



IMSA

INTERNATIONAL MEDICAL SCIENCES ACADEMY

Oct. - Dec. 2006
VOL. 19 NO. 4

BOARD OF TRUSTEES

President

Dr. K. Jagadeesan

Vice-President

Dr. R.R. Thukral

Members

Dr. (Miss) S. Padmavati

Dr. Ramdas M. Pai

Dr. Sandip Mukherjee

Dr. K.B. Sharma

Dr. P.V. Chalapathi Rao

Dr. N.K. Ganguly

Dr. Harvinder S. Luthra (U.S.A.)

Central Executive Committee (CEC)

Dr. P.K. Dave

Chairman, India Region

Dr. H.K. Chopra

Secretary General

Dr. Tarun Gupta

Addl. Secretary General

Dr. R.C.Sharma

Treasurer

Dr. P.D. Gulati

Editor - JIMSA

International Advisors

Sir Roy Caine

England

Allistair D. Beattie

Glasgow

H. Klinkmann

Germany

Susan Lim

Singapore

Secretarial Correspondence :

INTERNATIONAL MEDICAL SCIENCES ACADEMY

National Medical Library Building

Ansari Nagar, Ring Road,

New Delhi - 110 029

E-Mail : imsahq@ndf.vsnl.net.in

Website : www.imasonline.com

www.jimsaonline.com

PRESIDENT WRITES

Dear Fellows and Members,

The current issue of JIMSA is devoted to a very important health hazard, especially pertaining to the fetus as well as new born. Poisoning through placental transmission or by way of contamination in water and food as adulterants, insecticide, residues etc. is a widespread problem in the developing world. Contaminants carry major unnoticed, undetected health risks. Through the pertinent articles in JIMSA, academy wish to draw the attention of the health authorities as well as the administrators who should wake up and act, so that posterity can be safer from many major health problems hitherto seen or yet to be seen. Every fellow and member should strive hard with their research activities to find out the source of such contaminants and suggest ways and means to prevent such silent killers.

Our IMSACON-2006 on 3rd to 5th of November at Lahore, has been a very successful and a memorable event. Prof. Shaheena made all out efforts to organise an excellent meeting at Lahore.

Wishing all fellows, members and readers of JIMSA a very happy year 2007.



Dr. K. Jagadeesan,
President, IMSA

Free
Access

IMSA/ JIMSA WEBSITE

Free
Access

www.imsaonline.com
www.jimsaonline.com

All fellows and members of IMSA can have access to the site and get information about its objectives, benefits to the fellows/members, chapters and their activities including seminars, refresher courses, rural CME;s etc. and also IMSACON - a regular annual event of international standard; *application form for enrollment as fellow/member can also be downloaded. Fellows - members and even not fellows - members can have access to full text in the quarterly journal - jimsa from July - Sept. 2003 onwards by putting their E-mail address under 'user name' and using the password 'UserJimsa'.*

Presenting

The proven therapy to delay progression of
Chronic Kidney Disease

Ketosteril[®]

Protects and Preserves Renal Function

- Provides nitrogen sparing effect
- Reduces hyperfiltration of nephrons
- Improves metabolic complications



Recommended for all patients with:

- Proteinuria, even micralbuminuria
- Creatinine clearance < 50 ml/min

Delays the onset of dialysis and Prolongs life expectancy

Dose: 1 tab/5kg bw/day



 **Fresenius
Kabi**
Caring for Life

For further detailed information please contact

Fresenius Kabi India Pvt. Ltd.

Heritage House, 6-E, Ramabai Ambedkar Road, Pune - 411001, India

Ph. : 91-20-26053602-7 Fax : 91-20-26138258

www.fresenius-kabi-india.com



JIMSA

JOURNAL INTERNATIONAL MEDICAL SCIENCES ACADEMY

Oct. - Dec. 2006
VOL. 19 NO. 4

EDITORIAL BOARD

Editor	
P.D.Gulati	(Delhi)
Joint Editor	
S.N.A. Rizvi	(Delhi)
Asstt. Editor	
Pradeep Chatree	(Delhi)

MEMBERS

K.Jagadeesan	(Chennai)
Sandip Mukherjee	(Delhi)
D.D.S. Kulpati	(Delhi)
K.B. Logani	(Delhi)
Indira Bahl	(Delhi)
Prema Bali	(Delhi)
Veera Hingorani	(Delhi)
S.K. Bhargava	(Delhi)
I.P.S.Kalra	(Delhi)
P.N. Renjen	(Delhi)
H.K.Chopra	(Delhi)
Tarun Gupta	(Delhi)
Chintamani	(Delhi)
Sudershan K. Aggarwal	(Delhi)

ADVISORY BOARD - National

K.B. Sharma	(Delhi)
O.P. Gupta	(Ahmedabad)
B. Ramamurthy	(Chennai)
Habibullah Zargar	(J & K)
M. Natarajan	(Chennai)
P.M. Dalal	(Mumbai)
G.S. Sainani	(Mumbai)
S.A. Tabish	(J & K)
M. Sachdev	(Delhi)
V.H. Talib	(Delhi)
Sukumar Mukerjee	(Kolkata)
R.R. Thukral	(Delhi)
R.K. Bali	(Delhi)
S.S. Sethi	(Delhi)
Rattan Singh	(Delhi)
Sham Agarwal	(Delhi)
P.S. Gupta	(Delhi)
P.K. Dave	(Delhi)
V.K. Dada	(Delhi)
K.K. Malhotra	(Delhi)
H.P.S. Sachdev	(Delhi)
Kamlesh Kohli	(Delhi)
T.K. Biswas	(Kolkata)
R.R. Kasliwal	(Delhi)
S.P. Aggarwal	(Delhi)
Naresh Trehan	(Delhi)
S.D. Jeyaraj	(Chennai)
N.S. Neki	(Amritsar)
Richa Diwan	(Delhi)
M.Suresh Kumar	(Chennai)

ADVISORY BOARD - INTERNATIONAL

Swaraj Singh	(USA)
Leela Prasad	(USA)
J.Heinrich Joist	(USA)
Sir Roy Calne	(U.K.)
Alistair D. Beattie	(USA)
H. Klinkmann	(Germany)
Susan Lim	(Singapore)
J.D. Williams	(U.K.)
Harvinder S.Luthra	(USA)

Annual Subscription Rates for non fellow & member	
Inland	Rs. 500
Overseas	\$ 200
Single copy	Rs. 150

FROM EDITOR'S DESK

JIMSA will soon be entering the third decade of its existence. Besides the regular issues with improved scientific content, special issues and symposia on topics of current interest, have been published regularly. These issues have generated good response and earned wide appreciation. Requests have been pouring in from several teaching institutions for contributions to the special issues and symposia. JIMSA Best Article Award, instituted in 2004, has not only encouraged the contributors but has also raised the image of the journal.

In the present issue, a well written editorial by Prof. A.P.Dubey has brilliantly discussed the pattern and hazards of poisoning in children; this editorial review supplements the information given in the original work carried out on a large population of children, from Ludhiana (Punjab) India. A series of interesting original articles, case reports on some of the **practical topics** covering different disciplines of medicine are also published in this issue. An update on Non Cirrhotic Portal Fibrosis – a term first coined by Prof. A.K.Basu from Kolkata in the year 1967, elaborately highlights the epidemiology, clinical spectrum and management of complications of this common topical disorder. In another communication on Benign Prostatic Hyperplasia, the authors have focused on the increasingly popular medical treatment of this surgical condition. Also included in this issue is a **Symposium on An integrated approach in the management of peripheral vascular disease**, with **Dr. Ashok Gupta** as guest editor. The topics covered are really practical and provide an overview of what is evidence – based in vascular diseases; I am indeed grateful to Dr. Ashok Gupta and other contributors of this symposium. I am confident with wide variety of topics covered in this issue, this publication will make an interesting and informative reading for all.

I take this opportunity to thank all the members of editorial and advisory board and other peer reviewers of JIMSA, for their help in compilation of this publication. I would also like to extend my appreciation to all the advertisers of this issue.

Wishing all the readers of JIMSA Very Happy and Prosperous New Year 2007.

P. D. Gulati

JIMSA BEST PUBLISHED ARTICLE AWARDS

Journal of International Medical Sciences Academy has instituted award for **three (3)** best original articles published during the previous 3 years; **guidelines** are as below:

- (1) **Original articles** belonging to any discipline of medicine published in JIMSA during the previous three years.
- (2) Age Limit for the principal author/main researcher should be 45 years and below.
- (3) Number of awards: Three (3) annually, carrying a gold plated medal, citation and cash prize (1st Rs. 3000/-, 2nd Rs. 2000/-, 3rd Rs. 1000/-)
- (4) Awardee should preferably be a fellow/member of IMSA; non-fellows/ non members can also be considered for the award if the original work is outstanding; and if selected for the award will be required to apply for fellowship membership of IMSA.
- (5) Awardees should preferably plan to receive the award at the annual IMSA conference - IMSACON: in case he is unable to attend the conference, the award may be sent through courier, if desired.

Copy Right No part of this publication may be reproduced, or transmitted in any form or by any means, electronic or mechanical, including photocopy without written permission from the Editor. The Editor disclaims any responsibility or Liability for statements made and opinions expressed by authors.

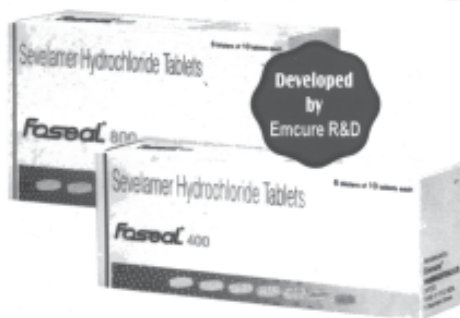
IMSA is now on website and our address is www.jimsaonline.com / www.imsaonline.com

JIMSA is indexed by *Experta Medica, Indian Science Abstracts/Chetna, Bibliographical Data base*

The first indigenous Sevelamer brand in India

Sevelamer™
Foseal
Seals Phosphorus Without Accumulation

- Recommended by NKF K/DOQI as The 1st Line Treatment Option for Hyperphosphatemia⁴
- Available in 25 Countries with a Clinical Experience of More than 7 years
- Significantly Reduces Serum Phosphorus & Ca x P Product to Target Levels^{3,5}
- Long-term Use Is Safe, Effective & Well Tolerated²
- Non-absorbed, Calcium & Metal-free⁶
- Lowers the Risk of Mortality⁷
- Reduces Risk of Hospitalization in CKD Patients⁵
- Halts Progression of Vascular Calcification¹
- Lowers LDL & Increases HDL Levels^{2,6}
- Effective Over a Wide pH Range⁸



1. Klemmer PJ. Blood Purif. 2005; 23 Suppl 1:12-9
2. Cherlow GM, et al. Kidney Int. 2002;62:245-262
3. Cherlow GM. J Am Soc Nephrol. 2003;14: S310-S314
4. NKF. Clinical Practice Guidelines for bone metabolism and disease in CKD. Am J Kidney Dis. 2003;42(Suppl3):S1-S201
5. Maurizio Galleni, et al. J Nephrol. 2001;14:176-183
6. Blayer AG, et al. Am J Kidney Dis. 1999;33:694-701
7. Collins AJ. Clin Nephrol 2000;54:334-341
8. Rosenbaum DP. Nephrology Dial Transplant. 1997;12:961-964
9. Cherlow GM, et al. Am J Nephrol. 2003;23:307-314



partners in health, healing & hope

POISONINGS IN CHILDREN

A.P. Dubey, K. Rajeshwari

Department of Pediatrics, Maulana Azad Medical College, New Delhi 110002, India

Abstract: Accidental poisoning is a world wide problem in children in the age group -5 years. Most pediatric poisoning is accidental and less than 1% is clinically serious. Majority of accidental poisoning is due to ingestion of non-toxic substances and only reassurance is needed. Only minority of poisoning in children are clinically serious requiring prompt attention. An effort has been made here to present an overview of pediatric poisoning including various management modalities. The best way to avoid accidental poisoning is education of parents and to prevent easy access of children to the toxic substances.

INTRODUCTION

Accidental poisoning in children is a global problem. The relative importance of poisoning as a cause of childhood morbidity and mortality increases when malnutrition and infections are brought under control. Most pediatric poisoning is accidental in nature and occurs between the ages of 1-5 years. Less than 1% of pediatric poisoning is clinically serious and death is rare. However some drugs including methadone, TCAs, iron, theophylline, antihistamines, methyl salicylate, phenothiazines, quinine, chloroquine and calcium channel blockers can cause severe toxicity after very small ingestions.

POISONINGS IN INDIAN CHILDREN

Accidental poisoning is the twelfth leading cause of admissions in pediatric wards in India and accounts for about one percent of the hospitalized patients. Most cases of accidental poisoning are preventable. The exact incidence of poisoning in Indian children is not known. In a study of 250 cases over a period of 2 years admitted to Dr. R.N. Cooper hospital, Mumbai for various poisonings, over all incidence of poisoning was 11.9% among hospital admissions. Of these 58.4% were seen in the age group of 1- 4 years. Male to female ratio was 1:7:1. Incidence of food poisoning was 48.8%, followed by that of kerosene (24%), pesticides (9.6%), chemicals and medicaments (8.4%), plants (3.6%) and animal bites (3.2%). Overall mortality was 0.8%. In another prospective study of 120 Indian children who were brought to hospital with history of acute poisoning, accidental poisoning was seen in 116 cases (96.7%). Most 78 (65%) children were in the age range 1 -4 years. Medical aid was sought earliest in case of children with animal bites and in infants. Kerosene and medications accounted for 72 (60%) of poisonings. None of the care takers of children received any instruction regarding prevention of accidents and poisonings prior to the episode inspite of multiple contacts with healthcare providers. In another perspective study from Punjab, published in this issue, poisonings constituted 0.6% of total pediatric admissions. Accidental poisoning occurred at home in 94% of cases. Kerosene oil followed by organophosphorus compounds were the commonest causes of poisoning. The National Poisoning Information Centre (NPIC) was set up in the Department of Pharmacology in 1995 at All India Institute of Medical Sciences (AIIMS), New Delhi. The center functions round the clock, 365 days in a year and provides information on various poisoning and treatment protocols on telephone, fax, e-mail and in person. The NPIC has the back -up of latest literature on poisoning due to a variety of products

Correspondence : Professor A.P. Dubey

E-mail : apdubey52@rediffmail.com

that include household items, agricultural and industrial chemicals, drugs, environmental toxins including plants, animals bites, stings and other miscellaneous products.

ECOLOGY OF POISONING

Interaction between the host and the environment (including easy access to the poisoning become very active and try to explore unfamiliar objects by putting these into their mouth and tasting these.

Large families and small accommodation: In large families living in small houses, there is little storage facility and therefore children living in small overcrowded houses are exposed to greater risk of poisoning.

Environment: Lead poisoning is common in children living in areas where there are workshops for repair of old automobile lead storage batteries or for manufacture of lead typesets for printings presses. Caustic soda poisoning used to be observed frequently in children of families which prepared washing soap for domestic or commercial purposes in their own houses. Insecticides, medicines, naphthalene balls and kerosene are common household things which are potential hazards.

Rural or urban areas: The pattern of poisoning varies in rural and urban areas due to exposures to different types of potential poisons. Snakebites are more common in those wandering in fields.

HOUSEHOLD POISONING

The household poisoning could either be a *non toxic* ingestion or a *toxic* ingestion. A non toxic ingestion is defined as that occurring after an individual consumes a non - edible product that usually does not produces symptoms, such as abrasives, adhesives, air fresheners, aluminum foils, antacids, baby products cosmetics, candles, chalk, erasers, ball point pen ink, lipsticks and lubricants etc. Household toxic ingestion consists of consumption of either of the following: soaps and detergents, shampoos, bleaches, disinfectants and deodorizers, acids and alkalis, boron compounds, cosmetics, nail polish remover (gamma butyrolactone), disk batteries, naphthalene moth balls, tobacco products, pica, insecticides, pharmaceuticals and paints. Nearly 75 percent of poisoning episodes are due to ingestion of non -toxic substances -which requires reassurance to the children and their parents. About 20 percent of poisoning episodes require urgent measures to remove the poison and approximately 5 percent of poisoning need intensive treatment.

MANAGEMENT OF POISONING

The basic elements of the medical management of poisoning are (1.) Support vital functions; (2.) Identify agent (when possible); (3.) Remove, neutralize or reverse toxic effects of poison; (4.) Hasten recovery; (5.) Treat damaged or poisoned organs systems and prevent further damaged whenever possible.

Initial Management

In a case of poisoning the immediate priority must be to maintain life. The general approach to evaluation and support of airways and cardio respiratory function remains same as taught in pediatric advanced life support course (PALS). During the initial evaluation and support of vital functions, a member of the emergency team should make effort to identify the poison. A constellation of signs and symptoms consistent with ingestion on exposure to a toxin is called toxidrome. (Table 1).

It is important to recognize toxidrome when an acutely ill patient does not have any obvious history of poisoning. For some of these toxidromes life saving therapies are available (table 2).

Immediate Care : The initial priority in treating seriously ill patient with poisoning is standard resuscitation, i.e. airway, breathing and circulation. Inadequate ventilation caused by airway compromise or reduced respiratory efforts may require oropharyngeal or nasopharyngeal airway and bag –mask ventilation with the provision of supplemental oxygen until a definite airway can be obtained through toxin reversal (for example, naloxone for opioids). Hypotension should be treated initially using intravenous fluids (an initial bolus of 10 -20 mL/kg of Crystalloid

titrated to clinical effect). Hypotension produced by poison such as opioids, beta blockers or digoxin can in addition be treated using the specific antidote (i.e naloxone, glucagon and digoxin specific antibodies respectively). Hypotension resistant to treatment with IV fluid or appropriate antidotes is managed by measuring central venous pressure to ensure adequate circulatory filling and then cautions administration of an appropriate isotropic agent.

Arrhythmias associated with poisoning should generally not be treated with anti -arrhythmic drugs as a first line approach. Factors precipitating or contributing to the arrhythmia such as acidosis, hypocalcaemia, hypomagnesaemia and hypoxia should be corrected. Correction of precipitating factors and the appropriate use of antidotal agents negates the need for anti arrhythmic agents in most cases. Sustained seizures should be treated using benzodiazepines (lorazepam or diazepam). It is important that a bedside sugar is checked early in any patient with seizures to exclude hypoglycemia as a cause. Patients with core temperatures of greater than 39°C should be aggressively treated with cool IV fluid and active cooling measures because prolonged hypothermia can result in significant complications such as rhabdomyolysis and disseminated intravascular coagulation.

Preventing Absorption : Most toxins are rapidly absorbed from the gastrointestinal tract or through inhalation. Many may also be well absorbed upon dermal contact. Prompt action to remove the toxin and minimize contact with the absorptive surface is crucial used to prevent absorption of a toxin from the stomach and gastrointestinal tract and each has limitations and risks. A decontamination procedure instituted after the drug is absorbed poses a risk to the patient with no potential for benefit. In general most liquid drug products are almost completely absorbed within 30 minutes of ingestion and most solid dosage forms within 1 -2 hours. Gastrointestinal decontamination beyond this time is of no value.

Investigations : All poisoned patients should have their heart rate, blood pressure, respiratory rate and temperatures recorded. Patients should undergo formal weight measurement as part of routine clinical care. An ECG may detect occult cardiac conduction abnormalities of diagnostic and prognostic significance. All unconscious patients and those with features of severe toxicity (seizures, hypotension, cardiac arrhythmias or respiratory depression) should have measurement of electrolytes, renal function, paracetamol concentration and determination of acid base status. Measurement of plasma drug concentration is not routinely helpful in treating poisoned patients and should not be part of clinical care. Exceptions include paracetamol, salicylates, iron, lithium, theophylline, ethylene glycol, ethanol, methanol, and to a lesser extent digoxin, phenobarbitone, sodium valproate and cabamazepine. Most poisoning should be treated on the basis of observed clinical toxicity rather than drug concentration.

Gut Decontamination : The role of gut decontamination procedures is outlined in a series of consensus statements “ published by the American Academy of Clinical Toxicologists (ACCT) and European , [Association of Poison Centers and Clinical Toxicologists (EAPCCT). Activated charcoal is a ; safe and probably effective agent used to decrease the amount of drug absorbed from the gastrointestinal (GI) tract into the blood stream. There is paucity of well controlled data from clinical studies. Activated charcoal (1g/kg) orally should be considered for patients who have ingested a potentially toxic overdose within the previous hour. It can be given to unconscious patients after intubation through a large bore nasogastric tube. Gastric lavage has no role in -routine GI decontamination

Table 1: Examples of symptom Complexes/Toxidromes.

Pupils	Respiration	Consciousness	Possible agent	Other associations
Pinpoint	↑↓	Coma	Organophosphorus	Cholinergic: Bradycardia, Wheeze, Salivation,
	↓	Coma	Opioids	Hypotension, hypothermia
	↓	Coma	Phenothiazines	Cardiac arrhythmias
Dilated	↑	Agitation	Atropine	Anticholinergic: Fever, Dry mucous membranes, Flushing, urinary retention.
	↓	Coma	Tricyclic Antidepressants	Cardiac arrhythmia, seizures, hypotension.
	↓	Coma	Sedatives, Barbiturates	Hypotension, hypothermia, hyporeflexia.
	↑	Agitation	Theophylline, Amphetamines	Seizures, tachycardia, hypertension, acidosis.
Normal	↑	Coma	Uremia	Acidosis, hyperkalemia,
	↑	Semi coma	Salicylates	Tinnitus, agitation, Diaphoresis, alkalosis followed by acidosis.

Table 2 : Toxidromes for which life saving therapies are available

Toxidromes	Therapy
1. Opioid: Miosis, CNS depression, Respiratory depression.	Intravenous naloxone
2. Cholinergic: (caused by organophosphates And carbamates)	Atropine and pralidoxime
3. Cyclical antidepressant toxidrome (Altered sensorium, wide QRS complexes, arrhythmias)	Sodium bicarbonate
4. Hypoglycemia: it should be suspected in any child with altered sensorium or seizures.	Intravenous 25% glucose.

(Occurs due to Oral Hypoglycemic, beta blockers, salicylates, ethanol)

of actually poisoned patients. There is no evidence that gastric lavage improves patient outcome. Gastric lavage should only be considered in a patient presenting within one hour of ingestion of a potentially life threatening overdose. Vagal stimulation and hypoxia during gastric lavage potentially increases risk of cardiac arrhythmias. Administration of syrup of ipecac to incidence vomiting after acute overdose is not part of accepted clinical care.

Whole bowel irrigation is a newer method of gut decontamination that entails administering polyethylene glycol (25-40 ml/kg/hour either orally or by way of nasogastric tube for 4-6 calcium channel blockers) Contra indications to its use include obstructed bowel, ileus or GI hemorrhage.

Antidotes: Antidotes are available for a limited number of drugs and poisons. Prompt administration of antidote can be life saving.

Enhancing Elimination: Enhancing excretion is useful for only a few toxins.

Diuresis: For most toxins, renal clearance is not proportionate to urine volume; thus diuresis alone does not increase elimination. Increasing the pH of the urine with intravenously administered bicarbonate increases the elimination of weak acids, such as salicylates and phenobarbital.

Dialysis: Few drugs or toxins are removed by dialysis in amounts sufficient to justify the risks and difficulty of dialysis. Examples of toxins for which dialysis may be useful include methanol, ethylene glycol and large symptomatic ingestions of salicylate or theophylline.

Hemofiltration: It is rarely used in children because of the risks associated with its use.

PREVENTION

Poison prevention education should be an integral part of all well child

visits, even before a child is mobile. Counseling parents and other caregivers about potential poisoning risks, how to make "poison proof" a child's environment and what to do if a poisoning occurs diminishes the likelihood of serious morbidity or mortality from an exposure. Poisoning exposures in children 6-12 years of age are much less common (4% of exposures). Toxic exposures in adolescents are primarily intentional (suicide or abuse) or occupational. Pediatrician should be aware of the signs of drug abuse or suicidal ideation in this population and should aggressively intervene. Future directions: Creation of centers in major cities and towns similar to the NPIC at AIIMS will facilitate early referral of poisoned patients to appropriate centers and institution of prompt treatment. Making life saving antidotes and anti snake venom widely available across the country will decrease morbidity and mortality. Dissemination of information to parents regarding prevention of poisoning by health care providers is easily feasible and requires only motivation. Only parent information can reduce the problem of poisonings in children in the long run.

SUGGESTED READING

1. Khare M, Bhide M, Ranade A, Jay Kar A, Panicker L, Patnekar PN, Poisoning in children analysis of 250 cases. *J Postgrad Med* 1990; 36: 203-206.
2. Mehta A, Kalsa KR, Bavdekar SB, Hathi as, Joshi sY. Acute poisoning in children. *J Indian Med Assoc* 1996; 94 (6): 219-220.
3. Greene SL, Dargan PI, Jones AL. Acute poisoning: understanding 90% of cases in a nutshell. *Postgrad Med J* 2005; 81: 204-216.
4. American Academy of Clinical Toxicology and European Association of Poisons Control Centres and Clinical Toxicologists. Position statement: gastric lavage. *J Toxicol Clin Toxicol* 1997; 35: 711-719.
5. American Academy of Clinical Toxicology and European Association of Poison Control Centres and Clinical Toxicologists. Position statement: whole bowel irrigation. *J Toxicol Clin Toxicol* 1997; 35: 753-762.
6. Watson WA, Litovitz TL, Rodgers ac et al. 2002 Annual Report of the American Association of Poison Control Centres Toxic Exposure Surveillance System *Am J Emerg Med* 2003; 21: 353-421.
7. CG Wilson. Accidents and Poisonings in children. In: IAP Textbook of Pediatrics. 3rd Ed. 2005 New Delhi: Jaypee Brothers Medical Publishers (P) Ltd; PP 971-982.

**THE UNIVERSITY
OF HONG KONG**

**World Class Postgraduate Training
in Hong Kong**

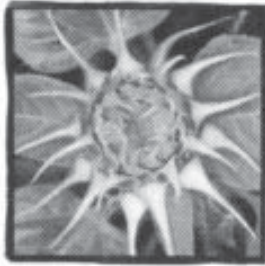
The World City of Asia

The Faculty of Dentistry, The University of Hong Kong offers a wide range of postgraduate programmes conducted in English in 2006-07.

Please note that you can apply now!

Please visit our website <http://www.facdenthk.org> for further information and application forms.

*Presenting
a novel immunosuppressant*



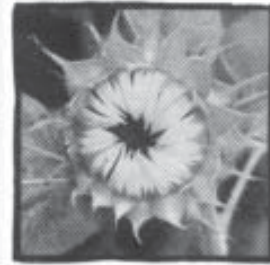
Takfa
Tacrolimus 0.5 mg, 1 mg & 5 mg Capsules

Redefines Protection

A Step Ahead

Mycofit-S
Mycophenolate Sodium 360 mg Tablet

Improved Performance for Improved Survival



*Presenting
for the 1st time in India*



Lonit

Minoxidil 5mg & 10mg tablets

Strong Hypertensive Solution

Cuprima
Viva
A Division of INTAG

INCIDENCE AND PATTERN OF ACCIDENTAL POISONING IN CHILDREN

Daljit Singh, Harmesh Singh Bains and Vinneet Arora

Department of Pediatrics, Dayanand Medical College & Hospital, Ludhiana, Punjab, India

Abstract : Accidental poisoning is a common problem in children due to their natural exploratory behaviour. The magnitude of this problem is associated with regional peculiarities. With this background, all children admitted in pediatric ward were studied over a period of 6 years to find out the incidence and type of accidental poisoning. Overall incidence was found to be 0.6%. Commonly observed poisons were kerosene oil (25.7%), organophosphorus compounds (21%) and drugs (20%). The mortality rate was 7.6%.

INTRODUCTION

Accidental poisoning in young children is often encountered by pediatricians and general physicians. The advent of various social and environmental changes has brought about a noticeable alteration in the pattern of poisoning now a day. Fresh hazards are constantly appearing with increasing use of various chemical substances in households and easy availability of drugs.

The pattern of poisoning varies from place to place because of difference in the social and epidemiological factors such as education, socio-economic status, local beliefs and customs and urban or rural distribution of population. Cumulative data about various categories of accidental poisoning from different parts of country are necessary to assess the magnitude of this childhood problem. The present study was conducted to determine the pattern of accidental poisoning in children admitted in this tertiary care hospital in Punjab.

MATERIAL AND METHODS

This prospective study was carried out in the department of pediatrics, Dayanand Medical College & Hospital, Ludhiana, Punjab. All children admitted to hospital with accidental poisoning during 6 years viz June 1996 to May 2002 were included. The detailed data recording included age, sex, urban/rural distribution, type of family, nature and mode of poisoning, occupation and education of parents. The time interval between the ingestion of the offending agent and admission to Children with food poisoning and patients with toxic and idiosyncratic reactions to prescribed drugs were not included in this study.

RESULTS

During the period of this study, 17838 children were admitted in pediatric ward. 105 children were diagnosed to be having accidental poisoning constituting 0.6% of the total admissions. Of the 105 children 10.5% were below 1 year, 41.9%, 28.6% and 19% were in the age group of 1-3, 3-5 and more than 5 years respectively (Table I). Males constituted 68.6% cases with male to female ratio of 2.2:1. Seventy five (71.4%) patients belonged to urban areas while thirty (28.6%) belonged to rural areas. The child belonged to nuclear family in 46 (43.8%) and joint family in 59 (56.2%). In majority of cases (84.8%) the mothers were housewives. (Table 2) the poison was accidentally consumed at home in 94% cases. Remaining six children consumed poison in the neighborhood. 36.2% patients were admitted within 6 hours of ingestion of the offending agent, 56.2% between 6-12 hours and 7.6% after 12 hours. A wide variety of

Table 1: Age distribution of various poisoning

Type of poison	Age group (yrs)				Total (%)
	0-1	1-3	3-5	>5	
Kerosene	1	18	5	3	27 (25.7)
Organophosphorus	1	7	5	9	22 (21.0)
Aluminium phosphide	0	1	1	3	5 (4.8)
Other pesticides	0	1	1	2	4 (3.8)
Drugs	2	10	8	1	21 (20.0)
Acids	1	4	2	1	8 (7.6)
Miscellaneous	6	3	8	1	18 (17.1)
Total (%)	11 (10.5)	44 (41.9)	30 (28.6)	20 (19)	105

agents were involved. Commonly observed poisons were kerosene oil (25.7%), organophosphorus (OP) compounds (21%), drugs (20%), aluminium phosphide (4.8%), corrosives (7.6%) and miscellaneous agents (17.1%). (Table I).

Table 2: Socio-demographic profile (N= 105)

Parameter	N	%	
Residence:	Urban	75	71.4
	Rural	30	28.6
Sex	Male	72	68.6
	Female	33	31.4
Mothers occupation	Housewife	89	84.8
	Service	16	15.2
Mother's education	Illiterate	23	21.9
	Primary	10	9.5
	Secondary	28	26.7
	Graduate	32	30.5
Type of family :	Postgraduate	12	11.4
	Nuclear	46	43.8
	Joint	59	56.2

Out of 27 cases of kerosene poisoning, majority (66.7%) were in the Poisoning due to drugs constituted 20% of total cases. The agents implicated included antiepileptics (28.6%), antipsychotics (28.6%), antihistaminics (9.5%), cough syrups (9.5%), iron tablets, antihypertensives and oral contraceptive pills.

Corrosive poisoning was due to ingestion of benzene oil, sulphuric acid and cleansing agents. Two patients developed dysphagia due to stricture formation.

Correspondence : Dr. Harmesh Singh Bains

E-mail : harmeshsinghi@sifyl.com

Miscellaneous agents included fire cracker powder, mosquito mats, detergents, thermometer mercury and naphthalene balls.

Seven patients expired. The mortality rate was 7.6%. These included 3 patients each due to aluminium phosphide and organophosphorus compounds and two due to kerosene oil poisoning.

DISCUSSION

Accidental poisoning is one of the important emergencies encountered in children. Hospital statistics reported periodically from different parts of the country indicate an incidence varying from 0.3% to 7.6% of total admissions. (j. 'J5. We found an incidence of 0.6%.

In the present study, 71% of poisoning occurred in children under 5 years with maximum incidence in 1-3 year age group. A similar age distribution has been reported from other studies. Usually, this pattern of occurrence is related to the development stage of the child.

The overall female ratio of 2.2: 1 is comparable to other reports 71.4% of the children in the present study come from urban areas. This could be due to difficulty of transport, as a result of which the rural patients may get treatment from nearby hospital or general practitioners.

Higher incidence was found in joint families (56.2%) as compared to nuclear families (43.8%) where the mother is overburdened by household chores and is more likely to be careless in storing potentially poisonous substances out of reach of children.

No seasonal variation of poisoning among different categories has been found in this study though some authors found higher incidence in summer months.

The commonest type of accidental poisoning in our study was *kerosene oil* (25.7%). This is in agreement with other reported poisonings from

this country which have found the incidence to be 30% to 44%^(2,9). Most cases of accidental poisoning due to pesticides involved *organophosphorus compounds*. Majority of these children came from rural areas (94%). This is attributed to wide use of these pesticides in this region as farming is common occupation in Punjab.

Accidental poisoning due to drugs accounted for 20% of cases in our 2-q study. This is in conformity with observations of other authors^(2,9).

The wide variety of agents implicated show that any substance available at home if accessible to a child can be accidentally consumed any time, to keep all medicines out of sight and reach, under lock, to place household chemicals out of reach of children, including detergents and antiseptics in bathrooms. All prescribed medicines for the children should be given under direct supervision. Do not permit the child to take the medicine on his own.

REFERENCES

1. Bhandari E. Accidental poisoning in children. *Indian Pediatric* 1981, 18: 153-155.
2. Buhariwala RJ, Sanjanwalla. Poisoning in children: A study of 303 cases. *Indian Pediatric* 1969,6: 141-145.
3. Satpathy R, Dass BB. Accidental poisoning in childhood. *Indian Pediatric* 1979, 13: 190-192.
4. Chatterjee E, Eanerjee DPo Accidental poisoning in children. *Indian Pediatric* 1981,18: 157-162.
5. Singh S, Narang A, Walia ENS, Mehta S, Kumar Lo Accidental poisoning in children. *Indian Pediatric* 1981,18: 163-166.
6. Sitaraman S, Sharma U, Saxena S. Accidental poisoning in children. *Indian Pediatric* 1985,22:757- 760.
7. Kumar V. Accidental poisoning in South West Maharashtra. *Indian Pediatric* 1991,28: 731-735.
8. KissonN, Vidyasagar D. Poisoning *Indian J Pediatric* 1991,58: 431-438.
9. Khadgwat R, Garg P, Eansal P, Arya A, Choudhary E. Accidental poisoning *Indian Pediatric* 1994, 31: 1555-1557.

ONCE-A-DAY
Olmezeest ¹⁰/₂₀
Olmesartan Medoxomil 10/20 mg Tabs.

**2 Digit BP reduction for
3 Dimensional benefit**

- **Efficacy**¹
 - The only ARB providing double digit BP reduction
 - Responder rates > 80%
- **Safety**²
 - Placebo like side effect profile
- **Protection**³
 - Additional impact on vascular inflammation
 - Targets two CV risk factors simultaneously

For Improved BP Control

AZURA
Life Sciences
A DIVISION OF SUN PHARMACEUTICAL INDUSTRIES LTD.

1. Supplement of Practising Medicine Aug 2005 p-16
2. Thomas Linger et.al, *Drugs* 2004; 64(24): 2731-39
3. Danilo Fliser et.al, *Circulation* 2004; 110: 1103-7

For the use of a Registered Medical Practitioner or a Hospital or a Laboratory only.

ROLE OF CORRECTIVE SERIAL PLASTER CAST APPLICATION IN MANAGEMENT OF CTEV PRESENTING WITH MODERATE DELAY

J.P.S. Walia B.S. Brar, Parveen Garg

Department of orthopedics, Govt. Medical College and hospital, Patiala, Punjab, India

Abstract: The present study aims at studying the role of corrective serial POP cast in the management of CTEV cases presenting with moderate delay. 30 patients with type II CTEV deformity were included in the study and evaluated clinically according to the grading in the oxford clubfoot programme before serial casting was begun. Radiographs of the foot were taken before casting was begun. Six corrective serial casts were applied at 15 days intervals. After a follow up period of 3 months, all clinical and radiological tests conducted at the start of the study were repeated. The degree of correction in each foot and residual deformity were noted. It was found that the more severe the initial deformity, the more resistant it was to conservative treatment particularly in case of equines. But this did not hold true for adduction deformity, which was corrected in most cases by casting irrespective of the initial severity.

INTRODUCTION

Congenital clubfoot is one of the most common foot disorders with an incidence of approximately 1 to 1.4 case per 1000 live births. The term talipes equinovarus is derived from Latin: talipes, a combination of the words talus (ankle) and pes (foot); equinus, meaning horse-like (the heel in plantar flexion at ankle joint); and varus, meaning inverted at subtalar joint and adducted at midtarsal joint as reported by Lehman¹. Boys are affected twice as girls as reported by Wynne Davies².

Clinical grading of main deformity of clubfoot done by Tibrewal et al³ and oxford clubfoot programme⁴.

CTEV is a highly dynamic disorder, which may vary from a relatively mild variant that is amenable to simple conservative treatment to a highly rigid type, which is almost resistant to all treatments available. Numerous studies have been done on the clubfoot since it was first described by Hippocrates⁵.

There are many advocated approaches to the treatment of clubfoot. Most researches agree that a period of casting can correct some clubfeet. In classical article on the treatment of congenital clubfoot by Kite JH⁶, a strong plea was made for conservative treatment of congenital clubfoot. The literature revealed significant gray areas in the field of treatment determination in type 2

CTEV. No well-defined criteria exist for cases that present moderately late, or have improper previous treatment.

Most centres internationally advocated non-operative treatment in cases <1 month. However the scene in the underdeveloped countries is unique in the sense that treatment is often delayed till as late as 6 months. In this aspect it was thought worthwhile to study the efficacy of serial POP casting in feet with isolated CTEV, and to try and identify factors that will lead to failure.

MATERIALS & METHODS

30 feet with type – 2 CTEV were included in this study. All the children were below 6 months and more than 1 month. No child had any associated medical/surgical illness.

A thorough clinical examination to assess the condition of skin, extent of deformity, muscle bulk, joint movement and neurovascular status of the foot was done along with clinical grading of main deformities of clubfoot.

Radiographs of the foot were taken before casting began by placing the foot in a position of maximum correction. Antero-posterior and lateral views were taken and the following angles were measured. Normal range of these angles are:-

Talocalcaneal angle (TC)	AP 30° - 50° LAT 25° - 50°
Talo-first metatarsal angle (TMT):	AP 5° - 15°
Talo-tibial angle (TT):	Stress lateral 62° - 85°
Tibio calcaneal angle (TiC):	Stress lateral 50° - 75°

METHOD OF POP APPLICATION

The skin was painted with an adherent such as tincture of benzoin. The surgeon applied the cotton in reverse direction pulling the foot into abduction. In a right clubfoot cast the surgeon's left hand mainly the first index finger, pull the heel out of inversion, the pulp of the left thumb fits in the sinus tarsi and hold the head of the talus medially. The thumb of the right hand pushes on the first metatarsal to push the foot out of adducts and also everts the forefoot. Once the cast is applied the patient parents will be explained clearly about plaster care and post cast complications. After 15 days the cast was removed. The foot was washed and thoroughly cleaned; degree of correction was assessed clinically and noted. The foot was re-manipulated to the maximum correctable position and cast re-applied. Six serial casts were applied at 15 days intervals. After a follow-up period of 3 months, all clinical and radiological tests were repeated. The degree of correction in each foot and residual deforming were noted.

CLINICAL ASSESSMENT

Tables 1,2,3&4 analyse the clinical assessment (pre & post operative), grading of equines and various deformities in the subjects studied.

Table 1 :Age and sex distribution.

