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INTERNATIONAL MEDICAL SCIENCES ACADEMY

October - December 2008

Vol. 21 NO. 4

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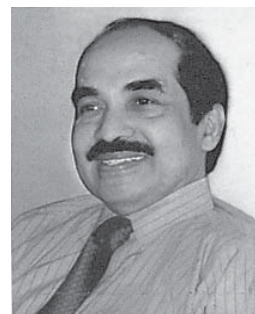
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PRESIDENT'S WRITES

Dear Fellows and Members,

It is indeed a great pleasure to write this message after a successful IMSACON 2008 at Dubai, UAE. Prof. Shaheena Asif and Ms. Nashi Khan along with an efficient team had ensured a very good meet in Dubai. This issue of JIMSA has very interesting array of articles underlining the multidisciplinary character of our organization. These articles will update all of us in a broad manner.

The financial melt down of recent days will cast its long shadow to fall on health care sector also and we must gear ourselves for the after effects. I am sure we will weather the storm, learn from the experience and take corrective measures.



Warm Greeting for a Happy & Prosperous Year 2009

K. Jagadeesan

Dr. K. Jagadeesan
President, IMSA

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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'.*



Dr. Pinnamaneni Narasimha Rao International Award

Appeal by Vice-President IMSA



Dr. P. Narasimha Rao

Ex. President, IMSA World H.Q.

Dear Fellows and Members

You are aware late Dr. P. Narasimha Rao, an international figure both in academic and teaching had been the President of this prestigious organization for more than a decade from 1990 to 2002. He was President of Medical Council of India and Vice Chancellor of various Universities. He had to his credit several outstanding contributions to the medical fraternity till his death. He had been in close association with IMSA since its very inception in 1981. The Academy has flourished tremendously during his tenure as President. Keeping in view his status, services rendered to the mankind and on the insistence of senior Fellows, the Academy has established an International Award in his honour named 'Dr. Pinnamaneni Narasimha Rao International Award', on the lines of Dr. B.C. Roy National Award. Substantial funds are needed for this prestigious award. Initially, the family of Dr. P. Narasimha Rao has contributed a fair amount of money and has also assured to contribute more.

I appeal to all our Fellows and Members to contribute generously for this noble cause in the memory of this dedicated acadamecian - Dr. P. Narasimha Rao. A separate account has been opened for this Award.

Dr. R.R.Thukral

Vice President IMSA World H.Q.

(R.R.Thukral)

IMSA Chapter Activities

CME Tamil Nadu Chapter

- 12-10-2008 Dr. L.V. Pathy: "Cardio Pulmonary Bypass"
 09-11-2008 Dr. V. Alamelu: "Recent Advances in Wound Healing
 with Special Note on Diabetic Foot".
 14-12-2008 Dr. M. Ilambarathi: "Common Lesions In Pharynx and Larynx"

RCME Tamil Nadu Chapter

- 16-11-2008 Prof. C.M.K. Reddy: "Common Surgical Emergencies"
 16-11-2008 Dr. C. Rajan: "Primary Health Care Delivery in India and
 Future Challenges"
 21-12-2008 Prof. S. Rathna Kumar: "Continuum of Care in Post Partum Hemorrhage-
 Simple Interventions For the Prevention of
 Major Catastrophe"
 21-12-2008 Dr. S. Jayachandran: "Diagnosis and Management of Ulcerative Lesions
 in the Oral Cavity"

CME Delhi Chapter

- 19-11-2008 Dr. Aru Handa: "Allergic Rhinitis"
 19-11-2008 Dr. Rajesh Sharma: "Managing Bronchial Asthma"
 29-11-2008 Dr. Ashwin Garg: "Interventional Radiology-New
 Dimensions What a Physician should know".
 29-11-2008 Dr. Pradeep Mule: Uterine Fibroid Embolization.
 17-12-2008 Dr. B. B. Khatri: Practical ENT Examination
 17-12-2008 Dr. Chanchal Pal: Practical ENT Examination

Election of Fellows and Members (October - December 2008)

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IMSA Fellows/Members Directory 2007

Dear Fellows and Members

International Medical Sciences Academy has published Directory of IMSA Fellows and Members containing information about their mailing addresses, telephone nos. email addresses, wherever available. The Directory was released at the inaugural function of IMSACON 2007 held at Manipal, Karnataka in November, 2007. I shall request you to send a demand draft of Rs. 250 soon to enable us to send to you a copy of the Directory by post. You can also collect in person from IMSA office if you so wish.

Secretary General, IMSA

Suggestions to Enhance Image of Medical Profession and Improve Doctor-Patient Relationship

President, Vice President and Trustees of IMSA have stressed that IMSA must engage itself in enhancing the image of Medical Profession by organizing seminars/conferences on various issues relating to medical profession, medico legal, patient—doctor relationship protocol of drug trials and research etc. It was also desired that suggestions be invited from all fellows and members, for improving relationship among doctors and patients.

The Fellows and Members are, therefore, requested to send their suggestions & ways and means to IMSA World Headquarter at New Delhi, for enhancing image of medical profession and improving doctor—patient relationship.

Secretary General, IMSA

Condolence

Dr. (Lt. Gen.) J.M. Grover, past Secretary General of IMSA from 04-04-1986 to 27-2-1997 left for heavenly abode on 17th Nov. 2008. Academy has suffer an irreparable loss. We pray to the Almighty for peace to the departed soul.

President, B.O.T. members, Fellows & Members IMSA

IMSACON-2009 at Chandigarh, Punjab

IMSA is pleased to inform its Fellows and Members that Annual Conference IMSACON 2009 will be held at Chandigarh, Punjab on 23, 24, & 25 Oct. 2009.

Secretary General, IMSA



JIMSA

October - December 2008

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FROM EDITOR'S DESK

Hospital acquired infections are often associated with antibiotic resistance, especially those caused by staphylococci. Prof. N.S. Neki, in an editorial, in this issue, has brilliantly discussed various aspects of this problem, frequently encountered in ICU setting. In a surveillance study from East Sikkim, the authors have emphasised the role of nasal carriage of Methicillin Resistant Staphylococcus Aureus (MRSA): the prevalence reported was 11%; interestingly the population residing close to the hospital did not pose a greater risk. In the other two original articles, CT and MRI have been reported to be powerful diagnostic tools in conditions like carcinoma colon & flourosis, respectively. An exhaustive review of poisoning by organophosphorous compounds highlights the harmful systemic effects of this poison: a need for a proper regulation for the use & storage of this compound has been rightly emphasised. A discussion about the health related challenges and opportunities afforded by the reproductive system during adolescence is well deserved, considering that 1/5th of India's population is in the adolescent age.

Paediatric Nephrology is an upcoming speciality in India. The spectrum and clinical course of Kidney Diseases is somewhat different in children from that seen in adults. The present issue of JIMSA contains a symposium on "Paediatric Nephrology". I sincerely thank **Dr. Sanjeev Gulati** for agreeing to be the Guest Editor for this symposium. The symposium covers wide ranging topics starting from nocturnal enuresis, nephrotic syndrome, obstructive uropathy to the ultimate devastating consequence of End Stage Renal Disease, requiring expensive renal replacement therapy: The write-ups have been contributed by experts from the country and abroad. I once again extend my gratitude to Dr. Sanjeev Gulati and other contributors of this excellent symposium.

I take this opportunity to thank all the members of Editorial and Advisory Boards for their assistance and also the various pharmaceutical firms, without whose help this publication would not have been possible.

*I wish to extend my good wishes to all readers of JIMSA for a
Happy, Healthy and Prosperous Year 2009*

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.

Editorial Correspondence: All corresspondance are to be addressed to **Editor JIMSA**
National Medical Library Building, Ansari Nagar, Ring Road, New Delhi - 110 029 India
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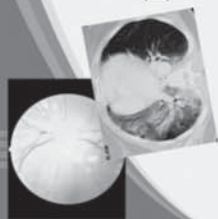


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NOSOCOMIAL INFECTIONS – THERAPEUTIC CHALLENGES

Nosocomial infections occur as a result of treatment in a hospital or a health care service unit, but secondary to the patient's original disease. Infections are considered nosocomial if they first appear 48 hours or more after hospital admission or within 30 days after discharge. Nosocomial is a greek word – *nosokomeion* meaning hospital (*nosos*=disease, *comeo*=to take care of). This type of infection is also known as a **hospital acquired infection** or more generally **health care associated infections (HAI)**. HAI's are inherent dangers of modern therapy especially for the critical ill patient in the ICU and lead to increased morbidity, mortality and costs. Increased incidence of nosocomial infections is due to chronic overcrowding in the hospitals, movement of medical staff from patient to patient providing a way for pathogens to spread, poor sanitation, underfunding, many medical procedures bypassing the body's natural protective barriers and emergence of antimicrobial resistance. Thorough hand washing and/or use of alcohol rubs by medical personnel before each patient contact is one of the most effective ways to combat nosocomial infections. More careful use of antimicrobial agents is also considered vital. In 1990 it was estimated that 5267 million population lived in developing countries. Of the 39.5 million deaths in developing countries, 9.2 million were estimated to have been caused by infectious diseases. The frequency distribution of major types of HAI is: UTI-28%, surgical wound infection -17%, pneumonia-17%, bacteraemia usually with intravascular devices 16% and others 20%. MS Magazine reports that as many as 92% of deaths from hospital infections could be prevented². The most common nosocomial infections are of the urinary tract, surgical site and various pneumonias³. Micro organisms are *transmitted* in the hospital by *five main routes* – *contact* (direct and indirect), droplet, airborne, common vehicle and vector borne. Direct contact transmission involves a direct body surface to body surface contact and physical transfer of microorganisms between a susceptible host and an infected or colonized person, such as occurs when a person turns a patient, gives a patient a bath or performs other patient – care activities that require direct person contact. Direct contact transmission also can occur between two patients, with one serving as the source of infectious microorganisms and the other as a susceptible host. Indirect contact transmission involves, contact of a susceptible host with a contaminated intermediate object, usually contaminated needles, instruments or gloves. *Droplet* transmission occur when droplets are generated from the source person mainly during coughing, sneezing and talking and during the use of procedures like bronchoscopy. Airborne transmission occurs by dissemination of either airborne droplet nuclei of evaporated

droplets containing microorganisms which remain suspended in the air for longer periods. Common vehicle transmission applies to microorganisms transmitted to the host by contaminated items such as food, water, devices etc. *Vector* transmission occurs when vectors like flies, mosquitoes transmit microorganisms. *Antibiotic resistance* with some microorganisms has become a worldwide concern. After Worldwar-II, penicillin resistance among gonococci and staphylococcal strains were first noted⁴. Methicillin resistant *Staphylococcus aureus* (MRSA) emerged in 1970's. Aminoglycoside resistant *Pseudomonas aeruginosa* was noted after widespread use of gentamicin while ceftazidime-resistant and ciprofloxacin-resistant *P.aeruginosa* remains a concern today. There has been a rapid increase in antibiotic resistance among respiratory microorganisms. Penicillin resistance in *Streptococcus pneumoniae* has increased in an epidemic manner in the past 10 years^{5,6}. Previously *Enterococcus faecalis*, now *Enterococcus faecium* has emerged commoner pathogen and it constitutes nearly all vancomycin-resistant enterococci (VRE) strains. This is not an example of increasing antibiotic resistance but rather a change in the selective pressures of the fecal flora favouring the widespread emergence of VRE as a colonizer⁷. Various factors leading to antibiotic resistance (AR) include antibiotic misuse or agent specific AR etc. A study has shown that low serum drug levels may be associated with an increased risk of selecting resistant mutants for a variety of bacteria⁸. Regarding agent specific antibiotic resistance, among the third generation cephalosporins, only ceftazidime has been associated with resistant *K.pneumoniae*, *Enterobacter* and *P.aeruginosa*, all other third generation cephalosporins have not been associated with significant resistance problems with these or other organisms^{9,10}. Similarly among aminoglycosides, gentamicin¹¹ and among fluoroquinolones, ciprofloxacin¹², have been associated with significant resistance to various organisms. So the usual recommendation is change of ceftazidime with cefepime, ciprofloxacin with levofloxacin, imipenem with meropenem and gentamicin with amikacin. As neither volume or duration of antibiotic use is a determinant or predictor of antibiotic resistance, there is no rationale for reserving an antibiotic with little or no resistance potential for further use¹³.

Prevention of hospital infection is essential by a big policing operation and consists of **infection control programme**. The *core committee* consists of a physician, a surgeon, a senior nurse, microbiologist and representatives from the operation theatres, CSSD and ICUS. Inputs are also required from others like housekeeping, laundry, food services and engineering, who work as a team to maintain the hygiene and cleanliness of the institution.

The committee performs three main functions: (i) The *first function* is to collect data regarding high risk areas such as ICUs, operation theatres, dialysis units and oncology services. Good microbiology laboratory is necessary to isolate organisms and also to indicate to clinicians trends and changes in hospital flora. For example **methicillin resistant staphylococcus aureus (MRSA)** has been a feared hospital pathogen in the past decade but is now overtaken by organisms such as E.coli and Klebsiella that secrete extended spectrum betalactamases (ESBL). MRSA is a bacterium responsible for difficult to treat infections in humans so that they are resistant to large group of antibiotics called betalactams. MRSA has evolved an ability to survive treatment with betalactamase resistant beta-lactam antibiotics, including methicillin, dicloxacillin, nafcillin and oxacillin. A 2007 report on Emerging Infectious Diseases, a publication of the Center for Disease Control and Prevention (CDC), estimated that the number of MRSA infections treated in hospitals doubled nationwide from approximately 127000 in 1999 to 278000 in 2005 while at the same time deaths increased from 11000 to more than 17000¹⁴. Mortality in MRSA is higher as compared to methicillin susceptible Staphylococcal aureus (MSSA) bacterium¹⁵. Staph.aureus most commonly colonizes the anterior nares (the nostrils), although respiratory tract, opened wounds, intravenous catheters and urinary tract are also potential sites for infection. MRSA can be detected by swabbing the nostrils of patients and isolating the bacteria found inside. Many people who are symptomatic present with pus filled boils and occasionally with rashes. In this issue, Majumdar Devjyoti et al in their article "Prevalence of nasal carriage of methicillin resistant staphylococci in healthy population of Gangtok, East Sikkim" recruited 280 apparently healthy adults out of which 247 (88.2%) subjects showed positive for staphylococcus and 31 (24%) subjects reported positive nasal swabs among those positive for S.aureus. The prevalence of MRSA in their study has been reported to be 11.1% which is of great concern. Vancomycin and teicoplanin are glycopeptide antibiotics used to treat MRSA infections and are given intravenously. Several newly discovered strains of MRSA show resistance even to vancomycin and teicoplanin and respond to linezolid, quinupristin/dalfopristin, daptomycin and tigecycline¹⁶. MRSA infections can be treated with oral agents including linezolid, rifampicin+fusidic acid, rifampicin and fluoroquinolone, prisinamycin, co-trimoxazole, doxycycline or minocycline and clindamycin¹⁷. Recently a new antibiotic-platensimycin and maggot therapy has been found to be successful to treat MRSA.

(ii) The *second function* of the infection control committee is to carryout surveillance at the local level, national/international level in order to understand the magnitude of the problem and to assess the impact of interventions in containing antimicrobial resistance. Public awareness, education of health care professionals is the need of hour with regard to prevention of antibiotic resistance. (iii) The *third function* of the committee is to enforce good infection control practices. An "infection prevention week" once a year can be used to galvanize the whole staff for prevention of hospital infections since hospital infections cannot be eliminated but can only be controlled.

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N.S. Neki

Professor, Department of Medicine, Govt. Medical College/Guru Nanak Dev Hospital, Amritsar (Punjab) and Trained Endocrinologist PGI, Chandigarh, India

Best Wishes for Very Happy & Prosperous 2009

Members of BOTICEC and Fellows/Members

JIMSA WHQ

PREVALENCE OF NASAL CARRIAGE OF METHICILLIN RESISTANT STAPHYLOCOCCI IN HEALTHY POPULATION OF GANGTOK, EAST SIKKIM

DEVJYOTI MAJUMDAR, ANKUR BARUA, BARNALI PAUL

Department of Microbiology Sikkim Manipal Institute of Medical Sciences 5th mile, Tadong, Gangtok, Sikkim-737102, India

Abstract: Methicillin Resistant *Staphylococcus Aureus* (MRSA) strains emerged in the last decade as one of the most important nosocomial pathogens. MRSA may invade the blood and cause potentially serious complications such as bacteremia, septic shock, and metastatic infections. MRSA infections have recently been identified in the community. There are few studies regarding carriage state of MRSA in the community and hence, the Epidemiology of MRSA in the community is little understood. Objectives of the study were to (1) to determine the prevalence of staphylococcal nasal carriers among healthy adults of Gangtok, East Sikkim. (2) to determine the proportion of Methicillin Resistant *Staphylococcus* species isolated from nasal carriers in healthy adults of the community. One Nasal swab from each of a total of 280 apparently healthy individuals belonging to 5 different areas of Sikkim was collected using Simple Random Sampling. The collected data was tabulated in spreadsheets of Microsoft Excel version Office 2000 and analyzed by Epi Info version windows 2000. 247 of 280 swabs (88.2%) out of them were found positive for staphylococcus. Among 247 staphylococcus nasal carriers, 129(52.2%) individuals were positive for *S. aureus*. Staphylococcal nasal carriage among healthy adults not exposed to hospital environment was found to be high (88.2%). It was also found that 31(24.0%) nasal swabs were positive for MRSA among those positive for *S. aureus*. The prevalence of MRSA in community was thus estimated to be of 11.1%. Majority of MRSA nasal carriers in the community belonged to the age group of 20 and 40 years. Proportion of MRSA nasal carriers was lower in Ranipool (16.2%) but higher in Loomse (38.5%) than in other areas. High carriage rates in different areas located far away from tertiary care level hospitals reveal that living close to a hospital is not a risk factor for MRSA or MRCNS colonization. Epidemiological studies including genotyping are required to understand in detail, the dynamics of spread of MRSA and MRCNS in the community.

Key words: Prevalence, Methicillin Resistant, *Staphylococcus aureus*, Nasal Carriers, Community

INTRODUCTION

Staphylococcus aureus (*S. aureus*), a Gram positive coccus, is frequently found as a part of the normal human microflora. The organism can be carried asymptotically for weeks or months on mucous membranes but only transiently on intact skin¹. Nasal carriers of *S. aureus* are more prone to skin sepsis and postoperative staphylococcal infections than non-carriers². Studies show that *S. aureus* teichoic acid, which is present in the surface of *S. aureus* and coagulase negative staphylococci, is the primary factor necessary for attachment to nasal vestibular mucosa³. *S. aureus* was the most common cause of nosocomial infections reported in USA during 1990-1996⁴. Methicillin Resistant *Staphylococcus Aureus* (MRSA) strains were initially described in 1961 and emerged in the last decade as one of the most important nosocomial pathogens⁵. MRSA may invade the blood and cause potentially serious complications such as bacteremia, septic shock, and serious metastatic infections (endocarditis, pneumonia, osteomyelitis, and arthritis)⁶. Healthcare workers' hands, the environment, and airborne transmission (in the case of staphylococcal pneumonia) are the most common means of spreading MRSA. Infected and colonized patients provide the primary reservoir and transmission is mainly through hospital staff⁷. Common factors associated with acquiring MRSA in any acute care setting include prolonged hospital stay, use of broad spectrum antibiotics, greater number and longer duration of antibiotic

use, stay in an ICU or burn unit, surgical wounds, decubitus ulcers, poor functional status and proximity to another patient with MRSA^{8,9}. MRSA is a strain of *S. aureus* that has developed resistance to methicillin and other beta β -lactamase-resistant penicillins and cephalosporins¹⁰. However, MRSA infections have recently been identified in the community, which raised a question of whether these infections were transmitted from hospital, or they were caused by different resistant strains. The sharp increase in the prevalence of MRSA acquired infections in many communities had led to the consideration of outpatients as a source of infection in an institution¹¹. However, there are few studies regarding carriage state of MRSA in the community. Majority of the studies, so far, had been conducted on the patients and staff members of the hospital⁶. Epidemiology of MRSA in the community is little understood or not studied at length. A few reports on MRSA in the healthy population of Nigeria, USA, Canada, Pakistan and Japan are available in the world literature. Till the beginning of study no report on the prevalence of MRSA in the community in India was available. Case reports of community acquired MRSA infections had been increasing since last 3 years in the tertiary care level hospitals in Gangtok of East Sikkim. Hence, there was an urgent need for evaluation of nasal carriage of staphylococci and Methicillin resistant staphylococci. With this background, a study was undertaken to determine the prevalence of MRSA among healthy subjects

Correspondence: Dr. Ankur Barua, Assistant Professor, Department of Community Medicine, Sikkim – Manipal Institute of Medical Sciences (SMIMS), 5th Mile Tadong, Gangtok – 737 102 India Fax.: 03592-231496, e-mail : ankurbarua26@yahoo.com

in the community in Gangtok of East Sikkim in India.

MATERIALS & METHODS

Background Information: Gangtok with Geographic-locations of (Lat/Lon Bounding Box: North=27.333332 South=27.333332 East=88.61667 West=88.61667 and altitude of 1547 m) has a population of 550,000. There are two tertiary care level hospitals, one government and the other private, at a distance of 5 miles apart in East Sikkim.

Study Period: Two months (March 2005 - April 2005).

Sample Size: One Nasal swab from each of a total of 280 apparently healthy individuals was collected for the study.

Sampling Technique: Simple Random Sampling by using the probability proportionate to sample size (PPS) method was used.

Selection Method: At the beginning, a spot-map of dwellings of different areas of East Sikkim was prepared. Then each village and nodal areas were identified in it and numbered serially. From these numbers, five spots (areas) in the map were randomly selected through lottery method. Thus, the areas selected for survey were - Deorali-Daragaon, Metro-point, Sarswati temple area, Loomse & Ranipool in East Sikkim. Households in the selected survey areas were numbered serially and specific number of households in each area (as calculated by power analysis from software package of epi-info version windows 2000) was chosen according to PPS method. Individual households were selected by using the random number table. Only one individual from each household was selected for the study through lottery method.

Study Area: Five areas that include Deorali-Daragaon, Metro-point, Sarswati temple area, Loomse & Ranipool.

Inclusion Criteria: Only one individual was included in the study from each household. Selection was done through lottery method after arranging all household members in ascending order of age.

Exclusion Criteria: Since, *Staphylococcus aureus* (*S. aureus*) was frequently found as a part of the normal human micro flora, children below 13 years of age were excluded from the study. Persons who had been admitted in a hospital in the preceding 12 months or had used any antibiotic during that period or worked in a health care center were also not included in this study.

Materials used for the survey: Sterile cotton-swabs, sterile test tubes, nutrient agar (HiMedia Laboratories Private Ltd.), Mueller-Hinton agar (HiMedia Laboratories Private Ltd.) supplemented with 4% NaCl, Oxacillin disk-1 μ g (HiMedia Laboratories Private Ltd.), Control strain NCTC 6571 (ICMR, Dibrugarh), Other reagents for catalase, oxidase, Coagulase, phosphates, DNase and sugar fermentation tests.

Data collection procedure: Nasal swabs were collected by sterile, dry cotton swabs from anterior nares of each nostril of a subject, inserting the swab and then gently rotating the swab three times¹². The swabs were immediately placed in test tubes for further processing in the laboratory. All the isolates were

tested for coagulase production following standard procedures. *Staphylococci spp* isolated were tested for Methicillin resistance by using modified Stokes same plate comparative disc diffusion method²³ using 1 μ g Oxacillin disk. Mueller-Hinton agar with 4% NaCl medium was used to detect Oxacillin resistance, incubated at 35°C for 24 hours¹³. Zone diameter of the test strain was measured in millimeter with a scale. Strains were classified as resistant or sensitive following standard procedure.

Data Analysis: The collected data was tabulated in spreadsheets of Microsoft Excel version Office 2000 and analyzed by Epi Info version windows 2000.

RESULTS

Nasal swabs from 280 healthy adult subjects were examined and among them 247(88.2%) were found to be positive for staphylococcus. Of 247 *Staphylococcal* nasal carriers, 129(52.2%) were positive for *Staphylococcus aureus* (nasal carriers of *S. aureus*) and the remaining coagulase negative staphylococci. Out of 129 *S. aureus* isolates, 31(24%) isolates were Oxacillin resistant and these are referred as MRSA. The prevalence of MRSA in community was thus estimated to be of 11.1%.

Among 247 staphylococcus nasal carriers, 171(69.2%) were males and 76(30.8%) were females. *S. aureus*, isolated from 19(21.6%) out of 88 male, and 12(29.3%) from the 41 female carriers were Methicillin resistant. However, difference in carriage rates of MRSA among male and female subjects was statistically not significant [$\chi^2=1.79$, $p=0.181$ (Yates corrected)].

MRSA nasal carriers in the community were high (26.6%) in age group of (20-40) years of age and less (10%) in age groups below 20 years and above 40years. MRSA nasal carriage was lower in Ranipool (16.2%) and higher in Loomse (38.5%) than in other areas. But these differences are statistically not significant [$\chi^2=1.72$, $p=0.156$ (Fisher exact 2-tailed)].

Out of 247 staphylococcal isolates, 118 (48%) were Coagulase Negative Staphylococci (nasal carriers of CNS) and among them, 26(22%) CNS was found to be resistant to oxacillin, referred to as Methicillin Resistant Coagulase Negative Staphylococci (MRCNS). Sex-wise break up of nasal carriers of CNS and MRCNS did not show any significant difference [$\chi^2=0.04$, $p=0.835$ (Yates corrected)] in the rates of nasal carriage among male and female carriers. MRCNS prevalence was high near the Saraswati temple area (28.6%) of lower Tadong and Loomse (28.6%). MRCNS nasal carriage rate was also higher in the age group below 40 years of age (24.75%).

DISCUSSION

S. aureus nasal carriage rates in various populations have been investigated in the developed countries with temperate climate¹⁴ but no such study among healthy population had been reported from India so far. Researchers reported that nasal carriage of *S. aureus* varied in different communities. The

results of the present study showed that nasal carriage of staphylococci was as high as 88.2% and in 52.2% cases, *S. aureus* were isolated. The prevalence of MRSA in the apparently healthy community of East Sikkim was estimated to be of 11.1%. A total of 129(46.1%) among 280 healthy individuals screened were nasal carriers of *S. aureus*. Similar findings were reported by Anwar *et al* in their study in Lahore, Pakistan who screened 1024 and 636 apparently healthy persons from urban and rural area respectively for nasal carriage of *Staphylococcus aureus* and MRSA and reported that in urban areas prevalence of nasal carriers of *S. aureus* was estimated to be 16.99%, but in rural areas, it was 11.32%. In urban areas prevalence of nasal carriers of MRSA was found to be 22.98% as against 11.11% in rural areas¹¹. In a study by Lamikanra *et al* it was observed that 56.4% of healthy Nigerian students were nasal carriers of *S. aureus*¹⁴. Tanaka *et al*, while studying *S. aureus* in healthy individuals in Japan reported 24.3% of them to be of nasal carriers¹⁵. In a study conducted at University of Texas, F. Moreno *et al* reported that 99 (58%) of 170 isolates of *S. aureus* were from community cases; the community to nosocomial case ratio was 2:1; no significant risk factors differentiated patients with community MRSA from community MSSA¹⁶.

There was no statistically significant difference in the prevalence of *S. aureus* nasal carriage between male and female subjects in the present study. This finding was contrary to that observed in the study done in Nigerian population where females harbored *S. aureus* significantly more often than males¹⁴.

An area-wise analysis of methicillin sensitive vs. resistant strains of CNS infections showed that statistically there was no significant difference in nasal carriage rate of MRCNS in areas near a tertiary care level hospital and away from the hospital. The reason for much higher rate of MRSA nasal carriage in Gangtok needs to be further investigated. A surveillance centre is necessary to be established for monitoring the problem of MRSA and MRCNS among the general population in India since Methicillin Resistant strains are increasing in other parts of the world. It is clear that epidemiological studies including genotyping are required to understand in detail, the dynamics of spread of MRSA and MRCNS in the community. Moreover, acute and recurrent infections with *S. aureus* and MARSAs are a possibility of developing drug resistant staphylococcal strains in the community. As the threat of acquiring multi-drug resistant staphylococcal infection increases with increasing prevalence of MRSA in general population, it is recommended that more studies be carried out in a larger scale in the general population along with the hospitals in order to keep updated information on nasal carriage of MRSA.

CONCLUSION

Case reports of community acquired MRSA infections had been increasing since last 3 years in the tertiary care level

hospitals in Gangtok of East Sikkim. Hence, there was an urgent need for evaluation of nasal carriage of staphylococci and Methicillin resistant staphylococci. The prevalence of MRSA in the apparently healthy community of East Sikkim was estimated to be of 11.1%. Majority of MRSA nasal carriers in the community belonged to the age group of 20 and 40 years. Proportion of MRSA nasal carriers was lower in Ranipool (16.2%) but higher in Loomse (38.5%) than in other areas. Staphylococcal nasal carriage among healthy adults, not exposed to hospital environment, was found to be high (88.2%). It was found in this study that there was no age / gender / location specific difference in nasal carriage rate of MRSA or MRCNS around the tertiary care level hospitals. High rate of MRSA nasal carriage among healthy adults in general population needed further investigation. High carriage rates in different areas located far away from tertiary care level hospitals reveal that living close to a hospital is not a risk factor for MRSA or MRCNS colonization. Epidemiological studies including genotyping are required to understand in detail, the dynamics of spread of MRSA and MRCNS in the community.

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PREOPERATIVE EVALUATION OF COLORECTAL CARCINOMA BY COMPUTED TOMOGRAPHY

*Rajul Rastogi, *Satish Kumar Bhargava, **Satish Kachhawa

* Department of Radiology and Imaging, University College of Medical Sciences & Guru Teg Bahadur Hospital, Dilshad Garden, Delhi-110095, India;

** Department of Radiodiagnosis Sardar Patel Medical College and PBM Hospital, Bikaner, Rajasthan, India

Abstract : Colorectal cancer is a disease in which malignant cells form in the tissues of the colon and rectum. The incidence of the colorectal cancer (CRC) varies greatly throughout the world. Computed Tomography (CT) is a powerful technique for detecting and staging carcinoma of the colon and rectum. In general, the sensitivity, specificity and accuracy vary with the stage of the CRC. Positive findings are highly indicative of neoplastic spread. Thus an effort has been made through this study to evaluate the role of preoperative CT in the staging of CRC

INTRODUCTION

Colorectal cancer is a malignant disease arising in the colon and rectum. The incidence of the colorectal cancer (CRC) varies greatly throughout the world. The lowest rates are found in the population of Africa, Asia, and Latin America. However, in northwestern Europe and North America, CRC ranks as one of the three most common fatal malignancies, along with lung and breast cancer, and members of these populations face a lifetime risk of developing the disease of 5% to 6%.^{1,2} Moreover, because the survival statistics in patients who undergo surgical treatment for symptomatic CRC have improved marginally over the last four decades,³ the calculated risk of dying of CRC is 2% to 3%.^{4,5} Risk factors for CRC are many and include age above forty years, preexisting adenoma, cancer family syndromes, hereditary nonpolyposis colon cancer (Lynch syndrome), inherited polyposis syndromes, chronic ulcerative colitis, Crohn's enterocolitis, etc.

MATERIAL AND METHODS

A prospective study of fifty(50) biopsy proven cases of adenocarcinoma of colorectal region was undertaken. These patients were subjected to pre-operative computed tomographic examinations using the Siemens Somatom Series CT Scanner.

The patients were administered 500-600 ml of diluted water-soluble contrast media orally one hour prior to the CT examination followed by another 200-300 ml immediately before the examination to get the optimal opacification and distension of the bowel loops. Unless the contrast material is contraindicated, the patients were administered water-soluble contrast material through an intravenous route as well. Air insufflations of the colon through the per-rectal route were done to achieve optimal colonic and rectal distension, unless contraindicated.

CT examination was done in supine position. Decubitus and prone position were utilized whenever necessary. Scans were taken both prior and after the intravenous contrast administration. Trans-axial images 10X10 mm were taken covering the entire abdomen and pelvis in the cephalocaudal direction. Additional 5X5 mm trans-axial images were taken through the region of interest. Scanning was performed during

suspended respiration. All scans were viewed at varying window widths and levels. CT staging was performed and the following parameters were established and evaluated:

- ❖ Tumor characteristics (intra-luminal / extra-luminal mass, thickness of the affected bowel segment & location)
- ❖ Local extramural invasion (irregular serrated / spiculated outer contour, tumor mass or strands of soft tissue extending out, and / or streakiness of the pericolic / perirectal fat)
- ❖ Regional nodes (a single adjacent node 1cm or larger or a cluster of three or more nodes, each less than 1cm in diameter, in their short axis)
- ❖ Distal and / or extensive disease (liver metastases, intraperitoneal and mesenteric tumor, distal retroperitoneal lymphadenopathy, and direct extension into adjacent solid or hollow organs).

The adjacent organs were considered involved, if a recognizable interface was not present between tumor and organ associated with irregular, spiculated or thickened adjoining surfaces. Omentum was considered involved when it showed enhancing discrete nodules or omental cakes. Mesenteric involvement was considered with presence of disorganized, stellate or discrete tumor masses. Peritoneal involvement was considered with presence of enhancing small nodules or diffuse peritoneal thickening and enhancement. In distal retroperitoneum 8 mm diameter in short axis was taken as upper limit.

The patients who underwent CT examination were then followed up till surgery (palliative / curative). The CT findings were then compared with those of operative findings and wherever possible, with the histo-pathological evaluation of the resected tumor or other specimen. Finally, the CT staging was compared with the Surgico-pathologic staging of the disease.

A criteria⁶ for CT staging of primary colorectal tumors is as follows

- ❖ **Stage I** – Intra-luminal mass without thickening of wall
- ❖ **Stage II** – Thickened wall (> 0.6 cm) or pelvic mass, no invasion or extension to sidewalls
- ❖ **Stage III a** – Thickened wall or pelvic mass with invasion of adjacent structures but not to pelvic sidewalls or abdominal wall
- ❖ **Stage III b** – Thickened wall or pelvic mass with extension to pelvic sidewalls and / or abdominal wall without distant metastases
- ❖ **Stage IV** – Distant metastases with or without local abnormality

Correspondence: Prof. Satish Kumar Bhargava, 201, Fancy Apartments, 19, Vasundhara Enclave, Delhi
Tel: 011-22629011, 9818312946

The above-mentioned criteria of CT staging correlates very well with the following surgico-pathologic staging system. A criterion of Surgico-pathologic staging is as follows ⁶:

- ❖ **Stage A** – Limited to mucosa
- ❖ **Stage B1** – Extension into, but not through, the muscularis propria
- ❖ **Stage B2** – Extension through muscularis, no nodes
- ❖ **Stage C1** – Limited to bowel wall, positive nodes
- ❖ **Stage C2** – Extension through bowel wall, positive nodes
- ❖ **Stage D** – Distant metastases

(Note: This staging system represents the Astler-Coller version of the Dukes classification, as modified by Turnbull)

RESULTS

- **Age:** Patients in our series ranged from second to eighth decade. The youngest patient was 19 years old and the oldest being 75 years. In the study, the largest group is formed by patients in the range of 60-69 years (16) followed by 50-59 years (9), 40-49 years & 20-29 years (7 each), 70-79 years (6), 30-39 years (4) and 10-19 (1) years in the decreasing order of frequency.
- **Sex:** In our study of 50 patients, 34 were males and 16 were females. Among the 20 patients with rectal carcinoma, 11 were females and nine were males. Among the patients with colonic carcinoma, 22 were males and four were females.
- **Location of tumor:** Among all the patients with CRC in our series, the largest group were formed by those in which rectum was involved i.e. 20 out of 50 (40%). The smallest group was formed by those in which splenic flexure was involved i.e. one of 50 (2%). In four patients, sites of involvement were multiple. These included two patients with cecal & ascending colon involvement and one patient each with transverse colon & sigmoid colon and ascending colon & rectal involvement.
- **Relation to lumen & mural thickness (fig. 1, 2, 3, 4, 5, 6):** All the patients in our series had intraluminal masses with associated increase in bowel wall thickness. None of the patients showed extraluminal masses or lack of mural thickening.
- **Local extramural invasion (fig. 2, 4, 5, 6):** In our study, CT revealed local extramural invasion in 35 out of 50 patients with a sensitivity of 91.43% and specificity of 80%. Positive and negative predictive values for the same finding were 91.43% and 80% respectively with an overall accuracy of 88%. The above results were obtained when CT finding was compared with surgical finding. Surgically, 35 of 50 cases showed extramural invasion. Comparison of the CT finding of local extramural invasion with histopathological data revealed a totally different scenario. On histopathology, only 11 of 33 patients who underwent surgical resection showed evidence of periserosal invasion. Thus when CT results were compared with that of histopathology, it yielded a sensitivity and specificity of 100% and 50% respectively. Positive and negative predictive values for the same finding were 50% and 100% respectively with an overall accuracy of 66.67%.
- **Nodal metastases (fig. 2,4):** In our study, CT detected lymphadenopathy in 20 of 50 patients & surgery in 30 of 50 patients. When of lymphadenopathy was assessed by CT and surgery, it yielded a sensitivity, specificity and accuracy of 66.67%, 100% and 80% respectively with positive & negative predictive values of 100% and 66.67%, respectively. Histopathologically, nodal metastases were detected in 15 out of 50 patients. When lymphadenopathy detected by CT was

compared with histopathological metastatic involvement of lymph nodes; the sensitivity, specificity and accuracy was 83.3%, 58.3% and 73.3% respectively with positive & negative predictive values of 75% and 70% respectively.

