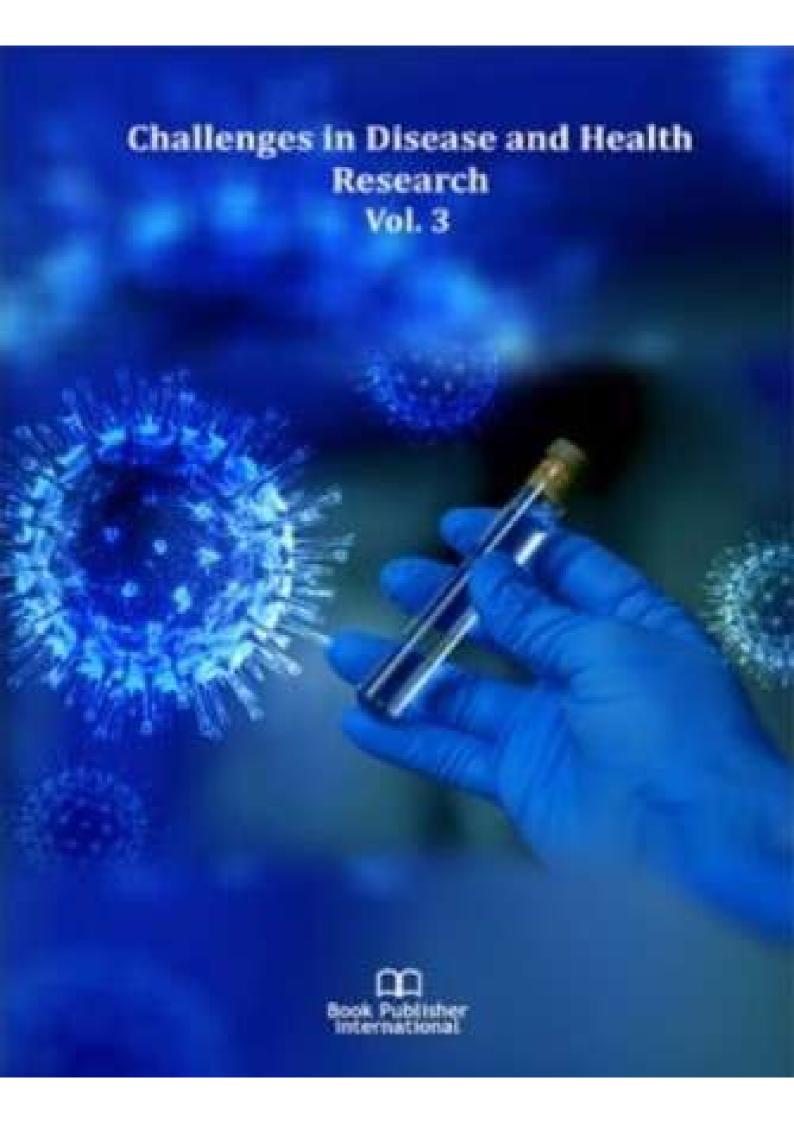
Department of Conservative Dentistry and Endodontics, SRM Kattankulathur Dental college & Hospital, SRM University of science and technology, Potheri, SRM nagar, Kattankulathur, Tamilnadu – 603 203, India.

He is currently working as an Associate Professor in SRM Kattangalathur Dental college & Hospital, completed his undergraduation in 2007 and post graduation in the speciality of Conservative Dentistry & Endodontics from Sree Balaji Dental college & Hospital in 2010. He has more than 10 years of teaching & clinical experience in dentistry and has over 15 publications to his credit.