Age (months)	Male	female	Total
1-2	3	2	5
2-3	8	3	11
3-4	6	3	9
4-5	1	0	1
Total	18	8	26

Correspondence : Prof. J.P.S Walia

70-E, Police Lines, Patiala - 147001

Table 2: Pre & post POP assessment of equinus deformity

Equinus deformity	Post – POP equinus deformity			
	Grade – 0	Grade – I	Grade – II	Grade – III
Grade – III	0(0%)	0(0%)	6(30%)	14(70%)
Grade – II	6(60%)	1(10%)	3(30%)	0(0%)
Grade – I	6(20%)	1(3%)	9(30%)	14(47%)

Table 3: Pre & post POP assessment of varus deformity

Varus deformity	Post – POP varus deformity			
	Grade – 0	Grade – I	Grade – II	Grade – III
Grade – III	0(0%)	8(32%)	14(56%)	3(12%)
Grade – II	2(40%)	3(60%)	0(0%)	0(0%)
Grade – I	2(7%)	11(37%)	14(46%)	3(10%)

Table 4 : Pre & post POP assessment of adduction deformity

Adduction deformity	Post – POP adduction deformity			
	Grade – 0	Grade – I	Grade – II	Grade – III
Grade – III	14(78%)	4(22%)	0(0%)	0(0%)
Grade – II	10(84%)	2(16%)	0(0%)	0(0%)
Grade – I	24(80%)	6(20%)	0(0%)	0(0%)

It was seen that the equinus deformity persisted in most cases and was most resistant to treatment. While varus and adduction deformities including hindfoot mobility improved significantly with POP casting; adduction being most amenable to POP casting treatment.

Radiological Assessment: The measurements of various angles on radiography before casting are depicted in Table – 5, the results after POP casting are depicted in Table – 6.

Table: 5 Pre-casting radiological assessment of foot

Measuring angle	Number of cases in relation to angle (in ^o)								
	0-10	11-20	21-40*	41-80	81-90	91-110	111-130	131-150	Total
TC angle (AP)	12	10	8						30
TMT angle (AP)				3	10	5			30
TC angle (Lat.)	13	15	2						30
TiC angle (Lat.)					3	11	16		30
TT angle (Lat.)					7	9	10		30

*31-40 : NIL; 41-50 : 30 (TMT-AP); >150: 4 (TT ANGLE)

Table: 6 Post-casting radiological assessment of foot

Measuring angle	Number of cases in relation to angle (in ^o)									Total
	0-10	11-20	21-40	41-80*	81-90	91-110	111-130	131-150		
TC angle (AP)	3	10	16	1*					30	
TMT angle (AP)	18	2	10						30	
TC angle (Lat.)	3	14	13						30	
TiC angle (Lat.)				6	1	6	3	12	30	
TT angle (Lat.)					6	3	12	10	30	

*40-50 : NIL; >150: 2 ; TT =2

It was seen that change in talocalcaneal angle (AP), talo-first metatarsal angle and talocalcaneal (Lat) angle was significant. In case of tibio-calcaneal and talo-tibial angles there was not significant changes in the angles.

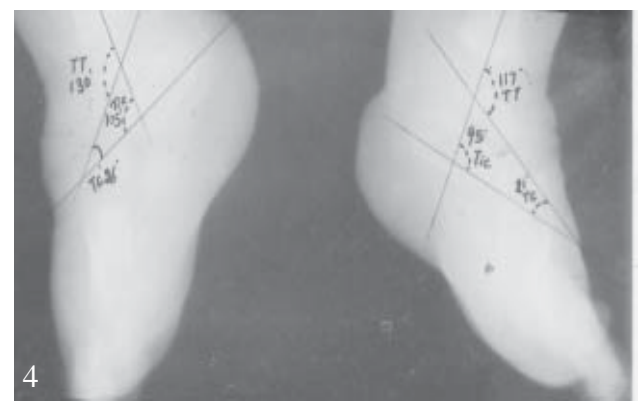
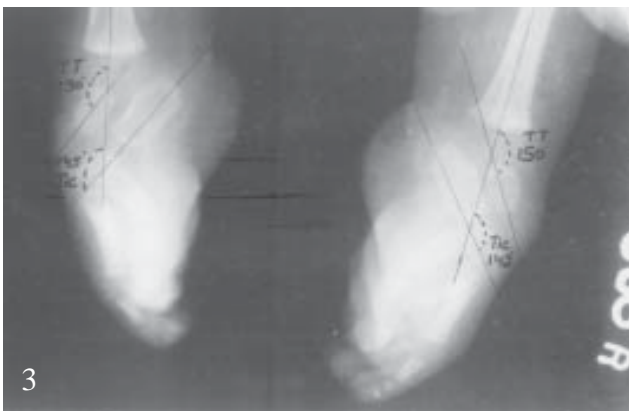
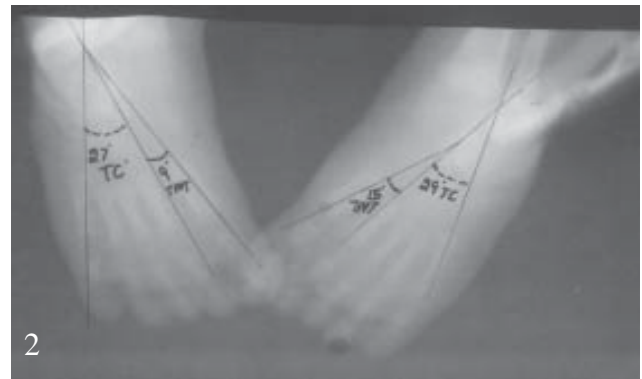
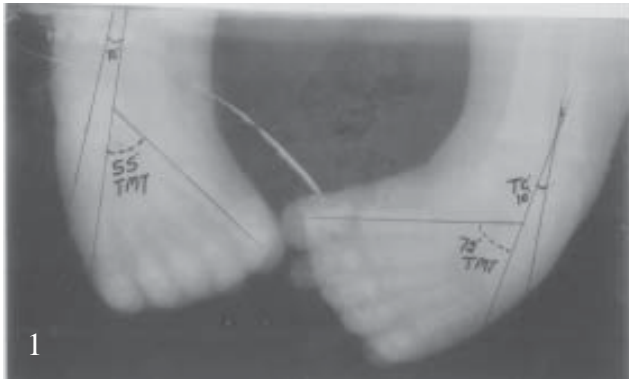
DISCUSSION

The basis upon which nonoperative techniques rest is the correction of the deformity through the production of plastic (permanent) deformation (lengthening) of the shortened ligaments and tendons in the involved foot. Serial manipulation and cast immobilisation relies on the viscoelastic nature of connective tissue to produce plastic deformation through a process known as stress relaxation. Deformity is corrected as much as possible with gentle stretching, which places the shortened tissues under tension. As the foot is held by the maximally corrected position in the cast, the tension in the shortened tissues decreases over time. When the tension decreases sufficiently, more correction can be obtained by repeating the process⁷.

After analysis of the results it was seen in our study that equinus deformity was most resistant to casting treatment. Out of 30 feet, with Grade – III equinus deformity, 14 feet (70%) persisted as Grade – III and 6 feet (30%) improved to Grade – II. Out of 10 feet with Grade – II equinus deformity 3 feet (30%) persisted as Grade – II, one foot (10%) improved to Grade – I and in 6 feet (60%) the equinus was fully corrected. Grade – III equinus deformity when compared to Grade – II had less chance of correction. So for complete, tenotomy of Z – Plasty lengthening of tight tendoachilles is required. In the feet treated by casting. Simons⁸ stated that the equinus is usually the last and most difficult deformity to correct with conservative treatment, Which is also consistent with our findings. In case of varus deformity out of the 25 feet with Grade – III varus deformity 3 feet remained at Grade – III, 14 feet with Grade – II and 8 feet improved to Grade – I varus after casting. Out of 5 feet with Grade – II varus deformity 3 feet improved to Grade – I and in remaining 2 (40%) feet the deformity was fully corrected. It was seen that the severity of varus did not have a significant influence on the outcome. The talocalcaneal (AP) and talocalcaneal (Lat) indicative of varus improved after treatment. The degree of correction of varus deformity was proportional to the improvement in hindfoot mobility.

In our experience forefoot adduction deformity was most amenable to casting and correction was achieved in most of the cases. The talo-first metatarsal (AP) angle (indicative of adduction deformity) before and after casting improved and the improvement was significant.

There was a positive co-relating b/w clinical assessment & radiological



Photographs (1) , (2) , (3) ,(4) are of case A presenting with B/L CTEV. Photograph (1) Photograph of X- ray (AP View) both feet before POP application It shows Talocalcaneal (TC) and Talo-first Metatarsal (TMT) angles of both feet. Rt. Side Lt Side
TC Angle - 00 TC Angle - 100

scores. Other studies also emphasized that radiological score is an objective representation of structure and function of the foot and can be used to distinguish the foot which will be easy to treat from those that will be difficult as stated by Bansal et al ⁹.

None of the previous studies have tried to focus clearly on the role of serial corrective plaster cast application in type 2 rigid CTEV. Researchers like Ikeda¹⁰ stress that conservative methods can achieve good outcome in the treatment of idiopathic clubfoot and criticises surgical intervention; as observed by other workers ^{6,11,12,13}.

In our study we found that the more severe the initial deformity, the more resistant it was to conservative treatment particularly in case of equinus. But this did not hold true for adduction deformity, which was corrected in most cases by casting irrespective of the initial severity.

CONCLUSION

Serial POP correction is a good option in the treatment of type II CTEV, in cases presenting with moderate delay.

BIBLIOGRAPHY

1. Lehman, Wallace B. The clubfoot. Phil J.B. Lippin Cott 1980; 1 – 5.
2. Wynne Davies R. Family studies and the cause of congenital clubfoot. J Bone Joint Surg 1964; 46(B) 445 – 453.
3. Tibrewal SB, Benson MKD, Howard C, Fuller DJ. The Oxford Clubfoot Programme. J Bone Joint Surg 1992; 74 (B): 528 – 33.
4. Fuller, D.J. (1984) Oxford Clubfoot Programme; Proceeding. Journal of Bone and Joint Surgery 66B, 142-43.
5. Carroll NC. Clubfoot: What have we learned in the last quarter century. J Pediatr Orthop 1997; 17: 1 – 2.
6. Kite JH. Nonoperative treatment of congenital clubfoot. Clin Orthop 1972; 84: 29 - 38.
7. Cummings RJ, Davidson RS, Armstrong DF, Lehman WB. Congenital clubfoot. J Bone Joint Surg Am 2002; 84(2): 290 – 308.
8. Simon GW. Analytical radiography of clubfoot. J. Bone Joint Surg 1977; 59-B: 485-489.
9. Bansal VP, Daniel J and Rai J. Radiological score in the assessment of clubfoot. International Orthopaedics 1988; 12: 181 – 185.
10. Ikeda K. Conservative treatment of idiopathic clubfoot. J Pediatr Orthop 1992; 12: 217 – 223.
11. Blumenfeld I, Kaplan N and Hicks EO. The conservative treatment of congenital talipes equinovarus. J Bone Joint Surg 1946; 28: 765-776.
12. Kuhlmann RF. Conservative management of congenital clubfoot deformity. Am J Dis Child 1954; 87: 440 – 447.
13. Ponseti IV. Clubfoot management. J Pediatr Orthop 2000; 20: 699 – 700.

CONFERENCE NEWS

16th Annual Conference of Indian Society of Otology – ISOCON 2007 will be from 16th to 18th November, 2007. The venue will be Taj Krishna, Hyderabad. **Guest Speakers:** Prof.Mario Sanna from Italy; Dr.Matthew Yung from U.K.; and Dr.Jahnke Klaus from Germany. The conference will be one day lectures, panel discussion and oration, two days of live surgeries, instructional courses and ENT quiz.

Contact : Dr. T.V. Krishna Rao, Organising Chairman, ISOCON 2007 “UMA KRISHNA”, 5-9-30/1/27AB, Basheer Bagh Palace Hyderabad – 500 063. Tel : 040-23222255; e-mail: dr Rao@mmdsofttech.com

3-D spectrum

MAGNEX

Sulbactam/cefoperazone (1:1) 1g, 2g Vials

IV/IM
q12h



- ✦ Provides 3-D spectrum of action¹
Dependable empirical therapy
- ✦ Achieves high peak serum concentrations within 5 minutes²
Rapid bactericidal action
- ✦ Sulbactam lowers MIC values of cefoperazone for β -lactamase producing & non-producing strains^{3,4}
High kill ratios
- ✦ Ensures high cure rates with dependable clinical efficacy and safety^{5,6}
Overall side effects ~ 4%
Common side effects - diarrhea, rash & fever (> 1%)
Very low discontinuation rate (2%)

SUMMARY OF PRESCRIBING INFORMATION

Composition: Magnex 1g/2g IV/IM injection- cefoperazone sodium 500 mg + sulbactam sodium 500mg; cefoperazone sodium 1000mg + sulbactam sodium 1000mg.

Indications: Monotherapy or combination therapy for the following infections when caused by susceptible organisms: Respiratory tract infections, urinary tract infections, peritonitis, cholecystitis, cholangitis, and other intra-abdominal infections, septicemia, meningitis, skin and soft tissue infections, bone and joint infections, pelvic inflammatory disease, endometritis, gonorrhoea, and other infections of the genital tract. **Contraindication:** Known hypersensitivity to penicillins or any of the cephalosporin class of antibiotics. **Warning and precautions:** Magnex should be given cautiously to penicillin-sensitive patients. As with other antibiotics, overgrowth of resistant organisms may occur during prolonged use of Magnex. The safety of Magnex during pregnancy or during lactation has not yet been established. Magnex has been effectively used in infants, but the drug has not been extensively studied in premature infants and neonates and safety has not been established in such patients. In patients with both hepatic dysfunction and concomitant renal impairment, Magnex serum concentrations should be monitored and dosage adjusted as necessary. As with other broad spectrum antibiotics, vitamin K deficiency has occurred in patients treated with Magnex, but has been reversible with discontinuation of the drug. **Adverse Reactions:** In pooled clinical trial data from comparative and non-comparative studies in approximately 2,500 patients the following was observed: reversible neutropenia (with prolonged administration) 0.5% (9/1696), positive direct Coombs' test 5.6% (15/269), anacnia 0.9% (13/1416), reduced hematocrit 5.6% (15/269), transient eosinophilia 3.5% (40/1130), thrombocytopenia 0.8% (11/1414), hypoprotrombinemia 3.8% (10/262), headache 0.04%, fever 0.5%, and chills 0.04%. Diarrhea/loose stools (3.9%) have been reported most frequently followed by nausea and vomiting (0.6%). As with all penicillins and cephalosporins, hypersensitivity manifested by maculopapular rash (0.6%) and urticaria (0.08%) has been reported. These reactions are more likely to occur in patients with a history of allergies, particularly to penicillin. Transient elevations of SGOT, SGPT, alkaline phosphatase and bilirubin levels have been noted in 1.2% to 6.2% of the reported cases. Phlebitis (0.1%) at the site of infusion or transient pain on intramuscular administration (0.08%) may occur in some patients. In post-marketing experience the following additional undesirable effects have been reported: anaphylactoid reaction (including shock), hypotension, pseudomembranous colitis, leucopenia, pruritus, Stevens Johnson Syndrome, hematuria, and vasculitis.

Dosage guidelines:

Usual Adult Dosage	Dosage in Renal Impairment	Dosage for Most Pediatric Patients [†]						
2g to 4g per day IM or IV, in equally divided doses every 12 hours. Maximum dosage: up to 8g per day. In cases where doses above 80mg/kg/day of cefoperazone activity are necessary, additional cefoperazone should be administered separately.	<table border="1"> <thead> <tr> <th>Creatinine clearance</th> <th>Maximum recommended dosage</th> </tr> </thead> <tbody> <tr> <td>15-30mL/min</td> <td>2g b.d.</td> </tr> <tr> <td><15mL/min</td> <td>1g b.d.</td> </tr> </tbody> </table>	Creatinine clearance	Maximum recommended dosage	15-30mL/min	2g b.d.	<15mL/min	1g b.d.	Usual dosage of MAGNEX is 40-80mg/kg/day, in two to four equally divided doses. In serious or refractory infections, dosage may be increased up to 160 mg/kg/day, in two to four equally divided doses. [†] See prescribing information for important additional information on dosage in neonates.
Creatinine clearance	Maximum recommended dosage							
15-30mL/min	2g b.d.							
<15mL/min	1g b.d.							

References: 1. Jones RN, et al. *Am J Clin Pathol* 1985; 84:496-504. 2. Data on file, Pfizer Inc. 3. Klasterky, Auwera PV. In-vitro activity of sulbactam in combination with various β -lactam antibiotics. *Diagn Microbiol Infect Dis*. 1989; 12: 1655-1690. 4. Ueda T, Matsuo K. *Jpn J Antibiot* 1989; 42(4):696-906. 5. Kuni O. In: β -lactamase Blocking Agents, Ueda Y, Neu HC (eds) University of Tokyo Press, 1986:61-67. 6. Kawada Y, Nishura T. In: β -lactamase Blocking Agents, Ueda Y, Neu HC (eds) University of Tokyo Press, 1986:69-76.

* Trademark of Pfizer Inc. U.S.A. (Pfizer Limited-Licensed User)
Full Prescribing Information Available on Request.

For the use of a Registered Medical Practitioner or a Hospital or a Laboratory only.



Pfizer Limited
Pfizer Centre, Patel Estate, S. V. Road,
Jogeshwari (W), Mumbai - 400 102.

MEX-03-04

VARIATIONS OF THE SPINE OF SPHENOID

Gohil K. Garg

Department of Anatomy, I.T.S. Center of Dental Studies and Research,
Murad Nagar, Delhi Meerut Road, U.P. India

Abstract : Spine of the sphenoid is related to few important structures like chorda tympani nerve and auditory tube, medially and auriculotemporal nerve laterally, each of which has an important function in the body. The present study is done, as there is scarcity of data on the length, shape and direction of spine of sphenoid and to study there variations of the spine as any variation in the spine can lead to the compression of the nerves and structures related to it. Sixty-six areas of thirty-three (33) dry skulls were studied and the length, shape, direction of the spine was noted. The length of the spine of the sphenoid varied from absence or minimally projecting spine, to a long spine.

The shape of the spine of the sphenoid varied from a pointed or rounded structure to a broad plate of bone. The spine was directed downward but the tilt was in every direction. In three specimens there was the presence of the pterygospinous plate of bone. Since the two ligaments, the anterior ligament of the malleus and the sphenomandibular ligament (both are remnants of the sheath of intermediate part of the Meckel's cartilage) are attached to the intervening spine of sphenoid, it may be conjectured that his spine also develops from the Meckel's cartilage; the pull of these two ligaments in different directions may lead to different lengths and shapes of spine, which may cause pressure on the structures related on either side of the spine.

INTRODUCTION

The base of the skull is related to number of important nerves, vessels and structures that enter the skull or exit from it. These nerves, vessels and structures are at times, related to some bony prominence or at times also groove or perforate the bone through which it travels.

One of the important bones at the base of the skull is the sphenoid bone. The pentagonal, infra-temporal surface of the greater wing of sphenoid. The spine is present lateral to the sphenopetrous fissure i.e. the sulcus from the auditory tube). Its medial side shows a faint anteroinferior groove for the chorda tympani nerve. Laterally the auriculotemporal nerve is related to it mentions that the persistence of the sheath of the intermediate part of the Meckel's cartilage, which gives rise to the anterior malleolar ligament of the malleus and the sphenomandibular ligament.

Halim¹ said that, *the anterior malleolar ligament connects the anterior process of the malleus to the spine of the sphenoid and is developmentally continued with the sphenomandibular ligament. He illustrates in his textbook of Anatomy (fig 244 on page 218 of Volume 2), all the three i.e. anterior ligament of the malleus, the spine of the sphenoid and the sphenomandibular ligament, are derivatives of 1st branchial arch (remnants of Meckel's cartilage).*

Synder and blank² mentioned the bridge of bone between the lateral surface and the base of the lateral pterygoid plate and the spine of the greater wing of sphenoid (lateral to the foramen ovale) and this place provides passage for some or most of the motor fibres of the trigeminal nerve,

The variations in the spine are expected and are not uncommon, as the size, shape, length and curvature of the spine of the sphenoid depends on the length and the pull of these two ligaments.

The present study was undertaken there is scarcity of data on the length, shape and direction of spine of sphenoid and to study there variations of the spine as any variation in the spine can lead to the compression of the nerves and structures related

to it.

MATERIALS AND METHODS.

The study was conducted on sixty-six areas comprising of thirty-three dry skulls. An important finding did not show common features of the spine of the sphenoid, thus the number of specimens were taken as one on one basis. The right and the left half of the skulls were studied, nothing the length, size, shape and direction of the spine of the sphenoid. The length of the spine was measured from the base of the spine (the base was taken as sphenotemporal suture, at the posterior most end of the infratemporal surface of the greater wing of the sphenoid) to the apex of the spine.

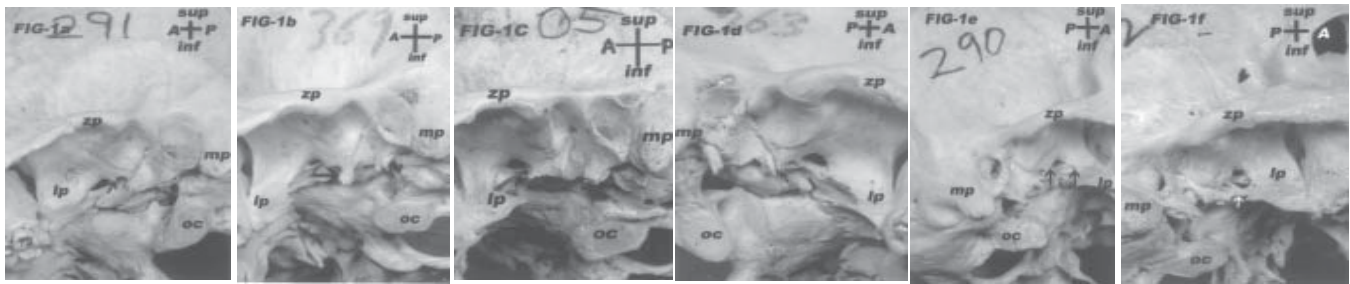
RESULTS

The length of the spine of the sphenoid varied from absence of the spine or a spicule, (Fig. 1(a)) to a long spine, (Fig.(b)). The shape of spine of the sphenoid varies from, a spine with broad base and broad rounded apex, (Fig.1 (b)) to a long and broad piece of bone, Fig.1 (c) or with a broad base with a pointed apex, (Fig 1(d)).

The spine was directed downwards but the tilt was downwards and anteriorly, fig. 1(b); downwards and extending posteriorly and fusing with tympanic plate of temporal bone (Fig. 1 (c)) downwards and posteromedially, forming the posterior and the medial wall of the foramen spinosum, Fig. 1 (d).

No half of the skull showed common features of the spine of the sphenoid, thus numbers of specimens were taken as one on one basis, (i.e. no right and the left half of the skull showed a similarity in the spine of the sphenoid).

In three specimens there was the presence of the pterygospinous plate of bone, which develops from the ossification of the pterygospinous ligament extending between spine of sphenoid and lateral pterygoid plate. Two of them were partly ossified with a large gap, Fig 1 (e), for the vessels and the nerves for the medial pterygoid muscle and in one; it was a well developed thin plate of bone with small and large foramina Fig1 (f).



The results were tabulated as below :

Spine of the sphenoid :

Absent	=	07 (10.6%)
Shape		
<i>Pointed</i>	=	28 (42.4%) Grooved anteriorly : 01 (3.5%) (Range of length 02 cm to 12 cms, mean 07 cm)
<i>Plate</i>	=	16 (24.2%) (range of length 0.2cm to 1.2cms means 0.7cm)
<i>Spicule</i>	=	12 (18.2%)
Ossified Pterygospinous ligament	=	03 (4.5%)

DISCUSSION

Our results on pterygospinous ligament in three out of 66 cases were in agreement with the study done of the spine of sphenoid by Synder and Blank² where the authors mention the ossification of the pterygospinous ligament with a forament in the ossified ligament which allows the passage of the nerves and the vessels

for the medial pterygoid muscle.

The anterior ligament of the malleus and the speno-mandibular ligament, both are remnants of the sheath of intermediate part of the Meckel's cartilage^(3,4). Since both these ligaments are attached to the intervening spine of sphenoid, it may be conjectured that this spine also develops from the Meckel's cartilage. {This fact has been shown only by Halim (illustration no. 24.4 on page 218 of his textbook of anatomy (volume 3). The pull of the two ligaments, in different directions may be responsible for varying shape of size of the spine, which in tum can cause pressure on the two nerves related on either side of the spine.

REFERENCE

- 1 Halim, A. Human Anatomy, In : The Bear, the Facial and Vestibulocochlear nerv. First edition, Vol. 3. Modern Publishers, New Delhi pp 218 (2001).
- 2 Synder, L.H. and F. Blank. (1994). Studies inhuman inheritance XXIV. Bridged sella and a genetic trait. Ohio Med. J. 40 : 318-320.
- 3 Williams, PL; bannister, LH; Berry, MM; Collings, P; Dyson, M; Dussek, JE; Ferguson, MWJ. Gray's Anatomy. In: Embryology and Development. 38th Edition, Edinburgh : Churchill Livingstone, pp. 278 1995)
- 4 Williams, PL; bannister, LH; Berry, MM; Collings, P; Dyson, M; Dussek, JE; Ferguson, MWJ. Gray's Anatomy. In : Skeletal system. 38th Eition, Edinburgh : Churchill Livingstone, pp. 586-87. (1995).

Compiled by Dr. P. Chhattree

Literature Review

Thirteen years experience of treatment of renovascular hypertension with transluminal angioplasty shows that this is a feasible treatment option.

K.A. Overhus et al, 15th Scientific Sessions, ESH, Milan, 2005.

Percutaneous transluminal renal angioplasty (PTRA) is a feasible treatment option to achieve control of renovascular hypertension, as per a study reported at the just concluded scientific session of ESH. In this follow-up study 121 patients with renal artery stenosis treated with PTRA in the period from 1991 to 2003 were selected. The methodology adopted by the study authors is described as follows: (a) screening with conventional renography with Tc- DTPA; (b) in cases with positive screening renography, the examination was repeated with/ without ACE - Inhibition; (c) plasma renin was measured before/after ACE - Inhibition; (d) If relative renal function was changed by the administration of ACEI or plasma renin increased more than 4 fold, renal angiography was performed. Based on above data the patients were further treated: (i) PTRA was performed if renal artery stenosis was found. (ii) The blood pressure and anti hypertensive medications were recorded before and after PTRA and at 1 month, 6 month, 1 year and the latest follow-up; (iii) The patients were divided into three groups: *Group 1* : normotensive without medication, *Group 2* : improved blood pressure control, *Group 3*: unchanged blood pressure. **Renal artery stenosis dilated with PTRA in 121 patients (72 men, 49 women);** stent was implanted in 71 patients. At the end of the follow-up period (*mean 41 months, 1 1/2 - 155 Months*) Patients numbers in various group : *Group i* = 13 Patients; *Group ii* = 96 Patients; *Group iii* = 12 Patients; managable complications with this treatment The authors concluded that PTRA is a feasible treatment of renovascular hypertension as 90% of the patients treated had better blood pressure control, and 11% were normotensive without medication throughout the follow-up period.

Use of Tamsulosin results in stone expulsion in almost all patients allowing complete home treatment *Dellabella M, Milanese G, Muzzonigro G J Urol. 2005 Jul; 174(1):167-72*

Resent studies show the interesting efficacy of different drug combinations for the spontaneous expulsion of distal ureteral stones. We performed a randomized, prospective study to assess and compare the efficacy of 3 drugs as medical expulsive therapy for distal ureteral calculi. A total of 210 symptomatic patients with distal ureteral calculi greater than 4 mm were randomly allocated to home treatment with phlorogucinol, tamsulosin or nifedipine (groups 1 to 3, respectively). Each group was given a corticosteroid drug and antibiotic prophylaxis with an injectable nonsteroidal anti-inflammatory drug was also used on demand. The primary end point was the expulsion rate and the secondary end points were expulsion time, analgesic use, need for hospitalization and endoscopic treatment as well as the number of workdays lost, quality of life and drug side effects. The expulsion rate was significantly higher in group 2 (97.1%) than in groups 1 (64.3%, P<0.0001) or 3 (77.1%, p<0.0001). Group 2 significantly achieved stone passage in a shorter time than the other 2 groups and showed a significantly decreased number of hospitalizations as well as a better decrease in endoscopic procedures performed to remove the stone. the control of renal colic pain was significantly superior in group 2 compared with the other groups, resulting in fewer workdays lost. Compared with group1. No difference in side effects was observed among the groups. Medical expulsive therapy should be considered for distal ureterolithiasis without complications before ureteroscopy or extracorporeal lithotripsy. The use of tamsulosin in this treatment regimen produced stone expulsion in almost all cases in a short time, allowing complete home patient treatment.

CIRCADIAN VARIATION IN THE ONSET OF ACUTE MYOCARDIAL INFRACTION IN KASHMIR

S.A. Tabish, A.M. Bhat, M.S. Alai, S. Jalal

Departments of Emergency Medicine & Cardiology, Sher-e-Kashmir Institute of Medical Sciences, Srinagar - 190011, Jammu and Kashmir, India

Abstract : A prospective observational study of two hundred patients of acute myocardial infarction admitted in Accident & Emergency Department and the Coronary Care Unit of a premier hospital, Sher-e-Kashmir Institute of Medical Sciences, Srinagar, India was carried out to determine the time of onset of chest pain and whether onset of myocardial infarction " Occurs randomly or observes circadian variation in the frequency of its onset" 50% of the patients developed infarction between 4 am to 10 am with anterior ST elevation myocardial infarction in 50% Second peak of 22% was observed from 4 pm to 10 pm as compared to trough 100/0 between 10 pm to 4 am. 18% of myocardial infection occurred between 10 am to 4 pm. This study revealed variation in circadian rhythm in the onset of acute myocardial infarction and its complications. The phannacological modulation of the physiological triggers can be tried to delay or prevent the occurrence of infarction.

INTRODUCTION

Myocardial infarction (MI) is the result of prolonged myocardial ischemia precipitated by an occlusive coronary thrombus in most cases, at the preexisting site of stenosis. Human body is a master computer with circadian rhythm, which are endogenously generated by self sustained oscillators called biological clocks -their relation being governed by Central Nervous System through suprachiasmatic nucleus of the hypothalamus region. Pineal gland has also been implicated in the control of circadian as well as circannual rhythm. The circadian rhythm study has numerous clinical implications in medical Science.

Cardiac disorders account for the vast majority of natural sudden deaths. In the United States, acute myocardial infarction develops suddenly in over 600,000 patients each year. These patients are either completely free of cardiac symptoms or have mildly symptomatic chronic stable angina pectoris¹. It is now well established that myocardia' infarction is usually preceded by coronary thrombosis, which in turn is often superimposed on disrupted intima covering an atherosclerotic plaque^(2,3). Little is known about the events or circumstances that trigger these pathologic events or transform a chronic sable condition to an acute life threatening disease. The anatomic distribution of the occluded vessel., adequacy of collateral circulation and presence of additional stenotic lesion status determines the location and extent of infarction. However it is well established that onset of the pain of myocardial infarction has circadian periodicity, with a peak incidence between 6 am and 12 noon^(4,5,6). The rhythmic processes that drive the circadian rhythm are endogenously mediated and governed by suprachiasmatic nucleus of hypothalamus and pineal gland^(7,8) Various key physiological secretions like endogenous tissue plasminogen activator (tpa) activity, PAI-1 levels, plasma cortisol, plasma epinephrine and other parameters like heart rate, blood pressure and blood viscosity exhibit circadian variation. Existence of this marked circadian variation in these parameters including platelet aggregation in the morning and upon assuming upright posture may ac-count for the observed circadian variation in the onset of Myocardial Infarction^(9,10)

MATERIAL AND METHODS

Two hundred consecutive patients of acute myocardial infarction with history of chest pain of more than 30 minutes duration., -cardiac by description with ECG showing characteristic changes of evolving myocardial infarction were included in the study. Enzyme studies where carried out for SGOT, SGPT, and CPK-MB estimation. Exact time of onset of events was recorded

Correspondence : Dr. S.A. Tabish,
E-mail : amintabish@yahoo.com

Following *criteria* satisfying the diagnosis for an acute evolving or recent myocardial infarction has been followed while conducting this study. Typical rise and gradual fall (troponins) or more rapid rise and fall (CK-MB) with at least One of the following, features (a) Ischemic symptoms; (b) Development of pathogenic Q waves on each reading; (c) ECG changes indicative of ischemia (ST -segment elevation or depression)

RESULTS

The results are tabulated in table 1 and table 2

Table 1: Distribution of patients according to onset of chest pain

Time of onset	No. of patients	Males	Females
4 am to 10am	100	76(38%)	24(12%)
10am to 4pm	36	24 (12%)	12(6%)
4pm to 10pm	44	40 (20%)	4(2%)
10pm to 4am	20	16(8%)	4(2%)

Table 2 : Temporal relationship of infarction type and death to time of onset of chest pain

Type of infarction	patients(n)	Time of onset of chest pain			
		4am to 10am	10am to 4pm	4pm to 10pm	4am to 10pm
Anterior wall MI	100	56	12	24	8
Inferior wall MI	0	40	16	16	8
Anteroseptal MI	16	4	4	4	4
Subendocardial	4	4			
Death	0				

DISCUSSION

Circadian variation in the frequency of myocardial infarction with morning resistance to thrombolytic therapy has been observed. Their may be an improvement in diagnosis and treatment of illness after understanding the role of circadian rhythm in the pathophysiology of acute myocardial infarction. Understanding of possible risk of atherosclerotic disease could improve the perception of pathophysiology of illness and increasing sensitivity to management.

Various studies have demonstrated a marked circadian periodicity in the time of onset of myocardial infarction with peak incidence between 6am to 12 noon. Master was the first to show the existence of periodicity in the occurrence of acute myocardial infarction (IOf Subsequently isolated reports showed its peak occurrence in the morning hours ! The authors

observed that the peak in the onset of acute MI occurs in the morning hours (4 am to 10 am), which confirm the results of study conducted by Pells D' Alonzo¹¹.

Summary of similar results of various studies regarding time of onset of myocardial infarction pain were first published in 1983¹². The peak onset of pain was different in one study conducted by Dim troy¹³. In this study it peaked from 4pm to midnight with a second peak from 6 am to 8 am. A number of studies including Millis data reported a secondary peak in the late evening hours which the authors also confirmed. However, this peak was not present in summary findings of the World Health Organization report¹⁴. Other study from Sovelunivn showed peak incidence of chest pain occurring in the evening hours. He observed that these patients were usually young males and persons who preferred giving night duties. This probably reflects different processes involved in altering the circadian rhythm in this patient population from those causing myocardial infarction in the morning hours.

Most of the studies used subjective parameters to determine the time of onset of myocardial infarction ignoring the effect of sleep on minor episodes of pain and circadian rhythm in pain threshold.

Other studies were conducted using CK-MB elevation for considering that the myocardial infarction has occurred 4 hours before the initial elevation.

Numerous exogenous and endogenous daily rhythms have been found to have correlation with the variation in the onset of myocardial infarction. Among the exogenous daily rhythms, which bear direct correlation with the occurrence of MI, is physical and mental stress. Substantial increases in these daily rhythms occur after waking. Endogenous daily rhythms involve rise in cortisol and catecholamine levels during morning hours resulting in myocardial infarction operating through multiple mechanisms like, plaque rupture thrombosis, coronary vasoconstriction; and systemic vasoconstriction increasing the myocardial oxygen demand. Circadian variation in the tendency of the blood to clot is possibly related to decreased fibrinolytic activity of the blood and time dependent changes in the platelet activities¹⁵⁻¹⁸.

The onset of acute MI shows characteristic circadian variation, that is a definite morning peak related to biological rhythms and a vague nighttime peak related to socioeconomic factors.

The incidence of onset of myocardial infarction was found to be more frequent in the early morning hours and unaffected by geographical distribution as observed by other. Understanding the role of circadian variation in the path physiology of illness may lead to improvement in the perception and increasing sensitivity to diagnosis circadian variation has also been observed

REFERENCE

1. Rana J.S., Kenneth J.M., Morgan J.P. et al. Circadian Variation in the onset of myocardial infarction: effect of duration of diabetes. Diabetes, June 2003,
2. Muller J.E., Stones P.H., Turi Z.G., Rutherford .D., Czeisler C., Parker C., et al: Circadian variation in the frequency of onset of acute myocardial infarction. N Eng J Med 1985;313:1315-1322
3. Miltner, M.M., Krippl, D.F. Circadian variation in myocardial infarction N Eng J Med 1986; 314:1187-1188
4. Braunwald, E; Morning resistance to thrombolytic therapy. Circulation 1995; 91: 1604
5. Willich, S.N., Linderer T, Wegscheider K, et al: Increasing morning incidence of myocardial infarction in the ISAM Study. Absence with prior adrenergic blockade. Circulation 1989; 80:853-54
6. Ridker, P.M., Manson J.E., Buring, J.E, et al: Circadian variation of acute myocardial infarction and the effect of low dose aspirin in a randomized trial of physicians: Circulation 1999; 82:897-98
7. Nahata U, Lodha A.A., Sulemani S.J. Circadian variation in different patterns of acute myocardial infarction in patients belonging to North -West Rajasthan: Indian J of Cardiology 1998, 1 : 15-16
8. Tanaka A, Kawarabayshi T, Fukuda D, et al: Circadian variations of plaque rupture in acute myocardial infarction. Am J Cardio 2004Jan 1,93: 1-5
9. Kunihiro Kinjo, Hideyuke Sato, Hiroshi Sato et al: Circadian variation of the onset of Acute Myocardial Infarction in the Osaka Area, 1998-1999: Characterization of Morning and Night-time peaks. Jpn Cir J 2001; 65:617-620.
10. Master AM. The role of effort and occupation (including physician) in coronary occlusion. JAMA 1960; 174:942-948.
11. Pells D. Alonzo CA. Acute myocardial infarction in a large industrial population: report of a 6 year study of 1356 cases. JAMA 1963;185:831-838.
12. Reinberg G A, Smolensky MB: Biological rhythms and medicine, cellular, metabolic, physiopathologic aspects. New York. Springer- Verlag, 1983.
13. Dimitrov I, Khadzichristiv A. Dynamics of the incidence of myocardial infarction in Smoljan District for the period 1965-1979. Vutr Boies 1983; 22(4):40-46.
14. World health Organization. Myocardial infarction community registers: results of a , WHO international collaborative study coordinated by the Regional Office of the Europe. In: Public Health in Europe, No.5, Copenhagen Regional Office for Europe.WHO 1976; 1:232.
15. Weitzman ED, Fukushima D, Nogeire C, et al. 24-hour pattern in the episodic secretion of cortisol in normal subjects. J Cl Endocrinology Matab 1971;33: 14-22.
16. Turton MB, Deegan T. Circadian variation of Plasma catecholamine, cortisol and immunosecretive insulin concentrations in supine subjects. Cl Chim Acta 1974; 55:389-397.
17. Wertheimer L, Hassen AZ, Delman AJ. The 24-hour circadian rhythm of cardiovascular system. Clin res 1972 ; 20:404 (Abstract).
18. Miller-Craig MW, Bishop CN, Raftery EB. Circadian variation of blood pressure. Lancet 1978; 1: 795- 797.