- **Invasion into adjacent organs:** In our study, 14 of 50 patients were diagnosed to have invasion of adjacent organs as determined by CT. On surgery, all these 14 cases were confirmed; but additional 7 cases were identified that were missed by CT. Thus our study yielded a sensitivity & specificity of 66.67% and 100% respectively, when CT results were compared with surgery with positive & negative predictive values of 100% and 80.56% respectively. For this finding no histopathological data was available for comparison with CT.
- **Invasion into pelvic/abdominal wall (fig. 3 & 5):** In our study, 8 out of 50 patients were diagnosed to have invasion of pelvic/

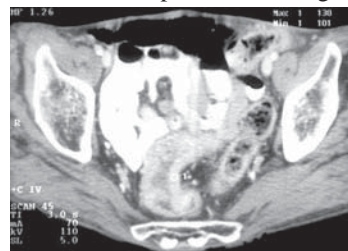


Figure 1: CT scan showing rectosigmoid carcinoma with mural thickening and intraluminal narrowing

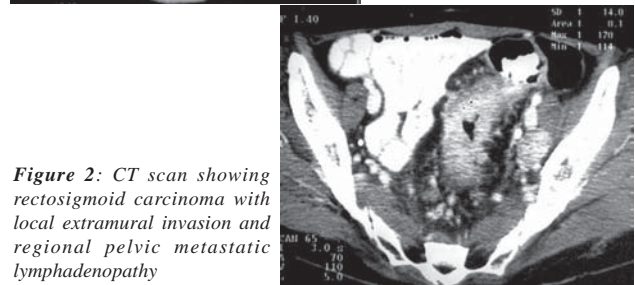


Figure 2: CT scan showing rectosigmoid carcinoma with local extramural invasion and regional pelvic metastatic lymphadenopathy

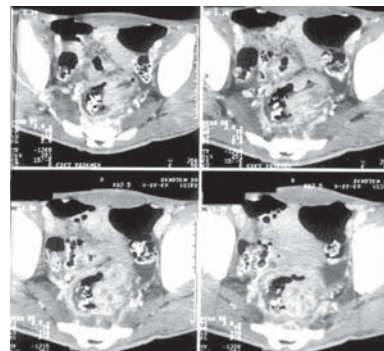


Figure 3: CT scan showing rectosigmoid carcinoma with invasion of pelvic walls posteriorly and posterolaterally with minimal ascites



Figure 4: CT scan showing carcinoma of ascending colon with pericolic metastatic lymphadenopathy, local extramural invasion and carcinoma peritonei

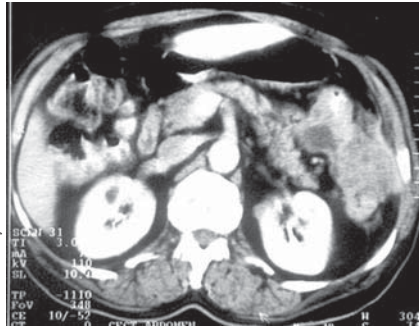


Figure 5: CT scan showing carcinoma of splenic flexure with local extramural and abdominal wall invasion

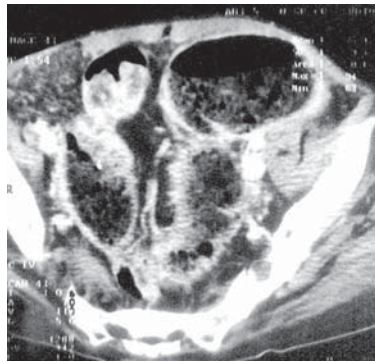


Figure 6: CT scan showing rectosigmoid carcinoma with local extramural invasion and proximal intestinal obstruction

abdominal wall as determined by CT. On surgery, all these cases were confirmed; but additional one case was identified that was missed by CT. Thus our study yielded a sensitivity and specificity of 88.89% and 100% respectively when CT results were compared with surgery with positive predictive, negative predictive values and accuracy of 100%, 97.62% and 98% respectively. For this finding no histological data was available for CT comparison.

- **Metastases (fig. 4):** In our series, 12 patients had peritoneal/mesenteric and hepatic metastases including one case that had metastases of both varieties. Out of above 12 patients, three had histologically proved peritoneal/mesenteric metastases, out of which two cases were correctly detected by CT. Similarly, out of 10 cases of histologically proved metastatic deposits in liver, CT could detect nine cases. This yielded sensitivity, specificity, positive predictive, negative predictive and accuracy values of 91.67%, 100%, 100%, 97.44% and 98% respectively.
- **Staging:** in our study, CT correctly staged 33 out of 50 cases (66%) when compared with surgicopathologic findings. CT understaged eight (16%) and overstaged nine (18%) cases. The distribution of cases is shown in the *table*.

All stage patients were represented well in our series except stage A, which was insignificantly represented. In our study, 18 out of 27 (66.67%) stage II lesions; six out of 12 (50%) stage III lesions and nine out of 10 stage IV lesions were correctly staged by CT. Of the 24 patients with rectal and rectosigmoid carcinoma, CT correctly staged – none of one stage I; nine of 12, stage II; five of seven, stage III and four of four stage IV lesions.

DISCUSSION

Colorectal cancer is treated by surgical removal of the tumor, or with adjuvant therapy. Hepatic metastases are resected surgically or palliated by cytotoxic drugs, cryosurgery or laser therapy.⁷ The chances of cure in patients with CRC depends upon the stage at which it is diagnosed. Treatment at an early stage allows 50% of patients to survive five years and 29% for 10 years, while, of those with advanced disease,

91% are dead within five years, and 97% of those patients who receive only symptomatic treatment die within five years.⁸ In our study, the percentage of patients in whom the rectum was involved formed the largest group i.e. 20 (40%), followed by cecum,

Table: Showing comparison between Computed Tomography and Surgico-Pathologic staging in fifty cases of colorectal carcinoma

CT	SURGICOPATHOLOGIC				
	1	2	3	4	TOTAL
1	0	0	0	0	0
2	1	18	7	0	26
3	0	8	6	1	15
4	0	0	0	9	9
TOTAL	1	26	13	10	50

eight (16%); hepatic flexure, six (12%); ascending colon, five (10%); transverse colon, sigmoid colon & rectosigmoid region, four each (8% each); descending colon, two (4%) and splenic flexure, one (2%) in the decreasing order of frequency.

The percentage involvement of various sites from appendix to anus as per the trends is rectum 38%, sigmoid colon 21%, cecum 12%, rectosigmoid region 7%, transverse colon 5.5%, ascending colon 5%, descending colon 4%, splenic flexure 3%, hepatic flexure & anus 2% each and appendix 0.5%.⁹

Our study shows the higher incidence in the right-sided colon while maintaining its highest incidence in the rectum. This may reflect the changing trends or may be because of smaller sample volume & selection bias so that our results may not be accurately extrapolated over the entire population.

When the CT finding of local extramural invasion was compared with histopathological data (which was obtainable in 33 of 50), sensitivity, specificity and accuracy of 100%, 50% and 66.67% respectively was achieved with positive & negative predictive values of 50% & 100% respectively. Our study results of CT versus histopathological data (*table*) are quite different from those obtained by Emil J. Balthazar et al¹⁰ and Patrick C. Freeny et al¹¹ in their studies. The use of thinner collimated slices in our series (5mm*5mm) than in other series (10mm*10mm) resulted in higher sensitivity at the cost of lowered specificity; however, the overall accuracy was comparable — 66.67% in ours, 57.9% in Emil’s & 68.75% in Patrick’s. Thus, it is clear that thinner scans do not significantly affect the overall CT accuracy of detecting local extramural invasion. CT criteria of metastatic lymphadenopathy when compared with histopathological data yielded a sensitivity, specificity and accuracy of 83.3%, 58.3% and 73.3% with a positive & negative predictive value of 75% & 70% respectively. Our results when compared with those obtained by Emil J. Balthazar et al and Patrick C. Freeny et al showed a comparable accuracy of 68.4% and 72.5% respectively. However, the sensitivity, specificity and positive & negative predictive value of only Emil’s study correlated with ours, as the criteria used were same. But the sensitivity and specificity values are very different from Patrick’s study viz. 25.9% and 96% respectively. This was because they used 1.5 cm as the upper limit of normal for labeling nodal metastases. Thus, it is clear that the lower cut-off criteria improve the CT sensitivity for detecting nodal metastases but lowers specificity significantly. But even this is advantageous as the CT detected lymph nodes can be subjected to FNAC before surgery for accurate preoperative staging and can also guide the surgeon to look for specific

lymph nodes so that they could be sent for biopsy for histopathological staging, thus allowing proper postoperative management and determining the prognosis of the patient.

When CT results for invasion into adjacent organs were compared with surgery findings in our study, it yielded sensitivity, specificity and accuracy of 66.67%, 100% and 86% respectively with a positive and negative predictive value of 100% and 80.56% respectively. No histopathological data was available related to this finding for comparison with CT data. A study by Emil J. Balthazar et al shows that CT detected nine out of 14 cases of tumor invasion into adjacent solid or hollow organs yielding a sensitivity of 64.29%. Our study results are comparable to that of Emil's study results.

In our series, CT detected pelvic / abdominal wall in eight out of nine cases confirmed on surgery. This yielded a sensitivity, specificity and accuracy of 88.89%, 100% and 98% respectively with a positive and negative predictive value of 100% and 97.62% respectively. No histopathological data were available for comparison with CT finding. This finding has not been separately considered and studied in previous reports. However, our study reveals that CT is quite an accurate method for determining the invasion into pelvic / abdominal wall.

In our series, CT could correctly identify 9 out of 10 cases of histopathologically proven hepatic metastases. The case missed on CT showed minute 2 - 5 mm hepatic nodulation. This may be because the size of nodules was beyond the resolution of the scanner or because of respiratory misregistration or partly because delayed hepatic scans were not taken. Our results are comparable to those obtained in Emil's and Patrick's series

Out of three cases of mesenteric / peritoneal metastases, CT could correctly diagnose two cases, thus yielding a sensitivity of 66.67%. The case missed on CT showed minute 2 - 5 mm mesenteric / peritoneal nodulation. This may be because the size of nodules was beyond the resolution of the scanner. The above result is similar to that of Emil J. Balthazar et al where four out of six cases were correctly diagnosed by CT, thus yielding a sensitivity of 66.67%.

In our study, 33 out of 50 cases (66%) were correctly staged by CT when compared with surgicopathologic findings. CT understaged eight (16%) and overstaged nine (18%) cases. Our study correlated well with the study conducted by Emil J. Balthazar et al i.e. 64% and G. Scott Gazelle et al¹² i.e. 76.67%.

The slightly higher staging accuracy achieved in Gazelle's study is due to the use of water-enema during CT scanning and use of dynamic sequential scans.

The higher staging accuracy achieved in our study as compared to some previous studies is due to good colonic preparation; good bowel opacification; improved CT scanning techniques and better resolution CT scanners. The accuracy may further increase with improvements in technology.

The staging accuracy in our study was much higher in patients with rectal and rectosigmoid carcinoma i.e. 79.2% which included an accuracy of 75% in stage II lesions, 71.4% in stage III lesions and 100% in stage IV lesions. This accuracy achieved in our study is higher than that achieved by B. Adalsteinsson et al¹³ i.e. 60 - 70%. This may be due to use of thinner collimated scans, bowel preparation & larger amount of positive oral contrast for good bowel opacification and also because of improved resolution of CT scanners. However, the accuracy achieved was lower than that of Ruedi F. Theoni et al¹⁴ i.e. 92%, as that study mainly included stage III and IV lesion where the CT accuracy is higher as 81.8% in our study.

CONCLUSION

In conclusion, Computed Tomography (CT) is a powerful technique for detecting and staging carcinoma of the colon and rectum. The

sensitivity, specificity and accuracy for staging primary colonic and rectal carcinomas range from 48 to 100% with a mean accuracy of 75%. In general, sensitivity, specificity and accuracy increase as disease progresses from mucosal to extramucosal stages and further especially in detecting hepatic metastases. Although negative findings on CT do not help staging colorectal carcinoma but positive findings are highly indicative of neoplastic spread. Following reasons thus justify the use of Computed Tomography in preoperative evaluation of colorectal carcinoma -

- CT is very accurate in establishing the cause of obstruction and detecting perforation in patients with colorectal carcinoma; the former being an independent prognostic factor in colorectal carcinoma and the latter determining the duration of disease free survival.
- Clinically unsuspected CT findings may lead to significant changes in either the preoperative management or type of surgery or may altogether preclude surgery; thus lessening the need for exploratory, noneffective, costly surgical procedures, reducing the hospital stay, directing FNAC / biopsy of suspected lesions, permitting application of chemotherapy & radiotherapy to be instituted promptly and effectively e.g. preoperative or intraoperative radiotherapy to control local tumor spread or to make previously inoperable lesions operable, resection of hepatic metastases, etc.
- CT is complementary to clinical assessment in high-located rectal tumors especially when preservation of rectal function is contemplated. It may provide the surgeon with additional information that can become essential during surgery as relationship between ureter and colon. CT is considered to be the best initial test for elderly frail patients with large bowel disease including colorectal carcinoma.
- Last but not the least, in patients with extensive local spread and in the absence of a specimen for pathological examination, the CT can give an objective and permanent record of the local extent in line with the pathological extent in most cases thus serving as the base-line for follow-up studies as in determining the response to therapy.

Finally, it would be apt to conclude that though CT findings cannot be solely relied upon but since the Computed Tomography delineates multiple abnormalities with a fair degree of accuracy than any other single diagnostic method, it should be considered as the investigation modality in preoperative assessment of colorectal carcinoma.

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MRI CHANGES IN COMPRESSIVE MYELOPATHY IN FLUOROSIS- STUDY OF 18 CASES FROM NORTH WEST INDIA

Ashok Panagariya, Ravindra Singh, Paresh Sukhani, Bhawana Sharma
Department of Neurology, SMS Medical College, Jaipur, Rajasthan, India

Abstract : This study was carried out to highlight the spectrum of magnetic resonance imaging changes in fluorotic spine, its frequent occurrence as cause of cord compression in this part of country and to correlate the radiological changes with the duration and severity of neurological deficit. 18 patients with clinically and biochemically proved fluorosis had MRI of whole spine on 1.5 tesla super conducting magnet between Jan 2002-Jan 2004. Clinical manifestations included pain and stiffness in spine, motor weakness, radicular pain, numbness and tingling sensation of limbs and retention of urine. Cord compression was seen in all patients. Thickening of PLL was seen in 14 patients out of which 7 patients showed ossification. Thickening of Ligamentum Flavum was seen in 16 patients, 11 of them showed ossification, intramedullary hyperintense signals representing cord edema was noted in 17, neural compression in 9 and target sign in 2 patients. There was a direct correlation between neurological deficit, duration of disease and radiological changes. Fluorosis should be considered as a possible cause of compressive myelopathy secondary to ossification of PLL or LF in the endemic areas and the neurological deficit parallels with duration of disease and radiological changes. Target sign pathognomonic of ankylosing spondylitis was seen in two patients.

Keywords : Magnetic resonance imaging, Fluoride poisoning, Ligaments. Spine, cord compression.

INTRODUCTION

Endemic skeletal fluorosis is a chronic metabolic disease caused by ingestion of large amount of fluoride through either water or food in geographic areas where high levels of fluoride occurs naturally. Although the prevalence of this disease has decreased considerably it still occurs in some parts of the world.¹ In contrast to global scenario prevalence of fluorosis is still high in developing countries like India; especially states like Punjab, Haryana, Rajasthan, Andhra Pradesh² are considered endemic for the disease. In Rajasthan, almost 27 districts are considered endemic zones for this disease.

Chronic toxicity of fluoride in human beings manifests predominantly on dental and skeletal tissue. Beside this other organs like thyroid, kidney cardiovascular and hemopoietic systems are also involved. Neurological complications, mainly compressive myelo radiculopathy, occurs in about 10% of skeletal fluorosis.³ Skeletal fluorosis was first reported as an endemic disease in India in 1937⁴. Since then various studies using plain skiagrams⁵, myelography^{6,7}, CT scan⁸ have been used to evaluate, the radiological changes in fluorotic spine but little has been written about spectrum of MRI findings⁹. Since fluorosis affects almost entire spine at multiple levels thus MRI because of its multiplanar capacity is considered superior as it can evaluate entire spine in single study. We evaluated the spectrum of MRI appearance in 18 patients of this disorder with the idea of highlighting its frequent occurrence as a cause of cord compression in endemic areas and to differentiated from other metabolic bone diseases.

MATERIAL & METHODS

This study was carried out in 18 patients of skeletal fluorosis admitted in dept of Neurology BMRC Jaipur India between

Jan 2002 - March 2004. Clinical manifestations included pain and stiffness in the spine, motor and sensory deficits in limbs, radicular pain and retention of urine.

Diagnosis of fluorosis was confirmed on the basis of urinary fluoride levels and AP skiagrams of forearm bones revealing ossification of interosseous membrane (*Fig.1*). Patients were subjected to routine investigations like blood sugar. KFT, LFT urine complete and microscopic, X-Ray fore-arm bones. Apart from these all patients were subjected to MRI of whole spine on 1.5 Tesla super-conducting magnet. T1 and T2 images were obtained using spin echo sequences in axial and sagittal planes with slice thickness of 3 mm, interslice gap of 0.4 mm and matrix 195 x 256. Conditions mimicking fluorosis such as : Ankylosing spondylitis, Diffuse idiopathic hyperostosis, Schonberg disease, Secondaries spine were excluded.



Fig.1: X-ray fore arm bones (AP view) showing ossification of interosseous membrane

RESULTS

There was male preponderance (M:F ration=14:4). Most of the patients were active manual workers doing unskilled labour on farms and living in the endemic area since birth. Most of the areas from where they belonged were fairly hot and dry, the temperatures touching 47°C. This necessitates drinking of large quantities of water and thus predisposing to higher amounts of fluoride deposition. The age ranged between 30-75 years (mean age 54 years).

Neurological examination revealed mild tenderness and stiffness in spine in 16 patients, quadriparesis in 8 patients, paraparesis in 6 patients, radiculopathy in 12 patients and bladder involvement in 2 patients .

All 18 patients had evidence of cord compression of MRI . Thickening of PLL was identified in 14 patients (77%) out of which 7 patients showed ossification. This thickening was most commonly seen in the cervical region (8 patients) followed by thoracic and cervicothoracic regions. Mean thickness of PLL

Table 1: Posterior longitudinal ligament changes

	No. of patients	Range	Mean duration of illness
Thickening	14	5-9mm	3.6 years
Ossification	7		5.8 years
Site			
Cervical	8		
Thoracic	4		
Cervicothoracic	2		

was 6.7 mm (range 5-9 mm)(table 1).

Ligamentum flavum thickening was seen in 16(88.8%) patients out of which 11 patients (69.2%) had ossified ligamentum flavum (OLF). Ligamentum flavum thickening was most commonly seen in cervicothoracic (9 patients) followed by thoracic (5 patients) and cervical spine (2 patients), the thickness of ligamentum flavum ranged from 6-9 mm with

Table 2: Ligamentum flavum changes

	No. of patients	Mean duration of illness
Thickening	16	3.5 years
Ossification	11	5.4 years
Site		
Cervical	2	
Thoracic	5	
Cervicothoracic	9	



Fig. 2: Sagittal T2 w scans of dorsal spine showing ossified posterior longitudinal ligament and ligamentum flavum thickening causing compressive myeloradiculopathy at multiple levels

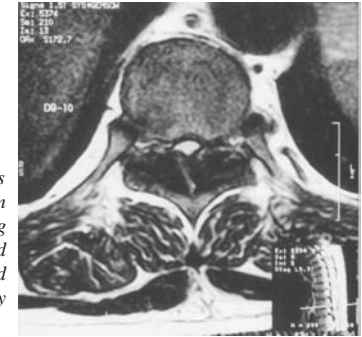


Fig. 3 Axial T2 W scans showing marked ligamentum flavum hypertrophy causing severe canal stenosis and compressing and displacing cord with focal intramedullary hyperintensity.

mean thickness of 7.4mm (table 2). (Fig. 2&3)

Intramedullary hyperintense signals representing cord edema were seen in 17 patients (94%). Neural compression was seen in 9 patients out of which herniated disc and posterior osteophytes were the cause in 6 patients and thickened PLL in 3 patients. Two patients in our series showed alternate bands of low and high signal intensity in intervertebral disc giving target sign appearance(Fig. 4).



Fig. 4 Sagittal T2 W scans of lumbo-sacral spine showing alternating bands of high and low signal intensity (Target sign appearance)

DISCUSSION

Consumption of fluorine contaminated water gives rise to fluorosis as has been reported from many parts of India by Shrott et al⁴, Satyanaryan Murthi et al⁷, SS Jolly et al³. Earliest radiological investigation was plain X-ray. In the later series myelography and CT Scan were used in addition to X-ray. Plain skiagrams show generalized increased bone density with ossification of interosseous membrane and ligaments. Myelography primarily assesses the site of extradural block. Calcification and ossification of spinal ligaments is better seen on CT scan. However MRI is by far the only modality which can give us the complete details of radiological changes in fluorotic spine including ligament calcification ossification, disc protrusion, disc changes, cord and neural foraminal compression and moreover we can visualize the whole spine in a single study.

Ligamentum flavum extends from second cervical to first sacral vertebra and gives low signal on all SE images. Ligamentum flavum thickening more than 3 mm in cervical and thoracic regions and more than 4 mm in lumbar region was considered significant in our study.

Posterior longitudinal ligament is normally seen as thin low intensity linear structure in mid sagittal plane. In parasagittal

plane it is interrupted and is present only at intervertebral levels. Posterior longitudinal ligament thickening of more than 2 mm was considered significant in our study.

Ossified spinal ligaments give signal similar to yellow marrow on T1 and T2 scans¹⁰. Thickening of posterior longitudinal and ligamentum flavum were first reported in 1836 and 1920 respectively and are seen in conditions like ankylosing spondylitis, secondary to trauma, diffuse idiopathic skeletal hyperostosis (DISH), calcium pyrophosphate deposition disease, hematochromatosis and hyperthyroidism¹¹ but still exact cause remains undetermined in many cases.

We found correlation between duration of illness & ossification of PLL and LF. In 7 cases where ossification of PLL was seen the mean duration of disease was 5.8 yrs as compared to 3.6 yrs. where PLL was only thickened & not ossified. Similarly mean duration of disease was 5.4 yrs in 11 cases of if ossification as against 3.5 yrs where LF was only thickened & not ossified. Thus, it takes on an average 5.5 yrs for PLL & LF to become ossified. It was seen that the neurological deficit was more in the patients having ossified ligaments.

Cord edema was seen in 92% cases and a good correlation was observed between extent of extradural compression on MRI and clinical severity. Nine patients had nerve root compression, in six of these it was due to herniated disc and in three patients extensive posterior longitudinal ligament extended far across midline to involve neural foramina. In two cases we noticed an interesting finding of alternating bands of low and high signals in intervertebral disc on T1 and T2W images giving target appearance. They represent dark nucleus pulposus in centre followed by bright inner annulus the dark outer annulus with bright signal of

syndesmophyte marrow at periphery. This appearance is considered characteristic of ankylosing spondylitis. However, this is a preliminary observation which requires further studies to confirm.

Till date only a small series of four cases has been reported by Gupta et al⁸ Our study has shown a direct correlation between duration of disease with neurological deficit and MRI changes, along with this we also observed target sign in 2 patients. These observations were not documented in the earlier study.

Aim of our study was to study the spectrum of MRI changes in fluoritic spine and their correlation with duration of disease and neurological deficit. However, further studies having large sample size are required for correlation of radiological changes on MRI with the prognostic outcome both by conservative and surgical methods.

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DRUG PROFILE

RANOLAZINE

Ranolazine is a compound that is approved by the US FDA for the treatment of chronic angina pectoris in combination with amlodipine, beta-adrenoceptor antagonists or nitrates, in patients who have not achieved an adequate response with other anti-anginals.

Mechanism of Action: The anti-anginal effect of ranolazine does not depend on changes in heart rate or blood pressure. The mechanism of action of ranolazine for anti-anginal effect has not been fully characterised. Ranolazine is an inhibitor of several ion channels, including the late inwards sodium (I_{Na}) current which reduces calcium overload during ischaemic conditions. Reducing excess intracellular calcium can lead to improvement of left ventricular diastolic dysfunction by decreasing diastolic tension and thereby oxygen consumption. Ranolazine has been shown to improve left ventricular regional diastolic function in patients with ischaemic heart disease. Thus, inhibition of the late I_{Na} current by ranolazine is likely to contribute to the anti-anginal effect, but other mechanisms may also be involved.

Pharmacokinetics: Following administration of an oral solution or IR capsule, peak plasma concentrations (C_{max}) are observed within 1 hour. After administration of radiolabelled ranolazine, 73% of the dose was excreted in urine, and unchanged ranolazine accounted for <5% of radioactivity in both urine and faeces. The absolute bioavailability ranges from 35% to 50%. Food has no effect on rate or extent of absorption from the ER formulation. Ranolazine protein binding is about 61-64% over the therapeutic concentration range. Volume of distribution at steady state ranges from 85 to 180 L. Ranolazine is extensively metabolised by cytochrome P450 (CYP)

3A enzymes and, to a lesser extent, by CYP2D6, with approximately 5% excreted renally unchanged. Elimination half-life of ranolazine is 1.4-1.9 hours but is apparently prolonged, on average, to 7 hours for the ER formulation as a result of extended absorption (flip-flop kinetics). Elimination occurs through parallel linear and saturable elimination pathways, where the saturable pathway is related to CYP2D6, which is partly inhibited by ranolazine. Oral plasma clearance diminishes with dose from, on average, 45 L/h at 500 mg twice daily to 33 L/h at 1000 mg twice daily. The departure from dose proportionality for this dose range is modest, with increases in steady-state C_{max} and area under plasma concentration-time curve (AUC) from 0 to 12 hours of 2.5- and 2.7-fold, respectively. Ranolazine pharmacokinetics are unaffected by sex, congestive heart failure and diabetes mellitus. AUC increases up to 2-fold with advancing degree of renal impairment.

Dosages: Initial studies used an oral solution or an immediate-release (IR) capsule, but subsequently an extended-release (ER) formulation was developed to allow for twice-daily administration with maintained efficacy. Usual dose of extended release (ER) is 200mg twice daily.

Drug Interaction: Ranolazine is a weak inhibitor of CYP3A, and increases AUC and C_{max} for *simvastatin*, its metabolites and HMG-CoA reductase inhibitor activity <2-fold. *Digoxin* AUC is increased 40-60% by ranolazine through P-glycoprotein inhibition. Ranolazine AUC is increased by CYP3A inhibitors ranging from 1.5-fold for *diltiazem* 180 mg once daily to 3.9-fold for ketoconazole 200 mg twice daily. *Verapamil* increases ranolazine exposure approximately 2-fold. CYP2D6 inhibition has a negligible effect on ranolazine exposure.



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CASE REPORT

A CASE OF MYOPATHY CAUSED BY SIMVASTATIN IN A HYPERTENSIVE DIABETIC PATIENT- A CASE REPORT

N.S. Neki* , H. L. Kazal**

* Department of Medicine, Govt. Medical College/Guru Nanak Dev Hospital, Amritsar (Punjab), India

** Department of Medicine, G.G.S. Medical College, Faridkot, (Punjab), India

Abstract : Simvastatin induced myopathy is rare but an important adverse effect. A case of myopathy in a hypertensive diabetic patient presenting as proximal muscle weakness in both upper extremities induced by long term use of simvastatin is being reported.

INTRODUCTION

Simvastatin and other statins are the most frequently prescribed medications for hyperlipidemia with rare adverse effect of myopathy^{1,2}. Various megatrials have reported the incidence of myopathy as 0.025%^{3,4}. Myopathy secondary to statins is defined as unexplained muscle pain, weakness or muscle tenderness with a rise of creatinine kinase to more than 10 times the upper limit of normal which is reversible on stoppage of drug^{2,5}. Other features of statin induced myopathy include lack of pre-existing muscular symptoms, delay in onset of symptoms after exposure, lack of any demonstrable cause for myopathy and disappearance of symptoms after their cessation⁶. We report a case of myopathy presenting as proximal muscle weakness in both upper extremities following the use of simvastatin, which disappeared on its stoppage.

CASE REPORT

A 60 year old obese post-menopausal female with history of hypertension and diabetes for 10 years and history of myocardial infarction had triple vessel disease and had undergone CABG. She was taking atenolol 100 mg od, glimepiride 2 mg od, ramipril 5 mg od, metformin 500 mg tds, simvastatin 20 mg od and clopidogrel 75 mg od. After 5 months of simvastatin treatment, her total cholesterol, triglycerides, LDL and HDL changed from 220, 200, 160 and 36 mg% to 160.20, 122.60, 99 and 40 mg% respectively. The dose of simvastatin was reduced to 5 mg daily. After one month of giving simvastatin in dosage of 5 mg daily i.e. a total of 6 months, she presented to us with symptoms of weakness in both arms and difficulty in raising arms above head since 10 days but there was no weakness of hand and wrist muscles. The lower extremities did not show any weakness. There was no history of muscle pain, swelling, tenderness, fasciculation of muscles or atrophy, headache, vomiting, diplopia, ptosis, nasal regurgitation of food and water, speech involvement, root pains, painful neck movements, bladder or bowel involvement, seizures or loss of consciousness. There was no history of concomitant administration of drugs like erythromycin, corticosteroids, ketoconazole, risperidone, amiodarone, gemfibrozil, cyclosporine, nicotinic acid, clofibrate etc. There was no evidence of severe infection, hypotension and electrolyte imbalance. On examination, her pulse rate 62/min, BP 130/80 mmHg, respiratory rate 16/min. Higher functions, speech, cranial nerves, muscle bulk and tone (both upper and lower limbs), were normal. The power at both shoulder joints was 3/5. The deep tendon reflexes in both upper and lower limbs were normal with normal power in both lower extremities. There were no signs of meningeal irritation. Gait, skull and spine were normal.

Her laboratory profile included Hb 10 gm%, TLC 9000/mm³, DLC N70 L28 M1 E1, ESR 18 mm in first hour, FBS 96 mg%, B urea 30 mg%, S. creatinine 1.2 mg%, S. bilirubin 0.9 mg%, SGOT 35 IU, SGPT 38 IU, S. Na+ 138 meq/L, S. K+ 4.2 meq/L, Hb A1C 7.1% with normal urine examination. CPK levels were 2600 IU/L, serum aldolase 30 IU/L and LDH level 600 IU/L. Tests such as rheumatoid factor, antinuclear antibodies and HIV Elisa were negative. Thyroid function tests were normal. The patient did not allow for taking muscle biopsy. The diagnosis of statin related myopathy was entertained and she was asked to continue all medications except simvastatin. During next 3-4 days, her muscle weakness improved to normal in both upper limbs and her CPK, serum aldolase and LDH levels returned to normal i.e. 150 IU/L, 5 IU/L and 150 IU/L respectively further

confirming the whole episode as simvastatin induced myopathy. She was followed up for 6 months without reporting any recurrence.

DISCUSSION

Statins play an important role in the management of patients with hyperlipidemia, hypertension, diabetes and coronary artery disease with studies showing improved morbidity and mortality outcome with their appropriate use reporting three cases of simvastatin (given in dosage of 5-40 mg per day) induced myopathy in 12000 patients (approximate incidence 0.025% or one case per 10000 patients - years)^{3,7}. Simvastatin, HMG - Co A reductase inhibitor, inhibits cytochrome P450 enzyme resulting in accumulation of drug leading to myotoxicity by causing lysis of muscle cells in the form of reduction in muscle cell wall cholesterol⁷.

Statins should be stopped temporarily in conditions predisposing to rhabdomyolysis such as hypotension, severe infections, trauma, major surgery, uncontrolled seizures as well as severe endocrine, electrolyte and metabolic disorder. Concomitant administration of statins should be avoided in patients on use of erythromycin, clarithromycin, ketoconazole and protease inhibitors etc. Patients with severe hepatic or renal disease need lowering of dose of simvastatin⁸.

Myopathy is dose dependant and is rapidly reversible if diagnosed early and treated with volume repletion and withdrawal of drug. So these patients on simvastatin use need close monitoring. Myopathy secondary to simvastatin in a type 2 diabetes patient has also been reported by other workers.⁹ But simvastatin induced myopathy is rare yet important adverse effect hence the case report.

CONCLUSION

This report raises the concern about the safety profile of statins. Physicians should be made aware about the possibility of late adverse reactions in the form of myopathy. There is also need of awareness on the part of physicians regarding potential drug-drug interactions which predispose to statin toxicity thus leading to myopathy. Patients need to be educated as to signs and symptoms requiring immediate physician intervention.

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Correspondence: Professor N.S. Neki, Department of Medicine, Govt. Medical College/Guru Nanak Dev Hospital, Amritsar (Punjab) India. e-mail : drnsneki_123@yahoo.com

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SOLITARY OSTEOCHONDROMA OF THE SCAPULA: A RARE DIFFERENTIAL DIAGNOSIS OF SHOULDER PAIN

J.P.S. Walia, Nitin Bansal, Baljeet Singh, Sameer Gupta

Department of Orthopaedics, Rajindra Hospital, Patiala-147001 (Pb.) India.

Abstract : A 13 year old female child having left shoulder pain presented with a hard oval mobile swelling in the scapular region; skiagram showed a large tissue mass overlying the left scapula; biopsy showed typical morphological features of osteochondroma. Wide excision with removal of tumor en bloc gave satisfactory result on follow-up.

CASE REPORT

A 13 years old female child having unspecified shoulder pain, presented with history of swelling left scapular region for one year which increased for last six months. Swelling was hard and oval with its edges-clearly defined. Skin over the swelling was normal. On palpation temperature of the swelling was normal with no tenderness. It measured 5×4cm in size and was not attached to overlying skin. No fluctuations or pulsations could be elicited, the edges were well defined with hard consistency. The swelling was mobile from side to side and was difficult to palpate with scapular muscles made taut; overlying skin was free (Fig. 1 & 2).



Fig. 1



Fig. 2

Investigations: There was no anemia, jaundice or cyanosis. All systems were named; hemogram, unanalysis etc. were normal. X-ray Left shoulder showed large soft tissue mass overlying the left scapular region. No calcification was seen. Bony alignment was normal with no erosion and normal joint space. Bone density was normal. Biopsy showed a cartilaginous cap and bony tissue; cartilage cap covering the entire surface and merging into underlying spongiosa; few double nucleated chondrocytes were seen. chondrocytes were arranged in vertical row. Spongiosa of the stalk was continuous underneath and

new bone formation was seen (Fig. 3 & 4). Wide excision was done under GA and patient was put on antibiotics for a week. On follow up, result was satisfactory.

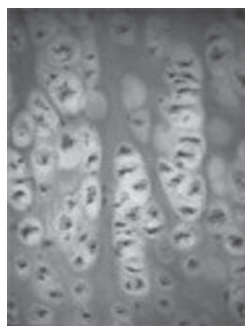


Fig. 3

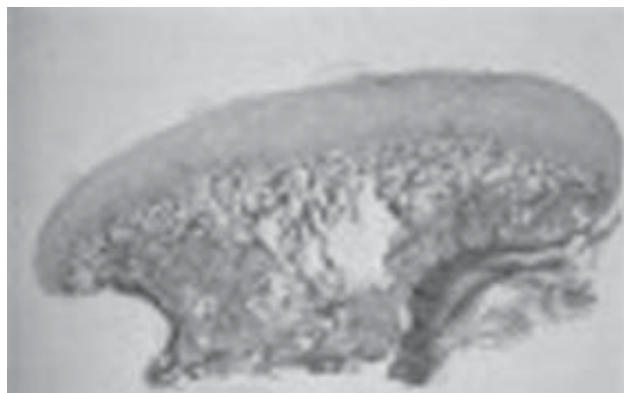


Fig. 4

DISCUSSION

Osteochondroma is the most common benign tumor. Most are asymptomatic, but they can cause mechanical symptoms depending on their location and size^{1,2}.

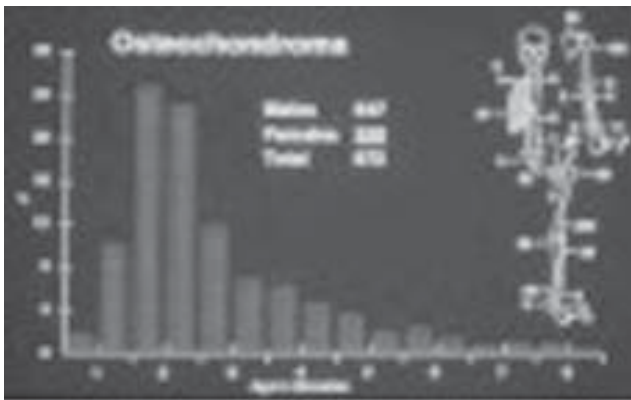
In fewer than 1% of solitary osteochondromas, malignant degeneration of the cartilage cap into secondary chondrosarcoma has been described. Male preponderance and a predilection for flat axial bones (scapula, vertebrae etc) were observed for secondary osteochondroma. The osteochondroma may be stalked (pedunculated) or may have broad base of

Correspondence: J.P.S. Walia, Department of Orthopaedics, Rajindra Hospital, 70-E, Police Lines, Patiala- 147001 (Pb.) India. Cell.: 098140-35706

attachment and considered sessile. Whether sessile or pedunculated, the medullary canal of the stalk and the bone are in continuity. It is a hamartoma and patients most commonly present in second decade of life. Wide excision of the osteochondroma and that too at early age had lowest recurrence rate³.

The actual frequency of osteochondroma is unknown because many are not diagnosed. Most are found in patients younger than 20 years. The male to female ratio is 3:1 (Fig. 5). It can occur in any bone that undergoes endochondral ossification, but they are most common around knee^{4,5}.

There has been a lot of debate about whether an osteochondroma is a hamartoma or a true neoplasm. But, now it is considered to be a true neoplasm due to presence of loss of heterozygosity (LOH) and aneuploidy in the cartilaginous tissue of osteochondroma⁶.



(Fig. 5)

Plain radiography is the mainstay of imaging for this clinical condition. Classic radiographic features include the lesion being oriented away from the physis and medullary continuity. In certain bones, such as the pelvis and scapula, CT scanning can be useful in planning surgery and localizing the lesion in the tissues. MRI is only needed in cases in which malignancy is a clinical concern or the relative anatomic structures in the soft tissues need to be localized. MRI is the modality of choice to assess the cartilage cap thickness. Thick cartilage caps (>4cm), especially when they are associated with pain, are suggestive of malignant degeneration⁷.

Grossly, the stalk is contiguous with the intramedullary marrow. The stalk is made up of mature bone. The cartilage

cap, which can be quite thick in children, is replaced by enchondral bone formation in maturing patients.

Microscopic examination reveals that the lesion is topped with a cartilage cap that can exhibit varying amounts of cellularity. The cap has an overlying fibrous layer that contains the mesenchymal cells that are thought to be responsible for the lesion's growth. The cells in the cartilage are orientated vertically, as is found in a growth plate. These lesions are benign lesions and can be staged under the Musculoskeletal Tumor Society (MSTS) staging for benign lesions.^{7,8}

No medical therapy currently exists for these lesions. The mainstay of treatment is observation because most lesions are asymptomatic. The treatment for symptomatic lesions is resection. Ideally, the line of resection should be through the base of the stalk; thus, the entire lesion is removed en bloc with its fibrous covering. Atypical or very large lesions should be fully investigated to exclude the remote possibility of underlying malignancy. MRI is useful in assessing the cartilage cap thickness.

Follow-up: The local recurrence rate after resection of osteochondroma is about 1.8%. Complications after surgical resection are rare. Considerations include epiphyseal disturbance or arrest, host bone fracture after resection, recurrence, incorrect diagnosis, and hematoma formation. For solitary osteochondromas, the outcome and prognosis after surgery are excellent, with excellent local control and a local recurrence rate of less than 2%. The process is a benign one; thus, the prognosis is usually one of complete recovery.