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Correction of Skeletal Class II Malocclusion – An Accelerated Osteogenic Orthodontic Approach

A. Arif Yezdani

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Abstract

Selective alveolar decortication and periodontal augmentation with a bone graft were the two procedures used for the correction of the skeletal Class II malocclusion in the case reported. A 25-year-old male patient presented with a skeletal Class II malocclusion with increased bi-maxillary dentoalveolar protrusion, increased overjet, deep bite and imbricated & rotated mandibular incisors with bilateral presence of supernumerary teeth in the maxillary right and left premolar region. Extraction of the supernumerary tooth in the maxillary right and left premolar region as also the impacted UL5 was done. Pre-adjusted edgewise appliance, Roth's prescription (0.022 x 0.028-inch slot) was strapped up and a week later full thickness labial and lingual flaps were reflected in the maxillary and mandibular arches. Circumscribed corticotomy cuts were done and subsequently augmented with a bone graft. Orthodontic treatment was commenced immediately after surgery and orthodontic adjustments were carried out every 2 weeks. The entire orthodontic treatment was completed in 9 months. The primary objective was to evaluate whether selective alveolar decortication could accelerate orthodontic tooth movement and reduce the duration of orthodontic treatment. It was observed that regional acceleratory phenomenon, triggered by alveolar decortication was responsible for the rapid correction of the malocclusion and augmentation with the bone graft further provided adequate bone volume for housing the teeth. This combined procedure might probably contribute to the decrease in the possibility of the tell-tale relapse.

Issues and Developments in Medicine and Medical Research Vol. 5



New Horizons in Medicine and Medical Research Vol. 12



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This book covers key areas of Medicine and Medical Research. The contributions by the authors include Contraception, intrauterine device, Human sexuality, buss's evolutionary psychology theory, Radiotherapy, chemoradiotherapy, oral cavity toxicity, inflammation, tooth loss, Nutritional care, cancer treatment, dietary factors, urology practice, Cystatin C, contrast-induced nephropathy, coronary angiography, percutaneous coronary intervention, chikungunya, skin manifestations, febrile illness, bicornuate uterus, pregnancy, uterine malformation, Autologous Conditioned Serum, Platelet-Rich Plasma, Osteoarthrosis Knee, Intra-Articular Injections, Metabolic syndrome, combined oral contraceptives, Type 2 diabetes, hyperinsulinemia, Saxagliptin, Bilateral maxillary posterior crossbite, mandibular functional retrusion, banded rapid palatal expansion appliance, Roth's pre-adjusted edgewise appliance therapy, Liver engineering, decellularization, recellularization, liver regeneration, implantation, Sound resonance, and mother-fetus attunement. This book contains various materials suitable for students, researchers and academicians in the field of Medicine and Medical Research.

Current Practice in Medical Science Vol. 8



Sella Turcica Bridging - An Orthodontic Perspective

A. Arif Yezdani

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Abstract

Background: Sella turcica bridge is a developmental anomaly formed as a result of calcification of the interclinoid ligaments. Its detection at an early age could foretell impending palatal canine impactions, tooth transpositions and other dental anomalies as also other craniofacial deviations, syndromes and underlying endocrinological disorders. The objective of the study was therefore to use published data to highlight the importance of sella turcica bridging and its correlation with dental anomalies and skeletal malocclusions.

Methods: Pertinent articles pertaining to anatomy, morphology, topography, radiology & prevalence of sella turcica bridging and its association with dental anomalies, skeletal malocclusions and congenital syndromes were extensively searched in bibliographic databases and perused, with the salient points conclusively delineated and highlighted.

Results: A correlation of sella turcica bridging and its occurrence with dental anomalies especially impending palatal canine impactions and concomitant occurrence with skeletal malocclusions and craniofacial deviations was found to be reported widely in literature. Though lateral cephalograms were accurate in diagnosing partial bridging and no bridging, CBCT was more accurate in diagnosing partial and complete bridging. Though visualized in a 2-D lateral cephalogram, greater clarity and visibility of the same is best achieved with imaging with the 3-D cone-beam computed tomography.

Conclusion: Detection of sella turcica bridging at an early age could foretell impending palatal canine impactions, tooth transpositions, maxillary lateral incisor, second premolar and third molar agenesis and occurrence of various other dental anomalies, thereby serving as an invaluable screening tool for the practising orthodontists as also aid the neurosurgeons who perform complex surgical procedures in this critical area characterized with rich vascular and neuronal elements.