Dependable Anti-Diabetic Care

Diapride

Glimepiride 1mg/2mg/4mg tablets

Dibizide-M

Glipizide 5mg+Metformin 500mg tablets

Melmet

Metformin 500mg tablets

Rosinorm

Rosiglitazone 2mg & 4mg tablets

Rosinorm-G

Rosiglitazone 2mg+Gliclazide 80mg tablets

Diapride Plus

Glimepiride 1mg+Metformin 500mg tablets

Diapride Forte

Glimepiride 2mg + Metformin 500mg tablets

Rosinorm-M

Rosiglitazone 2mg + Metformin 500mg tablets

For further information please write to :



MICRO LABS LIMITED

No. 3, Queen Road, Bangalore-560001.

email : micropmt@microblsltd.com

PROTECTIVE EFFECT OF VIT.E WITH CYPROHEPTADINE AGAINST LETHAL EFFECTS OF EXUDATES FROM BURNT RAT SKIN

V. Krishnaraju, K. Krishna Rao

Department of Pharmacology, Mediciti Institute of Medical Sciences, Ghanpur, Medchal Mandal, R.R. District, AP, India

ABSTRACT: To evaluate the protective effect of vit.E with cyproheptadine against lethal effects of exudates from burnt rat skin. the steps of the procedure were: **Step 1:** A pouch was made with air on the dorsal side of the albino rats and dipped in hot water. Tyrode solution was injected into the pouch and withdrawn after two minutes. The procedure is repeated for not more than 5 times to collect maximum exudates. **Step 2:** Albino rats were divided into three groups receiving three different doses of exudates and monitored for 24 hours for the mortality. The lethal dose is determined and served as control group. **Step 3:** Albino rats are divided in five groups. Group 1 received cyproheptadine and Group 2,3,4&5 received same dose of cyproheptadine with increasing doses of Vit.E. (0.9 to 7.2mg/100g) and monitored for 24 hours for the mortality. Group 1 and 2 showed same reduction in mortality rate. Group 3 and 4 showed increase in mortality rate while group 5 has the same effect as that of group 4. Vit.E. with cyproheptadine reduced the mortality rate confirming the presence of free radicals in the exudates along with antihistaminic and anti serotonin properties of cyproheptadine .

INTRODUCTION

Literally speaking, burns induced injury and death are ridiculous, Compared to adults, children are the major victims, caused by accidents with kettles, pans, hot drinks and bath water¹⁻³. Burns cause damage in a number of different ways, but by far the most common organ affected is the skin. However, burns can also damage the airway and lungs, with life threatening consequences. Airway injuries occur when the face and neck are burnt, Respiratory system injuries usually occur if a person is trapped in a burning place and is forced to inhale the hot and poisonous gases. Fortunately, marked decreases have seen in both mortality rates and length of hospitalizations since 1970⁵. This improved prognosis due to better understanding of the systemic effects of massive burns and discoveries of better ways to prevent wound infection and facilitate healing of skin surface¹.

Rocha E Silva and Rosenthal⁶ have reported that the exudates from burnt rat skin contain histamine, bradykinin, adenosine derivatives and possibly serotonin and other as yet unidentified pharmacologically active and toxic substances^{1,4}. It was confirmed by Rao:5 that two newer antihistaminic and anti serotonin compounds Cyproheptadine and BC 105, possess significant protective effect against the lethal effects of exudates from burnt rat skins. It is also stated that burns release free radicals and prostaglandins, which also account for the mortality³.

MATERIAL AND METHODS

The method of Rocha E sliva and Rosenthal⁶ was utilized to obtain the exudates. Animals weighing between 120 and 150g were anesthetized with thiopental sodium (40mg/kg, i.p.) and then 30ml of air was injected beneath the dorsal skin to raise a pouch of 7x4x3cm. This dome was submerged in water at 95° C for 15 to 20 sec. After scalding, the animal was suspended by its paws and 5 ml of tyrode solution was injected into the pouch. The animal was then shaken for 2 min after which the fluid was withdrawn by syringe and needle. The washing was repeated at regular intervals

after burning and a maximum of 5 washings were done to each animal Determination of control dose Animals were divided into three groups often each. The exudates were injected intraperitoneally at three different doses. Group I received (2ml/100g), Group 2 received (4ml/100g) and Group 3 received (6ml/100g). Animals were monitored during the next 24 hrs for the mortality. The dose, which is prior to the 100% mortality dose, is selected as the control dose, to prevent overloading in the peritoneal cavity and for better efficacy

Drug Treatment Animals were divided, into five groups of 10 each. Group I received cyproheptadine (0.05mg/100g, s.c.). Group 2,3,4 and 5 received same dose of cyproheptadine (0.05mg/100 g, s.c.) and 0.9,1.8,3.6 and 7.2mg/100g, s.c., of vit E respectively. The animals were monitored for the next 24 hrs for the mortality.

Animals: Albino rats of either sex (120-150 g) were used. The animals were bred and housed under standard environmental condition and fed with standard diet and water ad libitum. The institutional animal ethics committee has approved the animal studies.

RESULTS

Table1: Percentage mortality of rats injected with exudates from burnt rat skin

Groups	Control dose of exudate (ml/100g,i.p.)	% Mortality in 24hrs.
1	2	50
2	4	70
3	6	100

Table 1 indicates the percentage mortality of animals when exudates were administered intraperitoneally. A dose of 6ml/100g) showed 100% mortality.

Table2 indicates the influence of drugs on toxic effect of exudates. Groups showed almost partial reduction in mortality rate (40%). In case of Vit-E added groups, at lowest dose (Group 2) of vit E) it has no effect in reduction of mortality rate.

Correspondence : Dr. V . Krishnaraju

E-mail : krishcology@yahoo.co.in

Table 2: Percentage mortality of rats injected with 4ml/100g, 1hr after administration of test drugs.

Groups	Drug	Dose mg/100g,s.c.	Mortality in 24hrs.
1	Cyproheptadine	0.05	40
2	Cyproheptadine + Vit-E	0.05+0.9	40
3	Cyproheptadine + Vit-E	0.05+1.8	30
4	Cyproheptadine + Vit-E	0.05+3.6	40
5	Cyproheptadine + Vit-E	0.05+7.2	40

At the dose of 1.8 and 3.6 mg/100g (Group 3 and 4), the mortality rate was reduced to 30% and 20% respectively. Group 5 received the highest dose and showed no reduction in the mortality rate when compared to the prior dose (Group 4).

The maximum and minimum reduction of mortality rate were at 3.6 and 1.8 mg/100g respectively.

DISCUSSION

The present investigation carried out on the effect of Vit-E in enhancing the protective effect of cyproheptadine against lethal effect of exudates from burnt rat skin reveals that moderate decrease in mortality was there with increasing dose of Vit-E, suggestive of destructive role of free radicals in burns exudates.

Rocha E, SIL V A, et al⁴ have already reported that exudates contain histamine and serotonin. Our present study reveals the presence of free radicals in the exudates from burnt rat skin. Though many research projects suggested the beneficial role of various anti-oxidant in burns⁷⁻¹³, the protective action against exudates is not yet reported. It may therefore be

anticipated that the histamine, serotonin and free radical contents of the exudates are the major cause of death in animals and the drugs protect the animals due to their antihistamine, anti serotonin and anti-oxidant properties only.

In clinical cases of extensive burns, antihistaminic, antiserotonin and antioxidants are rarely used. They are therefore possibly therapeutically important in the management of cases of extensive burn. Fat soluble vitamins rarely cause hypervitaminosis in burnt patients and so the safety of Vit.E should be extensively studied.

ACKNOWLEDGEMENT

We are grateful to Dr. Surender Reddy, Principal, Mediciti Institute of Medical Sciences, Medchal, A.P., India, for offering the requisite permission and lab facilities to undertake this work and publish the paper.

REFERENCES:

1. Lawrence M Tiemey, Stephen J Mephee, Maxine A Papadakis, editors. Current medical diagnosis and treatment. 43rd ed. St. Francisco. Lange medical books;2004. P.1534 —1538
2. Pramod Kumar, San.C.Bose, editor. Fundamentals of burns management. I Hyderabad. Paras Medical Publishers; 1988. Page 14-24.
3. Marela L Hanumandass, Mathangi Ramakrishnan. Handbook of burns management. 1st ed. New Delhi, Jaypee Brothers; 1991. P 83-90.
4. Rosenthal SR, Finnamore SJ, Hunter FR, Williams AD. Fed.Proc.1956; 15: 156
5. Rao KK. Protective effects of BW.501 C67 and BW.204 C67 against lethal effects of exudates from burnt rat skin. Japan J Pharmacol 1972; 22:309-311
6. Rocha E Silva M, Rosenthal SR. J.Pharmac. Exp. Ther 1961; 132:110.
7. Clayton MC, Solem LD. Advice on management of burns for primary care physicians. Post graduate Medicine 1995;97:151-165.
8. Saw A, Anderson J, Hayward A. The early management of Large burns. Br.J.Ho.sp.Med 1995; 53:247-250.
9. Guyton AC, Hall JE. Textbook of medical physiology 9th ed. Philadelphia: WB Saunders company; 1996. P.285-294.
10. Parrillo JE. Pathogenetic mechanisms of septic shock. The New England journal of Medicine 1993; 328 1471- 1477
11. Currer PW. Nutritional replacement modalities. Journal of Trauma 1979; 19:906-908.
12. Deitch EA. Nutritional support of the burnt patient. Critical care clinics 1995; 11:735-750.
13. Pasulka PS, Wachtel TL. Nutritional consideration for the burnt patient. Surgical Clinics of North America 1987; 69:109-131.

Drug Profile

Diacerein

Mechanism of Action : *Rhein*, the active metabolite of diacerein inhibits the production of interleukin-1 beta by human monocytes which in turn reduces the collagenase production and collagenolytic activity in articular cartilage. Diacerein decreases the number of urokinase receptors on chondrocytes to normal levels and reduces fibrinolytic activity of synovial fibroblasts. It, dose dependently inhibits superoxide anion production, chemotaxis and phagocytic activity of neutrophils and macrophage migration and phagocytosis. In Patients with active osteoarthritis, diacerein increases the lymphocyte number and synovial membrane fluidity and reduces the ratio of chondroitin 6-sulphate to chondroitin 4 and thereby protects the proteoglycan aggregation and helps the articular cartilage to resist compression under load. It does not alter renal or platelet cyclooxygenase activity and may therefore be tolerated by patients with prostaglandin dependent renal function.

Pharmacokinetics : Oral diacerein undergoes first pass metabolism and is deacetylated to its active metabolite *rhein*, which is metabolized to glucurono and sulpho-conjugates. In healthy volunteers, the maximum plasma concentration (C_{max}) of *rhein* was 3.2 mg/L at 2.2 hours after administration of a single oral dose of diacerein 50 mg. The plasma protein binding is approximately 99%. Area under the plasma *rhein* concentration time curve (AUC) from time zero to infinity was 21.2 mg/L.h, apparent volume of distribution was 13.2L, terminal elimination half life ($t_{1/2}$) was 4.3 hours, apparent total plasma clearance was 1.6L/h and renal clearance (CL_R) was 0.13 L/h. The total quantity excreted in the urine is approximately 30%. The elimination half life of *rhein* is approximately 4.5 hours. *Rhein* is eliminated in urine 80% as sulfo and glucurono conjugated forms and 20% in unchanged form.

For doses ranging between 50 and 200 mg of diacerein capsules in a single intake, all the pharmacokinetic parameters are independent of the dose. The concomitant administration of diacerein capsules with food delays the absorption but increases the bioavailability presents a low accumulation. Among patients with severe renal impairment (creatinine

clearance less than 30 ml/min), the area under plasma concentration-time curve and elimination half life are doubled and urinary elimination is reduced by half. Among elderly subjects, taking into account the good tolerance of diacerein capsules, it is not necessary to modify the dose, despite slower elimination.

Indications : Diacerein is indicated for the symptomatic treatment of osteoarthritis of the knee or hip.

Warnings and Precautions : (i) Diacerein should not be administered to children (less than 15 years), (ii) Caution is advised in patients with inflammatory organic disease of colon (ulcerative colitis, Crohn's disease, etc.) or abdominal painful syndrome of unspecified cause. (iii) With prolonged treatment with any medication, a complete blood test, including liver enzymes and urinalysis should be conducted every 6 months. (iv) Diacerein capsule should not be used during pregnancy, and in a woman during the breast feeding period. **Drug Interactions :** The concomitant administration of hydroxides of aluminium, calcium or magnesium may cause reduction in the absorption of diacerein from gastrointestinal tract.

Side effects : (A) Diarrhea, soft stools and abdominal pain. (B) A yellow-brown colouring of the urine and pigmentation of the colonic mucosa (colonic melanosis) can be observed occasionally. (C) Other side effects like pruritis, eruptions and eczema may occur.

Dosage and Administration : As diacerein may cause acceleration in intestinal transit time during the first 2 weeks of treatment, it is recommended that therapy be started with one capsule per day administered with the evening meal for 4 weeks. The capsules should be swallowed whole with water, preferably in the middle of the meals.

The duration of treatment should not be less than 6 months. In clinical trials diacerein has been administered for up to 2 years with no safety problems. NSAID or analgesics for the first 2-4 weeks of treatment, may be needed. Modification of the dosage of diacerein capsules in patients with hepatic impairment is not required.

Renal impairment : In mild to moderate renal insufficiency, it is not necessary to modify the dosage of diacerein capsules while in patients with severe renal insufficiency (creatinine clearance less than 30 ml/min), dose should be reduced by half.

LEFT OVER FOOD IN TRAY BY INDOOR PATIENTS

Hem Chandra, Arvind Srivastava, Leela Masih, K. Jamalddin

Department of Hospital administration, Sanjay Gandhi PGIMS, Lucknow U.P, India

Abstract : Hospital diet plays important role in recovery from illness amongst indoor patients. Usually hospital diets are not well accepted. The refusal of food served, partly or whole may be due to many reasons. The refusal pattern of breakfast differs from lunch. The study conducted at SGPGIMS revealed that the refusal may be as high as 15.75% in case of breakfast and 19.50% in case of lunch. The major factors for refusal of breakfast were anorexia / vomiting (32%), hospitalization (17%), fasting for tests (12.25%), feeling of satiety (8%), fever (7%) etc. Whereas in case of lunch, salt free diet (27%), cyclic menu (18%), anorexia /vomiting (11%), taste of food (10%), hospitalization (7%) were the major factors. Majority of factors have administrative background and some have disease related for which little can be done, as they can only be overcome with recovery. But administrative reasons can be removed gradually by putting in efforts and acceptance of food can be improved. Still some amount of food will go waste.

INTRODUCTION

The life cannot be sustained without adequate nourishment Man needs adequate food for growth, development and to lead active and healthy life importance of good diet could have on their recovery is well established¹. But one can see physiologic stress like in many hospitalized patients as a consequence of infections, fever, surgery, anorexia, nausea, vomiting, food aversions, burns, or other traumas all which adversely affect oral Intake². Therefore these patients are unable to ingest sufficient food to meet the increased needs . It is the prime responsibility of the hospital to take care of the adequate quantity and quality of the food served to the patients This can be achieved by keeping in mind the aspects like portion size, seasonal foods, ingredients, storage, preparation, cooking methods palatability, holding and service methods so as to provide and maintain good nutritional quality of food. For proper acceptance of food one should also consider, the appearance colour, flavor, and texture of food. But usually hospital diets are not well accepted.

There is a great wastage of food portions since many of the meals prepared for patients are not eaten³. This may be due to many reasons like different meal timings, unfamiliar hospital environment, bland diet, taste of food, due to cultural difference, repeated menus, fasting due to tests, nausea, vomiting, constipation, poor quality of food and many more. As a consequence one can see left out food in trays in hospitals Food wastage is a problem in many hospitals and the problem may be due to number of reasons as mentioned above⁴. As such it was thought to conduct this study with the following objectives: (1.) To find out amount of breakfast and lunch consumed and not consumed by the patients; (2.) To find out the reasons for the food left over in trays of hospitalized patients, it breakfast and lunch; (3.) Based on above to make recommendations for better acceptance of food to reduce the wastage of food.

MATERIAL AND METHODS

Survey was concluded at SGPGIMS Hospital between 10-04-2004 to 19-04-2004 to ascertain the information on the followings –

- amount of food consumed by the patients.
- Reasons for the food left over in trays.

Selection of subjects : 20 patients per ward per day for 10 consecutive days (total 400) were randomly selected from indoor patients of Nephrology and Medical Gastroenterology wards of SGPGI Hospital.

Correspondence : Dr. Hem Chandra, Medical Superintendent, Sanjay Gandhi PGIMS, Rai Bareilly, Lucknow, U.P., India

Development of questionnaire : For obtaining the required information a questionnaire was formulated. It consist of the following information.

- Breakfast or lunch taken or not taken
- Amount of breakfast or lunch consumed
- Reasons for the food left over in trays.

Collection of data: After the development of questionnaire, interview method was followed to collect the data for the present study. For reference intake the consumption in the patients attendant was also taken.

RESULTS

After the data was collected, tabulation was done and the respective percentage for left over food with reasons were calculated

(i) Break fast Consumption

Respondents : 84.25% of the respondents take their breakfast, where as 15.25% of them skips their breakfast.

Amount of Breakfast consumed

Figure 1 shows that out of 84.25% of the respondents who were consuming their breakfast only 46.29% of them consumed 3/4th of their breakfast. 17.21% ate 1/2 of their breakfast and the rest 9.29% ate only 1/4th of their breakfast; 27.29% who did not have any breakfast

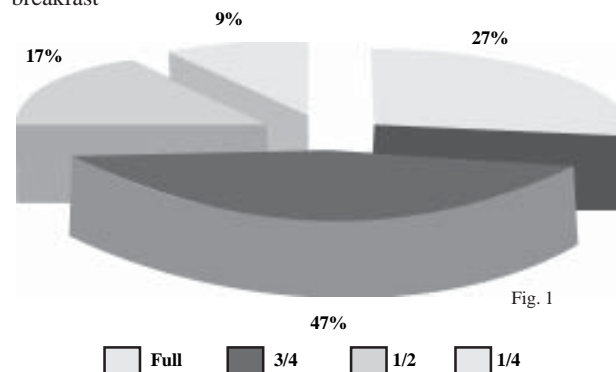


Fig. 1

Reason for left over Breakfast

Food was usually seen left out in trays of hospitalized patients due to various reasons (table 1), major reason in 31.75% was to anorexia and vomiting, whereas 17.75% of them did not take their full breakfast because of hospitalization; 12.25% each did not take due to fasting for test and abdominal distension; 10.25% due to constipation; 6.75% had fever; 8% of the patients reported

actual appetite; 6% did not eat because the taste of food was not good and remaining 4% meal timing were different from their daily schedule.

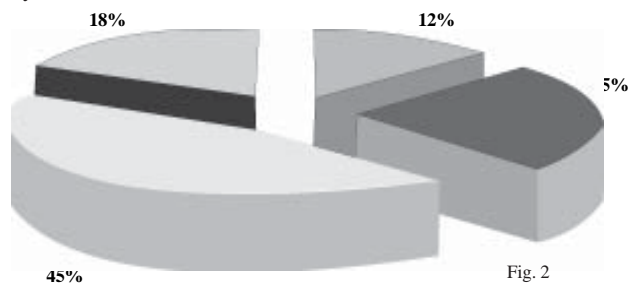
Table 1: Distribution on the basis of reasons for left over breakfast

Reasons	No. of Respondent (n=400)	%-age
Fasting for Investigations	49	12.25
Different meal time	16	04.00
Taste of food	24	06.00
Constipation	41	10.25
Anorexia/vomiting	127	31.75
Hospitalization	71	17.75
Feeling of satiety	32	08.00
Fever	27	06.75

Lunch Consumption

(i) *Respondents:* Analysis revealed that 80.5% respondents took their lunch, remaining 19.5% did not take lunch.

(ii) *Distribution on the basis of lunch consumed:* Fig 2 shows that out of 80.5% of the respondents who were taking lunch 44.45% of them consumed 1/2 of their lunch followed by 25.15% who were taking 3/4th of the lunch; 18.32% ate 1/4th of their lunch and the rest of them did not have any lunch.



Legend: Full (light grey), 3/4 (dark grey), 1/2 (white), 1/4 (medium grey)

(iii) *Reasons for left over lunch (table 2):* In 29% salt free diet was main cause for left over lunch; 18% disliked because of cyclic menu (especially vegetables); 11% to anorexia and vomiting; 7% of them because of were depressed due to hospitalization; 8% did not eat properly due to fasting for various tests/dialysis. 4% of the patients had conditipations; 3% had actual appetite loss. In 3% each reason was high fever and food fads; respectively.

Table 2: Distribution on the basis of reason for left over lunch

Reasons	No. of Respondent (n=400)	%-age
Fasting for Investigations	32	8
Different meal time	16	4
Taste of Food	40	10
Constipation	16	4
Anorexia/Vomiting	44	11
Hospitalization	28	7
Feeling of Satiety	12	3
Food fads	12	3
Fever	12	3
Cyclic menu	72	18
Salt free diet	116	29

Relative's response to left over food

Amongst the 63 respondent patient's relatives, all (100%) took the breakfast when whole of it was left over, none of them ate 3/4, 1/2, or 1/4 the breakfast left over by the patients. In the case of lunch, 88.25% of the 68 respondent relatives took left over lunch; only 11.75% took when 3/4th lunch was left over; none of the relatives took 1/2 or 1/4th left over lunch.

DISCUSSION AND CONCLUSION

The present study conducted on 400 indoor patients revealed that most of the patients consumed their breakfast and lunch i.e., 84.25% and 80.50% respectively. Out of these, 46.29% of the subjects consumed 3/4th of their breakfast followed by 27.29% who ate full amount which was served. The rest of them ate 1/2th and 1/4th of the breakfast served. As far as lunch was concerned, most of the patients i.e 44.72% ate only 1/2 the amount of the lunch followed by the 25.15% who ate 3/4th of the amount 18.32% ate 1/4th of the lunch and only 11.8% ate full amount served to them; in most of the cases the left over food was in the form of vegetables.

The study revealed that: (i) breakfast intake by the patients was slightly better (84.25%) as compared to lunch (80.50%); (ii) The major reasons contributing to over lunch were: salt free diet (29%), cyclic menu (18%), anorexia & vomiting (11%), personal taste (10%), hospitalization; (iii) The major factors contributing the left over lunch were anorexia & vomiting (31.75%), hospitalization (17.75%), The acceptance of left over food by the relatives was good (breakfast 100%, lunch 88.25%).

There were valid administrative reasons which could be removed. It is apparent that the total quality of food to be served to patients should be reduced only marginally.

Major Recommendations includes:

- The food prepared in hospital kitchen should be divided into two portions - salted and unsalted .
- Long term cyclic menu should be used so that weekly repetition of food item is avoided.
- There should be a provision for hot case tiffins or facility of reheating of food in the ward pantry for the patients who skip their meals because of tests.
- The standardization of each recipe should be done under strict supervision; food served should be palatable and attractive.
- Counselling is important in case of the patients who do not eat due to some food fads or dietary regime, related particularly to underlying diseases.
- There should be provision for specific therapeutic, attractive and palatable snacks.

RECOMMENDED READING

- 1) Peter Kandela; Hospital food; Lanchet, Feb. 27, 1999
- 2) Ruth Williams et al; Room service improves patients food intake and satisfactions with hospital food; Journal of Association of pediatric oncology nurses, 1998,
- 3) Michael Bezzina; An evaluation of the food service system of Goza general hospital: Health measures, Mar 1997.
- 4) L Kelly; Audit of Food wasteage; Differences between a plated and build system of meal provision: Journal of Human nutrition and dietetics, 12: Oct. 99, 415-424.

RENAL PSEUDOCYST SIMULATING AS A SIMPLE CYST: AN ULTRASOUND CASE REPORT

Rajul Rastogi, Satish K. Bhargava, Suchi Bhatt

Department of Radology, UCMS & GTB Hospital Dilshad Garden, New Delhi- 110019, India

Abstract : Renal involvement by pancreatitis is uncommon. Pseudocysts in the kidneys carry the potential for massive hemorrhage if they erode the renal vessels or can cause thrombosis due to vascular compression. They are not as benign as simple cysts and need timely management. Hence we report a case of renal pseudocyst that simulated as a simple cortical cyst.

INTRODUCTION

Classically, pancreatitis is a disease process where spread is not limited by adjacent organs, mesenteries or the omentum. While pancreatitis most commonly involves the pararenal spaces and lesser sac it can extend to and involve adjacent organs. Renal involvement is typically inflammatory extension into the anterior and sometimes posterior pararenal space^{1,2}. Uncommonly, a pseudocyst can track into the perirenal space and even beneath the renal capsule. This pseudocyst can at times, even simulate a simple renal cyst. When pancreatic fluid tracts beneath the capsule it can result in a Page kidney due to compressive forces on the renal parenchyma; percutaneous drainage may be needed.

CASE REPORT

A 37-year-old male patient was referred to the radiology department for ultrasound examination of the abdomen with pain in the epigastrium. Patient was a chronic alcoholic for the last 5-7 years. The laboratory findings were within normal limits except for the mildly raised erythrocytic sedimentation rate. Serum Pancreatic amylase was within normal limits. The *ultrasound* of the patient revealed small, atrophic, calcific pancreas with a dilated main pancreatic duct (figure 1). There was a cystic mass in the lesser omentum in relation to the distal body and tail of the pancreas. Another cystic lesion was seen in the left kidney in the superomedial part resembling a simple cyst. On careful scanning, the cyst appeared along and subcapsular in location with an interface between it and the renal parenchyma. Further examination revealed a possible communication between the cyst in lesser omentum and the left kidney as they were both tapering towards each other. Based on the above findings the diagnosis of the chronic calcific pancreatitis with pseudocyst in the lesser omentum and the left kidney was made.

Computed tomography of the patient revealed chronic, calcific, atrophic pancreatitis with a large lesser omental cyst dissecting into the left kidney in the subcapsular region with a very narrow neck of communication in between the two cysts confirming the diagnosis of renal pseudocyst as suggested by ultrasonography (Figure 2).

Biochemical analysis of the aspirated fluid from the cyst revealed increased pancreatic amylase confirming the diagnosis of left renal pseudocyst as suggested by ultrasonography.

DISCUSSION

Pseudocyst is a fluid collection that has developed a well-defined non-epithelialised wall in response to extravasated enzymes. It is generally spherical in shape and distinct from the other structures. Most commonly, pseudocyst formation is associated with alcoholic or biliary pancreatitis. Classically, a pseudocyst is seen on ultrasound as a well defined, smooth-walled, anechoic structure with acoustic enhancement. Pseudocyst

Correspondence : Prof. Satish K. Bhargava, E-3, GTB Hospital Complex, Dilshad Garden, New Delhi, Fax No. : 91-11-22590495



Figure 1: Us scan through the epigastrium showing calcific, atrophic pancreatitis

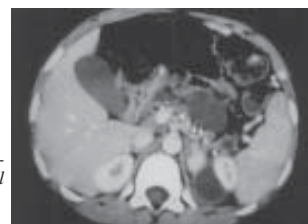


Figure 2 : CT scan showing possible communication between lesser omental and left renal cyst and atrophic, calcific pancreatitis

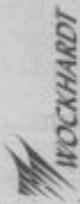
may become very large or may be strategically placed and cause obstruction of the stomach, small bowel (especially duodenum), colon or the bile ducts. They can also dissect into the adjacent organs such as the liver, spleen, and kidney. When subcapsular pseudocyst is very large it can result in a Page Kidney due to compressive forces on the renal parenchyma. Percutaneous drainage may be needed. Other unusual complications include renal vascular abnormalities such as narrowing of the renal vein, renal vein thrombosis, perirenal varices and asymmetric renal enhancement due to extrinsic pressure on one of the renal arteries.

US and CT findings of a pancreatic tail pseudocyst extending into the subcapsular space of the left kidney has been described by Lo et al³ and Singh et al⁴ also described renal pseudocysts in patients of pancreatitis and have emphasized the role of computed tomography in the diagnosis. Similar case report also appeared in Japanese literature⁵.

Our case report emphasizes the role of the ultrasound in the diagnosis of renal pseudocyst and its differentiation from the simple renal cyst.

REFERENCES

- Blandino A, Scribano E, Aloisi G, Visalli C, Pandolfo L. Subcapsular renal spread of a pancreatic pseudocyst. *Abdom Imaging*. 1996 Jan-Feb; 21 (1) : 73-4.
- Rauch RF, Korobkin M, Silverman PM, Dunnick NR. Subcapsular Pancreatic pseudocyst of the kidney. *J Comput Assist Tomogr*. 1983 Jun; 7 (3): 536-8.
- Lo J, Tag S. CT of multiple subcapsular pseudocysts of the kidney complicating acute pancreatitis. *J Comput Assist Tomogr*. 1995 Sep-Oct; 19 (5): 823-4.
- Singh SP, Vashisht S, Sharma R, Mukhopadhyay S, Berry M. Pancreatic pseudocyst of the kidney: computed tomographic diagnosis. *Trop Gastroenterol*. 1993 Jul-Sep; 14 (3): 114-7.
- Oba S, Mizutani K, Ito M. The subcapsular and perirenal pancreatic pseudocysts. *Rinsho Hoshasen*. 1988 Feb; 33 (2): 301-2.



Help your patients with anaemia

Move on with

Life Energy

Human Recombinant Erythropoietin

WEPOX

Pre-filled Syringe

A True Regard For Life



Feroject

Iron Sucrose Injection

100 mg/5 ml ampoule

Unleashing energy... unrestrained

BLEOMYCIN - INDUCED FLAGELLATE HYPERPIGMENTATION

V Talwar ; Ashok K Vaid ; Dinesh C Doval

Department of Medical Oncology, Rajiv Gandhi Cancer Institute & Research Centre, Sec. V, Rohini, New Delhi, India

Abstract : This male patient, a diagnosed case of Hodgkins Lymphoma (nodular sclerosis) developed linear hyperpigmentation on the chest, abdomen, trunk, when on combination chemotherapy which included bleomycin. Bleomycin is metabolised in all parts of the body by bleomycin hydrolase except in skin and lung, resulting in cutaneous and pulmonary toxicities. The cutaneous lesions usually appear on normal skin without preceding inflammatory lesions. Although many hypothesis regarding the pathogenesis have been postulated but the exact cause is not known.

CASE REPORT

A 52 years old male patient was diagnosed as Hodgkin's Lymphoma, (nodular sclerosis,) stage IIIA at our Institute. He was planned for ABVD combination chemotherapy (adriamycin, bleomycin, vinblastine, and dacarbazine). Four days after the first course of the chemotherapy, he noted linear hyperpigmentation on his chest, abdomen, trunk (Fig.). On close examination the rash was linear, erythematous, excoriated plaque on the chest and abdomen with a flagellate appearance. He denied permission for biopsy of the lesions. During this time the patient developed similar, linear eruptions at new areas by scratching the skin. The patient was continued with COPP chemotherapy instead (cyclophosphamide, vincristine, procarbazine, prednisolone), following which, hyperpigmented lesions resolved completely over a period of three months of discontinuation of ABVD regimen.

DISCUSSION



Bleomycin induced hyperpigmentation

Bleomycin is an antineoplastic antibiotic derived from streptomyces verticillius. After intravenous administration it is widely distributed through out the body. Bleomycin has cell cycle specific cytotoxic effects. The most pronounced inhibition of cell growth is during the S phase. The drug also damages prophase chromosomes and induces a G₂ phase maturation arrest. It is rapidly inactivated in all organs by bleomycin hydrolase except the lungs and skin where it is deficient. This results in

primarily cutaneous and pulmonary toxicities. In addition to pneumonia and pulmonary fibrosis, mucocutaneous reactions associated with the use of bleomycin are common and include stomatitis, alopecia, ulcers on palms and soles, warty keratotic plaques and inflammatory nodules¹. Almost every patient may experience fever within first 4 to 12 hours after

Correspondence : Dr. Vineet Talwar, 202, Ambika Apartments, Sector-14, Rohini, New Delhi-110 085., (Fax) 011-27931342

Email: drvineettalwar@yahoo.com

Bleomycin injection which is usually brief and not clinically troublesome. Chills, myalgias, nausea, vomiting and anorexia may accompany fever but less frequently. Anaphylactoid reactions and rarely anaphylaxis² were noted exclusively in lymphoma patients receiving first dose of Bleomycin and it was recommended to give test dose of Bleomycin prior to the actual dose. However, flagellate linear hyperpigmentation is seen in a majority of cutaneous reactions, which occur in 8-20% of cases³. These generally occur after a cumulative dose of 90 and 285mg. However, some cases have been reported with doses as low as 15mg given parenterally; as was in our case. The time lapse between the administration of drug and onset of clinical signs and symptoms ranges from 1 day to 9 weeks³ and may persist for upto 6 months⁴. The flagellate dermatitis occurs primarily on the upper trunk and limbs^{1,5}. They usually appear on normal skin without preceding inflammatory lesions. The exact pathogenesis of these lesions is not known. Some authors consider that the linear lesions result from increased leakage of the drug from dilated vessels after rubbing or scratching the skin, but others have been unable to reproduce linear hyperpigmentation by these means. It is also speculated that scratching induces subclinical local vasodilatation by a dermographic mechanism resulting in an excessive in situ accumulation of bleomycin². The reason for the increased pigmentation is thought to be due to increased melanocyte stimulation by melanocyte stimulation hormone, inflammatory oncotaxis and stimulation of melanocytes by adrenocorticotrophic hormone¹.

REFERENCES

- 1) Mowad C.M., Ngu Yen T.V., Elenitsas R, Leyden J.J., Bleomycin induced flagellate dermatitis: a clinical and histopathological review British Journal of Dermatology (1994), 131, 700-702.
- 2) Chabner BA, Myers CE, Coleman CN, Johns DG et al. The Clinical pharmacology of antineoplastic agents. N Engl J med 1975;292:1107-1113, 1159-1168.
- 3) Nelly G, Rubeiz, Ziad Salem, Rania Dibbs, Abdul-Ghani-Kibbi Cameo Bleomycin induced Urticarial flagellate drug hypersensitivity reaction. International Journal of Dermatology 1999, 38, 140-141.
- 4) Duhra P, Ilchysyn A, Das RN. Bleomycin-induced flagellate erythema. Clin Exp Dermatol 1991;16:216-7.
- 5) Rubeiz NG, Salem Z, Dibbs R, Kibbi AG. Bleomycin-induced urticarial flagellate drug hypersensitivity reaction. Int J Dermatol 1999;38:140-1.

Check-List

- (i) Copyright statement/declaration (not submitted or published elsewhere) signed by all the authors.
- (ii) Three hard copies of manuscript with illustrations attached to each; **CD should also accompany hard copy.**
- (iii) **Title page :** Title of manuscript, Name(s) and affiliation of author(s); institution(s) and city(ies) address of corresponding author (Tel; Fax; e-mail).
- (iv) **Abstract** should highlight objectives, methods, results, conclusions.
- (v) **Article** (double-spaced on A/4 size paper) : material & methods, results, discussions ; **Indian literature must be**

Manuscript Submission : For JIMSA

- referred, references numbered in text as they appear.*
- (vi) **References** maximum number of references for update-20, original-10, Case reports-6.
 - (vii) Each table on separate sheet; maximum number=4 in original article; 2 in case report.
 - (viii) Photographs/Figures in envelope, each marked figure number on reverse with legends on separate sheet. Number not to exceed 3, preferably.
 - (ix) Statement regarding adherence to **standard ethical guidelines** prescribed by ICMR 2000.

SPONTANEOUS CANDIDA PERITONITIS

H.S.Hira, Punit Pruthi, Didar Singh, Yasir S. Rizvi

Department of Medicine, Maulana Azad Medical College and Assoc. Lok Nayak Hospital, New Delhi - 110002, India

Abstract : Spontaneous fungal peritonitis caused by candida albicans is very rare. A middle aged male who was a known case of chronic pancreatitis and chronic liver disease presented in hepatic encephalopathy. On investigations he was diagnosed to be suffering from peritonitis caused by candida albicans with no evidence of bacterial infection. There are very few case reports of spontaneous candida peritonitis in this literature.

CASE REPORT

A 43 year old male, chronic alcoholic for the last 20 years, was a known case of chronic alcoholic pancreatitis for the year. The patient was operated for pancreatic pseudocyst (cystogastrostomy was done) 1 year back. During work-up he was incidentally diagnosed as having cirrhosis with portal hypertension. Ascites was not present at that time and patient never had any complication due to cirrhosis. He was on irregular pancreatic enzyme supplements.

This time he presented with the history of pain in abdomen of 4 days duration which was diffuse, non-colicky, continuous, not aggravated by meals. There was no history of vomiting or loose stools. Pain was associated with distension and constipation. Patient was in altered sensorium for last one day before admission, without any focal neurological deficit. There was no history of fever, jaundice, upper GI bleed or any recent drug ingestion. On examination his vitals were stable, there was mild pallor and mild pedal edema. There was no icterus. His chest and cardiovascular system examination were unremarkable. His per-abdomen examination revealed free fluid with normal bowel sounds. There was no organomegaly. His CNS examination revealed grade III encephalopathy.

On investigating the patient, his hemoglobin was 10 gm%, total leukocyte count (TLC) was 10,500 with differential count of 90% polymorphs and 10 % lymphocytes. His blood sugar was 87 mg %, blood urea 45 mg/dl, S. Creatinine 1.2 mg/dl, serum electrolytes were within normal range. His total bilirubin was 0.9 mg/dl, ALT – 38 (normal 20-40), AST – 46 (normal 20-40), alkaline phosphatase 10 KAU (normal < 13), serum total protein 4.8 gm % and serum albumin 2.4 gm % , serum amylase 31 Units. Ascitic tap was turbid with TLC - 16000, $DLC P_{80} L_{20}$, protein 1.2 gm % and sugar was 10 mg %. Gram staining revealed numerous Candida (yeast form), AFB staining was negative. His HIV 1 & 2 were negative. Awaiting ascitic fluid culture for bacteria and fungus he was started on intravenous ceftriaxone, intravenous fluconazole and supportive treatment. Amphotericin was avoided in view of poor general

Correspondence : Dr. Yasir S. Rizvi, 2, Doctors Apartments, Vasundhara Enclave, Delhi – 110096. e-mail : rizvis_2000@yahoo.com

condition and bilateral hydronephrotic kidneys found on ultrasound examination which also revealed coarsened echotexture of liver with irregular surface and moderate ascites . Pancreas could not be assessed because of bowel gas. Ascitic fluid culture revealed dense growth of candida albicans (both hyphae and yeast form), bacterial culture was sterile. In spite of treatment, his condition deteriorated with worsening of renal function and oliguria. Patient went in hypotension and was started on inotropic support, he could not be saved.

DISCUSSION

Spontaneous peritonitis caused by candida albicans is extremely rare. Search of literature revealed only 4 reported cases : two with liver cirrhosis secondary to hepatitis B¹ and two with alcoholic cirrhosis^{2,3}. There is only one previous case report³ of candida peritonitis in alcoholic cirrhosis who also had alcoholic pancreatitis and this is the second case report. There is a single case report of spontaneous fungal peritonitis caused by candida glabrata in a cirrhotic patient⁴. Candida albicans is not uncommonly found in patient with history of previous surgical procedure or who are on peritoneal dialysis³. In the present patient surgery was performed 1 year back and it may be postulated that candida gained entry during the procedure , lying dormant till host immunity decreased and then causing peritonitis. Finding of neutrocytic ascites with sterile bacterial culture and culture positive for a single fungus along with immunocompromised state (chronic alcoholic with cirrhosis and pancreatitis) with past history of surgical procedure goes in favour of candida peritonitis rather than non-pathogenic contaminant⁵.

REFERENCES

1. de Luis D, Aller R, Boixeda D, Meseguer M, Bermejo F, Martin de Argila C. Spontaneous peritonitis caused by ascitic fluid with Candida albicans. Rev Clin Esp. 1997 Jul;197(7):500-1.
2. Suarez A, Oero L, Navascves CA et al. Ascitic peritonitis due to candida albicans. Rev. Esp. Enferm. Dig. 1994, 86, 691-3.
3. Yang C, Yeh CT, Hung CF, Liaw YF. Case report: spontaneous peritonitis caused by Candida albicans. J Gastroenterol Hepatol. 1999 Oct;14(10):1041-4.
4. Nair S, Kumar KS, Sachan P, Corpuz M. Spontaneous fungal peritonitis (Candida glabrata) in a patient with cirrhosis. J Clin Gastroenterol. 2001 Apr;32(4):362-4. Bayer AS, Blumenkrantz MJ, Montgomerie JZ, Galpin JE, Coburn JW, Guze LB. Candida peritonitis. Report of 22 cases and review of the English literature. Am J Med. 1976 Dec;61(6):832-40.