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ETHICAL GUIDELINES FOR BIOMEDICAL RESEARCH

The need for uniform ethical guidelines for research on human subjects is universally recognised. It has acquired a new sense of urgency as the critical issues in the area of biogenetic research involving human subjects have become acute. Apart from the mandatory *clinical trials* on new drugs, a number of *diagnostic procedures, therapeutic interventions and prevention measures* including the use of vaccines, are being introduced which involve human subjects. Further the advent of *new medical devices and radio-active materials* and therapeutic benefits of *recombinant DNA products* have added a new dimension to the ethical issues that need to be considered before evaluating these for their efficacy, utility and safety.

Any research using the human beings as subjects shall bear in

mind the following principles of : i) **essentiality**, (ii) **voluntariness**, **informed consent**, (iii) **non exploitation**, (iv) **privacy and confidentiality**, (v) **precaution and risk minimisation**, (vi) **professional competence**, (vii) **accountability & transparency**, (viii) **maximisation of public interest and distributive justice** (ix) **institutional arrangements** (x) **public domain** (xi) **totality of responsibility** and (xii) **compliance**.

Recent advances in the field of **Assisted Reproductive technologies, organ transplantation, Human genome analysis, and gene therapy** promise unquestionable benefits to mankind. At the same time, they raise many questions of law and ethics, stimulating public interest and concern.

(Source : ICMR Publication 2000)

AMIODARONE INDUCED SYSTEMIC LUPUS ERYTHEMATOSUS – A CASE REPORT

N.S. Neki

Department of Medicine, Govt. Medical College/Guru Nanak Dev Hospital, Amritsar (Punjab) India

Abstract : Drug induced lupus (DIL) is an uncommon entity. Various drugs like hydralazine, procainamide, isoniazid, D-penicillamin, practolol, methyldopa, alpha-interferon, quinidine, phenytoin, oral contraceptives and ethosuximide etc. have been reported to induce lupus. But there are very few reports in the world literature regarding amiodarone induced systemic lupus erythematosus (SLE). A case of hypertension and atrial fibrillation in a 70 year old male patient treated with digitalis, amiloride and amiodarone (200 mg twice daily) for the last two years in being reported for its rarity.

INTRODUCTION

Amiodarone induced SLE is uncommon in India. On extensive review of Indian medical literature, only one case of amiodarone induced SLE could be found on repeated attempts and that too in a male patient. Probably, this could be the second case of amiodarone-induced SLE from this part of India. Hence the case report.

CASE REPORT

A 70 years old male patient presented with complaints of intermittent fever (39°C), dyspnoea on exertion, non productive cough and pleuritic chest pain since 3 weeks. He also had history of weight loss, loss of appetite, weakness and malaise for more than 2 months. He was a known case of hypertension and atrial fibrillation treated with amiodarone given 200 mg two times daily, amiloride and digitalis for the past two years. There was no history of Raynaud's phenomenon, oral ulcers and photosensitivity. Physical examination revealed pulse rate 80/min, regular of normal and equal volume in all the four limbs, BP 150/92 mmHg in the supine position, temperature 39°C, respiration rate 24/min. Malar rash and mild anaemia was also noticed. On auscultation of cardiovascular system, an aortic systolic murmur was heard (Grade II/VI). The examination of other systems was not contributory. Investigations revealed Hb 9.3 g/dl, normocytic-normochromic, anaemia, TLC 3900/mm³, DLC-P₆₈, L₂₄, M₁, E₁, ESR 110 mm/first hour, platelet count 190000/ml, MP slide -ve and urine C/E NAD. B.urea, S.creatinine, fasting blood sugar, serum bilirubin were within normal limits. Widal test, ECG, coagulation profile, Mantoux test, Coomb's test, C reactive protein, VDRL, ELISA test for HIV and M.Tuberculosis as well as T₃, T₄, TSH were non contributory. X-ray chest revealed small bilateral pleural effusion without fibrosis or cardiomegaly. The pleural fluid on aspiration was exudative with lymphocytic predominance without cytological evidence of malignancy. Cultures of pleural fluid for bacteria, including for M.tuberculosis, blood and urine cultures were negative. 2-D echocardiogram showed mild aortic stenosis. The histopathological examination of biopsy specimens of the skin, including immunofluorescence stain, muscle and temporal artery did not show any abnormality. In view of the symptomatology and laboratory findings, the patient was subjected to total collagen profile. The results showed: rheumatoid factor +ve 1:320, antinuclear factor (ANF)+ve 1: 640, circulating immune complexes (IgG-C1q)+ve but other autoantibody tests were negative.

A diagnosis of amiodarone-induced lupus was considered. The amiodarone was stopped and the patient started improving progressively. No corticosteroids were given. After one year, the patient was symptom free without any clinical, analytical or radiological findings of lupus. The patient on further follow up after one year and five months, remained free of symptoms while ESR, TLC, DLC and radiological profile were normal. The titre of ANA decreased but remained weakly positive at 1:40. The patient is now on digitalis, amiloride and is totally asymptomatic.

DISCUSSION

A syndrome resembling SLE may be induced by various drugs like hydralazine, procainamide, isoniazid, D-penicillamin, practolol, methyldopa, alpha-interferon, quinidine, phenytoin, oral contraceptive and ethosuximide¹. Only few cases have been reported in the world

literature. The first case was reported by Susano R et al in 1992² and the second case by Sheikh Zadeh A et al in 2002³. In the west, it is estimated that 3-7% of all patients of SLE might have drug induced lupus (DIL)^{4,5}. Clinically it is difficult to differentiate between SLE and DIL, but there are certain distinguishing features between them: the patient with DIL is usually older; the prevalence of male and female is equal; and the common presenting symptoms are usually mild with the patient usually complaining of malaise, fever, arthralgia with or without arthritis whereas involvement of skin, renal and central nervous system is rare. Pleuropericardial disease is frequent and as in classic SLE, anaemia and leucopenia may be present. Serum complement levels are usually normal. ANF is positive, anti-dsDNA and anti-SM antibodies are negative while antihistone-antibodies are positive in majority of the patients⁶. Amiodarone induced side effects range from 40-93% and are in the form of nausea, vomiting, hepatitis, alveolitis, photosensitivity, pulmonary fibrosis, microdeposits in cornea, bluish skin, peripheral neuropathy, bradycardia, Q-T prolongation and thyroid function abnormalities⁴.

The exact pathogenesis of DIL is not known but could be cross reactivity between the drug and nucleic acid, hapten complex formation between drug and nucleic acid, or structural damage to the chromosomal DNA, action of drug as an adjuvant or immunostimulant, which in concert with appropriate immune response genes, triggers polyclonal B/T cell activation, and interference with the complement pathway⁵. This case, presenting with fever, malaise arthralgia, circulating immune complexes, and autoantibodies strongly suggests an immunological underlying condition. Moreover, according to 1982, American Rheumatism Association revised criteria for the classification of SLE⁷, this patient meets four SLE criteria, i.e. malar rash, serositis, leucopenia and lymphopenia as well as positive ANF.

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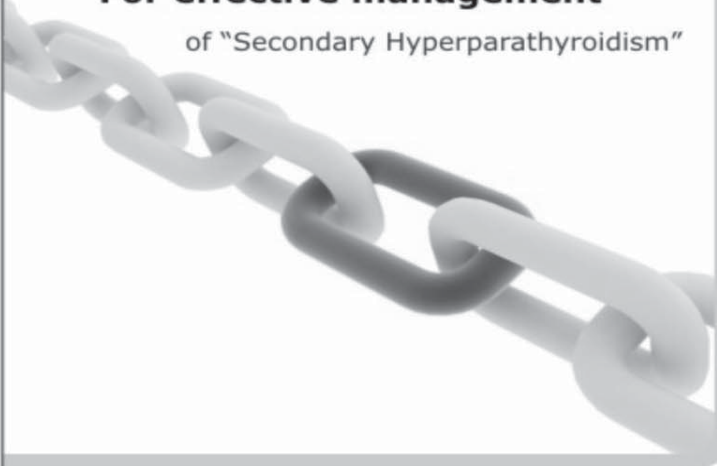
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Correspondence: Professor N.S. Neki, Department of Medicine, Govt. Medical College/Guru Nanak Dev Hospital, Amritsar (Punjab) India. e-mail : drnsneki_123@yahoo.com

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NEUROLEPTIC MALIGNANT SYNDROME – A CASE REPORT

N.S. Neki

Department of Medicine, Govt. Medical College/Guru Nanak Dev Hospital, Amritsar (Punjab), India

Abstract : Neuroleptic malignant syndrome (NMS) is an uncommon condition, a purely clinical entity, characterised by hyperthermia, muscle rigidity, autonomic instability and altered mental status. Autonomic dysfunction is characterized by tachycardia, labile blood pressure, profuse diaphoresis, dyspnoea and urinary incontinence. Extrapyramidal dysfunction is characterized by catatonic behaviour, dystonia, generalised rigidity and pseudoparkinsonism. NMS occurs after use of potent neuroleptics like haloperidol, thiothixene or piperazine, phenothiazines. The exact mechanism of NMS is not known but could be (i) dopaminergic blockade at various levels (ii) glutaminergic excitatory amino acids influencing dopaminergic activity and (iii) low serum iron. The differential diagnosis is from serotonin syndrome, malignant hyperthermia, infection and alcohol withdrawal. Prevention is better than treatment, which is carried out by use of bromocriptine and dantrolene sodium.

INTRODUCTION

Neuroleptic Malignant Syndrome (NMS) which though rare, is treatable, if diagnosed early. The 'criteria' for diagnosis of NMS are (a) history of treatment with neuroleptic drug (s) within 7 days of onset of symptoms (2-4 weeks for depot preparation), (b) hyperthermia equal to or more than 38°C, (c) muscle rigidity, (d) exclusion of other drug induced, systemic or neuropsychiatric illnesses, and (e) any five of the following: change in mental status, tachycardia, hypertension or hypotension, tachypnoea or hypoxia, diaphoresis or sialorrhoea, tremors, urinary incontinence, raised CPK or myoglobinuria, leucocytosis or metabolic acidosis.

CASE REPORT

A 40 years old female was admitted with complaints of high grade fever with chills, stiffening of body and altered sensorium since one day. There was no history of headache, vomiting, seizures and loss of consciousness. Her clinical examination revealed pulse 112/min, blood pressure 160/94 mmHg, temperature fluctuating between 102-103°F, respiratory rate 32/min. She was drowsy to stuporous. She had no signs of meningeal irritation but had generalised rigidity with a characteristic waxy flexibility in the limbs suggestive of catatonic rigidity. Within four hours, her blood pressure came down to 106/60 mmHg. CSF examination for meningitis was non-contributory. Other investigations included Hb 10.2 g%, TLC 14200/mm³, DLC P72, L28, E0, M0, ESR 10 mm/1 hour, urine C/E NAD and MP slide negative. PBF showed microcytic hypochromic anemia. Blood glucose was 80 mg%, blood urea 30 mg%, serum creatinine 1.3 mg%, LFT's normal, X-ray chest NAD, widal test negative, blood culture negative and HIV non-reactive. Further questioning of her husband revealed that his wife (index patient) was a known case of endogenous depression since 2 years and was taking imipramine 75 mg/day off and on, till 6 months ago. For the last 8-10 days, she had restarted taking the drug on her own with thrice the original dose. In view of clinical presentation and drug history, a provisional diagnosis of NMS was made on the third day of admission. Her CPK levels were 110 U/L. The offending drug i.e. imipramine was stopped immediately. She was put on IV fluids and tablet bromocriptine 5 mg thrice daily. Fever subsided after 72 hours of initiating therapy and she became asymptomatic within four days.

DISCUSSION

It is a rare but serious complication of treatment with phenothiazines, as well as butyrophenones especially haloperidol and rarely metoclopramide and pimozide². The sites at which these drugs act are hypothalamus (causing fever), corpus striatum and basal ganglia (causing extrapyramidal syndrome), mesolimbic system and mesocortical pathway (alteration of mental status) and spinal cord (dysautonomia and altered sympathetic tone). Schizophrenia is the most common disease reported with NMS². NMS has been reported in a patient of systemic lupus erythematosus³. Only rare case reports describe NMS after tricyclic antidepressants like imipramine⁴, as described in the present case and others also⁵. The chances of

developing NMS with the use of neuroleptics are 0.02 – 3.23%. It occurs in young and middle aged adults and is more common in males (M:F 2:1). Predisposing risk factors include organic brain disorders, psychomotor activity or agitation, underlying genetic factors, dehydration, physical exhaustion and past history of NMS¹. The exact pathophysiology of NMS is not fully known but is attributed to neurohormonal disruption within brain dopaminergic system. The central dopaminergic blockade within basal ganglia leads to extrapyramidal rigidity while hyperthermia, mental changes and dysautonomia are attributed to dopaminergic blockade in the hypothalamus. In addition hyperthermia occurs as a result of increased muscular activity. A peripheral mechanism also seems to play a role in which dopamine mediated skeletal muscle contraction is inhibited by neuroleptics^{1,6}. Even low serum iron has been reported to be responsible for NMS⁷. The differential diagnosis includes infection, malignant hyperthermia, alcohol withdrawal state as well as serotonin syndrome (SS). The clinical picture of NMS usually resolves within 1 to 3 days and lasts for 5 to 10 days after withdrawal of the offending drug whereas mortality is 20-25% if untreated. Death is due to renal failure, arrhythmias, acidosis, hypercalcaemia, myocardial infarction, aspiration pneumonia, pulmonary embolism, rhabdomyolysis (with acute renal failure), DIC or ARDS. Prognosis is poor in patients with underlying brain disorder, hypotension, rhabdomyolysis and acute renal failure. Regarding treatment, prevention is always better. The awareness about NMS, during neuroleptization, early recognition by careful observation of signs and symptoms is of utmost importance. Once the clinical diagnosis is made, immediate omission of offending drug and institution of specific and supportive measures are helpful. Treatment is to increase dopamine activity by giving bromocriptine 2.5 to 5.0 mg thrice daily (as high as 10 mg tds). Amantidine 100-200 mg twice a day can be given. Skeletal muscle relaxants like dantrolene 1-3 mg/kg 8 hourly are advocated¹. Neuromuscular paralysis may need ventilation.

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ORGANOPHOSPHORUS POISONING – REVISITED

N.S. Neki

Department of Medicine, Government Medical College & Rajinder Hospital, Patiala, Punjab, India

Abstract: Organophosphorus (OP) compound was synthesized about one and half century ago in France. Tetraethyl pyrophosphate (TEPP) was the first to be manufactured in liquid form in 1950. Since then numerous compounds have been synthesized and used as agricultural insecticides. They are easily available in the market on account of inadequate regulations controlling their use and storage. OP pesticide intoxications are estimated at 3 million per year worldwide with approximately 3,00,000 deaths. The fatality rate following deliberate ingestion of OP pesticides in developing countries in Asia is about 2% and may reach as high as 70% during certain seasons and at rural hospitals. More than 100 OP compounds are currently available under different brand names. Acute poisoning in human occurs due to suicidal ingestion and accidental exposure while spraying. Ops inactivate acetyl-cholinesterase (AChE) by phosphorylation leading to accumulation of acetylcholine (ACh) at cholinergic synapses. Recovery follows the reappearance of active AChE following synthesis or spontaneous hydrolysis of phosphorylated AChE. The phosphorylated AChE may lose a chemical group so that its inactivation becomes irreversible; this is well known as compared to diethyl compounds. Sequential triphasic illness follows OP intoxication starting from acute cholinergic phase to intermediate syndrome resulting in organophosphate induced delayed polyneuropathy. Cholinesterase (che) estimation (plasma butyryl cholinesterase and red cell AChE) are the only useful biochemical tools for confirming exposure to Ops, but are a poor guide to management and prognosis. Regarding management, complete and early atropinisation is essential in early management and treatment should be started immediately on clinical grounds without waiting for laboratory investigations. Speed of administration is as important as use of sufficient doses. Oximes have a definite role and a response should be seen within 30 minutes with resolution of fasciculation, convulsion muscle weakness and coma. Ventilatory support should be instituted before a patient develops respiratory failure. The need of the hour is framing of regulations by the govt. of India controlling the use and storage of Ops.

Key words: Organophosphorus compound, acetyl cholinesterase; atropinisation; oximes

INTRODUCTION

The commonest poisoning in India is with pesticides, most commonly organophosphate compounds (OPC) on account of their ready and easy availability in the market since there are inadequate regulations controlling their use and storage. Acute OPC poisoning is a major health problem¹. Poisoning is seldom included as a priority for health research India, though every year, hundreds of people are losing their life prematurely for pesticide poisoning. According to WHO, it is estimated that 3 million cases of pesticide poisoning with 2000 deaths every year occur world wide particularly in developing countries^{1,2,3}. Organophosphate compounds (OPC) are common insecticide exclusively used by farmers. More than 100 OP compounds are currently available under different brand names, so that their identification becomes very difficult until/unless the patient's relative/family members bring the said container to the doctor^{1,3}. The pesticides include *organophosphorus compounds* and *carbamates*. Quite often the victim is brought to the doctor within an hour of consumption of the pesticide. This is the *'golden hour'* for clinical intervention, before irreversible "ageing" of toxic compounds in blood occurs.^{4,5} OP compounds have been in use for pest control since many years and unfortunately are common agents of suicidal and accidental poisoning.^{6,7} Highly toxic agricultural insecticides like TEPP (Tetraethyl-pyrophosphate) was used as a nerve gas in chemical warfare during world war II by Germany^{8,9}. The use of OP compounds as nerve gas agents has been banned by Geneva Convention in 1974 as part of a large ban in chemical warfare. However they have been used in recent wars in Iraq and Tokyo⁹. Among OP group, the most common cause of human poisoning and fatality is with the use of parathion and the mortality varies from 7-12%. Less commonly used and less

toxic Ops have now almost replaced; DDT, an organochloride compound thus becoming popular insecticide¹². Majority of cases (60-70) of OP poisoning result from suicidal ingestion^{13,14}. Accidental and occupational exposure such as spraying of crops are less routes of poisoning^{15,16}.

CLASSIFICATION OF ORGANOPHOSPHATES

A. Based on clinical toxicity⁴:

- Highly toxic:** Agricultural insecticides e.g. i) TEPP ii) Parathion-symptoms toxicity occur late by -24 hrs because it has to be converted in to paraxon iii) phorate iv) disulfoton v) mevinphos
- Intermediate toxic:** animal Insecticides e.g. cholor-pyrifos, trichlorfos, coumaphos.
- Low toxicity:** Household use .e.g. malathion, dichlorovos, diazinon and carbamate insecticides which include aldicarb, propoxur (Baygon), Carbaryl and bendiocarb (Ficam) Therapeutic carbamates include ambenonium, neostigmine, physostigmine and pyridostigmine. The commonly available products are methyl parathion (Folidol, Paramar, Metacid, Paramet), malathion (malathion, Cythion) and phallone (Zolone, sumithion Faithion, Timidan, Ektakin).

B. Based on pharmacokinetics⁴:

Organophosphorus compounds and carbamates are a family of compound that share structural similarities. The kinetics of each group are highly dependant on multiple factors like onset, duration and severity of poisoning, route of administration (ingestion, injection, inhalation, transdermal and transmucosal absorption), distance from target organs, local versus systemic metabolism and activation, route of elimination, endogenous hydrolysis and consumption of the compound by various nonspecific esterases before reaching target organs. Structural consideration includes the group attached to the

Correspondence: Professor N.S. Neki, Department of Medicine, Govt. Medical College/Guru Nanak Dev Hospital, Amritsar (Punjab) India. e-mail : drnsneki_123@yahoo.com

sulfur, carbon or phosphorus moiety, the tightness of the bond to the central atom and the affinity of the compound for cholinesterases.

C. Based on characteristics of compound:

1. **Nature of compound** i) *Water soluble*: Effects are acute and short lived e.g. tepp. ii) *Liquid soluble*: Effects are chronic and of longer duration e.g. Chlor-fenthion, fenthion, difenthion
2. **Mode of action**
 - i) **Direct agent** - directly inhibits acetyl-cholinesterase e.g.
 - ii) **Irreversible** - has to be converted in to active metabolite metabolite e.g. parathion
3. **Type of binding**
 - i) **Reversible** - effects are acute and short lived
 - ii) **Irreversible** - effects are more sustained e.g. parathion
4. **Route/Severity of Exposure**
 - i) Oral/GIT - acute toxicity
 - ii) Skin - acute toxicity
 - iii) Inhaled - acute on chronic
5. **Toxicity of the poison**
 - i) High
 - ii) Intermediate

The fat soluble compounds may not manifest toxicity for several days to weeks because the toxic substance must be "leached out" of the fat until sufficient amount of cholinesterase is inhibited to cause symptoms.

PATHOPHYSIOLOGY OF OP POISONING

The major neurotransmitter in CNS released by the terminal nerve endings of all the postganglionic parasympathetic nerves and in both sympathetic as well as parasympathetic ganglia is the acetylcholine (ach). Other sites of ach release are neuromuscular junctions. The enzyme acetyl-cholinesterase exists in 2 forms (a) *true cholinesterase* mainly present in the nervous tissues and RBCs (b) *pseudo-cholinesterase* present in liver and serum only.⁷

Ops bind to the active serine residue of acetylcholinesterase irreversibly and convert the enzyme into inactive protein complex, resulting in excessive accumulation of Ach at the synapses / receptors. This results in over stimulation and subsequent disruption of nerve impulse transmission in both the brain as well as sympathetic and parasympathic system.

Over a period of time organophosphate compounds can permanently affect the acyl pocket so that endogenous hydrolysis of the serine phosphate bond can not occur and antidote function becomes limited. This is called "ageing". During the "ageing reaction" the acyl group is lost from the phosphorylated enzyme and the pocket shape change becomes permanent. Carbamates dissociate from Ache molecule within 24 hours, so they do not causing limited CNS toxicity.

Most Ops are well absorbed from skin, GIT, lungs, oral and conjunctival mucous membranes. After absorption, they are hydrolyzed by enzymes e.g. esterases or paroxenases, which are not inhibited by OP compounds. Then their metabolic products are excreted in the urine. Ops binding to acetylcholinesterase (ach-ase) inhibit the conversion of acetylcholine (Ach) to its degradation products like acetic acid and choline. This results in excessive accumulation of Ach at synapses, which becomes the root cause of toxicity of OP compounds.

CLINICAL MANIFESTATIONS OF OP POISONING (CHOLONERGIC CRISIS)

Signs and symptoms of acute poisoning occur within 24 hours of ingestion of OP compound. Toxicity due to carbamates is shorter in duration and usually less severe than that due to organophosphates

Muscarinic Effects i) *Ocular*: pinpoint pupils, blurring of vision, increased lacrimation. ii) *Respiratory* rhinorrhoea, dyspnoea, bronchorrhoea laryngeal spasm, bronchospasm, wheezing cough respiratory depression and pulmonary edema (due to uncontrollable bronchorrhoea)

iii) *CVS*: bradycardia, hypotension, arrhythmias including multiple ectopics, junctional rhythms and AV block. iv) *GIT* excessive salivation, nausea, vomiting, abdominal pain, diarrhea, fecal incontinence iv) *Genitourinary*: urinary frequency and incontinence vi) *CNS*: impaired consciousness, bilateral hyperreflexia, extensor plantar response vii) *Skin*: increased sweating.

Nicotinic effects: Musculoskeletal weakness

Fasciculations, twitching, cramps, paralysis ii) *CVS* tachycardia, hypertension, iii) *respiratory*: weakness paralysis of respiratory and oropharyngeal muscles and finally respiratory arrest.

Central receptor stimulation These features characterize isomnia, anxiety, convulsions, restlessness, coma, hyperreflexia, Cheyne strokes breathing, circulatory collapse and respiratory depression^{15,16}.

Neurological manifestations in OP poisoning most commonly result in the following effects

(A) **Type-I paralysis or acute paralysis**: It appears within 24-28 hours resulting from inhibition of enzyme acetylcholinesterase. It is characterized by fasciculations, cramps twitching and weakness of muscles and these features respond to atropine 16. Muscle paralysis may also invoke respiratory muscles resulting in acute respiratory failure in 33# patients.

(B) **Type-II Paralysis or Intermediate Syndrome or Wadia Syndrome**: This term was first coined by Wadia and later on by Senanayake¹⁸ since then many authors have described this clinical entity^{16,19,20,21}. This syndrome develops after the acute cholinergic crisis, 24-96 hours after the poisoning i.e. development of signs of paralysis appearing after admission and before the delayed neurotoxicity sets in; the incidence of this syndrome is 8% - 49%^{19,21,22,23}. Majority of the patients present with respiratory insufficiency, cranial nerve palsies and proximal muscle weakness. The presentation of these patients usually starts with marked weakness of neck flexion resulting in inability to lift the head from the pillow and inability to sit up. The common cranial nerves involved are those supplying the extra-ocular muscles resulting in to ophthalmoparesis and slow eye movements. Cranial nerves VII and X are least affected. Wadia⁶ in a study of 350 cases of OP poisoning reported 87 patients as having inability to lift neck, 99 patients having inability to sit, up 27 patients having ophthalmoparesis, 39 patients slow eye movement, 2 patients facial weakness, 14 patients swallowing difficulty, 86 patients proximal limb weakness, 52 as are flexia, 37 as respiratory failure and 33 died. *Nerve conduction and EMG studies* show that the primary type of involvement is an axonal neuropathy.^{24,25,26} This syndrome is also due to anterior cell or toxin induced muscular instability. It lasts for about 4-18 days and most patients survive this period with the use of mechanical ventilation

(C.) Type-II Paralysis or OP induced delayed Polyneuropathy:

It is a sensory motor distal axonopathy which appears with ingestion of certain Ops like triortho-cresylphosphate (70 CP) and tricesylphosphate (TCP).^{27,28,29} It develops usually 2-3 weeks after the acute poisoning episode and is characterized by distal muscle weakness with sparing of neck muscle, cranial nerves and proximal muscles. These patients show a pure motor axonal neuropathy with wrist drop and foot but no sensory loss. Usually the pyramidal tracts in the spinal cord are involved resulting in brisk tendon reflexes and spasticity. It is probably due to depression of a different esterase called neurotoxic esterase or neuropathic target esterase (NTE) in the nervous system and this form of toxicity occurs in small epidemics in India due to adulteration of cooking oil with TOCP6. The EMG studies suggest denervation and recovery is delayed up to 6-12 months²⁶.

Other neurological manifestations/neuropsychiatric features, especially occurring in chronic poisoning³⁰ are usually short lived and include irritability, confusion, lethargy, impaired memory and psychosis. Extra pyramidal manifestations³¹ usually appear after 4-40 days following poisoning in the form of resting tremors, dystonias, cog-wheel rigidity and choreoathetosis. Neuro-ophthalmological sequelae seen in chronic poisoning include retinal degeneration, optic atrophy, myopia due to spasm or paresis of accommodation³². Other rare neurological manifestations include isolated bilateral recurrent laryngeal nerve paralysis³³, sphincter involvement³⁴, Gullain-Barre syndrome³⁵ and ototoxicity³⁶.

Cardiovascular Manifestations: Saadh et al³⁷ reported various cardiac manifestations in the form of sinus tachycardia (35%), sinus bradycardia (28%), atrial fibrillation (9%), ventricular tachycardia (4%), extrasystole (6%), ST segment elevation (24%), inverted T waves (17%). Cardiac toxicity is due to direct toxic effect on the myocardium, hypoxemia, acidosis, electrolyte disturbances, over activity of nicotinic or cholinergic receptors as well as high dose atropine therapy.

Respiratory Manifestations

They occur in the form of rhinorrhoea, bronchorrhea, bronchospasm, laryngeal spasm, airway obstruction, paralysis of respiratory and oropharyngeal muscles. Even respiratory failure/arrest may occur¹⁷.

Gastrointestinal Manifestations

They occur in the form of nausea, vomiting and diarrhea. Rarely acute pancreatitis³⁸ and hypoglycemia³⁹ may occur.

DIAGNOSIS OF OP POISONING

The diagnosis is based on H/o ingestion or exposure to spray and combination of clinical features in the form of vomiting, diarrhea, pin pointed pupils, muscle fasciculations and proximal muscle weakness. measurement of plasma or serum red cells ChE levels are diagnostic. True and pseudo cholinesterase levels can be measured these levels are markedly reduced in OP poisoning True ChE levels usually correlate with severity at presentation but pseudo cholinesterase levels do not⁴⁰. Plasma cholinesterase levels are also reduced in other diseases like metastatic carcinoma, alcoholism, malnutrition, congestive heart failure with hepatomegaly and dermatomyositis. A 25% or greater reduction (less than 50%) in RBC cholinesterase level in diagnostic of OP poisoning¹². Other useful test is resistance to atropine action If

1.8 2.4 mg atropine does not cause significant tachycardia or papillary dilatation diagnosis is always certain¹⁰. Post mortem study shows cerebral edema in early cases. Some poison centers can identify the compound from the stomach contents.

Grading of severity of OP Poisoning Bardin et al⁴¹ validated a 3-grade system for poisoning at the time of admission

- i) *Mild poisoning*: History of intake/exposure, normal consciousness with mild increase in secretions and fasciculations.
- ii) *Severe poisoning*: Altered sensorium with excessive secretions and multiple fasciculations.
- iv) *Life threatening poisoning*: Suicidal attempt, stupor, abnormal chest roentgenogram and PaO₂ < 60 mm Hg. These groups of patients usually require mechanical ventilation with prior treatment in the form of atropine, suction and clearing of airway.

MANAGEMENT

Treatment should be started immediately on clinical grounds without waiting for laboratory investigations.

1. Non pharmacological treatment (General measures)

- a) *Decontamination*: Thorough decontamination of the skin with soap and water and subsequently with ethyl alcohol after removing all clothes of the patients in very important in order to prevent further absorption through the skin. Gastric decontamination is either done by forced emesis or through a gastric lavage is further facilitated with the addition of a new drug—serotonin adipinate, which increases the propulsive function of the GIT, resulting in shortening of the toxigenic phase and reduction in mortality⁴².

PHARMACOLOGICAL TREATMENT (SPECIFIC THERAPY)

The main stay of pharmacological treatment of acute OP poisoning is co-administration of atropine and oximes.

- i) **Anticholinergic drugs**: They are the main stay of treatment and should be given as soon as the airway has been maintained, atropine is given initially mg/I/V bolus doses and then at doses of 2-5 mg I/V bolus every 5-15 minute until signs of atropinization appear. Atropine effectively ameliorates the muscarinic hyperactivity, prevents pulmonary edema and excessive secretions. It should be continued for 4-7 days depending upon the severity of poisoning as atropine crosses the blood brain barrier so over dosage (toxicity) occurs in the form of delirium, hallucinations, confusion, fever and tachycardia. Alternative to atropine, glycopyrrolate – a quaternary ammonia compound does not cross the blood brain barrier and so gives better control of secretions and less tachycardia⁴¹. The maximum total dose in OP poisoning is 140-167 mg⁴³.
- ii) **Oximes**: They are nucleophilic agents which reactive phosphorylated acetylcholinesterase by binding to organophosphorus molecule⁴⁴. They are (a) pralidoxime methylsulphate (b) obidoxime (c) H 16 (d) HL07(e) B169f) TMB4 (trimedoxime). All these are not considered as universal reactivators; the use of oximes in acute OP poisoning has been derived from early observations of their protective effect in experimental nerve gas poisoning⁴⁵. Regarding the continuation of oxime therapy and their dosages in acute OP poisoning, electrophysiological studies have documented the decrement response to high frequency 30 Hz RNS (repetitive nerve stimulation), which is an electro diagnostic marker for the intermediate poisoning³⁶.

Pralidoxime iodide – It is water insoluble and given only I/v. It contains

82 mg/ml sol, so large volumes are required for administrations. High doses and repeat administration can cause iodism.

Pralidoxime chloride – It is water soluble and can be given I/v, I/M as well as orally. It contains 640 mg/ml; so small volumes are required for administration. The oral form of the compound was used in Gulf war as a preventive measure in the event of a nerve gas exposure.

Pralidoxime methylsulphate or methanansulphate – It is given I/M
Obidoxime – This drug is available for use in Europe. However, even with dimethyl compounds such as oxymedon, obidoxime are ineffective after 24 hours. However, high and prolonged doses lead to liver toxicity. This drug is available for use in Europe. However, even with dimethyl compounds such as oxymedon, obidoxime is ineffective after 24 hours; high and prolonged doses lead to liver toxicity.

The use of pralidoxime in acute OP poisoning is controversial¹⁴⁶. A recent large, randomized clinical trial compared the use of a single dose of pralidoxime (i.e. 1 gm single bolus dose) with a continuous infusion of 12 grams/day for 3 days, outcome was similar.

Ventilatory support

Mechanical ventilation is needed for several days when respiration is markedly depressed or when chest infection or aspiration of secretions is present. A case series involving 16 patients with continuous infusion of pralidoxime, atropine and ventilatory support has reported mortality as 12.5%.

Role of High dose methyl prednisolone: It has been shown to be beneficial in Type-III paralysis in animal studies^{54,57}.

Role of intravenous diazepam: It is often used to treat marked agitation and seizures in acute OP poisoning. A new drug, Gacyclidine (GK 11) has been shown to ameliorate CNS toxicity.

CONCLUSION

OP compounds are the most widely used toxic agent, for suicidal poisoning in developing countries; accidental poisoning occurs in workers engaged in spraying operations. They irreversibly phosphorylate cholinesterase leading to the accumulation of acetylcholine at the cholinergic nerve endings such as autonomic ganglia, parasympathetic nerve endings and motor end plates. Regulations controlling their use and storage must be made by Govt. of India and this is the need of the hour.

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ADOLESCENT SEXUAL AND REPRODUCTIVE HEALTH IN INDIA: CHALLENGES AND OPPORTUNITIES

A. Nath, S. Garg, M. M. Singh

Department of Community Medicine, Maulana Azad Medical College, New Delhi -110002, India

Abstract : In a country like India wherein adolescents (aged 10–19 years) represent over one fifth of the population, the health consequences of neglect of their reproductive health needs takes on enormous proportions. Adolescent reproductive health is poorly understood and ill served in India. While national strategies and programmes have focused on children and pregnant women, neither services nor research has focused on adolescent health and information needs with overall perspective. The objective of the current paper is to focus on the reproductive health profile of adolescents in India, the burning issues in adolescent reproductive and sexual health which still serve as a challenge in the way of bringing about reproductive well being of the adolescent and to explore the various opportunities that would be of further help to overcome these challenges in improvising the quality of adolescent reproductive health care services. These challenges include the consequences of early marriage, unsafe abortions, high risk behaviour, lack of awareness about contraception and reproductive health issues, RTIs/STIs including HIV/AIDS and non-consensual sex. The programme managers have ample opportunities to address these challenges with the main focus of raising awareness about reproductive health issues, making the adolescent health services friendly and accessible and encouraging involvement of the teachers, parents, community leaders and last but not the least –involve the adolescents themselves.

INTRODUCTION

Approximately 1.5 billion of today's world population consists of young people between 10 and 24 years old and 85% of them live in developing countries¹. The Government of India considers the age group between 13 to 19 years as a special group of adolescents². However the Planning Commission of India as well the W.H.O consider 10 to 19 years as the age group for adolescents^{3,4}. The origins of the term is from the Latin word 'Adolescere' meaning, "to grow, to mature," which indicates the defining features of adolescence.

Adolescents also represent a resource for the future whose potential can either be wasted or nurtured in a positive manner. However, in the absence of appropriate and effective programmes for sexuality and gender equation, and appropriate reproductive health services, adolescents continue to remain at risk, thus calling for development of need based interventions. Therefore, the present paper has been framed with the objective to review the reproductive profile of adolescents in India, the challenges that pose in the way of the adolescent's reproductive well being and exploring the opportunities that are available to overcome these challenges as well the initiatives that have been undertaken in this direction to improve the quality of adolescent reproductive health care services.

PROFILE OF ADOLESCENTS IN THE SOCIAL CONTEXT IN INDIA

About one-fifth of India's population is in the adolescent age group of 10–19 years. It is estimated that there are almost 200 million adolescents in India.⁵

The following indicators have a bearing on the adolescent's reproductive health.

Adverse sex ratio : Female feticide is very much rampant and there is a high maternal mortality among teenage mothers. The National Family Health Survey –2 (NFHS –2), findings have reflected the adverse ratios amongst adolescents wherein the sex ratio in the 10-14 years age group was found to be 902 and 915 in the urban and

rural areas, whereas the sex ratio in the 15-19 year age group was 893 and 953 in the urban and rural areas respectively.⁶

Educational Status : There is a wide disparity in the educational achievements of the adolescent boy and girl. According to NFHS reports, only 67% of the young adolescent girls(10-14 years) attended school as compared to 80.2% males. In the 15-17 year age group, only 40.3% of the females attended school as compared to 57.7% males.

CHALLENGES AND OPPORTUNITIES TOWARDS ADOLESCENT REPRODUCTIVE AND SEXUAL HEALTH IN INDIA

1) Challenge: Reproductive health challenges of the unmarried adolescent

(a) **High risk behavior:** Over the recent years in India, the decline in old family structures, greater liberalization of economy and the advent of technological aids like internet, mobile phones etc have appeared to have a major impact on the sexual behavior of the adolescent thus bringing in its wake a number of health consequences which pose as a major challenge. Family Planning Association of India (FPAI), in their multicentric study amongst 4,709 youth males and females noted that premarital sex was relatively more acceptable to boys (18%), particularly in the group aged 20-23, than girls (4.2%).⁷ Homosexual activity is fairly common among adolescents as a study conducted among 121 street children in Bangalore observed that 74 of them engaged in homosexual as well as heterosexual activities to the same degree.⁸

(b) **Low contraceptive usage:** Among the unmarried adolescents, contraceptive usage is quite low as observed by Abraham in a study conducted among male college students in Mumbai wherein less than half of them who claimed to be sexually active said that they used condoms or some other form of contraception.⁹

- (c) **Lack of awareness about reproductive health issues:** Adolescents tend to be extremely poorly informed regarding their own sexuality and reproductive health issues. In rural Haryana, less than 50 % of the girls preferred to consult parents and doctors for help at times of having reproductive health problems.¹⁰ Regarding the experience in an urban slum of Delhi, it was seen that a culture of silence surrounds menarche, an event that took the adolescents by surprise.¹¹ Even in a Mumbai urban slum, as many as 40 % of the adolescent boys considered nocturnal emission and masturbation as major health concerns.¹²

OPPORTUNITIES

- (i) **Strengthening of Life Skill Development among Adolescents:** Many Adolescent Reproductive health programmes include “life skills” either as one component or as the central focus of their work. Life skills are behaviors which help equip an individual to adapt and deal effectively with all the challenges in life. The CEDPA (Centre for Development and Population Activities) has been conducting a life skills development programme entitled as “Better Life Options” for out-of-school adolescent females since 1987. School teachers could also be trained so that they are well equipped to impart life skills to school going adolescents.

