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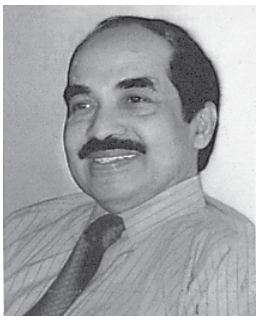
PRESIDENT WRITES

Dear Fellows and Members,



We had an interesting annual conference on the 4th and 5th of November 2011 at Hyderabad organized by our trustee, Dr.Bhaskar Rao. Many of our fellows from various parts of the world attended the meeting. Scientific papers were of high standard both in presentation and scientific content. I appeal to fellows and members to actively participate in the annual conferences.

I like to call upon all the fellows and members to contribute your valued articles in JIMSA; our journal as you aware, is now an indexed one. With your contribution, we can make it to one of the very best, globally.

Finally, may I request you to donate and motivate others to donate for the construction of our Head Quarters Building at Delhi; which is needed very much for the proper functioning of our organisation.

K. Jagadeesan

Dr. K. Jagadeesan
President, IMSA

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IMSA/ JIMSA WEBSITE

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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 CMEs 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 non 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'.***

APPEAL FOR IMSA BUILDING FUND

Dear Colleagues,

International Medical Sciences Academy (IMSA) is a global organization established as a registered society on 28th March 1981 with world headquarters at New Delhi. It is the only international body which encompasses all disciplines of medicine. It has regions in America, Australia, Europe, Africa, rest of Asia and India. There are 28 chapters world over. IMSA is run by Board of Trustees apart from other executive committees. IMSA is an associate member of Council for International Organizations of Medical Sciences (CIOMS). It has about 3300 members world over and the membership is expanding. Many Nobel Laureates are its fellows.

The main objectives of IMSA is to bring together national and international medical scientists, medical educationists, medical and public health administrators and research workers in medical and health sciences on a world wide basis for advancement of health of all the people in the world. The academy also arranges courses, training programs, CME programs and Rural CME programs. IMSA publishes quarterly journal, JIMSA in which original articles updates, symposia, special issues on topics of current interest are published.

An annual conference - IMSACON is a regular feature; being an International organization every alternate year, the annual conference is held outside India. This year's ***IMSACON*** *was held at Royal Society of Medicine, London, UK between 10th and 11th September 2010 and was an extremely successful event.*

Though IMSA has been in service of medical profession and has been encouraging development of medical sciences by bringing information technology into the profession thus improving the health of nations, yet we do not have our own building to work more effectively. Our organization is committed to the medical profession for promoting Continuing Medical Education and also hold educational programmes on topics of National and public health importance. We need to conduct seminars, organise lectures by National and International experts and hold regular workshops and group discussions. For arranging such activities we are badly in need of our own building with adequate infrastructure and facilities like an Auditorium , projection room, library, committee rooms for interactive sessions etc. So far we have been operating from small rented space which can hardly accommodate our office.

Friends, we have been fortunate to get a piece of land about one acre allotted to us by the Lt. Governor of Delhi for developing the IMSA World Head Quarters at Delhi. I am approaching all Fellows and Members to donate at least Rs. 5000/- each to meet the cost of the land as well as construction of our own building. The donations are exempted from tax under 80G; the cheque may please be made in the name of ***"IMSA – Building Fund"*** *payable at New Delhi, and sent to the Headquarters.*

Thanking you in anticipation and warm regards,

Yours Sincerely,

Dr. K.Jagadeesan, *President, IMSA,WHQ*

IMSA Chapter Activities/ CME Programmes

Karnataka Chapter

02.11.2011	***Dr. Murali Duggirala:***	*Analysis of Survival Curves.*
02.11.2011	***Dr Gerard Kamath:***	*Physician -Assisted Suicide.*
02.11.2011	***Dr Nisha Manek:***	*Recent Advances in Pathogenesis & Management of Osteoarthritis.*
02.11.2011	***Dr Paola Sandorini:***	*Autonomic Disorders.*
02.11.2011	***Dr Gurinder Vasdev:***	*Anaesthesia Concerns of Robotic Surgery.*

Election of Fellows and Members

Fellows

Dr Harpreet Singh
Dr K J Vedavathi
Dr Mary Prem Jayarajan
Dr T Kesavan
Dr Sunil Goel
Dr Sudhaa Sharma
Dr Annil Mahajan
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Dr Arun Kumar VS
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Dr Navin H K
Dr Anish Ahmed M K
Dr K Poongkodi

IMSACON 2012

IMSACON 2012 Conference will be held on Friday, 12th October, 2012 at Gulf Medical University, Ajman, United Arab Emirates.

Dr. R.K. Thukral, Secretary General, IMSA, WHQ, New Delhi

Obituary

Professor K B Sharma, MBBS, PhD (Paris), FAMS, FRCPath (London), FIMSA, FISCD. After graduating in Medicine in 1954, Professor K B Sharma obtained Ph.D in Medical Microbiology from Pasteur Institute, Paris in 1961. In his forty years of professional career, more than thirty years were spent in teaching and research. He started his teaching career in Microbiology in Lady Hardinge Medical College, New Delhi where he worked till 1981, having taken the Chair in 1967. In 1981, he moved as Dean, Maulana Azad Medical College, New Delhi, a post he held for five years. After a brief stint as Deputy director general Health Services of India, he joined WHO as Regional Advisor in Health Laboratory Services in 1988 from where he retired in 1995. His main research contributions have been in epidemiology of streptococcal infections and their sequelae; Rheumatic fever and acute glomerulonephritius, epidemiology of Salmonella infections in India and South East Asia Region and epidemiology of plasmid mediated drug-resistance and virulence factors in bacteria. He authored 150 publications in national and international journals and has written and edited several books including Hindi translations of Microbiology by Criuckshank, Health Laboratories in support of Primary Health Care in Developing Countries (WHO), monographs on Quality Assurance and Accreditation in Laboratory Medicine, Organization and Management of National Blood Transfusion Service. He was awarded F.R.C. Path. (London) and fellowships of National Academy of Medical Sciences and International Medical Science Academy as well as several national awards for his contributions to development of microbiology in India. He has lectured extensively on issues of infectious diseases eg. Emerging infections, antibiotic resistance trends, hospital infection control, vaccinology, quality assurance in laboratory medicine, global warming etc., in many Instituions all over the world. He joined as Trustee of IMSA 1997 and has been actively associated with its various activities. He was the organizing trustee of IMSACON 2002 in Cambridge, UK. Recently he received lifetime achievement awards of the Indian Association of Medical Microbiologists and Academy of Clinical Microbiology & IMSA NDB. *Scientific Contributions include:* (1.) Reference programme for epidemiology of streptococcal infections and their sequels – Rheumatic fever and acute glomerulonephritis. (2.) Epidemiology of Salmonella infections in India and South East Asia Region. (3.) Epidemiology of plasmid mediated drug-resistance in Salmonellae. (4.) Plasmid mediated virulence factors in bacteria. (5.) Annual national workshops on laboratory investigations of streptococcal infections, 1973-1990. (6.) National workshops on epidemiological investigations of salmonellosis, hospital acquired infections, monitoring of antimicrobial resistance, 1974-1988. Prof.. Sharma has been the recipients of several awards such as, (1.) *Dr. Y S Narayana Rao* (Indian Council of Medical research) for epidemiology of streptococcal and salmonella infections 1981. (2.) *Dr. B C Roy Award* (Medical Council of India) for development of specialities (Microbiology), 1982 (3.) *Dr. S C Agarwal Oration* (Indian Association of Medical Microbiologists) for Eidemiology of Multi-drug resistant salmonellae, 1982 (4.) *Dr. Om Parkash Oration* (All India Institute of Medical Sciences, New Delhi), 1984 (5.) *Dr. H I Jhala award* (Indian association of Medical Microbiology in India, 1991. Edited and Prepared South East Asia Regional Publication No 24, entitled *"Health Laboratory services in Support of Primary Health Care"*, in 1994. Which incorporated three elements eg.: Policy guidelines for health laboratory services, appropriate technology for Primary Health Centres and quality assessment of laboratory techniques; Second edition of the same publication has been published in 1999, monographs on Quality Assurance and Accreditation in Laboratory Medicine, Organization and Management of National Blood Transfusion service. As capacity building of laboratories, he has conducted Group Educational Activities in the fields of cost effective HIV testing, blood transfusion services, distance learning materials for blood safety, vaccine quality control, appropriate diagnostic technology, quality assurance in laboratory medicine and health laboratory service networks.

Dr K.B. Sharma left for his heavenly abode on 28-10-11, we at IMSA will miss him; but certainly he has left impeacable impressions of his valuable advice and pleasing personality on all of us to remember him always in times to come.

President, BOT Members, Fellows/Members of IMSA

JIMSA

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FROM EDITOR'S DESK

Dear Colleagues,

Although breast cancer risk estimation is now a part of standard healthcare screening in the West; in developing countries like India, it is yet to take off. **Prof. A.K. Attri,** from Chandigarh, in an editorial on **Risk Stratification of Breast Cancer,** has rightly emphasized the fact that optimizing breast cancer screening, creating public awareness and early application of the preventive strategies will go a long way in achieving this goal. This issue contains a series of interesting articles and case reports from different desciplines of medicine, which will provide valuable information to the readers of JIMSA. Published in the issue is an update on '**Sleep Disorders in Neurology**' by **Prof. K.S. Anand** - an entity which has remained under-recognised in clinical practice, though it can have significant cause and effect relationship with some of the life-threatening diseases. In another article, **Dr. Ankur Barua** and his collaegues, focus on a public health problem of **Depressive disorders**, which affect 10% to 25% of the elderly population.

The present issue also contains a 'Symposium' on **'Diabetic Foot-New Dimensions';** contributed by **Dr. Ashok Damir**- a versatile diabetologist with deep interest in this very common and one of the dreaded complications of diabetes and account for over 80% of lower limb amputations in India. I am grateful to Dr. Ashok Damir and his collaegues for brilliantly describing various aspects including gene transfer and stem cell therapy.

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 one years.

(2) Number of awards: Three (3) annually, carrying a gold plated medal, citation and cash prize (1st Rs. 3000/-, 2nd Rs. 2000/-, 3rd Rs. 1000/-)

(3) 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.

(4) Awardees should preferably plan to receive the award at the forthcoming annual **IMSACON 2012.**

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Risk Stratification of Breast Cancer.

Ever since the first reference was made in The Edwin Smith Surgical Papyrus dating back to 1600 BC, number of developments has taken place in understanding and management of breast cancer. Until recently, the primary message of Breast health awareness programs has been that early detection is a woman's best protection against breast cancer. But, with the availability of additional screening and prevention options for women at different levels of risk, breast cancer risk stratification in becoming increasingly popular.

The risk factors associated with breast cancer are grouped into different categories like familial/hereditary (family history, known or suspected BRCA1/2, TP53, PTEN or other known gene mutations associated with breast cancer risk); factors related to demographics (e.g. age, race/ethnicity); reproductive history (age at menarche, parity, age at first live birth and age at menopause); environmental factors (prior) history of irradiation before the age of 30, hormone therapy and alcohol consumption); and other factors (numbers of biopsies, atypical hyperplasia or lobular carcinoma in situ, breast density, body mass index). Based on these risk factors number of risk prediction models exists but none of them is perfect and each has its own limitation. Mitchell Gail developed one of the earliest models in 1989[1]. Though, this model is most commonly used, there are certain major limitations of this model-i) predicted risk increases substantially with the number of previous breast biopsies upto two-irrespective of pathology and ii) it only accounts for first degree relative with breast cancer and does not make any adjustment for age at diagnosis. Therefore, to overcome the limitations of gail model and to incorporate the other breast cancer related risk factors including BRCA1/2 mutations-Claus[2], IBIS by Tyrer and Cuzick[3], and other models were introduced. BRCAPRO and BOADICEA are currently used to estimate the risk based on BRCA mutations[4,5] and more recently breast density is recognized as a tool to assess cancer risk[6]. As none of these models takes in to consideration all known risk factors, no single model is appropriate in all circumstances. Some of these models may underestimate while others may overestimate the risk. To provide patient with best estimate of risk may therefore require use of more than one model and resulting risk needs to be evaluated keeping in mind the known limitation of each model. Breast cancer risk estimates are currently being used to determine which patients may benefit from screening with breast MRI, use of tamoxifen as chemoprevention on surgical risk reduction strategies like bilateral salpingoopherectomy or prophylactic mastectomy and genetic counseling/ testing. The role MRI in addition to routine mammography in detecting early lesions in high-risk women is now well established. It was outcome of the first large scale chemoprevention trial conducted in the United States, the NSABP P-1, that necessitates the need to evaluate breast cancer risk as standard of acre. This trial showed that tamoxifen lowered the breast cancer risk by 49%[7]. Further trails are underway to evaluate other medications that may decrease the risk of breast cancer. Data is also available regarding the efficacy of surgical strategies to reduce breast cancer risk. However, women who are being considered for interventions to reduce risk of breast cancer must be counseled about the demonstrated benefits with potential morbidities of the interventions, as surgical risk reduction strategies may have psychosocial consequences and drugs like tamoxifen is associated with certain adverse effects like endometrial cancer. The risk threshold required for a woman to consider the use of risk reduction therapy therefore must depend on an evaluation of efficacy, morbidity and expense of proposed intervention. Determining the net risk/benefit ratio in turn depends on the ability to quantify accurately a woman's likelihood of developing breast cancer.

Although, breast cancer risk estimation is now a part of standard care in west but, developing countries like India still has to cover a long way in this direction. Lack of awareness because of illiteracy, poverty and access to health care programs is major hindrance. It has been four decades since mammography was introduced as a screening tool to detect non-palpable lesions, but still studies suggest that majority of patients present with advanced stage of the disease. Limited data on the role various risk factors for breast cancer in Indian women, is another reason. No single risk assessment model exists which is based on risk profile of Indian women. Also, the cost of testing and limited knowledge of prevalence of gene mutations responsible for breast cancer in Indian women limits the detection of familial/hereditary breast cancer.

To conclude, it is important to incorporate preventive measures of breast cancer as incidence of affected individuals is rising. Options for breast cancer risk assessment continue to evolve, and risk reduction strategies will expand as well. But for these to be really effective, in optimizing breast cancer screening and prevention, adequate awareness of the population is very essential.

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Prof. A. K. Attri

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JIMSA is now IndMED indexed

*The present issue marks the **25th year** of publication of the **Journal International Medical Sciences Academy.** It is a matter of pride for all fellows/members that Journal Selection Committee (constituted by **ICMR),** in its meeting held on August 3, 2011, **has approved the indexing of JIMSA in IndMED,** the best known Indian Medical Database http://indmed.nic.in. The Journal will host full text of the articles at MedIND http://medind.nic.in and the readers will have access to the full text of articles from **January-March 2003 onwards.** These articles will be linked for IndMED to JIMSA website.*

I wish to express my gratitude for the help and guidance received from the Members of Board of Trustees and the Central Executive Committee members, of International Medical Sciences Academy, World Headquarters, New Delhi. I am also grateful for the valuable cooperation extended by the members of JIMSA Editorial and Advisory Boards; and also the peer reviewers, for their consistent and continuous effort and support to maintain a high standard of quality of the articles published in the journal. Friends, this is an important milestone in the history of our journal; this will broaden accessibility to all published articles. The journal should now attract original articles of even better quality. We should enforce rigorous peer review of the submitted articles and also on time publication of the issue, every quarter.

Dr. P. D. Gulati, Editor, JIMSA

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Breast Cancer Risk Factor Profile in Indian Women.