Future Special Issues/ Symposia

Special Issues :

- Interventional Radiology: Current Trends
- Challenges of Diabetes in the Developing World
- Organ Transplantation: Current Scenario
- Advances in Neuro Surgery
- Obesity: New Challenges

Symposia :

- Sexually Transmitted Diseases Current Scenario
- Prevention of Chronic Kidney Disease
- Metabolic Bone Disease : An update
- Advances in surgical Oncology
- Advances in Endourology

NON-CIRRHOTIC PORTAL FIBROSIS

H. S. Sandhu, Shamsher Singh

Department of Medicine, Govt. Medical College, Patiala, Punjab, India

Abstract : Non- Cirrhotic Portal Fibrosis (NCPF) characterized by splenomegaly and well tolerated episodes of variceal bleeding is very commonly seen in India. The aetiopathogenesis is not well understood but various physical, chemical, biological and immunological factors have been documented to have a role. It presents in 90% cases as variceal bleed which is massive, painless, recurrent and well tolerated. Signs of chronic liver failure are in variably absent- Endoscopy usually reveals Grade - III or IV oesophageal varices. The basis of diagnosis is exclusion of extra hepatic portal vein obstruction and, cirrhosis. NCPF is a benign disorder and has a good long term prognosis. Mean survival is 25 years from the time of diagnosis.

DEFINITION

Non Cirrhotic Portal Fibrosis (NCPF) is a distinct syndrome of portal hypertension of obscure aetiology, characterized by splenomegaly and well tolerated episodes of variceal bleeding in the absence of cirrhosis of the liver and extra hepatic portal vein obstruction (EHPVO). *SYNONYMS* Idiopathic portal hypertension (IPH), Non —Cirrhotic portal hypertension (NCPH), Hepatoportal Sclerosis (HPS). Obliterative portal venopathy (OPV) & Banti's syndrome (BS).

HISTORICAL ASPECTS

First noticed by Banti in 1883, it was Basu who coined the term NCPF in 1967. Marleau in 1975 & Futagawa in 1980 described it as NCPH & Idiopathic Portal Hypertension, respectively.

EPIDEMIOLOGY

The disease is very common in India, less common in Japan & least in Western countries. It accounts for 15-35% of all cases of PHT in India. The worldwide incidence is 3-5%. NCPF is a disease of young age. The mean age is 35 years although cases have been reported from 10-60 years. In India NCPF is more common in young males whereas in Japan it is more common in older females. The predominant patients are from the middle income group. In India it is reported more among urban dwellers, whereas in Japan most patients hail from rural areas.

ETIOLOGY OF NCPF

Despite its common occurrence, the aetiopathogenesis of NCPF is not well understood. The various aetiological factors are:

- i). **Physical agents:** NCPF has been reported following irradiation in the treatment of certain tumours e.g. Wilm's tumour.
- ii). **Chemical agents :** a) *Arsenic:* Present in water, opium and some indigenous medicines, chronic exposure can lead to NCPF¹. b) *Vinyl Chloride:* Chronic exposure to monomer and polyvinyl chloride leads to sclerosis of portal venules². c) *Copper:* Chronic exposure to copper e.g. in vineyard sprayers² d) *Vitamin A:* Chronic intoxication². e) *Methotrexate* and *Azathioprine* exposure.
- iii). **Biological agents:** Infections due to parasites (malaria and schistosomiasis), bacteria (E Coli), and viruses (Hepatitis B) either as recurrent clinical or sub-clinical forms has been incriminated in NCPF.
- iv) **Immunological Factors:** NCPF has been associated with

increased incidence of HLA, DRS & DR7 and decreased incidence of HLADR2 suggesting an auto immune basis for the disease. There is decreased levels of serum IgA, C3, C4 and CD 8+ cells and an increased ratio of CD 4: CD83

CLINICAL FEATURES

(1) Age of presentation is 20-40 years (2 decades earlier than cirrhosis and one decade later than EHPVO); (2) In India. M.F :: 2: 1 to 4:1.; (3) Mode of presentation is variceal bleed (90%), splenomegaly (10%) and rarely anemia; (4) Other symptoms may be abdominal pain because of enlarged spleen and edema feet; (5) Characteristics of bleed are that it is massive, painless, recurrent and well tolerated. Overt or subclinical encephalopathy is not a feature of portal hypertension except after shunt surgery⁵. **On Examination :** 1) Signs of chronic liver failure like clubbing, spiders, palmar erythema, loss of axillary and pubic hair are invariably absent. 2) Rarely mild edema presents following a bleed; 3) Liver span may be normal or increased (not decreased), palpable in 60% cases firm nontender with a smooth surface; 4) Spleen is enlarged usually more than 9 cm; 5) Ascites is present in 20% cases after bleed (Esp, if poor dietary intake is present). It responds well to decreased sodium intake and diuretics.

INVESTIGATIONS

- 1) **Hematological:** Anemia -hypochromic normocytic or normocytic normochromic may be present and is often due to gastro intestinal hemorrhage. In hypersplenism there is anemia leucopenia and thrombocytopenia. Bleeding time, clotting time, prothrombin time, thrombintime, are all normal. Platelet aggregation test may show hypoaggregation.
- 2) **Biochemical:** Liver function tests are normal. Serum cholesterol, serum phospholipids are normal, some patients show low serum albumin which is often due to malnutrition rather than liver dysfunction. Basal and pentagastrin stimulated gastric secretion are reduced often due to portal hypertension and collateral circulation and not due to hepatocyte dysfunction. Bromosulphthalein excretion is abnormal in 20% of cases². **4) Radiology:** a) *Ultrasonography :* Shows marked dilatation and thickening of portal vein walls esp. intrahepatic branches, dilatation of splenic vein & massive splenomegaly. Spleen shows marked congestion
b) *Spleno -porto venography (SPV) :* Dye is injected into spleen and picture of spleno -portal axis is taken. It helps in diagnosis and suitability of shunt operation. Findings are :- i) Paucity of

Correspondence : Prof. H.S. Sandhu, H.No. 23, Street No. 9, Guru Nanak Nagar, Patiala, (Punjab), India

middle sized portal vein branches and they assume a “weeping willow” withered tree” appearance. ii) Absent or abruptly cut off peripheral branches (4th or 5th order radicals) – Distal cut off sign
 iii) Avascular area in immediate subcapsular area. In Cirrhosis, pathology is in 2nd and 3rd order branches. In EHPVO pathology is in portal vein itself or its main branches (Proximal cut off sign)
 5) **Haemodynamic Studies:-** These are mainly used for research purpose and to demonstrate that site of PHT in NCPF is pre sinusoidal. Intrasplenic pulp pressure is increased, portal vein pressure is increased and Wedge hepatic vein pressure is normal.

6) **Liver Pathology And Liver Biopsy :-** Macroscopic appearance : Typically the liver is smooth and firm. In about 25% of the patients only the surface of the liver may show nodules (which may be restricted to only one lobe) whereas the parenchyma is bereft of such nodules. The cut surface shows irregular areas of fibrosis primarily around the portal tracts, with thickening of the capsule due to subcapsular fibrosis. The portal veins are dilated and show sclerosis of their walls and evidence of thrombosis in the large and small portal vein branches.

Microscopic Appearance:- By definition, the lobular architecture and hepatic parenchyma are unaffected. The fibrosis starts in the subcapsular region and then creeps inside the liver parenchyma to surround primarily the portal tracts. The classical changes observed in intrahepatic portal vein branches which are markedly thickened, sclerosed and studded with organised or recanalising thrombi resulting in disappearance of portal venous radicals. The entity is appropriately designated as “Obliterative portal venopathy of the liver”⁶.

Ultrastructural appearance:- The characteristic findings are deposition of collagenous material in the widened intracellular space and the perisinusoidal space (space of Disse). Capillarisation of the sinusoids and development of microvilli between the hepatocytes are also occasionally observed. There is reduction of smooth endoplasmic reticulum in the hepatocyte. The basic aim of liver biopsy is to exclude the diagnosis of cirrhosis of liver. Percutaneous needle biopsy is certainly better than a laparoscopic punch biopsy, because not only may the nodular variety of NCPF be confused with cirrhosis but a punch biopsy obtained Rt laparoscopy may reveal only the subcapsular fibrosis and hence an incorrect diagnosis of Cirrhosis may be made. The histopathological features of liver biopsy include normal liver architecture, variably increased fibrosis in portal tract with focal lymphocytic infiltration and obliteration of small portal vein radicals. There may be fibrosis of space of Disse particularly in centrilobular zone.

DIFFERENTIAL DIAGNOSIS :- This includes cirrhosis, EHPVO, tropical splenomegaly syndrome (TSS), Budd-chiari syndrome, congenital hepatic fibrosis, partial nodular transformation, nodular regenerative hyperplasia, Felty’s synd., CHF, myeloproliferative disorders.

The differentiating features between NCPF, EHPVO and cirrhosis are given in Table 1

A scoring system to differentiate NCPF from Cirrhosis liver is given in Table – 2

TREATMENT

Acute Bleed : Steps in management includes

Table -1 : Differentiating features between NCPF, EHPVO & CIRRHOSIS

	NCPF	EHPVO	CIRRHOSIS
Age:	20-40 Yrs	<20Yrs	>40Yrs
Presentation:	GI bleed, rarely splenomegaly	GI bleed, rarely splenomegaly	Asymptomatic hepatomegaly, ascites, jaundice encephalopathy, GI bleed.
Bleed	good	good	poor
Tolerance			
1. Signs of Ch liver Disease	--	--	+
2. Abd. Veins	+	--	prominant
3. Liver	n or increased in size, firm	N, soft	firm, shrunken nodular
4. Spleen	>9 cm	<9 cm	1-3 cm
5. Jaundice, aseites, flaps	--	--	+
INVESTIGATIONS			
1. Paneytopenia	+++	++	+
2. LFT (Includ. PTI)	N	N	Deranged
3. BSP ex. test	<10%	N(<5%)	>1%
4. SPV	Distal cut off Sign	Proximal cut off Sign	Involvement of 2 nd & 3 rd Order Branches; periphery normal
5. WHVP	N	N	Increased
6. Biopsy	subcapsular Changes, patchy Portal Fibrosis	N	diffuse changes, necrosis, regeneration

NCPF = Noncirrhotic portal fibrosis ;

EHPVO = Extrahepatic portal vein obstruction;

SPV= Splenoportovenography;

WHVP= Wedged hepatic vein pressure

Table -2 : Scoring system to differentiate NCPF from Cirrhosis Liver

Variable	Points
Age	< 30Years -2 > 30 Years +2
Ascites	Present +6 Absent -2
Liver Scan	Abnormal +2 Normal -4
Serum Albumin	< 3 +4 3 to 3.5 0 > 3.5 -3

Score : Less than 5 = NCPF
 More than 5 = Cirrhosis

- (1) Put patient in lateral position to prevent aspiration.
- (2) Ryles tube gravity drainage; nil orally, monitor vitals.
- (3) I/V fluids and blood transfusion as required; do not overload patient; keep the patient slightly hypovolemic.
- (4) No role of antacids / H2 blockers
- (5) *Balloon tamponade* with Blakemore Sengstaken tube (3 lumen) or Minnesota tube (4 lumen) with oesophageal and gastric balloons. It is quite effective in controlling bleed for 24-48 hrs. Rebleeding follows tube withdrawal in 50% cases. Complications occur in 15% or more of patients and include aspiration pneumonitis as well as oesophageal rupture. If the gastric balloon bursts or deflates, the oesophageal balloon may migrate into the oropharynx causing asphyxia. Ulceration of the lower oesophagus occurs due to prolonged or repeated use. The oesophageal tube should not be kept inflated for more than 24 hrs. and preferably for not more than 10 hrs.
- (6) Intravenous *infusion of vasopressin* at a rate of 0.1 to 0.4 μ m/c results in generalized vasoconstriction leading to diminished blood flow in the portal venous system. Control of bleeding can be achieved in upto 80% cases, but bleeding recurs in more than half after the Vasopressin is tapered and discontinued. Serious side effects include cardiac and gastro intestinal ischaemia, acute renal failure and hyponatremia. Concurrent use of venodilators such as nitroglycerine as an I/V infusion or isosorbide dinitrate S/L may enhance the effectiveness of Vasopressin and reduce complications.
- (7) *Somatostatin* and its analogue Octreotide act as direct splanchnic vasoconstrictors. Comparison of somatostatin and Octeotide and given in table 111. Somatostatin is given in dose of 250 mcg. Bolus followed by 250 mcg/hour infusion for 48-72 hrs. Maximum duration of treatment is 5 days. Side effects include transient episodes of vertigo, nausea and flushes. Orthostatic hypotension has been rarely reported; in the case, keep the patient supine during administration. Octreotide in dose of 25-30 mcg/hr is given as a continuous i.v. infusion for a maximum of five days. Side effects include local reactions like pain, a sensation of stinging, tingling 01. burning at the site of injection, with redness and swelling. (See table 3)

Table - 3 : Comparison of somatation with octreotide

PARAMETER	SOMATOSTATIN	OCTREOTIDE
Action on bleeding	well established ⁸	controversial ⁸
Spectrum of activity	broad ⁸	narrow ⁸
Half-life in normal human	1-2 min ⁷	90 min ⁷
Half-life in hepatic disease	1-2 min ⁸	240 min ⁸
Effect on portal pressure	quick reduction ⁸	no action
Hepatic blood flow		
Down regulation	no ⁹	yes ⁹
Transfusion requirement	low ⁹	high ⁹
Side effects	less ⁸	more ⁸

(8) *Emergency sclerotherapy* with absolute alcohol, ethoxysclerol, sodium tetra decyl sulfate, sodium mauruvate or ethanolamine eleate controls bleed in more than 90% cases. After acute sclerotherapy chronic injection of varices is done every 1-4 weeks till all varices are obliterated. Prophylactic sclerotherapy has no role in prevention of bleed. Side effects of sclerotherapy include transient effects like fever, dysphagia and chest pain. Mucosal ulceration may occur and result in further hemorrhage or stenosis. Endoscopic band ligation of varices is as effective as sclerotherapy

and is devoid of side effects of sclerotherapy.

(9) *Surgery* has a limited role in the management of patients with NCPF. The present day **indications** for surgery include:-

- i) Failure of sclerotherapy to control bleeding.
- ii) Bleeding from large gastroesophageal varices or isolated gastric varices which cannot be controlled by sclerotherapy.
- iii) Symptomatic hypersplenism spontaneous bleeding episodes requiring transfusion.

Non selective shunt surgery: The procedure decompresses the entire portal system and includes *end to side* and *side-to-side* portocaval and proximal splenorenal shunt.

Selective shunt surgery: This is done to decompress only the varices while maintaining blood flow to liver. This includes distal splenorenal shunt.

Non selective shunts are more likely to be complicated by *encephalopathy* than selective shunts. Emergency portal systemic non selective shunts may control acute hemorrhage but such surgery is usually used only as a last resort because early operative mortality is greater than 30%. Surgically created shunts effectively reduce the risk of recurrent hemorrhage, but the overall mortality of patients undergoing such surgery is comparable to medical therapy for control of bleed.

(10) *TIPS:- Transjugular intrahepatic portasystemic shunt* offers an alternative to shunt surgery. The main drawback is stenosis and occlusion of shunt over a period of months.

PREVENTION OF RECURRENCE OF BLEED

- 1) *β -blocker* propranolol in a dose sufficient to decrease the resting pulse rate by 25%.
- 2) *Chronic sclerotherapy:-* One absolute indication for sclerotherapy is no availability of vein for shunt surgery as revealed by SPV.
- 3) *Shunt Surgery :-* One absolute indication for shunt surgery is hypersplenism.

PROGNOSIS

The disease is benign and has a good long - term prognosis. Mean survival is 25 yrs. from time of diagnosis (5 yrs. for cirrhosis).

After successful eradication of varices a 2 yr. And 5 yr. survival (100%) has been observed. After splenorenal shunt surgery, a 5 yr. survival rate of 87% has been reported.

REFERENCES

1. Morris J.S Schmid M., Newman S., et al., Arsenic and non-cirrhotic portal hypertension: Gastroenterology, 1974;66:86-94.
2. Sama S.K., Bhargawa S., Gopinath N., et al., Non-cirrhotic portal fibrosis. Am. J. Med., 1971;51:160-9.
3. Nayyar A.K., Sharma B.K., Sarin, S.K., Broor S.L., Characterization of peripheral blood lymphocytes in patients with non-cirrhotic portal fibrosis- a comparison with cirrhosis and healthy controls. J. Gastroenterol hepatol, 1990.
4. Koshy A., Relationship between NCPF and EHO. In: Okuda K., Omata M., eds Idiopathic portal hypertension. Tokyo: University of Tokyo press, 1983:13-17.
5. Sarin S. K Nundy S., Subclinical encephalopathy after portasystemic shunts in patients with non-cirrhotic portal fibrosis. Liver, 1985;5, 142-6
6. Nayak N.C., Ramalingaswamy B., Obliterative portovenopathy of the liver. Arch. Pathol., 1969; 87:359-69.
7. Burroughs A.K. et al, Scand J Gastroenterol 1998;33 suppl 26:14-24.
- 8) Bosch J et al. Scand J Gastroenterol 1998 ; 33 suppl 226:14-24.
- 9) Avgerinous A. Digestion, 1998;59(Suppl 1): 1-22.
- 10) Sarin S.K., Nanda R., Gaur S.K., et al., Repeated endoscopic sclerotherapy for active variceal bleeding. Ann. Surg., 1985; 202: 708- 711.
11. Nundy S., Tandon B.N., The proximal lieno-renal shunt in the management of varices. In: Okuda K., Omata M., eds. Idiopathic portal hypertension, Tokyo: Univ. of Tokyo Press, 1983: 535-44.

With best Compliments from



We Impart Health to Life



CENTAUR PHARMACEUTICALS PVT. LTD.

CENTAUR HOUSE, Near Grand Hyatt,
Shantinagar, Vakola, Santacruz-East, Mumbai - 400 055
Tel. : 5649 9100 Email : centaur@centaurilab.com
Website : www.centaurpharma.com

makers of

Met@Z[®]
Metolazone 2.5 mg & 5 mg
Tablet

Losatrust[™]/H
Losartan 50 mg, Hydrochlorothiazide 12.5 mg Tablet

Preface[™]/H
Ramipril 2.5 mg , Hydrochlorothiazide 12.5 mg

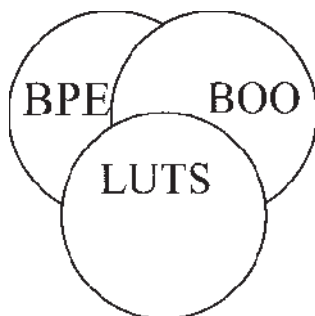
CAN BENIGN PROSTATIC HYPERPLASIA BE MANAGED BY PILLS? - OUR EXPERIENCE

N.K.Mohanty, Uday Pratap Singh, R. P.Arora, Nitin K. Sharma,
Department of Urology, V.M. Medical College & Safdarjang Hospital, New Delhi, India.

Abstract : This communication is to provide a critical overview of the currently available guidelines in management of benign prostatic hyperplasia & also to give the revolution of changes that has taken place in its management paradigm in the last four decades. Open prostatectomy was the only treatment modality available till 1970. Development of transurethral procedure by Nesbit in 1943 brought a total revolution in its management in 1970 till dates. Many other minimally invasive procedures have developed in the recent past using different sources of energy like laser, heat, radio frequency and ultrasound. Medical management for BPH using pills was dreamt till 1910 when α -adrenergic receptors were identified by Shapirio in 1967 with these recent developments, now a days, management of BPH has not only become very safe with low morbidity, no morbidity but also cost effective giving better quality of life to the patient.

INTRODUCTION

Until recently benign prostatic hyperplasia (BPH) was thought of as a relatively uncomplicated disease process, resulting from age related enlargement of the prostate gland. Current thought leaders view BPH as a syndrome in which BPE (Benign Prostate Enlargement), BOO (Bladder Outlet Obstruction) and LUTS (Lower Urinary Tract Symptoms) are inter related but distinct entities with possibly different etiologies and divergent natural histories. (Figure below)



Benign hyperplasia of the prostate (BPH) usually affects men after 40 years of age. It is the commonest disorder of ageing males worldwide, affecting one out of four men over 50 years of age. The prevalence is expected to increase as the mean age of the male population is increasing in our society and in years to come this malady will be a great health problem in ageing males of our society. Although 70% of men over 60 years of age will develop BPH, but only 35% of them may require surgical intervention for relief of their symptomatology. Therefore, there is a need for medical management of rest of BPH patients who are symptomatic. Again various co-morbid factors in the geriatric age group may be a contraindication for undergoing surgical treatment. This group would greatly benefit from medical management.

The weight of the prostate at birth is 1gm in weight. This gland undergoes first involution at the age of 14 years when man enters adulthood. From 14 years to 40 years of age the prostate growth is

slow as its main function remains as an accessory gland for sexual activity of the man. After 40 years of age when the peak sexual activity of man starts declining, serum testosterone level also falls, an imbalance occurs between serum testosterone and oestrogen resulting in uncontrolled enlargement of prostate gland. The size and the degree of growth vary from individual to individual depending on the stimulation of various growth factors like EGF (epidermal growth factor), FGF (fibroblast growth factor) and TGF (transition growth factor). The prevalence of BPH is 8% at the 4th decade of life, rises to 50% by 6th decade of life and 80% by 8th decade of life.

The concept of medical management of BPH came into focus after the identification of effect of α -adrenergic receptors at the bladder neck, prostate capsule, smooth muscle of prostate and prostatic urethra in 1970-75 when it was proved that stimulation of these receptors control the tonicity at the bladder neck & prostate resulting in obstruction to urinary flow i.e. the dynamic factor. Hence relaxation of these receptors by giving α -adrenergic antagonist will relax the tonicity at the bladder neck thereby releasing obstruction. Simultaneously it was proved that the increased volume of the prostate gland also results in obstruction at the bladder neck i.e. the static factor. Therefore, shrinkage of the prostate gland can be achieved by giving 5 α reductase inhibitors so that DHT (di-hydro testosterone) production from serum testosterone and androgens can be reduced thereby causing reduction in volume of prostate adenoma.

Age is the greatest prognostic factor for BPH. BPH decreases quality of life. Raised serum insulin, waist to hip ratio and coffee drinking increase incidence of BPH. Incidence of BPH is declining in developed countries but mortality is on rise in underdeveloped countries.

AUTHOR'S EXPERIENCE

The author in the last ten years has tried to establish the importance of medical management in BPH and herewith present his experience & research work with result chronologically.

The first α -selective α -adrenergic blocker available in Indian market was Terazosin in 1990. We conducted a trial using Terazosin 5mg once a day (in divided dose) for three months on BPH patients not having absolute indication for surgery but symptomatic of

Correspondence : Dr. N.K. Mohanty,
C-II/124, Moti Bagh-I, New Delhi – 110 021, India
e-mail : nayankm@yahoo.co.in

prostatism. These patients showed 50-55% improvement in their subjective and 40-45% improvement in their objective symptoms at the end of therapy but showed adverse side effects in the form of postural hypotension, dizziness, headache in 20% of patients and had symptoms returned once drug was stopped. (Paper published – Indian Journal of Urology, March 1998)

With the introduction of *Doxazocin* later in 1998 as a highly selective α -adrenergic blocker with a longer half life (22 hours) and gradual onset of action 2-6 hours we conducted a trial in 1999 using 4mg of *Doxazocin* once a day at night for three months. At the end of the therapy we recorded 50-55% subjective improvement and 60% in objective improvement with a decrease in the post residual urine volume by 21%. Though there was no significant improvement in symptoms score and flow rate as compared to *Terazocin* but the incidence of adverse side effect was comparatively much lower than *Terazocin*. In *Doxazocin* group, headache, dizziness and hypotension was seen in 10% only. (Paper published – Indian Journal of Urology, Sept. 2000).

Though medical management with above α -adrenergic blocker showed 50-55% improvement in symptomatology and flow rate but it did not bring satisfaction to the patient as was expected as patients continued to have lower irritative symptoms like urgency, frequency & nocturia.

In 2001, *Tamsulosin* a new uroselective α -adrenergic receptor antagonist was introduced for medical management of BPH. This salt has the advantage of being uroselective as it takes care of both the bladder outlet obstruction symptoms hesitancy, intermittency, terminal dribbling & weak stream and bladder instability symptoms like nocturia, frequency and urgency. Since it has a dual mode of action blocking not only α_{1a} but also α_1 responsible for bladder irritative symptoms.

We undertook a trial to study the safety & efficacy of *Tamsulosin* in management of BPH using a dose of 0.4mg once a day at night for three months. At the end of therapy there was 70-75% improvement in subjective symptoms score and 75-80% improvement in objective symptoms. Post residual urine volume decreased by 39% from baseline.

The adverse effect in the form of dizziness & headache was found in 7% of patients and less than 4% of patients had postural hypotension as compared to *Terazocin* & *Doxazocin* because the ratio of binding affinity for α_{1a} receptor to α_{1b} receptors was 29 times for *Tamsulosin* as compared to 1-2 times for *Terazocin*, *Doxazocin* & *Prazocin*, thereby making *Tamsulosin* a much safer drug. (Paper published – Indian Journal of Urology, Sept. 2003 & Annals of the College of Surgeons, Aug. 2003)

Since at present medical management is a well established modality of management of BPH for patients not having absolute indication for surgery, more and more geriatric males and males not suitable for surgery due to associated co-morbid factors are willing for medical management as the first line of treatment for their prostatism symptoms.

The MTOPS (Medical Therapy of Prostatic Symptoms Trial) study have established the use of two drugs – a uroselective α -blocker in combination with 5 α -reductase inhibitor (type I & type II) is very effective in management of BPH.

To give more benefit to the patients the author undertook another trial in 2003-04 using a combination of α -adrenergic blocker (*Tamsulosin* 0.4mg OD) and 5 α -reductase inhibitor (*Finasteride* 5mg OD) for six months. The result of this combination has proved to be most beneficial in improving the symptoms score, urinary obstruction and greatly reducing irritative symptoms and post residual urine volume as compared to all other previous trial therapy. Before starting this combination a baseline PSA is mandatory and periodic PSA estimation during course of therapy is recommended as 5 α -reductase inhibitor cause reduction in PSA. (Accepted for publication in Indian Journal of Urology 2004-05). The result of this study is very encouraging with regard to reduction in prostate size, post residual urine volume, improve IPS score, uroflow rate & decrease hesitancy time with the minimum adverse effect.

The author invariably faces one query while treating such patients. *How long can I continue with medical management?* The author is of the opinion to continue medical management on BPH patients as long as the patients do not develop absolute indication for surgery. In authors opinion retention of urine and back pressure changes of kidneys are the two only indications for surgery for BPH. At present the author has patients who are satisfied with medical management for more than five years.

DISCUSSION

Medical management with α -adrenergic antagonist and 5 α -reductase inhibitor as monotherapy or in combination is a well established modality of management of BPH patients not having absolute indication for surgery but symptomatic or having associated risk co-morbid factors as contraindication for surgery.

Selection of patients with periodic follow up should be meticulously done so that patient gets maximum benefits.

By doing so the author in the last ten years have not only prevented unnecessary prostate surgery or over-doing of prostate surgery in many patients of BPH but also has reduced the surgical morbidity & mortality rates from prostate surgery in the department apart from establishing medical management of BPH as a reality and there by giving better quality of life in a sizeable geriatric male population of our society.

Currently the author is involved in management of BPH with newer drug combination and phytotherapies. *Alfuzosin* and *Dutasteride* are newer drug on study trial with the author. *Lycopene* an antioxidant derived from tomatoes and guava have shown to reduce serum testosterone in human beings and causes apoptosis in prostate of rats in experimental study.

CONCLUSION

Medical management is now the first line treatment option for patients with BPH not having indication for surgery. In the past five years medical management for BPH has greatly reduced the incidence of surgery for prostate worldwide simultaneously reducing the mortality & morbidity incidence resulting from the same.

The author is of the firm opinion that 65-70% of patients with BPH not requiring surgical intervention greatly benefit from medical management as first line of treatment option for their prostatism.

A VISION FOR THE FUTURE HEALTH SYSTEM DEVELOPMENT

Dr. B.C. Ghosal

Retd. Regional Adviser (Health), World Health Organization, New Delhi, India

The world is in transition-actually in a great hurry to move on, Recent developments have made people and machines move faster than ever before; values are shifting. With the rapid changes in political, socio-economic and environmental scenarios unfolding right before our blurry eyes, a clear vision for the future becomes all the more necessary, however difficult the task may be.

The 21st Century will see many more remarkable breakthroughs in science and technologies, bringing the World closer in one way and making it more disparate in another. The development field itself will be riddled with conflicts, Will techno-friendly advances also be eco-friendly? Will economic reforms also benefit the economically depressed? Will the balance between materialistic and spiritual values tilt in favour of the former or latter? Such balances, in our opinion, will be influenced by many forces. For example greed for money or power will be balanced by the compulsions for equity, waste by conservation and violence by peace. Health too, will hang in the balance - delicately positioned between the haves and have-nots, between abundance and want, between access and deprivation. Which way the balance will tilt will depend on the way we want it to tilt. In the vision that I have of the future

- I see ethics prevailing, to ensure health as a fundamental right of every citizen of the world, regardless of race, colour, economic or social status. The near-impossible survival conditions for a significant proportion of the world's population in deprived pockets of developing countries must begin to touch the conscience of the rich.

- I see people as central to this movement. A growing disenchantment with political systems riddled with nepotism and corruption has already begun. Enlightenment will grow, literacy levels will improve and communication highways will increasingly help in exposing the 'games' being played internationally and nationally by small elitist groups that aim to preserve, even widen present-day disparities. Government structures developed over the last half a century will not change easily. In fact, as the population grows, as people begin to understand how the determinants of health can be controlled; as men and women more closely see the strong relationship between health and quality of life, responsibility for health will move from the centralized health sectors more peripherally towards the community. Through nongovernmental organizations, the media and community based groups, people's voices will be heard. Their demands will be expressed loudly and more boldly. Collective expression will encourage collective leadership and, action. Coalition and collaboration will, hopefully, replace confrontation.

- As far as the rich, the privileged, the well-endowed are concerned, humanitarian concerns will surface for a variety of reasons. This will lead to more tolerance, more concern for poor neighbours and friends and more generosity being extended for the promotion of equity.

- Harsh realities will shake complacency. Communicable diseases have never respected national boundaries. Their movements across the globe are even faster today. They have also shown a healthy disrespect for class,

or country. The HIV/AIDS pandemic is a stern warning to all those who believed that this disease is somebody else's problem, not theirs.

- The role of the government health sector in meeting the new situations arising out of enlightenment and conscientiousness will also become more relevant. Health structures as such may not change significantly but strategies and approaches will. This will help to bring health closer to the people through greater decentralization, viable district health systems and, most importantly, a willingness and motivation to work with other than the health sector to create supportive conditions for health.

- With growing realization of the importance of health for long-term development gains, planners and policy makers will begin to see the wisdom of placing health high on the political agenda. Development sectors will increasingly appreciate the relationship between health and development.

- The people's perspective to development will be recognized, For people, it does not matter who provides them what they need. What matters is that they get what is required to live a life of dignity and that their basic needs are met at a price they can afford. They will demand opportunities for growth and upward mobility to improve the quality of their lives. Alliances will be built between various partners, providers and receivers

In the vision of the future I also see:

- health partnerships forming, growing and maturing as strong holds for health action
- government and people appreciating the powerful contribution that health can make to social cohesion and quality of life,
- government protecting at all costs and the underserved and poor and providing, a high quality of health care, rationalizing high technology applications, opening up health issues for national and international debate
- parliamentarians, community leaders, religious groups, environmental forums and other opinion leaders making health an important part of their mission and work various UN agencies and world bodies working more closely together- for health concerns with a solidarity of purpose
- various UN agencies and world bodies working more closely for health concerns
- the private sector and nongovernmental organizations joining hands with government and with the people in the pursuit of common goals;

These are glimpses of a vision for future health: (i) framed by the values I hold most dear - *solidarity, cohesion, harmony* and *peace*. (ii) inspired by the binding power partnerships hold for health; (iii) sparked by the dedication and commitment shown by member countries in their pursuit for health for all; (iv) created by a strong and growing conviction that as we enter the 21st century, partnerships for health could well become the turning point for health development in the South-East Asia Region.

Correspondence : Dr. B.C. Ghosal,

mobile- 9350814238

With Best Compliments

from:

UNITED BIOTECH PVT. LTD.

makers of :

Tablet AMINESS-N

(Dialysis - sparing essential amino acid)

For queries:

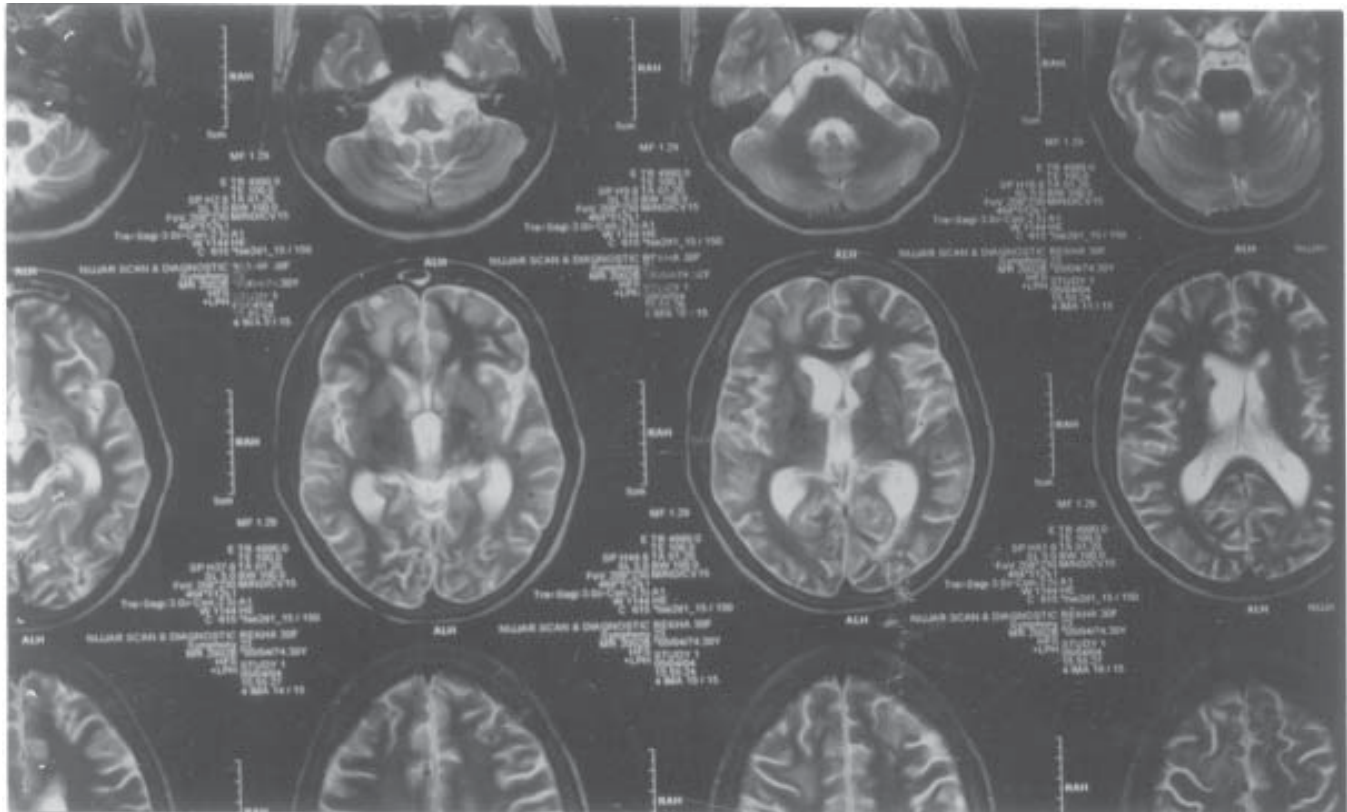
Contact **Mr Deepak Arora**, 9811231278

MULTIPLE NEUROCYSTICERCOSIS IN ALL 3 STAGES

N.S. Neki

Department of Medicine, GGS Medical College, Faridkot, Punjab, India

A 30 years female presented with tonic –clonic convulsions suggestive of grand mal type of epilepsy. Subsequently she got her MRI brain done which revealed distinctly seen multiple neurocysticercosis lesions in vesicular, colloidal vesicular and granular nodular stages along with ventriculomegaly (third and fourth ventricles dilated – See photograph). **Vesicular** is first stage in which larvum appears as a round CSF line ecyst with a mural nodule that represents scolex, rarely associated with edema and contrast enhancement. **Colloidal vesicular stage** is the second stage in which larvum dies, begins to degenerate thereby releasing metabolic products resulting in edema and cyst wall enhancement. Ring like enhancement is seen in 2/3rd of cases. **Granular nodular stage** is next stage in which cyst retracts with calcification of scolex and thickening of cyst. Occasionally target or Bull's eye appearance is seen with calcified scolex in the centre of mass. Residual cyst which is isointense to brain, nodular or microsing enhancement is common at this stage suggesting granuloma. Surrounding edema is still present and enhancement following contrast persists. In **nodular calcified stage** (final stage), a small calcified nodule without mass effect or enhancement is not observed or MRI. Although solitary cyst is more common, but the presence of all the 3 stages in the same patient at the same time is not commonly seen. The patient was put on carbamazepine and albendazole to which she responded satisfactorily and is now on regular followup.



Correspondence : Professor N.S. Neki

E-mail : drmsneki_123@yahoo.com

The most comprehensive range of Nephrologicals

TRANSPLANTATION

siromus
The Non-Nephrotoxic Immunosuppressant

Tacrolimus
Tacromus
The Superior CNI for a better tomorrow

Azathioprine 50 mg
Zymurine
The "FIVE" rupee Azathioprine

Renal Specialist

Committed to
a better & brighter tomorrow

In service of Medical Profession

**Zydus
Biogen**
We, Better Life

'Zydus Tower', Satellite Cross Roads, Ahmedabad 380 015, India.
Phone : +91-79-26868100 (20Lines) Fax : +91-79-268 68 453
www.zyduscadila.com

CHRONIC RENAL FAILURE

Erythropoietin
ZYROP 1K|2K
3K|4K
The World's Only Thermostable EPO

Nexiron
Iron Sucrose Injection
The Safest Next Generation Iron

Bandroner Hydrochloride 400 mg / 800 mg
Zynagel
The *non-calcium* phosphate binder

PHOSTAT
Calcium Resorb 600 mg
The Ideal Phosphate Binder

Calcitriol 0.25 mcg.
Calcit
The Most Active Vitamin D₃ Analogue

K-BIND
Calcium Polystyrene
Sulphonate
The No.1 Potassium Binder

Zavinex
INTERFERON ALFA 2B
The Unique Interferon with TSA

“AN INTEGRATED APPROACH IN THE MANAGEMENT OF PERIPHERAL VASCULAR DISEASES”

EDITORIAL

PERIPHERAL VASCULAR DISEASES IN THE 21ST CENTURY

It is indeed a pleasure and great honour for me, to be writing for the JIMSA as a guest editor. The concept of Vascular Surgery as a stand-alone speciality has not progressed as rapidly in India and the sub-continent, as it has in the United States or Europe.

Peripheral vascular surgery started as an off-shoot from cardio-thoracic surgery way back in the 1930s. As an entity it has gone from strength to strength since then. Today we can confidently say that, there exists a vibrant peripheral vascular surgery training program in most countries, with India also trying to catch up.