- (ii) **Involvement of the adolescent in creative activities:** The formation of youth clubs and forums which would serve to channel the energy of youths towards constructive activities and encourage participation in sports, martial arts, talent competitions etc should be encouraged. A recent approach in this aspect was undertaken by CEDPA in collaboration with four other NGOs, namely Prayatan, and Young Women’s Christian association in Delhi slums, Bhartiya Grameen Mahila Sangh in Madhya Pradesh and Society for the promotion of Youth and Masses in Haryana wherein a comprehensive package consisting of reproductive health, nutrition services and skills development as well as recreation was provided to more than 9000 adolescent boys in girls.

- (iii) **Development of a separate curriculum incorporating lessons on sexual health:** A variety of educational programs are underway which are being implemented at the school and college level by government and non-governmental sectors. These include programs such as the National Population Education project (A Govt. and United Nations Population Fund collaboration) as well as the programs run by Indian NGOs’ such as Family Planning Association of India and Parivar Sewa Sasthan

- (iv) **Involvement of the adolescent themselves :** Establishment of Youth forums wherein the adolescent can play the role of a peer educator should be promoted. A Youth convention was recently organized by CARE international in Jabalpur wherein as many as 4500 adolescent boys were involved in spreading messages about reproductive health through posters, quiz programmes, slogans and street plays.

- (v) **Parental involvement:** Parents should be involved in reproductive education which would require that parents be

able to communicate with their children about various reproductive health issues without any hesitation.

- (vi) **Making health services accessible and friendly:** As the adolescents in India face a number of social obstacles and other constraining factors in accessing adolescent health services, the same could be overcome by adopting the following strategies: (a) Provide clinic based preventive, promotive and curative services. (b) Specialized training of the staff to understand the felt needs of the adolescents needs to be stressed upon during the training. (c) Ensure the establishment of services in poorly served areas (d) Clinic should also be open after school/college hours and on holidays as well. (e) Availability of a Help line service.

- (vii) **Addressing Special needs of Adolescent boys:** In Indian settings, boys are generally raised to be self-reliant and independent, not to show emotions and not to be concerned with or complain about their physical health, nor to seek assistance during times of stress. These beliefs, and other factors significantly affect boy access to health care. Efforts to address the special needs of adolescent boys are being undertaken by NGOs’ like CEDPA and India-INCLIN in Lucknow etc

2) Challenge: Married adolescents: the health consequences of early marriage and childbearing.

In India, traditionally the transition from childhood to adulthood among females has tended to be sudden as a result of early marriage. According to NFHS-2, nearly one third of female adolescents were ever married compared to only 6 % of male adolescents.⁶ The awareness level amongst the female adolescents about the legal age of marriage has been found to be less. Pattanaik D. et al in their study conducted amongst 254 girls aged 13 to 17 years belonging to a rural area in Haryana observed that only 65 % of them knew the correct legal age and only a few could correctly define the needs and advantages of a small family.¹⁰

Consequences of early marriage :

- (i) **Impact on maternal health and pregnancy outcome:** Findings of NFHS – 2 reflected the infant mortality rate (IMR) of 93 per thousand live births to be much higher among children born to adolescent mothers. Early pregnancy also has an impact on population size as adolescent mothers will have more children than those who start childbearing later. Moreover the poor nutritional status of adolescent girls in India has been well documented.¹³ Pregnant adolescents are more likely to suffer eclampsia and obstructed labor than women who become pregnant in their early twenties.¹⁴

- (ii) **Unmet need for contraception:** The findings of NFHS-2 also revealed that only 8 percent of married adolescents were currently using a method of contraception to avoid pregnancy. The use of contraceptives was lower in rural areas compared with urban areas, at 7.7 percent and 9.9 percent, respectively.

- (iii) **Accessibility to Reproductive health services :** The married adolescent female is also prone to face social and psychological barriers in accessing reproductive health services. In rural Maharashtra a study showed that many of them did not seek treatment for several reasons: shame and embarrassment; not being taken seriously by those with influence (husband and mother-in-law); and lack of financial

independence.¹⁵

Opportunities:

(i) Raising the age of marriage among adolescent girls

It is important to raise awareness among girls, their parents, schools and communities of the harmful health consequences of early marriage and early pregnancy. This can be done by means of (i) Educating the community (ii) A stricter enforcement of the law regarding the legal age of marriage of girls (iii) Women empowerment. The National Population Policy 2000 underscores the need for such programs which encourage delayed marriage and child bearing. The Adolescent girl scheme which has been launched under the ICDS also envisages imparting skills and involvement in useful economic activities. At present the scheme covers 3.9 million adolescent girls in 507 blocks across the country.¹⁶

(ii) Addressing the adverse health implications of married adolescent girls : Very few programs have been able to distinguish between the special reproductive health needs of married and unmarried adolescents. For example the Planned Parenthood Federation has implemented a project known as "Couple to couple" wherein peer couples are employed to work with newly weds and young couples so as to motivate them to plan their families and attain positive reproductive health.

3) Challenge: Unwanted pregnancy and induced abortions amongst adolescents

The female adolescent is highly vulnerable to unplanned, unwanted and mistimed pregnancy, mainly as result of lack of contraceptive usage and high risk sexual behaviour. Also, a large number of abortion seekers become pregnant as a result of rape or sexual coercion. Adolescents comprise about 1 to 10 % of the abortion seekers.¹⁷ Although the Medical Termination of Pregnancy (MTP) Act (1972) has legalized abortion, yet the existing MTP health services are generally ill equipped to address the needs of these young girls.

Opportunities:

- (i) Ensuring availability, accessibility and quality of safe and client friendly abortion services
- (ii) Use of safer methods of abortion such as manual vacuum aspiration techniques and medical.
- (iii) Raise awareness about the legal implications of abortion and rights of the woman in availing safe abortion services
- (iv) Expansion of access and use of Emergency contraception. Various studies have shown the existence of inadequate levels of knowledge about emergency contraception, such as a study which was conducted in Bhopal among the sexually active group in the age group of 15-25 years wherein as many as 83 % of them had low levels of awareness.¹⁸

4) Challenge : Reproductive tract and sexually transmitted infections including HIV/AIDS

The vulnerability of adolescents to reproductive tract infections (RTI s') and sexually transmitted infections (STI s') are mainly attributed to their high risk behavior. Moreover, adolescents who are involved in a steady relationship tend to use oral contraceptives because of the fear of risk of an unwanted pregnancy. Inexperience with proper use of condom is also an important cause of failure of protection

offered by it. About a third of the 333 million new sexually transmitted disease (STD) cases each year, excluding HIV occur among people younger than 25.¹⁹ Findings from NFHS -2 have shown that as many as 32.1 % of the ever married adolescents complained of abnormal vaginal discharge or symptoms of UTI.

Opportunities:

- (i) **Raising awareness levels , availability and utilization of barrier contraceptives:** Easy accessibility to condoms, especially by the unmarried adolescents would significantly enhance their utilization rates. This could be done by installation of vending machines in public toilets, games arcades, internet cafes, night clubs etc. Easy accessibility should also be combined with peer education and proper diagnosis, treatment and referral services in the Adolescent health clinic.
- (ii) **Range of Choices :** Availability of a range of choices such as abstinence, fidelity, monogamy and condom use could give a greater momentum to STI prevention initiatives, as this helps to bring about a respectful recognition of the different choices of the adolescent.

5) Challenge : Sexual violence as an emerging issue of concern

Sexual abuse is a violation perpetrated by a person who holds, or is perceived to hold, power over someone who is vulnerable. It includes such sexual violations as rape, sexual assault, sexual harassment, incest and sexual molestation. As a taboo subject, sexual violence is rarely reported or studied. Sexual abuse results in acute as well as long term consequences. The acute consequences for both male and female victims include physical injury, sexually transmitted infections (STIs), and psychological trauma whilst for female victims, there is the added danger of unwanted pregnancy. The long term consequences include a likelihood to engage in high-risk sexual activity, inability of self defense. Patel et al in their study on sexual abuse in schools in Goa reported that one third of the students had experienced at least one type of sexual abuse in the previous 12 months.²⁰

Opportunities:

- (i) Imparting training skills in self defense
- (ii) Raising awareness about laws which protect the victim and punish the accused
- (iii) Victims of sexual abuse should be identified by health providers and teachers by including questions about abuse in health assessments
- (iv) Supportive services should aim at addressing the physical, mental and emotional needs of the abuse victims.

CONCLUSIONS

The present has sought to provide a brief overview of sexual and reproductive health situation of adolescents in India and the strategies that could have been adopted by various agencies dealing with adolescents. Further research and evaluation on some issues such as investigating the sexual and reproductive choice among married youth, adolescent's access to health care and the problem of non-consensual sex is no doubt genuinely needed. There is a need for evolving information, education and communication strategies to

focus on raising awareness on reproductive and sexual health matters and gender sensitive issues and for the programme managers and various stakeholders to gain a wider vision pertaining to this issue.

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LITERATURE REVIEW

Correction of Anemia with Erythropoietin in Chronic Kidney Disease (stage 3 or 4): Effects on Cardiac Performance Konstantinos D. Pappas et.al. *Cardiovasc. Drugs Ther.* 2008, 22,37-44

It is not clear whether the correction of anemia with erythropoietin (rhuEpo) in patients with chronic kidney disease (CKD) has any benefit on cardiac function and geometry. Most studies are based on indices of systolic function and left ventricular mass (LVM) and the results are conflicting. Authors sought to investigate the effect of rhuEpo on LV systolic and diastolic performance using conventional and novel echocardiographic indices. Thirty one patients with CKD (stage 3 or 4) were included. Fifteen patients (group I) treated with rhuEpo targeting at Hb e¹³13.0 g/dL, while the remaining (group II) were not treated. Clinical and laboratory parameters were recorded at baseline and 1 year later. Ejection fraction (EF) and LVM were carefully determined. Diastolic function was assessed by mitral inflow indices (E and A wave velocities, Edt deceleration time and E/A) and novel indices of mitral annulus motion using Tissue Doppler Imaging (Em, Am, and E/Em). An index of global cardiac function (Tei) was also calculated. At baseline, the 2 groups had comparable clinical and laboratory characteristics. After 1 year, a significant improvement in Hb levels (13.6 ± 1.2 vs 10.3 ± 1.2 g/dL, $p < 0.05$) as well as in systolic and diastolic function indexes was observed in group I compared to group II patients: EF (70.5 ± 7.6 vs 63.4 ± 9.3%, $p < 0.05$), LVM (116.5 ± 34.9 vs 155.6 ± 51.6 g/m², $p < 0.05$), Edt (233.9±98.6 vs 166.9±45.1 ms, $p < 0.05$), Tei index (0.35±0.12 vs 0.51±0.17, $p < 0.01$) and E/Em (9.7 ± 2.4 vs 14.8 ± 5.2, $p < 0.05$), respectively. Blood pressure and heart rate did not show significant changes. Correction of anemia with rhuEpo in patients with CKD seems to improve cardiac performance and geometry.

LITERATURE REVIEW

Mumbai Stroke Registry (2005-2006) - Surveillance Using WHO Steps Stroke Instrument - Challenges and Opportunities PM Dalal, Madhumita Bhattacharjee, Jae Vairale, Priya Bhat JAPI 2008, 56, 675-678

India will face enormous socioeconomic burden because life expectancy is increasing placing larger numbers of older people at risk of stroke and other chronic diseases. In order to plan prevention strategies, reliable information on stroke epidemiology is required. For uniform data collection (population based), WHO recommends use of STEPS Stroke instrument. A well-defined community (H-ward) with verifiable census data, and representative of population structure of Mumbai (Bombay), was selected. The manual on WHO STEPwise approach to stroke surveillance (STEPS; <http://www.who.int/chp/steps/Manual.pdf>) was the operational protocol. During the two year study period (Jan 2005 to Dec 2006), 521 new stroke (CVD) cases (males- 275 and females- 246) were identified; of which 456 (238 males and 218 females) had "first ever stroke"(FES) indicating an annual incidence of 145 per 100,000 persons (CI 95%: 120-170); age adjusted Segi rate:152 /100,000/year (CI 95% 132-172). Two thirds of the FES cases were admitted to health care

facilities (Step I: "in-hospital" cases), the remaining 150 (32.8%) either died outside of hospital or were treated at home or nursing homes (Step II: Fatal events in community and Step III: Non-fatal events in community). CVD Diagnosis was supported by CT (Computed Tomography) in 407 (89%) of 456 FES cases: 366 (80.2%) had Ischaemic CVD, 81 (17.7%) had hemorrhagic CVD and 9(1%) were of unspecified category. The mean age was 66 yrs SD±13.60 and women were older compared with men (mean age 68.9rs SD ± 13.12 versus 63.4yrs SD ± 13.53). Hypertension (BP more than140/90 mm Hg) alone or in various combinations was present in 378(82.8%) cases. Case fatality at 28 days after the FES stroke was 29.8%. Of 320 surviving patients 38.5% had moderate to severe disability. WHO STEPS stroke surveillance Instrument is simple to use and, practical for community surveys. The data are useful for planning stroke prevention campaigns on public awareness and education with regard to diet, exercise, blood pressure control and early symptoms of minor strokes.

PICTORIAL CME

NEUROPATHIC EDEMA AND CHARCOT FOOT IN A DIABETIC PATIENT

N.S. Neki

Department of Medicine, Govt. Medical College/Guru Nanak Dev Hospital, Amritsar (Punjab), India



FIG. 1

FIG. 2

A 58 years nonalcoholic, non smoker, non obese with type 2 diabetes mellitus since 13 years, presented with wound on left big toe on its plantar aspect (Fig. 1) and decreased vision for six months. He was agriculturist by profession with history of working barefooted in the fields. he was taking oral hypoglycemic agents off and on. He was also having hypertension and retinopathy for 10 years, without treatment. On examination, he had ulcer on plantar aspect of left big toe with atrophy of foot muscles (Fig. 1). The right foot was swollen with dry, brittle skin diagnostic of neuropathic edema and nails thickened with clawing of toes (Fig. 2). X-ray both feet showed calcification of vessels especially dorsalis pedis artery of right foot as well as destruction of distal phalanges of left 1 big toe (auto-amputation) with involvement of first metatarsophalangeal joint of the right foot, diagnostic of neuro-arthropathy (Charcot foot). A charcot joint is a relative painless progressive arthropathy of a single or multiple joints caused by underlying neuropathy. The neuropathic joints commonly involved are in order of tarso-metatarsal, metatarsophalangeal, ankle and subtalar joints. the initial presentation is often a hot, swollen foot as seen in right foot, the precipitation event usually being a minor trauma.

LETTERS TO THE EDITOR

Dear Editor,

This writeup is meant to create awareness about "Asthma as Public Health Problem" amongst the medical fraternity
Thanking you,

Your sincerely,
Ranabir Pal, Ankur Barua

SLOW EPIDEMIC OF BRONCHIAL ASTHMA

Asthma is a serious global health problem. Prevalence of occupational asthma has been variable; it is detectable 10 or 11 years after beginning exposure and is much greater in cigarette smokers¹. People of all ages in countries throughout the world are affected by chronic airway disorders that can be severe and sometimes fatal. The prevalence of asthma is increasing everywhere, especially among children. Asthma causes significant burden, not only in terms of health care costs but also of lost productivity and participation in family life².

In addition, public health officials require information about the cost of asthma care, how to effectively manage this chronic disease, and best education methods in order to develop asthma care services and programmes responsive to the particular needs and circumstances within their countries. Accordingly, in 1993, the National Heart, Lung and Blood Institute collaborated with World Health Organization to convene a workshop that led to the global strategy for asthma management and prevention. A workshop report that presented a comprehensive plan to manage asthma with the goal of reducing chronic disability and premature deaths while allowing patients with asthma to lead productive and fulfilling lives³.

Throughout the world in the last 30 years there has been a steady, relentless increase in the prevalence of childhood asthma. According to the 50-nation international Study of asthma and Allergies in Childhood (ISSAC): (a) Asthma is a very common condition; (b) Its prevalence varies widely from country to country; (c) At age of six to seven years, the prevalence ranges from 4% to 32%; the same range holds good for ages 13 and 14⁴. The UK has the highest prevalence of severe asthma in the world⁵. In India, a questionnaire based study measured the prevalence of asthma in nine randomly selected Delhi schools. The current prevalence of asthma was found to be 11.9%. Assuming Delhi represents the whole of India, this means there are 40 million children in India, who suffer with

asthma⁶. the prevalence of asthma worldwide is 200 million with a mortality of around 0.2 million per year. Through the prevalence is more in the developed countries, the developing countries have a higher total burden of the disease due to differences in population. In India, the estimated burden of asthma is believed to be more than 15 million⁷. The population prevalence of asthma reported in different field studies is reported to be quite variable⁸.

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Ranabir Pal, Ankur Barua
Department of Community Medicine,
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Symposium : Pediatric Nephrology

OUR GUEST EDITOR



Dr. Sanjeev Gulati

Dr. Sanjeev Gulati is currently working as Sr Consultant in Nephrology at Fortis Hospitals, Vasant Kunj, New Delhi, India. He was previously working as Additional Professor in Nephrology at Sanjay Gandhi Post Graduate Institute of Medical Sciences, Lucknow, *He has also worked as Associate Professor in Nephrology at McMaster University, Hamilton, Canada.* He has post MD experience of 18 years and post DNB experience of 14 years. He has dual qualifications in adult and pediatric nephrology. He has acquired special expertise in managing children with renal diseases and has experience at leading hospitals in UK, Australia and Canada. He played a pivotal role in the Pediatric Dialysis and Transplant programme at SGPGI, Lucknow which is amongst the largest programmes in the country. He has presented papers at several International and National Conferences and published more than 120 scientific papers in indexed journals including NEJM, Kidney International and American Journal of Kidney Diseases. He has also authored 9 chapters in textbooks (including the prestigious Oxford textbook of Nephrology) besides numerous guest lectures. He has received several awards for his original contributions to the field of kidney diseases. His work has received recognition from the Indian Council of Medical Research, Indian Academy of Pediatrics, Indian Society of Nephrology, the Australian College of Pediatrics, Royal college of Pediatrics and Child Health UK Royal College of Physicians and Surgeons of Canada and the Japanese Society of Nephrology.

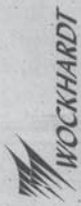
He is a reviewer for several prestigious journals like Pediatrics, American Journal of Kidney Diseases, Pediatric Nephrology and Indian Pediatrics and have had other editorial responsibilities also. He has also written several articles in newspapers and magazines for creating public awareness about kidney related issues.

EDITORIAL

It is indeed a great honor to be asked to edit a section on pediatric nephrology in this prestigious journal. This subspecialty was conceived nearly 30 years ago in our country through the collective vision of pioneers like Dr. R.N.Srivastava, Dr. Kumud Mehta and Dr. Nammalwar. Over the next few years there were significant advancements in management of common renal disease like urinary tract infection, acute renal failure and nephritic syndrome. A major lacuna was lack of dedicated pediatric nephrology training programmes as well as infrastructure for pediatric dialysis and transplantation. Thus this subspecialty had a prolonged gestation period and delayed development. During this period a unique experiment was initiated at SGPGI, Lucknow. The credit for this goes to Prof. Vijay Kher, an adult Nephrologist who was then heading the department of Nephrology at SGPGI, Lucknow. I dedicate this section to him who has not only been my mentor but also laid the foundations of what emerged as one of the first centres for pediatric dialysis and transplantation in our country in a very short span of time.

In this symposium on "Pediatric Nephrology" we will trace the development of pediatric nephrology in our country, update ourselves with the management of common problems like bed wetting, steroid resistant nephrotic syndrome and management of obstruction uropathies. In the end we will look at recent advances in dialysis and transplantation in children.

Dr. Sanjeev Gulati
Sr Consultant , Nephrology,
Fortis Hospitals, Vasant Kunj, New Delhi, India



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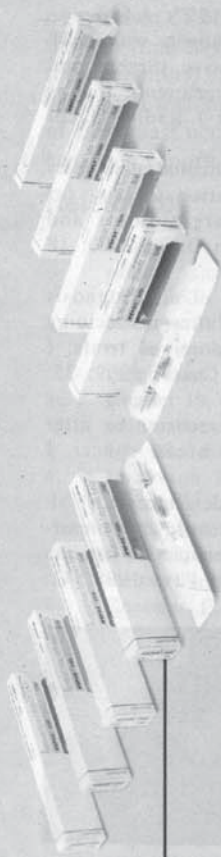
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DEVELOPMENT OF PEDIATRIC NEPHROLOGY IN INDIA

Vijay Kher

*Director, Nephrology & Transplant Medicine, Fortis Hospital
Sector B, Pocket 1, Aruna Asaf Ali Marg, New Delhi - 110070, India*

Pediatric Nephrology is a well established sub-specialty in the western world. However in India, though there are few pockets of excellence, there are very few trained pediatric nephrologists and even fewer institutions with separate pediatric nephrology divisions or departments and only one centre providing a one year training (post graduate diploma / certificate) course.

There has always been a debate as to whether pediatric nephrology subspecialty should develop around the departments of Pediatrics or Nephrology. In my opinion at the initial stages it should be both. The parent specialties need to provide active support. It is advantageous to be tethered to the parent specialty say pediatrics for overall connectivity and growth. However infrastructure for the subspecialty would need to be provided for, if the pediatric nephrology is developed around the department of pediatrics. In contrast developing it around Nephrology could mean utilizing the adult department's infra structure of dialysis and transplantation and this may save the cost of separate infrastructure for dialysis and transplantation. That is why I think that in an ideal setting, support and nurture from both Nephrology and Pediatrics would allow growth with Pediatrics and also allow utilization of adult nephrology infrastructure and trained manpower. However it needs committed support from both Pediatrics and Nephrology departments. Pediatric nephrologists developed with the co-operation of both departments need to cultivate and work along with both the teams. This way Pediatric Nephrology may come of age earlier and develop faster like in the developed world.

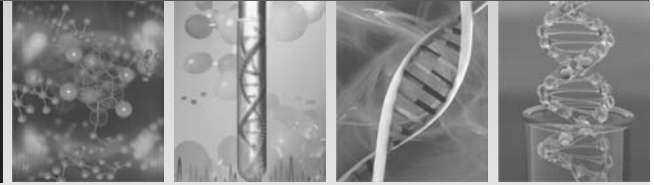
A survey of the pediatric nephrology centers across the country revealed that dedicated infrastructure for pediatric dialysis was available only in 4 centres and in one of them it was not being utilized because of absence of trained manpower. Even in these three centres, pediatric transplantation was being carried out in close collaboration with the adult transplant surgeon and utilizing the same transplant nurses and ICUs. In rest of the centres the facilities for pediatric dialysis and transplant were being shared with adult hemodialysis and transplant units. There are few institutions in the country where pediatric nephrology is well developed with infrastructure for their use under their command. These institutions have carved out a niche not only in our country but internationally, e.g. under stewardship of Prof. Srivastava and Prof. Arvind Bagga at AIIMS, Dr. Kumud Mehta and Dr. Uma Ali at KEM & Wadia hospitals; Dr. Nammalwar and Dr. Vijay Kumar at Institute of Child Health, Chennai and Dr. Phadke at St. John's Hospital, Bangalore. These stalwarts have spearheaded the pediatric nephrology flag in the country. A lacuna

in these institutions has been the slow pace of development of facilities for pediatric dialysis and transplantation. At SGPGI Lucknow, we made a concerted effort to develop pediatric nephrology along with adult nephrology in early nineties and inducted pediatricians Dr. Sanjeev Gulati & Dr. Ajay Sharma into our training programme, to open new avenues for growth of Pediatric Nephrology. Over the next few years this department was able to quickly make a mark for itself and both these are making significant contributions nationally and internationally. This has been followed up with similar inputs by many Nephrology Departments across the country. Over these years, the 2 largest centres for pediatric end stage kidney disease programme have been CMC Vellore and SGPGIMS, Lucknow. Thus this seems to be preferred method to get more Pediatricians to learn Nephrology particularly with regard to end stage care. It also economises on the infrastructure and trained manpower this model has been the one that is being followed in majority of the private sector hospitals across the country. There remains a need to have more training courses in the subspecialty especially in the institutions like AIIMS, PGI, St. Johns hospital, SGPGI and others.

There are about 800 nephrologists for a large country like India with more than a billion people and obviously a dismally minuscule number of pediatric nephrologists for the care of huge number of children. Treating children with kidney diseases pose many different challenges in comparison to treating adult – nephrology patients, the challenges of correction of congenital urological anomalies, the negative impact of kidney disease on growth of children – a huge challenge providing dialysis and transplantation in children and the social and financial impact on the family and the society. A clinician requires all the skills to manage these time consuming and difficult challenges. Simultaneously one also needs to train nurses, technicians and other paramedics for full fledged growth as well as make easily available the small sized consumables like vascular catheters, PD catheters, vascular instruments and other consumables to provide effective care of dialysis and kidney transplantation to the growing number of children with kidney diseases, wanting and requiring these modalities of treatment in India. We also need to train and sustain a whole range of allied persons like social workers, psychologists, pediatric urologists, pediatric transplant surgeons to take care of pediatric CKD patients. This is my opinion can only be achieved by a multi pronged directed approach preferably by public and private partnership which should be spearheaded by the Health Ministry.

Correspondence: Vijay Kher, Director, Nephrology & Transplant Medicine, Fortis Hospital, Sector B, Pocket 1, Aruna Asaf Ali Marg, New Delhi - 110070, India

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MANAGEMENT OF BEDWETTING IN CHILDREN

M Kanitkar

Department of Pediatrics, Armed Forces Medical College, Pune 411040, India

Abstract : Nocturnal enuresis or bed wetting is a benign condition, yet needs treatment to relieve the child and parents of the accompanying anxiety and the stigma attached. More than 85% children attain complete bladder control by 5 years. The underlying cause of enuresis is not clear; various proposed pathophysiological mechanisms have been described. In most children with enuresis, extensive investigations are not required. A simple and structured evaluation that includes a detailed history, clinical examination and measurement of the voided volume is sufficient. The various treatment modalities available are bladder training, behavioral modification using the alarm, medications such as oxybutinin and desmopressin along with good supportive care. No treatment plan is ideal and in a given child the modality may be selected based on information obtained from the structured evaluation and the parent and child's preference. Often a combination works best. This communication discusses a therapeutic approach.

Key words: Nocturnal enuresis, Evaluation, Treatment

ETIOLOGY & CLASSIFICATION

Enuresis is a common problem encountered in clinical practice. It is not enough to tell parents seeking attention, that the child will grow out of the problem. A child having nearly complete evacuation of the bladder at least twice a month after the fifth year of life definitely warrants attention. As a rule the bed will be soaking wet as against incontinence, which is loss of urine without normal emptying of the bladder. Bladder control is usually attained between the ages of one and five years. More than 85% children will have complete diurnal and nocturnal control by five years of age¹.

At the outset it is important to classify enuresis as *primary* when the child has never been dry and *secondary* when bedwetting starts after a minimum period of six months of dryness at night. It is considered monosymptomatic if the child has no daytime symptoms like urge, frequency or daytime incontinence². Primary monosymptomatic enuresis does not require extensive evaluation. Secondary enuresis on the other hand warrants investigations.

There is no single definite underlying cause for enuresis, it is often multifactorial. Evidence points towards maturational delay, inadequate arousal during sleep, genetic predisposition, reduced functional bladder capacity and an altered secretion or response to antidiuretic hormone, as some of the factors responsible for enuresis³. A recent study found that breast feeding the infant for more than three months may protect against bedwetting in childhood⁴. Attempts to identify the possible cause in a given child can help translate the information into therapeutic options.

INVESTIGATIONS

Most children with primary monosymptomatic nocturnal enuresis considered as uncomplicated enuresis require no further evaluation. A detailed history and clinical examination helps differentiate these children from ones with a more complex problem (Table 1). At times the history of daytime

symptoms such as holding maneuvers, urgency and day time wetting may not be forthcoming on history alone and a voiding diary maintained for at least two days yields a lot of information⁵. It is therefore advisable to request parents to maintain a record of the time of each void and the volume of urine passed each time, along with a record of any "accidents" as noted from a dampness of the underpants. This record helps identify a child with a relatively small functional capacity of the bladder where a frequent small quantity-voiding pattern is noted. In a child with reduced functional bladder capacity the average maximum volume of urine voided at urge is much less than the expected bladder capacity for the age as determined using standard formulae as under⁶.

Age < 2 yrs Bladder capacity in milliliter = Weight in kg x 7

Age > 2 yrs Bladder capacity in milliliter = (Age in yrs+2) x 30

Table 1 Initial evaluation for Enuresis

	<i>Uncomplicated</i>	<i>Complicated</i>
Onset	Primary	Secondary
Diurnal symptoms	Absent	Present
Urinary stream	Normal	Abnormal
Examination*	Normal	Abnormal
Urinalysis	Normal	Abnormal

* Examination includes developmental and neurological assessment, examination of the abdomen, genitalia and spine.

A special mention needs to be made of any history of holding maneuvers used by the child such as crossing of the legs, bending forward or squatting. Such children possibly have a functional voiding disorder and may require further evaluation. Though a normal urodynamic study provides reassurance of

normal bladder function, it is a costly, invasive and unpleasant procedure in young children and offers little in the management of uncomplicated enuresis.

TREATMENT

Timely treatment of nocturnal enuresis prevents psychological damage to the child and provides relief to the family. It should be started without wasting time on investigations in any child who wants to sleep dry and has uncomplicated enuresis. No single therapeutic plan seems ideal for all patients. Assessing the level of motivation of the patient and his parents prior to offering the choice of treatment is important. Emotional support may be required when the family history reveals psychosocial stress especially in adolescents and those with complicated enuresis.

Withholding fluids in the evening, random awakening of the child to void or punitive measures result in significant stress to the child and family. However caffeinated drinks like tea, coffee and sodas should be avoided in the evening. Adequate fluid intake during the day ensures lesser intake during the evening, as the child would then have received his daily fluid requirement during the first half of the day. This also helps in reducing the often associated problem of constipation which can aggravate bladder dysfunction.

The success of any form of therapy depends to a large extent on the child being motivated to work towards sleeping dry. The child is reassured and provided emotional support. Every attempt is made to remove any feeling of guilt. The benign nature of the disorder is explained to the child and parents. The child should be encouraged for total involvement in the therapy with maintenance of a dry night diary. Dry nights merit praise and encouraging words from the parents. Various modalities of treatment are available for the treatment of enuresis. The final choice of modality for treatment depends on the likely cause of enuresis and the patient's preference.

Bladder training exercises

With an aim of increasing the functional bladder capacity, children are encouraged to drink more water during the daytime and hold urine for an increasing duration after feeling a desire to void. They are also told to try voluntary cessation of micturition during the process of voiding. This increases the ability to withstand uninhibited bladder contractions. The



Figure 1 Child using the alarm while sleeping

efficacy of these measures along with bed time resolution by the child and encouragement from the treating physician is comparable to that of desmopressin or alarm therapy⁷.

Enuresis alarms

This form of therapy involves the use of an alarm device to elicit a conditioned response of awakening initially to wetting and later to the sensation of a full bladder. Gradually bladder distention evokes micturition. The alarm device consists of a small sensor attached to the child's underwear, or a mat under the bed-sheet and an alarm placed at the bedside. When the child starts wetting the bed, the sensors are activated causing the alarm to sound. This conditions the child to sense a full bladder; subsequently the child awakens at a critical time when

Table 2 Medications in enuresis

Drug	Dose	Side effects	Age for use
DDAVP nasal spray	10-40µg per day	Nasal stuffiness, hyponatremia, seizures	Any if supervised
DDAVP tablets	0.2-0.6 mg/day	Headache, epistaxis, nausea	Any
Oxybutinin	5-20mg per day	Dryness of mouth, flushing, palpitations blurring of vision	>6y
Imipramine	0.9-1.5mg per kg/day	Anxiety, personality change palpitations	>7y
Tolterodine	1 mg twice a day	Mild effects similar to oxybutinin	>5

the bladder is full and the child still dry. These devices are now available in the country and a prototype is depicted in Figure 1

Pharmacotherapy

A number of medications are used in the treatment of nocturnal enuresis (Table 2). *Tricyclic antidepressants* like imipramine alter the arousal-sleep mechanisms and exert some anticholinergic effects. The effect of these medications is rapid and should be given a couple of hours before bedtime. Side effects have put this group of medication on the back burner. *Anticholinergic drugs* like oxybutinin reduce uninhibited bladder contractions and are useful in children who manifest with urgency and urge incontinence during the daytime or those with a reduced voided volume as calculated from the voiding diary. Oxybutinin maybe also be used as an adjunct to the alarm or treatment with desmopressin, when either of them fails as single therapy⁸. Tolterodine a newer anticholinergic is better tolerated and may be used in children above 5 years. *Desmopressin (DDAVP)* is an analogue of the hormone vasopressin that acts by reducing the nocturnal urine output to a volume less than the functional bladder capacity. Administration of DDAVP as an intranasal spray an hour before bed time is particularly useful in patients showing high nocturnal urine production or a less concentrated urine prior to therapy. In non-responders the dose may be increased upto 40 mcg/day in a stepwise manner. Oral desmopressin in a dose

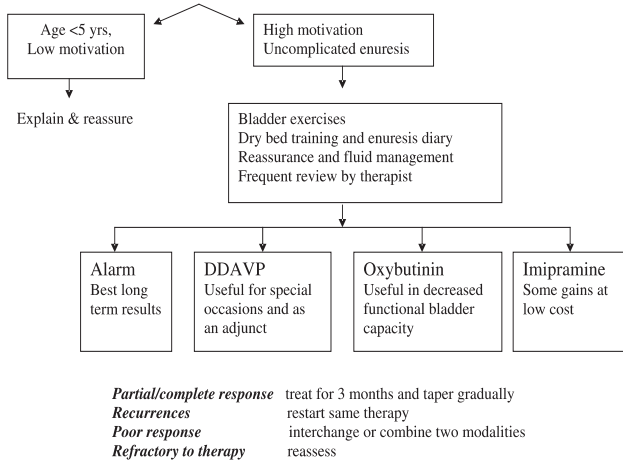


Figure 2 Treatment for primary monosymptomatic nocturnal enuresis

of 0.2 mg increasing to 0.6 mg daily may be given an hour before bedtime. This is now available in the country. Prolonged desmopressin bioactivity may increase the risk of water intoxication, a possible side effect of free water intake by the child when on desmopressin⁹.

While therapy is initiated, certain *guidelines* are recommended. The child is started on a low dose of the medication. Thereafter the dose is adjusted every two weeks to the maximum dose required to achieve dry nights. Therapy is continued for 3-6 months of dry nights and thereafter weaned over three to four weeks. In case of a relapse the same therapy is restarted or behavioral modification using an alarm device, is considered in conjunction. A structured withdrawal of therapy rather than tapering the dose of medications seems to improve the outcome¹⁰. This is achieved by administering therapy alternate day, followed by twice a week etc.

The various treatment modalities available are not used exclusive of each other and often a combination works best. Failure of one form of therapy should result in substitution or

addition of another. The three system model, suggesting desmopressin for low vasopressin release, oxybutinin along with bladder training for instability when suspected and the alarm to enhance arousability from sleep works well. A combination of one of these with motivational therapy is ideal. Comparative studies have shown that DDAVP has better short-term results, but the alarm has better long-term outcome. Hence, DDAVP is best used under special situations, e.g., if the child needs to remain dry when camping out or staying over at a friend's place. If long term efficacy, cost and safety are taken into consideration, the enuresis alarm comes out superior¹¹. In patients with enuresis and a voiding dysfunction DDAVP can enhance the effect of oxybutinin by reducing urinary output and bladder filling, thus reducing uninhibited bladder contractions. Reassurance and motivation of the child for involvement in the therapy and direct frequent contact with the therapist improves the outcome. An algorithmic representation for the treatment of primary monosymptomatic enuresis is depicted in Figure 2.

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ADVANCES IN THE PATHOGENESIS AND MANAGEMENT OF IDIOPATHIC STEROID RESISTANT NEPHROTIC SYNDROME IN CHILDREN

Rajendra Bhimma

Department of Mother and Child Health, Nelson R Mandela School of Medicine, University of Kwazulu-Natal, Durban, South Africa

Abstract : 20% children with idiopathic nephrotic syndrome are steroid resistant (SRNS) according to ISKDC report (1970); they are at the risk of developing ESRD, especially those with FSGS criteria; specific gene mutation could be likely mechanism. Clinically, hypertension, haematuria, elevated serum creatinine, massive proteinuria are some of the possible predictors of steroid resistance. Optimal approach to SRNS is uncertain; newer immunosuppressive agents may benefit a small proportion of these subjects.

INTRODUCTION

The idiopathic nephrotic syndrome (NS) of childhood is a heterogeneous disorder characterised by massive proteinuria, hypoalbuminaemia, hyperlipidaemia and oedema. Histological characteristics are non-specific and range from minimal change disease, focal and diffuse mesangial proliferation to focal and segmental glomerulosclerosis (FSGS). Immunofluorescence is usually negative and electron microscopy shows fusion of the epithelial cell foot processes¹. Over 80% of children presenting with an initial episode of NS respond to steroids (steroid sensitive), whilst the remaining 20% do not respond and are considered steroid resistant (SR)². On follow up, 50-60% of children in the steroid responsive group have frequent relapses or develop steroid dependent disease. This group of children together with those that are SR are at risk for extrarenal complications of NS, as well as progression to end-stage renal disease necessitating renal replacement therapy. In children with SRNS (particularly FSGS) who undergo transplantation, the overall risk for recurrence of the primary disease is about 25%¹. The aim of therapy is to control the nephrotic state and thus prevent complications and to especially try and halt or delay progression to end-stage renal disease. To date the plethora of agents in our therapeutic armamentarium has failed to produce a drug that is the panacea for this condition. Thus management of SRNS poses a major therapeutic challenge to the attending clinician.

MECHANISM OF STEROID RESISTANCE

Why some children develop resistance to steroids is not well understood [6]. There are certain clinical, laboratory, and histological characteristics that may predict the likelihood of steroid resistance (Table 1). Recent studies have shown that specific genetic mutations constitute a principle mechanism for steroid resistance. Mutations of *NPHS1*, *NPHS2*, *ACTN4* and *WT1* genes are responsible for severe forms of SRNS in childhood, progressing to end-stage renal failure³. Positional cloning has revealed defects in these 4 different genes as monogenic causes of SRNS in familial cases (Table 2)⁴.

Children presenting with NS in the first year of life are steroid

Table 1 Clinical, laboratory, and histological characteristics that may predict the likelihood of steroid resistance.

Clinical Characteristics	Laboratory
Hypertension (50-60% likelihood)	Selectivity index >0.2
Haematuria (30% likelihood)	Elevated plasma creatinine
Hypertension plus haematuria (20% likelihood)	Tubular proteinuria (Increase excretion of B ₂ -microglobulin, retinol-binding protein, lysozyme)
Black race	Massive proteinuria (>10g/day)
Age of first presentation in infancy, after 8 years or post puberty.	
Primary vs. secondary steroid resistance.	
Histology	
Tubulointerstitial disease on renal biopsy or collapsing FSGS and >50 percent of globally sclerosed glomeruli	
Non minimal change disease on histology.	