Navneet Kaur, Amit Attam, Sudipta Saha, S. K. Bhargava

Department of Surgery and Radiology, University College of Medical Sciences & GTB Hospital, Delhi, India

***Abstract**: In India, the incidence of breast cancer is on the rise. However there is little data about the role of various known and/ or presumptive risk factors for breast cancer. This case-control study was conducted on 115 cases with diagnosed breast cancer and 127 controls. Socioeconomic, demographic, reproductive and other known risk factors were analyzed for their prevalence and odds ratio in the study population.*

Prevalence of risk factors determining endogenous or exogenous hormone exposure was low. However there was a statistically significant increased risk with reproductive risk factors such as : early menarche (<14 years vs >16 years, Odds ratio (O.R) 4.36, 95% confidence interval (CI) 108-10.1, p<0.001. chi square test), higher number of live births (<3vs >6, O.R 2.5 ; 95% CI, 1.0-5.7; p=0.026), higher number of abortions (>2 or nil, O.R 4.5; 95% CI, 2.2-9.0; p = <0.001) and duration of breast feeding 9<4vs => 10years, O.R 3.5 ; 95% CI 1.5-7.8; p = 0.006). Height (<145vs >161, O.R 3.0; CI 1.0-9.9; p=0.039), history of breast biopsy (0 vs > 1, O.R 4.6; CI 1.2-16.9; p= = 0.010) and higher mammographic density were found to be independent predictor of risk

(75% VS 0%, O.R 5.9). This study suggests that many known reproductive risk factors have an association with increased risk for breast cancer though their prevalence is low in our population. Breast therapy and mammographic density are independent predictors of risk and may become useful tools in breast cancer risk assessment.

***Keywords:** Breast cancer, Risk factors, Mammographic density, Indian women.*

INTRODUCTION

The risk factors for breast cancer in western populations have been extensively investigated, and it has been suggested that reproductive and life-style related factors are strongly associated with increased risk for breast cancer[1,2]. Various risk assessment models such as Gail, Clause, BRACPRO have been developed and validated in white women[3, 4]. They are used to recruit women for breast cancer screening protocols. However racial/ethnic differences exist in both prevalence as well as risks associated with particulars factors[5,6]. Many low or intermediate risk countries have studied risk factor profile of their populations and developed their own risk assessment protocols[7,8]. Not much data is available about the role of various risk factors for breast cancer in Indian women. A few earlier studies have reported the association of reproductive risk factors with increased risk for breast cancer[9-12]. In this study we examined the stratus of various known and presumptive risk factors for breast cancer and their relative risk in our population.

METHODS

This hospital based case control study was carried out during the period between April 2003 to March 2005 after approval from institutional review board; on 115 cases of histogically confirmed breast cancer; for the control females ≥ 35 years of age, without to the hospital with no complaints related to the breast or gynecological system, were included after an informed consent. Each control was examined in detail to exclude the presence of any breast lump and subjected to screening mammography to evaluate for in-situ lesions. Standardized structured questionnaire was used for the interview. The questionnaire was divided into sections comprising of demography, anthropometric measurements, reproductive history and established and potential risk factors for breast cancer. Mammographic density of the breasts of all controls and contra-lateral breast of breast cancer patients was measured by a qualified radiologist who was blinded to the identity of the subjects. Classification of densities using a six-category scale was done.[13] Demographic profile of cases and controls was compared. Prevalence of various risk factors in the study population was estimated and Chi square test was used to look for any significant difference in both the groups. Odds ratio for each risk factor were estimated with the help of univariate logistic regression analysis. Calculation of odds ratio for the risk factors assessed the relative value of each risk factor in the study population.

RESULTS

A total of 115 female patients with histologically confirmed breast cancer were compared with 123 controls. The maximum number of cases were in the age group of 35-44 years 939.1%), followed by 45-54 years (32.2%). Mean age of cases was 47.14 years and controls was 47.90 years. The most common histological type was infiltrating ductal carcinoma (92.1 %). Sixty eight present of cases presented at stage III or IV of breast cancer.

Socio-demographic data showed no difference in the literacy status between case and control group (58.5% of control and 49.6% of cases were illiterate). As regards religion72.9% of controls and 79.1% of cases were Hindus, 23.4% controls and 19.6% cases were Muslims and rest were Sikhs and Christians. Ninety six percent controls and 96.5% cases were married and over 85% in both groups were housewives. Awareness about breast cancer was recorded in 19.5% of controls and 16.5% of cases. Breast self examination was practiced by 4.8% of controls and 3.5% of cases.

Reproductive characterstics of the subjects (Table 1): mean age os menarchae in case group was 14.05 and control group was 14.85 years. Only 32.2% of cases and 14.6% of control subjects had early menarchae (<13years). Mean age at first live birth was 19.76 in study group and 18.69 in the control group. 67.8 % cases and 79.8% of control subjects had their first issue before the age of 20years. Mean number of live births in the study group were 3.63 and in control group were 4.26. Four control subjects and 3 cases were nulloparous. Majority in either group breast fed for 5-9 years. Mean value for the study group was 5.519 and control group was 7.159 years. As regards the difference between the age at first live birth and age at menarche (AGEFLB-AGEMEN) the mean was 6.2411 in the study group and 4.4958 years in control group. Study group also had

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a significantly higher number of abortions (Mean-1.12) compared to 0.52 in control group. Forty seven percent of cases were premenopausal and 35.7% were postmenopausal. Eight patients had undergo hysterectomy before menopause for benign indications.

Table 1: *Reproductive factors*

Reproductive factors	Cases		Controls		P value
	N	%	N	%	
Age at menarchae (Yrs)					
>=16	10	8.%	41	33.4	
14-15	68	59.1	64	54.0	<0.001(s)
<=13	37	32.2	18	14.6	
Age at the first live birth (Yrs)					
<=17	8	7.1	18	15.1	
18-21	83	74.1	88	74.0	(0.170 9NS)
>=22	21	18.8	13	10.9	
AGEFLB-AGMEN (yrs)					
0-3	17	15.2	52	43.7	
4-6	61	54.4	40	33.6	<0.001 9S)
>=7	34	30.4	27	22.7	
Number of live births					
>=6	18	15.8	25	20.3	
3-5	69	59.9	75	60.9	0.026 (S)
0-2	28	24.3	23	18.7	
Duration of breast feeding (yrs)					
=10					
5-9	14	12.2	30	24.4	
0-4	58	50.4	67	54.5	0.006 (S)
	43	37.4	26	21.1	
Number of abortions					
0	46	40.0	80	65.0	
1	30	26.1	28	22.8	<0.001 (S)
>=2	39	33.9	15	12.2	
Menopausal status					
Premenopausal	54	47	53	43.1	0.575
Postmenopausal	41	35.7	54	43.9	
Hysterectomy/Perimenopausal	20	17.3	16	13.0	

ANTHROPOMETRIC CHARACTERISTICS OF THE SUBJECTS

Mean height of the study group was 155.67 cm and control group was 154.01 cm (p = 0.039). There was no significant difference in the BMI of either group. Mean BMI of case group was 22.800 kg/m^2 and 22.368 kg/m^2 for the control group. BMI when considered separately for pre-menopausal and postmenopausal women was also not different.

Other known risk factors: History of breast cancer in the family was present in 3 patients but in none in the controls. None of the subjects in either group had history of ovarian or endometrial cancer in the family. Fourteen patients and six controls reported use of oral contraceptive pills (OCP) and one patient hormone replacement therapy 9HRT). Majority of subjects were pure vegetarian. None of the subjects in either group consumed alcohol. None had history of ionizing radiation. Three (2.4%) subjects in control group and twelve (10.4%) patients in the case group gave history of previous breast biopsy and the difference was significant.

Mammographic density patterns: (Table 2 & 3): There was no significant difference in distribution of subjects in the two groups according to the percent breast density seen on mammograms. We reanalyzed both the groups after dividing the study population in two age groups, based on the mean age at menopause for both the groups combined. The difference in mammographic density between the two groups was found to be significant in younger women (Subjects M=47 years of age)

Odds ratio for various risk factors: Table IV shows the results of univariate logistic regression analysis. We found that women who had menarche at 13 years years of age had 3.42 times risk compared to women who had menarhcae at 16 years and above. Women with first live birth at 22 years of age and later had 3.6 fold increase in risk of breast cancer as compared to a women with first live birth at 17 years and earlier. The risk of breast cancer rose to 3.8 times when the interval between age at first live birth and menarche was more than 7 years relative to an interval less than 0-3 years. Women with three live births had a 2.5 fold risk of breast cancer compared to women who gave birth to six or more children. Breast feeding of four or less years exposed women to 3.5 fold risk breast cancer compared to women who breast fed for ten or more years. Women with two or more abortions had a 4.5 fold risk of breast cancer as compared to women with no history of abortions. Women with height >=161 cm had a 3.1 times risk of breast cancer as compared to a woman with height <=145 cm. women who consumed non vegetarian food at least once a week were 2.8 timely more likely to develop breast cancer as compared to women who were pure vegetarians. Women with one or more previous breast biopsy had 4.7 times risk breast cancer compared to women with no breast biopsy. Women with breast density of 75% or more, the breast cancer risk rose to 5.9 fold as compared to women with breast density 0%.

Table 2*: Distribution according to mammographic density (%) for age group <=47 years*

Mammographic density (%)	Case group		Control group		Total
	N	%	N	%	N
0	1	2.0	10	14.7	11
0-<10	10	20.4	17	25.0	27
10-<25	8	16.3	10	14.7	18
25-<50	8	16.3	17	25.0	25
20-<75	13	26.5	9	13.2	22
>=75	9	18.4	5	7.3	14
Total	49	100	68	100	117

Chi square value 11.735, p value 0.039 (significant)

Table 3: distribution according to mammographic density (%) for age gropu >47 years

Mammographic density (%)	Case group		Control group		Total
	N	%	N	%	N
0	9	17.3	17	30.9	26
0-<10	18	34.6	16	29.1	34
10-<25	12	23.0	11	20.0	23
25-<50	8	15.4	5	9.1	13
50-<75	3	5.8	6	10.9	9
>=75	2	3.8	0	0	2
Total	55	100	52	100	107

Chi square value 6.236, p value 0.284

Table 4: *Results of univariate logistic regression analysis for all the factors combined*

Risk factors	Beta	Odd ratio	CI of odds ratio	Significance
Age at menarchae 9Yrs)				
=16	1.470	1.000	1.879-10.063	0.001 S
15	1.474	2.348	1.870-10.185	0.001 s
14	2.132	2.365	3.455-20.557	<0.001 s
<=13		3.428		
Age at the first live birth 9Yrs)		1.000		
1-17	0.425	1.530	0.543-4.311	0.421
18	0.742	2.100	0.789-5.591	0.138
19	0.855	2.352	0.850-6.507	0.009
20	1.121	3.068	0.982-9.591	0.054
21	1.291	3.635	1.231-10.731	0.019 S
>=21				
AGEFLB-AGMEN (Yrs)		1.000		
0-3	1.172	3.229	1.386-7.523	0.007 S
4	1.668	3.302	2.292-12.267	<0.001 S
5	1.945	3.492	2.463-19.848	<0.001 S
6	1.349	3.852	1.829-8.114	<0.001 S
>=7				
Number of live births				
>=6		1.000		
5	-0.445	0.641	0.257-1.599	0.340
4	0.113	1.120	0.502-2.500	0.782
3	0.904	2.469	1.069-5.702	0.034 S
0-2	0.525	1.691	0.745-3.836	0.209
Duration of breast feeding (Yrs)				
>=10		1.000		
5-9	0.618	1.855	0.898-3.831	0.095
0-4	1.265	3.544	1.593-7.885	0.002
Number of abortions				
0		1.000		0.053
1	0.622	1.863	0.993-3.498	<0.001 S
>=2	1.509	4.522	2.252-90.80	
Height (cm)				
<=145	0.020	1.000	0.371-2.804	0.968
146-150	-0.210	1.021	0.311-2.109	0.667
151-155		0.810	0.384-2.410	0.934

DISCUSSION

In contrast to a high prevalence of various reproductive factors in women in the west[1,2] we found a low prevalence in our study. Almost similar trend has been in other reports from India as well. In our study, only 32.2% patients and 14.6 % of cases had menarche below 13 years of age. The means age of menarche in our and other studies had been reported to be around 14 to 14.5 years[9, 10]. in our study the average age at first live birth was 19.76 years in cases and 18.69 in controls. First live birth before 20 years of age was seen in 67.8% of cases and 79.8 % of controls respectively. Other studies to report an average age at first live birth as 19.5-20.5 years [9-11]. Mean number of live births in our study were 3.63 and 4.26 in cases and controls respectively. Only four controls and 3 cases were nulliparous. An average parity of 3-5 has been reported in other studies as well.[10, 11] however the difference in number of live births in cases and control was statistically significant in our study as well as other studies. In our study majority in either group (i.e. 50.4% cases and 54.5% of controls) breast fed for 5-9 years. Other studies too report a high rate of breast feeding practice in Indian women[10-12]. Thus it can be seen that though some reproductive factors are significantly more prevalent in breast cancer patients compared to controls, but their overall prevalence is much lower in Indian women than women in the west. In our study only few patients underwent breast biopsy before the onset of illness. (2.4% in the control group and 10.4% in the case group). The difference was found to be statistically significant. Women with one or more biopsy had 4.7 times risk of breast cancer compared to women with no biopsy. However a large proportion of Indian women do not have access to hospitals with facilities for breast biopsy. Illiteracy and poverty further add to the problem. In our population a history of lumpiness instead of history of biopsy should be given some place in risk assessment.

Percent breast density is an expression of the mammary gland mass as a fraction of the total breast area, and thus presumably the total number of breast cells at risk for malignant transformation. There is a significant positive relationship between dense mammographic patterns and subsequent risk of breast cancer and the association has been particularly strong when the exposure is defined as % breast density[14]. In our study we found that the premenopausal women with breast density of 0%. Thus the highest category of percent density was found to exceed the Odds ration of most other risk factors in the study population. In a multiethnic case control study it was found that women with breast density of more than 50% had 3.6 times higher risk of breast cancer than women with less than 10% density, but the risk varied with ethnicity. Whereas the odds ratio was 5.3 for Caucasians and 4.2 for Native Hawaiians, it was only 3.2 for women of Japanese ancestry[15]. In other studies, it was seen that risk associated with dense patterns persisted for 8 years ad was greater in younger women than older women[16, 17]. Thus knowledge of a woman's breast density might be useful in determining the indication for screening.

Limitations of our study are that size of the study population is small and we were not able to do multivariate logistic regression analysis. However our study has identified mammographic density as an important risk factor which has not been investigated in Indian women in any other study so far. Benign breast biopsy and mammographic density need to be evaluated in larger studies for their potential role in risk assessment for breast cancer.

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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 trails* 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) **essentiallity**, (ii) **voluntariness, informed consent**, (iii) **non exploitation**, (iv) **privacy** and **confidentially**, (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 2008)

A Single-masked, Randomized, Controlled Trial of Ginger Extract in the Treatment of Nausea and Vomiting of Pregnancy.

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***Abstract**: In order to evaluate the efficacy and tolerability of an oral ginger extract formulation in comparison to oral fixed dose combination of doxylamine 10 mg plus pyridoxine 10 mg, seventy eight (78) women between 6-16 weeks of pregnancy, complaining of nausea and vomiting (NVP), were randomized to receive either ginger formulation or pyridoxine-doxylamine preparation in a single blind fashion. Efficacy variables were the severity of nausea and vomiting scored by visual analog scale, on the day of each visit, as well as averaged over the past week; the average number of nausea spells or vomiting episodes per day over the past week; and subjective well-being assessed as a binary variable. Study was completed by 63 women (34 on ginger extract). Statistically, no appreciable difference in efficacy parameters was noted between groups. Tolerability of ginger extract was satisfactory with no severe or serious adverse events noted. Ginger extract can provide a safe and effective alternative for management of NVP.*

***Keywords:** Ginger, pyridoxine, doxylamine, nausea and vomiting in pregnancy, randomized controlled trial, Indian medicinal plant*

INTRODUCTION

Approximately 80% of pregnant women experience nausea and vomiting (NVP) to some degree, which usually occurs between 8 to 12 weeks of gestation, although 10% women will exhibit symptoms past the 20th week and less than 1% have the severe form for hyperemesis gravidarum[1]. Many women are hesitant to take conventional medicines for NVP from fear of harming the fetus. However, they are often interested in natural remedies. The pharmacological effects of ginger [Zingiber officinale] has been investigated in various studies ranging from animal experiment top observations in healthy human volunteer and patients[2-4] and the antiemetic potential in pregnancy has been explored in clinical trial[5-7]. Ginger is an important plant in traditional Indian[8-10] and Chinese pharmacopoeias and World health Organization monographs on selected medicinal plants also list nausea and vomiting among indication among ginger[11]. Ginger is also listed in the United States Pharacopoeia[12]. The effectiveness and safety of its use in NVP is being studied more intensively through randomized controlled trials over the past few years[13-16]. Against this backdrop, the present study was conceived to evaluate the efficacy and tolerability of a single ingredient orai formulation of ginger in Indian women suffering from nausea and vomiting of pregnancy.