Keywords: Sella turcica bridge; dental anomalies; skeletal malocclusions; syndromes

Association of Epstein - Barr virus with Oral Squamous Cell Carcinoma and Oral Potentially Malignant Disorders

S. Leena Sankari; K. Mahalakshmi; G. M. Kailash Kumar; K. M. K. Masthan; V. Naveen Kumar

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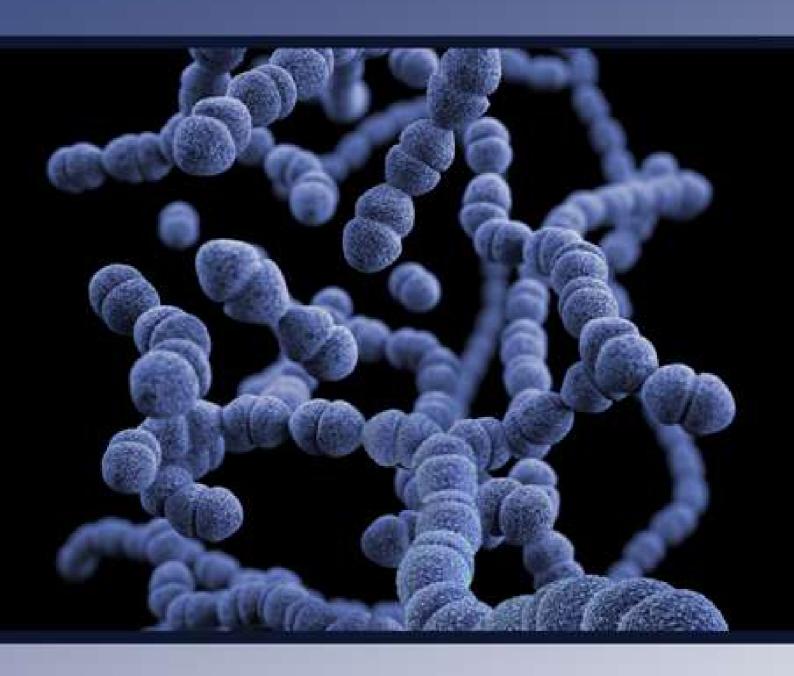
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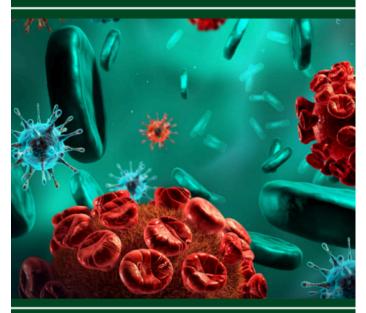
Oral Squamous Cell Carcinoma (OSCC) has varied etiology. Genetic predisposition or the presence of oncogenic viruses are two etiological variables that might disrupt the physiological processes that limit cellular proliferation. The study was aimed to determine the association of Epstein- Barr virus (EBV) with oral squamous cell carcinoma and oral potentially malignant disorders (OPMD). The objective of the study was to quantify the EBV in oral exfoliated cells of OSCC and OPMD patients. Oral exfoliated cells were collected from the subjects diagnosed with OSCC (n=19), OPMD (n=23) and healthy subjects without any deleterious condition (n=39). The DNA extraction was performed with DNeasy Blood & Tissue Kits (Qiagen, Germany). Quantitative Real-Time PCR was then carried out with QuantiNova® SYBR® Green PCR Kit (Qiagen, Germany). Compared to healthy subjects, very high EBV load was observed in the oral exfoliated cells of OSCC and OPMD patients. The presence of EBV DNA in all three groups of individuals indicates that EBV is an oral resident. Aside from its presence, the high prevalence of EBV DNA in OSCC and OPMD shows a link between the two diseases. The elevated odds and risk ratio for EBV copy number point to a substantial link between this virus and OSCC and OPMD. This could be the first study to measure EBV DNA in OSCC and OPMD oral exfoliated epithelial cells.