Table 2 Genetic mutations associated with SRNS in childhood.

GENE	TYPE OF NS
NPHS1	Recessive mutations, encoding nephrin, (OMIM No. 602716) causes congenital NS of the Finnish type.
NPHS2	Recessive mutations, encoding podocin (OMIM no. 604766), causes SRNS Type 1.
ACTN4	Mutations encoding actinin 4, (OMIM no. 604638), causes autosomal dominant form of SRNS. An additional locus for an autosomal dominant form of NS has been mapped to chromosome 11q21-q22 (OMIM no. 603965).
WT1	Mutations are associated with congenital NS and diffuse mesangial sclerosis in the Denys-Drash syndrome and Frasier syndrome.

resistant. Two thirds of NS manifesting in the first year of life can be explained by mutations in 4 genes only (*NPHS1*, *NPHS2*, *WT1*, or *LAMB2*)⁵. Interestingly, *NPHS1* mutations occur in congenital NS only. However there are likely to be additional

Correspondence: R Bhimma, Department of Mother and Child Health, Nelson R Mandela School of Medicine, University of Kwazulu-Natal, Durban, South Africa e-mail : bhimma@Ukzn.Ac.Za

unknown genes mutated in early-onset NS that have still not been detected. NS associated with syndromes in childhood are SR and progress to end stage renal disease. The *Denys-Drash syndrome* is characterised by early onset of NS progressing rapidly to end-stage renal disease, male pseudohermaphroditism, and Wilm's tumour⁶. The *Frasier syndrome* is characterised by the association of male pseudohermaphroditism and progressive glomerulopathy⁷.

CLINICAL PRESENTATION

The majority of patients present between 2-7 years of age. There is a preponderance of males with a ratio of males: females of 2:1. The disease is characterized by the sudden onset of oedema; anasarca may develop with ascites, pleural and pericardial effusions. Blood pressure is usually normal but is sometimes elevated. Abdominal pain is occasionally due to complications such as peritonitis, thrombosis, or rarely pancreatitis. Sometimes the rapid development of ascites with concomitant hypovolaemia leads to abdominal pain and malaise. In some patients oedema is minimal and the nephrotic state is only discovered during routine urine analysis. Macroscopic haematuria may occur in a few cases. Common complications of SRNS include the following: acute or chronic renal failure, growth retardation, increased susceptibility to infections as a result of secondary immunodeficiency from malnutrition, and arterial or venous thrombosis.

TREATMENT

Symptomatic treatment is similarly to that of children who are steroid sensitive. This includes dietary recommendations of no added salt and adequate intake of proteins and vitamins with reduced intake of foods high in cholesterol. Diuretics are used for the treatment of oedema. If there is anasarca, salt free albumin together with loop diuretics is given for control of oedema. Treatment includes prevention and appropriate treatment of infections and thromboembolic complications, and treatment of hypovolaemia, hypertension, and hyperlipidaemia. If the latter is not controlled by dietary restriction alone, lipid lowering agents are used.

Immunosuppressive Therapy

The optimal approach to SRNS is uncertain. Reports of the large number of agents used as specific therapy for SRNS bears testimony to the lack of a single effective agent for the treatment of this condition.

Alkylating Agents

Cyclophosphamide and chlorambucil have been used either alone, in combination with oral steroids or with high dose pulse steroids. These regimens have met with variable success rates of inducing remission ranging from 10% to 70%. Many patients exhibit features of steroid toxicity. The use of pulse dose cyclophosphamide over a few months induced remission in 25-60% of children with SRNS^{8,9,10}.

In a review of 223 children with SRNS, Bhimma et al¹⁰ showed distinct racial differences with respect to response to oral cyclophosphamide therapy in Indian and Black children. In this study, a total of 183(82.1%) underwent renal biopsy; 84(45.9%) were Indian and

99(54.1%) were black. Sixty-six (36.1%) had minimal change disease, 66(36.1%) FSGS, 15(8.2%) proliferative forms of NS, and 36(19.7%) had other forms of NS. Of the 50 children who were biopsied and treated with oral cyclophosphamide and corticosteroids only, 29(57%) achieved complete remission and 5(12%) partial remission, all were Indian. In view of the large number of Indian patients that responded to oral cyclophosphamide but the dismal response in black children, the authors recommend a trial of oral cyclophosphamide therapy in non-black children with SRNS before resorting to kidney biopsy¹⁰.

Cyclosporin

Initial studies evaluating the efficacy of cyclosporin in patients with SRNS showed a relatively small benefit. In eight uncontrolled studies involving 60 patients, complete remission was induced in only 12 (20%). In the study by the French Society of Pediatric Nephrology involving 65 children with SRNS, complete remission was observed in 42% of children (48% with minimal change disease and 32% with FSGS). Eight of the 27 responders became steroid-sensitive when they subsequently relapsed¹¹. Patients who respond to cyclosporin often relapse when the dose is tapered or discontinued. Many reports indicate that the prolonged use of cyclosporin is associated with chronic nephrotoxicity. The most prominent histological feature of chronic cyclosporin nephrotoxicity is the presence of *tubulointerstitial lesions*, characterised by striped interstitial fibrosis containing groups of atrophic tubules. *Cyclosporin associated arteriopathy* is rarely observed. Other side effects include elevation of blood pressure, hyperkalaemia, hypertrichosis, gum hypertrophy, and hypomagnesaemia.

Mycophenolate Mofetil

Mycophenolate Mofetil (MMF) is the prodrug of mycophenolic acid (MPA) which is formed by hydrolysis. MPA is a potent, selective, uncompetitive, and reversible inhibitor of inosine monophosphate dehydrogenase. The latter is an enzyme required for de novo purine synthesis. MPA inhibits B and T-lymphocyte proliferation, as these cells are critically dependant upon de novo purine synthesis for their proliferation whereas other cell types can utilize salvage pathways for purine synthesis.

MMF has been used in SRNS and FSGS. Although several reports of the use of MMF in steroid dependent NS have been published, a paucity of data exists concerning its use in SRNS. In a study by Mendizabal et al¹³, MMF was given to 5 children with SRNS. Only one achieved complete remission. Withdrawal of the drug led to relapse with one patient developing chronic renal failure¹³.

The advantage with the use of MMF is its benign side effect profile compared to prednisone and cyclosporin. Its use is not associated with nephrotoxicity, hepatotoxicity, neurotoxicity, hyperglycaemia or abnormalities of lipid metabolism.

Tacrolimus

Tacrolimus is a calcineurin inhibitor that is more potent in cytokine suppression than cyclosporine. The main mechanism of action of tacrolimus is through the inhibition of IL-2 dependant T-cell activation, a process occurring during the

early phase of T-cell activation. Tacrolimus also inhibits B-cell activation, in part through its action on T-cells and also directly by blocking TNF- α gene transcription by anti-Ig antibody. The drug only becomes active when complexed with a distinct endogenous intracellular receptor (cystocolic binding protein-FRBP₁₂) known as immunophilin. The immunophilin drug complex interferes with intracellular calcium-dependent signal transduction pathways, processes that are central to T-cell activation. The common biological target for the resulting complex is the calcium and calmodulin-dependent protein phosphatase, calcineurin. Case reports and single centre studies have shown tacrolimus to be effective in treating SR FSGS. In a prospective, open labeled study of 20 children with SR FSGS given tacrolimus (0.2-0.4mg/kg per day in 2 divided doses over 12 hours adjusted to achieve a trough level between 7-15ng/ml) for 12 months in combination with low dose steroids and angiotensin converting enzyme inhibitors, Bhimma et al showed tacrolimus to be a safe and effective agent in the management of SR FSGS. At the end of the treatment period of 12 months of tacrolimus therapy, 8(40%) children were in complete remission, 9(45%) children were in partial remission, and 3(15%) failed to respond. The average period of follow-up following cessation of tacrolimus treatment was 27.5 months (range 13.7-43.7). At last hospital follow-up 5 (25%) of children were in complete remission, 10 (50%) in partial remission and 2 (10%) in relapse. 3 children demised from dialysis related complications following cessation of tacrolimus treatment. Adverse events included sepsis (2), nausea (2) diarrhea (2), anaemia (4) and worsening of hypertension (4). None of the 14 children who underwent repeat biopsy after follow-up for 6-18 months post treatment showed evidence of calcineurin toxicity¹³.

In another prospective, open labelled study, Gulati et al treated 22 consecutive children with SRNS, 11 having FSGS, 9 minimal change disease and 2 diffuse mesangial hypercellularity. Tacrolimus was withdrawn in 3 children because of side effects. Of the remaining 19 children, complete remission was attained in 16(84%) children, 2(10.5%) attained partial remission and 1(4.5%) was non responsive¹⁴.

Both of these studies together with several other case reports an single centre studies have shown that tacrolimus is a safe and effective form of treatment in children with SRNS. Several patients included in the above studies were also cyclophosphamide and/or cyclosporine treatment failures and thus tacrolimus can be used as rescue therapy in these patients.

Monoclonal antibodies

The lack of efficacy and side effects of the various forms of immunosuppressive have lead to the consideration of the use of other, less typical, immunosuppressive drugs. Recently, several case reports have suggested that the monoclonal antibody *rituximab* could be an effective treatment for steroid-dependant nephrotic syndrome¹⁵. Rituximab has also been used in SRNS and a prospective multicentre, opened labelled study of 22 patients with severe steroid dependant or SRNS,

but cyclosporine sensitive disease, showed the drug to be effective in 19 of 22 patients.

The exact mechanism of action of rituximab in idiopathic NS is not known. The following effects have been found that may possible explain its efficacy viz. down regulation of α -cell receptors, shedding of CD 23 cells and apoptosis of CD20⁺ cells, general regulatory effects on the cell cycle, and increases in MHC II and adhesion molecules LFA-1 and LFA-3 (lymphocyte function – associated antigen).

The finding that rituximab is effective as rescue therapy in patients with decreased or complete cessation of therapy using other immunosuppressive agents, even when infused during a proteinuric phase (when significant amounts of CD20 antibody are likely to be lost in the urine) bears testimony to its efficacy. Its efficacy has been reported in idiopathic NS in several other case reports.

Other Agents

Other agents used in steroid dependent or SRNS include *inter alia* vincristine, azathioprine, sirolimus and mizoribine. Immunoglobulin transfusions have also been used with varying success.

CONCLUSION

Childhood SRNS poses a major challenge to the attending physician. Although specific genetic factors such as mutations in the *NPHS2* and other genes have been identified, suggesting a possible genetic basis for the SRNS in a subgroup of patients. However in the majority of patients the pathogenesis remains elusive. The large numbers of agents used in the treatment of this condition bears testimony to the lack of an optimal approach in managing this condition.

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RENAL REPLACEMENT THERAPY IN CHILDREN

Sanjeev Gulati

Department of Nephrology, Fortis Hospitals, Noida, U.P., India

Abstract : Chronic kidney disease (CKD) is characterized by an irreversible deterioration of renal function that gradually progresses to end-stage renal disease (ESRD). Once the estimated GFR declines to less than 30 mL/min per 1.73 m² and the child is in Stage 4 CKD, it is time to start preparing the child and the family for renal replacement therapy. Some form of renal replacement therapy will be needed when the weekly renal Kt/Vurea falls below 2.0, which approximates a creatinine clearance between 9 to 14 mL/min per 1.73 m². Children usually have a range of treatment options for kidney failure. The family should be provided with information related to preemptive kidney transplantation, peritoneal dialysis, and hemodialysis. The best rehabilitation of uremic children can be achieved by renal transplantation. This is the only modality that facilitates growth and development in children. In an ideal scenario, pre-emptive kidney transplantation is the gold standard as it gives superior patient and graft survival with minimal side-effects. The other advantages are economic because of the cost savings in terms of dialysis expenses. The aim of dialysis is to bridge the period of terminal renal insufficiency until transplantation becomes possible. Many children begin with dialysis to stay healthy until a suitable kidney becomes available. Sometimes, a transplant itself may stop working, and the child may need to return to dialysis. Peritoneal dialysis is much more common in infants and younger children, in large part due to vascular access issues, and hemodialysis becomes more common in older adolescents. Although transplantation is the treatment of choice for children with ESRD, maintenance dialysis can provide satisfactory life expectancy for patients with no possibility of transplantation or highly sensitized patients. Peritoneal dialysis can be performed by parents at home, overnight with a cycling machine. Hemodialysis usually takes place three times a week, but it may be required more often in smaller children. Each treatment lasts from 3 to 4 hours. An early diagnosis of CKD and prompt referral to an appropriate centre would help in increasing the rates of pre-emptive renal transplantation in children in our country. For those in whom transplant is not an immediate option dialysis offers a bridge till this therapy becomes an option.

INTRODUCTION

Chronic kidney disease (CKD) is characterized by an irreversible deterioration of renal function that gradually progresses to end-stage renal disease (ESRD). Children develop end-stage renal disease (ESRD) at an annual rate of 0.5 to 5.5 per million population. CKD has emerged as a serious public health problem. In the past decade, the incidence of the CKD in children has steadily increased, with poor and ethnic minority children disproportionately affected¹.

The definition and classification of chronic renal disease may help identify affected individuals, possibly resulting in the early institution of effective therapy. To achieve this goal, the Kidney Disease Outcomes Quality Initiative (K/DOQI) working group of the National Kidney Foundation of the United States defined CKD as "evidence of structural or functional kidney abnormalities (abnormal urinalysis, imaging studies, or histology) that persist for at least 3 months, with or without a decreased glomerular filtration rate (GFR), as defined by a GFR of less than 60 mL/min per 1.73 m²"².

ESTIMATION OF GFR

The GFR is equal to the sum of the filtration rates in all of the functioning nephrons; thus, estimation of the GFR gives a rough measure of the number of functioning nephrons. A reduction in GFR implies either progression of the underlying disease or the development of a superimposed and often reversible problem, such as decreased renal perfusion due to volume depletion. The normal GFR varies with age, gender, and body size. Children achieve adult values for mean GFR at approximately two years of age. The estimation of the GFR by the creatinine clearance in a 24-hour urine collection is easy to perform, but has limitations including frequent incomplete collections, especially in infants and young children who are not toilet-trained.

The work group on chronic kidney disease (CKD) for the Kidney Disease Outcome Quality Initiative (K/DOQI) recommends that in children, the level of GFR should be estimated from the Schwartz. In the Schwartz equation, GFR is calculated by the following:

$$\text{GFR} = k \times \text{Height (cm)} / \text{Pcreat}$$

Height represents the body height measured in centimeters, and Pcreat is the plasma creatinine. The constant k is directly proportional to the muscle component of body, and varies with age. The value for k is 0.33 in premature infants through the first year of life, 0.45 for term infants through the first year of life, 0.55 in children and adolescent

girls, and 0.7 in adolescent boys.

CLASSIFICATION

The observation that many of the complications of CKD can be prevented or delayed through early detection and treatment prompted the K/DOQI workgroup to develop a formal staging system for stratification of CKD based on the level of kidney function, independent of the primary renal diagnosis:

- **Stage 1** disease is defined by a normal GFR (≥ 90 mL/min per 1.73 m²)
- **Stage 2** disease is a GFR between 60 to 89 mL/min per 1.73 m²
- **Stage 3** disease is a GFR between 30 and 59 mL/min per 1.73 m²
- **Stage 4** disease is a GFR between 15 and 29 mL/min per 1.73 m²
- **Stage 5** disease is a GFR of less than 15 mL/min per 1.73 m² or ESRD.

TREATMENT CHOICES FOR KIDNEY FAILURE IN CHILDREN

Once the estimated GFR declines to less than 30 mL/min per 1.73 m² and the child is in Stage 4 CKD, it is time to start preparing the child and the family for renal replacement therapy. Some form of renal replacement therapy will be needed when the weekly renal Kt/Vurea falls below 2.0, which approximates a creatinine clearance between 9 to 14 mL/min per 1.73 m². However, renal replacement therapy is often initiated before children reach these levels for the following reasons:

- Limitations of total calorie intake resulting in failure to thrive
- Clinical symptoms attributable to uremia
- Delay in psychomotor development and/or educational issues from progressive CKD

Children usually have a range of treatment options for kidney failure. The family should be provided with information related to preemptive kidney transplantation, peritoneal dialysis, and hemodialysis. In most cases, the goal is to have a successful transplant that allows the child to lead the most normal life possible. The best rehabilitation of uremic children can be achieved by renal transplantation³. This is the only modality that facilitates growth and development in children⁴. The aim of dialysis is to bridge the period of terminal renal insufficiency until transplantation becomes possible⁵.

Correspondence: Sanjeev Gulati, Department of Nephrology, Fortis Hospitals, Noida, U.P., India e-mail : sgulati2002@hotmail.com

In an ideal scenario, pre-emptive kidney transplantation is the gold standard as it gives superior patient and graft survival with minimal side-effects. The other advantages are economic because of the cost savings in terms of dialysis expenses⁶. There is a greater potential for preemptive renal transplantation in children due to having parents who are a half haplotype match, are relatively young and healthy, and are willing to donate a kidney. But viable kidneys are not always readily available, and not all children can have a transplant. Many children begin with dialysis to stay healthy until a suitable kidney becomes available. Sometimes, a transplant itself may stop working, and the child may need to return to dialysis. The registry of the North American Pediatric Renal Transplant Cooperative Study (NAPRTCS) reports that of patients initiating renal replacement therapy in pediatric centers:

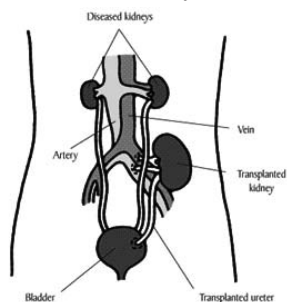
- One quarter of children underwent preemptive renal transplantation
- One half were started on peritoneal dialysis
- One quarter were started on hemodialysis

TRANSPLANTATION

Transplantation means that a healthy kidney from a donor is placed inside a child's body to take over the job of filtering wastes and extra fluid from the blood. The donor may be a stranger who has just died or a living family member or friend. Once kidneys fail because of chronic kidney disease, function cannot be restored, so transplantation is the closest thing to a cure we have. A child with a transplant will still need to take medicines every day, follow a restricted diet, and get regular checkups to make sure the new kidney is accepted and functioning in the body. Over the last decade there has been a progressive improvement in result of kidney transplantation in children. A retrospective analysis was done of 39 pediatric transplants (age at transplant <18 yrs) done at our centre over the last 10 years. The 1-year patient and graft survival was 89%. Three year patient and graft survival was 70%. Kaplan Meier revealed actuarial graft survival at 5 years of 50%. The major cause of graft loss was noncompliance with immunosuppressive agents⁷. An analysis of the next 61 transplants however revealed a distinct improvement when due attention was paid to compliance. In a long-term Swedish study of children who received cyclosporine, prednisolone, and azathioprine, 5- and 10-year allograft survival rates were 77 and 66 percent, respectively. Patient survival is better in pediatric renal transplant recipients than adults^{8,9}.

Preemptive Transplantation

Preemptive transplantation means that the child receives a donated kidney before dialysis is needed. Some studies indicate that preemptive transplantation reduces the chances of rejecting the new kidney and improves the chances that it will function for a long time. Another advantage especially in a country like ours is the cost saving because of avoidance of dialysis⁶.



Kidney transplantation

Living Donor Kidneys

About half of the kidneys transplanted into children are donated by family members—usually a parent—or a family friend. Potential

donors need to be tested for matching factors and to make sure that donating a kidney will not endanger their health. Most people can donate a kidney with little risk.

A kidney from a living donor often has advantages over a kidney from a person who has just died.

- A kidney from a parent is guaranteed to match on at least three of six proteins; mismatched proteins may cause rejection.
- Living donation allows for greater preparation and for the operation to be scheduled.
- A kidney from a living donor may be in better condition because it does not have to be transported from one site to another.

Deceased Donor Kidneys

The cadaveric transplant programme in India is in infancy. In US every person who needs an organ from a deceased donor is registered with a central network which maintains a centralized computer network linking all regional organ gathering organizations and transplant centers. How long the child will have to wait for a transplant depends on many things but is determined primarily by how good the match is between the child and the cadaveric donor. When a kidney becomes available, the hospital that has obtained the kidney reports to the network registry, where the central computer generates a list of compatible recipients. In our country the cadaveric donor programme is yet to take off and living donor transplantation remains the predominant choice.

DIALYSIS

There are 2 types of dialysis : hemodialysis and peritoneal dialysis. When preemptive transplantation is not an option, the choice between the two forms of dialysis is generally dictated by technical, social, and compliance issues, as well as family preference. Peritoneal dialysis is much more common in infants and younger children, in large part due to vascular access issues, and hemodialysis becomes more common in older adolescents. However, hemodialysis can be performed successfully in infants and very young children.

(a) Hemodialysis

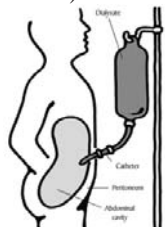
Although transplantation is the treatment of choice for children with ESRD, maintenance HD can provide satisfactory life expectancy for patients with no possibility of transplantation or highly sensitized patients. In hemodialysis, the child's blood is sent through a filter to remove harmful wastes, extra salt, and extra water. Hemodialysis helps control blood pressure and keep the proper balance of potassium, sodium, calcium, and bicarbonate. Hemodialysis uses a special filter called a dialyzer. During treatment, blood travels from the child's body through tubes into the dialyzer, which filters out wastes and extra water. Then the cleaned blood flows through another set of tubes back into the child's body. The dialyzer is connected to a machine that monitors blood flow and disposes of the wastes. Regarding *dialysis technique*, the extracorporeal circuit ('tubing') must be adapted to the size of the patient. The entire circuit volume should not exceed 10–15 per cent of the total blood volume of the child. In small children and infants, dialyser and tubing should be 'primed' with blood to prevent circulatory collapse. Heparin is used to prevent clotting in the extracorporeal circuit. The usual loading dose at initiation of HD is 2000 U/m², the maintenance dose 400 U/m²/h; monitoring is usually performed by measuring activated clotting times (ACT). In patients with high risk of bleeding or heparin-induced thrombopenia, regional citrate anticoagulation should be used.

Hemodialysis usually takes place in a centre three times a week, but it may be required more often in smaller children. Each treatment lasts from 3 to 4 hours. A recent advancement is home hemodialysis, which allows more flexibility in scheduling but requires the caregiver to take weeks of training. During treatment, the child can do homework, read, write, sleep, talk, or watch TV10. Children who are to receive

hemodialysis will need evaluation of their vasculature for placement of an arterio-venous (AV) fistula several months before the first treatment. Alternatively a cuffed double lumen catheter can be placed. The use of AV fistula, the recommended type of vascular access in adults, is limited in children due to the size of their vessels. The NAPRTCS database reports that 78.6 percent of children receiving hemodialysis use an external percutaneous catheter for vascular access, 11.8 percent have an AV fistula, and 9.2 percent have an arterio-venous graft¹¹. The 5 year patient survival rate for children receiving chronic HD was 95 per cent, being comparable with the results of living-related donor transplantation (92 per cent). Long-term results of chronic HD in infants are worse; in one single-centre report (including 20 infants with 11 receiving transplants) the overall 14 year survival was 60 per cent and significantly better in children weighing greater than 5 kg (73 per cent) than those weighing less (20 per cent) at initiation of HD¹².

(b) Peritoneal Dialysis

Peritoneal dialysis can be performed by parents at home, overnight with a cycling machine. This potentially allows the least disruption of home life, school, and work attendance, when compared to ambulatory peritoneal dialysis, which often requires a dialysis exchange procedure to be conducted during school hours and hemodialysis which requires three weekly treatments of at least 3 to 4 hours (not counting travel time). In developing countries like India, pediatric hemodialysis facilities are scarce and there is no maintenance hemodialysis program in most of the nephrology centers. Thus CPD remains the only available option as a bridge between ESRD and transplant in remote areas¹³. In addition, access to a nearby hemodialysis center may not be readily available to patients and their families or the personnel may not be trained to care for children, especially pre-pubertal children and infants. Peritoneal dialysis uses the lining of the child's abdomen, called the peritoneal membrane, to filter blood. CPD is most often based on patient and family preference, center philosophy and availability of desired expertise. Children who are to initiate peritoneal dialysis undergo abdominal surgery for placement of a peritoneal dialysis catheter. Ideally, there should be a period of 10 days to 3 weeks to provide for healing of the abdominal wound to occur prior to the initiation of dialysis¹⁴. Peritoneal dialysis is more common in infants and young children than hemodialysis due to the above mentioned vascular access problem. The peritoneal dialysis solution contains a mixture of minerals and dextrose dissolved in water and is inserted into the abdomen through a soft tube. The dextrose, draws nitrogenous wastes, electrolytes and extra water from the tiny blood vessels in the peritoneal membrane into the dialysis solution. After some time, the used solution—now loaded with the wastes and extra fluid that the kidneys would have filtered out—is drained from your child's abdomen through the tube. The period that dialysis solution is in the abdomen is called the dwell time. The abdomen is filled again with fresh dialysis solution, and the cycle repeats. The process of emptying and refilling the abdomen is called an exchange and takes about 30 to 40 minutes. Following catheter placement, PD is started with a low exchange volume (300 ml/m² or 10 ml/kg). Small amounts of heparin (200 IE/l) can be added to prevent catheter obstruction by fibrin clots.



Peritoneal dialysis

The exchange volume is slowly increased over several days and the exit site is repeatedly checked for leakage of dialysis fluid. The exchange volumes are increased to 1000–1500 ml/m², the final volume, during the second week. Some centres have gained experience with intra-abdominal pressure measurements, which may be helpful in adjusting the dialysis dose to the individual need of the patient¹⁵. Peritoneal dialysis can be done with or without a cycling machine.

- **Continuous ambulatory peritoneal dialysis (CAPD).** CAPD requires no machine and can be done in any clean, well-lit place. The dialysis solution passes from a plastic bag through the catheter and into the abdomen, where it stays for several hours with the catheter sealed. After the dwell time, the child drains the dialysis solution into a drain bag for disposal. Then the same catheter is used to refill the abdomen with fresh solution so the cleaning process can begin again. With CAPD, the dialysis solution stays in the abdomen for 4 to 6 hours or more. Most people change the dialysis solution at least four times a day and sleep with solution in their abdomen at night. With CAPD, it is not necessary to perform an exchange during the night.
- **Continuous cycling peritoneal dialysis (CCPD).** CCPD uses a machine called a cyclor to fill and empty the child's abdomen many times at night during sleep. In the morning, the child begins one exchange with a dwell time that lasts the entire day. An additional exchange without the cyclor may be added in the middle of the afternoon to increase the amount of waste removed and to reduce the amount of fluid left behind.

Both types of peritoneal dialysis can be performed in the home without help from a nurse or doctor¹⁵. If your child is very young, you will need to help with the exchanges or set up the cyclor. Older children can do it themselves. The child and the family needs detailed instructions and extensive training so that they feel confident when performing these exchanges.

The most common problem with peritoneal dialysis is peritonitis, a serious abdominal infection that can occur if the opening where the catheter enters the body becomes infected or if contamination occurs as the catheter is connected or disconnected from the bags. Peritonitis requires antibiotic treatment.

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OBSTRUCTIVE UROPATHY IN NEWBORNS

S. K Chowdhary

Department of Pediatric Surgery, Indraprastha Apollo Hospitals, Sarita Vihar, New Delhi – 110076, India

Abstract : One percent babies are born with varying grades of obstructive uropathy. In less than half of them surgical intervention may be necessary at the right time to protect the kidney from deterioration. Bilateral obstruction is commonly due to infravesical obstruction secondary to lesions as bladder outlet or urethra i.e., posterior urethral valves in boys and ureteroceles in girls. Majority of them are symptomatic and may require intervention in the neonatal age. The corner stone of diagnosis is a well performed micturating cystourethrogram. Endoscopic procedure under direct vision and video recording can take care of the vast majority of the lower urinary tract lesions in newborns. The commonest aetiology of upper urinary tract obstruction are pelviureteric junction obstruction and vesicoureteric junction obstruction. A pelvic diameter of more than 15 mm and ureteric diameter more than 10 mm are significant dilatation and requires serious attention. The low GFR of a newborn kidney does not allow the functional imaging to be very reliable. Accurate and serial measurement of the pelvic dilatation along with drainage studies with isotope renogram can allow an reliable assessment by one month. In a small percentage, intervention may be necessary as early as the first month.

Key words : Obstructive uropathy, posterior urethral valve (PUV), ureteroceles, Pelviureteric junction obstruction (PUJ obstruction).

INTRODUCTION

Obstructive uropathy is defined as obstruction to the urinary tract in such a way that the renal function of individual kidney is at risk from deteriorating. One percent babies are born in our country with various grades of urinary dilatation and approximately half of these may need intervention¹. It is important to segregate those babies who are at risk from deterioration and prevent renal dysfunction. This review paper is an attempt to introduce the physicians to common causes of obstructive uropathy in newborns, early detection and currently available technology to treat them and prevent renal damage.

The urinary tract develops in the third month of intrauterine life and the urine starts flowing at about the same time. Any obstructive disease in the urinary tract at this stage leads to changes in the urinary bladder, ureter, and kidneys depending on the level of obstruction. Progressive dilatation is a definitive evidence of significant evolving obstruction. The decision regarding the need for intervention in a baby with upper tract urinary obstruction is not an easy one as the obstruction is never absolute, however if left alone, it has the potential to lead to renal deterioration in a significant majority.

ANTENATAL DIAGNOSIS AND INTERVENTION

In the last decade there has been ever increasing availability of antenatal fetal ultrasound being done in our country. It is important to appreciate that in fetal life, towards the third trimester the fetal urine production is as high as 30mL/hr which is 90 % of the amniotic volume. There are two implications of this knowledge, that babies with lower urinary tract obstruction have oligohydramnios and mild dilatation of the upper urinary tract (Pelvic anteroposterior diameter 5 – 10 mm) does not require any investigation other than serial US follow up. In general, earlier the diagnosis of urinary tract dilatation (<28 weeks), prognosis is poorer.

There is a popular grading system for antenatal dilatation of kidneys and ureter which is the objective system accepted by the society of fetal urology².

The dilatation of the urinary tract reflects the level of possible obstruction. In case of infravesical obstruction, one is able to see a persistently dilated bladder with bilateral hydronephrosis. When the obstruction is at the level of vesicoureteric junction, there is hydronephro-nephrosis. However, if the obstruction is at the level of pelviureteric junction one will see only hydronephrosis. Whereas, the milder grades of dilatation in third trimester

Table 1. : Growing of Antinature dalation of Pelvicalycecal system

Renal image	Renal Complex Pelvis, calyces	Renal Parenchymal thickness
0	Intact	normal
1	Slight splitting	normal
2	Splitting, Pelvis within	normal
3	Wide splitting, pelvis extra renal	normal
4	Calyceal dilatation Pelvic and calyceal dilatation	thin

Grade of ureteric dilatation (UD) (I)<7 mm; (II) 7 – 10 mm ; (III)> 10 mm

may reflect minimal obstruction or fetal diuresis leading to transient dilatation, severe grades are associated with obstructive uropathy.

In a case of infravesical obstruction, the situation is far more serious than unilateral obstruction. This is because of the potential for damage to both kidneys ! Therefore, the effort to evolve prognostic criterion to predict outcome for infravesical obstruction and segregate those who need are likely to benefit from antenatal intervention has been going on. The *poor prognostic criteria* worse outcome include³.

- Dilatation before 24 weeks gestation.
- Moderate/severe hydronephrosis (Pelvis AP dia > 10 mm).
- Thick walled bladder with oligohydramnios.
- Echobright renal cortex with microcystic changes.
- Fetal urine NA > 100 meq/L, Cl >90 meq/L and osmolality > 210 mosm/L.

Whereas, for obvious reasons in unilateral obstructive uropathy there is no role for fetal intervention, those babies who have evidence of bilateral dilatation need a much more serious evaluation in a dedicated centre. If the evaluation suggests a poor outcome the parents may exercise the option of terminating pregnancy. Fetal intervention is available in select centres world wide in the form of vesico amniotic shunt and even direct cystoscopic ablation of posterior urethral valves^{4,5}. However, majority of the centres have not been able to demonstrate a huge difference in the outcome in favour of fetal intervention. However, that should not be used as evidence to discredit the technology of fetal intervention as this has been offered to selectively only those who were going to have the worst outcome anyway ! while, the technology of fetal intervention continues to undergo continuous refinement, at present there is limited role of fetal intervention, only in those babies with bilateral obstructive uropathy and poor prognosis.

Correspondence: S. K Chowdhary, Senior Consultant (Pediatric Urology & Pediatric Surgery), Department of Pediatric Surgery, Indraprastha Apollo Hospitals, Sarita Vihar, New Delhi – 110076, India e-mail : sujitchowdhary@hotmail.com

POST NATAL INVESTIGATIONS

The babies who are born with obstructive uropathy generally have had serial ultrasound scans and in properly performed scans the diagnosis is made before birth. However, in our country largely only screening ultrasound is done outside dedicated fetal centre. The vast majority are asymptomatic at birth unless they have associated pulmonary hypoplasia and bilateral obstructive uropathy with infravesical / urethral obstruction. The symptoms in these babies may be related to the presence of obstruction to urine flow or secondary complications like urinary infection or renal failure. The obstruction in urine flow depending on the degree and level of obstruction leading to dribbling, overflow incontinence, palpable bladder, renal lump and rarely palpable ureters. Urinary tract infection can be severe and is commoner in the first three months. The role of prophylactic antibiotics continue to be debated, however a recent large series over a ten year period has supported its use⁶.

In a asymptomatic baby, investigations should be started 48 – 72 hours after birth in order to allow the fetal urine production to recover from oliguric phase and serum levels to reflect the true levels in the baby. The investigations should start with an ultrasound measuring renal pelvis AP diameter and micturating cystourethrogram. If renal pelvis is less than 15 mm, no further investigation may be necessary other than US at 3 months. However, if renal pelvis measurement is greater than 15 mm a micturating cystourethrogram has to be done. If it shows vesicoureteric reflux, prophylactic antibiotic has to be used. However, if the MCU demonstrates a primary pathology like posterior or anterior urethral valves and vesicoureteric reflux is secondary, the primary pathology needs treatment. A DMSA scan should be done in either case of primary or secondary vesicoureteric reflux. If MCU does not show reflux, an isotope scan MAG3/DTPA has to be done between 4-6 weeks.

Obstruction to the urinary tract in baby can be conclusively proven on palpable lump (bladder, kidney), progressive dilatation of urinary tract, falling differential function on MAG3/DTPA over a period of observation. The other features are an initial differential function less than 35 % and dilated pelvis greater than 30 mm or recurrent urinary tract infection with dilated and slow draining systems. The correlation of a pelvis with greater than 50 mm pelvis alone versus need for surgical intervention based on fall of differential function was 100 % in the largest published series⁷. Therefore, in a case of PUJ obstruction with pelvic dilatation larger than 30 – 50 mm, there may be need for intervention earlier than three months.

MANAGEMENT OF NEONATAL OBSTRUCTIVE UROPATHY

Infravesical Obstruction

The most serious symptoms in neonatal period are produced by significant infravesical obstruction. This leads to dribbling micturition, palpable abdominal lump, septicaemia, dyselectrolytaemia, features of acute renal failure and palpable abdominal lump.

The common lesions in a newborns producing these symptoms in newborns include posterior urethral valve, ureterocoele. Rarely, anterior urethral valve, congenital urethral stenosis, syringocoele, urethral diverticulum, urethral atresia can produce similar symptoms. The initial management of all these conditions is insertion of a urethral catheter, assessment of biochemical parameters and intravenous antibiotics. If the metabolic and infective parameters reverse with these simple measures, the current management includes cystoscopic ablation of valves, deroofting ureterocoele or syringocoele depending on the diagnosis. The diagnosis is based on a good voiding cystourethrogram done under intravenous antibiotic cover.

The technical feasibility of doing a satisfactory clearance of obstruction endoscopically is dependent on the size of urethra. Usually, a 3 kg baby

has a urethral caliber which allows a neonatal resectoscope to be safely negotiated and obstruction relieved satisfactorily. However, if the baby is smaller than term, that can be difficult and in that case a cystoscope with straight working channel with cold knife could be used. The use of any other instruments as in the past and continuing even now in many centres for the want of appropriate instrumentation has lead to a lot of morbidity seen in older children. In current day and age one can video record all the neonatal endoscopic procedures and that is the surest way of ensuring that appropriate treatment for the pathology has been done. It is reproducible and can be used to compare with future findings. All babies must undergo a check cystoscopy at three months to ensure that adequate clearance has been done.

The resolution of the pathology is suggested by the improvement of symptoms, but the follow up must include radiological evaluation and biochemical tests. For example, in a baby with posterior urethral valve a pre and post ultrasound evaluation can tell the reduction in bladder wall thickness, post voiding residue, and dilatation of upper tract. Similarly, endoscopic deroofting of ureterocoele, diverticulum etc requires careful follow up and delayed reconstruction in 50 % of the babies who undergo endoscopic management in the neonatal period⁸.

In a small but significant proportion it is not possible to relieve obstruction by endoscopic technique or because of the associated bladder neck hypertrophy. Under those circumstances it may be necessary to temporarily divert the urine at the level of the bladder called vesicostomy. Although, initial studies raised concerns about harmful effects on the function of bladder more recent studies have failed to show any ill effects.

In fact, there should be no hesitation in considering vesicostomy in the interest of long term safety of the baby⁹.

However, if a baby continues to have a raised serum creatinine level or persistent urosepsis there may be a case for high diversion. In some units, one would consider a percutaneous nephrostomy before going on to high ureterostomy.

Vesicoureteric junction obstruction

This is a rather uncommon abnormality in a newborn and characterised by unilateral or bilateral hydroureteronephrosis. In a case of hydroureteronephrosis, if there is no vesicoureteric reflux seen than the probable diagnosis intervention include symptoms, diameter of ureter (>10 mm) differential function <35% or fallen by 10% during the period of observation.

In a newborn, ureteric reimplantation is associated with a very high failure rate in case if obstructed megaureters. Therefore, one can try endoscopy, dilatation and insertion of DJ stent; the same procedure can be done with much higher success rate by open technique. However whereas this certainly can take the baby and the kidney through, the risk of insertion with foreign body remains. The other alternative is lateral or end ureterostomy.

Pelviureteric junction obstruction

This is one of the commonest obstructive uropathy in newborns. However a very small proportion of those who have antenatal diagnosis of pelviureteric junction obstruction actually will need intervention. The pelviureteric junction obstruction can be due to an actual atresia/stenosis at PUJ, high insertion of ureter, anteriorly crossing vessels etc.

Whereas, the vast majority do not need intervention, there are a few who may need intervention if the pelvic AP diameter has progressed to higher than 40-50 mm with an obstructed curve and differential function of less than 35%.