The formulation in question is manufactured by M/S Lupin Laboratories Ltd., Mumbai, from dried ginger rhizome but not yet marketed. The goal of the present study was to evaluate this monoherbal formulation, LHR-2445AE, for its efficacy and tolerability when used, in recommended doses, in nausea and vomiting of pregnancy. The assessment was done in comparison to an oral fixed dose combination of doxylamine 10 mg plus pyridoxine 10 mg (DOXINATE, of M?s Sigma Laboratories Pvt. Ltd., Mumbai), that is currently widely used in India.

MATERIALS AND METHODS

The resent study was designed as single blind, prospective, randomized, controlled trial and was conducted in accordance with good clinical practice guidelines. Enrollment was subject to signing of the informed consent from by the trial participants. Each of the two participating centers, namely the Departments of Gynecology & Obstetrics at Institute of Postgraduate Medical Education & Research (IPGME&R) and SSKM Hospital, Kolkata and R.G. Kar Medical College Hospitals, Kolkata, received ethical clearance first their respective institutional ethics committee. Subject recruitment period was from November, 2004 to April, 2005.

Subjects were selected only if they sought treatment for the symptoms of morning sickness between 6 to 16 weeks of pregnancy without having received any treatment earlier for the same. USG confirmed singleton intrauterine pregnancy in all cases. Women ere excluded from the study if they were beyond 16 weeks of gestation, had multiple gestation, gestational trophoblastic disease, hyperemesis gravidarum, ovarian cyst, gastroesophageal reflux disease or other forms of acid peptic disorders, chronic or serious diseases of major organs o if the containing food, spices, or beverages, or taking medication other than those permitted but eh study protocol were also excluded.

Subjects were randomly allocated (using computer generated random number list) to one of the following two treatment groups- Group a: the study drug LHR-2445AE, one tablet 9eavh tablet containing 150 mg of standardized extract of dried ginger) three times daily or Group B; the comparator drug DOXINATE, one tablet 9each tablet containing doxylamine 10 mg, as succinate, and pyridoxine 10 mg, as hydrochloride) two or three times daily. The medication was supplied by the sponsor in coded packaging to protect its identity from the subject. This was, however, known to the investigators. For each individual subject, the study consisted of 3 weeks of active treatment, with follow-up visits at the end of first and second weeks. Routine laboratory tests (blood counts, liver function tests, serum creatinine and fasting glucose) were done at baseline and repeated at the end of study to assess safety. The subjects were followed up as per routine hospital protocol till delivery to note any untoward long-term effects in the fetus or mother.

The efficacy variables for this study were the severity of the nausea and vomiting scored by a 100 mm visual analog scale (VAS), on the day of each visit as well as averaged over the past week. The average numbers of spells of nausea or episodes of vomiting per day over the past week were also recorded. In addition, the subjective feeling of

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well-being was assessed as a binary (yes/no) variable at each visit. A diary card was provided to each woman and explained carefully to enable them to keep track of the severity of their problem.

At each visit, subjects were closely questioned and examined clinically to detect treatment emergent adverse events. Compliance was assessed by the traditional pill count method i.e., determined by the balance between the quantity of medication dispensed and the quantum returned as unused. It was graded as excellent if 19 or more days medication was taken, good for 16 or more days medication used and poor for anything less than good.

Statistical Analysis

The study protocol specified that efficacy data was to be evaluated on an intention-to-treat basis for subjects who presented for at least one follow-up visit, but any subject randomized was to be included in adverse event count. Parametric data were compared by the students't test. Non-parametric data was compared within groups by Friedman's analysis of variance followed by Wilcoxon's matched pairs signed rank test, and between groups by Mann Whitney U test. Categorical data were compared between groups by Chi-square test or fisher's exact test. All analysis were 2-tailed with $p<0.05$ as the cut-off level for statistical significance.

STATISTICA version 6 [Tulsa, Oklahoma: Stat soft Inc., 2001] and SPSS for Windows version 11.5 [Illinois, Chicago: Spss Inc., 2002] were the statistical software used for analysis. The initial database was created in Microsoft Access.

RESULTS AND DISCUSSION

Out of the total 78 subjects, 15 subjects [19.23%], six in Group A and five in Group AB were lost to follow-up, and an additional four (two in each group) were non-eligible due to protocol-violation. The difference in withdrawal numbers between groups was not statistically significant. The efficacy analysis, in essence was carried out with the 63 subjects who competed the study as per protocol, since withdrawn subjects did not present for even the first follow-up visit.

There were 82.35% primigravida women in Group A [28 out of 34] and 65.52% in Group B [19 out of 29]- this difference was statistically non-0 significant [p=0.154]. The age and anthropometric profile of the study subjects at recruitment were evenly matched at baseline, with the exception of the height parameter. A median age of 21 and 22 years in two groups, both close to their respective means, indicates a preponderance of young adult women subjects in both the groups (Table 1). Abnormalities were detected in a few women during systemic examination at baseline, including a history of rheumatic fever in one patient in Group A who was on long-term penicillin prophylaxis for rheumatic heart disease. However none were considered serious enough to preclude inclusion into the study.

Tables 2 and 3 present the changes in the efficacy variables in the two groups while the changes in nausea and vomiting VAS scores have been depicted in Figure 1. Evidently, in both groups there was a steady decline in the severity of nausea and vomiting that generally achieved statistically significant improvement from baseline by the time of the second follow-up visit. Vomiting scores in particular showed a precipitous decline, with the median values tending towards 0 at study end in both groups. However, nausea persisted, with considerably reduced severity, in both groups at study end.

Table 1: *Baseline age and anthropometric profile summary of study subjects*

Parameter	Ginger extract Preparation [n=34]	Doxylamine-Pyridoxine preparation [n=29]
Age [Y]	21.7 ± 3.06 Median: 21.0	22.7 ± 4.46 Median: 22.0
Weight [Kg]	47.6 ± 8.38	48.1± 8.29
Height [cm]	151.3± 5.85	147.6 ± 4.99*

Abbreviations are standard; Values are Mean ± Standard deviation, unless otherwise stated.

*p< 0.01 in comparison to group A by independent samples t test.

Table 2: *Serial changes in efficacy parameters in Ginger extract group (n=34)*

	Baseline	End of week 1	End of week 2	Study end
Nausea severity by VAS scores:				
Median	34.50	22.00###	5.50###	0.00###
Interquartile range	25.00	31.50	21.00	10.00
Range	0.00-91.00	0.00-64.00	0.00-78.00	0.00-52.00
Vomiting severity by VAS score;				
Median	14.50	0.00#	0.00##	0.00###
Interquartile range	33.00	18.00	0.00	0..00
Range	0.00-73.00	0.00-72.50	0.00-26.00	0.00-30.00
Average number of nausea spells Per day in the last week:				
Median	3.00	1.76###	1.11###	0.43###
Interquartile Range	3.00	2.57	1.86	2.00
Range	1.00-10.00	0.00-7.28	0.00-11.00	0.00-12.00
Average number of vomiting Episodes per day in last week:				
Median	1.00	0.5.	0.14###	0.14###
Interquartile Range	2.00	1.00	0.71	0.57
Range	0.00-6.00	0.00-5.57	0.00-3.71	0.00-5.50
Average severity of nausea in the last week by VAS score:				
Median	–	29.50	15.70##	5.00###
Interquartile range	—	32.00	25.30	13.30
Range	—	0.00-72.70	0.00-85.70	0.00-89.20
Average severity of vomiting in 'the last week by VAS score;				
Median	—	9.40	2.30##	1.60#
Interquartile Range	—	23.40	9.70	9.00
Range	—	0.00-76.00	0.00-65.1	0.00-88.20

VAS score = Visual Analog Scale Score; Repeated measures comparison by Freidman's test showed highly significant differences (pd"0.001) between time points, with respect to all the parameters; #/##/### denote 2-tailed p< 0.05 / 0.01/ 0.001 in comparison to baseline 9Comparision to first follow-up data in case of last two parameters) by Wilcoxon matched pairs signed rank test.

Table 3: Serial changes in efficacy parameters in Doxylamine-Pyridoxine group (n=0.294)

	Baseline	End of week 1	End of week 2	Study end
Nausea severity by VAS scores:				
Median	30.40	17.00#	10.00##	0.00###
Interquartile range	34.00	30.00	23.00	18.00
Range	0.00-100.00	0.00-100.00	0.00-72.00	0.00-65.00
Vomiting severity by VAS score;				
Median	22.00	0.00#	0.00##	0.00###
Interquartile range	35.00	15.00	11.00	0..00
Range	0.00-87.00	0.00-48.00	0.00-48.00	0.00-47.00
Average number of nausea spells Per day in the last week:				
Median	4.00	2.14###	1.28###	0.60###
Interquartile Range	4.00	1.99	2.28	1.70
Range	1.00-1.20.00	0.00-6.00	0.00-8.00	0.00-7.70
Average number of vomiting Episodes per day in last week:				
Median	2.00	0.43.	0.42###	0.00###
Interquartile Range	2.00	143	1.14	0..60
Range	0.00-6.00	0.00-3.14	0.00-3..30	0.00-2.80
Average severity of nausea in the last week by VAS score:				
Median	–	.37.50	22.00##	7.00###
Interquartile range	—	24.90	28.10	21.80
Range	—	0.00-78.00	0.00-88.00	0.00-70.00
Average severity of vomiting in 'the last week by VAS score;				
Median	—	13.2	10.30##	0.00##
Interquartile Range	—	27.40	18.00	14.20
Range	—	0.00-48.50	0.00-90.00	0.00-26.00

VAS score = Visual Analog Scale Score; Repeated measures comparison by Freidman's test showed highly significant differences (pd"0.001) between time points, with respect to all the parameters;

#/##/### denote 2-tailed p< 0.05 / 0.01/ 0.001 in comparison to baseline 9Comparision to first follow-up data in case of last two parameters) by Wilcoxon matched pairs signed rank test.

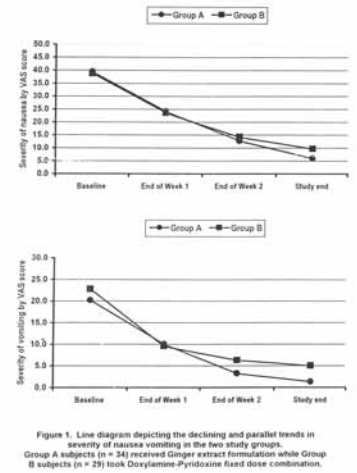

Figure 1. Line diagram depicting the declining and parallel trends in severity of nausea vomiting in the two study groups. Group A subjects (n = 34) received Ginger extract formulation while Group B subjects (n = 29) took Doxylamine-Pyridoxine fixed dose combination.

Between group comparisons of the nausea and vomiting parameters, did not reveal any difference at any time point. Thus the groups were comparable at baseline and remained so at study end and at both the intervening follow-up visits. Similarly, the subjective feeling of well—being showed an improving trend in both groups from baseline to study end, with no inter-group differences at any of the visits (Table 4).

Table 4.: *Distribution of well being status in study subjects at different time points*

Time Point	Group	Well- being YES	Well –being NO
Baseline	A	25 [73.53%]	9 [26.47%]
	B	17 [58.62%]	12 [41.38%]
End of Week 1	A	2 [64.71%]	12 [35.29%]
	B	20 [68.97%]	9 [31.03%]
End of week 2	A	11 [32.35%]	23 [67.75%]
	B	15 [51.72%]	14 [48.28%]
Study end	A	27 [79.41%]	7 [20.59%]
	B	29[68.97%]	9 [31.03%]

* Group A subjects (n=34) received Ginger extract formulation while Group B subjects (n=29) took Doxylamine –pyridoxine fixed dose contribution

* Beween group comparaison was non-0significant at all time points (Chi-square test).

There'was a modest but statistically increase in body weight in both groups, which is to be expected in pregnancy. There was also clinically insignificant (1.5 beats per minute) but statistically significant decline in heart rate in Group A. all other parameters, in both groups, showed no significant deviations from baseline. Between group differences were also minor and neither significant statistically nor clinically. So far as the biochemical safety parameters are considered, there'was no clinically significant difference between baseline and study end means, in either group. A few abnormalities were noted when individual subjects, rather than group means, were considered. This is to be expected in any clinical study. However, the abnormalities present at baseline were not severe enough to preclude inclusion in the study. Similarly, the abnormalities at study end were not severe enough to be reported as adverse events by the investigators. Anemia was noted in a substantial proportion of subjects in each group.

Regarding treatment emergent clinical adverse events, only 1 subject out of the 34 [0.68%] evaluated from Group A, complained of two different adverse events. This was body ache and loose stools, occurring at different times. Two subjects out of the 29 in group B [0.585] suffered from hyperacidity. The duration, in all three instances, was short (<2 days), the intensity moderate, and the outcome satisfactory. None of these events was considered to be related to study drug by the investigator concerned.

Serious adverse events (those that could be fetal, life-threatening, disabling or requiring hospitalization for management) were not encountered during the course of the present study. There were no withdrawals on account of adverse events and both preparations were well accepted by study subjects. Compliance was excellent for 28 subjects [82.35%] in Group A and 22 [75.86%] in Group B. only one subject in each group showed poor compliance.

All subjects reported normal pregnancy outcome without any stillbirths, congenital malformations of the fetus or neonatal complications altogether, 16 subjects out of the total study population of 63 (25.4%) had their pregnancy terminated by Caesarian section at term due to obstetrical indication only. Thus the caesarian section rate found in the study population was not higher than that to be expected in the normal course of institutional deliveries.

The results of the present study are in concordance with other randomized controlled trials conducted recently. This include an equivalence trail, comparing ginger to pyridoxine, in 291 women less than 16 weeks pregnant undertaken at a teaching hospital in Australia[15]. These women took 1.05 g of ginger or 75 mg of pyridoxine daily for 3 weeks, and ginger was found to be equivalent to pyridoxine. In another study in 138 women in a teaching hospital in Thailand[16], ginger 500 mg and pyridoxine 30 mg per day, administered orally in divided doses, for 3 days, proved to be equivalent in relieving the symptoms of morning sickness.

However, the major limitation of the present study has been that the sample size, currently attained, does not give it enough power to detect aq small difference between groups even if that exists. Taking nausea score, as assessed by Visual Analog Scale, as the primary efficacy parameter, and assuming a standard deviation of 20 mm, it would be require 64 evaluable subjects in each group to detect a 10 mm difference in mean nausea scores with 80% power and 5% probability of Type1 error. Another limitationhas been that the study was single masked rather than double masked. The logistical difficulties inherent in genuine double binding is considerable and could notbe overcome in our case.

Therefore, the present study should be viewed as a preliminary report regarding the efficacy of the test preparation in pregnant Indian women.

CONCLUSION

The present study has shown that both the formulations used are effective to comparable extents in reducing the severity of nausea and vomiting, this effect being evident from the end of the first week of treatment. Tolerability of the preparations was excellent, with respect to the clinical safety profile as well as the biochemical parameters. No severe or serious adverse events were encountered and there were no hospitalizations or withdrawals on account of adverse events. Study subjects showed satisfactory compliance. Thus, ginger extract can provide a safe and effective alternative for management of nausea and vomiting of pregnancy in lieu of the doxylamine-pyridoxine formulation that is currently widely used in Indian women, A larger multicentric study, conducted in a double blind design, can provide confirmation of the encouraging trend noted in the current study.

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Matrix Metalloproteinase-2 and its Relation with Incisional & Inguinal Hernia.