Emerging Trends in Disease and Health Research Vol. 8



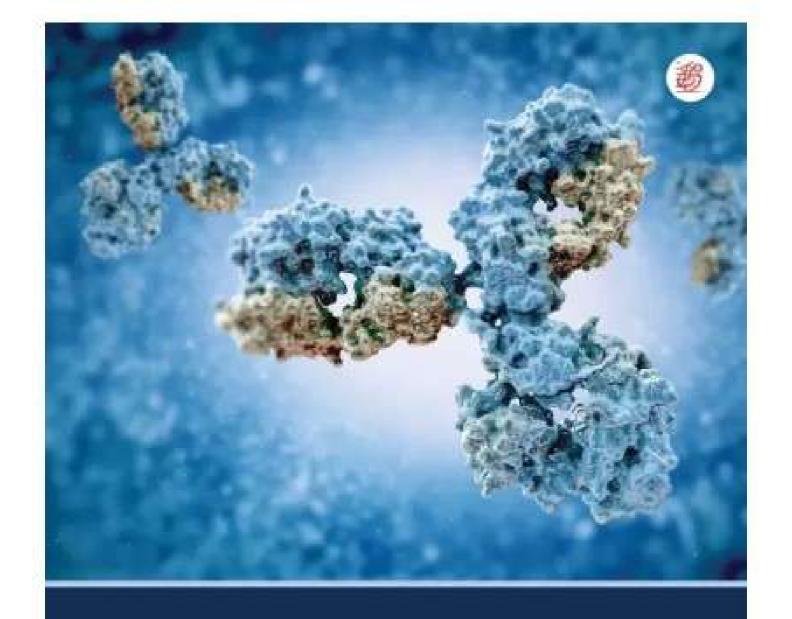


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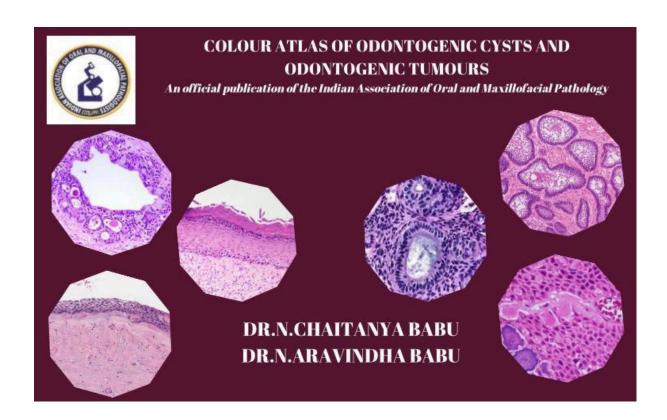
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Parasitic infestations of the Human Oral Cavity – Intruders unveiled

Dr. K. Padmavathy¹, Dr. A. Kiruthiga²* and Ms. A. Iswarya³

¹Professor, Department of Microbiology, Research Laboratory for Oral and Systemic Health, Sree Balaji Dental College and Hospital, BIHER, Chennai, India

^{2*}Associate Professor, Department of Microbiology,

Madha Dental College and Hospital (Affiliated to the T.N. Dr. M.G.R. Medical University), Kundrathur, Chennai.

³Lecturer, Department of Microbiology, Madha Dental College and Hospital, (Affiliated to the T.N. Dr. M.G.R. Medical University), Kundrathur, Chennai.

Abstract

Infestations caused by parasites constitute different members of unicellular protozoans, unicellular eukaryotic organisms and multicellular helminths. Severe forms of parasitic infections occur in the gastrointestinal, cutaneous and various parts of the body with ingestion as the common route of transmission. The oral cavity serves as an abode for the colonization of various types of emerging parasites leading to the development of lesions.