In these cases in our hospital the protocol is to do a retrograde pyelogram, DJ stenting and Anderson Hynespyeloplasty. Unless there is poorly developed parenchyma, the post operative results are worth all the efforts in doing the procedure in newborn period.

The Apollo experience (2004-2007) with neonatal obstructive uropathy

is outlined in the accompanying Table 2.

Table 2: Apollo experience with neonatal obstructive uropathy 2004 – 2007 (n = 49)

Diagnosis		
<i>Bladder outlet obstruction</i>		
Posterior urethral valve	17	
Ureteroceles		07
Anterior urethral valve	01	
Congenital urethral stenosis		01
Dysfunctional voiding	03	
<i>Vesicoureteric junction obstruction</i>		
<i>Pelviureteric junction obstruction</i>	15	
Follow up results 15 PUJ		01-36 months
		Mean = 12
Death due to renal failure		
Living with renal failure	01	
Fall in differential renal function	03	
Improvement in Diff renal function	05	
No significant change	05	
Improvement in drainage		10
Growth of cortical matter		10
Success defined as stable differential renal function or improvement, reduction in pelvic dilatation, improvement in drainage and increase in cortical thickness 10/15.		

Pelviureteric junction obstruction can be severe enough in a small proportion of babies to require intervention early. The outcome of surgery in newborn is dependant on the quality of renal parenchyma, length of the obstructing segment, quality of surgery and feasibility of DJ stenting.

CONCLUSION

Neonatal obstructive uropathy is one of the commonest cause of reversible urosepsis and renal failure in newborns. The symptoms are more

pronounced if there is infravesical obstruction or obstruction in a single functioning system. The corner stone of diagnosis of infravesical obstruction is a micturating cystourethrogram.

The vast majority with obstructive pathology below the bladder can be managed by a neonatal resectoscope (9 F) or a cystoscope and cold knife (7.5 F). The babies who undergo such treatment must have a check at 3 months for improvement in clinical symptoms and radiological sign with reversal of biochemical parameters. A small proportion will need temporary urinary diversion.

Vesicoureteric junction is not common. However, in case it warrants intervention, it is usually temporary and definitive repair is done at one year.

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IMSACON 2008, Dubai



ABSTRACTS of IMSACON 2008, Dubai

ORTHOPAEDICS

Surgery for TB Spine. Aziz, A., Pakistan

Tuberculosis is the world's leading cause of death, from a single infectious disease with two million deaths in 1990. It is most endemic, chronic infection, which paralyzes the society when it affects the spine due to its resultant neurological deficit. Despite the adequate control of pulmonary tuberculosis, the incidence of musculoskeletal tuberculosis is increasing. Tuberculous spondylitis being endemic in underdeveloped countries including Pakistan has considerable socioeconomic and orthopaedic concern. In spite of all the advances regarding diagnosis, treatment and total control of many diseases, this slow but grave disease still affects considerable number of cases and makes them disabled and even paralyzed. Being a tertiary care center, Ghurki Trust Hospital entertains more than 100 patients of T.B Spine per year who require operative treatment. In the last 30 months we have performed more than 300 Anterior Decompressions of spine and more than 80% of them were for T.B Spine. Patient selection, indications of surgery, surgical procedures and follow-up of patients with T.B Spine will be discussed in detail.

Controversies and Newer Advances in Fractures of the Scaphoid.

Kotwal, P. P. & Gupta, V., India

The Scaphoid is the most commonly fractured bone, the second commonest fracture in wrist injuries after fracture distal radius. The Scaphoid bone is one of the eight carpals bones in the wrist and occupies an important position in the proximal row. It plays a key role in the kinematics of the wrist joint, yet its precarious blood supply makes it vulnerable for the fractures to go into nonunion. Although a plethora of methods are available for the treatment of fracture of the Scaphoid varying from cast application to internal fixation, a lot of controversy exists about the choice of method. If not treated properly, a fracture of the Scaphoid can go into non-union, malunion and may subsequently result into carpal instability and finally degenerative arthrosis. There are many newer advances in the implants as well as techniques in the treatment of fractures of the Scaphoid. We have treated a total number of 50 cases of fractures of the Scaphoid, at the All India Institute of Medical Sciences, New Delhi, India during the period 1997 to 2008. All cases were treated by internal fixation using K-wires/ Herbert screw/ Herbert Whipple screws; with or without bone grafting. The following is the break up of cases where internal fixation has been done: Different method of bone grafting such as non-vascularised, vascularised, muscle pedicle bone grafting etc. were employed in addition to internal fixation. The following types of bone grafting methods have been employed:- Iliac crest bone graft - 15; Distal radius bone graft - 8; Pronator Quadratus based muscle pedicle graft - 12; Vascularised bone graft - 15; Total 50 Cases; Good results were obtained in about 80% of cases. This paper discusses the controversies and newer techniques in the treatment of fracture Scaphoid, besides the results in 50 cases.

Compressive Myelopathies. Hammack, J. E., USA

The mechanisms of compressive myelopathy span the spectrum of human disease, the most common of which are traumatic and degenerative. Inflammatory, neoplastic, and even metabolic disorders must be considered in the differential diagnosis. The patient's history and clinical examination are the most important diagnostic tools. The history should include a detailed past medical history including a history of malignancy, infection (HIV and otherwise), autoimmune disorders, diabetes mellitus, drug abuse, spinal surgery or injection, and spine trauma. The examination should include visualization and palpation of the entire spine, looking for deformities and point tenderness. A complete motor and sensory examination (including a search for a sensory level) is essential as is an evaluation of sphincter tone. MRI of the spine or myelography is an important diagnostic adjunct. MRI is the best tool for visualization of the spinal cord, roots, discs, and paraspinal soft tissues. I shall focus my review on the diagnosis and treatment of non-traumatic compressive myelopathies including degenerative spinal stenosis and epidural cord compression by metastatic tumor.

Mechanism(s) for Premature Aging in Inflammatory Disease.

Clowes, J. A., USA

Subjects with Rheumatoid Arthritis (RA) have decreased longevity, at least in part, due to increased cardiovascular disease. Our understanding of the mechanisms behind the premature senescence observed in RA is currently in its infancy. There is however an increasing body of data which examines mechanisms involved in aging which may explain our observations in RA. We will explore the evidence supporting premature senescence in inflammatory diseases. We will examine the current theories and mechanisms of aging and translate these findings to explain the premature senescence observed in inflammatory arthritis. We will present some novel theories and data relating to stem cells and their role in premature aging. Finally, we will summarize existing research and discuss potential interventions to prevent and treat patients with chronic inflammatory diseases.

Our Experience with SIGN Nail at Ghurki Trust Teaching Hospital/ Lahore Medical and Dental College, Lahore, Pakistan – The Results and Difficulties. Akram, R. & Aziz, A., Pakistan

The SIGN Program started at Ghurki Trust Teaching Hospital in 2004 November, since then 250 poor patients got benefit from this program. Beautifully designed Sign nail proved a nail with variety of options for the use as well as an implant with user friendly technique, which does not require the image intensifier or even the radiograph pre-operatively for the locking bolts placement. The simple jig design popularized this system world wide. The most important aspect of any surgery in the Orthopaedics is the financial burden of implant prize on the patient, even in cases where the Orthopaedic surgeons are working on no profit bases or volunteer bases the implants are needed for the surgery. In the SIGN SYSTEM credit goes to the SGN Organization specially Dr Lewis G Zirkle, Jr., M.D The Founder and the President of this Surgical Implants Generation

Network (SIGN), for providing the Implants and the instrument free of cost in the third world countries for the poor patients and to create the Equality in fracture management world wide. I will discuss the results of surgery, variety in the use of nail (Indications), and the difficulties faced at Ghurki Trust Teaching Hospital, Lahore, Pakistan.

MEDICINE

Role of Anti-CCP Antibodies. *Luthra, H. S., USA*

Citrulline is a non-natural amino-acid which occurs from post-translational modification of arginine by peptidylarginine deiminase enzymes (PAD 1, 2, 3, and 4). Citrullination of proteins is found in many inflammatory conditions. PAD 2 and 4 are found in high concentrations in the rheumatoid synovial fluid and thus citrullinated proteins are increased in this disease. Interestingly, for reasons which are unclear, patients with rheumatoid arthritis (RA) make high titers of anti-cyclic citrullinated protein (Anti-CCP) antibodies. This observation has led to the use of this test for the diagnosis of RA. The anti-CCP antibodies are measured using the ELISA assays in which citrullinated peptides derived from human filaggrin are used as the antigen. More recently the second generation test has been developed in which true conformational epitopes selected from libraries of citrullinated peptides were synthesized and have become the standard of the commercially available tests. Studies have shown that anti-CCP antibodies are both sensitive and specific for the diagnosis of RA and can be of prognostic significance in predicting more severe and erosive disease. Compared to IgM rheumatoid factor, it has become a more valuable test. Although very specific (>90%), this test can be positive in low titers in other connective tissue diseases e.g. SLE, Sjogren's, Polymyositis and Dermatomyositis. Scleroderma and infectious states like pulmonary tuberculosis, hepatitis C etc. This presentation will focus on the role of this test in management of patients with RA.

Copper Deficiency Myelopathy. *Kumar N., USA*

Acquired copper deficiency can present as a myelopathy or myeloneuropathy in adults. The neurologic manifestations may be present without the more commonly recognized hematologic abnormalities. The clinical picture bears striking similarities to the syndrome of subacute combined degeneration associated with vitamin B12 deficiency. Typical findings include a spastic gait and prominent sensory ataxia. Copper and vitamin B12 deficiency may coexist. Somatosensory evoked potential studies may show delay in central conduction. Clinical or electrodiagnostic evidence of a peripheral neuropathy is commonly present. Spinal cord magnetic resonance imaging in patients with copper deficiency myelopathy may show increased signal on T2-weighted images, most commonly in the paramedian cervical cord. Early recognition and prompt copper supplementation may prevent neurological deterioration. The commonly identified causes of acquired copper deficiency include a prior history of gastric surgery, excessive zinc ingestion, parenteral alimentation or enteral feeding without adequate supplementation, and malabsorption. Often the cause of the copper deficiency is unclear. Hyperzincemia may be present even in the absence of exogenous zinc ingestion. The clinical, biochemical, electrophysiological, and imaging features of copper deficiency myelopathy will be presented using a single-institution series of 25 patients. The differential diagnosis of copper deficiency myelopathy will be discussed and a practical treatment algorithm will be provided.

High Performance Team Development in Critical Care. *Patel, B., USA*

In hospital cardiac arrest outcomes are poor and have remained unchanged despite standard care algorithms such as Advanced Cardiac Life Support. Contributing to this outcome is lack of resuscitation team training. High proficiency response teams may be associated with improved outcomes. The development and training of these teams at Mayo Clinic Hospital will be reviewed.

Potential Mechanisms of Global Epidemics in Type 2 Diabetes Mellitus. *Nair, K. S., USA*

Type 2 diabetes is rapidly emerging as the major global chronic disease of 21st century with its incidence rate increasing most rapidly in South Asia and Middle East. The diabetic epidemic is related to the global demographic transformation with a decline in fertility rate and increased life expectancy. Type 2 diabetes increases with age and life style changes. The talk will focus on studies performed to determine the impact of age on metabolic process involving muscle mitochondria and how the muscle changes contributes to insulin resistance, type 2 diabetes and related metabolic problems resulting in increased cardiovascular death. Muscle changes related to age cause reduction in activity levels and contribute to increase in body fat, especially of abdominal fat. Insulin sensitivity is negatively correlated to abdominal fat and may explain insulin resistance related to aging. The impact of regular exercise on age-related changes in muscle mitochondria, body composition, insulin resistance, and other longevity markers will be discussed.

Acupuncture: Applicability in Common Medical Conditions. *Vincent, A., USA*

Practiced in China and other Asian countries for thousands of years, acupuncture is one of the key components of traditional Chinese medicine, a whole system of medicine. It is practiced worldwide both as a primary and adjunctive treatment for a wide range of conditions. Traditional Chinese medicine views health as a balance of two opposing and inseparable forces in the body called yin and yang and disease as an imbalance of these forces that blocks the flow of Qi or vital energy in the body. Qi flows along pathways in the body called meridians on which acupuncture points are located and Qi can be unblocked by needling these points. Acupuncture involves the stimulation of anatomical points on the body with thin, solid, metallic needles that are manipulated by hands, heat, herbs or electricity. The objectives of this talk are

- Highlight the philosophy of acupuncture
- Describe explanatory models for the effects of acupuncture
- Describe the array of conditions for which acupuncture has been studied and the models and outcome measures used
- Describe challenges in designing acupuncture studies
- Outline practical uses of acupuncture for the practicing physician

Targeted Screening of First Degree Relatives of Patients with Non-Diabetic Chronic Kidney Disease. *Aggarwal, S. K., Soumita, B., & Gupta, S., India*

Aim: First-degree relatives (FDR) of patients of chronic kidney disease (CKD) are reported to have high prevalence of CKD and its risk factors. There is no data from India on this aspect. Present study was conducted to screen FDR of patients with non-diabetic CKD for the prevalence of CKD and its risk factors. **Methods:** Adult FDR of patients with non-diabetic CKD followed at our hospital were assessed. Patients with diabetes mellitus, obstructive Uropathy and CKD with known Mendelian inheritance were excluded. Age, sex, lifestyle habits, history of diabetes, hypertension and renal disease were elicited from each subject. Height, weight and blood pressure (BP) were recorded. Fasting blood sugar, serum creatinine, serum cholesterol, serum uric acid and a urinalysis were evaluated. A subject was labeled diabetic or having impaired fasting glucose by the ADA criteria. Hypertension was defined if subjects were using antihypertensive drugs or a BP/140/90 mm of Hg. eGFR was calculated using the 4 variable MDRD formula. **Results:** Among the 123 patients whose families were screened, 6(4.9%) had one more family member who was suffering or had died of CKD. Out of 510 FDR screened, 266 (53%) were males (mean age-39.14; A14.80) and 244 (48%) females (mean age-39.93; A14.71). 5 (0.98%) had a history of some renal disease. 24 (4.71%) were obese (BMI > 30) and 88 (17.25%) were overweight (BMI 25-29.9) with no gender specific difference. 59 (11.57%) gave a history of smoking. 140 (27.45%) had hypertension. 42 (8.24%) had history of hypertension of which 36(85.71%) had uncontrolled BP. 20 (3.92%) had diabetes of which 9 (1.76%) were known diabetics. Screening identified 98 (19.22%) new cases of hypertension, 11 new cases of diabetes (2.16%), 115 subjects with previously undetected IFG (22.55%) and 95(18.63%) with serum cholesterol>200mg/dl. There was no significant difference in the prevalence of hypertension, diabetes and hypercholesterolemia between males and females. Serum uric acid more than 7mg/dl was found in 53 (10.39%), significantly more in males than females (44,16.54% vs 9, 3.69%, p<0.0001) and in hypertensive FDR (34/140, 24.29%, p<0.0001). 7 FDR (1.37%) had serum creatinine more than 1.5 mg/dl (5 males, 2 females, p=ns). 24 (4.71%) had proteinuria (dipstick ?+) and 27 (5.29%) had hematuria and/or pyuria with no significant difference between males and females. Stage-1, 2, 3, 4+5 CKD was found in 25 (4.90%), 198 (38.82%), 180 (35.29%), 17 (3.33%) and 1 (0.20%) cases respectively. Impaired eGFR (<90ml/min/1.73 m²) was significantly more in females than males (48.36% vs 30.08%, p<0.0001). On multivariate analysis, older age, female sex, increased serum creatinine, proteinuria and BMI>30 were significantly associated with impaired eGFR and male sex, diastolic BP>90mmHg and impaired eGFR had an association with increased serum uric acid level. **Conclusion:** It is concluded that in India, CKD and its risk factors show a familial clustering. Targeted screening of individuals with family history of CKD identifies those with previously unrecognized/ poorly controlled risk factors of CKD. This can be an acceptable strategy for prevention of CKD in India.

The Diagnostic Sensitivity of F-Wave Latency in Diabetic Polyneuropathy.

Taksande, B., Jain, A. P., & Jajoo, U., India

Background and Aim: Non insulin dependent diabetes mellitus is frequently asymptomatic and the reported prevalence of diabetic neuropathy varies from less than 5 to 60%. Diabetic patients have a 12 times higher risk of amputations when compared with non-diabetic subjects, due to diabetic neuropathy. Diabetic polyneuropathy is characterized by a combined axonal loss and demyelinating sensorimotor peripheral neuropathy. Nerve conduction studies, primarily nerve conduction velocities are considered one of the most sensitive indices of the severity of neuropathy. To investigate this condition, nerve conduction studies with the determination of latency and velocity, are commonly used as they are considered to be the most sensitive, reliable, noninvasive, and objective means. **Material and Methods:** This was a prospective study of 30 subjects of Type 2 Diabetes mellitus admitted in medicine ward during a period of 6 months. Individuals with a diagnosis of endocrine disorders or any other disease capable of causing polyneuropathy were excluded. All patients underwent a detailed neurological examination of both the extremities and were included in the study, who had sensory symptom in the form of paresthesia or dysesthesia symptoms or reduced vibratory sense below knee or reduced/absent ankle jerk. Nerve Conduction Velocity (NCV) measurements were made using the standard RMS EMG EP machine. Nerve conduction studies of the bilateral median, ulnar, tibial and peroneal nerves are performed with surface recording, using the standardized technique. DML (Distal Motor Latency), CMAP (compound muscle action potential) Amplitude and FWL (F-wave Latency) were recorded. The minimum F wave latency defined as shortest latency to the onset of first deflection from the baseline. In total 240 motor nerves of 30 diabetic patient (60 limbs) were studied. Statistical analysis was performed using SPSS version 10. **Results:** The 30 diagnosed patients of type 2 diabetes comprised of 24 males and 6 females with their age ranging from 40 years to 60 years. Tingling was the most common symptom (38%), followed by tingling and numbness (22), tingling and burning feet (16%). Burning feet alone (10%), weakness of the limbs (6%) and combination of tingling, numbness and burning feet were the other findings. The minimum F wave latency had a larger Z score than the MCV of the median, ulnar, peroneal or tibial nerves and was larger than z score for the amplitude of the CMAP in all the four motor nerve. There was a significant correlation between the minimum F wave latency and NCV in all the four motor nerve. The bivariate correlation coefficients were $\bar{a} = -0.41$ (p<0.05), $\bar{a} = -0.757$ (p<0.05), $\bar{a} = -0.759$ (p<0.05) and $\bar{a} = -0.74$ (p<0.05), for the median, ulnar, peroneal and tibial nerve, respectively. **Conclusion:** Abnormal NCV is a common finding in NDD subjects. Different patterns of Fwave abnormality have been demonstrated in patients with various peripheral nerve disorders, as well as in diabetic neuropathy. F-waves may show clinically significant and measurable changes even before conventional nerve conduction studies are informative.

Prevalence of Hypertension in School Going Children in Rural Area of Wardha District,

Maharashtra. Taksande, A., Chaturvedi, P., Jain, M., & Vilhekar, K., India

Objectives: To study the blood pressure level in the children at rural area and its relationship with the anthropometric indices. Also to know the prevalence of hypertension in the school children in rural areas of Wardha Districts of Central India. **Material and Methods:** This was a prospective, cross-sectional study carried out from November 2006 to December 2007 on school children between the ages of 6-17 years, drawn from 8 different schools in rural areas of Wardha Districts.

The height, weight, systolic and diastolic blood pressure were recorded for both sexes followed by complete clinical examination with special stress on cardiovascular system. Hypertension is defined as the arterial BP above the 95th percentile with reference to age and sex. Coefficient correlation tests were employed to see the relation between blood pressure (BP) and anthropometric variable. **Results:** Of 2643 school children, 1416 were girls and 1227 boys with a male to female ratio of 1:1.16. In boys, SBP & DBP increases with age groups except at a) 17 year of age, slight declination in SBP i.e. -0.09 and b) -1.29 declinations in DBP at 16 year. In girls, SBP & DBP also increases with age groups except at a) 11 year of age, slight declination in SBP i.e. -0.09 and b) -0.24 declinations in DBP at 11 year age. Correlation coefficient analysis showed positive and significant correlation of age, height, weight, and body mass index with each SBP and DBP. The prevalence of hypertension was 6.73% (i.e. 3.90% for systolic HT and 2.83% for diastolic HT). **Conclusion:** We recommend that the need for regular check up of BP in the children to find out the hidden cases of hypertension in children.

Role of Serum Bile Acids in Diagnosis of Intrahepatic Cholestasis of Pregnancy and Effect of Ursodeoxycholic Acid Therapy on Bile Acids and Perinatal Outcome. Agarwal, N., Mahey, R., Kriplani, A., Saraya, A., Sachdeva, V., Garg, P., & Agarwal, S. K., India

Introduction: Diagnosis of intrahepatic cholestasis of pregnancy (ICP) is difficult by liver function tests (LFT). Bile acids are specific markers for ICP but not studied in India. **Objectives:** We conducted a prospective clinical trial to assess the role of serum bile acids in diagnosis of ICP, effect of ursodeoxycholic acid (UDCA) therapy on bile acid levels and perinatal outcome in relation to bile acid levels. **Materials and Methods:** Serum bile acids were assessed in 100 cases, 50 of ICP (group I) and 50 asymptomatic pregnant women (group II) between 16-36 weeks POG. UDCA was administered 300mg thrice daily to group I till delivery. Bile acids were repeated 4 weeks later. LFT was done at 2 week interval. **Results:** The mean serum bile acid levels in study group were 76.47 ± 39.74 μ mol/L. and control group were 29.18 ± 5.67 μ mol/L. (p value < 0.001). The severity of itching was directly correlated with bile acid levels. After 4 weeks therapy the mean serum bile acids were 44.6 ± 15.4 μ mol/L (41.6% reduction, p value < 0.001). There was significant reduction in itching score within two weeks of therapy. The incidence of perinatal complications i.e. preterm labour, MSL, fetal distress and caesarean section rates were high in study group and were directly correlated to bile acid levels. Serum bilirubin was raised only in 12% patients. **Conclusions:** Rise in serum bile acids helps in diagnosis of ICP and to differentiate it from other conditions. Their levels also help in prediction of severity of disease and perinatal outcome.

GYNAECOLOGY

Assisted Reproduction Technology – Brave New World? Robertson, D., UAE

Since the first IVF baby was born in the UK in 1978, there has been a veritable explosion in both the development and use of assisted reproduction techniques. More than 3 million babies have now been born as a result of these treatments and it is undoubtedly true that many previously infertile couples are now able to have children. It is becoming clear, however, that this technology is being over-used, and that many patients are not aware of the potential risks and the complications that can arise. Is it time to take a step back and review where this path is leading us?

Endometriosis – The Chameleon Caged ??? Kodati, V. L., India

Endometriosis is the presence of endometrial cells and stroma at ectopic sites located outside the uterine cavity. The natural history of endometriosis is uncertain, its etiology is unknown; the clinical presentation is inconsistent, (changing colors like a chameleon) diagnosis is difficult and the treatment is poorly standardized. It causes significant morbidity due to pelvic pain and infertility among 15 – 25% of women during their reproductive age. The benign disease causes peritoneal inflammation, fibrosis, formation of adhesions and ovarian cysts but displays features of malignancy, ranging from neo-vascularization to local invasion and distant metastasis. Mechanical, hormonal, immunological, environmental and genetic factors have been implicated in its etiology but provide inconclusive explanations. An 'Infection hypothesis' is being put forward as the possible etiology of this disease which is not yet proposed in the world literature. It is hypothesized that shigellosis, a bacterial infection of the colon, progresses beyond the limits of the large bowel into the pelvic peritoneum leading to endometriosis. Endometriosis is perhaps the extra-intestinal manifestation of shigellosis. This mechanism proposes "Infection hypothesis" as the most convincing explanation for the etio-pathogenesis of endometriosis.

SURGERY/ RADIOLOGY

Postoperative Rhabdomyolysis in Bariatric Surgery.

Halmi, D., Kolesnikov, E., & Kolomiets, N. N., USA

Background: As the number of bariatric surgeries has been increasing, several reports of postoperative rhabdomyolysis (PR) have appeared in the literature. PR is uncommon, but a recognized cause of renal failure. The mortality rate following acute PR is very high reaching 40-70%. **Objectives:** The aim of this study was to identify the patients at high risk of PR to develop a routine postoperative monitoring method for early diagnosis of PR and to develop preventative measures to avoid Acute Renal Failure. **Methods:** 850 patients underwent Roux-en-Y Gastric Bypass (RYGB) via minilaparotomy incision between January 2001 and June 2006. All patients were divided in two groups: Group 1 - 300 patients and Group 2 - 550 patients. Group 1 consisted of 34 Males and 266 Females with average age: 39.5 years, and average BMI: 48 kg/m². Routine postoperative monitoring for PR was not performed in first group of patients operated on between January 2001 and June 2003. The second group 550 patients operated on from July 2003 through June 2006. Group 2 consisted of 97 Males and 453 Females with average age: 42.3 years, and average BMI: 47.1 kg/m². Patients of this group did receive the established routine postoperative monitoring of Creatinine Phosphokinase (CPK) and electrolytes. Postoperative serum CPK levels were measured (using VITROS CK Slides) on: day of surgery, postoperative day 1 and postoperative day 2. Risk factors of OR time, weight, BMI and comorbidities were considered and postoperative monitoring for PR was established. Patients were also grouped into low, intermediate and high risk groups. Preventative treatment measures were developed and implemented for the high risk groups. **Results:** In Group 1 (without CPK monitoring) 4 (1.3%) patients developed acute renal failure secondary to PR. 2

patients received temporary hemodialysis. In Group 2 CPK was closely monitored. CPK level > 1000 was in 58%, 1001-2000 in 25% and > 2000 in 17% of patients. Three patients in this group developed subclinical PR after mini-open RYGB with prolonged more than 2 hours operating room time. Patients at high risk and with signs of sub-clinical PR were aggressively treated according to our protocol. No patient in this group developed ARF. **Conclusion:** Subclinical PR is more frequent than anticipated even in shorter operative procedures in bariatric patients. Routine postoperative monitoring of the serum CPK levels on the first and second postoperative days may be warranted on all bariatric patients. Screening for risk factors and routine monitoring of CPK levels with early aggressive treatment may prevent serious complications associated with rhabdomyolysis including ARF and death.

CO₂ Laser: The Cutting Edge in Otolaryngology. Nagarkar, N. M., India

The use of lasers has revolutionized the surgical management of various ENT conditions. The CO₂ laser is the one with the widest applications presently available. Various benign and malignant conditions are amenable to treatment. I will be presenting a series of patients with laryngeal, nasal, oral and head & neck lesions. These patients have been operated by me in the ENT Department of the Govt. Medical College & Hospital, Chandigarh, India. The benign conditions include vocal cord nodules and cysts, laryngeal papillomas, laryngotracheal stenosis, leukoplakia of oral cavity. The malignant conditions include Ca tongue and early laryngeal cancers.

3D Echo-Cardiography in Assessing and Quantifying Mechanical Dysynchrony in Patients with Normal and Abnormal LV Systolic Function. Kapur, K. K., India

Introduction: Assessment of mechanical dysynchrony is of paramount importance for considering patients with LV dysfunction who are likely to benefit from biventricular pacing. Conventional and tissue Doppler have been used to quantify dysynchrony. However the angle dependency of tissue Doppler combined with artifacts due to motion of translation and respiration are major drawbacks of these techniques. The recent introduction of live or real time 3Decho allows functional assessment of all the LV myocardial wall segments in one full volume acquisition of 110o x 110o sector. This enables the time to the attainment of the minimum systolic volumes (TMSV) of all the myocardial wall segments to be estimated and compared instantaneously. Standard deviation of the TMSV of these myocardial wall segments and expressed as a percentage of the cardiac cycle length enables calculation of systolic dysynchrony index (SDI%). Patient with SDI of > 9% are considered to have significant mechanical dysynchrony. **Materials & Methods:** 53 pts., 37 M, 16 F, mean age 58.2 years formed the basis of this study. CAD was present in 24, cardiomyopathy in 23 and 6 pts had a normal heart. Wide QRS (> 120 msec) was seen in 27 pts and narrow QRS (< 120 msec) in 26 pts. Conventional 2-D Echo, Pulsed Doppler as well as 3-D Echo and tissue Doppler were performed in all patients. 3-D LVEF, SDI% and Bax Index by Tissue Doppler were computed. Co-relations were obtained between the SDI%, the QRS width, the LVEF and the Bax Index by Tissue Doppler. **Results:** There was good correlation between mechanical dysynchrony by 3-D Echo using the SDI% and the severity of LV dysfunction (LVEF), r = 0.71, p = < 0.0001. However there was no correlation between SDI% and QRS width, r = 0.19 and p = 0.92. There was fair correlation between Bax Index and LVEF (r = -0.47, p = < 0.01) and no correlation between Bax and QRS width, r = 0.29, p = 0.13. **Conclusion:** 3-D Echo has a powerful tool to assess mechanical dysynchrony for biventricular pacemaker implantation. It shows a better correlation with LVEF than the Tissue Doppler. There was however no relationship between SDI and QRS width.

Aesthetic Breast Surgery. Bhargava, K. S., USA

Various aspects of aesthetic surgery will be discussed. The following topics will be addressed breast augmentation, breast reduction, breast ptosis, breast asymmetry, Poland's syndrome, gynaecomastia. The author will discuss each of the above topics and illustrate each aspect with clinical cases and highlight the salient points. Velocity Vector Imaging – A New Promising Echocardiographic Tool with Potential to Detect Sub-Clinical Myocardial Dysfunction in Patients with

Normal Conventional 2D Echo. Kapur, K. K., India

Introduction: While 2-D echocardiography is an excellent tool to quantify left ventricular systolic and diastolic function, abnormalities of contractile and relaxation properties of the myocardium occur much earlier than observed on standard 2-D echocardiography. Tissue Doppler imaging has been a useful technique to detect subclinical myocardial contractile abnormalities. However it has severe limitations arising from angle dependency as well as being severely affected by motion or translation and respiration. Over the last couple of years a new technique has emerged which is based on tracking of ultrasound myocardial back scatters called "speckle". From the speckle tracking algorithm the myocardial velocity data can be traced over the entire cardiac cycle and important contractile data obtained. **Methodology:** High quality 2-D images are obtained in the parasternal short-axis as well as apical 4C and 2C planes. The entire left ventricular myocardium is traced along the entire circumference and these traced images are then selected. The tracking algorithm then provides velocity and direction data of the left ventricular myocardium along the entire circumference and from apex to base. Important velocity, strain rate data is made available from which several essential parameters are derived. These data include angular rotation of the LV apex with respect to the base as well as velocity of angular displacement. This is measured as torsion and torsional velocity. The timing of the onset of the velocity trace, 2D strain and strain rate imaging allows for the identification of dysynchrony segments and thereby quantification of dysynchrony. **Results:** Initial results with velocity vector imaging have shown that it can reliably assess mechanical dysynchrony. Using radial strain in 6 mid-ventricular wall segments, > 130 msec. in the time to the peak strain had 89% sensitivity and 83% specificity for predicting a 15% or > 15% in LVEF at 3 months. Moreover using the torsion and the torsional velocity, it is possible to assess sub-clinical early left ventricular systolic and diastolic dysfunction in the longitudinal follow up of a patient with hypertension. **Conclusion:** Using the recent innovative technique of velocity vector imaging (Speckle Tracking) it is possible to reliably assess left ventricular dysynchrony by the time to peak velocity and time to peak strain. Moreover using the torsional indices it is possible to detect early sub-clinical left ventricular myocardial dysfunction in patients with hypertension with or without Pulmonary Artery Disease. This has an exciting potential in therapeutic planning especially with novel pharmacological agents.

CARDIOLOGY/ ONCOLOGY

Echocardiography: The Most Powerful Predictor of Masked CVD in Metabolic Syndrome.

Chopra, H. K., Aggarwal, K. K., Krishna, C. K., & Sambhi, R. S., India

Background : Several studies have demonstrated that metabolic syndrome is associated with increased cardiovascular morbidity and mortality. In our study we analyzed the impact of the Metabolic Syndrome on cardiac structure and function by 3D echocardiography. **Methods:** We used echocardiographic data from the prospective study done by us- "Echocardiographic and Carotid Colour Doppler Profile in patients of Metabolic Syndrome". The study population which consisted of 100 subjects, admitted as indoor patients or attending the outdoor patient departments, were divided into three groups: Group A, Group B and Group C on the basis of age < 40 yrs, 40 - 60 yrs, and > 60 yrs respectively. On the basis of history, physical examination and biochemical parameters, they were diagnosed as MS according to the modified National Cholesterol Eradication Program (NCEP) Adult Treatment Panel (ATP) III definition and then subjected to 3D echocardiographic evaluation of following parameters: left ventricular myocardial performance index (LVMPI), left ventricular mass index (LVMI), left ventricular diastolic dysfunction (LVDD), systolic function (LVEF), and left atrial volume index (LAVI), left ventricular filling pressures and carotid composite intima media thickness. **Results :** The mean LVMPI was abnormal in all the groups and showed an increasing trend with the lowest value in Group A. Of the total population 74 (74.0%) had abnormal LVMPI > 0.4, of which 9 (69.2%) in Group A, 39 (68.4%) in Group B, 26 (86.7%) in Group C. The mean LVMI indexed to Body Surface Area (BSA) was normal in all the groups, but showed an increasing trend from Group A to Group C. LVMI and RWT were normal in 13%, whereas 76% had concentric remodelling; only 11 % had concentric hypertrophy, but none had eccentric hypertrophy. Mean LVM when indexed to height and BMI, also showed similar results. The mean LVEF was normal in all the groups and of the total population only 9 % had systolic dysfunction. Normal LVDD was found in 32 % of patients but, 68% had impaired diastolic function of which 53 % had grade I LVDD, 12 % patients had grade II LVDD and 3 % had grade III diastolic dysfunction. None of our patients in our study population had grade IV diastolic dysfunction. The mean LAVI was normal in all the groups, but LAVI increased with worsening DD. Most of our patients in Group C & Group B had higher mean Composite CCIMT (0.84 ± 0.42 & 0.73 ± 0.33 respectively). **Conclusion:** MS is associated with masked CAD as evident by echo in our series of patients. LVMPI was an early indicator and most robust marker of early LVDD. Concentric left ventricular remodeling was the most common pattern of LVH. Grade I LVDD was highly prevalent. Most of our patients had increased CCIMT on the contrary LAVI was less robust predictor of LVDD in our series of patients. Thus 3D Echocardiography is most useful for early detection and necessary timely therapeutic intervention in patients with masked CVD in MS. **Key Words:** Metabolic Syndrome, Myocardial Performance Index, Diastolic Dysfunction, Left Atrial Volume Index, Left Ventricular Mass Index, Ejection Fraction.

Optimal Medical Therapy for Chronic Stable Angina. Manchanda, S. C., India

Optimal Medical Therapy (OMT) for chronic stable angina (CSA) can be defined as control of precipitating and risk factors, intensive life style modifications and maximally tolerated pharmacologic therapy with hemodynamic acting drugs (beta blockers, calcium channel blockers, nitrates) and metabolically acting anti anginal drugs. We have demonstrated that intensive life style modification (yoga) can decrease anginal episodes by as much as 73% when added to the antianginal drugs. Hence intensive life style modification including stress management should be an important modality to control angina. Addition of metabolic acting anti anginal drugs trimetazidine, ranolazine in addition to the conventional hemodynamic acting drugs has also been demonstrated to control angina in significant number of patients with CSA. This approach of optimal medical therapy for CSA goes beyond the definition used in the 'COURAGE' trial where metabolic antianginal drugs and intensive life style modification were not used. Even then, it was demonstrated in 'COURAGE' trial that medical therapy for CSA is as good as PCI. However if the present definition of optimal medical therapy is used, it should be possible to control angina in most patients with CSA and 'optimal medical therapy' may be superior to PCI in such patients.

What a General Practitioner Needs to Know About Interventional Cardiology.

Sandhu, G. USA

We shall discuss a variety of clinical presentations of coronary artery disease and their medical as well as invasive management. Recent issues of interest to physicians, including stent thrombosis and post-stent management of antithrombotic medications shall be addressed. Interesting cases shall also be discussed in an interactive manner.

Heart Transplantation. Pereira, N., USA

Heart failure is one of the most common causes of hospitalizations in the United States due to increasing incidence and prevalence of this disease. Despite significant advances in medical and device therapy, 5 year mortality remains at 50% for patients with advanced heart failure. Heart transplantation remains a useful therapeutic option for these patients. Careful selection of appropriate candidates is essential for good outcomes and use of increasing scarce donor hearts. The use of pre-operative left ventricular assist devices, longer waiting time, and older donor hearts recently has increased the complexity of post heart transplant management. Advances in post transplant monitoring and immunosuppression continue to lead the way for reduced morbidity and mortality in heart transplant recipients.

Breast Cancer: Approach to Diagnosis and Management. Sandhu, N., USA

The worldwide impact of breast cancer will be discussed. Diagnosis of breast cancer using clinical examination, mammography and sonography will be addressed. The role of MRI will be explored. New horizons in breast imaging being developed at Mayo Clinic, Rochester will be presented. Breast conserving surgery and mastectomy will be addressed, focusing on individualizing surgical recommendations. Adjuvant therapy for breast cancer will be addressed, including systemic therapy (both chemotherapy and endocrine therapy) and radiation therapy (both whole breast radiation and accelerated partial breast radiation). Surveillance after breast cancer treatment will then be addressed, highlighting the risk of recurrence and guidelines for surveillance. Finally, some special high-risk

situations will be addressed, including genetic risk, patient with a prior history of breast cancer, women with a history of mantle radiation for Hodgkin's lymphoma and women with Her2/neu positive breast cancer.

PREVENTIVE MEDICINE

Health Care Seeking Behavior of Mothers for Their Pre-School Children in Urban Slum of Bahawalpur City, Pakistan. Aziz, N., & Ramzi, W., Pakistan

In order to improve the preventive measures and control of various childhood diseases the Health Care Seeking Behavior of care taker/ mothers must be modified. The urban slums are neglected parts of cities where immigrant from rural areas live with minimal health facilities. This study was done in an urban slum area of Bahawalpur City of Pakistan. This is a cross sectional survey of mothers having children from age 1-4 years who has had any illness in last 2 weeks. They were selected from a list of such households present with lady health workers. Two hundred mothers who fulfilled the criteria were selected so no sampling procedure was adopted. A structured questionnaire was used for interviewing the mothers. The results showed that 53.5% children had diarrhea, 42% ARI and 4.5% other diseases in last two wks. Classification of Severity of disease was done using IMNCI Criteria According to that 95% had mild disease while 5% had severe disease. The choices made about selection of health personnels were Govt. Medical Centre & MCH Centre 13%, GPs. 30%, Dispensers 18%, Quacks Hakeems 32%, and Mosque Molvi Peer etc 7%. Broadly classifying 43% mothers went to some qualified person while 51% went to quacks. If going to a qualified health personal for treatment is taken as correct health seeking behavior then correct health seeking behavior was significantly associated with the severity of the disease, $p < 0.001$, distance of the health personnel from home ($p < 0.01$), education level of the mother ($p < 0.01$) and socio-economic status of the family ($p < 0.01$). No significant relationship was found between the appropriate behavior and their believes, traditions and influence of the head of the family. In conclusion, for bringing a change in health care seeking behavior of that community, interventions should not only focus at providing health education but also lay stress on provision of an easy access to health facilities, make some efforts to improve literacy rate of females & raise economical status of the community.