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***Abstract**: Abnormal collagen metabolism is thought to play an important role in the development of primary inguinal and ventral hernia. The detection of an impaired collagen balance both in the tissue as well as in cultured fibroblasts underlines the suspicion that the development of hernia is likely to be implemented primarily by a disturbance of the fibroblast function and their collagen genes. Based on these results we assume that the altered collagen synthesis in hernia patients can be regarded as a genetically linked deregulation serving as a basic initiating or promoting factor for the development of primary inguinal hernias. With the hypothesis that hernia is a local manifestation of a systemic disease manifested by increased expression of MMP 2, a study was planned with the objectives : 1)To establish a causal association between incisional & inguinal hernia and MMP 2 ; 2) To test the hypothesis that hernia is a local manifestation of a systemic disorder rather than being a mere local mechanical defect. A case control study was conducted on 10 cases of incisional hernia, 30 cases of indirect hernia & 30 cases of direct inguinal hernia with 30 controls. DAC ELISA test was used for analysis of serum (preoperative) and tissue samples (rectus sheath/fascia transversalis) in patients as well as controls. Statistically, Serum levels of MMP-2 were significantly increased in all the hernia patients as compared to controls. This maximum increment was seen in patients of direct hernia. MMP-2 was not detectable in any of tissue samples. Therefore, we can draw conclusion that hernia is a local manifestation of a systemic disease rather than being a mere local mechanical defect.*

***Keywords:** MMP-2, Matrix Metalloproteinase-2, inguinal hernia, DAC-ELISA, collagen metabolism, PBST- Phosphate Buffer Saline Tween-20, Incisional hernia*

INTRODUCTION

Usually an abdominal wall hernia is regarded as a mechanical problem with a local defect which has to be closed technically, either by sutures or, in modern time with meshes. In the long history of hernia repair, even the most experienced surgeon, irrespective of the utilized technique, has to face recurrences that have been treated by him and correspondingly have to be regarded as his personal technical failure. That's why it is obviously impossible in hernia surgery to make mechanical repair with success rates being expected similar to those for engineering[1, 2].

The close causal relationship between one technical component and its failure is reflected by s-shaped survival curve. If the recurrence is considered just as a technical failure, this should occur either soon or with a certain delay, but in any case the outcome curve should reveal an s-shaped configuration. However, this contradicts the actual proportions. On the contrary, in incisional and inguinal hernia formation, the cumulative incidences show a linear rise over years without any s-shaped deformation[3,4]. This course is in contradiction to any significant direct causal relationship between technique and recurrence. Instead, an underlying multifactor process has to be suggested. Furthermore, because most of the recurrences occur after 1 year within the linear rise of the cumulative incidences, a multifactor process seems to be far more important than any accusable factor of the early postoperative course.

There is a close association between inguinal hernia and collagen metabolism. A decreased collagen types I / III ratio is found in adult patients with groin hernia as well as in the scar of patients with recurrent hernia[5,6]. Collagen type I is characteristic for mature scars or fascial tissue while the collagen type III represents the mechanically instable, less cross-linked collagen synthesized during the early days of wound healing. Correspondingly, in patients with recurrent hernias, there seems to be an impaired maturation of scar tissue which is not able to close the hernia gap or fix the mesh in place for long. Consequently, a recurrence may develop either through a scar or at the border of a synthetic mesh through its scary fixation.

Abnormal collagen metabolism is thought to play an important role in the development of primary inguinal hernia. This view is strengthened by detection of altered collagen metabolism and structural changes of the tissue in these patients. Several connective tissue diseases have been related to an abnormal collagen metabolism. Patients with an aortic Abdominal Aortic Aneurysm[7,8], Ehlers-Danlos Syndrome[9], Polycystic Kidney Disease[10,11] show an increased risk for inguinal herniation. Furthermore, previous studies on protein level indicate that patients with an inguinal hernia present a disturbed collagen proportion with a reduced ratio of type I and type III collagen as well as abnormal ultra-structural changes of the deposited collagen[12,13]. A defective collagen metabolism contributes to a decreased tensile strength and mechanical stability of both the connective tissues and the induced scar tissue. Therefore these alterations in collagen formation should be of central relevance in the pathophysiology of hernias.

The altered ratio of the collagen subtypes can result either by a modified synthesis or by an imbalanced breakdown. The cleavage is regulated by the activity of the matrix metallo-proteinases (MMPs), proteins of a family of zinc-dependent endopeptidases. Among them MMP-1 and MMP-13 are the principal matrix enzymes cleaving fibrillar type I, II and III collagen. In particular, the alterations in MMP-1 and MMP-13 protein expressions could have been responsible for the changed ratio of type I to type III collagen on the protein level. Nevertheless, as firstly shown in investigations by Bellon *et al*. in 1997, cultured fibroblasts in fascia transversalis from patients with inguinal hernia showed no difference in the expression of matrix metallo-proteinase-1, whereas the same author later detected a MMP-2 over expression in these patients[14,15]. These results on protein level appear to suggest that in comparison to MMP-1 and MMP-13, MMP-2 is an active part of degradation system of the extracellular matrix in hernia patients. Based on above facts, a hypothesis was generated that hernia is a local manifestation of a systemic disease which is manifested by increased expression of MMP 2. Thus a study was planned with research objectives to establish a causal association between hernia and mmp 2 and to test

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the hypothesis that hernia is a local manifestation of a systemic disorder rather than being a mere local mechanical defect.

MATERIALS & METHODS

A Case Control Study was designed in which patients admitted in the department of General Surgery of CSM Medical University, Lucknow constituted the study and control group. In study group patients operated for direct, indirect inguinal and incisional hernia (n = 30 each for direct and indirect hernia & n=10 for incisional hernia) were included. Randomization was done according to Table of Random Number Method. Controls (n=30) were age and sex matched patients who were operated for abdominal trauma in emergency. Neither of the controls had any type of abdominal wall hernia. Patients suffering from any type of connective tissue disorder and with chronically raised intra abdominal pressure e.g. COPD, pregnancy, intra abdominal tumour etc were excluded from the study.

Sample Collection and Transportation

Serum Samples: Blood samples were taken preoperatively. Serum was separated from blood after allowing it to stay in a test tube for about 30 minutes followed by centrifugation at 3000 rpm for 10 minutes. Serum was stored in eppendorf vials till further processing.
Tissue samples: In the study group, a section of about 1x1 cm of fascia transversalis tissue (inguinal hernia) & rectus sheath (incisional hernia) was taken while in the control group, section of rectus sheath was taken of same size. Tissue samples were kept in normal saline after washing with distilled water. Both serum and tissue samples were transported to the laboratory at National Botanical Research Institute, Lucknow in ice cooled boxes within 2 hours of extraction. There these samples were kept at –70°C till commencement of the analysis.
Direct antigen coating ELISA (DAC-ELISA) test was done for detection of serum and tissue MMP-2 levels.

RESULTS

All the cases of direct hernia were males, while 8/10 (80%) cases of incisional hernia were females. Amongst indirect hernia, 1 out of 30 patients (3.33%) was female. Controls were aged between 22 to 57 years; the mean age of control group subjects was 35.90±10.67 years; patients of indirect hernia were aged between 22-42 years with a mean age of 31.03±5.60 years and patients of direct hernia were aged between 33-60 years with a mean age of 49.33±7.21 years. The patients of incisional hernia were aged between 30-52 years with a mean age of 43.00±6.98 years.
The mean **serum concentration of MMP 2** in control group was 745.37±30.05 ng/ml with a range from 667 to 803 ng/ml; mean serum concentration in incisional hernia group was found to be 1091.00±286.73 ng/ml (range - 761-1573 ng/ml). while that in direct hernia group was 1473.37±118.95 ng/ml with a range of 1244-1678 ng/ml. Mean value of serum MMP 2 in indirect hernia group was 1076.07±80.06 ng/ml with values ranging from 967-1247 ng/ml, thereby showing a statistically significant difference among groups. (table-1 & diag-1)
Intergroup comparison revealed a statistically significant difference between indirect hernia and direct hernia ($p<0.001$) but no statistically significant difference between indirect hernia and incisional hernia groups ($p=0.986$). As compared to control group, the indirect hernia, the direct hernia group and incisional hernia group had a difference of 330.70±30.76; 728.00±30.76 and 345.633±43.499 ng/ml which was significant statistically. Thus all the study groups had higher mean serum concentration values as compared to control group ($p<0.001$).

Table 1: *Mean serum concentration of MMP2 in different groups*

	N	Mean	SD	Minimum	Maximum
Control	30	745.37	30.05	667	803
Ind Hernia	30	1076.07	80.06	967	1247
DIR Hernia	30	1473.37	118.95	1244	1678
INC Hernia	10	1091.00	286.73	761	1573
Total	100	1097.54	307.0675	667	1678

F=187.264; P<0.001 (ANOVA)

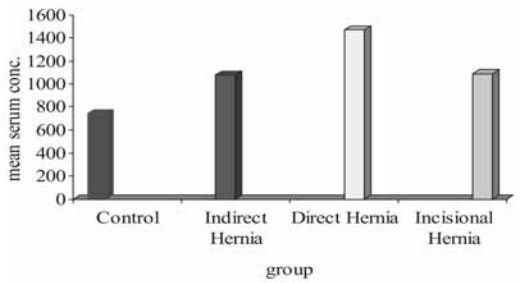

Diagram-1:*Barred diagram Showing mean serum concentration of MMP2*

Intergroup comparison showed significantly higher values in direct hernia in comparision to all the other groups ($p<0.001$).
On the basis of above observations the serum MMP 2 concentration could be shown as:
Control < Indirect Hernia ~ Incisional Hernia < Direct Hernia
Analysis of Tissue samples: We were not able to find any detectable amount of MMP 2 in tissue samples (neither in controls nor in test samples)

DISCUSSION

In a study conducted by J. Smigielski, K. Kolomecki et al from the department of Endocrinological and General Surgery, Medical University of Lodz, Poland in 2007[16], significant increase in serum mmp 2 levels of indirect, direct and recurrent inguinal hernia as compared to controls was found. There was also significant difference with respect to age. The levels were higher in subgroup of younger patients as compared to subgroup of older patients (highest levels were found in young patients with direct hernia). In our study the patients of direct hernia showed highest levels of serum mmp2 but no significant difference was found with respect to age Juan M. Bellon, Ana Bajo, Natalio G et al[17] performed a cell culture of fibroblasts from fascia transversalis of young patients with direct inguinal hernia and observed significant expression of active mmp2. These findings were confirmed by immunosorbent assay, immunoblotting, immunocytochemistry and zymography in the culture media. In our study, we directly used the tissue samples after crushing them in liquid nitrogen. Probably cell culture would have been beneficial for amplification of mmp2 expression. Immunocytochemistry can be more sensitive but it requires long duration of time for sectioning, staining etc. We adopted a simple procedure which was easy to perform and required a shorter time span.
R. Rosch, et al in 2005[18] aimed to investigate the MMP-2 expression in patients with recurrent incisional hernias with and without mesh-materials. In primary fibroblast cultures obtained from skin scars of patients with and without recurrent incisional hernias, MMP-2 synthesis and gene expression were investigated. Furthermore, MMP-2 synthesis and gene expression of fibroblasts were compared after incubation with two different mesh materials: polypropylene and absorbable polyglactin filaments. MMP-2 enzyme activity was determined by semiquantitative zymography and mRNA synthesis by quantitative RT-PCR. Both

MMP-2 enzyme activity and mRNA expression were similar in hernia and control fibroblasts in vitro. In control fibroblasts mesh incubation did not significantly affect MMP-2 expression, whereas polypropylene mesh contact of fibroblasts from patients with recurrent incisional hernias led to a major decrease of MMP-2 activity and of mRNA expression. In the absence of biomaterials fibroblasts from recurrent hernia, patients have no alterations of their MMP-2 synthesis compared to control, whereas a specific response was found after biomaterial contact indicating the differences in fibroblast phenotype.

Based on international research and our own results, we found that increase in MMP-2 activity could be considered to play a significant role in the etiology of inguinal hernias. The increased activity may lead to the dysfunction of collagen fibers, which are responsible for forming fascial structures, and as a result it can weaken their durability.

CONCLUSIONS

Because in present study, there is statistically significant increase in serum MMP 2 levels in patients of indirect and direct hernia both as compared to controls, we can conclude that hernia is not a mere local defect but a local manifestation of a systemic disease. This is more apparent in patients of direct hernia group, as mean serum concentration of serum mmp 2 is highest in these patients. Development of incisional hernia may also be regarded partly as manifestation of systemic effect. However, further study with more Meta analysis is needed to derive a definite conclusion.

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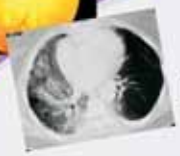

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Effect of Pulsed Magnetic Field on Wound Healing Property in Wistar Rats: A Preliminary Study.

T.M.R. Panicker*, N.S. Jayamohan, M.Kaul Korath**, K. Mohandas*, K Jagadeesan****

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Abstract*:The wound healing properties of Pulsating Magnetic Field (PMF) therapy are well known. The normal healing process manifests in four stages : 1) Debridement. 2) Contraction, 3) Epithelialisation and 4) Remodeling. By exposing the wound to PMF of very low frequency and intensity it was found that the healing process could be accelerated. At our centre a four coil assembly has been fabricated with a function generator which supplied a pulsating electric current of sine wave mode to the coil to treat small animals. Two groups of Wistar rats six in each with artificial wound created on the dorsal area of 1cm diameter, leaving one group to natural healing and the other subjected to daily 30 minutes PMF therapy was given for a period of 15 days. Daily measurement of the wound area was noted in each animal in both groups and rate of healing calculated and responded graphically. It was seen that the experimental group with PMF showed a faster rate though small, than the control group which received no PMF.*

Key words: *Pulsating Magnetic Field (PMF), wound healing process in animal model.*

INTRODUCTION

Magnets are purported to aid wound healing despite a paucity of clear scientific evidence. Although there is ample experimental and clinical evidence supporting the use of magnetic field to aid bone healing, its application for soft tissue healing, including skin and tendons, is still ambiguous. Promising research along these lines was first produced in the 1960s by Becker. Studying amphibians, he described the presence of an electromagnetic skin circuit, alterations which accompanied limb regeneration[1] but still the effects of Pulsed magnetic Field (PMF) on treatment purpose are a promising unearthed area of research. The purpose of this study was to evaluate the effect of pulsed magnetic fields produced by a four coil co-axial assembly one parallel to the other placed in east west directions using a given wave form current from a function generator, which produces a pulsing magnetic field of known frequency and amplitude is used for healing in medicine. In the present project this pulsed magnetic field therapy with low frequency and intensity in sine wave form[2] was used in Wistar rats.

MATERIALS AND METHODS

We used healthy wistar rats weighing 100-150g classified into 1 and II groups each having six animals. Both the animal groups were shaved on the dorso-trunk area, 1.5 cm from the midline. After anaesthetizing with measured quantity of diethyl ether a circular wound was created on both groups, using a skin biopsy punch to ensure maximum uniformity in the area of the wound 9 see plate1. the animals were given standard feed, water, light and temperature environment during study. The test group animals are exposed to PMF of 1Hz of ±250nT of field strength for duration of 30 minutes every day till 15th day and an additional five days observation of the wound is to be carried out. The areas of the wound in test and control animals were measured using tracing paper-graph sheet planimetry every day till 20th day. The wound area was measured in millimeter square in both groups and recorded and the changes in the rate of wound healing area were noted.

RESULTS

The mean rate of contraction of the wound is compared between the control and test groups noting the percentage of decrease I area from 0 day to 20th day. The rate of heating was calculated as the ratio of decrease in area to the preceding area in a given interval in percentage. The mean area of the wound in each animal group versus time elapsed from wound creation was serially measured (Table I & Figure 2) and this was the indicator for the rate of wound healing. The Table 2 depicts the percentage difference of healing in test and control in three days interval in succession till the 15th day, which indicates a tendency of greater delay in healing (figure 3). Regarding the rate of healing related to the test and control groups, the mean value shows a small difference and 'P' value being 0.559, the difference in not statistically significant.