The peripheral vascular surgeon has given way to the concept of a vascular specialist in the new millennium. As we understand more and more regarding the patho-physiology and natural history of peripheral vascular diseases, we hope to use a combined approach of vascular medicine, surgery, endovascular and complimentary techniques in the treatment of these conditions. Times are changing fast and the future is bound to bring in rapid and far reaching changes in vascular care, therefore it is important that we integrate our knowledge, skills and resources to provide the state of the art care for our patients.

Apart from giving an overview of what is evidence based in a modern vascular practice, it has been my endeavor to promote an integrated approach to patient care. I am grateful to Dr. Vinod Sharma, Dr. V.K.Gujral , Dr. Amar Pal Singh Suri and Dr. Deepak Chaudhary, my colleagues at the Centre for Integrated Care for Vascular Diseases, at the National Heart Institute, in New Delhi for joining me in presenting a holistic view of management of vascular diseases.



Guest Editor
Dr. Ashok Gupta

*Senior Vascular and Endovascular Surgeon,
National Heart Institute, East of Kailash, New Delhi, India*

Hopace
Ramipril 1.25 / 2.5 / 5 / 10 mg Capsules

Hopace-H5

Ramipril 5 mg + Hydrochlorothiazide 12.5 mg capsules

Torsinex
Torsemide 10 / 20 / 100 mg tablets / Injection 10 mg / ml

VASCULAR, SURGICAL & PERCUTANEOUS INTERVENTIONS – A BALANCING ACT

Ashok Gupta

Senior Consultant, Vascular and Endovascular Surgeon, National Heart Institute, East of Kailash, New Delhi, India

Abstract: Peripheral vascular diseases (PVD) encompass an entire gamut of conditions related to arteries and veins of the body. This niche speciality has come a long way since its origins in the 1950's. Today, it is perhaps the only speciality where the barriers between surgery, percutaneous interventions and vascular medicine are becoming blurred and the providers of care are becoming multi-skilled to provide the patients with the most appropriate care under evidence based medicine. This article touches on the aspects of a multi-specialized approach to vascular interventions, where time tested results of standard surgical procedures are now being matched by percutaneous techniques in many areas. It also highlights the importance of good patient selection for a particular procedure rather than having a single point program of treatment for all patients suffering from a particular condition. Treatment of carotid stenotic disease is changing, surgical results have been excellent from most reputed centres. However a subset of patients may be suitable for percutaneous techniques particularly with modern imaging and hardware at our disposal. Percutaneous approach to the thoracic aorta is novel and extremely promising; it may become the approach of choice in times to come. Treatment of aneurysmal as well as stenotic disease of the abdominal aorta has changed as well. The clinical evidence in favour of percutaneous techniques, in well selected patients is mounting; surgery as well as stent-grafting will almost certainly have a role in treatment in the future. Infra-inguinal vascular disease has also become amenable to treatment by percutaneous techniques. Again patient selection seems to be the key to success. In conclusion, percutaneous techniques are here to stay and are the way forward as well, the key factor being good training and committing our practices to evidence based medicine.

INTRODUCTION

Surgical treatment in its entire range, for a particular condition in the body, undergoes change from time to time. This was proven when the laparoscopic revolution overtook open surgery in the last decade of the previous millennium.

Vascular surgery is a highly specialized field, requiring good training & experience. However, the era of endo vascular treatment is here and it is for the surgeons to understand, appreciate and actively join others to become endovascular specialists.

CAROTID INTERVENTIONS

Nowhere else has the usage of endovascular techniques caused more confusion than in the carotid circulation. The carotids remain a victim of the 'oculo-stenotic' reflexes of most interventionists. The results of surgery in indicated cases of carotid endarterectomy (both symptomatic and asymptomatic), have been established over the last fifty years or so^{1,2}. First reported cases of carotid angioplasty came way back in 1988-89, way before a safe protection device or durable stent was designed or conceived^{3,4}. However carotid angioplasty with stenting (CAS), with modern hardware is becoming more acceptable with the providers and the patients. Much of this enthusiasm for CAS has been fostered by nonsurgeons.^{7,8}

Indications for Carotid Angioplasty/ Stenting in High-Risk Patients

1. Severe chronic obstructive pulmonary disease (a) requiring home oxygen (b) FEV-1 < 20% predicted (forced expiratory volume one second)
2. Severe chronic renal insufficiency (a) Serum creatinine > 3.0 mg% (b) Currently on dialysis
3. Prior carotid endarterectomy (CEA) (restenosis); contralateral vocal cord paralysis
4. Surgically inaccessible lesions (a) at or above the 2nd cervical

vertebra (b) inferior to the clavicle

5. Radiation-induced carotid stenosis

6. Prior ipsilateral radical neck dissection

Limitations/Contraindications to Carotid Angioplasty/ Stenting

- Inability to obtain femoral artery access
- Unfavorable aortic arch anatomy
- Severe tortuosity of the common or internal carotid arteries
- Severely calcified / undilatable stenoses
- Lesions containing fresh thrombus
- Extensive stenoses (>2cm)
- Critical (99%) stenoses ("string sign")
- Lesions adjacent to carotid artery aneurysms
- Contrast-related issues
- Chronic renal insufficiency
- Previous life-threatening contrast reaction
- Preload dependent states—severe aortic valvular stenosis

In conclusion, CAS is an evolving technique that has significantly improved our ability to treat patients with carotid bifurcation disease, especially those at high risk for carotid endarterectomy. It is currently approved for use in high-risk patients, as defined by clinical trials. As with CEA, proper patient selection and attention to procedural detail are imperative to produce exemplary results.

The raging controversy in this field remains good patient selection between surgery and stenting as well as lesions that need to be treated. To answer these basic questions, it is important that the interventionist is well read and informed regarding the natural history of carotid stenotic disease as well as the evidence based information regarding need for intervention. This is of course, essentially in the interest of the patient who is our primary concern.

THORACIC ENDOGRAFTING

Since the first report of endovascular therapy for descending thoracic

aortic pathology in 1994 by Dake et al, the advent of commercially available devices has been relatively slow. This is primarily due to the relatively lower volume of thoracic aortic aneurysms as compared with infra-renal aortic aneurysms. Technical and anatomic challenges in thoracic endografting, such as proximity of the great vessels and tortuosity around the arch, also pose a challenge. In addition, a larger device profile and hostile hemodynamic forces complicate the technical aspect of the deployment procedure.^{7,8}

Surgical repair of thoracic aortic aneurysms (TAA) is demanding both for the surgeon and the patient. The experience and expertise of the surgical team including the anesthesiologist and the post operative care for patients undergoing TAA repair, is crucial in producing successful results. This fact along with the morbidities involved, including that of ischemic injury to the spinal cord has contributed to a large extent in compelling providers to look for alternative means of treating this difficult problem.

Endovascular technology is expected to result in more pronounced benefits in the treatment of aneurismal disease in the chest than in the abdomen because of the higher morbidity of thoracic aortic procedures. Peri-operative mortality and morbidity, particularly with respect to SCI and cardiopulmonary complications, have been noticeably lower than those observed in open surgical repairs. These endografts have been applied to a variety of clinical settings beyond aneurismal disease, including aortic dissections, transections, and most other pathologies of the descending thoracic aorta.⁹

No device-specific results are yet available. All devices tested to date carry a large profile, ranging from 20F to 25F, and require a large access vessel for introduction. Access to the thoracic aorta continues to be a main source of complications. Almost 15% of the patients required access proximal to the femoral artery. The increased prevalence of TAA in women compared with abdominal aneurysms clearly exacerbates this problem.¹⁰

Although the incidence of spinal ischemic injury was low and less than that reported with open repair, it does occur with thoracic endograft repair. Although previous aortic surgery and coverage of long segments of aorta have been reported to portend a higher risk of paraplegia with endovascular repair of TAA.^{10,11} To conclude, endovascular treatment may become more acceptable for higher-risk patients, with TAA and new trials are expected to expand indications of this technique. The hope is of a viable alternative to surgery with consistent results in the near future.

ENDOGRAFTING FOR ABDOMINAL AORTIC ANEURYSMS

Surgical repair of an infra-renal aortic aneurysm was first done by Matas in the early 1900s. He repaired the aneurysm from within calling the technique as endo-aneurysmorrhaphy.

In the decades that followed with the advancement of anesthetic techniques and post operative care the mortality associated with this surgery has steadily declined, to the current figure of 3% for elective repairs.¹⁶ Most if not all, the large surgical invasion that the patient's body has to undergo to have the repair done. As would be expected majority of these people are in their seventies or above.

A need for a more minimally invasive procedure, which would produce similar results, was felt since the mid eighties. Credit must be given to pioneers such as Parodi et al. who dared to attempt endovascular management of abdominal aortic aneurysms with most

primitive hardware and imaging techniques in the early nineties¹³. Endovascular repair of abdominal aortic aneurysm was introduced in the early 1990s as a minimal access alternative to conventional repair. The first stent-grafts implanted were homemade devices and served to establish the feasibility of the technique. We are today in the midst of a quiet revolution, where we find minimally invasive and minimal access techniques have gained credibility, with suitable support from the industry, and a teamwork approach from the providers.

To be effective, a stent-graft needs to maintain fixation, hemodynamic seal, mechanical integrity, and patency over many years. However, a stent-graft implanted in an aortic aneurysm is subjected to several adverse factors that tend to compromise these functions.^{14,15}

The EUROSTAR comparative analysis is indeed one of the most comprehensive multicenter registry of its kind.

EUROSTAR Project

EUROSTAR (European Collaborators on Stent-graft Techniques for Abdominal Aortic Aneurysm Repair) project was launched in 1996 in response to the introduction of the new technique of repairing aortic aneurysms. The project was designed as a voluntary pan-European multicenter registry to allow collection of as much data as possible in as short a time as possible for expeditious scientific evaluation of this technique.

Patient Sample : During the observation period, 6787 patients (6341 men; mean age 72 years, range 28–100) from 181 hospitals (Appendix) in 19 countries were included in this analysis.

Statistical Analyses: The primary aim of the analysis was to compare patients who were treated by the different stent-graft models.

Adverse events during follow-up were examined to characterize the performance of different models. In order to render this comparison quantitative, annual incidence rates (IRann: number of events/person-years at risk) for each complication were calculated for the entire cohort and for each stent-graft model.

RESULTS

Endoleaks Device-related endoleaks were observed at 1 month in 10% (n=673) of the 6787 patients. Overall, the annual incidence rate was 6.2%.

Change in Aneurysm Diameter Aneurysm diameter increased in 6%; the annual incidence was 3.3%, ranging from 2.2% to 4.3%. Shrinkage of the aneurysm diameter occurred in 5 times as many patients (30%, n=2031). The overall annual incidence rate was 22.7%.

Migration: Graft migration was observed in 5% (n=323). The annual incidence rate, which was 2.8% overall

Kinking: Stent-graft kinking occurred in 4% (n=257) of the patients. Overall, the annual incidence rate of kinking was 2.3%.

Occlusion : Stent-graft occlusion was also reported in 62% lower in patients with a Ze-5% (n=367) of the patients

Reinterventions: Conversion to open repair was performed in 3% (n=234) of all patients. Of these, 76 conversions were performed within 30 days of the initial operation. The annual incidence for conversion was 2.0% overall.

One or more secondary interventions were necessary in 11% (n=771) of the patients. Although the eurostar study, had its share of

Table: Annual Number of Registered Stent-Graft Implantations

	Total	1995	1996	1997	1998	1999	2000	2001	2002	2003
AneuRx	999 (15%)	—	4	89	265	273	205	90	49	24
EVT/Ancure	176 (3%)	11	10	41	30	34	16	6	23	5
Excluder	808 (12%)	—	—	—	29	90	108	153	190	238
Stentor	308 (5%)	165	143	—	—	—	—	—	—	—
Talent	1579 (23%)	—	9	60	101	168	223	282	306	430
Vanguard	929 (14%)	—	89	372	304	149	15	—	—	—
Zenith	1988 (29%)	—	—	—	15	159	317	483	487	527
Totals	6787	176	255	562	744	873	884	1014	1055	1224

limitations, it has provided us with objective evidence that endografting for aortic aneurysms, is safe and can be performed with acceptably low rate of complications and mortality.

With the newer generation devices on smaller sized delivery systems, the technique is set to become more attractive both to the patients and operators. On the basis of this analysis, one can safely hope to have wider usage of stent-grafting for AAAs. There will perhaps always remain a subset of patients in whom a surgical repair would be a more suitable and therefore the decision regarding patient selection must involve people who have intimate knowledge regarding advantages and limitations of both these techniques.

INFRA – INGUINAL ENDOVASCULAR INTERVENTIONS

Surgical treatment of infra-inguinal arterial disease remains the gold standard even today. However a definite shift towards minimal access and percutaneous techniques is taking place in most centers around the world. The TASC (Transatlantic Inter-Society Consensus) recommendations have been modified and as in other blood vessels, the hardware has improved by leaps & bounds to make it more acceptable, durable and user friendly. Almost all infra-inguinal lesions from high grade symptomatic stenosis to occlusive disease have become approachable by endovascular means. There are a few studies that support the usage of modern stent grafts in the short and medium term (upto four years) in the superficial femoral artery (SFA), results being comparable to those of surgical bypasses.¹⁶

Usage of stent grafts in popliteal aneurysms, particularly behind the knee, is controversial, but is gaining support as technology advances further. Popliteal artery aneurysms (PAA) account for the most frequently seen peripheral aneurysms. They are potentially dangerous, with a 5-year cumulative risk for complications of 68%. The most common complications are acute thrombosis, with occlusion of the aneurysm, and distal^{17,18} embolization.

Open surgical treatment with a venous bypass graft is still the treatment of choice for most surgeons.

Advantages of the endovascular treatment include the minimally invasive character of the procedure, with only a small incision in the

groin, minimal morbidity, and a shorter operation time and hospital stay. A particular problem associated with this technique is that the stent graft crosses the knee joint. Repetitive stress on the device in this bending zone may lead to complications, including kinking, fracture of the stent-graft material, and occlusion. The newer generation of stent grafts address the problems of the tortuous course of the SFA and the need to maintain integrity, when deployed behind a joint.¹⁹ Endovascular management of focal lesions in the aorto-iliac segment is standard procedure now, but once again, it is worth mentioning that the wire may not be the best approach in all patients with these lesions.

CONCLUSION

A few facts emerge as an overall conclusion of this article. Firstly vascular surgery has emerged as a stand alone specialty and endovascular techniques are an integral extension of our field. The future will belong to groups of providers who are capable of working together and come up with complete treatment plans for vascular patients. The vascular specialists of the future will need to have in-depth knowledge on surgical, percutaneous and evidence based techniques, if our patients are to be offered treatments that meet the international standards.

REFERENCE

1. North American Symptomatic Carotid Endarterectomy Trial Collaborators: Beneficial effect of carotid endarterectomy in symptomatic patients with high-grade carotid stenosis. *N Engl J Med* 325:445-453, 1991
2. Executive Committee for the Asymptomatic Carotid Atherosclerosis Study: Endarterectomy for asymptomatic carotid artery stenosis. *JAMA* 273:1421-1428, 1995
3. Gruntzig A: Transluminal dilatation of coronary artery stenosis. *Lancet* 1(8058):263, 1978
4. Kerber CW, Cromwell LD, Loehnd OL: Catheter dilatation of proximal carotid stenosis during distal bifurcation endarterectomy. *AJNR Am J Neuroradiol* 11:348-349, 1980
5. Yadav JS, Roubin GS, Iyer S, et al: Elective stenting of the extracranial carotid arteries. *Circulation* 95:376-381, 1997
6. Jordan WD, Schroeder BS, Fisher WK, McDowell HA: A comparison of angioplasty with stenting with endarterectomy for the treatment of carotid artery stenosis. *Ann Vasc Surg* 11:2-8, 1997
7. Dake MD, Miller DC, Semba CP, Mitchell RS, Walker PJ, Liddell RP: Transluminal placement of endovascular stent-grafts for the treatment of descending thoracic aortic aneurysms. *N Engl J Med* 1994; 331:1729-34.
8. Duebener LF, Lorenzen P, Richardt G, Misfeld M, Notzold A, Hartmann F, et al. Emergency endovascular stent-grafting for life-threatening acute type B aortic dissections. *Ann Thorac Surg* 2004;78:1261-6.
9. Amabile P, Collart F, Gariboldi V, Rollet G, Bartoli JM, Piquet P. Surgical versus endovascular treatment of traumatic thoracic aortic rupture. *J Vasc Surg* 2004;40:873-9.
10. Sacks D, Marinelli DL, Martin LG, Spies JB. Reporting standards for clinical evaluation of new peripheral arterial revascularization devices. Technology Assessment Committee. *J Vasc Interv Radiol* 1997;8:137-49.
11. Makaroun MS, Dillavou ED, Kee ST, Sicard G, Chaikof E, Bavaria J, et al. Endovascular treatment of thoracic aortic aneurysms: results of the phase II multi-center trial of the GORETAG thoracic endoprosthesis. *J Vasc Surg* 2005;41:1-9.
12. Chuter TA, Green RM, Ouriel K, et al. Transfemoral endovascular aortic graft placement. *J Vasc Surg* 1993;18:185-197.
13. Zarins CK, White RA, Schwarten D, et al. AneuRx stent graft versus open surgical repair of abdominal aortic aneurysms: multicenter prospective clinical trial. *J Vasc Surg* 1999;29: 292-308.
14. Bush RL, Najibi S, Lin PH, et al. Early experience with the bifurcated Excluder endoprosthesis for treatment of the abdominal aortic aneurysm. *J Vasc Surg* 2001;33:497-502.
15. Criado FJ, Wilson EP, Fairman RM, et al. Up-date on the Talent aortic stent-graft: a preliminary report from United States phase I and II trials. *J Vasc Surg* 2001;33:S146-149.
16. Dawson I, Sie RB, van Bockel JH. Atherosclerotic popliteal aneurysm. *Br J Surg* 1997; 84:293-9.
17. Carpenter JP, Barker CF, Roberts B, Berkowitz HD, Lusk EJ, Perloff LJ. Popliteal artery aneurysms: current management and outcome. *J Vasc Surg* 1994; 19:65-73.
18. Shortell CK, DeWeese JA, Ouriel K, Green RM. Popliteal artery aneurysms: a 25-year surgical experience. *J Vasc Surg* 1991; 14:771-9.
19. Galland RB, Magee TR. Management of popliteal aneurysm. *Br J Surg* 2002; 89:1382-85.

DIABETIC FOOT CARE

Dr. AMAR PAL SINGH SURI

Foot Care Specialist, National Heart Institute, East of Kailish, New Delhi, India

Abstract : Diabetes is a serious chronic disease. In 2003 the global prevalence of diabetes was estimated at 194 million. This figure is predicted to reach 333 million by 2025 as a consequence of longer life expectancy, sedentary lifestyle and changing dietary patterns. This rise is likely to bring a proportional increase in the numbers of people with diabetes complications, including problems of the foot. Without action, more amputations are likely. 40-70% of all lower extremity amputations, are related to diabetes. 85% of diabetes-related amputations are preceded by foot ulcers. A co-ordinated foot-care strategy can reduce amputation rates by between 49% and 85%. This will require: (a) prevention; (b) multi-disciplinary treatment of foot ulcers; (c) appropriate organization; (d) close monitoring; (e) education of people with diabetes and healthcare professionals

INTRODUCTION

More than 190 million people in the world and 38 million in India have diabetes mellitus and too many of these patients suffer from diabetic foot disease, which may eventually lead to a lower limb amputation. Foot complications are one of the most serious and costly complications of diabetes. Foot disorders are a major source of morbidity and a leading cause of hospitalization for persons with diabetes mellitus. Foot ulcers and amputations are a major cause of morbidity and disability for people with diabetes. Approximately 15% of patients with diabetes will have an ulcer and 50% of patients will have diabetic peripheral neuropathy in their lifetime. Diabetes is one of the most common causes of lower limb amputation in our country; there are about 1-lakh diabetes-related foot amputations per year. The early recognition and management of risk factors for diabetic foot disease can prevent these adverse outcomes.

OBJECTIVES OF DIABETIC FOOTCARE

The main objectives of diagnosis and treatment of diabetic foot squel is around maintaining the patient ambulatory, productive member of the society. This may require the expertise of many different specialists on the diabetic foot care team.

EPIDEMIOLOGY OF DIABETIC FOOT

Three major pedal complications of diabetes are: (i) foot ulcers, (ii) foot infections and, (iii) Charcots foot; most common being foot ulcer. It is estimated that 15% of patients with diabetes will develop a foot ulcer. Several reports from population-based studies indicate an annual incidence for diabetic foot ulcers of 2-3%. About 20% of patients with foot ulcers subsequently require an amputation. While most ulcers can be successfully treated in the clinic or outpatient setting, infected and/or ischaemic foot ulcers are a major cause for diabetes related hospitalization.

RISK IDENTIFICATION

Risk identification is fundamental for effective preventive management of the diabetic foot disease. The risk of development of diabetic ulcers is increased in people who had diabetes > 10 years, are male, have poor glucose control or have cardiovascular, eye, or renal complications. The most important risk factors for ulceration are: (i) peripheral sensory neuropathy, (ii) peripheral vascular disease, (iii) structural foot deformity, limited joint mobility, (iv) ill fitting shoes, increased pressure- callus, erythema, (v) history of prior ulcers or amputation, (vi) trauma, high sugars, old age.

FOOT EXAMINATION

Every diabetic should get a thorough foot examination once a year from the Podiatrist (foot specialist). This examination includes an assessment of protective sensation, vascular status of feet, foot biomechanics, and high-pressure areas like callus and skin condition. The presence of erythema (redness), warmth, or callus formation indicates areas of tissue damage with impending breakdown. Bony deformity in feet, limited joint mobility and problems with gait and balance should be assessed.

Do's: (i) Close look, at the top and bottom of the feet, use a mirror or ask a family member for help; (ii) Check for red spots, bruises, cuts, swelling or cracks; don't forget to feel under and between the toes; (iii) Wash the feet every day with warm-not hot water and a mild soap; dry between the toes, if skin between the toes is wet and soggy (macerated), clean with spirit using cotton and apply antifungal powder; if the foot skin is dry, apply lanolin, urea base cream; (iv) Wear good fitting, soft shoes and thick, soft socks; (v) Cut your toe nails straight across and file the edges, this is to prevent ingrown toe nails; (vi) One should always avoid injuries on the feet by wearing sleepers or shoes all time.

Don'ts: (i) Do not use hot water bottles or heating pads on your feet as they can cause skin burns in someone with diminished sensation. (ii) Never cut a corn or callus with a blade or use a corn pads as they contain salicylic acid. (iii) Don't wear tight or torn shoes and tight socks.

PREVENTION OF FOOT PROBLEMS

The development of neuropathy or loss of sensation can be delayed significantly by maintaining good sugar control. Smoking should be stopped to reduce the risk of vascular complications and gangrene of the foot. People with neuropathy or high planter pressure (warmth, erythema or callus) should use well-cushioned shoes that redistribute the pressure. Callus can be debrided with a scalpel by a foot specialist only and not by self. Diabetic people with bony deformity (hammertoes, bunions) should wear extra wide shoes or with high toe box. Any injury or infection in a diabetic foot is a direct threat to the leg and should be treated promptly and aggressively.

Management of Foot Ulceration: Essentials are: (a) early control of infection; (b) maintenance of blood circulation; (c) regular debridement; (d) proper offloading.

Patient Education Patients with diabetes and high-risk foot conditions should be educated regarding the risk factors and their appropriate management. They should understand the implications of the loss of sensation in the feet, the importance of foot monitoring on a daily basis, proper foot care including nail and skin care, and the selection of proper footwear. Patients with neuropathy should always break in new shoes gradually to minimize the formation of injuries or ulcers. *Smoking cessation* is mandatory for diabetics. Proper education of the patients and good foot care team is necessary for reducing the number of amputations and improving the quality of foot care in our country.

RECOMMENDED READING

1. Kolte, M.L., Nielsen, B., Dolmer, M. Exsudat-management mit silberhaltigen Verbanden. Poster presented at the 7th conference of the Deutsche Gesellschaft für Wundheilung und Wundbehandlung (DGfW), Augsburg, Germany, 2003
2. Kolte, M.L., IARSEN-jOCHUMSEN, U., Nielsen, B. eXUDATE management of silver containing dressings. Poster presented at the 12th conference of the European Wound Management Association (EWMA), Granada, Spain, 2002.
3. White, R. (2001); British Journal of Nursing, The Silver supplement Part One, p.3-8
4. Lasdown, A.B.G et al. (2003); J of Wound Care, Vol 12(6)
5. Serup, Jergen, MD, Ph.D., A double-blind Comparison of two creams Containing Urea as the Active Ingredient, Published in Acta Derm Venereol, Suppl, 177, 34-38, 1992.

PULMONARY EMBOLISM - A PULMONOLOGIST'S PERSPECTIVE

DEEPAK CHAUDHARY

Senior Consultant Physician, National Heart Institute, East of Kailish, New Delhi, India

Abstract: Pulmonary embolism is an extremely common and lethal condition. It occurs when an artery in the pulmonary vasculature becomes blocked. Blockage is caused by one or more blood clots that travel to the lungs from another part of the body. Most of these blood clots originate in the legs, but they can also form in the arm veins, the right side of the heart or even at the tip of the catheter placed in the vein. A good clinician actively seeks the diagnosis as soon as any suspicion of pulmonary embolism is warranted. Prompt diagnosis and treatment can dramatically reduce the mortality and morbidity of the disease. Unfortunately the diagnosis is missed more often than it is made, because pulmonary embolism often causes only vague and nonspecific symptoms. It is a leading cause of hospital deaths and an increasing threat to passengers on long airplane flights. But a few simple measures can go a long way towards preventing pulmonary embolism. Immediate full anticoagulation is mandatory for all patients with suspected DVT or pulmonary embolism because effective anticoagulation with heparin reduces the mortality rate of PE from 30% to less than 10%. Anti coagulation is essential but anticoagulation alone does not guarantee a successful outcome. DVT and PE may recur or extend despite full and effective heparin anticoagulation.

INTRODUCTION

Pulmonary embolism (PE) is an extremely common and highly lethal condition that is a leading cause of death in all age groups. It is caused by sudden blockage in a lung artery, usually due to a blood clot that travelled to the lung from the leg. A clot that forms in one part of the body and travels in the bloodstream to another part of the body is called an embolus. In most cases, pulmonary embolism is a complication of a condition called deep vein thrombosis (DVT). In DVT, blood clots form in the deep veins of the body, most often in the legs, these clots can break free, travel to the lungs and cause pulmonary embolism.

Thrombosis in the veins is triggered by venostasis, hypercoagulability and vessel wall inflammation. These three underlying causes are known as the Virchow triad.

Although DVT starts in the calf veins, it has propagated above the knee in 87% of symptomatic patients before the diagnosis is made. Studies suggest that nearly every patient with thrombus in the upper leg or thigh will have a PE if a sensitive enough test is done to look for it. Thrombus in the popliteal segment of the femoral vein is the cause of PE in more than 60% of cases. Fatal PE often result from thrombus that originates in the axillary or subclavian veins or indwelling central venous catheters. One third of the cases of massive PE have their only identified source in the veins of the lower limbs.

INCIDENCE

More than 600,000 people in the United States have a pulmonary embolism each year and more than 60,000 of them die, most by within 30 to 60 minutes after symptoms start. PE is the third most common cause of death in the US and first or second most common cause of unexpected deaths in most age groups. Highest incidence of recognized PE occurs in hospitalized patients. In the absence of prophylaxis acute DVT may be demonstrated in, general medical patients advised bed rest for a week (10-13%), patients in medical intensive care units (29-33%), patients with pulmonary disease kept in bed for 3 or 7 days (20-26%), patients admitted to coronary care units after myocardial infection (27-33%), patients who are

asymptomatic after coronary bypass graft (48%).

In the Framingham study it was observed that about four times more medical patients die from PE than surgical patients, yet we focus on the prevention of thrombosis in postoperative settings, ignoring the medical patients.

Patients who survive an acute PE are at high risk for recurrent PE and for the development of pulmonary hypertension and chronic cor-pulmonale, which occurs in upto 70% of patients and carries its own attendant mortality and morbidity.

Race:- Subtle population differences may exist in the incidence of DVT & PE, but the incidence is high in all racial groups. If the differences are real, whether they are due to generic variation or to population differences in diet and activity is not known.

Sex:- PE is common in all trimesters of pregnancy and puerperium and the incidence of PE is increased in women receiving oral contraceptive or hormone replacement therapy; however sex alone is not an independent risk factor.

Age:- Although the frequency of PE increases with age, it is not an independent risk factor. Rather the accumulation of other risk factors, such as underlying illness and decreased mobility, causes the increased frequency of PE in older patients.

Cause:- *Hypercoagulable states* Prolonged venous stasis or significant injury to the veins can provoke DVT and PE in any person, but increasing evidence suggests that spontaneous DVT and PE nearly always are related to some underlying hypercoagulable state. Other identified causes most likely serve only as triggers for a system that is already out of balance. Hypercoagulable states may be *acquired* or *congenital*. An inborn resistance to activated protein C is the most common congenital risk factor for DVT that has been identified to date. Most patients with this syndrome have a genetic mutation in factor V known as "factor V Leyden," although other mechanisms also can produce a resistance to activated protein C. Primary or acquired deficiencies in protein C, protein S, or antithrombin III are also common underlying causes of DVT and PE.

SIGNS & SYMPTOMS

The classic triad of signs & symptoms of PE are haemoptysis,

dyspnoea and chest pain but these are neither sensitive nor specific. They occur in fewer than 20% of patients in whom the diagnosis of PE is made. Nonetheless, the presence of any of these classic signs & symptoms is an indication for a complete diagnostic evaluation. Many patient with PE are initially completely asymptomatic and those who do have symptoms, have an atypical presentation. They may present as seizures, syncope, abdominal pain, high fever, productive cough, new onset of reactive airway disease, new onset atrial fibrillation or pleuritic chest pain.

Differential Diagnosis :- Although PE is known as a great masquerader, quite often other illness simulate PE . PE is likely diagnosis when dyspnoea, pain chest and an abnormal lung scan are present. In situations wherein pneumonia or heart failure coexist with PE, clinical improvement will often fail to occur despite standard medical treatment of concomitant illness, indicating possibility of coexisting PE. Whether the presentation is typical or atypical, the list of differential diagnosis remains extensive and the true diagnosis must be sought actively;

1. Acute coronary syndrome, conditions includes unstable angina and acute myocardial infraction.
2. Pneumonia, bronchitis, exacerbation of asthma or chronic obstructive lung disease..
3. Congestive heart failure, pulmonary edema.
4. Pericarditis.
5. Pleurisy, costochondritis, musculoskeletal discomfort.
6. Rib fracture, pneumothorax , pneumo-mediastinum
7. Primary pulmonary hypertension.
8. Anxiety, hyperventilation.

Laboratory Studies: Unfortunately no known blood or serum test can confirm pulmonary thromboembolism or vise versa.

■ **D-dimer** is a unique degradation product produced by plasma-mediated proteolysis of cross linked fibrin. It is measured by latex agglutination or by an enzyme linked immunosorbent assay (ELISA) test that is considered positive if the level is greater than 500 ng/ml.

■ **Latex agglutination tests** are notoriously unreliable with sensitivity of only 50-60% for DVT & PE. **ELISA test** is more sensitive than latex test. Under the best of circumstances, D-dimer study misses 10% of patients with positive pulmonary angiograms, while only 30% of those with a positive d-dimer will have a positive angiogram.

D-dimer alone is not sensitive or specific enough in diagnosing PE but it has a high negative predictive value and thus can be used to help exclude PE.

■ **White cell counts** (WBC) may be normal or elevated. A count as high as 20,000 is not uncommon in PE.

■ **Clotting studies** are normal in most patients of PE.

■ **Contrary** to classic teaching the PO₂ on **arterial blood gases** analysis has a zero or even negative predictive value in clinically suspected cases of PE. The reason for this is that other etiologies that masquerade as PE (eg COPD, pneumonia, CHF) are more likely to lower the PO₂ than is PE. It holds true not only for arterial PO₂ but also for the alveolar-arterial oxygen gradient and for the oxygen saturation level as measured for by pulse oximetry

Electrocardiogram:- Classic abnormalities include sinus tachycardia, new onset atrial fibrillation or flutter, and an S wave

in lead I, a Q wave in lead III and an inverted T in lead III. Often the QRS axis is greater than 90°. T inversion in leads V₁ to V₄ reflects right ventricular strain. One fourth of patients with proven PE have ECGs that are unchanged from their baseline state. An absence of ECG abnormalities has no significant predictive value

Noninvasive Imaging Modalities

The initial chest Xray findings of a patient with PE are virtually always normal. On rare occasions they may show the westermark sign, a dilatation of pulmonary vessels proximal to an embolism along with collapse of distal vessels, sometimes with a sharp cutoff. Later changes include a small pleural effusion and an elevated hemidiaphragm or focal infiltrates indistinguishable from an infectious pneumonia. Rare late finding of PE is 'Hampton hump' – a triangular or rounded pleural based infiltrate with apex pointed towards the hilum, frequently located adjacent to the diaphragm.

Chest CT:- Computer tomography (CT) of the chest with intravenous contrast (100ml administered at 3 to 4ml/sec via an antecubital vein) superseding lung scanning as the principal imaging test for diagnosis of PE. New generation multi slice scanners image the entire thorax with 1mm thin sections during a single 12 to 15 sec breath hold and can detect peripherally located thrombi in the fifth order branches.

Lung scanning:- Small particulate aggregates of albumin labeled with a gamma emitting radionuclide are injected intravenously and are trapped in the capillary bed. The perfusion scan defect indicates absent or decreased blood flow, possibly due to PE. Ventilation scans are obtained with radiolabeled inhaled gases such as Xenon or krypton, improve the specificity of the perfusion scan. A high probability scan for PE is defined as having two or more segmental perfusion defects in the presence of normal ventilation.

The diagnosis of PE is unlikely in patients with normal and near normal scans but is about 90% certain in patients with high probability scans. As many as 40% of patients with high clinical suspicion for PE and 'low probability' scans do in fact, have PE at angiography. A repeat V/Q scan is indicated before stopping anticoagulants in a patient with irreversible risk factors for DVT and PE because recurrent symptoms are common and a reference 'post treatment V/Q scan' can serve as new baseline for comparison , often sparing the patient the need for a future angiogram.

Magnetic Resonance (MR) pulmonary angiography utilizes gadolinium contrast agent, which unlike iodinated contrast agents used in CT angiography, is not nephrotoxic. Usually reserved test for pregnant woman and nephrocompromised patients MR also assesses right ventricular function, thus making it a promising single test for both diagnosis for PE and assessment of hemodynamic effect .

Echocardiography :- More than half of patients with PE will have normal echocardiograms. Mc Connell's sign ie right ventricular free wall hypokinesis with normal right ventricular apical motion, appears to be specific for PE. Detection of right ventricular dysfunction due to PE helps to stratify the risk, delineate the prognoses and plan optimal management.

Venous Ultrasonography :- Confirmed DVT is usually an adequate surrogate for PE. Ultrasonography of the deep venous system relies upon loss of vein compressibility as the primary criterion for DVT. About one half of the patients with PE have no

imaging evidence of DVT because the clot has already embolised to the lung or in the pelvic veins, where ultrasonography is inadequate.

Invasive Diagnostic Modalities

Pulmonary Angiography:- Is the most specific examination available for establishing the definitive diagnosis of PE and can detect an embolus as small as 1 to 2 mm. A definitive diagnosis of PE depends upon visualisation of an intraluminal filling defect in more than one projection. Secondary signs of PE include abrupt occlusion (Cuf off) of vessels; segmental oligemia or avascularity, a prolonged arterial phase with slow filling or tortuous tapering peripheral vessels. Chest CT scanning is replacing diagnostic pulmonary angiography because it is less invasive. In the current era of chest CT with contrast, pulmonary angiography is reserved for (1) patients with technically inadequate CT scans (2) scans performed on older machines which cannot image fourth or fifth order pulmonary arteries and (3) patients who will undergo interventions such as catheter embolectomy or catheter – directed thrombolysis.

Contrast Phlebography :- Venous ultrasonography has virtually replaced contrast phlebography, which is costly, uncomfortable and occasionally results in contrast allergy or contrast induced phlebitis.

TREATMENT

Primary therapy consists of clot dissolution with thrombolysis or removal of PE by embolectomy. Secondary prevention constitutes anticoagulation with heparin and warfarin and placement of inferior vena caval filter.

Risk Stratification:- is crucial for determining treatment strategy. The presence of hemodynamic instability, right ventricular dysfunction or elevation of troponin level due to right ventricular micro infarction can identify high risk patients. Such patients would warrant primary therapy to prevent adverse clinical outcome. When right ventricular function remains normal in a hemodynamically stable patient, a good clinical outcome is highly likely with anticoagulation alone.

Drug Therapy:- Fibrinolytics:- therapy has been the standard of care for patients with massive or unstable PE. Unless contraindicated, a rapidly acting fibrinolytic agent should be administered immediately to every patient who has suffered hypotension (even if resolved) or is significantly hypoxic from PE. Fibrinolytic therapy has replaced surgical embolectomy as the primary mode of treatment for hemodynamically unstable patients with pulmonary thromboembolism. Surgical thromboembolectomy is now reserved for patients in whom fibrinolysis has failed or cannot be tolerated. Fibrinolytic regimen currently in use for PE include two forms of recombinant tissue plasminogen activator –t PA (alteplase) and r PA(reteplase) along with urikinas and streptokinase.

Retaplaste (r-PA, Retavase) –Second –generation recombinant tissue – type plasminogen activator. As fibrinolytic agent, seems to work faster than its forerunner, alteplase, and also may be more effective in patient with larger clot burden. Also has been reported more effective than other agents in lysis of older clots. Two major differences help explain these improvements. Compared to alteplase, reteplase does not bind fibrin so tightly, allowing drug to diffuse more freely through clot. Another advantage seems to

be that reteplase does not compete with plasminogen for fibrin – binding sites, allowing plasminogen at site of clot to be transformed into clot- dissolving plasmin.

Adult Dose :- Two, 10 Units, IV boluses, given 30 min apart In setting of cardiac arrest or impending arrest due to PE, single IV bolus of 20 U has been used successfully in small number of cases .

Contraindications :-Active internal bleeding; history of cerebrovascular accident; recent intracranial or intraspinal surgery or trauma; intracranial neoplasm, arteriovenous malformation, or aneurysm; known bleeding diathesis; severe uncontrolled hypertension.

Alteplase (rt-PA, Activase) – Drug most often used to treat PE in ED. One advantage of alteplase is that, it is used so widely for treatment of patients with acute MI that most ED personnel are familiar with its use.

Adult Dose :- 100mg IV infusion over 2 h (FDA- approved regimen for PE)

Accelerated 90- min regimen is used widely, and most authors believe it is both safer and more effective than 2-h infusion; for accelerated regimen, recommended total dose based upon patient weight, not to exceed 100 mg.

Heparin therapy should be instituted or reinstated near end of or immediately following alteplase infusion, when aPTT over thrombin time return to twice normal or less.

Contraindications :- Documented hypersensitivity : active internal bleeding ; history or cerebrovascular accident; recent intracranial or intraspinal surgery or trauma intracranial neoplasm, arteriovenous malformation, or aneurysm, known bleeding diathesis; severe uncontrolled hypertension

Urokinase (Abbokinase)- Direct plasminogen activator produced by human fetal kidney cells grown in culture . Relatively low in antigenicity.

When used for localized fibrinolysis, given as local catheter – directed continuous infusion directly into area of thrombus with no loading dose, When used for PE, loading dose necessary.

Adult Dose :- Loading Dose : 2000 U/lb infused IV over 10 min, maintenance dose : 2000 U/lb/h IV for 24 h.

Contraindications :- Active internal bleeding ; history of cerebrovascular accident ; recent intracranial or intraspinal surgery or trauma ; intracranial neoplasm, arteriovenous malformation, or aneurysm; known bleeding diathesis; severe uncontrolled hypertension.