Drug Surveillance: Its Importance and Current Status in Western Countries and India.

Medhi, B., India

Spontaneous reporting system is the oldest and to date most productive, source of new information about possible beneficial and adverse effects of marketed drugs. It was first proposed by finney after thalidomide tragedy, regulators, public health organizations and manufacturers have been faced with the difficult task of interpreting post-marketing adverse effect that arise from health care product surveillance programs. Health care product monitoring is based on data from four major data sources: spontaneous reports, medical literature, case report or case series, human studies and pharmacological and toxicological experiments. Of these spontaneous reporting is typically the largest contributor and it become the foundation of post marketing surveillance program because it demonstrated usefulness when supervised by experience evaluators. In United Kingdom, the committee of safety of drugs (CSM) was set up and spontaneous reporting scheme was introduced in 1964, by Sir Derrick Dunlop and presently it is the most successful system in the world. Spontaneous reporting system in the USA was started in 1968 by Division of Drug Experience, the ADR monitoring unit of Food and Drug Administration (FDA). Similar system was started in a number of other countries e.g. Australia, Canada, Germany, Japan and the Scandinavian countries. Although their details differ, they share the essential feature that reports of suspected ADRs encountered during clinical practice are solicited from doctors, pharmaceutical companies and in some countries from dentist, pharmacist and patients, for collection and analysis at a central monitoring agency. Spontaneous reporting ADR may be unorganized or non-systemized. Three steps that may occur before medical community received information on spontaneous adverse reactions are: the adverse reaction must be detected; it must be attributed to the medicine and must be reported. The reporting may occur to regulatory authority, manufacturer, or to the medical community. There are many reasons why physician present adverse reaction reports. Given these data are a valuable sources of new information although, they can result in the over generation of hypothesis. It is relevant to attempt to improve the reporting valid data. One approach is to encourage hospital to develop their own system for obtaining these data. At present most of industrialized countries and several developing countries have established organized or systemic spontaneous ADR reporting systems by which individual health professional may report suspected reaction to central/national ADR collection coordinating centre. In majority of the countries this coordinating centre is part of the drug regulatory authority. In some, a university or institution functions as the national centre. In addition, there are usually several regional centre for spontaneous ADR reporting, which connected to major medical institute which report to national centre. In most of the countries where ADR monitoring systems are operational; reporting of ADR is voluntary, but some countries it is legally bound. Many factors that can influence reporting bias such as volume of sales, how long the drug has been on the market, the type and severity of the ADR and publicity about the drug and the reaction. Another limitation of spontaneous reporting is the difficulty for doctors to recognizing previously unknown drug reactions. Rarely more than 10-15% of even severe ADR's are reported to the committee on safety of medicine (CSM) through the yellow card system, and the overall reporting may be even less than 1%. Most drug monitoring centre usually advice to report all ADR with a drug for the first 3-4 years after it licensing and thereafter ADR only serious ADR are solicited. Monitoring of ADR in India was started about two decade ago (1982) under chairmanship of DCGI. The first multi centric study for monitoring ADR in the Indian population was initiated in 1989 by Dr. Singhal with financial assistant from ICMR. The national Pharmacovigilance program was inaugurated in November 2004. Presently there are two zonal centres, five regional centers and 24 primary centers in India and these centers are working together with DCGI and WHO, but still in India spontaneous ADR monitoring is in very early stage. Despite of limitations, which are common to all spontaneous reporting system, it has been proven track record in identification of previously in recognized safety hazard. The spontaneous reporting system has undergone continual evaluation and development over the years and this will continue in the foreseeable future. The spontaneous reporting system requires its spontaneity, speediness, confidentiality and above all the

commitment of health professionals to report their suspicious ADR in the interest of protecting public health. **Key words:** Spontaneous ADR,

Capacity Building of District Level Trainers in IMNCI. Gupta, A. K., & Bhardwaj, A., *India*
Background: IMNCI is an integrated approach that includes the assessment, classification and major problems a sick infant or a child less than 5 years may have. Pneumonia, diarrhoea, malaria, and neonatal infections are most important causes of morbidity & mortality among this group. Training of district level trainers by the state level trainers so that they can percolate it to the grass root level to improve the health indicators. **Objectives:** To develop the Skills of District Level Trainers in IMNCI. **Material & Methods:** 5 day training was done for the pediatricians, Medical officers health and health supervisors from three districts Shimla, Solan & Bilaspur of Himachal Pradesh. The instruments used were Module reading, OPD & IPD Cases, Video and other demonstrations, Field visits etc. **Results & Conclusions:** These will be discussed at the time of Presentation

TDM Pattern of the Antiepileptic Drugs in Developed and Developing Countries: An Experience from Tertiary Care Centre. Medhi, B., & Prakash, A., *India*

Aim: Therapeutic drug monitoring (TDM) is a comparatively a new investigational procedure for developing world and it is considered very beneficial in the management of epilepsy patients. Aim of the study was to compare the pattern of antiepileptic drug level monitoring in different tertiary care centers in developed and developing countries. **Method:** Systematic literature search was carried out for a period of 1966 to July 2006 in Pubmed, Medline, Embase and Cochrane database. Manual search of related journals in the National Medical Library (New Delhi, India), library of the institute and conference abstracts were also checked to evaluate the pattern of TDM in different tertiary centers in developed and developing countries. **Results:** Studies from different parts of the world have evaluated the pattern of TDM of centre. Overall assessment showed values of TDM to be at therapeutic level in 68, 49, 56%, sub-therapeutic in 25, 41, 24% and toxic level in 7, 5, 20% respectively. For phenytoin it was therapeutic in 20, 34, 48 %, sub-therapeutic in 66, 49, 32% and toxic in 14, 17, 20% respectively. For carbamazepine it was at therapeutic in 77, 82, 70 %, subtherapeutic in 19, 13, 12% and toxic in 4, 5, 18% respectively. For phenobarbitone it was at therapeutic level in 85%, subtherapeutic in 13% and toxic in 2%. Studies reported, there increasing requests over the year in the above centers for TDM. Tertiary centre from developing countries reported therapeutic in 29, 56, 75%, subtherapeutic in 52, 39 and 19 % and toxic in 19, 6, 6% for phenytoin, phenobarbitone and carbamazepine respectively. **Conclusion:** The antiepileptic therapeutic drugs monitoring pattern is similar in developed and developing countries. **Key words:** TDM pattern, Antiepileptic drugs.

INFECTIOUS/ ORTHOPAEDICS

Isolation of Anaerobic Bacteria (Actinobacillus Actinomycetemcomitans) and Porphyromonas Gingivalis) from Subgingival Plaque and Their In-Vitro Susceptibility to Standard Drugs Seitz Filtered Lyophilized Ethanolic Extract of Terminalia Catappa L. and Terminalia Chebula L. Rajarajan, S., *India*

Periodontitis affects 65 % Of the Indian population (Beena .et al 1997) and leads to coronary heart diseases [Zaremba et al 2006]. The aim of present study was to isolate these anaerobic bacteria – Actinobacillus actinomycetemcomitans and Porphyromonas gingivalis which are strongly associated with periodontitis. After careful removal of supragingival plaque, a pooled sample was taken from these using sterile paper point and was inoculated into a test tube containing 1.5 ml BHI broth kept at 4°C until the processing procedure was carried out. Tryptic Soy-serum in Bacitracin Vancomycin Agar (TSBV) for Actinobacillus actinomycetemcomitans as described by (Slots. J 1986) and Blood agar supplemented with hemin and vitamin are the enriched and selective medium used for Porphyromonas gingivalis as described by (Sheila et al 2005). Anaerobic condition was maintained inside the anaerobic jar by placing a Gas pack in it. Indicator tablet was placed inside the jar. After 5-7 days colony morphology was observed. Further characterization by biochemical tests and antibiogram showed that these anaerobic bacteria were highly sensitive to Norfloxacin followed by novobiocin, amoxicillin and gentamycin. Besides these the antibacterial activity of Seitz filtered lyophilized ethanolic extract of Terminalia chebula (Fruit rind) and Terminalia catappa – unripe (Fruit rind) was assayed by two fold Microdilution assay. After 4 days of anaerobic incubations MIC of plant extracts was estimated as 400µg/ml for both the bacteria. The present report seems to be the first successful clinical isolation of the anaerobic bacteria (Actinobacillus actinomycetemcomitans and Porphyromonas gingivalis) from India and on the positive efficacy of lyophilized ethanolic extract of two medicinal plants with their MIC value and the sensitivity profile of the isolates to standard antibiotics.

Osteoporosis in Men. Amin, S., *USA*

Osteoporosis in men is not a rare problem. It is estimated that one in eight men over age 50 years will experience an osteoporosis-related fracture in their lifetime. The morbidity and mortality following a fracture is higher in men than women, especially for hip fractures, and roughly 30% of all hip fractures occur in men. As the aging population increases, there is growing recognition that osteoporotic fractures in men will soon become an even greater burden to society and health care systems worldwide. Thus, a better understanding of the epidemiology, pathogenesis, diagnosis, and treatment of osteoporosis in men is increasingly important for health care providers. An overview of the epidemiology of fractures in men will be provided, with particular attention to the differences observed between men and women. The role of declining sex steroid levels and other hormonal changes, which likely contribute to age-related bone loss in men, will be discussed, as will the ongoing controversy regarding the criteria to be used to diagnose osteoporosis in men. Finally, the different treatment options available (both non-pharmacological and pharmacological) for the management of osteoporosis in men will be reviewed.

Prevalence of Chlamydia Pneumonia Seropositivity in Patients Presenting with Acute First Episode of Middle Cerebral Artery Territory Ischemic Stroke – A Case Control Study from a Tertiary Care Centre. Shanavas A. R., *India*

Chlamydia pneumoniae has been linked with increased risk of cardiovascular disease, but data on stroke are sparse. I examined whether seropositivity to Chlamydia pneumoniae was associated with the risk of ischemic stroke in a nested case-control study. Data on Chlamydia pneumoniae serology, conventional risk factors, and medical history were obtained at baseline. Forty consecutive patients (Age > 45) admitted with acute (< 7 days) first episode of ischemic Middle Cerebral Artery territory stroke were included. The diagnosis of Ischemic Middle Cerebral Artery territory stroke was established from consistent clinical features & CT scan findings. All patients with any one of the following criteria were excluded from the study—Hemorrhagic stroke, Posterior circulation stroke, Lacunar stroke, Young stroke, Previous history of stroke, Sub acute & Chronic presentation. Verified cases (n = 40) were compared with age, sex and risk factor matched controls (n = 40). Patients were classified clinically as per National Institute of Health Stroke Scale (NIHSS). Chlamydia pneumoniae IgG, IgM and IgA antibodies were evaluated by ELISA. Attempts were made to correlate the titre of Chlamydia pneumoniae antibody and the severity of disease. To elucidate the associations and comparisons between different parameters, Chi square (χ^2) test was used as nonparametric test. Risk of case group with respect to control group was estimated using Odds ratio along with Chi square analysis. Student's t test was performed as parametric test to compare different variables. For all statistical evaluations, a two-tailed probability of value, < 0.05 was considered significant. Chlamydia pneumoniae IgG serology was positive in 10 out of the 40 patients studied (25%). Only 3 out of the 40 controls had a positive serology for Chlamydia pneumoniae (7.5%). Since P value is < 0.05, this is statistically significant. 42.5% of cases had a positive Chlamydia pneumoniae IgA titre as compared to 10% in controls. Since P value is < 0.01, this is highly significant statistically. Both the cases & controls had a 7.5% positivity regarding Chlamydia pneumoniae IgM titre. So it is not statistically significant (p > 0.05). Positive IgA (> 1.1) or IgG (> 22) titres were associated with an increased risk of acute ischemic stroke. These results partly support the hypothesis that serologic evidence of Chlamydia pneumoniae infection may be associated with an increased risk of ischemic stroke mainly of atherothrombotic origin. However, a large-scale prospective confirmation of the finding is required. Among the cases the positive IgG titre was highest (50%) in patients with NIHSS score between 15-25, closely followed by 40% in patients with a score 5- 15. The least positivity (10%) was in patients with a score < 5. As the score increases the chance of getting IgG titre positivity also increases. Among the cases the positive IgA titre was highest (58.8%) in patients with NIHSS score between 5-15 closely followed by 35.3% in patients with a score between 15-25. The least positivity (5.9%) was in patients with a score < 5. As the score increases the chance of getting IgA titre positivity also increases, but the increase in positivity of the titre is not linearly related to increase in score. Since P value is < 0.05, this is statistically significant. This means that a positive titre of IgG and IgA is more likely in patients with higher NIHSS score & therefore in patients with increasing severity of stroke. There is no positive correlation between IgM titre positivity & NIHSS score. But since this study enrolled only 40 patients further study may be required to confirm this finding. Among the cases the IgM titre positivity was equally positive (33.3%) in patients with NIHSS score < 5, 5-15 & 15-25. Since P value is > 0.05, this is statistically not significant. There is no positive correlation between IgM titre positivity & NIHSS score. Another observation which was found statistically significant was that as age advances the chance of IgG getting positive is increased when compared to IgA. So in advanced age group IgG may be a better marker than IgA. Again as this study enrolled only 40 patients, further study may be required to confirm this finding.

Falls in Elderly. Singh, S. B., Kalra, A., & Mansharamani, G. G., *India*

Falls are very common in elderly. It is sixth important cause of mortality. The subject of fall has not been given any importance in text books of Medicine. However hardly a patient comes to us for consultation unless and until he developed some complication. Prevention of fall is very important. Epidemiology Falls are very common in elderly a major problem especially for women. Some 30% of community-dwelling elderly individuals fall each year. Aetiopathogenesis of fall Falls are due to physiological changes in elderly. Some may be related to disease. Few are due to environmental problem. Some of them are enlisted: 1) Postural instability; 2) Changes in blood pressure homeostatic mechanisms; 3) Disease related factors. These are attributable to a disability or disordered function in the patient. They are caused in many patients by potentially treatable conditions. Therefore, they can also be called medical falls. I. Drop attacks; II. Cardiovascular disease; III. Neurological disorders Seizures; IV. Musculoskeletal disorders; V. Iatrogenic conditions; VI. General causes 1. Systemic illness. 2. Disuse of the lower limbs. 4) Extrinsic/ Environmental Factors Accidental falls account for nearly 50% of falls in the elderly. These falls occur owing to an inability to compensate for common environmental hazards due to the presence of multiple pathological conditions in the elderly. **Diagnosis and Evaluation of a Patient of Fall** Any elderly person who voluntarily or on questioning admits to falling should be thoroughly investigated by detailed history, clinical examination and relevant investigations in order to find out any underlying pathological conditions, many of which may be potentially treatable. Diagnosing includes all of the following: 1. History 2. Physical examination 3. Investigations 4. Who should be involved in prevention? **Prevention** Putting prevention into practice **Primary Prevention:** This means taking measures to prevent falls in people who have not fallen. **Secondary Prevention:** This means taking measures to prevent further falls in those who have had a previous fall/falls (with or without injury).

Total Knee Replacement – Our Experience with All Poly Tibial Components. Ahmad, I., & Aziz, A., *Pakistan*

Arthroplasty, the surgical refashioning of joint, aims to relieve pain and to retain or restore movement. Both articular bone ends are replaced by prosthetic implants. Different designs and systems of total knee replacement are available in the market. These include metal on poly, metal on metal backed poly, RPF etc., etc. Patient selection results & follow up of more than 50 patients who under went total knee replacement (PFC – 2000) with all poly tibial component will be discussed.

Detection of Mycobacterium Tuberculosis by Conventional Methods and by PCR in Patients of Tuberculosis. Sarfaraz, Shukla, I., Ahmed, Z., Malik, A., Fatima, N., & Shahid. *India*

Introduction: Tuberculosis (TB) is one of the most common preventable infectious diseases of the world and it has been estimated that about 30% of TB patients reside in India. Due to emergence of multidrug resistant TB (MDR-TB) the situation has become alarming. The disease is fast emerging due to HIV pandemic. The laboratory diagnosis of TB is a long and tedious process. Though culture continues to be the gold standard for definitive diagnosis of TB, it is time consuming and susceptible to contamination process. Rise in TB statistics and recent outbreaks of MDR-TB have highlighted the importance of rapid diagnosis of this disease. Polymerase chain reaction (PCR) is one such technique, which is of great value today in providing sensitive and rapid diagnosis. **Aims and Objectives:** 1. To compare the conventional methods and PCR in the diagnosis of suspected cases of pulmonary and extrapulmonary TB.; 2. To find out the efficacy of PCR in the diagnosis of extrapulmonary TB.; 3. To determine prevalence of drug resistant strains of Mycobacterium tuberculosis (M.tb). **Material and Methods:** The study was conducted in the Department of Microbiology, Jawaharlal Nehru Medical College & Hospital, A.M.U. on patients attending OPD and IPD of the hospital over a period of 2 years. 781 patients of pulmonary and 450 of extrapulmonary TB were included. Sputum and extrapulmonary specimens (blood, pus, spinal, pleural, gastric, synovial and ascitic fluids etc.) were subjected to microscopy (ZN method) and culture (on LJ media). Drug susceptibility testing was performed by 1% proportion susceptibility method for Streptomycin(S), Isoniazid(INH), Rifampicin(R), Ethambutol(E), and Pyrazinamide(Z). Nested PCR was performed on 70 (37 sputum, 6 gastric aspirate, 19 endometrial biopsy & 8 CSF) specimens. **Results:** Smear and culture examination of sputum obtained from 714 cases of pulmonary TB revealed that in 59 cases (7.55%) smear was positive and in 87 cases (12.18%) culture was positive. Extrapulmonary samples yielded smear positive in 4 cases (0.89%) and culture positive in 23 cases (5.11%). Out of 70 cases of TB studied for PCR, 28% (20/70) cases could be diagnosed by AFB smear, 34.29% (24/70) by culture and 74.29% (52/70) by PCR. PCR results showed a positivity of 4(66.7%) for gastric aspirate, 14(76.8%) for endometrial biopsy and 6(75%) for CSF. For the 30 strains tested for drug susceptibility maximum resistance was seen for INH 23% followed by R 20%, S 6.67% and E 0%. 16.6% (5/30) were multi drug resistant strains. **Conclusion:** 1. ZN smear and culture positivity was much higher for pulmonary TB (7.81% & 12.55% respectively) than extrapulmonary TB (0.89% & 5.11% respectively). 2. Mycobacterial PCR from various types of specimens could be helpful in diagnosing AFB smear, culture negative cases of pulmonary & extra pulmonary TB where number of bacilli is very less. 3. Prevalence of MDR M.tb was found to be 16.67%.

PSYCHOLOGY/PSYCHIATRY

Stress, Depression and Anxiety among Mothers of Children with Thalassemia. Kausar, R., & Zehra, S. K., Pakistan

The present study examined psychological implications of Thalassemia for mothers. It was hypothesized that mothers of children with Thalassemia experience significant stress, depression and anxiety and that there is positive relationship between stress, anxiety and depression in mothers. A sample of forty mothers of children having Beta Thalassemia. Major were recruited through National Thalassemia House, Rawalpindi. Depression, Anxiety and Stress Scale (DASS-42) was translated into Urdu for use in the present study. Interview schedule was used as a method of data collection and mothers were assessed at the premises of Thalassemia House. Data was analyzed using descriptive and correlation analysis. Mothers were found to be stressed out and depressed and there was significant positive correlation between stress, depression and anxiety. Findings have very important implications for provision of psychological services as part of Thalassemia management. **Key Terms:** Thalassemia, Stress, Depression, Anxiety.

Effect of Family Psycho Education on Burden in Families of Patients with Schizophrenia.

Nasr, T., & Kausar, R., Pakistan

Background: The majority of patients with schizophrenia live with their relatives in Pakistan. Because of the patient's behavioral disturbances and other negative symptoms, family experiences a considerable burden. **Aims and Hypothesis:** To evaluate whether family psycho education reduces the burden on families of patients with schizophrenia. It was hypothesized that families receiving psychoeducation would report significantly less burden compared to those who did not receive psycho education. **Method:** 115 patients with schizophrenia and their family members were recruited from out patient departments of a teaching hospital in Lahore. Patients and their family members were randomly assigned to two groups, i.e. psycho education and non psycho education group. Both groups received psychotropic drugs but one group received psycho education and other did not. The burden on families was assessed using the family burden interview schedule (Pai & Kapur, 1981). The family members of both groups were assessed twice; once at the time of recruitment and second at six months follow up i.e. post intervention. **Results:** 99 patients and their relatives completed the treatment and data was analyzed using independent sample and paired sample t-test analyses. The results showed significant reduction in the score of all sub scales of family burden schedule in the group who received psycho educational intervention as compared to the group who did not receive psycho education. There was also significant reduction in burden at post intervention assessment in psycho education group. **Conclusion:** Family psycho-education reduces family burden experienced by family members of patients with schizophrenia and has very important implications for rehabilitation of patients with schizophrenia. **Key Terms:** Family Burden, Schizophrenia

A Comparison of the Perception of Expressed Emotions in the Patients with Schizophrenia, Depression & Obsessive Compulsive Disorder.

Mirza, M., & Kausar, R., Pakistan

Several theories and research findings explain in detail about the blunting of affect in schizophrenia and the consequent difficulties of its victims to appropriately perceive and respond to the expressed emotions of their immediate others. On the contrary the patients with depressive disorder and OCD present high sensitivity in their emotional interactions because of their anxious and negative cognitions. The present study aimed to compare the type of perceived expressed emotions of the aforementioned groups. It was hypothesized that the patients with schizophrenia are less emotionally responsive to

the high expressed emotions than that of the patients of depression, OCD and non patient individuals. To explore this phenomenon, a list of high expressed emotions scenarios was generated and administered to 100 participants (N=25 of each group) for their possible responses. Then similar type of responses were categorized and scored according to their emotional tone. It was found that majority of the patients with schizophrenia rendered responses which were less emotional than that of the subjects of the other groups. While the patients with depressive disorder, OCD & non patient participants hierarchically reported more emotional responses to the given scenarios. This type of findings may initiate further research in this direction and open new avenues in the management and relapse prevention strategies for schizophrenia, Depression & OCD. **Key Words:** Schizophrenia/ Blunting of affect/ Perceived expressed Emotions/ Depression/ O.C.D.

Development of Working Women's Stressors Scale (WWSS).

Asad, S., & Najam, N., Pakistan

Objective: The present research was carried out to identify stressors of Pakistani professional women and to develop the Working Women's Stressors Scale (WWSS). **Method:** Focus group discussions on multiple roles of professional women were conducted on three groups of professional women (N=18) comprising of doctors, bankers, human resource officers and from medicine and textile factories. Age range of the participants was 26 to 57. There were 11 married and 7 unmarried women. The groups were asked to describe their lives which could be attributed to multiple roles. Working women identified additional load in seven categories and these were summarized in five sub categories. **Results:** Stressors which classified were life events, daily stressors, family stressors, work stressors, personal stressors, social stressors and catastrophic (extremely painful events). However their were variables such as "finance" came up under more than one category of stressors, e.g. identified as (a) life event variable, (b) as daily hassle, and also (c) as a personal variable. Variable such as "in laws" identified in three categories of stressors (a) daily hassles, (b) as family stressors, (c) as catastrophic. Social and personal factors were also suggested as stressors. Married women reported more stressors related to family, finance, social, health, catastrophic, where as unmarried women reported work stressor, personal stressors, daily hassles. On the basis of these findings Working Women's Stressors Scale WWSS was developed. The 63 items of WWSS were further provided with Likert scale (5-point). A pilot study was conducted to collect responses from a sample of 30. Reliability analysis was computed which revealed that reliability coefficient was very high with alpha = 0.92. Significant correlation between the stressor was found which provided good preliminary support of scale's validity. **Conclusion:** Working Women's Stressor's Scale WWSS can be used to identify stressors of Pakistani working women. **Key Terms:** Stressors, Working women, WWSS: Working Women Stressor's Scale.

Construction of Scale to Measure Job Autonomy.

Fida, K., & Najam, N., Pakistan

Objectives: To construct a scale to measure job autonomy among employees of private and privatized organizations. **Method:** Focus group technique was used to explore the Job Autonomy (JA) among 26 employees of private and privatized organizations. Discussions from the focus groups were utilized in the generation of 28 statements. These statements were classified into 7 sub-areas of J.A. i.e. 1. Job functioning, 2. Scheduling, 3. Decision making, 4. Physical environment, 5. Gender, 6. Social interactions, and 7. Dress code. Likert scale (5-point) was adopted for these 28 statements to collect the responses from the sample. Pilot study was conducted on a sample comprising of 32 employees, selected from private and privatized organizations. JA Scale was administered and data was collected for further statistical analysis. **Results:** Using the response obtained from 32 employee of private and privatized organizations reliability analysis was computed which reveals a significantly high internal consistency reliability for the JA scale with coefficient alpha = 0.62. Correlation coefficient was computed among the sub-areas of JA and found with relatively low correlations. Inter-statements' correlation was also computed to find-out the relationship among the each statement. Data from correlation analysis supported the construct and discriminant validity of the JA scale. **Conclusions:** Results of the statistical analysis reveal that, the JA Scale is reasonably reliable and valid and is expected to prove useful for the assessment of JA of employees of private and privatized organizations. This scale may contribute to conducting further studies related to measure JA of employees of private and privatized organizations. **Key Words:** JS; Job Autonomy, private and privatized organizations, employee.

INTERNAL MEDICINE/ OBSTETRICS

Neuromyelitis Optica. Cross, S., USA

New research is providing the basis for a revised understanding of Neuromyelitis Optica (NMO). NMO, or Devic's disease, has been characterized by the presence of optic neuritis that is often bilateral, simultaneous and severe, myelopathy with longitudinally extensive spinal cord imaging abnormalities, and no brain MRI abnormalities typical of multiple sclerosis (MS). There is often rapid progression to debility and death. These clinical features have been used to distinguish NMO from MS. An antibody marker of NMO binding selectively to the aquaporin-4 water channel has been identified. This may play a causative role in the disease. Aquaporin-4 is the most abundant water channel in the central nervous system, and lesions in NMO frequently correspond in location to its distribution. This marker has been identified in Japanese patients with opticospinal MS, prompting the suggestion that NMO and Japanese opticospinal MS are the same disease entity. The NMO antibody predicts the frequent relapses of optic neuritis and myelitis. It is also found in some patients with Sjogren's syndrome and lupus erythematosus, implicating a close relationship between NMO and these auto-immune disorders. Because the antibody is found in patients with brain abnormalities atypical of MS, the diagnostic criteria for NMO have been revised to allow the inclusion of patients with these MRI abnormalities. The distinction between NMO and MS is critically important because these two disorders respond differently to immune modulatory therapy.

Economic Cost in Novel Cancer Treatment: Biggest Dilemma in Developing

Countries. Sharma, K., Mohanti, B. K., & Rath, G. K., India

The incidence of cancer and its treatment cost is increasing worldwide and it is becoming a major impediment in attaining the state of optimum health in developing countries like India, where practices like health insurance, economic cost analysis, cost-effectiveness ratios are rare practices.

A major challenge for these countries is to find strategies in which their limited resources can be properly utilized in managing this disease. With the increasing use of novel diagnostic and treatment modalities, the overall treatment cost for cancer is increasing and often it becomes the biggest controversy whether such practices are justified in poor or medium resource countries. In recent years, market forces and political processes have generated growing interest regarding the economic costs of diseases. Also, increasing influence of market forces in clinical practice, lack of proper guidelines, awareness amongst patients regarding themselves as consumers, and lack of political willpower amongst governing agencies adds to these cost inflations. Cancer interventions have outcomes that affect patients and their families who pay out-of-pocket costs and time, people (not yet "patients") who are falsely screened positive, providers of care, third party payers who cover costs of health care, the employer, the government, and society as a whole. Since there is a growing need in health sector to live within budgets in a country like India, there is a great need for incorporating economic cost assessment practices for effective health care delivery so that patients and their families can access the care adequately. **Keywords:** Cancer, treatment, cost-analysis, economic-cost

Non-Invasive Treatment of Osteoarthritis with Quantum Magnetic Resonance (QMR).

Vasishtha, V. G., India

Quantum Magnetic Resonance Therapy TM utilizes highly complex quantum electromagnetic beams in the sub-radio and near-radio frequency spectrum. The beams can be precisely controlled and focused onto tissues therein generating streaming voltage potentials. In osteoarthritis, this flow in the joint causes forced movement of hydrogen protons in the extra cellular matrix (ECM) due to the alteration in QMR spin in the hydrogen atoms and stimulates the chondrocytes. After the publication (2004) of the results of a pilot study on the effect of QMR on 35 patients with osteoarthritis, 300 more patients with osteoarthritis have been treated with QMR as a follow up study. The patients were assessed on the basis of well-established internationally recognized knee society rating system and scores prior to immediately after treatment and further after three months were computed. In addition, MRI of the knees was done using standard protocol before and after three months of treatment with a view to measure the changes in the cartilage thickness in the knee joints. By the end of the treatment the patients could walk up to five times more than before treatment without any difficulty. MRI showed a remarkable increase in the thickness of the cartilage in the knee joint. It needs the emphasized here that cartilage in one of the tissues in which the cells (chondrocytes) have stopped reproduction (mitosis) since they have reached the final stage of differentiation. QMR Therapy TM has now been successfully employed to induce mitotic activity in the fully differentiated chondrocytes. This has been established as an increase in cartilage thickness in MRI. QMR Therapy TM is a method for regeneration of cartilage and is effective for treatment of osteoarthritis of the knee joint.

A Randomized, Double-Blind, Clinical Trial Comparing Different Concentration of Topical Diltiazem and Assessment of Quality of Life in the Indian Patients Suffering from Chronic Anal Fissure.

Medhi, B., Prakash, O., Prakash, A., Kaman, L., & Pandhi, P., India

Objective: Aim of the study was to compare efficacy and safety diltiazem 2% with 4% gel prospectively including quality of life in patients diagnosed with chronic anal fissure. **Materials and Methods:** 50 outpatients with chronic anal fissure, 25 patients were randomized to topical diltiazem (2%) gel and 25 patients to diltiazem (4%) gel once daily for 8 weeks as per inclusion criteria. All the biochemical investigations and detailed examination were carried out. During the course of treatment each patient was seen three times (15, 30 & 60th day). Adverse drug reaction, healing and quality of life were recorded during the patients visit. **Results:** Healing occurred in 23 of 25 patients treated with diltiazem (2%) and 18 of 25 patients were cured with diltiazem (4%) ($P < 0.05$). 2 patients complain of itching and one patient with dizziness. Quality of life was improved in both the group and with 2% diltiazem most of the patients showed improved quality of life. **Conclusion:** Both diltiazem preparation were effective in healing anal fissure and improved quality of life with in fewer side-effects. However study indicates more efficacies with diltiazem 2% gel. **Key words:** Diltiazem, Chronic anal fissure, chemical spinteractomy

Effect on Glycated Hemoglobin (HbA1c) of Iron Deficiency Anemia and Its Response to Treatment.

Gupta, N., & Niin, S., India

Background & Purpose: Glycated hemoglobin (HbA1c) is formed by non-enzymatic glycosylation of hemoglobin. This rather slow process occurs throughout the life span of red blood cells. Hence, a given HbA1c value represents the glycaemic status over preceding 2-3 months. This fact is often used to assess the glycaemic status of diabetic patients. Amongst the variables, hemolytic anaemias are shown to affect HbA1c levels. Effect of other anaemias including iron deficiency anaemia is less well defined. We studied the effect of iron deficiency anemia, which is the most common type of anemia, on HbA1c levels, and how these respond to successful treatment of iron deficiency. **Methods:** Fifty adult patients of proven iron deficiency anemia were included, against another fifty healthy controls. Disorders known to alter HbA1c were excluded from this prospective study and a baseline Hb electrophoresis excluded haemoglobinopathies. Diagnosis of iron deficiency anemia was based on microcytic picture along with a low serum ferritin level. The treatment included oral ferrous sulphate in appropriate doses. Baseline and follow-up investigations included HbA1c at baseline and during the 2-month follow-up. **Results & Conclusion:** Mean value of HbA1c 4.6 ± 0.6 % was significantly lower than control 5.5 ± 0.55 % at baseline. Following treatment, there was a significant rise in HbA1c values and were 5.9 ± 0.56 at 2 month, being significantly higher than control. No significant changes were encountered in fasting blood sugar over the two months. Such findings are not reported earlier and are discussed including the possible role of nutrition.

Neural Computers: A Model.

Varadarajan, S., UAE

The Nervous System is composed of multiple feedback loops which range from 2-neuron recurrent inhibitory loops to multiple polysynaptic loops. It is particularly prevalent in the cortical regions that are important for memory i.e., the hippocampus. An intrinsic component of these loops is the presence of time delays like conduction time along the axon and across the synapse, and processing times. Consequently, mathematical models take the form of delay differential equations. When the time delays become sufficiently large it produces multistability. This multistability plays a role in

active short-term memory i.e., the electrical form of memory before the memories are stored in the form of macromolecules. Neural circuits constructed from *Aplysia* (sea snail) provide convincing evidence of this phenomenon. It has also profound implications on the dynamics of closed-loop hybrid neural computer devices. Here, time delays take the form of sensor response time, and computing time, which are longer. Hence, multistability arises more readily. This helps treating neurological disorders through Prosthetics which are partly human and partly machine. The recent demonstration that two-way communication can occur between a living neuron and a *Silicon Chip* has made possible to minitarize hybrid neural computer devices to almost cellular level. The use of hybrid neural devices for lost limbs by robotic ones, and for epileptic seizures by embedding computer chips in the brain has become a reality. This paper analyses the recurrent feedback circuits in the brain and presents a model of a hybrid neural computer.

OBSTETRICS/ GYNAECOLOGY

Acquired Hemophilia – Cause of Life threatening PPH.

Khanna, S. B., & Dash K., India

Objectives: 1. To discuss about two cases of acquired hemophilia leading to life threatening PPH. 2. To discuss about the emerging role of recombinant factor VII a in the management of acquired hemophilia. **Case Reports:** 1. Mrs. X, 32 years old P2 delivered two weeks back presented with complaints of severe PPH for one week. She had multiple D&Es and blood transfusions. After admission she was managed with Laparotomy with internal ligation, hysterectomy and multiple transfusions with PRC, Cryo Precipitant and FFP. Still she did not respond and on thorough investigation diagnosed to have acquired hemophilia; 2. Mrs. Y, 24 years old P1 who had LSCS three weeks back presented with persistent pyrexia and abnormal coagulation profile. She had laparotomy with drainage of abdominal wall haematoma, D&E. She also had received multiple transfusions with PRC and FFP. On thorough investigation diagnosed to have acquired hemophilia. She responded well after giving a single dose of recombinant factor VII a. **Discussion:** Acquired Hemophilia is a severe bleeding diathesis, resulting from production of auto anti bodies against Factor VIII impairing coagulation. It may be idiopathic, drug induced, immune mediated or following pregnancy and delivery. Diagnosis is made by prolonged PTTK, decreased Factor VIII level and normal PT & Platelet Count. Recombinant Factor VII has been proved to be an effective agent in the treatment of this condition.

An Indian Survey of Awareness and Use of Complimentary and Alternative Medical (CAM) Therapy in Infertile Couples Attending a Private Tertiary Assisted Reproduction Unit.

Verma, S., & Pujá, D., India

Background: Substantial improvement has been made in various areas of infertility including IVF (in vitro fertilization), ICSI (intra cytoplasmic sperm injection) and cryopreservation technology, however overall pregnancy and "take-home baby" rates still remain low at approximately 25-30 percent per cycle. Alternative medicines commonly known as "CAM (Complimentary and Alternative Medicine) therapy" are gaining increasing popularity all over the world. In the absence of any assured solution, the infertile couples constitute a vulnerable group, ready to try any medical or non-medical therapy without being aware of its proven benefits or potential harmful effects. With the huge tide of demands, markets are flooded with enormous number of CAM products and therapies with often highly deceptive claims and advertisements. Scientific data regarding the exact prevalence and beneficial role of the CAM therapy is sparse. Some studies have even reported lower pregnancy rates following IVF treatment in the couples using CAM therapy. **Aim(s)/ Objective(s):** To study the prevalence and pattern of the use of complimentary alternative medical therapy in infertile couples attending a tertiary level assisted reproduction unit. **Material(s)/ Method(s):** 200 infertile couples (total 400 patients) with various etiologies affecting either or both partners, attending a private tertiary level assisted reproduction unit of Indraprastha Apollo Hospitals, New Delhi, India were interviewed between January and July 2008. The information was collected by voluntary participation after an informed written consent ensuring confidentiality. A predefined proforma using questionnaire methodology was filled in person where clear, simple, comprehensible, easily understandable language was used and most questions needed tick in the box under yes or no option. **Result(s)/ Observation(s):** The results of the practice pattern, prevalence and type of CAM used, its perceived indications, safety and efficacy were analyzed. The survey revealed that 37 % of all patients attending a tertiary level assisted reproduction unit had used CAM therapy for their infertility. The most popular CAM therapy in this study was found to be Ayurvedic therapy which was used by 27% of all CAM users. The next two commonly used CAM therapies were Yogic (12%) and Herbal (11 %) medicines. Forty percent of the patients used more than one type of CAM therapy at the same time. 82 % of the CAM therapy users were not aware that there could be any potential side effects and 75% did not volunteer the information of their use of CAM to their infertility specialists. **Conclusion:** Our study revealed that an unexpectedly large Indian population even those attending a private tertiary ART unit is using CAM therapy. Their preferred choice is Ayurvedic therapy followed by Yogic and Herbal sciences. Most of these infertile patients undergoing various assisted reproductive treatment do not even voluntarily disclose this information to their physician. To the best of the author's knowledge, this study is the first reported Indian survey of CAM therapy use in infertile population.

Pregnancy After Bilateral Dysgerminoma of the Ovary.