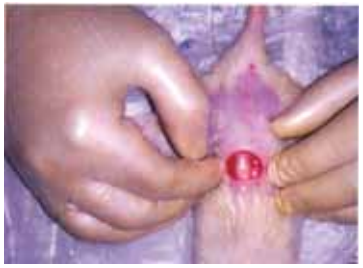

Plate1: *A skin biopsy punch to ensure maximum uniformity in the area of the wound 9 see.*

(X axis shows the percentage of healing)

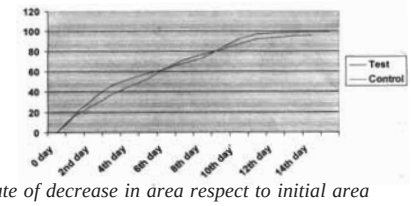

Figure 1: *Rate of decrease in area respect to initial area*

Table 1: *Rate of Healing with respect to initial area*

Days	Percentage of healing in test group	Percentage of healing in control group	Days	Percentage of healing in test group	Percentage of healing in control group
1	18.9	17.1	9	83.1	81.2
2	33.2	27.2	10	92	87.1
3	46.2	37.1	11	91.1	91.9
4	52.5	45.2	12	98.4	93.3
5	58	52.8	13	98.9	95.4
6	62.2	63.9	14	99.1	95.9
7	68.7	71.7	15	99.1	97.8
8	73.3	76.7			

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Table 2: *Percentage difference in Healing*

Days	Test	Control	Days	Test	Control
0-3	2.60%	2.36%	9-12	0.86%	0.77%
3-6	0.90%	1.70%	12-15	0.04%	0.28%
6-9	1.19%	1.11%	**Mean**	**1.118**	**1.244**
			S.D.	**0.93**	**0.81**

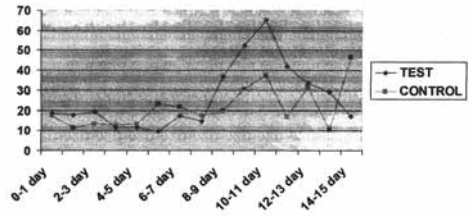

Fig 3: *Rate of decrease in area compared with previous day area*

DISCUSSION

Indirect evidences suggest that PMF therapy could augment peripheral blood flow via reflex vasodilation following epigastric in normal subjects[3]. However there have been no direct measurements of PMF effect on blood flow at the site of application which ultimately would be a target of potential wound healing interventions[4]. Less consistent results have been reported in investigations of the direct effect of magnetic energy on cutaneous blood flow. Miura and Okada showed that the arterioles of frog's webs dilate on response to pulsed electromagnetic radiation. This effect was shown to be independent of heat and was postulated to involve the modulation of calcium balance in vascular smooth muscle cells[5].

The wound contracts owing to the vaso-elastic properties. A wound of say five cm diameter can close completely by the contraction property. This depends on the growth of blood vessels and tissue into the contracting margin of the wound. Exposing the wound to PMF of low frequency and intensity quickens the wound healing[6]. The modes of action of PMF said to be

1. Vaso-dilatation by increasing the local blood supply which accelerates the vasodilatation process[7].
2. Increasing the oxygen supply to the tissues and helpful to control infection as well as increasing the local metabolism[8].

In the present pilot experiment as indicated graphically in fig IV the test group animals as the wound undergoing PMF throughout is showing although not significant a quicker rate of healing. It can also be noted that from 9th day the healing rate variation of test animals become marked as seen in fig IV.

CONCLUSION

We have found that wounds of animals which had PMF therapy healed faster than those which was left to natural process, which was the control group. Whether PMF could be an effective adjunct in quickening the healing processes of the wound could be reconfirmed by taking more number of animals and subjecting them to bigger wounds instead of 1cm diameter.

ACKNOWLEDGEMENT

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LITERATURE REVIEW

Short-term Outcomes of Induction Therapy With Tacrolimus Versus Cyclophosphamide for Active Lupus Nephritis: A Multicenter Randomized Clinical Trial.

Wei Chen , Xueqing Tang, Qinghua Liu, et al. American Journal of Kidney Diseases, Volume 57,(2):235-244. 2011

Intravenous cyclophosphamide with prednisone is an effective treatment for lupus nephritis, but with significant toxicities. We compared the efficacy and safety of tacrolimus versus intravenous cyclophosphamide as induction therapy. Multicenter randomized controlled trial, analysis data on 81 patients with biopsy-proven lupus nephritis from 9 nephrology centers in China from 2006-2008. patients were treated with Prednisone and either tacrolimus (n = 42) or intravenous cyclophosphamide (n = 39) for 6 months. Tacrolimus was started at 0.05 mg/kg/d and titrated to achieve a trough blood concentration of 5-10 ng/mL. Intravenous cyclophosphamide was initiated at 750 mg/m^2 of body surface area, then adjusted to 500-1,000 mg/m^2 every 4 weeks for a total of 6 pulse treatments. The primary outcome was complete remission (proteinuria with protein excretion <0.3 g/24 h, serum albumin ≥3.5 g/dL, normal urinary sediment, and normal or stable serum creatinine level) at 6 months. Response (complete or partial remission), clinical parameters, and adverse effects were secondary end points. After the 6-month induction therapy, the tacrolimus group achieved higher cumulative probabilities of complete remission and response (52.4% vs 38.5% and 90.5% vs 82.1%, respectively) than the intravenous cyclophosphamide group, but differences were not statistically significant (log-rank test, $P = 0.2$ and $P = 0.7$, respectively). Proteinuria (log-transformed) was significantly decreased in tacrolimus- versus intravenous cyclophosphamide–treated patients after the first month of treatment, even with adjustment for baseline proteinuria (protein excretion, 0.01 vs 0.23 g/d; $P = 0.02$). After treatment, serum creatinine levels and estimated glomerular filtration rates were not significantly different between treatment groups. Adverse effects, such as leukopenia and gastrointestinal symptoms, were less frequent in the tacrolimus group. **Conclusions:** In conjunction with prednisone, induction therapy with tacrolimus is at least as efficacious as intravenous cyclophosphamide and prednisone in producing complete remission of lupus nephritis and has a more favorable safety profile.

LITERATURE REVIEW

Mortality and cardiovascular risk associated with different insulin secretagogues compared with metformin in type 2 diabetes, with or without a previous myocardial infarction: a nationwide study. *Tina Ken Schramm, Gunnar Hilmar Gislason, Allan Vaag etal. European Heart Journal 2011, 10, page 1093*

The impact of insulin secretagogues (ISs) on long-term major clinical outcomes in type 2 diabetes remains unclear. Authors examined mortality and cardiovascular risk associated with all available insulin secretagogues compared with metformin in a nationwide study in patients of type II diabetes. All Danish residents >20 years, initiating single-agent ISs or metformin between 1997 and 2006 were followed for up to 9 years (median 3.3 years) by individual-level linkage of nationwide registers. All-cause mortality, cardiovascular mortality, and the composite of myocardial infarction (MI), stroke, and cardiovascular mortality associated with individual ISs were investigated in patients with or without previous MI by multivariable Cox proportional-hazard analyses including propensity analyses. A total of 107 806 subjects were included, of whom 9607 had previous MI. Compared with metformin, glimepiride (hazard ratios and 95% confidence intervals): 1.32 (1.24–1.40), glibenclamide: 1.19 (1.11–1.28), glipizide: 1.27 (1.17–1.38), and tolbutamide: 1.28 (1.17–1.39) were associated with increased all-cause mortality in patients without previous MI. The corresponding results for patients with previous MI were as follows: glimepiride: 1.30 (1.11–1.44), glibenclamide: 1.47 (1.22–1.76), glipizide: 1.53 (1.23–1.89), and tolbutamide: 1.47 (1.17–1.84). Results for gliclazide [1.05 (0.94–1.16) and 0.90 (0.68–1.20)] and repaglinide and [0.97 (0.81–1.15) and 1.29 (0.86–1.94)] were not statistically different from metformin in both patients without and with previous MI, respectively. Results were similar for cardiovascular mortality and for the composite endpoint. **Conclusion** Monotherapy with the most used ISs, including glimepiride, glibenclamide, glipizide, and tolbutamide, seems to be associated with increased mortality and cardiovascular risk compared with metformin. Gliclazide and repaglinide appear to be associated with a lower risk than other ISs.

Acetabular Profile and its Correlation in South Indian Population.

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***Abstract**: Orthopaedic surgeons face great difficulty in placement of screws during uncemented total hip arthroplasty and fixation of acetabular fractures. The screws need to be placed with great care to avoid injury to the nearby neurovascular structures. Knowledge of the important structures and a preoperative determination of the length of the screw would help the orthopaedic surgeons to achieve adequate fixation and hence better results. Literature on the acetabular profile including the diameter and thickness of South Indian acetabuli are scarce. The objective of this study is to find the average acetabular diameter, thickness and to find the correlation between the two in South Indian population. 108 pelvic bones without any pathology were studied. The acetabulum was divided into four quadrants based on standard guidelines. The diameter of the acetabuli were measured along a single plane and the thickness was measured in all the four quadrants using a vernier caliper. The results were analyzed statistically. The mean diameter was found to be 48.74 $\pm$ 3.62 mm. The average thickness of the posterior quadrants was calculated to be about 70% of the acetabular diameter (about 33 mm). Thickness of three quadrants except the antero-inferior quadrant showed a linear correlation with the diameter. The posterior quadrants were found to be the most safe zone for placement of screws and the anteroinferior quadrant the least safe.*

***Key words :** acetabular fractures, acetabular profile, screws, safe zone, correlation*

INTRODUCTION

The acetabulum is an incomplete hemispherical socket with an inverted horseshoe shaped articular fossa[1]. According to Judet and Letournel[2], the acetabulum is supported by two columns of bone-anterior and posterior. The iliac crest, the iliac spines, the anterior half of the acetabulum and the pubis forms the anterior column . The ischium, the ischial spine, the posterior half of the acetabulum forms the posterior column. The acetabular fractures are classified based on the involvement of fracture in these columns. The surgical approach for internal fixation of these fractures is also planned based on the column involved in fractures.

Acetabular fractures are usually due to high energy trauma. The nearby neurovascular structures including the iliac vessels, the lumbosacral trunk and obturator artery are at great risk for injury both at the time of initial trauma and also later during the surgical treatment[1]. Iatrogenic injuries may occur due to the usage of drills, reduction forceps and over lengthed screws during surgery. Also screws with inadequate length fails to achieve adequate fixation. Therefore it is very important for the orthopaedic surgeons to know the average length of the screws that can be placed safely at various quadrants of the acetabulum as a part of the pre-operative assessment. This study is aimed at correlation of the diameter and thickness of South Indian acetabuli and its relevance to clinical application in terms of assessing the safe zone for placement of screws in acetabulum and also a guide for pre-operative determination of screw length.

MATERIALS AND METHODS

For this study, 108 dry hip bones without any pathology belonging to the bone banks of VMKV Medical College, Salem, Annapoorana Medical College, Salem and Vinayaka Mission's Homeopathy Medical College, Salem were utilized. Of these, 58 belonged to right side and 50 belonged to left side. Gender and age of the bones were not determined. Vernier caliper was used to measure the parameters. Four quadrants as described by Wasielewski et al (1990)[3] were determined. Two lines A and B were drawn to divide the acetabulum into four quadrants (R1, R2, R3 and R4). Line A was drawn from the anterior superior iliac spine through the center of the acetabulum Line B was drawn perpendicular to the Line A at the mid-point of the acetabulum (Fig.1). R1 is the antero-superior quadrant. It includes the region of the anterior part of the acetabulum and the pubic bone. The postero-superior quadrant (R2) represented the part lying over the posterior part of the dome of the acetabulum and the postero-inferior quadrant (R3) is the posterior part of the acetabulum and the area over the tuberosity of the ischium. The antero-inferior quadrant (R4) is the inferior part of acetabulum including the part lying in front of the obturator foramen.

***Fig. 1:** Hip bone lateral view showing acetabular quadrant delineation*
***Line A:** From anterior superior iliac spine through the center of acetabulum*
***Line B:** Line drawn perpendicular to the line A at the mid-point of the acetabulum*

The diameter was measured along the line A. Thickness of the acetabular wall was measured in all the quadrants near the rim using a vernier caliper. All the readings were repeated by two other observers by staging method.

The results were analyzed using SPSS 12. 0 system.

RESULTS

The average acetabular diameter was found to be 48.74 $\pm$ 3.62 mm (range 42-56 mm). The mean diameter for 58 right sided bones was 48.39mm and for 50 left sided bones it was 49.09 mm.

The mean thickness of acetabulum was found to be 25.85 mm in R1,

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36.33mm in R2, 33.32 mm in R3 and 5.63 mm in R4.
The correlation between the acetabular diameter and thickess for R1 quadrant (25.85 mm), for example, was 0.504 & R square was 0.254. This was highly significant ($p< 0.01$). R2 and R3 also showed significant correlation ($p<0.01$) but in case of R4 it was not significant ($p= 0.158$) (Table 1).

Table-1: *Correlation analysis of acetabulum (n= 108)*

Quadrant	Mean Thickness (mm)	R	R^2	Significance
R1	25.85	0.504	0.254	<0.01(S)
R2	36.33	0.472	0.222	<0.01(S)
R3	33.32	0.480	0.231	<0.01(S)
R4	5.63	0.158	0.025	0.158(NS)

S-Significant NS- Not significant

The histogram of the dependent variable (thickness of acetabulum) showed a normally distributed curve (Fig. 2). The scatter plot of the dependent variable to the diameter was found to be within the linear best-fit line (Fig.3).

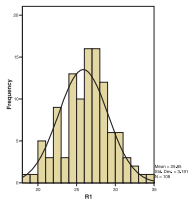

Figure 2 *The histogram of the thickness of acetabulum showing normally distributed "Bell" shaped curve (R1 –Antero superior quadrant thickness of acetabulum in mm)*

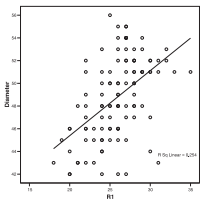

Figure 3 *The scatterplot of the dependent variable to the diameter of acetabulum (R1 – Anterosuperior quadrant thickness of acetabulum in mm)*

Mean thickness at R1 was found to be about 50% of acetabular diameter. The average thickness at R2, R3 & R4 was found to be about 75% , 68% and 11.7% of acetabular diameter respectively. The average posterior quadrant thickness (posterosuperior and posteroinferior) was the maximum (33mm) and it was found to be about 70% of the acetabular diameter . The antero-inferior quadrant was found to have the minimum thickness (about 11 % of acetabular diameter).
Interobserver analysis showed more than 90% agreement (k=90%). It was found to be a better agreement.

DISCUSSION

The average acetabular diameter in our study is found to be 48.74 ± 3.62 mm (n=108). Our findings are similar to that as observed by Eric Vandenbussche et al(2008)[4](48.5 ± 4.4 mm) but differs with that of the average observed by Namchai Varodompun et al(2002)[5] (51.82 mm)in their study on Thai population. Chauhan R. et al (2002)[6] in their study on North Indian hip joints in cadavers, have reported the average acetabular diameter in males on the right side as 47.10 ± 2.09 mm and on the left side as 47.48 ± 3.05 mm. In females they found it as 44.38 ± 3.01 mm on the right side and 46.0 ± 2.28 mm on the left side
Namchai et al(2002)[5] noted the thickness of the postero-superior and postero-inferior quadrants to be 85% and 72% of the average acetabular diameter. In our study the thickness of R1 quadrant was found to be about 50% of acetabular diameter and at R2, R3 & R4 it was found to be about 75% , 68% and 11.7% of acetabular diameter respectively.
The present study revealed that the posterior quadrants (R2 & R3 together) are the thickest quadrants with maximum bone stock and can accommodate screws ranging from 33 mm to 36 mm safely. Stranne SK et al (1991)[7] have reported that the screw fixation over the superior part of ilium, posterior column and over the ischium was the strongest since these areas possess the maximum bone stock for adequate and safe fixation of screws. The antero-inferior quadrant is the quadrant with least thickness and least available bone stock. Transacetabular placement of screws in this quadrant therefore needs special care since improper placement may cause damage to the external iliac vessels, obturator vessels and nerve. Our study showed a statistically significant linear correlation between the acetabular diameter and thickness in South Indian population. Therefore we strongly feel that the diameter of the acetabulum can be used as a guideline in the pre-operative assessment of the thickness of the different acetabular quadrants and length of screws that can best fit that particular quadrant and hence achieve adequate fixation. Gender and Age of the bones were not taken into account in the present study. These factors can be included in future studies.

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Radioiodine Induced Hypoparathyroidism in a Patient of Hyperthyroidism:A Case Report.