Keywords: Parasitic infestation, Ingestion, Oral cavity, Lesions

Introduction

Parasitic infections in the oral cavity

The human oral cavity serves as the portal of entry for numerous parasites. Very few parasites thrive in occupying the oral cavity as their habitat. Parasitic members of the oral cavity include harmless commensals turning into opportunistic pathogens such as *Trichomonas tenax* [1] and *Entamoeba gingivalis* [2], while the serious pathogenic forms include *Naegleria fowleri* and *Acanthamoeba encephalitis* [3] causing meningoencephalitis following their way to the brain after entering through the oral cavity. These parasites may reach the nasal cavity and olfactory nerve finally resulting in the invasion of the brain [3-5].

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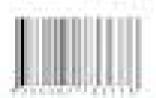
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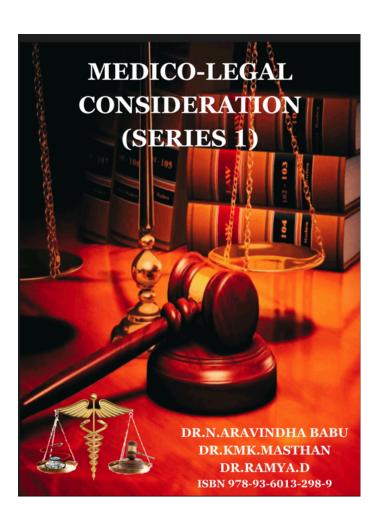


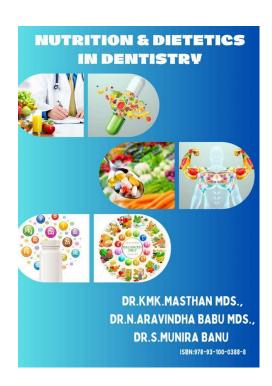
HALITOSIS REMEDIAL MEASURES



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Dr. Masthan KMK MD5, is a professor in Department of Oral Pathology & Microbiology as well as Director of Centre for Oral Cancer Prevention, Awareness and Research (COCPAR) at Sree Balaji, Dental College and Hospital, Chennal, BHER, Taminadu. He has an extensive 28 years experience in teaching Oral Histology, Oral Pathology and Oral Microbiology for undergraduate and postgraduate

Oral Microbiology for undergraduate and postgraduate students. He is also the editor-in-chief of Indian Journal of Multidisciplinar, Destinate (MD). He has present as 40 hooks to his credit.



Dr. N. Aravindha Babu MDS, is the Professor and Head of Department of Oral Pathology & Microbiology as well as Assistant Director of Centre for Oral Cancer Prevention, Awareness and Research (COCPAR) at See Bailly Dental College and Hospital, Chennai, BiHER, Tamilnadu, He has IB years experience of teaching in teaching Oral Histology, Oral

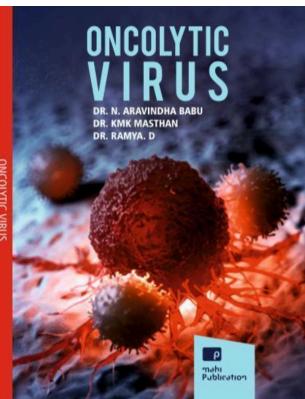
postgraduate students. He is the Vice President of Indian Association of Oral & Maxillofacial Pathology (IAOMP) and co-editor of Journal of Oral & Maxillofacia pashology (JOMPF). He has more than 40 books and a number of national an international publications to his credit.





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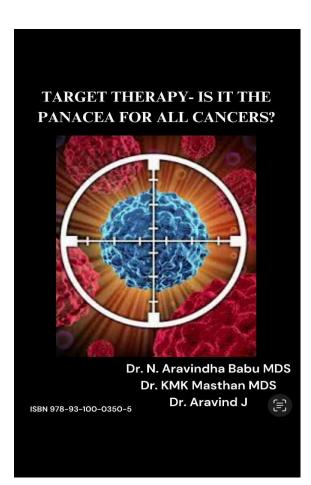


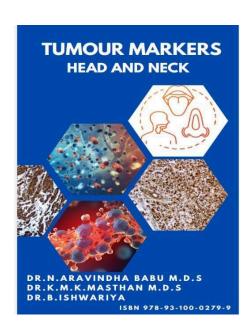


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