Shami, N., Anwar S., Shaharyar, A., & Asif, S., Pakistan

Background: Pregnancy after treatment of germ cell tumours of ovary is common. However patients with bilateral dysgerminoma treated with unilateral oophorectomy, wedge biopsy of opposite ovary, and conservation of uterus face difficulty in conception. This study was conducted with the objective to evaluate the fertility status of ovarian dysgerminoma patients treated with conservative surgery and BEP chemotherapy. **Methods:** Patients of bilateral dysgerminoma who underwent conservative surgery and chemotherapy with cisplatin 20 mg / m² and etoposide 100 mg / m² day 1 to 5 and bleomycin 30 mg on day 1, 8 and 15 of three weekly cycles were eligible. A normal AFP and beta HCG at baseline was required. Post treatment CT scans of abdomen and pelvis were obtained. Patients were regularly followed on monthly basis. Pregnancy was allowed 2 years after completion of last cycle of chemotherapy. **Results:** From January 1998 to December 2003, 11

patients were enrolled. Median age was 16 years (range 13-18). All patients had complete disappearance of disease after treatment. Treatment related amenorrhea did not last beyond one year. During a median follow up of 5 years, all patients conceived and a total of 14 pregnancies were completed successfully. Three patients required use of clomiphene citrate for ovulation induction. No patient was treated with gonadotrophins. Six patients underwent lower segment caesarean section for obstetric indications and seven delivered vaginally. All babies were healthy without the signs of birth abnormalities or retardation. **Conclusions:** With conservative surgery and BEP chemotherapy for treatment of bilateral dysgerminoma the fertility is retained with good pregnancy outcome, when conception occurs at least two years after the last dose of chemotherapy.

Pre-Pregnancy Weight and Risks of Adverse Pregnancy Outcome.

Anwar, S., Shami, N., & Asif, S., Pakistan

Pre-pregnancy maternal weight is an important indicator of fetal outcome and fetal weight. Maternal nutrition and drug usage have important implications and effect fetal outcome. Maternal Body Mass Index (BMI) < 19 is associated with babies of low birth weight, whereas maternal BMI > 25 is associated with heavier and bigger babies. However, the number of preterm deliveries increases in both groups. The ratio of LSCS also increases with both extremes in BMI. IUGR babies are more commonly delivered by mothers whose BMI is less than normal range. Therefore it is concluded that pre-pregnancy counseling, care and management has important implications on pregnancy outcome. **Key Words:** BMI, Nutrition, IUGR, LGA.

Effect of Motile Sperm Count After Swim Up on Outcome of IUI. Khan, A. A., Pakistan
IUI is one of the treatment options for infertile couples before proceeding to other invasive and expensive techniques. Several semen parameters correlate directly with outcome of IUI, one of it is total processed motile sperm count and it can be helpful in counselling of patients. **Study Design:** Retrospective study was conducted from January 2004 to July 2006 at Surgimed Infertility Centre, Lahore. **Objective:** To analyze the prognostic value of motile sperm count after gradient method sperm wash in IUI in large group of semen samples. **Method:** 600 couples under 800 infertility treatment cycles. After ovulation induction and follicle monitoring HCG was given, pregnancy rate was calculated in relation to motile sperm count. **Results:** A non linear increase in pregnancy rate per cycle was increased with number of motile sperm in IUI sample. IUI with, 2 x 10⁶ motile sperm after gradient method sperm wash resulted in pregnancy rate of < 1%. With motile sperm count above this level the pregnancy rate was 18%. **Conclusion:** Strict analysis of motile sperm count after gradient sperm wash technique is a useful prognostic factor for predicting pregnancy rate for IUI. In patients with post wash sperm count < 1% other treatment options should be offered to them.

PSYCHOLOGY/PSYCHIATRY

Neuropsychology: Challenges and Opportunities for Emerging Neuroscience in the Region (with Special Reference to Clinical and Research Training and Practice). Najam, N., Pakistan
The present paper would give a review of the historical development of Neuropsychology in Pakistan from its inception in Pakistan to the present day. From the late 19th and early 20th century, Neuropsychology emerged out of three major traditions around the world i.e. the European, the American and most importantly the Russian branches (psychology, neurology and physiology). In Pakistan, Neuropsychology began as an alien word in Psychology in the early 80's, but gradually it has achieved recognition as an important specialization in Psychology. The research and assessment training programs have expanded effectively to pediatric, adult and geriatric issues. Similarly additions, developmental disorders, cognitive and memory functions, psychopathological conditions have been researched and assessed using various neuropsychological tools and batteries such as the Luria Nebraska Neuropsychological Battery (LNNB), Halstead Reitan Neuropsychological Battery (HRNB) and the Boston Protocol. This has given a new perspective to clinical assessment and direction for effective and focused rehabilitative programs. The opportunities for this discipline to grow are indicated by the need for a larger number of trained neuropsychologists to work in hospitals and clinical settings. However, even though research has indicated the efficacy of looking at the neuro-psychological profiles in clinical decisions, we still are a long way from accepting the assessment as a matter of routine evaluation. The challenges of a changing paradigm are great which include overcoming hard drawn lines between disciplines (within psychology, neurology and psychiatry).

Demographic Characteristics and Family Correlates of Dhat Syndrome in

Pakistan. Khan, N., Kausar, R., & Choudhry, H. R., Pakistan

Dhat Syndrome also known as Semen Loss Concern is commonly reported in the Indian Subcontinent. Main objective of the present study was to examine demographic profile and family correlates of Dhat Syndrome in Pakistan. 318 Dhat Syndrome patients meeting ICD-10 criteria were recruited from clinics of Homeopaths, Hakims, Infertility Specialists and General Medical professionals. Semi Structured Interview Schedule was used to gather data and individual assessment was carried out at the premises of the professionals. Data was analyzed using descriptive and inferential statistics. Analysis indicated that a vast majority of patients were consulting Hakims and Homeopaths. Typical profile of a Dhat Syndrome patient in Pakistan emerged to be a young, single, less educated man with poor socioeconomic status. Most of the patients were working as labourers (skilled and unskilled) and in non official capacity. Majority of the patients perceived their family atmosphere being strict. Half of the patients perceived their parents strict and among those, one third perceived their fathers being strict. Most of married patients reported having extra/premarital relations. Findings from the present study have very important implications for provision of psychological intervention to patients reporting with Semen Loss Concern in Pakistan. **Key Terms:** Demographic Characteristics, Family Correlates, Dhat Syndrome, Semen Loss Concern.

Psychiatric Morbidity and Trends of Patients Seeking Psychological Help

Munaf, S., Pahnwar, M., Iqbal, N., & Shaheen, M., Pakistan

Introduction: The Objective of the present research is to determine Psychiatric Morbidity and trends of patients seeking psychological help at Institute of Clinical Psychology, University of Karachi, Pakistan. **Method:** One hundred and twenty five case files were analyzed, out of four hundred and thirty clients of Institute of Clinical Psychology, University of Karachi, Pakistan registered

during one-year duration from January 01, 2005 up to December 31, 2005. These files indicated client's diagnosed on Axis-I and Axis-II disorders on Multi Axial system of DSM-IV-TR (2002). Their age range was between 18 upto 50 years, their minimum education was primary and all of them belonged to upper and middle socioeconomic level. Out of 125 patients, 119 were diagnosed on Axis-I-Clinical disorders and other conditions that may be a focus of Clinical attention and 06 were diagnosed on Axis-II-Personality disorders on DSM-IV-TR. In order to determine prevalence of psychiatric morbidity on Axis-I, Axis-II and trends of the patients seeking psychological help, percentages were calculated taking into consideration number of cases on various categories of Axis-I, Axis-II disorders and separate percentages of gender, marital status, education and socioeconomic level of the patients diagnosed on same approach were also taken out. **Results:** It is clear from the results that prevalence of psychiatric morbidity on Axis-I disorders is more (95.2%) than Axis-II disorders (04.8%). Prevalence of psychiatric morbidity on different diagnostic categories was also calculated. Looking into trends, it is towards males (60.80%) seeking more psychological help than females (39.20%). Furthermore it was also noted that more males (Axis-I=56.80%, Axis-II=04%), unmarried people, (Axis-I=48.80%, Axis-II=02.40%), more educated (Axis-I=52.80%, Axis-II=03.20%) and people belonging to middle socio economic class (Axis-I=77.60%, Axis-II=04.00%) seek psychological help or / and suffer more from Axis-I and Axis-II disorders than females (Axis-I=38.40%, Axis-II=0.80%) married (Axis-I= 46.40%, Axis-II=02.40%) less educated (Axis-I=42.40%, Axis-II=01.60%) and those belonging to Upper socio economic class (Axis-I= 17.60% , Axis-II=00.80%). **Discussion:** Our results of prevalence of psychiatric morbidity and trends of the patients seeking psychological help, corresponds with the gender difference findings reported in previous years by Clinical Psychologists of Pakistan, which indicate that in the city of Karachi male seek more psychological help than females. It seems that the trend has not yet changed in Pakistan of gender biases of giving preference to males and bringing them more to Clinical Psychological for psychological assistance. Hence, awareness program may be introduced in different communities in order to develop psychological sophistication among people and to motivate those segments of society who avoid seeking psychological help. **Keywords:** Psychiatric, Morbidity, Prevalence, DSM-IV-TR, Trends.

Power Spectral Density Analysis of Lullaby Songs in South Indian

Languages – Tamil. Ravindran, S., & Ravindran, G, India

It is medically proved that, music has soothing effect on human neurological system. Especially Indian Carnatic music has different ragas which has specific pattern of modulation of sounds. Each ragas has specific notes while going up (Arohanam) and different while coming down (Avarohanam). In Tamil Nadu (Southern Part of India) there are specific types of songs (lullabies) that help to relax both sensory and motor system of neonates and children. This sets the baby into sleeping mode. In the present work, the power spectral density (i.e. the energy content of audio signals in each frequency band) is being computed. The result indicates that, these songs contains frequency components spread over 1 to 40 KHz, instead of concentrating on specific frequency. The next observation noted is that the energy is not equally spread over the entire frequency range, but concentrates on frequencies like 1.2 KHz, 3 KHz, 7 KHz, 13 to 16 KHz, 22-24 KHz, 27-30 KHz, 35-37 KHz and 40-42 KHz. Of these frequencies, higher concentration is in the vicinity of 15 KHz and 30 KHz. In these songs notes are maintained for a particular time period. These results agree with the previous researchers results that white noise can help the neonates to relax. From time in memorial the Tamil lullaby songs are sung to the South Indian infants by their mother and are found to be useful in making the neonates to sleep. Further analysis in this area can result in the development or safe audio stimulates for neonate relaxation.

GERIATRICS/ORTHOSURGERY

Ageing Revolution (Ageing-Magnitude, Problems, Research, Myths & Prevention).

Mansharamani, G G, Bhalla, S., & Kalra, A., India

Ageing has fascinated mankind from time immemorial but it is only after world war two lot of research is being done on this aspect. No ageing was seen in Stone Age period. All deaths were accidental or sudden. Hardly one in million Robin dies of old age. World is ageing fast. Large number of people is seeing prospects of longer life opening before them. There was a time, when hardly 30% of the population could reach the age of 60 but now there are places where 30% of the population is above 60. Dependency ratio is rising. In short health, psychological, financial, nutritional and social problems will be discussed in these ageing nations (Graying of Nations). There will be some aspects of research going on in Ageing.

Rheumatology Physician Attitudes Towards Complementary and Alternative Medicine:

Results from a National Survey. Manek, N. J., USA

Objective: To describe US Rheumatologist's use of common Complementary and Alternative Medicine (CAM) treatments and to determine if their personal or professional characteristics and attitudes were associated with having recommended each CAM modality. **Methods:** A sub-sample of data from a recent NIH cross-sectional physician survey about CAM was analyzed. A random sample of 600 rheumatologists in clinical practices listed in the American Medical Association Physician Master file received a 12 page questionnaire by mail. Response items included participant characteristics, and experience with common CAM therapies. Dependent variables included attitudes toward 6 common CAM therapies: spinal manipulation, acupuncture, Reiki, meditation, bodywork and glucosamine +/- chondroitin. For each therapy we asked if they had ever recommended the CAM therapy. Independent variables included respondents' demographic information, practice characteristics, as well as the relative role of patient preferences, clinical experience, and published research in their decision making. Chi-square tests were used for comparisons. **Results:** A total of 345 rheumatologists responded (58%) of which 254 were male (74%), 80 were female (23%); 214 participants were age > 50 years (62%), and 117 were < 50 years (34%). Most participants reported white race (86% vs. 11% non-white). Majority reported a group practice setting (46%), followed by solo practice (28%), academic (20%), and institutional (3%). Female rheumatologists were more likely to have ever used meditation (38%), and body work (massage) (48%), compared to their male counterparts (20% and 30% respectively; p<0.01). Non-white practitioners were more likely to recommend acupuncture compared to physicians who are white (69% vs. 52%) (p=0.01). Younger rheumatologists (<50 yrs) were more likely to have recommended acupuncture than older rheumatologists (62% vs. 50%) (p=0.013). Published research was uniformly very important across

all practice settings. However, one in six female rheumatologists, (17%) rated patient preference as the "most important factor" in formulating a treatment recommendation compared to one in thirty male rheumatologists (3%; $p < 0.001$). **Conclusions:** In this first national survey of conventional rheumatologists, we found physician characteristics including younger age, ethnicity and gender were all associated with favorable attitudes toward CAM therapies. Gender differences in attitudes toward CAM may be mediated by concurrent differences in the relative role of patient preferences in clinical decision-making relative to research evidence and clinical experience. Further research is required to determine to what extent CAM can be or should be integrated into the practice of Rheumatology in the US.

Limb Salvage in Patients with Diabetic Foot – An Option Worth Considering.

Gupta, A., & Trehan, N., India

Published data has shown that peripheral arterial insufficiency occurs in 11 – 15 % of all long standing diabetic patients. In addition, another 5% patients have neuro-ischemic ulcerations or necrosis. Regular assessment of peripheral circulation is mandatory in all diabetics and re-vascularization procedures must be considered whenever possible. We present a prospective analysis of the 1 year outcomes, of diabetic patients who underwent a range of procedures with a view to limb salvage. A prospective outcome analysis of 34 diabetic patients (n = 34) between Jan 2007 – Sept 2007, with critical limb ischemia was done. Femoro- above knee popliteal bypass with two vessel runoff – 6, Fem – above knee popliteal bypass with single vessel runoff – 6, Fem – Anterior Tibial – 10, Fem – Posterior Tibial-7, Fem – peroneal 2 and 3 patients were un-reconstruct able by direct bypass but were found suitable for the stem cell program. They therefore underwent an autologous stem cell implantation as per our approved protocol. The overall functional limb salvage rate was 76.4% (26/34). 12 patients with Fem – below knee procedures had a primary patency of 63% (12/19), we however managed to salvage 14 limbs. Two out of the three patients with stem cell implantation salvaged their limbs. Our results are encouraging and strongly support an aggressive evaluation as well as re-vascularization policy for effective limb salvage, in long standing diabetics, with critical limb ischemia.

Ozone Discectomy (Ozonolysis) for Acute Disc Herniation with

Intractable Radiculopathy, A New Paradigm. Kumar, V. S., & Kumar, A., India

Introduction: Direct injection of ozone (ozonolysis) has been proven to be a safe and effective alternative to open surgery for patients suffering from disc herniation in many centres around the world. We report on our experience using ozone discectomy as the primary therapeutic modality in patients suffering from discogenic radiculopathy since we first introduced this therapeutic modality in India. **Methods:** Five hundred patients suffering with MRI proven disc herniation with intractable radiculopathy who had failed to respond to a minimum of twelve weeks of conservative treatment were treated by ozonolysis. Patients with a cauda equina syndrome were excluded. Percutaneous injection of the disc(s) or foraminal injection of gas was performed in prone position using a postero-lateral approach in an outpatient setting. Over a three-week period, one injection of 4ml intradiscal ozone oxygen mixture at 29mcg% conc. was followed by biweekly injections of 10ml of O3O2 in the pararadicular region. **Results:** 88% had a successful outcome (55% excellent, 33% good) and 12% were failures measured on the modified McNab's criteria. There was no ozone related morbidity and no patient had to be hospitalized for any complication related to the procedure. **Conclusions:** Ozone discectomy (ozonolysis) is a valid and safe alternative to an open surgical intervention with a minimal morbidity that can be utilized in many cases of discogenic radiculopathy with favorable results.

The Indications of Ilizarov External Fixator at Ghurki Trust Teaching Hospital.

Javed, S., Pakistan

Ilizarov is the biggest discovery in Orthopaedics after total joint replacement. Present day limb reconstruction is based on the principle of tension-stress, which is the generation of new tissue in response to gradual increases in tension. Discovered in the 1950's by Gavril Ilizarov in Russia, the application of this principle to orthopaedic conditions represents a significant departure from old; it has opened opportunities for treatment in conditions which otherwise were poorly treated or even untreatable. The term 'Ilizarov method' embraces the various applications of this principle and its emphasis on minimally invasive surgery, coupled with an early return to function. In many ways, it has redefined deformity correction in the late 20th century. In our unit, we use Ilizarov External Fixator for the following indications. 1. Treating non-union of Fracture of long bones (Septic and non-Septic). 78 cases; 2. Treating mal-unions. 33 cases; 3. Limb lengthening. 29 cases; 4. Correction of rotational and angular deformities. 15 cases; 5. Correction of neglected and recurrent CTEV. 05 cases; 6. Hip osteotomies. 04 cases; 7. Treating Perthes disease. 03 cases; In the last 03 years we have operated and closely followed more than 150 such patients. Usual complications of pin track infection, AV fistulas and joint stiffness have been a great hurdle in some cases. A few cases of septic nonunion had failure of procedure and led to amputation as well. Recently, we have started following Catagni's recommendation of one schanzscrew and one pin in our cases of Ilizarov. The indications of Ilizarov at our institute, results, follow-up and problems (complications) faced will be discussed in detail.

The Functional Outcome of Vertebroplasty. Ahmad, N., Zaman, A., & Aziz, A., Pakistan

We described a dedicated therapeutic vertebroplasty technique that uses newly designed instruments, acrylic cement, and guidance with image intensifier for pain control in patients with bone failure, and report their experience. Between October 2004 to February 2007, we performed 22 percutaneous cementoplasty procedures in patients with severe osteoporosis, vertebral tumors. In patients with osteoporosis, satisfactory results were obtained in 83% of cases; in patients with vertebral tumors, satisfactory results were obtained in 75% of cases.

Evaluation of Functional Outcome of Knee After ACL Reconstruction By

Modified Clancy Procedure. Zaman, A., & Aziz, A., Pakistan

Background : When you twist your knee or fall on it, you can tear a stabilizing ligament that connects your thighbone to the shinbone. An anterior cruciate ligament (ACL) unravels like a braided rope when it's torn and does not heal on its own. Fortunately, reconstruction surgery can help many people recover their full function after an ACL tear. **Objective:** To evaluate the functional outcome of knee after ACL reconstruction by MODIFIED CLANCY procedure. **Setting and Methods:** We present one year follow-up of 70 previously diagnosed patients having ACL tears (diagnosed clinically as well as MRI proven) fulfilling the inclusion criteria, seen at the Orthopaedic outpatient department of Lahore Medical and Dental College/ Ghurki Trust Teaching Hospital

Lahore. Each patient was examined for the knee range of motion and clinical features of instability with the feeling of "giving way". These patients were later operated and ACL reconstruction (open using bone-tendon-bone graft technique) was done. None of these patients was subjected to arthroscopy and the procedure was carried out through the donor site defect of patellar tendon. Postoperatively, patients were followed for one year and evaluated regarding the functional outcome of knee. **Results:** All the patients were male having mean age of 32 years and mean duration of their symptoms was 03 months. Postoperatively, in all patients, drain was removed after 48 hours and skin stitches were removed on 10th POD. ACL brace was applied to all the patients and knee flexion was started after the removal of skin stitches. Superficial wound infection was noted in 02 cases which later settled after repeated wound wash, dressings and parenteral antibiotic administration. Four patients reported with stiff knees postop. owing to poor compliance, irregular follow up and lack of physiotherapy. Fortunately, they gained near complete range of motion after MUA. One patient had to be reoperated because of recurrence of symptoms in spite of full care. Perop. slippage of graft was noted. Rest of the patients experienced complete alleviation of symptoms, re-gained full range of knee motion and quadriceps power and returned to their pre-injury status within one year. The athletes started light practice after 09 months and returned to their normal sports after 01 year. One of our patients was national "Kabaddi" champion who started his natural game only after 09 months. Thanks mainly to good patient compliance and rigorous physiotherapy. **Conclusion:** There is no conservative treatment for a torn ACL. Only surgical reconstruction (open and arthroscopic) offers complete cure. Fortunately, compliant patient returns to the pre-injury status within one year. **Key Words:** ACL Reconstruction; Modified Clancy procedure

The Value of 3D Ultrasound Measurement of Placental Volume in Prediction of IUGR, in Cases of Pre-Eclampsia. Fiaz, M., & Rahim, A., Pakistan

Design: Prospective study. **Setting:** Department of Radiology Surayya Azeem Hospital & Department of Ghulab Devi Hospital, Lahore from October 2006 to October 2007. **Aim of the Work:** Is to study the possible correlation between the placental volume estimation using 3D ultrasound in cases of pre-eclampsia (P.E.) and the associated IUGR and to identify if the placental volume is a reliable index of fetal welfare in pregnancy complicated by pre-eclampsia. **Patients and Methods:** Hundred and fifty pregnant women were included in this study, with gestational age between 36-38 weeks and they were followed till delivery. They were classified into 3 groups: Group I: 50 normal pregnant women as control group; Group II: 50 pregnant women with mild pre-eclampsia; Group III: 50 pregnant women with severe pre-eclampsia All cases were subjected to history taking, laboratory investigations and 3D ultrasonic examination for gestational age, biophysical profile, placental volume (measured by a parallel ultrasonographic section scan method). All 3-D ultrasonographic data were recorded at 36 weeks of gestation to be statistically analyzed. After delivery the newborns were evaluated by Apgar score and birth weight. The placental weight and thickness were determined. **Results:** The severe P.E group had the smallest placental volume (612.7+31.6ml) compared to mild P.E (740.1+36.9ml) and control group (850.3+40.1ml). There was a positive correlation between placental volume measured by 3D U/S and the placental weight and thickness measured after birth. The severe P.E group had significantly higher IUGR rate (82%) compared to (24%) and (12%) for mild P.E and control groups. Severe P.E group had significantly lower mean birth weight (2.53+0.38kg) V.S. (3.08+0.24kg) and (3.48+0.32kg) for mild P.E and control groups. There is significant negative correlation between placental volume measured by 3D U/S and the incidence of IUGR in cases of pre-eclampsia. There were significant positive correlation between placental volume and the biophysical profile and Apgar score in cases of severe P.E. **Conclusion** 3-D ultrasound measurement of the placental volume well correlated with placental weight and thickness and neonatal birth weight. 3-D ultrasound measurement of the placental volume is a reliable index of fetal growth and welfare in cases of pre-eclampsia. It can be used as a predictor of IUGR in these cases.

MEDICINE

Role of Ultrasound in Chest Diseases. Bhargava, S. K., & Bhargava, S., India

Ultrasound is a non-invasive, non-ionising, relatively cheap modality and is used widely in developing country in almost every system of human body. However due to its limitation of penetrating through the Air and bone, its application in chest and musculoskeletal system was unheard almost a decade before. Due to availability of High frequency Transducers, it is now in prevalent use to diagnose the chest wall tumors, rib fracture, osteomyelitis of ribs, abscesses, consolidation and collapse of the lung, lung tumors. It is also helpful not only to diagnose the cases of pleural effusion but also give its etiological diagnosis. The presentation will highlight the application of Ultrasound in chest diseases.

Medical Tourism – Global Initiative in Providing Affordable Best in Class Healthcare.

Singh, S., India

Acceleration of unsustainable healthcare costs in many developed economies is expected to propel 10 million Americans alone to seek medical solutions world wide resulting in an annual loss of \$ 160 billion to American Healthcare Providers by 2010. However, the current market stands at 60,000 to 85,000 inpatient medical travelers a year as opposed to earlier higher projected numbers. Tens of millions of uninsured middle class will keep driving this both in the developed and developing world. Today 40% of all foreign patients actually plan travel to access Most Advanced Technology (40%), Quality (32%), Quicker access (15%) Low cost (13%). Hospitals in Asia and Latin America rival or surpass many in the developed world for safety and quality. How will this impact the healthcare delivery system in the developing world? Will a flood of overseas patients divert money and manpower from state health systems to private or will this create local jobs and possibly tempt émirg doctors to return and value add to health services at home. Either which way we look at it the flood looks unstoppable for the moment though the numbers are debatable.

Surgical Treatment of Thoracic Carcinoid Tumor. Nabi, M. S., Pakistan

Objective: To analyze results of surgical treatment of Thoracic carcinoid tumor. **Methods:** Retrospective analysis of 14 patients of thoracic carcinoid in the last 5 years. **Results:** 14 cases of thoracic carcinoid tumor were managed surgically. There were 13 cases of pulmonary carcinoid tumors: typical (n= 11) and atypical (n= 2) and one case of atypical carcinoid tumor of Mediastinum. The female to male patient ratio was 4:10. Bronchial obstruction and tumor ulceration was the cause of most of the presenting symptoms and signs and included hemoptysis, obstructive pneumonitis, pleuritic chest pain, atelectasis, and dyspnea in pulmonary carcinoid tumors. Features of Carcinoid syndrome was absent in all patients and carcinoid crisis occurred in only one patient during surgery. Most of the tumors (12) arose in the major bronchi. Diagnosis was made using fiber optic bronchoscopy in 8 patients without evidence of endobronchial hemorrhage. Nodal involvement

occurred in 2 patients in the atypical group, and in 1 patient in the typical group. The treatment of choice was surgical: lobectomy (6), sleeve lobectomy (3), bilobectomy (1), pneumonectomy (3) and in one patient excision of anterior mediastinal tumor. Follow-up of 6-48 months revealed 2 mortalities after 3 yrs. **Conclusion:** Thoracic carcinoma is an uncommon tumor. With early diagnosis and aggressive surgical therapy, long-term prognosis is good in this group of patients.

Correction of Palatal Crossbite in Adults Using Surgically Assisted Rapid Palatal Expansion – A Case Report. Ahmed, F. Pakistan

Rapid palatal expansion is used to correct posterior palatal cross-bite. The type of expansion depends on age of the patient. Rapid palatal expansion is frequently used for adolescents but can not be applied to adults. Surgically assisted rapid palatal expansion as a form of distraction osteogenesis can be used to treat severe maxillary constriction. Comprehensive diagnosis and three dimensional patient evaluations are mandatory. This case report enlightens the favorable effects of transverse expansion on vertical and sagittal aspect of the patient. The effect of the procedure on soft tissue profile is also discussed. **Conclusion:** Surgically assisted rapid palatal expansion is effective and efficient treatment option for correction cross-bite in adults with stable outcome.

To Study the Efficacy of Formoterol and Fluticasone (DPI) Fixed Dose Combination in the Management of Mild Persistent and Moderate/Persistent Asthma. Shameem, M., Bhargava, R., Ahmad Z., & Ahmad, A., India

Objective: To study the efficacy of formoterol and fluticasone (DPI) fixed dose combination in the management of mild persistent and moderate persistent asthma. **Material and Methods:** The study was open label, prospective, non comparative clinical trial carried out in the Department of Tuberculosis and Chest diseases: Jawaharal Nehru Medical College; Aligarh Muslim University Aligarh UP India, between December 2007 to April 2008. Inclusion criteria- a) Patients with Mild persistent and Moderate persistent asthmatics (as per GINA guidelines) was enrolled b) Fixed dose combination of Fluticasone and Formoterol was given twice a day d) Primary end point was change in FEV1 and FVC, secondary end points were change in PEFr from baseline and change in mean "as needed" inhaled β_2 agonist. Exclusion criteria 1. Daily requirements for >1000 μ g BDP, or equivalent. 2. Contraindication or known or suspected hypersensitivity to Fluticasone propionate or Formoterol or any other constituents of the investigational products. 3. Evidence of active concomitant pulmonary disease other than asthma. 4. Acute upper respiratory tract infection within 2 weeks of the screening visit. 5. Acute lower respiratory tract infections within 4 weeks of the screening visit. 6. Any change in asthma therapy (other than inhaled shortacting β_2 -agonists as rescue medication) or admission to hospital for treatment of asthma within 4 weeks preceding the screening visit. 7. More than 4 short courses of oral corticosteroids within the six months preceding the screening visit, or any oral corticosteroids in the preceding 4 weeks. 8. Concomitant severe decompensated systemic disease (cardiovascular, renal, hepatic, endocrine, haematological, neurological or immunological) Follow up schedule was baseline, week 4 (visit I), and week 8 (Visit II) **Results:** There was significant improvement in FEV1 and FVC values from baseline (p<0.005), there was also decrease in mean usage of β_2 agonist (p<0.005). **Conclusion:** Formoterol and Fluticasone (DPI) combination offers symptomatic and Spiro metric improvement in mild to moderate persistent asthma.

PREVENTIVE MEDICINE

Important Reason to Control Air Pollution in Flour Mills. Gandhi, A., Surange A. G., & Singh, S. H., India

Flour mill workers are exposed to flour dust, a health hazard to their respiratory system. Hence, pulmonary functions of workers engaged in flour mills were investigated. Lung functions were studied by recording forced expiratory spiogram in 65 non-smoker male subjects, aged 15 to 35 years. Thirty three subjects worked (exposure 4.32 + 3.9 years) in elevator operated flour mills, which produced large quantity of flour dust; whereas 18 subjects worked (exposure 7.08 + 4.08 years) in pneumatic flour mills-better designed to produce minimal flour dust. Fourteen subjects served as control. Subjects were anthropometrically and socio-economically matched. There was deterioration in pulmonary functions of workers of elevator type flour mills compared with controls: FEV1, FEV3, FEF 20-30% and FEF 45-55% (P<0.001); FVC & FEF 70-80% (P<0.01). All these parameters decreased in pneumatic type flour significance, despite longer (7.08 + 4.08 years) exposure to flour dust: FEF 45-55% (P<0.01); FEV1 (P<0.02); FEF 20-30% (P<0.5); FVC, FEV3 and FEF 70-80% (NS). To summaries, study shows that though flour dust is an occupational health hazard, yet its impact and be minimized by improving mill designs.

CYP3A5 and C3435T MDR1 Gene Polymorphisms Determines the Pharmacokinetics of Cyclosporine and Tacrolimus. Rao, P., Kiran, V., & Hasan, Q., India

Background: Cyclosporine (CsA) and tacrolimus (Tac), are immunosuppressants used to prevent organ rejection following renal transplant. Both drugs show highly variable pharmacokinetics due to variations in absorption and metabolism. Several genes influence serum drug levels. P-glycoprotein (Pgp) is a membrane transporter coded by MDR1 gene. The MDR1 single nucleotide polymorphism of exon 26, C3435T is associated with lower intestinal P-gp expression which affects the therapeutic drug levels. The CYP3A isozyme group, part of the CYP system is abundantly expressed in the liver and intestine. They are responsible for the phase I metabolism of CsA and Tac. A single base change (6986A>G) in intron 3 of CYP3A5 (designated CYP3A5*3) produces a truncated and nonfunctional protein. **Aim:** To evaluate the role of C3435T polymorphism of MDR1 gene and CYP3A5 A6986G polymorphism with respect to inter individual variability in CsA and Tac blood levels in a cohort of renal transplant recipients. **Results:** CYP3A5 A6986G polymorphism: Individuals with *1/*1 genotype showed low CsA (C2) levels in blood (mean 946.5 + 243.63ng/ml) while heterozygotes *1/*3 and homozygotes *3/*3 showed higher CsA C2 levels (mean 1090 + 288.68 ng/ml, 1222 + 298.30 ng/ml) respectively. CsA and Tac dose verses blood levels along with genotype showed significant association (p<0.05). MDR1 gene polymorphisms: Patients with TT had higher CsA dose to blood levels ratio compared to CC polymorphism (5.82 + 2.61, 4.41 + 1.58, p<0.001). TT patients had higher tacrolimus levels (11.11 + 5.01, 5.82 + 3.75 ng/ml, p<0.001) **Conclusion:** Genetic factors regulate absorption and metabolism of cyclosporine and tacrolimus.

Nursing Resource Utilization Based on Activity Score.

Chandra, H., Pandey, C. M., Jamaluddin, K., & Mastih, L., India

Background: The nursing resource is a scarce one and important in the hospitals. The utilization of nursing personnel remained debatable due to lack of definitenorms. The bed occupancy rate (BOR) and Nursing activities are the main factors that influence the workload and utilization of nursing personnel. **Aims:** The present study is aimed at to identify/develop the criterias / norms for the

allocation of nursing personals and their after optimal utilization in the hospital. **Methodology:** In this study about 29 nursing care activities (direct & indirect) were identified and each activity was allotted score based on involvement of nursing care. (Direct (25) e.g. - IV fluid infusion, bed sore, indirect (4) e.g. cardiac arrest death etc., - bed making, TPR, charting, drug distribution etc.). The study was conducted during April-May 2006 at Sanjay Gandhi PGIMS Lucknow U. P. India a tertiary care hospital of U. P. State Government and the same study was repeated after 02 months to confirm the consistency in findings of the first study. **Findings:** Both studies revealed that the nursing care workload (activity score) may increase with increase in the bed occupancy rate (BOR) but not in the same proportion. The wards having high BOR may not earn high activity score in proportionate manner. On the contrary, the workload increases with severity or criticality of the patients that involves more and more nursing activities and a ward may earn higher score even with low BOR. This facilitate the administration to identify the high work and low work area and to depute the appropriate number of nursing personnel, if required mobilizing them from low work area to high work area. **Conclusion:** The criterion to allocate nursing staff should be based on nursing care activities in a ward, which depends upon severity/ criticality of the patients rather than the BOR of that ward. **Recommendation:** The score used in the study may be taken as a model to justify allocation of nursing personnel and their optimal utilization. **Keywords:** Nurses, Utilization, Activity Scores, BOR, Norms/ Criterias

Treatment of Hypertension in Very Elderly People. Roy, C., India

Elevated blood pressure is common in persons 80 years of age or older, a group constituting the fastest-growing segment of the general population. Whether the treatment of patients with hypertension in this age group is beneficial is unclear. It has been suggested that antihypertensive therapy may reduce the risk of stroke, despite possibly increasing the risk of death. A recent study "Hypertension in very elderly Trial" had assigned 3845 patients from Europe, China, Australasia, and Tunisia who were 80 years of age or older and had a sustained systolic blood pressure of 160 mm Hg or more to receive either the diuretic indapamide (sustained release, 1.5mg) or matching placebo. The angiotensin-converting-enzyme inhibitor perindopril (2 or 4 mg), or matching placebo, was added if necessary to achieve the target blood pressure of 150/80 mm Hg. The primary end point was fatal or nonfatal stroke. At mean follow up period of 1.8 years active treatment was associated with a 30% reduction in the rate of fatal or nonfatal stroke a 39% reduction in the rate of death from stroke a 21% reduction in the rate of death from any cause a 23% reduction in the rate of death from cardiovascular causes and a 64% reduction in the rate of heart failure Fewer serious adverse events were reported. This landmark study showed that very elderly (over 80 years) people do benefit from treatment of Hypertension

POSTER PRESENTATION

Perceived Health Related Quality of Life of Renal Transplant Recipients.

Kamran, F., Pakistan

The present study aimed to investigate the perceived health related quality of life among RTR (renal transplant recipients) after a successful kidney transplant and healthy graft functioning in the post transplant period. The sample N= 70 (male=34, female= 36) comprised of kidney transplant recipients (age range 25 -45 years) recruited from renal units of various hospitals in Lahore, with a post transplant period up to five years. The RTR with the same medication group were asked to report their perception about Satisfaction with their QOL as well as the Importance that they attach to the QOL. Satisfaction and Importance with quality of life were measured by The Quality of Life Index, Kidney transplant version by Ferrens and Powers (1998) comprising of four sub scales i.e. Health and Functioning, Psychological and spiritual, Family sub scale, Social and economical sub scale. The results indicated that RTR are significantly satisfied with quality of life with increased level of health & functioning. (P<0.05) and attach a great significance to improved Quality of life (P<0.01), indicating their serious concern regarding their health status and daily life coping after a successful kidney transplant.

Thyroid Dysfunction in Genotype 3 Chronic Hepatitis C Patients Treated with Interferon and Ribavirin. Haque, I., Tayyab, G. N., Zafar, S., Khan, G. M., & Chaudry, N. U., Pakistan

Objective: Interferon (IFN) plus ribavirin therapy for chronic hepatitis C (CHC) virus infection has been associated with thyroid dysfunction. The aim of our study was to determine the pattern of thyroid Dysfunction in Genotype 3 Patients and to assess the risk factors and reversibility of thyroid disorders induced by interferon therapy. **Methods:** Patients with chronic hepatitis C, either biopsy proven or tested positive for HCV RNA by PCR and having only genotype 3(n=200), were treated with Interferon alpha 3 MIU TIW (n=150) or Pegylated Interferon alpha180Mcg (n=50) along with weight based Ribavirin and developed thyroid diseases were included in this study. Thyroid-stimulating hormone (TSH), free T3 and T4, and thyroid peroxidase autoantibodies were measured at 0, 3, and 6 months of treatment and also at 6 months after end of treatment. Sustained Virological response was defined as loss of detectable HCV RNA at 6 months follow-up. Thyroid dysfunction was defined as TSH level below or above the normal range (0.2–4.5MIU/L). Frequency was compared between groups using the chi square test with Yate's correction or Fischer exact test. A multiple logistic regression model was used in the statistical analysis of the various factors for the development of thyroid dysfunction. Variables which were used included age, gender, type of IFN used, presence or absence of thyroid auto antibodies before starting therapy, impact of RVR and SVR. The type of thyroid disease and its outcome were assessed during and post IFN therapy. The analysis was performed using the SPSS 10 statistical package (SPSS Inc., Chicago, IL, USA). P-value of <0.05 was considered to be statistically significant. **Results:** Thyroid dysfunction developed in 21 (10.5%) of 200 patients. Hypothyroidism was seen in 17 and hyperthyroidism in 4 patients. Thyroid dysfunction occurred in 15 (10%) of 150 patients who received conventional therapy as compared with 6 (12%) of 50 patients who received Pegylated IFN therapy (P = 1.0). Amongst 200 patients who completed all 6 months of HCV treatment, overall SVR was achieved in 162(81%) patients. While out of 21 patients who developed thyroid dysfunction SVR was seen in 16 of 21(76%) and 179 who didn't have thyroid dysfunction SVR was present in 145(81%) (P = 0.96). By multivariate analysis female gender and pre-treatment auto-antibodies presence were independent predictors of developing biochemical thyroid dysfunction (P < 0.01) while age, type of IFN used, RVR and SVR were not. These patients were followed for six months after interferon therapy. Out of 21 patients 19 became euthyroid six months after cessation of therapy, only two patients had to continue taking therapy after this time period and both were from Pegylated IFN group. **Conclusion:** Female gender and pretreatment auto-antibodies detection are associated with thyroid dysfunction while pegylation of IFN and age of patients did not induce thyroid disease in Chronic Hepatitis C.

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