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Abstract: *Hypoparathyroidism is a rare complication which can occur 3-45 years after radioiodine therapy. A case of Hypoparathyroidism following relatively small dose of I^{131} given for the management of hyperthyroidism is being reported here for its rarity.*

INTRODUCTION

Hypoparathyroidism following I^{131} therapy in a patient of hyperthyroidism is a rare but recognized complication. A rare case is reported here where a relatively small dose of I^{131} led on to development of hypocalcaemia.

CASE REPORT

A 40 years old non-pregnant lady presented with complaints of palpitation, sweating, and intolerance to heat and marked loss of weight. She was diagnosed to be a case of hyperthyroidism and was put on carbimazole. After 2 months of carbimazole, she developed hypersensitivity reactions to it and it was stopped. Subsequently she was considered for RAI (radioactive iodine) therapy. Her RAI study showed a one hour and 24 hours uptake of 25% and 75% respectively and the thyroid gland measured about 11 gm. She was given 5 millicuries of I^{131}. She presented with severe carpopedal spasm following 3 months of RAI administration and her plasma total calcium decreased to 6.1 mg/dl (normal range 8.5-10.5 mg/dl). She was admitted in the hospital and subjected to various laboratory investigations which revealed Hb 10.2 gm%; TLC 10800/mm^3; DLC P68, L30, E2, E0; Blood urea 35 mg/dl; Serum creatinine 1.1 mg/dl; X-ray chest NAD; ECG revealed sinus tachycardia; T3 1.4 pg/ml (normal range 1.4-4.2 pg/ml), free T4 1.4 ng/dl (normal range 0.86-2.4 ng/dl), TSH 1.2 mcu/ml (normal range 0.23-4.0 mcu/ml) and intact PTH was 1.5 pg/ml (normal range 12-72 pg/ml). She was immediately put on oral calcium and alfacalcidol. On the next day, her plasma calcium increased to 7.3 mg/dl and then the plasma calcium was estimated every 2 weeks. She receive d calcium lactate 10 g daily, alfacalcidol 1 ug daily and inj. Cholecalciferol 3 lakh I.U every 2 weeks for 4 months. At the end of 4 months, her plasma calcium increased to 7.5 mg/dl only. Further she was put on 6 lakh I.U units of cholecalciferol every 2 weeks, which increased calcium levels to 8.2 mg/dl. At the end of 5 months, she had a relapse of hyperthyroidism and free T_3 rose to 3.4 ng/dl, and free T_4 rose to 8.2 pg/ml. she was again put on carbimazole 10 mg daily and responded well. She is now on regular follow up without any ill effects.

DISCUSSION

Hypoclacimia following radiation has been commonly reported in patients of thyroid carcinomas[1] where larger doses of RAI therapy are given postoperatively. It has also been reported following 100 millicuries radiation of I^{131} in a patient of papillary thyroid carcinoma[2].

Few cases of hypocalcemia both permanent and temporary ones following 4 millicuries of RAI therapy have been reported in the literature [1,3,4,5,6,]. The onset of symptoms varied from 5 days to 6 months[1, 3, 6,] while 2 months [5] and more than 3 years[7].

The release of irradiated calcium from thyroid tissue leads to development of hypocalcaemia. Other factors include poor pre-existing parathyroid reserve[2], which makes the individuals to develop primary hypoparathyroidism on account of parathyroid injury.

CONCLUSION

Following I^{131} administration to a patient of hyperthyroidism, the development of hypocalcemia is due to hypoparathyroidism, which is a rare manifestation. Hence the case report.

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Ascaris lumbricoides and Duodenal Perforation : A Case Report.

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***Abstract**: Ascariasis is one of the most common parasitic illnesses in human beings worldwide. The physicians treating patients with ascariasis should be aware of the abdominal complications, since a delay in its management may have fatal outcome . Ectopic locations of the adult worm are a source of diagnostic confusions. Perforation of the gastrointestinal tract is common cause of peritonitis. In most instances, this perforation is caused by peptic ulcer, acute appendicitis, acute suppurative cholecystitis, or trauma. Gastrointestinal perforations resulting from ascariasis is a rare but distinct entity. We came across a patient, 24 years old male, who presented with severe abdominal pain and features of peritonitis. On laparotomy, duodenal perforation was found and ascaris lumbricoides adult worm was found free in the peritoneal cavity .It is suggested that heavy infestation with ascaris lumbricoides makes a diagnosis of intestinal perforation more likely in a patient with an acute abdomen.*

***Keywords** : Ascariasis, perforation, peritonitis*

INTRODUCTION

Ascariasis is one of the most common helminthic disease in humans[1] occurring mostly in countries with low standard of public health and hygiene, thereby making ascariasis highly endemic in developing countries[2]. In endemic areas 30% of adults and 60-70% of children harbour the adult worm[3]. Complications are not uncommon because of the wanderlust of the worm. Ascaris normally infests the small bowel with occasional migration of the adult worm into the biliary and pancreatic ducts, portal venous systems or the abdominal cavity, thereby causing ectopic forms of the disease[4,5]. Ascariasis can cause serious intra abdominal complications such as intestinal obstruction, cholangiohepatitis, biliary obstruction, liver abscess, pancreatitis, acute appendicitis, intestinal perforation and granulomatous peritonitis. Intestinal obstruction is most common complication[6]. The surgeon or physician treating patients with ascariasis should be aware of the abdominal complications, since a delay in management may have fatal outcome[7]. Perforation of the gastrointestinal tract is common cause of peritonitis. In most instances, this perforation is caused by peptic ulcer, acute appendicitis, acute suppurative cholecystitis or trauma. Gastrointestinal perforation resulting from ascariasis was suggested by Ovnatanian in 1959 to be a distinct entity. This is a report of a rare case presentation of ascaris lumbricoides with duodenal perforation.

CASE REPORT

A 24 years old adult male patient was admitted in our hospital with chief complaints of severe abdominal pain for last five days and vomiting and fever for three days. Patient had no history of smoking, he was non alcoholic was not a known diabetic or hypertensive. He had a positive history of passage of altered coloured blood in stools for many years since his childhood. The physical examination showed evidence of malnutrition, mild dehydration and tachycardia. On abdominal examination, there was diffuse tenderness all over the abdomen and guarding was present. On auscultation bowel sounds were absent. Other systems were normal. Laboratory investigations including complete blood analysis, blood urea, random blood sugar, serum creatinine, serum electrolytes, chest x –ray, ECG were done and found to be normal. X- ray examination of the abdomen in sitting position was done and it showed presence of free air under the domes of diaphragm. Patient was taken up for exploratory laparotomy, which was done under general anaesthesia with endotracheal intubation. Abdomen was opened through a midline incision and on exploration it was found that stained intestinal contents in the bile were present in peritoneal cavity. On further exploration perforation of first part of anterior wall of duodenum was found, standard omental patch repair was done by passing three sutures . Upon lavage of peritoneal cavity an adult worm of ascaris lubricoides was found in the peritoneal cavity, which was taken out of peritoneal cavity and measured and found to be 25 cm in length it was stored in a jar (picture 1). Thorough peritoneal toilet was done with normal saline and abdomen closed in layers over a drain. Patient was kept on intravenous fluids and triple antibiotic cover was given. Post operative period was uneventful and recovery was good and patient was discharged after suture removal after 7 days.

DISCUSSION

Ascaris is the earliest recorded human helminth and has a worldwide distribution being prevalent especially in the tropics such as China, India, Bangladesh and South East Asia. Of the clinical diseases which ascariasis cause in human beings, we come across intestinal obstruction, intussusception, ulcer perforation, appendicitis and rarely migration.

Perforation of hollow viscus by an adult worm is well known to tropical surgeons. Two types of intestinal perforation by normal worms are recognized, the primary and the secondary. In the primary type the worm perforates through healthy intestine, while in the secondary type there is associated intestinal disease like enteric fever, or a weakness in the intestinal wall. In primary perforation, it has been suggested that the worm produces a lytic secretion and this

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combined with the nibbling effect of the head of the worm can lead to perforation of the normally impenetrable bowel wall[8].

Intraperitoneal tumoral ascariasis results when the perforation is sealed spontaneously. This situation may be self limiting without recourse to emergency surgery. Destruction of the larvae and the adult worm is usual, but eggs are resistant and result in a specific granulomatous reaction. The presence of viable ascaris eggs suggest that they were deposited on site prior to female adult worm destruction[9].

Ascaris perforation may cause acute diffuse peritonitis, usual symptoms in these patients are abdominal pain and vomiting. Abdominal pain is present in almost all cases with vomiting found in 80% cases and fever in 16% cases. 70% cases usually have typical signs of peritoneal irritation, including tenderness, rebound pain and guarding[10].

It is suggested that signs of infestation with ascariasis lumbricoides make a diagnosis of intestinal perforation more likely in a patient with an acute abdomen. Ascaris has a propensity to migrate from its usual habitat, duodenum, to other areas. It is because of tendency of the adult worm to migrate that even a single worm can cause serious sequelae. Wandering worms may move to any organ of the gastrointestinal system including liver, biliary tract, gall bladder, pancreatic duct, appendix, or to the peritoneal cavity. They may come out of the anus, mouth or nose. The worm may move to the peritoneal cavity through intestinal ulceration or may itself perforate the intestine. The female worm lays eggs which produces a granulomatous inflammation, and itself dies leading to a large abscess, which presents as a tumour like mass in the abdomen, peritonitis associated has a high morbidity and mortality. Surgical intervention is the treatment of choice.

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Case Report

Radiological Features in Actinomycosis of Paranasal Sinus region and Base of Skull with Oro-antral fistula.

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Abstract*: Actinomycosis of paranasal sinus region occurs rarely. It's a clinical and diagnostic dilemma associated with significant morbidity. If untreated it can spread to the base of skull and lead to fistula formation. Computed tomography scan (CT) can reveal the type and extent of disease but the definitive diagnosis is by demonstration of actinomyces on histopathology. The authors report a rare case of actinomycosis of the paranasal sinus region spreading to the base of skull with formation of oroantral fistula; CT scan findings, differential diagnosis and review of literature, has been discussed.* ***Key words:*** *Actinomycosis, paranasal sinus, oroantral, fistula*

INTRODUCTION

Actinomycosis is caused by actinomyces israelii, a commensal bacteria harboring human oral cavity usually around teeth and tonsillar crypts. Its pathologic potential is minimal in normal individuals but is enhanced by trauma resulting in disruption of mucous membranes[1,2]. Out of the three forms; cervicofacial, thoracic and abdominal, the cervicofacial type occurring in form of soft tissue abscess and draining cervical fistulae is the commonest. Sinonasal, laryngeal and pharyngeal disease due to actinomycosis is rarely encountered[1,3]. Actinomycosis involving the base of skull has not been described in the medical literature.

CASE REPORT

A forty years old female with complaint of foul breath and purulent discharge in the oral cavity since 3-4 months visited our department for computed tomography (CT) scan of the nasal and paranasal sinus region. Patient gave the history of tooth extraction in the molar region of maxilla on left side 8-9 months back. Local examination of oral cavity revealed periodontal disease, multiple carious tooth and presence of communication between the oral & nasal cavity on left side with purulent discharge. No evidence of any external abnormality was noted in the facial region. Laboratory examination was unremarkable. Chest radiograph and ultrasonography of abdomen

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was unremarkable.

CT scan of the paranasal sinus region (Figures 1a & 1b) revealed variable degree of osseous destruction & resorption involving left antrum except the posterolateral wall; nasal septum; left lateral nasal wall; maxilla including its alveolar process, hard palate, body and greater & lesser wings of sphenoid with predominant involvement on the left side. Additionally noted was partial destruction of petrous apex on left side, oroantral fistula on left side and multiple sequestra especially on the left side. There was partial destruction of osteomeatal unit complex on right side as well. Mucosal thickening was noted in the bilateral inferior turbinate and right antrum along with partial opacification of the ethmoid air sinus complex on both sides. There was no evidence of any obvious mass or sclerosis / reactive bone formation except in the posterolateral wall of left antrum.

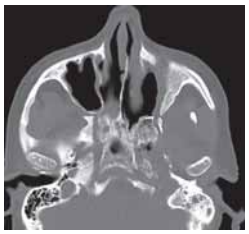

Figure 1a: *Transaxial CT image shows osteolytic destruction of medial and anterior wall of left antrum, nasal septum, sphenoid bone and petrous apex on left side along with opacification of mastoid air cells of left side*

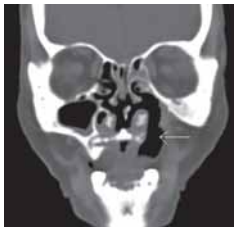

Figure 1b: *Transcoronal CT image shows osteolytic destruction of medial and lateral wall of left antrum, nasal septum and hard palate with formation of oroantral fistula on left side (arrow) along with partial opacification of ethmoid sinuses and mucosal thickening in the right antrum*

Based on the clinicoradiologic findings, the diagnosis of low grade / granulomatous chronic osteomyelitis involving nasal cavity, paranasal sinuses, hard palate and base of skull along with formation of oroantral fistula on left side was suggested. Biopsy of bone was suggested for further work up.

Histopathology of the biopsied bone fragment revealed areas of necrosed bone and degeneration of connective tissue stroma with chronic inflammatory cell infiltrate (figure 2). In addition, colonies of microorganisms with branching filaments were also noted. Modified acid fast staining ruled out Nocardia. Hence, the histopathological diagnosis of chronic osteomyelitis with actinomycosis as an etiologic agent was made.

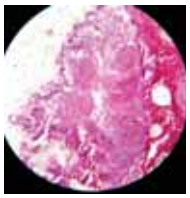

Figure 2: *H & E stained slide (high power) shows presence of colonies of microorganisms with branching filaments (sulfur granules).*

DISCUSSION

Actinomycosis is an uncommon chronic suppurative infection caused by actinomyces that are normal commensals of human oral cavity and pharyngeal region[1]. In this era of antibiotics, they rarely assume parasitic and pathologic role resulting in significant morbidity. Poor oral hygiene, oral disease and oral trauma are the predisposing factors for actinomycosis[4,5]. The disease is commoner in males and in middle aged and elderly, but uncommon in children, probably reflecting the higher incidence of periodontal and dental disease in higher age groups[4,6]. The disease is mainly seen in the tropics including Asia and Africa[6].

Actinomyces are slow growing, gram positive, anaerobic, non-acid fast, filamentous bacilli producing typical yellowish sulfur granules. They spread locally rather than by hematogenous or lymphatic route[5].

Cervicofacial region involvement is commonest. Ingestion of organisms results in abdominal involvement, while tracheobronchial aspiration results in thoracic involvement. Rarely, pelvic involvement may be associated with use of IUCD[4].

Irrespective of the region of involvement, the commonest feature is formation of phlegmon with increasing induration and fibrosis and resultant decrease in vascularity over several weeks followed by formation of discharging sinuses. But acute form with rapid suppuration is also seen[1]. The commonest site is cheeks, angle of jaw or submandibular region. The infection may spread contiguously to the adjacent areas disrupting fascial planes. Oral infection may further involve pharynx, larynx, salivary glands, tonsils and paranasal sinuses. Involvement of paranasal sinuses is rare and only few cases have been reported[1]. Involvement may occur in the form of pseudotumors causing sinus opacification; mucosal thickening and destruction of bony walls especially the medial wall. Destruction of posterior wall of antrum favors a malignant pathology[1]. Presence of hyperdense hyphae and calcification seen characteristically in fungal infection is absent in actinomycosis. Rarely actinomycosis can appear as an enhancing mass on CT scan making it difficult to differentiate from masses[7]. There may be formation of fistulas[4].

Primary actinomycosis of bone is rare, as seen in our case and is the result of adjacent soft tissue involvement. Unlike our case, where maxilla was involved, involvement of mandible is commoner by four times[4]. Osteolytic destruction ranging from minimal rarefaction or periosteal reaction to extensive osteomyelitis with sclerosis and periosteal reaction is the predominant radiologic manifestation. Sometimes, the appearance of osseous tumor may be simulated[4]. Besides, there may be formation of interosseous sinus tracts. In our case, extensive and contiguous osteolysis of bones of face & base of skull with formation of multiple sequestra was a predominant radiologic finding along with oroantral fistula and absence of any significant sclerosis or periosteal reaction except in posterolateral wall of left antrum, making it probably first instance of its type in medical literature.

Diagnosis of actinomycosis is based on the demonstration of sulphur granules in exudates, culture or histopathology[1]. Sulfur granules are, in fact aggregates of filaments of bacteria.