Anticoagulants :- Heparin augments the activity of antithrombin III and prevents the conversion of fibrinogen to fibrin. Full – dose LMWH or full dose unfractionated IV heparin should be initiated at the first suspicion of DVT or PE. With proper dosing, several LMWH products have been found safer and more effective than unfractionated heparin both for prophylaxis and for treatment of DVT and PE. Monitoring with aPTT is neither necessary nor useful when giving LMWH. Because the drug is active in a tissue phase and does not exert most of its effects on coagulation factor IIa

Fractionated LMWH administered subcutaneously is now the preferred choice for initial anticoagulation therapy . Unfractionated IV heparin can be nearly as effective but is more difficult to titrate for therapeutic effect. Warfarin maintenance therapy may be initiated after 1-3 d of effective heparinization.

Enoxaparin (Lovenox)—First LMWH released in US. Approved by FDA for both treatment and prophylaxis of DVT and PE.

LMWH has been used widely in pregnancy, although clinical trials not yet available to demonstrate that it is as safe as unfractionated heparin. Except in overdoses, checking PT or aPTT has no utility, as aPTT does not correlate with anticoagulant effect of fractionated LMWH.

Adult Dose:- Treatment of DVT and PE: 1 mg/kg SC q12h or 1.5 mg/kg SC qd

DVT prophylaxis: 30 mg SC q12h

DVT prophylaxis in abdominal surgery: 40 mg SC qd, with first dose given 2 h prior to surgery

Contraindications :- Documented hypersensitivity; major bleeding; thrombocytopenia

Dalteparin (Fragmin)—LMWH with many similarities

Except in overdoses, checking PT or aPTT has no utility, as aPTT does not correlate with anticoagulant effect of fractionated LMWH.

Adult Dose:- DVT prophylaxis in patients undergoing abdominal surgery : 2500 U SC qd.

Tinzaparin (Innohep)—Approved for treatment of DVT in hospitalized patients. Enhances inhibition of factor Xa and thrombin by increasing antithrombin III activity. In addition, preferentially increases inhibition of factor Xa.

Adult Dose:- For treatment of acute DVT : 175 IU/kg SC qd; give drug at same time each day and continue for at least 6 d and until long-term anticoagulation established with warfarin or another agent.

DVT prophylaxis in patients undergoing hip and knee surgery:- 50 U/kg SC q12h

Unfractionated heparin—when unfractionated heparin used, aPTT should not be checked until 6 h after initial heparin bolus, as an extremely high or low value during this time should not provoke any action

Adult Dose:- Initial bolus:- 120-140 U/kg IV or approximately 10,000 U/70-kg person Initial infusion:- 20 U/kg/h IV

After bolus, check aPTT q6h until stable, and heparin dosing should be adjusted as follow: if aPTT is low (<1.5 times control value), administer second bolus of 5000 U and increase drip by 10%. If a PTT is high (>2.5 times control value), decrease drip 10%. If aPTT is extremely high (>100s), hold heparin drip for 1 h and decrease drip 10%

Contraindications :- Documented hypersensitivity; subacute bacterial endocarditic; active noncompressible bleeding; any history of heparin-induced thrombocytopenia the drug is usually safe but benefits must outweigh the risks.

Warfarin (Coumadin):- The drug interferes with hepatic synthesis of vitamin K-dependent coagulation factors. Never give to patient with thrombosis until after patients has been anticoagulated fully with heparin, because first few days of warfarin therapy produce hypercoagulable state. Failing to anticoagulate with heparin before starting warfarin will cause clot extension and recurrent thromboembolism in about 40% of patients, compared with 8% of those who receive full-dose heparin before starting warfarin. Heparin should be continued for first 5-7 d of oral warfarin therapy regardless of PT, to allow time for depletion of procoagulant vitamin K-dependent proteins. Anticoagulant effect of warfarin adjusted by varying dose to keep INR within target range. An INR target range

of 2.5 to 3.5 makes sense for DVT and PE because rate of recurrence increases dramatically when INR drops below 2.5 and decreases when INR is kept above 3.0 the risk of serious bleeding (including hemorrhagic stroke) is approximately constant when INR is between 2.5 and 4.5 but rises dramatically when INR is 5.0 or higher. Patients who have difficulty maintaining adequate anticoagulation while taking warfarin may be asked to limit their intake of foods that contain vitamin K. Foods that have moderate to high amounts of vitamin K include brussel sprouts, kale, green tea, asparagus, avocado, broccoli, cabbage, cauliflower, collard green, liver, soybean oil, soybeans, certain beans, mustard greens, peas (black-eyed peas, split peas, chick peas), turnip greens, parsley, green onions, spinach and lettuce.

Adult Dose:- Initial dose: 5-15mg/d PO qd After initial anticoagulation obtained, adjust dose according to desired INR

Contraindications : Avoid or use extreme caution in patients with hereditary or acquired deficiencies of protein C or protein S, because these deficiencies are associated with higher incidence of tissue necrosis following warfarin administration. Warfarin is teratogenic and contraindicated in pregnancy

Prevention

Graduated compression stockings steadily squeeze legs, helping veins and leg muscles move blood more effectively. They offer a safe, simple and inexpensive way to keep blood from stagnating after general surgery. Compression stockings used in combination with heparin are much more effective than is heparin alone.

Pneumatic compression treatment uses thing high cuffs that automatically inflate every few minutes to massage and compress the veins in the legs. Pneumatic compression can dramatically reduce the risk of blood clots, especially in people who have had hip replacement surgery.

Physical activity :- Early mobilization as soon as possible after surgery can prevent pulmonary embolism and hasten recovery.

Preventive steps while traveling.

- Move around the aeroplane cabin once an hour or so. If driving, stop every hour and walk around the car a couple of times or do a few deep knee bends.
- Exercise while sitting- flex and rotate ankles or press feet against the seat in front or try rising up and down on your toes; Don't sit with crossed legs for long period of time.
- Wear support stockings as they help promote circulation and fluid movement
- Drink plenty of fluids before and during the trip to avoid dehydration as this can contribute to development of blood clots. Avoid alcohol which contributes to fluid loss.
- In high risk individuals planning to fly six hours or more, low molecular weight heparin 2 to 4 hours before departure is recommended.

CONCLUSION

In most cases, a pulmonary embolism is not fatal. Still, pulmonary embolism is a leading cause of hospital deaths and an increasing threat to passengers on long aeroplane flights. A few simple measures can go a long way towards preventing pulmonary embolism. When pulmonary embolism does occur, treatment with anti-clotting medications can greatly reduce the risk of death.

BIBLIOGRAPHY

- Antevil JL, Sise MJ, Sach DI, et al: Retrievable vena cava filters for preventing pulmonary embolism in trauma patients: a cautionary tale. *J Trauma* 2006 Jan; 60(1):35-40[Medline].
- Brown MD, Rowe BH, Reeves MJ, et al: The accuracy of the enzyme-linked immunosorbent assay D-dimer test in the diagnosis of pulmonary embolism: a meta-analysis. *Ann Emerg Med* 2002 Aug;40(2):133-44[Medline].
- Feied CF: Pulmonary embolism. In: Rosen and Barkin, eds. *Emergency Medicine Principles and Practice*. Vol 3. 4th ed.1998: chap 111.
- Feied CF: Peripheral venous disease. In: Rosen and Barkin, eds. *Emergency Medicine Principles and Practice*. Vol 3. 4th ed. 1998: chap 107.
- Feied CF: Pulmonary chest pain, cor pulmonale and pulmonary embolism. In: Gibler and Aufderheide, eds. *Emergency Cardiac Care*. Vol 1. 1994:243-303.
- Goldhaber S, et al. *JAMA* 1983; 74: 1023-1028.
- Heit JA: the epidemiology of venous thromboembolism in the community: implications for prevention and management. *J Thromb Thrombolysis* 2006 Feb; 21-(1):23-9 [Medline].
- Hogg K, Brown G, Dunning J, et al: Diagnosis of pulmonary embolism with CT pulmonary angiography: a systematic review. *Emerg Med J* 2006 Mar; 23(3): 172-8 [Medline].
- Junger M, Diehm C, Storiko H, et al: Mobilization versus immobilization in the treatment of acute proximal deep venous thrombosis: a prospective, randomized, open, multicentre trial. *Curr Med Res Opin* 2006 Mar; 22(3): 593-602[Medline].
- Kabrhel C, Mattis C, McNamara M, et al: A Highly Sensitive ELISA D-Dimer Increases Testing but No Diagnosis of Pulmonary Embolism. *Acad Emerg Med* 2006 Mar 21; [Medline]
- Kabrhel C, McAfee AT, Goldhaber SZ, et al: The probability of pulmonary embolism is a function of the diagnoses considered most likely before testing. *Acad Emerg Med* 2006 Apr; 13(4):471-4[Medline].
- Kabrhel C, McAfee AT, Goldhaber SZ, et al: The contribution of the subjective component of the Canadian Pulmonary Embolism Score to the overall score in emergency department patients. *Acad Emerg Med* 2005 Oct; 12(10):915-20[Medline].
- Kruse L, Mitchell AM, Camargo CA, et al: Frequency of Thrombophilia-Related Genetic Variations in Patients with Idiopathic Pulmonary Embolism in an Urban Emergency Department. *Clin Chem* 2006 Mar 30;[Medline]
- Le Gal G, Righini M, Roy PM, et al: Prediction of pulmonary embolism in the emergency department: the revised Geneva score. *Ann Intern Med* 2006 Feb 7; 144(3): 165-71[Medline].
- Quiroz R, Kucher N, Zor KH, et al : Clinical validity of a negative computed tomography scan in patients with suspected pulmonary embolism: a systematic review. *JAMA* 2005 Apr 27; 293(16): 2012-7[Medline]
- Roy PM, Meyer G, Vielle B, et al: Appropriateness of diagnostic management and outcomes of suspected pulmonary embolism. *Ann Intern Med* 2006 Feb 7; 144(3) 157-64[Medline]
- Silverstein et al. Trends in the incidence of DVT & PE. A 25 year population based study.
- Tillie-Leblond I, Marquette CH, Perez T, et al: Pulmonary embolism in patients with unexplained exacerbation of chronic obstructive pulmonary disease: prevalence and risk factors. *Ann Intern Med* 2006 Mar 21; 144(6) 390-6[Medline]
- Weiss CR, Scatarige JC, Diette GB, et al: CT Pulmonary Angiography is the First-Line Imaging Test for Acute Pulmonary Embolism: A Survey of US Clinicians. *Acad Radiol* 2006 Apr; 13(4): 434-46[Medline].
- Wells PS: Advances in the diagnosis of venous thromboembolism. *J Thromb Thrombolysis* 2006 Feb; 21(1):31-40[Medline].

IMSA News

IMSA CHAPTER ACTIVITIES - Oct. to Dec. 2006

Tamil Nadu Chapter

- 8-10-2006 : Dr. S. Ganapathy Ramanan, "Tumour Markers"
 22-10-2006 : Dr. P.Rajendra, "Etiology and Epidemiology of Chikungunya and Dengue Fever"
 : Dr. Ramasubramanian, "Tackling Chikungunya and Dengue"
 12-11-2006 : Dr. Thangam Varma, "Current Thoughts about HRT & Alternative"
 10-12-2006 : Dr. Leonard Ponraj, "Knee and Shoulder Injuries, Management"

Rural CME T.N. Chapter

- 29-10-2006 : Dr. Khurja, "Hypertension and Diabetes"
 Delhi Chapter
 29-10-2006 : Dr. Khurja, "Hypertension and Diabetes"

Fellows and Members elected during the quarter Oct.-Dec. 2006

Dr. Rahul Sarda	Jaipur	Prof. Tasnim Majid	Lahore, Pakistan	Dr. Ghulam Akbar Sial	Lahore, Pakistan
Dr. Vinod Kumar	New Delhi	Prof. Khalid Javed Rabbani	Lahore, Pakistan	Dr. Hasnat Butt	Lahore, Pakistan
Dr. Sunil Kumar	Jharkhand	Prof. Nusrat Ullah Chaudhry	Lahore, Pakistan	Dr. Huda Ghulam Mirza	Lahore, Pakistan
Dr. Shailini Singh	USA	Prof. G. A. Shah	Lahore, Pakistan	Dr. Shumail Zafar	Lahore, Pakistan
Dr. S. Jayachandran	Chennai	Prof. Javed Asghar	Lahore, Pakistan	Prof. Iqbal Butt	Lahore, Pakistan
Dr. Syed Najimudeen	Bangalore	Prof. Humaira Wyne	Lahore, Pakistan	Prof. Khalil Rana	Lahore, Pakistan
Dr. Pradip Kumar Shrivastava	New Delhi	Dr. Nabeela Shami	Lahore, Pakistan	Dr. Ambreen Akhtar	Lahore, Pakistan
Dr. Sanjeev Bagai	New Delhi	Dr. Shaila Anwar	Lahore, Pakistan	Dr. Amol Pramod Mahajan	Mumbai
Prof. Shaheena Asif	Lahore, Pakistan	Dr. Maimoona Hafeez	Lahore, Pakistan	Dr. Ghulam Hassan	Kashmir
Prof. Amer Aziz	Lahore, Pakistan	Dr. Waseem Talib	Lahore, Pakistan	Dr. Ramandeep Singh Virk	Chandigarh
Dr. Tahira S. Izhar	Lahore, Pakistan	Dr. Sajeela Hameed	Lahore, Pakistan	Dr. Amar Mohanrao Taksande	Wardha
Dr. Samir Riaz Qazi	Lahore, Pakistan	Dr. Amir Bashir	Lahore, Pakistan	Dr. (Mrs) Deepti Sarda (Jain)	Jaipur
Prof. Shahid Mahmood	Lahore, Pakistan	Prof. A. H. Nagi	Lahore, Pakistan		
Prof. Muhammad Yousaf	Lahore, Pakistan	Dr. Seema Daud	Lahore, Pakistan		

HONOUR

- **Dr. K. Jagadeesan**, President IMSA, has been re-elected as President of International Medical Sciences Academy (IMSA) for another term of 5 years w.e.f. 1/12/2006 by the IMSA governing body in its meeting held recently at Lahore, Pakistan
- **Dr. R.R. Thukral**, Vice President IMSA, ENT Specialist, has been re-elected as Vice President of International Medical Sciences Academy (IMSA) for another term of 5 years w.e.f. 1/12/2006 by the IMSA governing body in its meeting held recently at Lahore, Pakistan

IMSACON 2007 at Manipal, Karnataka

IMSA is pleased to inform its Fellows and Members that Annual Conference IMSACON 2007 will be held at Manipal, Karnataka on 3,4,5 November 2007. Manipal Academy of Higher Education (MAHE) will organize the conference, Dr. Ramdas M. Pai, President of MAHE and Trustee of IMSA will be the Patron.

The organisers will be issuing the first information brochure shortly. IMSA would like its Fellows and Members to participate in the conference in large numbers and derive benefit of latest medical scientific inventions. They should register themselves with the organizers well in time to avoid any confusion at the last moment regarding arrangements for their stay etc.

Dr. R.R. Thukral
Vice President

MANAGING DIABETES MELLITUS IN PATIENTS WITH VASCULAR DISEASES

Vinod K.Gujral, Vinod Sharma, Sanjiv Gupta

Departments of Diabetic & life StyleManagement & Interventional Cardiology,
National Heart Institute, East of Kailash, New Delhi, India

ABSTRACT : Diabetes mellitus is associated with a markedly increased prevalence of vascular disease. Therefore, management of diabetes mellitus in peripheral arterial disease (PAD) requires multifaceted approach in the form of more vigorous control of hyperglycemia, hyperlipidemia, hypertension, and other risk factors and use of antiplatelet agents.

INTRODUCTION

Diabetes mellitus is the most common endocrine disease. Type 2 diabetes affects >3% of all adults and >10% of adults >65 years old.^[1] Eighty percent of patients with type 2 diabetes will die of cardiovascular disease.^[2]

The risk of vascular diseases is 2-4 times greater in diabetes, occurs at a younger age, and is much higher in women with diabetes. The risk of peripheral arterial disease (PAD) is increased in patients with poor glycemic control, but studies have not shown a major impact of improved glucose management on mortality. This apparent contradiction may be due to the many potential mechanisms of increased cardiovascular damage in diabetes, including hypertension; abnormal clotting function due to changes in fibrinolysis, platelet adherence, and plasminogen activity; abnormal vascular reactivity; and abnormal lipid patterns and particles. Some, but not all, of these issues are related to lifestyle factors, including diet, exercise, and cigarette smoking. The treatment of hypertension and hypercholesterolemia has been more successful in reducing cardiovascular mortality than reducing HbA_{1c} levels. One of the major, unresolved questions is whether insulin resistance rather than hyperglycemia is the primary risk factor for cardiovascular disease (CVD).

(A) GLYCEMIC CONTROL

Serum glucose level not only defines the onset of diabetes but also is associated with an increased risk of future cardiovascular events among diabetic. Although there are abundant data linking both fasting glucose and impaired glucose tolerance to adverse events, the data demonstrating an improvement in cardiovascular outcomes with an aggressive glucose lowering treatment strategy have been lacking among patients with type 2 DM. Although data from UK Prospective Diabetes Study (UKPDS)-33 clearly demonstrate a reduction in microvascular complications with intensive glucose control, there was not a concomitant significant reduction in macrovascular complications.

About 80 % of all diabetic patients have type 2 diabetes mellitus, which characteristically occurs after age 40 years. The metabolic mechanisms of type 2 diabetes are the combination of insulin resistance and a genetically programmed defect in the pancreatic beta-cell secretion of insulin. Although a traditional goal of glycemic control in the treatment of diabetes mellitus is to normalize fasting plasma glucose, emerging data indicate that modulation of postprandial plasma glucose levels plays an important role in overall glycemic control. The glycemic threshold for the

development of macrovascular complications is lower than that for microvascular complications, so there is more evidence for an association with postprandial glycemia. Postprandial glucose elevations are associated with postprandial hyperinsulinemia and higher plasma levels of triglycerides, chylomicrons, chylomicron remnants, and free fatty acids. High concentrations of free fatty acids have been associated with endothelial dysfunction,^[6] and high triglyceride levels have been linked to low levels of high-density lipoprotein (HDL) cholesterol and a preponderance of small, dense, low-density lipoprotein (LDL) particles. Associated with carotid artery atherosclerosis in nonobese white subjects. In addition, high postprandial glucose levels result in protein and cellular glycosylation. Glycosylated LDL particles are more easily oxidized and taken up by macrophages through the scavenger receptor. This, in turn, leads to higher foam cell production, and, ultimately, atherosclerotic plaque. In addition, glycosylated LDL also stimulates platelet aggregation. Glycosylated HDL is less efficient than nonglycosylated in transporting cholesterol back to the liver for metabolism. Additionally, the formation of advanced glycosylated end products in the collagen of the vessel wall itself may directly stimulate or accelerate the atherosclerotic process.

Acute increases in plasma glucose also stimulate the production of free radicals, another factor involved in the atherosclerotic process.^[9] Excessive postprandial plasma glucose levels have also been associated with transient hypercoagulability resulting from increased thrombin production and decreased fibrinogen breakdown. These, in turn, result from the overproduction of plasminogen activator inhibitor, which directly inhibits tissue plasminogen activator activity. Control of postprandial hyperglycemia reverses this hypercoagulable state.

Endothelial dysfunction is another consequence of postprandial hyperglycemia. Activation of protein kinase C in the endothelium increases adhesion molecules that facilitate leukocyte uptake into the blood vessel wall; increases production of the vasodilators nitric oxide and prostaglandin; increases expression of the vasoconstrictor endothelin; and induces platelet aggregation.

The standards of care in patients with diabetes (American diabetes Association) are preprandial glucose levels of 80 to 120, time glucose levels of 100 to 140, and hemoglobin A_{1c} (HbA_{1c}) below 7 percent. The ADA recently (January 2004) recommended lowering the upper limit for normal fasting glucose (NFG) from 110 mg/dL to 100 mg/dL (Table 1) and designating the category of IFG to be at 100-125 mg/dL rather than 110-125 mg/dL.^[13] The basis for this recommendation was that the threshold of FPG, above which risk of a clinical or metabolic outcome rises sharply, was lower than 110 mg/dL. Plasma HbA_{1c} reflects the average glucose level of the previous weeks and allows a uniform measure for achieving a target as well as comparing the efficacies of different therapies.

Correspondence : Dr. Vinod K. Gujral

Table 1. Treatment Goals for Type 2 Diabetes

Parameter	Therapeutic Goal
Body mass index	< 25 kg/m ²
Blood pressure	< 130/85 mm Hg
Plasma glucose	
Fasting	80 - 100 mg/dL
Postprandial (2 h)	< 160 mg/dL
HbA _{1c}	< 7%
Total cholesterol	< 200 mg/dL
HDL-C	>50 mg/dL
LDL-C	d ⁿ 100 mg/dL
Triglycerides	< 150 mg/dL

MEASURES TO CONTROL HYPERGLYCEMIA

Lifestyle intervention

Diet since more than 80% of patients with type 2 diabetes are overweight, initial intervention mostly centers around dietary control and increased aerobic exercise.

Obesity has a demonstrated association with coronary heart disease. Numerous studies have shown an increased mortality rate in individuals with a BMI of at least 30. These individuals have a 50% to 100% increased risk of death from all causes compared with individuals at a BMI of 20 to 25. Weight loss of at least 7% of current body weight should be an initial goal, since this will produce significant metabolic improvement in glucose control and other associated risk factors, including blood pressure and dyslipidemia.

Cigarette smoking is a powerful predictor of mortality. Multiple large prospective cohort studies have demonstrated a 2-fold increase in the relative risk for all-cause mortality in smoking versus nonsmoking diabetic patients, and it has been calculated that the benefit of smoking cessation is the most cost-effective risk factor intervention for diabetic patients.

Exercise for 30-60 minutes of moderate-intensity activity 4-5 times weekly (walking, jogging, cycling). Increased in daily lifestyle activities (Stairs, gardening, household chores) is recommended by ADA. Particular emphasis on patients with hypertension, elevated triglyceride, elevated glucose levels.

Oral Hypoglycemic Agents (table 2)

Sulfonylureas are the typical therapy for lean patients with type 2 diabetes and are used in combinations with other agents in obese type 2 patients. Sulfonylureas bind to a receptor on the beta cells and inhibit the sodium-adenosine triphosphate (Na-ATP) channel and increase in intracellular calcium results in insulin exocytosis. Some experts point to a possible risk of increased myocardial damage in patients with known CAD or PAD who use sulfonylureas at the time of an ischemic event. Prevention of protective ischemic preconditioning of the heart by inhibition of the potassium (K)-ATP channel is the putative mechanism. The UKPDS data do not support this concern. Therefore use of sulfonylureas in appropriate patients with PAD.

Repaglinide newer insulin secretagogue binds to a different receptor site than the sulfonylureas on the K-ATP channel. 166 The half-life of this drug is 3.7 h, which makes it effective for postprandial rather than preprandial hyperglycemia, for use in the elderly and for diabetic patients with chronic renal failure.

Metformin is a biguanide drug that has main mode of action is

Table 2. Oral Drugs Currently Available for the Treatment of Type 2 Diabetes

Drug Class	Primary Mechanism	Potential Secondary Benefit	Potential Problems	Main Contraindications
Sulfonylureas/Meglitinides (repaglinide)	Augmented insulin secretion	More rapid onset of action	Weight gain, hypoglycemia	Hepatic disease
Biguanides (metformin)	Reduced hepatic glucose production	Reduction in lipids, less weight gain	Gastrointestinal side effects	Renal insufficiency, CHF
Thiazolidinediones	Enhanced insulin sensitivity	Reduced circulating insulin levels, possible beta-cell preservation and vascular protection	Hepatotoxicity, fluid retention, weight gain	Abnormal liver function, CHF
Acarbose	Delayed gut absorption of carbohydrates	Rare systemic effects	Flatulence	Gastrointestinal disease

through decreasing hepatic glucose output primarily by inhibiting gluconeogenesis, typically without hypoglycemia. Metformin is effective alone or in combination with insulin, sulfonylureas, and thiazolidinediones. The drug usually results in weight loss as a result of decreased appetite for up to 1 year after the initiation of the therapy.

Significant decreases in LDL cholesterol and triglycerides occur. The incidence of lactic acidosis with metformin is 9 per 100,000 person-years. Contraindications to its use include an elevated creatinine level (>1.4 in women, >1.5 in men), congestive heart failure, severe pulmonary disease, or any hypoxic state.

Thiazolidinediones promote insulin-stimulated glucose transport in muscles and adipocytes through a mechanism of action involving activating peroxisome proliferators activated receptor-gamma (PPAR- γ) ligands. Binding to the nuclear receptor promotes differentiation of adipocytes and increased expression of glucose transporter. Thiazolidinediones also may act by antagonizing the effects of cytokines such as TNF- α .

Endogenous C peptide is necessary for all the thiazolidinediones to be effective when used in combination with insulin. These agents can result in a reduction from two injections of insulin a day to one. The Thiazolidinediones are associated with weight gain partly resulting from improvement in glycemic control.

Rosiglitazone monotherapy results in a decrease of Hb A_{1c} of 0.8 to 1.5 percent greater than that seen with placebo, with the greatest reduction seen when it was given in two divided doses. 184, 185 Combination studies of rosiglitazone with metformin for 26 weeks resulted in a 1.0- to 1.2-percent placebo-adjusted decrease in Hb A_{1c}. 186 Although rosiglitazone is currently approved for use as monotherapy and in combination therapy with metformin, it also is expected to be efficacious with sulfonylureas or insulin. Rosiglitazone has been reported to result in an increase in LDL and HDL cholesterol concentrations between 12 and 19 percent, with changes in serum triglycerides similar to those seen with placebo.

Pioglitazone, the newest thiazolidinedione, has been approved for use as monotherapy and in combination with metformins, sulfonylureas, and insulin. In three randomized, double-blind placebo-controlled trials of 16 to 26 weeks duration, changes in Hb A_{1c} were 1.0 to 1.4 percent. 188 Increases in alanine aminotransferase (ALT) occurred in 0.26 percent of treated patients, a result that was not different from that with placebo. 188 Patients treated with pioglitazone showed a decrease in serum triglyceride (9.3 to 9.6 percent), increases in LDL (5.2 to 6.0 percent) with the 30- to 45-mg doses respectively.

Table 3. Pharmacologic Effects of Thiazolidinediones

• Improved glycemic control in type 2 diabetes patients and animal models by reduction of insulin resistance in muscle, liver, and adipose tissue
• Stimulation of differentiation and fat metabolism predominantly in subcutaneous adipose tissue depots +Reduction in circulating triglyceride and free fatty acid levels
• Reduction in circulating insulin and glucose levels
• Increased expression of glucose transporter molecules in insulin target tissues
• Reduction in proportion of atherogenic small, dense LDL-C particles
• Preservation of pancreatic β -cell mass (animal studies)
• Reversal of effects of tumor necrosis factor- α , which inhibits insulin action in target tissues (animal studies)

Insulin

The natural history of type 2 diabetes is one of progressive β -cell failure. Therefore, after approximately 10 years of the use of oral hypoglycemic agents, insulin will be required either in combination with oral agents or as the sole therapy. Although endogenous hyperinsulinemia is clearly associated with atherogenesis, there is no compelling evidence of increased risk of cardiovascular disease or increased mortality from exogenous insulin therapy.

Treatment Modalities that enhance insulin sensitivity

- Diet (caloric restriction)
- Weight loss if obese
- Aerobic exercise
- Thiazolidinediones
- Metformin

On one hand, fast-acting and regular insulin are absorbed too slowly to reproduce the typical secretory burst of native circulating insulin, whereas long-acting insulins, like Lente and NPH, are absorbed too rapidly to simulate a normal pattern of basal insulin secretion.

The advent of recombinant DNA technology has led to the development of novel insulin molecules with absorption and biological activity profiles that more closely resemble the physiologic pattern of insulin secretion.

This has, in part, been made possible by the recent development of insulin analogues that target both postprandial blood glucose excursions (rapid-acting analogues) and basal glucose levels (long-acting analogues). The analogues can provide better physiologic control of glycemia throughout the day with a lower incidence of hypoglycemic events than subcutaneously injected native human insulin.

Rapid-Acting Insulin Analogues Insulin lispro and insulin aspart are the 2 available rapid-acting insulin analogues. They have a shorter time to onset and shorter duration of action than regular human insulin. These analogues begin to work within 5-15 minutes of injection, achieve peak activity in about 60-90 minutes, and have a duration of action of approximately 4 hours. They are absorbed from the injection site twice as fast as is regular insulin, which begins to act 30 minutes after injection, reaches its peak at 2-4 hours, and lasts 6-8 hours or longer. These characteristics allow patients to administer rapid-acting insulins immediately before mealtime, providing more flexibility in scheduling mealtimes and better control of postprandial glucose levels. In

addition to achieving lower postprandial blood glucose at 1 and 2 hours after meals, rapid-acting insulin analogues maintain the same time-action profile regardless of dose, whereas a dose increase with human regular insulin increases the duration of action.

Insulin lispro has been shown to improve postprandial glucose control without increasing the risk for hypoglycemia in patients with type 1 and type 2 diabetes. Several studies on patients with type 1 diabetes show improvement in levels of HbA1c, ranging from 0.3% to 0.5% reductions in those receiving insulin lispro compared with those receiving regular human insulin, with no increase in the rate of hypoglycemia. Insulin lispro is also associated with a lower risk for severe hypoglycemia and coma. As part of a basal-bolus regimen with NPH, insulin lispro was associated with a lower incidence of nocturnal hypoglycemia than was regular insulin in patients with type 1 diabetes who maintain tight glycemic control. In patients with type 2 diabetes, the addition of lispro to a sulfonylurea has been shown to significantly reduce fasting and postprandial glucose concentrations as well as HbA1c values compared with sulfonylurea alone or sulfonylurea plus either metformin or bedtime NPH.

Similarly, studies show a significant reduction in HbA1c levels in patients receiving continuous subcutaneous insulin infusion (CSII) with insulin lispro compared with patients receiving pump treatment with regular human insulin.

Studies comparing insulin aspart with regular human insulin in patients with type 1 diabetes indicate that aspart improves postprandial glycemic control and reduces the number of hypoglycemic episodes requiring third-party intervention. A recent study by Raskin and colleagues showed that patients assigned to the insulin aspart group experienced a modest but significant reduction in HbA1c at 6 and 12 months of the study when compared with patients in the regular human insulin group.

Long-Acting Insulin Analogues NPH and Lente (insulin zinc) are intermediate-acting insulins that are twice as slow as regular insulin with an onset of action of 1-2 hours; NPH insulin exhibits a peak activity of 4-10 hours and a duration of 10-16 hours, whereas Lente peaks at 4-12 hours and lasts for 12-18 hours. Ultralente insulin is a long-acting insulin formulation that has a modest peak at 10 hours and duration of 18-20 hours. Ultralente insulin, however, varies greatly in its absorption characteristics from day to day. Glargine is a long-acting insulin analogue that has a flat, peakless profile of activity that lasts for more than 24 hours in most patients.

Premixed Insulin Formulations have the advantage of providing more convenience and greater accuracy for patients because the patient does not need to mix them. The premixed insulin formulations currently available for use are a combination of NPH and regular insulin (70/30 mixture or 50/50 mixture) and a combination of 75% neutral protamine lispro (NPL) and 25% insulin lispro (insulin lispro mixture 75/25). Insulin lispro mixture 75/25 has been shown to be more effective in reducing morning and evening postprandial glucose excursions [41] and in reducing nocturnal hypoglycemia than the NPH/regular insulin 70/30 mixture.

(B) TREATMENT OF HYPERTENSION

Hypertension (defined as a blood pressure 140/90 mmHg) is an extremely common co morbid condition in diabetes, affecting 20-

60% of patients with diabetes, depending on obesity, ethnicity, and age. In type 2 diabetes, hypertension is often present as part of the metabolic syndrome of insulin resistance also including central obesity and dyslipidemia.

Aggressive blood pressure control prevents further cardiovascular events more in diabetics than in nondiabetics. The ADA currently recommends a targeted blood pressure of 130/80 mm Hg.

(C) TREATMENT OF DYSLIPIDEMIA

The most common pattern of dyslipidemia in patients with type 2 diabetes is elevated triglyceride levels and decreased HDL cholesterol levels. The mean concentration of LDL cholesterol in those with type 2 diabetes is not significantly different from that in those individuals who do not have diabetes. However, qualitative changes in LDL cholesterol may be present. In particular, patients with diabetes tend to have a higher proportion of smaller and denser LDL particles, which are more susceptible to oxidation and may thereby increase the risk of cardiovascular events.

Life style modification should be the first step to improve lipid profile, followed by strict glycemic control which lessens hepatic VLDL production.

Statins (3-hydroxy-3-methylglutaryl-coenzyme A reductase inhibitor) are first-line agents for decreasing LDL cholesterol, but they also lower the apo B-containing lipoproteins, including atherogenic TGRLP or remnant lipoproteins. These agents result in a proportionately greater cardiovascular risk reduction in diabetic than in non diabetic subjects.

Both the 4S and Cholesterol And Recurrent Events (CARE) studies have demonstrated a significant reduction in future cardiovascular end points for patients with diabetes and PAD. In Heart Protection Study (HPS), which included 5963 subjects with diabetes, simvastatin decreased the risk of coronary death, non fatal myocardial infarction, stroke or revascularization by 25% in the diabetic group with PAD. The reduction risk even extended to patients with pretreatment LDL cholesterol levels below 100 mg/dl.

Fibrate, agonists of peroxisome proliferator-activated receptor-alpha (PPAR-alpha), modulate the expression of key genes involved in lipid transport and metabolism in liver and adipose tissue. These alterations result in reduced production of hepatic TG-rich lipoproteins, enhanced TG clearance, and increased HDL-C production of particles. The effect of fibrate therapy on the lipid and lipoprotein profile is characterized by elevation of HDL-C levels ranging from +5% to +20%, mean reduction in TG-rich lipoproteins ranging between 20% and 55%, and a shift in the dense LDL phenotype to receptor-active, buoyant LDL. Fibrates reduce triglyceride levels most effectively in patients with the highest levels. Several diabetes subgroup analyses from primary and secondary CHD prevention trials compared fibrate therapy with placebo; of these, the VA-HIT trial showed a significant CHD reduction of 24%, while the results of DAIS and the diabetes subgroup in the HHS were not statistically significant. In the Bezafibrate Infarction Prevention (BIP) study, which included 330 subjects (11%) with diabetes and 293 patients (9%) with IFG levels at baseline, the primary end point was fatal MI, nonfatal MI, or sudden death with secondary end points included hospitalization for unstable angina, percutaneous transluminal coronary angioplasty, and coronary artery bypass grafting. Bezafibrate

therapy raised HDL-C by 18%. Patients with diabetes mellitus and IFG, both at baseline or diagnosed during follow-up, had a significantly higher rate of secondary end points than patients with NFG ($P < 0.0001$). Bezafibrate treatment reduced secondary end points only in patients with NFG ($P = 0.04$). Thus, diabetes mellitus and IFG were predictive of a worse clinical outcome that was not attenuated with bezafibrate treatment.

The combination of a fibrate with statin therapy was evaluated by Wiklund and colleagues who compared the effects of gemfibrozil 1200 mg, pravastatin 40 mg, pravastatin plus gemfibrozil, or placebo in a 12-week randomized, controlled trial in 290 patients with total cholesterol greater than 232 mg/dL and TGs less than 354 mg/dL. Gemfibrozil plus pravastatin produced a 17% increase in HDL-C compared with a 6% increase by pravastatin alone and a 15% increase by gemfibrozil alone. The incidence of myopathy associated with statin therapy is increased when statins are used in combination with agents such as fibric acid derivatives that share common metabolic pathways.

(D) ANTIPLATELET THERAPY

Platelets play a major role in the ischemic manifestations of PAD. Patient with diabetes have a "prothrombotic" state which is characterized by the constellation of endothelial dysfunction, increased platelet adhesiveness and exaggerated platelet aggregation, ultimately resulting in intraluminal thrombus formation. In this milieu of "diabetic heightened platelet activity", therapy with antiplatelet agents is, therefore, expected to confer significant beneficial effects in reducing cardiovascular events.

Antiplatelet Therapy in Secondary Prevention of Cardiovascular Events in Patients With Diabetes & PAD

Diabetic patients with prior vascular disease are at a high risk for recurrent cardiovascular events and, in the absence of any absolute contraindication, should be treated with aspirin. In the CAPRIE (Clopidogrel versus Aspirin at Risk of Ischemic Events) trial of 19,185 patients with atherosclerotic vascular disease, clopidogrel (75 mg daily) was superior to aspirin (325 mg daily) in reducing the risk of MI, ischemic stroke or vascular death.[88] The rate of vascular events per year was 15.6% in the 1,914 diabetic patients randomized to clopidogrel and 17.7% in the 1,952 diabetic patients randomized to aspirin ($p = 0.042$); in the nondiabetic patients, the event rates per year were 11.8% and 12.7%, respectively ($p = 0.096$). It was concluded that clopidogrel is especially potent in reducing the elevated risk for recurrent ischemic events in diabetic patients with a prior history of vascular disease. In the CURE (Clopidogrel in Unstable Angina to Prevent Recurrent Events) trial, the effect of combination therapy with aspirin plus clopidogrel, versus aspirin alone, was evaluated in the 12,562 patients with non-ST elevation ACS. The primary composite outcome of death, nonfatal MI or stroke occurred in 9.3% of the aspirin plus clopidogrel group and in 11.4% of the aspirin alone group ($p < 0.001$). Although a specific analysis of the diabetic subgroup is not available, the combination of aspirin plus clopidogrel reduced the risk of composite endpoints from 16.7% to 14.2%, pointing out the potential efficacy of this regimen in diabetic patients.

CONCLUSION

Peripheral Vascular Disease is should be evaluated at least in part by their

effect on cardiovascular effect. Although there are no studies available to directly suggest beneficial effect of blood glucose control on macrovascular effect yet, present data strongly indicate tight glycaemic control of both fasting and postprandial glucose level is of help to achieve this goal. Glycaemic control can be achieved with lifestyle intervention, oral hypoglycaemic effect mainly metformin, thiazolidinediones which have properties that may be associated with cardiovascular disease benefit in the long run and recently available newer insulin analog. Use of ACEI or ARB should get precedence over others agents apart from optimum utilization of beta blocker for aggressive blood pressure control to currently recommended targeted level of 130/80 mm Hg. Although reduction of low-density lipoprotein cholesterol is the primary target of treatment to reduce the risk of cardiovascular events, including stroke reduction of elevated triglyceride levels is now considered a secondary target for risk reduction. Lower goals for triglycerides — including normal levels at <150 mg/dL — have also been set for triglyceride therapy. Dietary modifications and increased exercise remain the initial therapeutic approaches; however, pharmacologic intervention may be required for many patients. Selection of the appropriate agent from among the available medications, including statins, fibrates, nicotinic acid, and omega-3 fatty acids, depends on the degree of triglyceride elevation and the presence of other lipoprotein abnormalities. Platelet inhibition with oral or intravenous agents has “normalized” the increased risk of diabetic patients with PAD. Aspirin is effective in the primary prevention of fatal and nonfatal MI in patients with diabetes, and in the absence of contraindications, should be given to all diabetic subjects at high risk for vascular disease. Clopidogrel has been proven superior to aspirin, especially in diabetic patients.