Radical excision of the sinus tracts, wherever possible along with heavy and prolonged doses (3-12 months) of penicillin is the treatment of choice[1,4]. Oroantral fistula can be closed successively by buccal flap advancement.

To summarize, primary actinomycosis of bone involving paranasal sinuses and base of skull is rare and is best evaluated by computed tomography which not only determines the extent of involvement but also helps to narrow the differential diagnosis and in deciding the site of biopsy. Actinomycosis should be suspected if there is extensive osseous destruction especially involving the medial wall and preserved posterior wall with absence of hyperdense hyphae.

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Chronic Intestinal Ischemia with varied Presentations: A Case Report

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***Abstract**: Acute or chronic intestinal can be the result of many different pathophysiological processes. Presentation may be benign to life threatening, if not recognized swiftly. We present two acs4es of chronic intestinal ischemia with varied presentation resulting in hypoplasia of the intestinal wall with smooth serosa in one & hyperplasia of the intestinal wall in the other. Both patients underwent physical examination, blood analysis, X-Ray chest, abdomen & selective superior mesentereric arteriography (SMA). One patient showed filling defect at the root of SMA with poor blood flow and occlusion at the distal ileocolic artery suggestive of acute embolism of SMA with no bowel necrosis. Thrombosis was attached to the wall of SMA with 40- to -60 cms long ileum of sausage consistency and cyanotic at about 50cm from the caecum. In the other patient angiography showed an occlusion of SMA and formation of a huge Riolan's arch. The intestinal wall was like paper –thin. In one patient surgical embolectomy of the SMA and resection of disease, segment of ileum with end-to-end anastomosis was carried out. In other patient, an aorto-superior mesenteric bypass was done and the pulsation of the SMA returned. Postoperative recovery of both the patients was uneventful.*

***Keywords:** Intestinal ischemia, Small bowel ischemia*

INTRODUCTION

The diagnosis on intestinal ischemia begins with the ability of the clinician to suspect and recognize it. The clinical history of abdominal pain and non specific findings may be misleading. However, common clinical conditions should be quickly excluded and mesenteric vascular disease aggressively pursued, traditionally, conventional angiography has been regarded gold standard imaging method. Approximately 90% of patients with acute mesenteric ischemia who undergo angiography before the onset of peritoneal signs survive, demonstrating the value of angiography and early diagnosis. Advantage of angiography includes the ability for concomitant endovascular treatment. Multiple therapeutic approaches are available for intestinal ischemia, depending on acuity and extent of disease. Resection of infracted bowel as well as embolectomy can be accomplished during surgery.

CASE1

1 65 years old male was admitted to our hospital due to severe acute abdominal pain, nausea without vomiting for 3 days in Feb 2004. On examination abdomen was soft, and bowel sounds were present. The while cell count was 11,200/cmm, LDH 433 IU/L and Plain Abdomen X/Ray revealed intestinal distension in the right half of abdomen, Stool was positive for occult blood. He did not give past history of intermittent abdominal pain. Diarrhea, constipation, weight loss or diabetes. He had atrial fibrillation for 8 years. Selective superior mesenteric arteriography showed filling defect at its root with poor blood flow and on occlusion at the distal ileocolic artery. Collaterals between the common hepatic artery and SMA could be seen (fig 1a). a diagnosis of acute mesenteric embolism was made and before surgical SMA embolectomy, laparoscopy was planned, which showed no bowel necrosis. Patient did not consent for surgical embolectomy and was managed conservatively with 2,50,000 IU of urokinase perfusion via the angiographic catheter inserted into the SMA for angiography and the catheter was with drawn. He was discharged on 10^{th} day of admission.

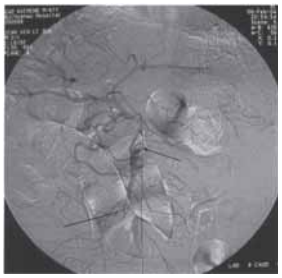

Fig 1a. Superior mesenteric arteriography with filling defect at its root and an occlusion of the distal ileocolic artery. Collaterals between hepatic artery and SMA seen.

Fig 1b. Intestinal wall hypertrophy with mesenteric involvement and narrow lumen.

After 6 days, he was readmitted with intolerable abdominal pain for nearly 16 hours. He was febrile. X-Ray abdomen showed multiple air fluid levels. This time, again he was managed conservatively in hospital for $3^{1/2}$ months. He lost 13 kg of weight. This time patient's family agreed for surgical embolectomy surgical embolectomy showed thrombus with partial fibrosis attached to the wall of artery. Approximately 40-60 cms long ileum sausage like-in consistency, cyanotic in color with smooth serosa at about 50 cm proximal to Caecum was found. Proximal intestine was slightly dialted, no other intestinal and peritoneal lesions were found. The diseased segment of ileum was resected with end-to-end ansatomosis.

The removed ileum was markedly thickened, hypertrophied without irregular appearance and with a much-narrowed lumen (fig 1b). On histopathology "an usual widening in the layers of sub mucosa and serosa with fibrous proliferation and cell infiltration mainly lymphocytes and plasma cell.

The patient had an uneventful recovery and was discharged after 10 days. Follow-up six months later he was completely asymptomatic

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and had gained 12 kg weight.

CASE 2

Another patient 69 years old woman had repeated abdominal pain and lower gastrointestinal bleeding for one and half year. She was anemic (Hb 4g %) and had lost 8 Kg weight. Angiography showed an occlusion of SMA and formation of a huge Riolan's arch. During surgery, intestinal wall was found thin like layers of paper in some areas, light of colonoscopic illumination could easily be seen from the lumen of thin layer intestine. After aorto-SMA bypass, the SMA pulsation could be felt and seen. Postoperative recovery was uneventful. She became asymptomatic, gained 5 Kg weight. Hemoglobin rose to 10G% at 4 weeks and was discharged.

DISCUSSION & CONCLUSION

Arterial insufficiency or ischemia produces the target tissue or organ hypoplasia even necrosis as in our case of mesenteric insufficiency and remarkable hypoplesia of the intestinal wall[1].

The variable vessels involved. Location of bowel affected, and different levels of acuity of illness all result in multiple possible presentations. The detection of such a serious condition can be a diagnostic and therapeutic dilemma[2]. The varied presentation seen in the two cases where in one had hypoplasia and the other had hyperplasia is rather perplexing. Could this be related to the rapidity of onset, duration and degree of ischemia? Could it be that different layers or parts of layers of intestine behave differently to ischemic insult?

Embolic occlusion of the superior mesenteric artery occurs in more than half of all cases[3]. Most emboli originate in the heart and are potentiated by cardiac arrhythmias or depressed systolic function due to ishaemic heart disease. In our case, unnecessary delay increased morbidity of the patient though this patient was lucky to have uneventful recovery after surgery.

Mesenteric ischemia most often results from SMA embolization or thrombosis, and less commonly, venous occlusion or nonocclusive process. Remobilization of the SMA accounts for nearly 50% cases, with thrombosis responsible for another 25% of cases[4, 5]. In our case, perhaps atrial emboli were responsible.

Conservative treatment with thrombolytic therapy did not help our patient. In fact, unnecessary delay could have jeopardized patient's survival. In most cases, as in our both cases surgical exploration was emergently performed to restore intestinal arterial flow and resect irreparably damaged bowel. Very thin ischemic bowel in second case is in contrast to the first case where ischemic bowel segment was remarkably thickened or hypertrophied with smooth and normal serosa without any other lesions. We fail to understand as to why is two cases where same etiology of mesenteric ischemia could lead to different pathological processes?

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Case Report

Ileal Carcinoid Tumor mimicking Carcinoma Cecum.

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Abstract*: We report a 28-year old female admitted to the surgical ward with pain and lump in right lower abdomen; on careful examination and inhertigation a presumptive diagnosis of carcinoma caecum was made. A standard right hemicolectomy was done. However, the histopathalogical report demonstrated carcinoid tumor in the ileum with free resection margins. Immunohistochemistery confirmed the diagnosis of carcinoid tumor ileum.* ***Keywords:*** *Carcinoid tumors, carcinoid syndrome, 5HIAA.*

INTRODUCTION

Historically, the term carcinoid was first coined by Oberndorfer in 1907[1]. The prevalence of carcinoid tumors is expected to be around 0.5 per 100,000, although autopsy studies suggest that it may be as high as 2 per 100,000[2]. In the great majority of cases, carcinoids remain silent. Symptomatic carcinoids declare either through their mass effect (pain, luminal obstruction) or secretary products. Carcinoid syndrome consists of a constellation of symptoms which arise as a result of massive release of serotonin and neuropeptides directly into the systemic system[3]. It has been observed that patients with carcinoids have an increased risk of developing secondary neoplasms[4]. Urinary 5-HIAA measured in a 24-hour urine sample is the most frequently applied test in the endocrine work-up of the carcinoid tumors[5]. Chromogranin A, a glycoprotein secreted y the neuroendocrine cells, has 80% sensitivity to carcinoids and serves as a valuable marker in the early detection of recurrences and during follow-up after the primary treatment[6]. Carcinoids frustrate the physicians by the complex symptoms and varied biochemical affections and demand a high index of suspicion. Surgery is the treatment of choice for such lesions, and patients should be follow-up with serial urinary 5-HIAA assays and somatostatin receptor imaging, where available.

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CASE REPORT

A 28-year old female presented to the surgery OPD of Rajindra hospital, Patiala, with pain and lump in the right lower abdomen of 15 days duration. Pain was of moderate intensity, off and on and aggravated after meals. Patient's examination revealed a mass in the right iliac fossa of approximate size of 10 X 10cm. it was nontender, mobile, firm. Non ballotable, with irregular surface and was dull on percussion. Routine blood investigations and abdominal X-rays (erect and supine) were unremarkable. An abdominal/pelvic ultrasounds showed around 180 ml fluid collection in the right iliac fossa, and reported this as appendicular abscess. Ct scan showed a neoplastic mass 8X7.7 cm in size, irregularly marginated, involving ileocaecal junction, cecum and the proximal ascending colon causing luminal narrowing, along with some small areas of necrosis within this. In ultrasound and CT liver was normal; there were no secondaries in liver. Barium enema showed a large filling defect in proximal ascending colon and caecum with mucosal irregularities and this was also reported as growth in the cecum. Operative findings demonstrated a big mass in the cecum. A standard right hemicolectomy was done with removal of 15 cm distal ileum, and an ileotransverse was done. Postoperative period was uneventful.

The histopathology reported carcinoid tumor in the ileum. There was no penetration of the muscular or serosal layer and the resection margins were free of tumor. On immunohistochemisttry, the tumor cells were positive for neuron specific enolase and focally positive for chromogranin, confirming the diagnosis of carcinoid tumor of ileum. The patient was planned to be regularly reviewed in the surgical clinic every 6 months for 3 years with urinary 5-HIAA assays.

DISCUSSION

In the present case there was no feature suggesting carcinoid syndrome. The presentation was with a palpable mass in the right iliac fossa along with CT (Fig-1) and barium finding suggesting the same; it was considered to be like a classical case of carcinoma cecum. Accordingly a right hemicolectomy was carried out. Even the gross specimen of Rt. Hemicolectomy (Fig.2) suggested a cecal tumor. Only on cut section (fig.3) it was found that there was no tumor in the lumens of

Fig.1 Gross specimen of right hemicolectomy of patient showing big mass in cecum

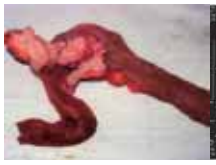

Fig.2 Cut section of specimen showing ileal carcinoid encroaching the cecal lumen

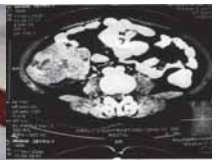

Fig.3 CT abdomen of the pt showing cecal mass

cecum although the lumen was being encroached upon by the big tumour which was actually in the terminal ileum. Histopathology and immunohistochemistery subsequently confirmed this to be carcinoid tumor.

On as exhaustive search of literature about ileal carcinoid clinically mimicking a carcinoma of the cecum, we could not find a single such reference. Hence it was considered fit for this case to be reported for its rare presentation. To conclude it is suggested that ileal carcinoid should also be kept in mind while evaluating a right iliac fossa mass, and should be considered in the differential diagnosis of cecal carcinoma as management is entirely different for both.

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Case Report

Rifampicin Induced Thrombocytopenia:A Case Report.

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Abstract: *Rifampicin is an essential drug in the treatment regimen for tuberculosis. It is generally well tolerated. But very rarely it can cause serious adverse reactions in the form of acute renal failure and thrombocytopenia. A case of acute thrombocytopenia occurring in a patient on Rifampicin for the treatment of pulmonary tuberculosis is being reported here.*

INTRODUCTION

Rifampicin is a crucial drug as well as essential component of the treatment regimen for tuberculosis. Apart from minor adverse effects in the form of nausea, vomiting and rash, very rarely it may cause life threatening side effects like acute renal failure and thrombocytopenia[1, 2].

The first case of Rifampicin induced thrombocytopenia was reported

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by Blajchman et al (1970) [3]. It is properly reversible if detected early.

CASE REPORT

A 45 year old male weighting 52 kg, nondiabetic, non hypertensive, chronic biri smoker since 10 years, non-vegetarian presented with complaints of cough, fever, dyspnoea and loss of appetite since $1^{1/2}$ mild anemia and pedal edema. There was no jaundice or clubbing. Chest examination revealed crepitations in apices of both lungs. His laboratory profile revealed Hb. 9.8gm%, TLC 16800/33[3], DLC P -$_{70}$L$_{28}$E$_{1}$M$_{1,}$ ESR 90 mm at the end of the first hour, Mantoux text +ve with 15 mm induration. HIV eliza was non reactive, ANA test and antibodies for dengue were also negative. Sputum smears on occasions were positive for tubercle bacilli by fluorescent microscopy, confirmed later on by positive cultures. X-ray chest showed infiltration of both lungs apices. Liver and renal profile was normal. In view of the sputum positivity, clinical findings and x-ray chest, he was put on treatment in the form of Rifampicin 600mg, isoniazid 300 mg, ethambutol 1000 mg, pyrazinamide 1500 mg daily for 2 months along with antianemic and supportive therapy. He was discharged from the hospital and advised to continue rifampicin 600 mg and isonizid for 4 months more. But after taking the therapy for 6 months, he reported back with hemorrhagic spots on the lower extremities. On examination, there was large sized ecchymosis involving lower extremities. But he was well oriented and afebrile. Investigations revealed a platelet count of 20,000 cells/mm^3 and bleeding time 6 minutes and clotting time of 12 minutes. Liver and renal profile were within normal limits. Bone n=marrow biopsy revealed megakaryocytosis. A diagnosis of acute thrombocytopenia was made. The patient was treated with I/V fluids, inj. Hydrocortisone 200 mg I/V thrice daily. Rifampicin was also stopped. The bleeding subsided with improvement in his general condition as well as improvement in the X-ray chest after continuous treatment with isoniazid, ethambutol and pyrazinamide without adverse effects. Rechallenge with 600 mg of rifampicin resulted in fall of platelets from 160000/mm^3 to 10200/mm^3 within 4 hours with positive antiplatelet lgG and lgM antibodies. Rifampicin was again stopped and patient continued on other antitubercular drugs. The steroid dose was gradually tapered off and shifted to oral prednisolone tablets 20 mg thrice daily which was also stopped after tapering off. He was discharged with a normal platelet count 2,30,000/mm^3 and bleeding time of 2 min and clotting time of 3 minutes. However the patient was lost on follow up.

DISCUSSION

The most common causes of thrombocytopenia are vital or bacterial infections, autoimmune disease, collagen vascular disorders including SLE, Myelolymphoproliferative disorder including leukemia, anemia including aplastic anemia, HIV, massive blood transfusion, hypersplenism, alchoholism, surgery, osteopetrosis, bone cancer, pancytopenia, DIC, dengue, leishmaniasis, syphilis, myelodysplastic syndrome, prosthetic heart valve, Gaucher's disease, snake poisoning, blood poisoning, non Hodgkin's lymphoma, thrombotic thrombocytopenic purpura, eclampsia and idiopathic thrombocytopenic purpura.[4] Important drugs[4] which may cause thrombocytopenia include chemotherapeutic agents, sulphoanamides, penicillins, cephalosporins, heparin, thiazide diuretics, pentamidine, valproic acid, PAS, cotrimaxozole, mercaptopurine, vancomycin, methyldopa, indomethacin, ticlopidine, captopril, quinidine, and sirolimus etc.