BIBLIOGRAPHY

- American Diabetes Association. Diagnosis and classification of diabetes mellitus. *Diabetes Care*. 2004;27(suppl 1):S5-S10.
- Barry J. Goldstein, MD, PhD and Susan E. Wiegiers, MD, FACC: Treatment Strategies for Type 2 Diabetes: Drug Benefit Trends 11(11sb):11-34, 1999.
- Bucala R, Cerami A, Vlassara H: Advanced glycosylation end products in diabetic complications. biochemical basis and prospects for therapeutic intervention. *Diabetes Rev* 1995; 3:258-268
- Ceriello A, Quatraro A, Marchi E, et al: Impaired fibrinolytic response to increased thrombin activation in type 1 diabetes mellitus: effects of the glycosaminoglycan sulodexide. *Diabetes Metab* 1993; 19:225-229
- Ceriello A, Falletti E, Bortolotti N, et al: Increased circulating intercellular adhesion molecule-1 levels in type II diabetic patients: the possible role of metabolic control and oxidative stress. *Metabolism* 1996; 45:498-501
- Garber AJ, Duncan TG, Goodman AM, et al. Efficacy of metformin in type 2 diabetes — results of a double-blind, placebo-controlled, dose-response trial. *Am J Med*. 1997;103:491-497.
- Gaster B, Hirsch I. The effects of improved glycaemic control on complications in type 2 diabetes. *Arch Intern Med* 1998;158:134-40.
- Goldberg RB, Einhorn D, Lucas CF, et al. A randomized placebo-controlled trial of repaglinide in the treatment of type 2 diabetes. *Diabetes Care*. 1998;21: 1897-1903.
- Groot PHE, van Sijpout WAHJ, Krauss XH, et al: Postprandial lipoprotein metabolism in normolipidemic men with and without coronary artery disease. *Arterioscler Thromb* 1991; 11:653-662
- Habib MP, Dickerson FD, Mooradian AD: Effect of diabetes, insulin, and glucose load on lipid peroxidation in the rat. *Metabolism* 1994; 43:1442-1445
- Harrower AD. Pharmacokinetics of oral antihyperglycaemic agents in patients with renal insufficiency. *Clin Pharmacokinet*. 1996;31:111-119.
- Intensive blood-glucose control with sulphonylureas or insulin compared with conventional treatment and risk of complications in patients with type 2 diabetes (UKPDS 33): UK Prospective Diabetes Study (UKPDS) Group. *Lancet* 1998;352:837-53.
- Koya D, King GL: Protein kinase C activation and the development of diabetic complications. *Diabetes* 1998; 47:859-866
- O'Keefe J, Miles J, Harris W, et al. Improving the adverse cardiovascular prognosis of type 2 diabetes. *Mayo Clin Proc* 1999;74:171-80.
- Patsch JR, Miesenböck G, Hopferwieser T, et al: Relation of triglyceride metabolism and coronary artery disease. studies in the postprandial state. *Arterioscler Thromb* 1992; 12:1336-1345
- Peter B. George, MD, Kenneth J. Tobin, DO, Roberto A. Corpus, MD, William H. Devlin, MD, and William W. O'Neill, MD: Treatment of Cardiac Risk Factors in Diabetic Patients: How Well Do We Follow the Guidelines? from the Division of Cardiology, *Am Heart J* 142(5):857-863, 2001.
- Report of the Expert Committee on the Diagnosis And Classification of Diabetes Mellitus. *Diabetes Care* 1997;20:1183-97.
- Stratton IM, Adler AI, Neil HA, et al. Association of glycaemia with macrovascular and microvascular complication of Type 2 Diabetes (UKPDS 35): prospective observational study. *BMJ* 2000;321:405-12.
- UK Prospective Diabetes Study (UKPDS) Group. Intensive blood-glucose control with sulphonylureas or insulin compared with conventional treatment and risk of complications in patients with type 2 diabetes. *Lancet*. 1998;352:837-853.
- Zimmerman BR. Sulphonylureas. *Endocrinol Metab Clin North Am*. 1997;26:511-522.

PEER REVIEWERS OF JIMSA

Peer Review process is essential for maintaining high standard of scientific content of the journal. Editorial board of JIMSA is extremely grateful to the following reviewers for rendering help in thoroughly scrutinizing the articles published during the year 2005

K.Jagadeesan (Chennai)	Surgery	S.A. Tabish (J & K)	Health Admn.
Sandip Mukherjee (Delhi)	Surgery	M. Sachdev (Delhi)	Medical Education
D.D.S. Kulpati (Delhi)	Pulmonology	V.H. Talib (Delhi)	Lab.Medicine
K.B. Logani (Delhi)	Pathology	Sukumar Mukerjee (Kolkata)	Phematology
Indira Bahl (Delhi)	Anatomy	R.R. Thukral (Delhi)	ENT
Prema Bali (Delhi)	Community Medicine	R.K. Bali (Delhi)	Dental
Veera Hingorani (Delhi)	Obst. & Gyne	S.S. Sethi (Delhi)	Plastic Surgery
S.K. Bhargava (Delhi)	Radiology	Rattan Singh (Delhi)	Derm. Ven & Leprosy
I.P.S.Kalra (Delhi)	Cardiology	Sham Agarwal (Delhi)	Endocrinologist
P.N. Renjen (Delhi)	Neurology	P.S. Gupta (Delhi)	Gestroentrologist
H.K.Chopra (Delhi)	Cardiology	P.K. Dave (Delhi)	Orthopedics
Tarun Gupta (Delhi)	Surgery	V.K. Dada (Delhi)	Ophthalmology
Chintamani (Delhi)	Surgery	K.K. Malhotra (Delhi)	Nephrology
Sudershan K. Aggarwal (Delhi)	Radiology	H.P.S. Sachdev (Delhi)	Pediatrics
K.B. Sharma (Delhi)	Microbiology	Kamlesh Kohli (Delhi)	Pharmacology
O.P. Gupta (Ahmedabad)	Endocrinology	T.K. Biswas (Kolkata)	Internal Medicine
B. Ramamurthy (Chennai)	Neurosurgery	R.R. Kasliwal (Delhi)	Cardiology
Habibullah Zargar (J & K)	Endocrinology	Naresh Trehan (Delhi)	Cardiologist
M. Natarajan (Chennai)	Ortho surgery	S.D. Jeyaraj (Chennai)	Cardiologist
P.M. Dalal (Mumbai)	Neurology	N.S. Neki (Amritsar)	Medicine
G.S. Sainani (Mumbai)	Medicine	Richa Diwan (Delhi)	Internal Medicine
		M. Suresh Kumar (Chennai)	Psychiatry

Most Economical Brand of Telmisartan

CRESAR

(Telmisartan 20/40mg)

CRESAR-H

(Telmisartan40+hydrochlorothiazide12.5mg)

Control BP. Activates PPAR- γ too

Indias's 1st Torsemide As 1st Line loop Diuretic

DYTOR

(Tosemide-5/10/20/100mg)

Now Also Available

DYTOR-40

(Torsemide-40mg)

Truly 1 step ahead

For Sequential Nephron Blockade

DIUREM

(metolazone2.5/5mg)

CONQUERS

DIURETIC RESISTANCE

Filtering complexities

Simplifying life

Courtesy: **CIPLA VITALIS**

IMSACON 2006 held at Lahore Medical & Dental College, Lahore, Pakistan

3rd - 5th November 2006



TV presentation by the President, the Vice President, the Secretary General of International Medical Sciences Academy and the Organising Secretary of IMSACON 2006 held at Lahore in November 2006 Venue of the conference was Lahore Medical and Dental College Lahore.

■ In the TV presentation the President, International Medical Sciences Academy said “My name is Dr. K. Jagadeesan. I am a transplant surgeon and President of International Medical Sciences Academy founded on 28.3.81. Since then it has established 28 centres all over the world. It is an international body in which medical specialities of various disciplines are included. This is a recognised International Academy and is a member of Council for International Organizations of Medical Sciences (CIOMS) Geneva. It supports and encourages all the departments of Medical Sciences and has been helping in new ways of cooperation. It also ensures the manufacturing of quality drugs. We as a part of society are keen to spread, the message that those who are associated with Medical Sciences should be accountable for their services rendered to the patients. We wish healthful life of whole mankind. In this regard Prof. Shaheena Asif has played a remarkable role and has set example for next generation to follow. I am proud of her professional qualities and this Academy will ever remember her contributions”.

■ Dr. R.R. Thukral, Vice President, IMSA introduced “My name is Dr. Rajpat Rai Thukral . I am the Vice President of International Medical Sciences Academy. We have come from India to participate in this IMSACON 2006 conference. We highly praise Dr. Shaheena Asif for the nice arrangements made for the conference. By holding such a wonderful conference in Pakistan she has set an example for the new generation. I belong to Delhi, India and am an ENT specialist. The basic purpose of the conference is to exchange among ourselves experience, knowledge and the new researches made. We are sharing our views with the doctors of India and Pakistan under one umbrella keeping in view the betterment of both of our countries in the light of research work done . We both are working under one roof for the welfare of humanity at large”.

■ Dr. H.K.Chora spoke “My name is Dr. H.K.Chopra. I am the Secretary General of the World Head Quarter of International Medical Sciences Academy. I hail from New Delhi. I am a Cardiologist by profession. I am immensely happy with the efforts put in by Prof. Shaheena Asif. The way she has organized this conference is commendable and unforgettable. Her hospitality, here has impressed us a lot. In fact I have no words to express this gesture. The arrangements done by her for this conference are unique. During the first session, Dr. A. N. Chohan meritoriously expressed views about the wonderful arrangements made.

■ Dr. Shaheena Asif said “The experience of holding conference in Pakistan is before you. The people called this conference unparalleled and unprecedented. For these remarks we are grateful to Almighty that He has translated our dreams into a reality. The credit goes to the executive committee, the professors and the workers of the Lahore Medical and Dental College for all this grand and successful conference. I salute and greet all involved from the core of my heart.

Conference News

IMSACON 2006

Published in Urdu Daily “Health” from Lahore, Pakistan (3-5th, Nov, 2006) (www.afroasianhealth.com)

Letter of Appreciation from**Dr. Tahir Ali Javed, Minister for Health, Punjab, Lahore, Pakistan to Dr. R.R. Thukral, Vice President as below:****Next Issue Highlights****Special issue: Interventional Radiology****Guest Editor : Col. Chander Mohan**

- Interventional Radiology : Cruising from a Glorious Past to a Successful Future
- Ethical Issues in Interventional Radiology Practice
- Interventional Management of Cerebral Arteriovenous Malformation
- Intracranial aneurysms: clipping or coiling? A Neurosurgical Perspective
- Endovascular treatment of ruptured intracranial aneurysms: Immediate result and long term follow up.
- Comparative Assessment of Intracranial Aneurysms using 3D Rotational DSA and 3T MRI: Initial Experiences
- CT guided Neurolytic Celiac Plexus Block (NCPB) in abdominal
- Current Status of Image Guided Interventional Techniques in the Management of Chronic Low Back Pain

- Interventions in Obstetrics and Gynecology : a concise review
- Pioneers in Interventional Radiology
- Prostatic Interventions
- Intra-arterial Thrombolysis in Acute Stroke
- Percutaneous Vertebroplasty
- RFA in oncology principles techniques applications
- Radiofrequency Ablation in Oncology: Principles, Techniques and Current Applications
- Percutaneous catheter drainage of abdominal abscesses and fluid collections.malignancies: Experience in a cancer hospital

ABSTRACTS OF PAPERS PRESENTED AT IMSACON 2006

3rd - 5th November 2006

Lahore Medical & Dental College, Lahore, Pakistan

SECONDARY CYTOREDUCTION AND POST-OPERATIVE SECOND LINE CHEMOTHERAPY WITH GEMCITABINE & CISPLATIN IN RECURRENT EPITHELIAL OVARIAN CANCER

Nabeela Shami, Anwar, Asif, Shaharyar, Lahore Medical & Dental College, Lahore

The role of secondary cytoreduction in recurrent epithelial ovarian cancer is not clearly defined. This study was designed to evaluate the efficacy of secondary cytoreduction and post operative and line chemotherapy with gemcitabine and cisplatin in recurrent ovarian cancer. Patients who had undergone primary cytoreductive surgery, had received chemotherapy and showed a complete response but have developed subsequent recurrence were included. Evidence of measurable disease on imaging study was required. Abdomen was opened with a vertical incision, ascetic fluid washings were removed, maximal cytoreduction was done to resect the tumor to <1 cm diameter. All patients were given gemcitabine 1250 mg/m² on day 1 and 8 and cisplatin 70 mg/m² on day 8 only. Cycles were repeated every three weeks. RECIST was used for response evaluation.

Fifty-four patients were enrolled from Dec 98- Jun 05, Median age was 52 years (range 40-68). Thirty-two had previously received cyclophosphamide and cisplatin while 12 had received paclitaxel and cisplatin. The disease free interval was more than 6 months in 38 patients and less than 6 months in 14. Optimal cytoreduction was achieved in 21 (38.8%) patients only. Gut injury was seen in 4 (7.4%) and bladder perforation in 4 (7.4%). Among 21 patients with optimal cytoreduction, 10 had a CR while 11 showed a PR with chemotherapy whereas in patients with sub-optimal surgery CR was seen in 7 patients, PR in 1 and NR in 7. All patients who had a CR previously had DFI > 6 months, 17 patients are still alive at a median follow up of 16 months (range 6-42 months). Secondary cytoreduction and postoperative second line with gemcitabine and cisplatin is a reasonable treatment option for patients with recurrent epithelial ovarian cancer who present after a disease free interval of more than 6 months.

EXTENDED SPECTRUM BETA-LACTAMASES -PREVALENCE AND CLINICAL IMPLICATIONS

Mateen Izhar and Sophia Khan Dept of Microbiology Shaikh Zayed Federal Postgraduate Medical Institute, Lahore

Hospital acquired infections are a major cause of morbidity and mortality in patients admitted to medical care units. The pressing requirement in treatment of severe nosocomial infections is: urgent and appropriate antimicrobial therapy. Initial antimicrobial therapy is usually empirical which can later be targeted towards a specific organism with a known sensitivity pattern once culture results have become available.

Increasing microbial resistance to antimicrobials poses a major therapeutic dilemma. The most recognised mechanisms of bacterial resistance are restricted entry of antimicrobial into the microbial cell, modification of target site and enzymatic destruction of the antimicrobial. This latter is the mechanism of resistance of most aerobic gram negative bacilli to beta-lactam antibiotics, including all penicillins, cephalosporins, monobactams and carbapenems. Beta-lactamase enzymes arose as a bacterial response to the introduction of antibiotics and were first isolated in the mid 1980s. These are known to encompass a large and rapidly increasing group of enzymes. Out of this group the Extended Spectrum Beta-Lactamases (ESBL) which arose in response to the oxyiminocephalosporins such as cefotaxime and ceftazidime are by far the largest and most important member.

Nosocomial prevalence and resistance data are useful tool in guiding the clinician towards the correct choice of antibiotic while initiating empirical therapy. This paper will review the national and international data on ESBL prevalence and discuss the diagnostic, therapeutic and infection control implications of infection with an ESBL producing organism.

NEW COMBINATION TREATMENT OF VITILIGO

Sheikh & S. H. Kazami

Vitiligo is an ever increasing problem in all ages in our country. Different regimens are in practice including sun exposure, UVR, oral & topical psoralens. My paper presents an original work with a new idea where NEEDLING is combined with narrow band UVB. The needling inoculates epidermal cells (including melanocytes) into the vitiliginous patches to create a substrate and the added UVB exposure enhances melanogenesis and hence pigmentation of the vitiliginous areas.

A study of this combination is being done over 70 patients, in both sexes, in different from Jan 2005 to date. A comparison is also being done with UVB alone (without needling) in the same patients at some patches. A 30-G needle with short stem is softly pushed through the normal edge in to the vitiligo patch at the level of the D.E junction which drags epidermal cells including melanocytes as micro-inoculation to produce a small population of melanocytes in the vitiliginous area, which is then exposed to increasing doses of narrow band UVB. Photographs of all patients were taken at the start and then

every 3 weeks. This combination treatment has proved very safe and effective in vitiligo as compared to UVB alone in all age groups.

Correspondence : Email : iftikhar96@hotmail.com

ABORTIONS IN THE LEGAL AND RELIGIOUS PERSPECTIVE.

Shabeen Naz Masood Local Government Health Department, Government of Sindh, Pakistan

In low-income countries, approximately 200 women die each day as a result of unsafe abortions (WHO). According to United Nations Population Fund (UNFPA), each year more than 20 million young women aged between 15 and 19 years undergo unsafe abortions, which results in around 78,000 deaths and because of unsafe abortions women are at risk of developing complications.

Most women do not even know that induced abortions are illegal and often the husband agrees to the procedure. The typical profile of women seeking an abortion is a married woman with a minimum of three children

POLICIES AND LEGISLATION: Abortion was considered a crime unless performed in the good faith to save the life of a pregnant woman. The policy makers in Pakistan slowly recognized that women practice induced abortion in this country, often in unsafe environment endangering their lives & causing a public health problem. Revised provisions of abortion laws 1997 declares abortion as an offence with a three years of imprisonment and a full Diah if a child is born alive.

The abortion laws are specified in PPC 338A 3380. Pakistani Law does not allow abortion in rape cases or even when the victim is insane. Pakistan's abortion law allows abortions to be performed to save the life of the woman or to provide "necessary" treatment. The law does not indicate which abortions constitute "necessary" treatment. Abortion is sometimes legal "with significant restrictions" and different verdicts for different sects of Islam. How vigorously laws are enforced vary globally. Following the International Conference on Population and Development (ICPD), held in Cairo in 1994, Pakistan has gradually integrated family planning with reproductive health services and adopted a voluntary and target-free approach to family planning services. In the end there are General Recommendations for improving Health Care, thereby reducing the back street procedures of abortion.

ACS AND LMWH FROM CLINIC TO CATH

H.k.Chopra, R.S.Sambi, Sukhwinder Kaur Dept. of cardiology, Moolchand Medcity, Lajpat Nagar, New Delhi

(ACS) is a major public health problem throughout the globe with very high morbidity and mortality. The mortality rate is 10% at 3 months sudden cardiac death 8% to 16% at one month. The Therapeutic approach of ACS has dramatically advanced few years. It is evident by various clinical Trials that Low (LMWH) is useful in stabilizing the vulnerable plaque in ACS by reducing the high sensitivity of CRP, Interleukin 6 and increasing Nitric Oxide levels. The data from CAPTURE, TIMI 11b, NICE (1), (3), (4), MULLER, ESSENCE, FRISC, FRIC, PRAXIS, ARMADA, EVET, INTERACT, ACUTE, CRUISE and SYNERGY studies will be presented. It is concluded that LMWH in ACS has tremendous potential in reducing the morbidity and mortality and can be used effectively from (clinic to cath before, during and after PCI with or without Glycoprotein IIb/IIIa, inhibitors.

ALTERATIONS OF P53 PROTEIN IN BENIGN AND MALIGNANT THYROID GLAND LESIONS

Gul-e-Rana Hameed, Khurshid and Tayab Dept of Gynecology, Services, Lahore

Alterations of p53 protein in benign and malignant thyroid gland lesions.

Study Design : An experimental 24 weeks.

Place and Duration : The study was carried out on tissue samples that were obtained from local medical colleges of Lahore including Post Graduate Medical Institute from April to September, 2004. The study included 80 cases of resected thyroid specimen with benign or malignant thyroid disease along with the relevant clinical history and provisional diagnosis.

Among 50 benign there are two major groups; non-neoplastic. 30 cases with malignant thyroid carcinoma that include papillary, follicular, medullary and anaplastic carcinoma. On the other hand among 30 cases malignant thyroid carcinoma 26 shows the positive slides for p53 while 04 slides shows the negative result for p53.

Conclusions : However, keeping in mind the limited number of subjects studied in each sub group and the rather low correlation coefficients, these possibilities would have to be substantiated in a larger study population

AN UPDATE ON LASERS IN DERMATOLOGY SYED ATIF HASNAIN KAZMI*Dept. of Dermatology, Kemu/Mayo Hospital, Lahore*

Advances in laser therapy have dramatically improved the clinicians' ability to treat cosmetic and non-cosmetic skin lesions safely and effectively. This has greatly enhanced the interest of physicians, the general public and the media as well. The number and variety of skin problems amenable to laser treatment continues to grow. Four categories of lasers are used in dermatology. These are lasers for vascular lesions, hair removal, pigmentary disorders and resurfacing, remodeling or rejuvenation. I shall give you a review of the major cosmetic and therapeutic applications of laser therapy including Nd: YAG 532 nm for freckles, lentigines, portwine stains; Long pulsed Nd: YAG 1064 nm for hair removal in Asian skin; CO₂ 10600 nm which is a cutinf- laser, used for removal of small tumors, moles, warts etc...; Flashlamp pumped pulsed dye 585 nm laser for vascular lesions; Q-switched Nd: YAG laser for pigmented lesions.

KASHMIRE : FOCUS OF CUTANEOUS LEISHMANIASIS Ali Syed & S.H. Kazmi DEPARTMENT OF DERMATOLOGY UNIT-I KEMU / MAYO HOSPITAL, LAHORE, PAKISTAN

Cutaneous leishmaniasis (CL) is a protozoal infection, endemic in many areas of Pakistan. This study was carried out to determine whether CL is endemic in District Kashmir of Province Sindh and to determine the various clinical patterns of leishmaniasis in that District. Patients from District Kashmir presenting to the Outpatient Department of Dermatology, Mayo Hospital, Lahore with a suspicion of cutaneous leishmaniasis, within a period of six months, were included in the study. The patients were diagnosed clinically and confirmed by demonstration of amastigote form of a leishmania in a Giemsa stained smear prepared from the lesions. Out of 300 patients enrolled, who had an average three months stay in District Kashmir, 55% had rural and 45% had urban leishmaniasis. The diagnosis of subtypes was based on history and clinical examination. Hundred patients had only one lesion, 121 patients had two lesions whereas rest of the patients had more than two lesions. The mean number of lesions was two with 75% involving legs and feet followed by 15% over upper limbs, 5% involving trunk and 5% over face and neck. At the end of the study, it was concluded that Cutaneous leishmaniasis is endemic in District Kashmir with predominance of rural followed by urban leishmaniasis and majority of patients have involvement of legs and feet.

ANTIBACTERIAL EFFECT OF ALLICIN A COMPONENT OF GARLIC IN INFECTIONS AND ITS COMPARISON WITH COMMONLY USED ANTIBIOTICS * Shahnaz Akhtar , Rukhsan Khurshid, and Bushra Farooqi.

** Department of Pharmacology and Biochemistry, Fatima Jinnah Medical College, Lahore*
Object : Study is carried out on the culture colonies of gram negative and gram positive organism to find out the antibacterial activity of allicin (an ingredient) and compared its antibacterial effect with commonly used antibiotics like Clarithromycin, Ciprofloxacin, Vancomycin and Enoxacin

Material and Methods: The colonies of gram negative and positive was taken from the department of Pathology of Fatima Jinnah Medical College, Lahore.

Results : It was observed that allicin shows a significant inhibitory effect on both gram negative and gram positive micro-organism as compared to Clarithromycin and vancomycin. On the other, the antibacterial activity of Ciprofloxacin and Enoxacin was significantly high as compared to the antibacterial activity of allicin.

Conclusion : It is suggested that the use of allicin along with antibiotics especially with Clarithromycin and 'vancomycin may give better response of treatment.

CHROMATOGRAPHIC DIFFERENCE OF SERUM PROTEIN INCLUDING GRANZYME H NORMAL AND BREAST CANCER PATIENTS. Z. Razvi, Khurshid and vagra Department of Biochemistry, Fatima Jinnah Medical College, Lahore,

Institute of Chemistry, University of Punjab, Lahore. Granzymes (serine protease) contained within the cytoplasmic T cells and Natural Killer (NK) cells that were kill their target cells by the process of apoptosis, Granzymes over expression is a marker of cytotoxic cell activation. Present study tried to find out the level of granzyme H in normal subject and compared its level with breast cancer patients by using the techniqui chromatography. Results shows a marked difference in the chromatographic profile of granzyme H in in breast cancer patients as compared to the chromatographic profile of normal subjects. Conclusions : However the level of granzyme should be further evaluated to delineate their potential value in predicting clinical outcome.

CLINICAL, EFFICACY AND SAFETY PROFILE OF A FIXED DOSE COMBINATION OF BISOPROLOL AND AMLODIPINE IN MODERATE ESSENTIAL - JNC VII REPORT N.S. NEKI Department of Medicine, Rajindra Hospital/Govt. Medical College, Patiala - Punjab (India)

Hypertension is an increasingly medical and public health problem. According to WHO, hypertension is an important risk factor for death throughout the world and is responsible for 62% of cerebrovascular disease and 49% of ischemic heart disease. Treating systolic blood pressure (SBP) and diastolic blood pressure (DBP) to targets <140/90 mmHg is associated with a decrease in CVD complications. Two thirds of hypertensive patients are not being controlled to BP levels less than 140/90 mmHg and majority need 2 or more antihypertensive drugs. JNC VII report has recommended that when BP is more

than 20/10 mmHg of above goal, consideration should be given to initiating therapy with 2 drugs, either as separate prescriptions or in fixed dose combinations. The aim of the study was to evaluate the efficacy, safety and tolerability of fixed dose combination of bisoprolol (2.5mg) and amlodipine (5 mg) in the form of 1 tablet was given once daily in the morning for a period of 8 week .Dose was treated at 7/15 days. All patients were subjected to routine laboratory investigations including blood urea, serum creatinine, SGPT and 12 lead ECG. BP was recorded at the end of 2 weeks, 4 weeks, 6 weeks and 8 weeks. The heart rate was also measured simultaneously . All laboratory investigations were repeated at the end of 8 weeks. Any side effects reported by the patient were noted at every visit.

Of the 50 patients, 30(60%) were males and 20(40%) were females. The mean age of the patient was 50.12 years (range 18-80 years). The mean heart rate was 87.12 beats per minute (68-105 beats/minute). The mean SBP and DBP was 163.00 mmHg range 160-179 mmHg and 101.20 mmHg (range 100-108 mmHg). The mean SBP at baseline was 163.00 ± 7.50 mmHg. This reduced significantly (p <0.001) to 146.20 ± 15.07 mmHg, 140.02 ± 12.36mmHg, 135.60 ± 10.2 mmHg, 132.6 ± 9.2 mmHg and 132.02 ± 8.3mmHg at the end of 1,2,4,6 and 8 weeks of treatment respectively. A mean fall of 20.2% from baseline was recorded in the SBP at the end of 8 weeks of treatment respectively. A mean fall of 20.2% from baseline was recorded in the SBP at the end of 8 weeks of treatment. The mean DBP at baseline was 101.20 ± 4.2 mmHg. This reduced significantly (p < 0.001) to 91.02 ± 8.2 mmHg, 85.31 ± 6.50 mmHg, 83.02 ± 5.6 mmHg, 81.25 ± 4.2mmHg and 80.34 ± 4.85mmHg at the end of 1,2,4,6 and 8 weeks of treatment respectively. A mean fall of 21.20% from baseline was recorded in the DBP at the end of 8 weeks of treatment. At the end of treatment period (8 weeks), the mean DBP was well below goal set by JNC VII for hypertension. The at baseline was 87.2 ± 11.02 beats per minute. This reduced (p<0.01) to 78.52 ± 10.25, 73.56 ± 9.52, 69.90 ± 7.56, 67.4 ± 6.4 and per minute, at the end of the 1,2,4,6 and 8 weeks of treatment respectively. 90% patients (n=45) responded well while 10% patients (n = 5) needed 2 tablets of amlodipine 5mg plus bisoprolol 2.5 mg plus bisoprolol 2.5 mg to achieve target blood pressure. Regarding side effects 4 patients (8%) reported edema feet, 2 patients (4%) headache. But these side effects were mild in nature and did not warrant stoppage of therapy.

Conclusion : The Combination of bisoprolol and amlodipine in fixed dose (2.5 mg and 5.0 mg) given as once daily dose having different and complimentary mode of actions reduce BP significantly without without any major adverse events. The systolic BP reached the target range as early as 4 weeks while DBP as early as 2 weeks therapy. This combination is safe, effective and well tolerated in patients suffering from moderate essential hypertension.

CLINICAL PROFILE OF PATIENTS IN GELATINOUS BONE MARROW TRANSFORMATION Harpreet Singh Dept. of Medicine Pt. B.D. Sharma PGIMS, Rohtak-Haryana India

The present study was planned to see the clinical spectrum associated with gelatinous bone marrow transformation (GMT). The study was carried out on bone marrow aspiration received between 1.02.1998 to 31.1.1999 pertaining to the patients attending outdoors/ admitted in various wards of Pt. BD Sharma PGIMS, Rohtak. All subjects whose bone marrow aspiration showed rial on Leishman stain underwent a detail history, clinical investigation biochemical/microbiological/radiological). Additionally, in each subject the smear was stained with special stains of Periodic Acid Schiff and Alcian blue.

Out of total 1498 marrows, 65 showed evidence of GMT. All of these had anaemia. The associated clinical spectra of diseases noticed were : Infection (31 cases), nutritional deficiency (5 cases) haematological disorders (a plastic / toxic depression) (17cases) malignancies (3 cases) , and miscellaneous (9 cases). Based on the heterogeneity of associated clinical disorders, GMT indicates severe illness and not a particular disease. GMT may be a result of bioregulatory process (which presently needs further prospective studies) that are activated in different pathologic conditions but resulting in similar lesion in the bone marrow and so till then it may be concluded that GMT is a symptom of bone marrow.

COMPARATIVE NEPHROTOXIC EFFECTS OF TWO AMINOGLYCOSIDES: GENTAMICIN AND TOBRAMYCIN Asima Malik, Khanum and Khurshid Dept. of Biochemistry, King Edward and Fatima Jinnah Medical College and Dept. Pharmacology, Allamah Iqbal Medical College, Lahore, Pakistan

Study was designed to see the comparative nephrotoxic effects of two aminoglycoside i.e. gentamycin and tobramycin . We evaluated the levels of serum creatinine and of electrolytes (sodium and potassium) in the serum of different group of rabbits considered as control group (group A), group 1 using gnetamycin and group 2 using tobramycin Rabbits in group 1 and 2 received laboratory diet and 32mg.kg day of gentamycin i/m and tobramycin twice daily for 7 days. Blood sample was collected on 1,10, 16 and 22 day of drug administration. Each rabbit of all groups was sacrificed on 22nd day of experiment. Kidneys were removed and histological studies mainly consisting of 4 components of renal tissue (glomerull, tubules, blood vessels and interstitial tissue) Level of serum creatinine was significantly increase in both group (1 , 2) as compared to control group A. On the other level of serum sodium and was insignificantly increased in both group whereas level of serum potassium was significantly decrease in both groups of rabbit receiving gentamycin and tobramysin as compared to control group of rabbit. Conclusion : It is therefore concluded that there was no significant difference in nephrotoxicity between gentamycin and tobramycin.

INTERNAL ROOT RESORPTION

Physiological or pathological resorption of the mineralized tissues i.e. dentine, cementum or bone by osteoclasts like cells is known as resorption.

If bacteria are coronal above an infamed pulp, internal resorption may occur.

External resorption can result from bacteria in the pulp cavity, surface of the root or gingival sulcus.

This paper presents the different types of resorption, how to diagnose them and how to treat them as well as case of a 30 years old lady having internal root resorption in the maxillary upper left central incisor having the history of trauma in the past diagnosed due to a routine x - ray with the complaint of mild pain in the central incisor region.

The patient's tooth was diagnosed, the effecting pathology was removed and obturated accordingly.

LIPID PROFILE AND RISK OF PRE-ECLAMPSIA.

Pre-eclampsia (PE) is a syndrome, which affects virtually all maternal organ systems. Without intervention, Pre-eclampsia progresses to eclampsia, which is characterized by malignant hypertension and epileptiform convulsions requiring emergency Caesarian section. Early pregnancy dyslipidemia is associated with an increased risk of Pre-eclampsia. Serum lipid profile (total lipids, cholesterol, triglycerides, HDL and LDL) of thirty two women with Pre-eclampsia (n=16), normotensive women (n=16) were reviewed.

The serum triglycerides and total lipids concentrations increased significantly (232.18 ± 106.41 vs 113.12 ± 21.3) P<0.01 and (806.12 U ± 243.11 vs 574.93 ± 47.55) P < 0.01, while Serum High density lipoproteins - cholesterol concentrations decreased significantly (39.75 U ± 11.99 vs 51.18 ± 06.09) P< 0.01 in preeclamptic group as compare to normal pregnant women.

Conclusions : Lipid metabolism plays a key role in the pathophysiology of Pre-eclampsia. Increased

levels and delayed triglycerides clearance and high blood pressure are the reasons for the development of preeclampsia.

LONG TERM EFFICACY OF TOPICAL THERAPIES IN KNEE OSTEOARTHRITIS : META-ANALYSIS OF RANDOMIZED PLACEBO CONTROLLED CLINICAL TRIALS. *Bikash Medhi, Biswal & Pandhi Department of Pharmacology, level 4, Research block B, Postgraduate Institute of Medical Education & Research, Chandigarh, 160012, India.*

Systematic literature search was carried out from 1966 to 31 Dec 2004 in Pubmed, Medline, Embase and Cochrane data base. Manual search of related journals in the National Medical Library (New Delhi, India), library of the institute and conference abstracts were also carried out. We included randomized controlled clinical trials of four weeks or more comparing any topical NSAID placebo or vehicle. Effect size for pain control was estimated using the software RevMan (version 4.2).

Out of 172 citations, 4 studies fulfilled all the specified criteria. Four of them compared topical NSAIDs with placebo or vehicle. Pooled effect of topical NSAIDs measured at 4 weeks or beyond was superior to placebo / vehicle in pain relief (effect size 0.28, 0.14 to 0.43)

In conclusion topical NSAIDs are effective for pain relief in knee osteoarthritis for a long duration, however this may not hold true for all the preparation.

ERB : YAG LASER RESURFACING FOR ACNE SCARS IN DARKER SKIN TYPES LONG TERM FOLLOW UP OF PATIENTS.

Acne scars are difficult to manage specially in Asian skin type III-V because of risk of complications. We evaluated the efficacy and safety to Erb : Yag laser for management of acne scars.

A total number of 50 patients with mild to severe acne scars were enrolled in the study after informed consent. Thirty were females and 20 males. Age range between 18-40 years and skin type III- V. All the patients were given sunscreen and hydroquinone 4% and Retionic Acid 0.1% one month before laser resurfacing. Erb : Yag laser with 1 variable pulse durations was used for resurfacing of face. Fluence range was between 500-800 millijoules. 3-6 passes of resurfacing was done to each area. Open wound dressing and antibiotic was given. Patient was reassessed after 7 days, 1 month, 3 month and then after 1 year to see the improvement and complications. Degree of improvement was assessed by grade 1 = 0-25%, grade 2 = 26-50%, grade 3 = 51-75% and grade 4 = 76-100%.

Intra operative bleeding was less in LP treated area but healing time was prolonged i.e 1-1.5 days with long pulse duration side. Degree of improvement seen was grade 1 = 20%, grade 2 = 45%, grade 3 = 35% and grade 4 = 0%. Side effects noted were erythema 100%, hyperpigmentation 20% of patients. Erb : Yag laser is effective in acne scars and is not associated with prolonged morbidity in darker skin types.

MDCT EVALUATION OF GUT PATHOLOGIES *Mian Waheed Ahmad Dept. of Radiology, Shalamar Hospital, Lahore, Pakistan*

In the first 50 abdominal CT scans of Shalamar hospital for suspicion of Gut pathologies, 33 were found positive. The patients were referred from surgical and Medical Indoor and Out door department. The CT scans were done with oral water ingestion and IV contrast of 100ml non ionic. Machine was Toshiba Aquilion 4 slice.

CT is a very useful tool for gut pathologies, especially when the clinical suspicion is high and the ultrasound is negative.

“NO DENTAL EXTRACTION -NO FACIAL COLLAPSE THE SLOGAN OF TODAY'S ORTHODONTICS” *Col. Hameed Ullah Jan Dept. of Orthodontics, Program Director, Armed Forces Institute of Dentistry (AFID), Rawalpindi Cantt., Pakistan*

In this esthetic conscious society, people are become more aware of their teeth straightening than they were ever before. They are more eager to have fuller labial profiles accompanied with a wider, radiant but a most attractive dental smile. With the advent of more sophisticated armamentarium and increased skill and dexterity in the field orthodontics, specialists are now more capable to handle and overcome almost all the imminent challenges being faced to them by the mushrooming growth of their diversified patients. Today's orthodontist can prevent, intercept and even comprehensively treat many patients with out dental extractions, which were deemed almost possible couple of years back. History is witness to the dental extractions of 4-8 teeth. Losing 4-8 teeth not only tortured the poor patient, it also undermined the dental profession, as the effected patient was inflicted with the "of dental extraction". No orthodontic procedure is without pits falls if not prudently managed. The same is the case with non extraction . It does create a devastating situation for tailored according to the needs and wants of each patient. Restoration smile, acceptable both to the patient as well as to the treating not be ideally made possible if maintenance of full compliment of teeth is not well respected. Flattened and sunken faces will super add the unskilled operator tailored accordingly to the needs and wants of a patient each and every orthodontist. Restoration smile, acceptable both to the patient as well as to the treating not be ideally made possible if maintenance of full compliment of teeth is not well respected. Flattened and sunken facial will super add the vacant buccal corridors conferring the young patient with an unacceptable progerian look and a compromised, narrow dental smile.

OFF-PUMP CORONARY ARTERY BYPASS : EVIDENCE BASED META - ANALYSIS *Ali Khan Department of Cardiovascular & Thoracic Surgery, Gulab Devi Cardiac Complex, Shaikat Khanum Memorial Cancer Hospital & Research Centre, Lahore, Pakistan*

Off- Pump CABG has emerged as the new fashion in the revascularization medicine. However the data for the procedure is little understood & the real benefit is not being achieved in the very patients that this technique was developed for. This paper will review the current literature & the recommendations & results. It will also present our results in the last 2 years in Pakistan in both a tertiary care center & a private community hospital.

PARAGONIMIASIS: AN EMERGING FOOD BORNE PARASITIC ZOONOSIS IN NORTH EAST INDIA. *T. Shantikumar Singh 1 Hiromu Sugiyama 2*

1. Department of Microbiology, Sikkim Manipal Institute of Medical Sciences 5th Mile, Tadong, Gangtok - 737102, INDIA. 2. Department of Parasitology, NIID, Toyama 1-23-1, Shinjuku Ward Tokyo 162 8640, Japan.

It is estimated that about 20 million people are affected by paragonimiasis worldwide. The disease is endemic in many parts of Asia, mainly China, Korea, Thailand, Philippines, Vietnam and Japan where variety of fresh water crabs and crayfish which serve as second intermediate hosts are eaten raw or undercooked. Although, India is the country from where Paragonimus westermani was first described by Kerbert (1878) from a Bengal tiger which was captured in India and died at a zoo in Amsterdam more than a century ago, paragonimiasis was never considered to be a public health problem. The first case of human pulmonary paragonimiasis in India was reported from Manipur in 1982. Since then till 1995 more than 300 cases were diagnosed and treated for paragonimiasis in Imphal, Manipur. A serological survey conducted in Manipur during 1986-1987 revealed that the disease is endemic in Imphal -East district of Manipur with a prevalence rate of 6.7%. Recently an endemic focus of paragonimiasis was also detected in Arunachal Pradesh. Thus paragonimiasis has emerged as an important food borne parasitic zoonosis especially in the north eastern states of India. Recent research studies revealed that *Potamiscus manipurensis* in Manipur (Singh et al., 1997) and *Barytelphusa lugubris* in Arunachal Pradesh (Narain et al., 2003) are naturally infected second intermediate hosts. Four types of Paragonimus metacercariae were described from Manipur and three were identified as *P. heterotremus*, *P. heterotremus*, *P. hueit' ugensis* and *P. skrjabini* on the basis of morphological features of metacercariae and adult worms. Paragonimus heterotremus was also described from Arunachal Pradesh. In Manipur, civet cats and toddy cats served as natural animal hosts of Paragonimus species prevalent. Puppies were found more suitable than Albino rats for experimental Paragonimus infection. Major symptoms of paragonimiasis and differential diagnosis Pulmonary paragonimiasis (lung fluke infection) caused by one or possibly a

combination of several species of the trematode parasite of the genus Paragonimus is one of the several important causes of recurrent haemoptysis. Haemoptysis (coughing with blood or blood stained sputum) as a disease symptom is alarming to the patients and a diagnostic dilemma to the doctors. An empirical diagnosis of pulmonary paragonimiasis can be made in patients usually children presenting with frequent spitting of blood stained sputum or recurrent haemoptysis, chest pain with a history of consumption of raw or undercooked fresh water crabs or crayfish in an endemic area. Diagnosis of paragonimiasis can also be confirmed by one of the serological tests for Paragonimus specific antibodies. However, availability of the serological test kits is limited to the country where these are produced. Pulmonary paragonimiasis clinically and radiologically mimics pulmonary tuberculosis and thus almost all the cases of paragonimiasis described here were diagnosed and treated for pulmonary tuberculosis. The problem of misdiagnosis and mismanagement of the two diseases is more significant in areas where both diseases are co-endemic as in

the north east states of India. Thus the importance of differential diagnosis of pulmonary paragonimiasis from tuberculosis is emphasized.

Treatment and control: Praziquantel (Biltricide) is the drug of choice for treatment of paragonimiasis with a cure rate of 100% when given orally in doses of 25mg per kg body weight in 3 times a day for 5 days. Bithionol was found to be a good alternative drug to be given in doses of 40mg per kg body weight daily for 10 to 15 doses for treatment of paragonimiasis. It was not available commercially but as an investigational drug in the powder form. An effective health education intervention program, changing habit by not-eating raw or undercooked crustacean hosts and mass treatment of cases are effective measures of control and prevention of paragonimiasis. Rarely paragonimiasis is included in the undergraduate as well as post graduate teaching curriculum in India till today. Now it is time to generate awareness among health personnel including clinicians and public about paragonimiasis which can be mistaken for pulmonary tuberculosis and it should be included in the curriculum of medical education.

PERINATAL OUTCOME IN MACROSOMIC PREGNANCIES AMONG DIABETIC AND NON DIABETIC MOTHERS AT TERM. Sara Saeed, Unit-II, Department of Obstetrics & Gynecology, Jinnah Hospital / AIMC, Lahore, Pakistan.

Macrosomia is defined as fetal weight above the 90th percentile, birth weight above 4000 gm or 4500 gm, or birth weight over + 2 SD of the mean birth weight by age. Pregnancies with fetal macrosomia are at increased risk of several maternal and perinatal complications. Total of 6 patients with fetal macrosomia at term were selected. Among them, 30 non-diabetic patients constituted group-A and 30 diabetic patients constituted group-B. These patients were monitored during labour. Caesarean section rate, mean neonatal birth weight and perinatal complications were compared between the two groups. The caesarean delivery rates were not statistically different between the two groups (63.3% vs 66.7%). Mean birth weight (4.43 +0.42) among diabetics was higher as compare to non- diabetic patients (4.13+0.14). Perinatal complications especially in terms of asphyxia and neonatal hypoglycemia were also encountered more often in diabetic pregnancies. Caesarean delivery rate is high in pregnancies with fetal macrosomia. Diabetic patients with fetal macrosomia are at additional risk of increased perinatal complications.

PLEURAL FLUID ESTIMATION AND TUBERCULAR INFECTION IN THE PEOPLE ADMITTED WITH PLEURAL EFFUSION : A FIVE YEAR SURVEY.

Najla Shore and Rukhshan Khurshid Department of Physiology and Biochemistry, Fatima Jinnah Medical College, Lahore, Pakistan.

We prospectively conducted this study to evaluate the diagnostic value of Pleural fluid estimation and tubercular infection in the people with pleural effusion. All patients aged 22 years and older with clinical and radiographic findings consistent with pleural effusion due to TB admitted to the hospital between January 1999 to 2005 were evaluated consecutively. The studies were performed on pleural fluid samples; glucose and protein were estimated. Specific gravity was calculated. Cell count, differential cell count, bacterial culture, acid-fast bacilli smear were performed using standard procedures. Specimen was cultured, if effusion contains more than 150 WBC/cumm. It was observed that the level of fluid glucose was increased in both sexes as compared to the normal reported values. Level of fluid protein was more in both sexes as compared to the normal reported values. However the level of pH was neutral in both sexes. Conclusion: Present study found that pleural TB is still a major cause of pleural effusion in the city of Lahore, and microbiological and biochemical investigation may be helpful in diagnosing the disease.

POT-BELLY -THE MOST POWERFUL PREDICTOR OF METABOLIC SYNDROME AND PREMATURE MORBIDITY AND MORTALITY H.K.Chopra, R.S.Sambi, Sukhwinder Kaur Dept. of cardiology, Moolchand Medcity, Lajpat Nagar, New Delhi

We aimed to evaluate the accuracy of abdominal waist circumference against the National Cholesterol Education Program Adult Treatment Panel III (NCEP A TP III) definition for defining the individual as Metabolic Syndrome (MS) in Indians. We used clinical and biochemical data from the prospective study done by us – "To Evaluate the Scenario of Metabolic Syndrome in the Hospital Based Community". Candidate definitions of MS were proposed by using the NCEP A TP-III and modified NCEP A TP III definitions. The modifications included the abdominal waist circumference cut offs to >90 cm in men and > 80 in women. 200 patients, 100 males and 100 females between the ages of 20 to 85 yrs were clinically and biochemically evaluated according to the NCEP ATP III and modified NCEP ATP III definitions.

On comparing the abdominal waist circumference of the two definitions with the > 3 criteria of the NCEP A TP III definition it was found that abdominal waist single most accurate (79%) predictor for determining the metabolic status of the individual and defining him as Metabolic Syndrome (p-value <0.001). The WC as predictor for metabolic status for males and females separately was also of high statistical significance (73% and 84%, p-value <0.001). The hospital based data has shown a significant statistical power that abdominal growth of >90 cm (36 inches) in male and >80 cm (32 inches) in females is the most powerful clinical predictor of metabolic syndrome as compared to other clinical, biochemical and ultrasonic variables (p-value <0.001). This may be considered for a premature morbidity and mortality. The whole data will be presented.

PREDICTION OF POSTMENOPAUSAL FRACTURE RISK WITH USE OF BONE MINERAL MEASUREMENT. * Asma Rasheed Rukhshan Khurshid * Department of Pathology and Biochemistry, Fatima Jinnah Medical College, Lahore, Pakistan.

Present study planned to relate the risk factors with use of bone mineral. The

female subjects wit- age range of 40-52 years included in the study. Bone density was scanned by bone scanner by applying a gel on the right heel. T score less than 2.0 indicate risk factor. Blood parameters like serum calcium, alkaline phosphatase, total protein and uric acid were also estimated. It is observed that although most of the women were physically active but they have excess of BMI. They have a history of taking hormone replacement therapy. Most of these have an increased level of calcium, alkaline phosphatase, uric acid and bone mass density as compared to control subjects. The study conclude that physiological and biochemical factors may predict a risk of osteoporosis in post menopausal women.

PREVALENCE OF ANTIBODIES TO HEPATITIS C VIRUS AMONG THE POPULATION OF LAHORE CITY, PAKISTAN. Tabassum, Khurshid, Khokar Department of Chemistry, University of Punjab Department of Biochemistry, Fatima Jinnah Medical College, Lahore, Pakistan.

The present study was conducted with an objective to evaluate the prevalence of anti-HCV antibody in major blood transfusion centers of Lahore city. Comparative study of prevalence rate with other developed and under developed countries was also done. Material and Methods: Four major blood transfusion centers of Lahore city were surveyed. Two hundred and forty nine subjects were found to be reactive for anti-HCV antibody, yielding an overall prevalence of 1.57%. The age distribution of anti-HCV reactivity showed a maximum prevalence rate of 1.4% in the age group of 20-29 years. It is concluded that there are deficiencies in practice such as an excessive, unwarranted usage of injections, a sizeable prevalence of unsafe injection practices, the short supply of injection equipment leading to a high incidence of needlestick injuries, and a lack of adequate sharps containers and disposal facilities in this part of Pakistan.

PREVALENCE OF ERECTILE DYSFUNCTION IN PAKISTANI SUBJECTS WITH AND WITHOUT TYPE 2 DIABETES: PRELIMINARY RESULTS OF LAHORE EPIDEMIOLOGICAL ADULT POPULATION-ERECTILE DYSFUNCTION (LEAP-ED) STUDY Zafar Niaz', Ali Java, Babar Rizvi, Imtiaz Ali, Sajid Abaidullah, Jawad Zaheer, Mumtaz Hasan, Department of Medicine, King Edward Medical University, Lahore, Pakistan.

Erectile dysfunction (ED) is especially common in male subjects with type 2 diabetes mellitus (T2DM), with frequency reported between 35% and 75%. The prevalence of ED increases progressively with age. We prospectively interviewed 24 consecutive male diabetic subjects presenting to diabetes clinic. Similarly; we interviewed 12 non diabetic non hypertensive male subjects. Degree of ED was determined by using sexual health inventory for men (SHIM) questionnaire, termed the IIEF-5. A score of 25 was considered to be typical for a healthy man, and 11 or less moderate-to-severe ED. For purpose of study, subjects scoring 20 or less were referred for serum FSH, LH and Total Testosterone (T) level measurement.

20/24 (83%) subjects with T2DM and 1/12 (8%) healthy subjects had some degree of erectile dysfunction.

Mean age (range) years	Mean BMI(range)	TotalGroupMean IIEF-5ScoreBetween25-21	IEEF-5ScoreBetween 20-12	IEEF-5Score < 11
(range)				IEEF-5Score
T2DM	51.4(30-73)	27.6(21-41)	7.4 (0.18)	
-	16 (n = 4)	5.2 (n = 20)		
Healthy (n=12)	40.5 (26.55)	21.2 (26.33)	23 (5.25)	25 (n=11)-5 (n = 1)

3/24 in T2DM group had labs drawn for FSH, LH, testosterone. 2/3 had low FSH, LH, and testosterone levels; 1/3 had normal testosterone and FSH, LH levels.

Erectile dysfunction is highly prevalent in male diabetic subjects residing in Lahore, Pakistan. Most cases of erectile dysfunction are not diagnosed due to cultural and social barriers. There is a feeling of embarrassment amongst patients and physicians alike in asking such personal questions. It is also interesting to see that in limited number of subjects with T2DM who had labs drawn, 2/3- had idiopathic hypogonadotropic hypogonadism (IHH). More laboratory data is needed before any definitive conclusions could be drawn regarding true prevalence of IHH.

PROFILE OF ANEMIA IN THE ELDERLY

N.S. NEKI, Department of Medicine, Rajindra Hospital/Govt. Medical College, Patiala – Punjab (India)

This prevalence of anemia in the elderly ranges from 6.30% for males and 10-20% for females 50 patients more than 60 years old with Hb <10 gm%. were studied over a period of year for the clinical presentation and type of anemia. All the patients were subjected to detailed clinical evaluation, BMI, complete hemogram, PBF, stool for M/E and occult blood. Bone marrow, serum ferritin and TIBC were done in selected cases if needed Similarly upper GI endoscopy was carried out in selected cases .

60% (30) cases were males and 40% (20) females. Maximum number of cases (40%) were in 60-64 years of age group with median age of 65 years. 62% of cases had comorbid illness and 33% had history of chronic blood loss. 70% had microcytic anemia, 40% normocytic normochromic anemia and 8% had macrocytic type. EM aspiration showed iron deficiency in 60%. Leukemia and lymphoma constituted 10%. 5% patients revealed megaloblastic anemia. Upper GI endoscopy revealed duodenal ulcer in 10 patients and esophagitis in 20 patients. 40 patients showed positive occult blood in stools. Anemia

related to chronic disease was found in 40% and that due to chronic blood loss in 30%. 30% cases showed decreased albumin (<3.5 gm%) with chronic blood loss. 40% patients showed iron deficiency anemia, while 45% patients showed low BMI. 25% patients showed ova of hook worm while 20% showed ova of round worms in stools.

Conclusions : 1.Iron deficiency and chronic illness were the most common causes of anemia (40% each) in the elderly. 2.The most common cause of GI blood loss was duodenal ulcer and gastric (3) Most patients with iron deficiency showed associated nutritional deficiency as revealed low BMI and low serum albumin.

PROFILE OF ACUTE RENAL FAILURE IN THE ELDERLY

N.S. Neki Department of Medicine, Rajindra Hospital/Govt. Medical College, Patiala – Punjab (India)

To study the aetiology, cause and prognosis of acute renal failure (ARF) in the elderly. 25 patients of ARF with serum creatinine >3 mg/dl and age >60 years admitted in Guru Nanak Dev Hospital, Amritsar over a period of 1 year were studied. The patients with acute or chronic renal failure were excluded from the study group.

60% of cases were males and 40% females. Majority of the cases (45%) were in 60-64 years age group. There was no definite difference in the age and mortality or prognosis. The commonest cause of ARF observed was septicemia (15 patients) followed by obstructive uropathy (10 patients). Regarding complications, metabolic acidosis was observed in 10 patients and hyperkalemia in 20 patients. 20 patients had severe renal failure i.e. creatinine >5 mg% and of which 7 patients died. The recovery time and mortality rate in oliguric patients (15) was prolonged (35%) as compared to non-oliguric patients (10) with mortality rate of (20%). Out of 25 patients, 20 were managed with conservative treatment and 5 patients needed hemodialysis.

Conclusion

The mortality and morbidity in elderly patients with ARF is high. Sepsis is an important cause of acute renal failure followed by obstructive uropathy in elderly population

PROSPECTIVE UNIVERSAL 75-GRAM ORAL GLUCOSE TOLERANCE SCREENING IN PREGNANT PAKISTANI WOMEN: PRELIMINARY RESULTS OF LAHORE EPIDEMIOLOGICAL ADULT POPULATION-GESTATIONAL DIABETES MELLITUS (LEAP-GDM) STUDY

Ali Jawa, Somia Iqtadar, Shahla Gulzar, Sajid Abaidullah, Jawad Zaheer, Naseem Niaz, Mumtaz Hasan -Ing Edward Medical University, Lahore, Pakistan, Department of Medicine 2Department of OB/GYN

Undiagnosed gestational diabetes mellitus (GDM) is associated with marked maternal and child morbidity and mortality. Asians are a high risk group for developing diabetes. We prospectively evaluated the prevalence of previously undiagnosed GDM in 24+week gestational age non-diabetic pregnant Pakistani females. 55 consecutively presenting subjects to OB/GYN clinic of a tertiary care center were offered 75 gram oral glucose tolerance test (OGTT). Fasting (FBS), 1 hour (1Hr) and 2 hour (2Hr) post glucose load serum blood glucose levels were tested. GDM was defined as 2/3 elevated glucose reading: FBS >95, 1-Hr >180 and 2-Hr >155 mg/dL. Isolated elevated FBS was defined as IFG, and 1/2 elevated postprandial reading as IGT.

40/55 subjects presented for OGTT. Mean age was 25(19-38) years and mean gestational age 28(24- 31) months.

Fasting mg/dL \pm SD (range) 1 Hr PPmg / dL U \pm SD (range) 2 Hr PPmg/dL \pm SD (range)

GDM(n = 10) 120 \pm 11 (100-140) 172 \pm 37 (100-200) 162 \pm 13 (140-184)

IFG(n = 14) 112 \pm 7.6 (100-126)

IGT (n = 3)

NGT(n=13)

Total(n = 40)

10/40 (25%) subjects had GDM, 14/40(35%) had IFG, 3/40(7.5%) had IGT, and 2/40 (5%) had both IFG and IGT.

Pakistani females develop GDM at a much higher rate. To our knowledge, this is the first prospective study to assess burden of undiagnosed GDM. Early intervention with medical nutrition therapy and/or Insulin therapy is needed to curb diabetes related complications in mother and fetus. Physician awareness of ADA guidelines for diagnosis based on OGTT is urgently needed. Universal OGTT screening should be performed in all \geq 24 gestational age pregnant Pakistani women. LEAP-GDM is an ongoing trial likely to yield further insight into pathogenesis of GDM.

PSEUDOMYXOMA PERITONEI IS A RARE ABDOMINAL TUMOR

Nasir Iqbal Department of Surgery FMH College of Medicine and Dentistry, Shadman, Lahore Pakistan

Pseudomyxoma peritonei is a rare abdominal tumor with a reported incidence of approximately 1 per million per year. It is invariably fatal as the space within the abdomen is eventually replaced by mucinous tumor. We report one case of pseudomyxoma peritonei. Case History: A forty years old male presented to us with history of pain abdomen and abdominal distention for last 2 years and was already diagnosed as a case of pseudomyxoma peritonei. Patient went under laparotomy at hospital and biopsy was just taken as tumor all over in the abdomen. Abdominal distention and pain was on increase till he was admitted to surgical department at Fatima memorial hospital. Re-exploration was done and cytoreduction surgery performed. Patient is fine upto one year follow up. So, this case report is highlighting the importance of surgery in PMP management

PAKISTAN AND QUACKERY ...IS THERE ANY LAW OF THE LAND !

Shabeen Naz Masood Co - Chaired hair Anti Quackery Committee Pakistan Medical Association, Pakistan

"A person who does not have knowledge of a particular system of medicine but practices in that system is a quack and a mere pretender to medical knowledge or skill."

There about 60,000 quacks in the city of Karachi and 600,000 quacks across the country. "Bohr report" in 1946, dealt with quackery. In the 1950s these quacks claimed that they could deal with "sex problems," in the 1960s dispensers also started practicing medicine due to the shortage of qualified doctors and the absence of legislation against quackery. A large number of homeopaths emerged on the scene without proper qualifications.

In 1973 the then government tried to make a law against quackery and prepared a draft ordinance called the "Sindh Magic Remedies Act of 1973". In 1977, quackery was promoted at the State level; the government permitted a dispenser to practice medicine if he or she had worked with a doctor for 10 years. The decades old law provides maximum financial punishments up to merely Rs 2,000 which is equivalent to one day income of most of the quacks. Under the decade old ordinance, any person can open a clinic in any part of the country without getting it registered with an official body as there is no legal provision. Under the law, a Drug Inspector cannot seal a clinic of the quack despite observing unhygienic and injurious environment nor is the clinic registered at the time of its opening.

PMDC made a law on quackery in 1962 and yet another law in 1982, which could send a quack to prison, but merely for two months if he harmed somebody.

Now, that sufficient number of doctors is available and after the promulgation of Medical, Dental Degrees Ordinance, 1982 it has become necessary that quackery should be banned and prosecuted by repealing Allopathic System (Prevention of Misuse) Ordinance 1962 and Rules of 1985.

RELATIONSHIP BETWEEN TRIGLYCERIDE LEVELS AND UNNATURAL FATALITIES

DEPT. OF FORENSIC MEDICINE, PGIHER CHAN

This was a prospective study conducted between April 2002 and March 2004 on 358 unnatural deaths that were brought to the mortuary andigarb7-ia for medico legal autopsy. Forty five healthy volunteers from the hospital staff, after due informed consent were taken, as controls for the study. 10 cc of blood was collected from the right femoral vein prior to the autopsy from the dead body and from the right cubital vein of the control groups. The serum was separated from blood by centrifugation at 1500 rpm for 10 minutes, Triglyceride levels were then estimated by enzymatic method using the kit supplied by Accurex biomedical Pvt. Ltd., Thane, India

It was found that the mean triglyceride level in accidental deaths was 303.60mg%, with males showing a mean triglyceride level of 303.24mg%, and females showing 304.92mg%. The mean serum triglyceride level in suicidal deaths was 326.55mg% with males showing level of 317.40mg% and females, 338.64mg%. Homicidal deaths exhibited a mean triglyceride level of 304.14mg% with male victims showing 298.33mg% and females, 318.67mg%. However, the controls showed a mean triglyceride level of 167.54mg% with males showing 164.76mg% and females, 172.58mg%.

The present study showed that the serum triglyceride levels were significantly raised in cases of unnatural fatalities as compared to controls.

"RESEARCH PRIORITIES IN DENTAL AND MEDICAL SCIENCES AND TECHNOLOGY IN ASIA AND AFRICA"

M. Rahmatulla Director, Indian Academy of Advanced Dental Education, India

The dawn of civilization began perhaps invention of wheel. There has been slow and steady progress in every field of human activity ever since. The world has benefitted immensely from the scientific discoveries in the last two centuries as never before. The discovery of new drugs has alleviated human suffering. The institution of Noble prize in medical sciences recognises outstanding research efforts. Developing countries budget normally goes to defence, armaments and Nuclear plants and not to Health sector. Pharmaceutical industry has little interest in developing vaccine for the third world country diseases, which gives little profit. The research efforts should be consistent with disease burden. While developing a vaccine for malaria is a priority in the third world, it is the private charitable foundation of Bill Gates and Warren Buffet of U.S.A which has pledged 60 Billion dollars to World health pharmaceutical company to conduct clinical trials for using promonyecin to treat Kala azar, a disease which kills around 1 lakh population every year in Bihar alone in India. These instances compel the developing countries of Asia and Africa to identify research priorities in Health sciences.

Dentistry till the 18th century was no more than barbaric extraction of teeth, until Pierre Fauchard of France efforts raised the status of dentistry as a profession. With the advent of foot engine to fill carious cavities in teeth, Dental science today has progressed to usher in a cosmetic revolution. The Dental industry is wholly responsible in the technological Development. While it may be appropriate for the privileged community, the progress in Dental technology has not benefitted the poorer lot. The present paper is an attempt to focus attention of the scientists on oral disease burden in the third world countries. It is also an attempt to foster international collaboration to maximize limited resources of these countries to benefit the population.

RESEARCH PRIORITIES IN DENTAL AND MEDICAL SCIENCES AND TECHNOLOGY IN ASIA AND AFRICA. ACHIEVEMENTS AND CHALLENGES -AN OVERVIEW *M. Rahmatulla Director, Indian Academy of Advanced Dental Education, India*

There is no doubt that the mankind today is far healthy than in the past. It is sorely due to the sustain research efforts to alleviate human suffering. The eradication and reduction of diseases such as small pox, poliomyelitis and dental caries, Increase in the life span, lower infant mortality are some of the examples of accomplishments of medical science in the recent times. Currently research is concentrated on issues pertaining to advanced countries. Hence, there is an urgent need to direct research to health disorders, faced by the under privileged, in the developing countries.

This paper is an attempt to present an overview of current research accomplishments, in both medical and dental field. The drugs discovered and the dental technology developed has not benefited the poorer lot. Hence, the present paper is an attempt to focus attention of the scientists' research on oral diseases burden in the third world countries. It is also an attempt to foster international collaboration to maximize limited resources of these countries to benefit the population.

This paper is also a curtain raiser for the proposed international symposium on research priorities in dental sciences and technologies to be held in India-Chennai, December 1 to 3, 2007, to be jointly sponsored by the Indian society for dental research in association with International association for dental research and the WHO.

REVERSE SURAL ARTERY FLAP AS AN OPTION TO COVER THE SOFT TISSUE DEFECTS OF LOWER ONE THIRD OF LEG *Saeed Ashraf Cheema*

Dept. of Plastic Surgery Services, Institute of Medical Sciences & Services Hospital Lahore, Pakistan

Lower limb trauma is very common in the third world countries. Main cause of trauma is road traffic accidents, although quite a big number of cases also result from etiologies like firearm injury, household trauma and burn injury, etc. Reconstruction of the soft tissue defects of the lower limb is a challenging job due to scarcity of the reconstruction options. Whereas a number of options were utilized to reconstruct defects in lower one third of leg, reverse sural artery flap acted as work horse in the area. Reverse sural artery flap is quite versatile flap as it can be used to reconstruct the soft tissue defects in the regions of middle and lower thirds of leg, ankle, heel, sole and dorsum of foot. In this paper, its use in defects of lower one third of leg is discussed and compared with other options.

THREE YEARS REVIEW OF MATERNAL MORTALITY IN A TERTIARY CARE CENTRE (JINNAH HOSPITAL, LAHORE) AND RECOMMENDATIONS

Shahnaz Kouser, Raana Shirin, Prof. Amtullah Zareen Dept. of Obstetrics & Gynecology, Unit -II, Jinnah Hospital, Lahore, Pakistan

Objectives of the Study to (1) To review the current status of maternity services and to review maternal mortality at a tertiary care hospital. To find out the short comings providing adequate services. to high light the basic causes of increased maternal mortality and to device recommendations. All maternal deaths occurring in 3 years. Inclusion of all serious patients having direct or indirect obstetric complications, who expired either immediately or after few days. There were 59 maternal deaths during the study period. The MMR was 523/100,000 LB. Fifty four patients were unbooked, who presented through emergency. Most of the patients 40 (67.7%) were of age group 20- 30 years. Most common presenting complaint was vaginal bleeding (APH, PPH) in 27 (45.7 %) cases, while 15 (25.4%) patients were received unconscious. The most common cause of death was hypovolaemia in 34(57.6%) patients and hypertensive disorders and related complications in 13 (22%) patients. One patient expired after mismatched transfusion.

Among all these patients, provision of ICU care was delayed in 4 cases due to non-availability of beds or of ventilators, while 8 patients did not receive blood either due non-availability of attendants or non-availability of blood in blood bank. This study highlights the fact that haemorrhage, hypertensive disorders and sepsis remain the major contributing factors for increased maternal mortality. This is coupled with untrained traditional birth attendants, compromised infrastructure and inadequate social attitudes. Need of the day is to put strong emphasis on all these components separately if we have to bring down alarmingly high maternal mortality rate.

TO STUDY THE LEVELS OF PHTHALIC ANHYDRIDE AND MALIC ANHYDRIDE IN WORKERS OF A CHEMICAL FACTORY AND THEIR EFFECT ON HUMAN HEALTH. *Iqbal, Shahid and Khursid Nimir Chemicals Sheikupura, Govt. College, Ravi Road Lahore and Fatima Jinnah Medical College, Lahore, Pakistan*

Present study tried to find out the exposure of maleic anhydride in a group of workers working in a chemical factory and find out its hazards on human health. 25 workers of Nimir chemical industry Sheikupura exposed with a period of 6 month and 10 non workers of the same area were included in the study. The technique of HPLC chromatography was used to analyze the serum for the presence of maleic anhydride. Only traces of maleic anhydride were found. It is that although traces of maleic anhydride were observed but we should considered a large no of people having a more duration of exposure with the chemical.

TO STUDY THE LIPID LOWERING EFFECT OF SIMVASTATIN IN HYPERTENSIVE PATIENTS. *Shahid and Khursid Dept. of Biochemistry, Nimir Chemicals Sheikupura, Govt. College, Ravi Road Lahore and Fatima Jinnah Medical*

College, Lahore, Pakistan

Present study is carried out to find the effect of simvastatin on controlling the blood pressure as well as its effect on lowering the serum lipid profile in hypertensive patients. Blood samples were taken before and after the dose of amlodipine. It was observed that the drug not only affect on the blood pressure of the patients but it also decreased the level of lipid profile. This shows the amlodipine is a drug of choice for lowering the level of lipid profile and also controlling the blood pressure of the hypertensive patients.

GEMCITABINE AND CONCURRENT RADIATION AS A SALVAGE TREATMENT OF CHEST WALL RECURRENCE IN BREAST CANCER *Shaharyar, Alauddin, Shabbir, Hafeez, Ehsan UR Rehman, Abbasi Department of Clinical Oncology, King Edward Medical University, Lahore, Pakistan.*

Chest wall recurrences in breast cancer are seen despite postoperative chemotherapy and radiotherapy. For with unresectable lesions who have previously received radiotherapy no standard treatment is available. We devised a protocol of low dose gemcitabine as radiosensitizer concurrent with low dose of on 8md conducted this study with the objectives to document the efficacy and toxicity of this protocol.

From January 2003 to August 2005, 48 patients were included in this study. A histopathological logical evidence of chest wall recurrence was required. Females between 18- 70 years, with D⁺-odified radical mastectomy, post operative radiation and adjuvant chemotherapy were included. Is with r, aetastatic disease were excluded. Written informed consent was obtained. A dose of 150 mg of gemcitabine in 200 ml of normal saline infused in 2 hour on day 1, 8, 15 and 22 of radiation. Ion was delivered 2 hours after the completion of infusion. Conventional fractionation was used to ratotal dose of 36 ay given in 3.5 weeks. RECIST and RTOG criteria were used.

Twenty recurrences were related to the scar, 10 to the involved internal mammary lymph node invading sternum and ribs and 18 were associated with the soft tissue masses outside the scar area. tients were evaluable for response. Complete response was seen in 6/148 (12.5%) patients, (95 %), 87-37.16 %), partial response was seen in 30/148 (62.5%) (95% CI, 44.92 -71.40%) with an Mlresponse rate of 75% (95% CI, 70.57-91.40). Stable disease was seen in 9/148 (18.8%) and progression in 31/48 (6.3%) patients. Grade I skin reaction was seen in 15/148 (31.2%) Is grade II in 11/48 (22.9%) and grade III in 3/148 (6.3%) patients. No systemic toxicity was seen. "Low dose gemcitabine and concurrent radiotherapy is a reasonable salvage treatment in wall recurrence in breast cancer patients who have previously received adjuvant chemotherapy and full dose of radiotherapy. This approach has acceptable toxicity.

STRUCTURAL PREDICTION OF MUCL VACCINE THAT MAY IMMUNIZE HUMAN AGAINST BREAST CANCER

The epithelial type 1 transmembrane mucin MUC 1 is long-established as a marker for monitoring recurrence of breast cancer. It is able to break tolerance and to induce humoral immune respons in healthy subjects and ih cancer patients, but, the response is generally weak the sinen was to overcome the weak immunogenicity of heavily O-glycosylated MUCL, attempts were made to define site-specific O-glycosylation and the structural requirements for efficient endosomal proteolysis by cathepsin

Sequences of amino acids of MUC 1 with heavy O-glycosylation was taken were from Swiss Prot Data Bank

Studies on clusters of sequence-variant repeats, which are interspersed in the repeat domain of MUCL at high frequency, have revealed that a limited set of concerted amino-acid replacements (Asp-ThrO-ArgI-ProI) to Glu-SerO-ArgI-AlaI) contributes considerably to increased peptide flexibility and to under-glycosylation of sequence-variant repeats which in concert modify immunological features of the mucin. This replacement may overcome the weak immunogenicity of heavily glycosylated MUC 1. Conclusion: It is suggested that modified MUC-1 maya promising target for immunotherapeutic strategies to treat cancer by active specific immunization.

SUBJECTS WITH TYPE 2 DIABETES MELLITUS COMPARED TO HEALTHY PAKISTANI ADULTS HAVE IMPAIRED VASCULAR REACTIVITY AT SIMILAR BODY MASS INDICES: PRELIMINARY RESULTS OF LAHORE EPIDEMIOLOGICAL ADULT POPULATION-BRACHIAL ARTERY REACTIVITY (LEAP-BAR) STUDY *Ali Jawa', B*^r Rizvi', Zaffir Niaz', Intiaz Ali, Ali Imran', Sltjid Abaidullah, J- Zaheer', M- Hasan.'*

Asians are at high risk of cardiovascular events. Patients with diabetes mellitus are more susceptible to the vascular complications than non diabetics. We investigated the extent of endothelial dysfunction in Pakistani subjects with type 2 diabetes mellitus (T2DM)

18 healthy subjects and 46 subjects with T2DM were enrolled after informed consent. Endothelial function was studied ultrasonographically in a healthy subset of Pakistani volunteers. Ischemia was induced by inflating a cuff over the forearm to 40 mm Hg higher than systolic pressure for 5 minutes. Brachial artery diameter was measured at baseline and at 60 seconds after deflation by use of a GE Logic Pro ~:5 ultrasonograph with a 10 MHz transducer. All subjects were non smokers and arrived fasting for at least 12 hours. All T2DM subjects had been diagnosed for at least 5 years. As expected, subjects with T2DM have impaired %FMD but preserved % NDD. The interesting fact was that their Body mass indices were similar, an unusual finding since T2DM is usually associated with obesity. To our knowledge, this is the first study ever in Pakistan to assess the endothelial dysfunction in subjects with T2DM. Much research is needed to identify additional risk factors contributing towards development of T2DM in subjects residing in Southeast Asia. In this ongoing project, plan to focus on measuring brachial artery reactivity in healthy obese, hypertensive as well as type 2 diabetes mellitus subjects with and without microalbuminuria.

SUBJECT INDEX

A	Abdominoplasty : A Clinical debate 174 Aesthetic Breast Surgery 170 Aesthetic Rhinoplasty 165 Abstracts of papers presented at IMSACON 2006 253	L	Lasers In Plastic Surgery 178 Left over food in tray by indoor patients 219 Liposuction 144 Literature Review 26, 60, 88, 214
B	Bleomycin induced flagellate hyperpigmentation 223 Breast cancer – A Radiologist’s Perspective 15 Breast cancer – Past, Present and the Future 7 Breast cancer – Conventional Surgical Technique 37 Breast conservation Surgery 43 Breast cancer – Management of axillary lymphnodes 33 Breast oncoplasty – A new dimension 49 Breast cancer – Mismatch Repair Genes 71 Breast cancer – Mullidesciplinary Approach 72 Breast cancer – Coservation Surgery: Partial Breast Irradiation 59 Breast cancer – Quantitative Dermatoglyphic Traits 69 Breast cancer – Staging and Pathology 11 Breast cancer – Which is new in Imaging? 21 Breast cancer – new pot pourri of markers 9	M	Managing Diabetes Mellitus in patients with vascular disease 245
C	Carotid Stenting in Stroke Prevention : Present Status 130 Circadian Variation in the onset of acute myocardial Infarction in Kashmir 215 Comparative Evaluation of Bupivacaine and Ketamine as Spinal Anesthetic Agents in Albino Rabbits 87 Correlation of expression of Androgen Receptors and Estrogen Receptors in female 66 Cosmetic Surgery : Curative or Creative Science 143	N	Multiple Neurocysticerci in all 3 stages 233 Non cirrhotic portal fibrosis 225 Non – Hodgkin’s Lymphoma 93 Non Surgical Facial Rejuvenation 158
D	Diabetic Foot Care 239 Dissection Room Reactions of First year Medical Students 89 Drug Profile: Pregabalin 53 Cilostazole 123 Diacerein 218	O	Oxidative Stress in Male Infertility : Role of Anti-Oxidants 95
E	Early Breast Cancer 27	P	Spontaneous candida peritonitis 224 Accidental poisoning in children: Incidence & pattern 207 Poisoning in Children 203 Probiotics – Revisited 98 Prostatic Hyperplasia: Management by pills 229 Pulmonary Embolism 240 Protective effect of vit E on burnt rat skin 217 Peripheral vascular diseases in 21st Century 235 Pictorial CME 108,233
F	Functional endoscopic sinus surgery: 7 Year’s Review 85	R	Renal Pseudocyst: An Ultrasound report 221 Interventional Neuroradiology in neurovascular disorders 115 Role of corrective serial plaster cast application in management of CTEV 209 Role of Apoptotic Markers in predicting the response to neoadjuvant Chemotherapy in Breast Cancer – A prospective clinical study 64
G	Genito –urinary fistula – A Review of 45 Cases 81	S	Acute ischemic Stroke – Is Thrombolysis need of the hour? 128 Acute ischemic Stroke – Management 124 Stroke : An Indian Perspective 136 Surgical Options for covering soft tissue defects in locally advanced and recurrent Breast cancer 44 Systemic Sclerosis – Diffuse Form 108 Subarachnoid Haemorrhage (SAH) – What should we know? 111 Surgical Facial Rejuvenation 152 Special Issue - Breast Cancer : Advances in Mangement 7 - Cometic Surgery : New Horizons 143 Symposia: - Brain Attack : Practical Issues 109 - An Integrated approach in the Management of Peripheral Vascular Diseases 235
H	Haemangioma of tongue 91 Hair Restoration Surgery 148 A Vision for Future Health System Development 231	V	Vesico-Vaginal Fistula – Problems in Management 79 Variations of the Spine of Sphenoid 213 Vascular, Surgical & Percutaneous Interventions – A balancing act 236
I	Imaging in Acute Ischemic Stroke 119 Innovative Training Programmes for Health Workers 104 IMSA NEWS 74,135,187,244		

AUTHOR INDEX

	A		Kulshreshtha Pranjal	37	
Agarwal Meenakshi		144	Kumar Vivek	170	
Aggarwal Gyaneesh		119			M
Ahuja R.B.		143, 165			
Alai M.S.		215	Mallick J.	81	
Arya D		69	Maneesh M.	95	
Arora R.P.		229	Mandlecha R.H.	87	
Arora Vineet		207	Masih Leela	219	
			Mehrotra G	93	
			Mohanty N.K.	229	
	B		Mohil R.S.	43	
Bahadur Anil K		53	Mittal A	69	
Bains Harmesh Singh		207	Mittal Suneeta	79	
Bajaj Y.		85			N
Bansal A		61			
Basu P.		81	Neki N.S.	98, 108, 233	
Baranwal P.		170			O
Behari M.		136			
Bhatnagar D		71	Ouseph M. M.	53	
Bhargava Satish K.		91,93,221			P
Bhatt Shuchi		91	Pandey H.I.	27	
Bhangoo Kulwant S.		152	Prasad Abhila	15	
Biswas S.C.		81	Pruthi Punit	225	
Bhatt Suchi		221			R
Brar B.S.		209			
Bhat A.M.		215	Rajeshwari K.	203	
			Raheja Shashi	89	
	C		Rao K. K.	217	
Chandra Hem		219	Rani Bidya	89	
Chintamani		7, 37, 61,66,69,71	Rastogi Rajul	93,221	
Choudhary Deepak		240	Rastogi Harsh	119	
Chug Manish		115	Rathi Arun K.	53	
			Rekhi Bharat	9,66	
			Reddy T.N.	85	
	D		Rehman K.M.	130	
Deo S V S		33,49	Rizvi Yasir S.	224	
Desai Soaham D.		136			S
Dixit Vijay K.		128	Sandhu H.S.	225	
Dhami Lakshyajit D.		144	Saijanani S	69	
Doval Dinesh C.		223	Saini Radha	72	
Dubey A.P.		203	Saxena Sunita	9, 61,66	
			Sethi Tejinder K	59	
	G		Sethi S.S.	178	
Garg Parveen		209	Sewlikar	87	
Ghosal B.C.		231	Singh D.K.	27	
Garg G. K.		213	Singla K.	27	
Goyal Hemant		41	Singh Kishore	53	
Goswami B.K.		81	Singh S.	85	
Goswami Sebanti		81	Singhal V	61	
Goel Arun		174	Singh Kuldeep	158, 178	
Gujral V.K		245	Singh Daljit	207	
Gupta Ashok		235,236	Singh Uday Pratap	229	
Gupta K		66	Singh Shamsher	225	
Gupta Nupur		79	Singh Didar	224	
Gupta P		91	Sharma Nitin Kr.	229	
Gupta Sanjiv		245	Sharma Vinod	245	
Gupta Vishal		21	Shukla N.K.	41	
Gupta Vipul		109,115	Shrivastava P	165	
Gupta V.		111	Somani Sapna	91	
			Srivastava Padma M.V.	124	
	H		Srivastava Arvind	219	
Hira H.S.		224	Sugandhi Nidhi	37	
Husain Shakir		130	Suri Singh A.P.	239	
			Sukumaran S.	130	
	J				T
Jalal S.		215	Tabish S.A.	215	
Jayalakshmi H.		95	Talwar Vineet	223	
Jha A.N.		111	Tuteja Amita	69	
Jha Binita P.		71			V
Jamaluddin K.		219	Vaithiswaran V	41	
			Vajpayee A.	130	
	K		Vaid Ashok K.	223	
Kakar Smita		89	Verma K.	111	
Kant Ravi		21			W
Kaul Pity		104	Walia J.P.S.	209	
Kazal H.L.		108			
Khan S.U.		130			
Khanna Manoj		148			
Khandelwal R		69			
Khazanchi R.K.		170			
Krishna S V S R		11			
Krishnaraju V.		217			
Kumar Sunil		27			