An extensive review of the literature revealed rarely occurring rifampicin induced thrombocytopenia[6-9]. It has been postulated that with the daily use of Rifampicin, there is neutralization of any antibody formed and the immune complexes are continuously removed without causing any allergic reactions[10]. In our patient, rifampicin induced thrombocytopenia may be due to formation of immune complexes which absorb to the platelet membrane resulting in platelet damage and their rapid removal from the circulation[3,4]. The binding epitope of the lgGantibody was found in the glycoprotein Ib/IX complex which is the target in Rifampicin induced immune thrombocytopenia[11,12]. Our patient recovered completely on stopping the drug along with steroid therapy.

Rechallenge and de-challenge of a drug are established tools but not accepted technique for the diagnosis of adverse events.[13] Bassi et al[14] found Rifampicin dependent antibodies in 10 out of 32 patients three weeks after discounting 600 mg daily. No antibodies were found the day after treatment was stopped. Any delay in re-treatment allows a sufficient amount of antibodies to build up during the antigen free interval. Occasional patients with platelet counts <10000 to 20000/- mm^3 hav-e severe hemorrhage and may require plasmaphresis or platelets transfusion while waiting for the platelet count to rise[4].

CONCLUSION

The presentation of this case report is to enlighten the medical fraternity about the rare occurrence of the life threatening Rifampicin induced thrombocytopenia which if detected early is completely reversible on stopping the drug. These patients must be instructed to avoid the offending drug in the future, since early minute amounts of drug are needed to set up subsequent immune reaction[4].

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APEAL

Readers of JIMSA are requested to send their suggestions regarding any alteration in the Scientific Content and Overall Format of JIMSA.

Editor, JIMSA

Vertigo with Migraine: A Diagnostic Challenge.

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Abstract: *Migraine and vertigo are both common disorders and therefore both may coexist,just by chance. However a entity called migrainous vertigo or migraine associated vertigo is being increasingly recognized. We here present a case of a 28 years old lady with history of recurrent episodic vertigo since last 3 years and migrainous headaches since last 5 years. She was suspected as a case of migrainoous vertigo and started on treatment with flunarizine 10 mg HS, following which both her headaches and vertigo responded. Treatment was slowly tapered off in 4 months and there after she was followed up for 6 months. In these 10 months her headaches aand vertigo have not recurred.*

INTRODUCTION

A strong association exists between migraine and vertigo.When recurrent vertigo attacks begin at an early age in patient with normal hearing and migraine,there are few other diagnoses other than migrainous vertigo that need to be considered[1]. Neuro-otological manifestations of acute MV are heterogeneous. Few patients show spontaneous nystagmus indicative of central vestibular dysfunction.In cases with predominantly torsional spontaneous nystagmus,a dysfunction of the vestibular nuclei at the pontomedullary junction or midbrain is most likely, while downbeating nystagmus indicates dysfunction of the vestibulocerebellum or underlying medulla and upbeating nystagmus is commonly reported with midline medullary lesions. Positional nystagmus of a central type has been reported in posterior fossa lesions adjacent to the fourth ventricle presumably involving an inhibitory loop between midline archicerebellar structures and the vestibular nuclei. In contrast few patients with predominantly horizontal spontaneous nystagmus and contralaterl semicircular canal paresis point to acute peripheral vestibular dysfunction[1,3]. There usually is no temporal relationship between migraine and vertigo attacks.A marked female preponderance has been recognized[6]. There is a possible casual relationship and its has been postulated that a migrainous aseptic inflammation probably creates a central sensitivity that spreads from trigeminal to the vestibular system[7].Treatment of MV currently paralles that of migraine headache,as proper studies of optimal MV management are just beginning[7]. Studies have shown topiramate to be effective in reducing the frequency and the severity of vertigo and headache attacks.The 50 mg/day dose seems to be appropriate as higher adverse effects were noted when 100 mg/day was used[2]. As for the acute attacks,several case reports have revealed variable treatment options.one study has revealed usefulness of intravenous methylprednisolone in abating the acute attacks[8]. Patients of MV usually have an attenuated or absent headache with their vertigo as compared with their usual headache of migraine.It has been reported that patients of MV when gives tripants suffered induction or exacerbation of headache with disappearance of vertigo, which may suggest that headache and vertigo of migraine may be inversely related to each other and suppression of one may induce or aggravate the other[4].

CASE

We present a case of a 28 years old lady with history of episodic rotational vertigo,lasting few days, occurring atleast once in six months since last 3 years. There was no history of tinnitus or subjective hearing impairment during the attacks of vertigo. She had motion induced dizziness since childhood.Since the age of 23 years she also had a history of episodic unilateral throbbing headaches association with nausea and occationally vomitings,photo and phonophobia and sometimes dizziness.The attacks occurred once in 15-20 days. No specific triggers had been identified. She had been diagnosed as a case of migraine without aura but was not on any prophylactic treatment for the same at the time of our evaluation. She was advised sumatriptan 25 mg tablet whenever headache occurred. No history of head trauma. On examination at the time of vertigo,she had normal hearing, rinne's and weber test and no evidence of positional nystagmus. She underwent routine and otoneurological investigations including CBE, ESE, CRP, pure tone audiometry, brainstem audiometry evoked response,electronystagmography and MRI brain. All investigations were normal.

She was managed with betahistine and cinnarizine for the episode of vertigo and advised diclofenac 50 mg and domperidone 10 mg whenever headache or nausea occurred. She was started on flunarizine 10 mg at night which she tolerated well except a 3 kg weight gain during the four months of treatment for which she was advised lifestyle modification measures.She was being followed up for six months thereafter during which she had no episode of vertigo and just one episode of headache which occurred during the second month of prophylaxis.

CONCLUSION

Migrainous vertigo should be considered in any young patient with history of migraine and vertigo[6] it responds well to prophylactic treatment of migraine,so could be worthwhile to keep a high degree of suspicion and start one of them[6].

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Thyroid Carcinoma metastasising in the Mandible: A Case Report.

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Abstract: *Metastatic lesions of primary tumours, which originate in different parts of the body, comprise almost 1% of oral cancers. They are highly significant because their appearance may be the only symptom of the underlying malignancy and/or the first evidence of dissemination from the primary site. These lesions can affect either bones or soft tissues in the maxillofacial region, the most common region being the molar region of the mandible. A case of metastatic tumour of the mandible from primary follicular carcinoma thyroid and its clinical, histopathological and immunohistochemical findings are discussed.*

INTRODUCTION

Metastases in the oral tissues are rare events that constitute approximately one percent of all oral malignancies. In the oral cavity, the most common site is the body of the mandible in the premolar-molar region. These tumours are of great clinical significance since at times, their appearance may be the only symptom of an undiscovered underlying malignancy and may be the first evidence of dissemination of the known tumour from its primary site[1]. The primary site differs among genders. Breast cancer is the most frequent metastatic oral cancer in females; lung cancer followed by prostate cancer is the most frequent metastatic tumour in males[2]. The lung is the most common source of metastases to the oral soft tissues, whereas the breast is the most common source of metastatic tumours to the jaw bones. Common oral sites other than the jawbones are gingival, buccal mucosa, soft palate and tongue. Most common presenting symptoms are pain, swelling, loosening of teeth and paraesthesia[3]. Sometimes, these lesions are asymptomatic, and may be overlooked. This is particularly true when the primary malignant tumour is far advanced and the patient has symptomatic metastatic deposits elsewhere.

Here, we present a rare case of metastatic thyroid carcinoma in the mandible, thus emphasizing that metastatic tumours should be included in the differential diagnoses of such lesions. Furthermore, it is suggested that thyroid should not be excluded as the primary source of metastatic jaw lesions.

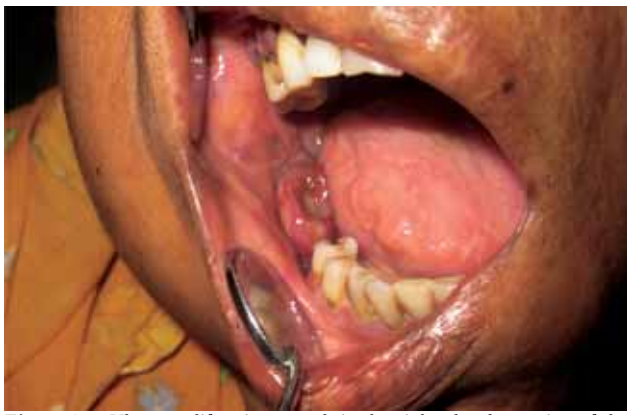

Figure 1 : *Ulceroproliferative growth in the right alveolar region of the lower jaw*

CASE REPORT

The patient was a 55 year old female who reported to the institution with the complaint of pain and swelling in the right lower face for the last 1 month, which started after the mobile teeth in the same region exfoliated spontaneously. There was uncontrolled bleeding from these sockets but the patient did not consult a dentist until a growth developed at the site. Examination revealed soft spherical swellings, 2 in the scalp region and 1 in the supra-orbital region; there was localised elevation of temperature in the same. Intra-orally, an exuberant growth was noticed in the edentulous mandibular molar region on the right side; with well defined borders, soft consistency and continuous mild bleeding.

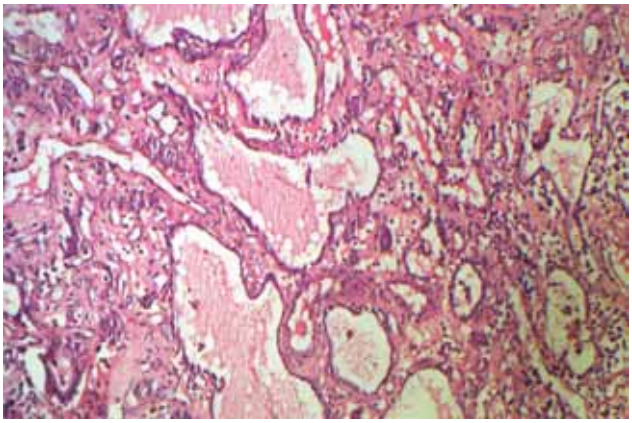

Figure 2: *H & E picture showing follicular arrangement of the malignant cells with eosinophilic secretory material (40X)*

Examination also revealed a solitary nodule in the left paramedian region in the neck; which moved on deglutition.

The patient had been diagnosed with Follicular Carcinoma Thyroid 2 years back, when she was admitted due to trauma. Investigations had revealed multiple lytic lesions in ileum, pelvis and vertebrae. Patient was advised radiotherapy, which she discontinued abruptly; had been on Morphine for the past one and a half years. Patient had also been under catheterisation for the same duration for urinary retention. Patient had been on a wheel-chair for the past 6 months.

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Radiographs revealed radiolucency in the right body and ramus of the mandible, with thinning of the lower border. Expansion and thinning of the buccal and lingual cortical plates was also evident; with intervening radiopaque septae in the radiolucency. There was radiographic evidence of osteolytic lesions in the skull, as well as mild osteoporotic changes in the long bones.

Serum acid phosphatase levels were mildly elevated (5.3 IU/L) and those of serum calcium were lower (7.2 mg/dl) than normal. Alkaline phosphatase levels were within normal range.

An incisional biopsy of the oral lesion was performed. The histopathological examination revealed cellular as well as sinusoidal like spaces which were typically lined by clear cells. Within follicle-like areas, secretory material was noticed. Most of the areas had papillae like appearance. Apart from this, connective tissue stroma showed mixture of homogenous areas, groups and nests of epithelial like cells which gave a malignant picture. The whole lesion was covered by atrophic epithelium, some of them even showed dysplastic cells but with intact basement membrane. Hence, based on the clinical features, erratic behaviour of the

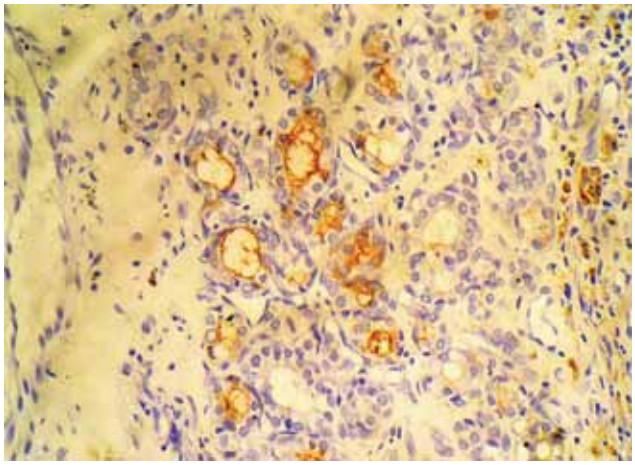

Figure 3 : *Follicular cells showing positivity for Thyroglobulin (40X)*

swelling, the histopathology is suggestive of metastatic thyroid carcinoma. Immunohistochemistry with Thyroglobulin showed the follicular cells taking up the stain, confirming the histopathological diagnosis.

DISCUSSION

Metastatic tumours to the oral region are uncommon, comprising only 1%-3% of all malignant neoplasms[4]. Because of their rarity, they are generally overlooked in the diagnosis, because these malignant lesions have the same clinical features as that of Squamous Cell Carcinomas which are the most common malignant lesions in the jaw bones. But the apparent rarity may be partially due to failure to recognize metastatic tumours in the jaws. Further, the jaws are not routinely examined at autopsy, so it is possible that some lesions are missed. Hence the true frequency of metastatic tumours in the jaws may possibly be higher. The typical tumours that metastasize to the jaws in order of decreasing frequency are : breast, lung, adrenal, kidney, bone, colorectum, prostate and thyroid[3]. Most of the bony metastatic lesions are osteolytic and appear radiolucent on the radiograph; those of prostate and breast are osteoblastic and appear radio-opaque[5]. There are no characteristic type of radiolucent lesions; and in case of involvement of areas about the teeth, they might simulate periapical lesions or severe periodontal disease.

The most common clinical manifestations are swelling, pain/ paraesthesia and lymphadenopathy[2,3,6]. Less frequently, the lesion can present as pain in the temporomandibular joint region or as an osteomyelitis in the jaw, or as trigeminal neuralgia. The increase in volume of the bone with a metastatic lesion is often associated with dental mobility and/or trismus[2]. A peculiar site for metastasis is the post-extraction site, with the latency period usually of about 2 months. Metastatic tumours of the jaw are difficult to diagnose for a number of reasons [5]

1.) The lesions are centrally located within the bone
2.) There are a very few subjective symptoms, except at a very late stage
3.) Radiographs are usually non-specific

Thyroid carcinoma is the most frequently diagnosed endocrine carcinoma. Bone metastasis is found in 1-3% of well-differentiated thyroid carcinomas, occurring more often in follicular carcinoma and in patients more than 40 years of age. The presence of distant metastasis in an adult is associated with poor prognosis[1]. Follicular Thyroid carcinoma (FTC) is a well-differentiated tumour which originates in follicular cells and resembles the normal microscopic pattern of thyroid. It is the second most common cancer of thyroid after papillary carcinoma. It rarely gives rise to oral metastasis[3]. Immunohistochemical marker for FTC is thyroglobulin, which is present in more than 95% of FTC cases.

Pathogenesis of metastasis to jaw bones is unclear but possible predilection for mandible is due to large amount of red bone marrow and increased flow of circulating blood. Most of the red marrow in the jaws is found in the third molar region that is most often the metastatic site[5]. Others opine that the mode of metastasis is hematogenous, the neoplastic cells become deposited in the vascular haemopoietic tissue; a reduced flow of blood in the area could help the cell deposition[1,2]. When the metastasis is in the mandible, the primary tumour is frequently associated with a tendency to develop osseous metastasis. Most authors agree that in patients with multiple metastases, the prognosis is highly unfavourable, and palliative treatment may be the only option available to improve the immediate quality of life in such cases.

This case report adds to the growing list of rare metastasis to mandible from a distant primary, and highlights the need for alertness and awareness of the diagnostician when dealing with such cases.

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Errata

Article: ***"A Comparative Study to Evaluate the Anticardiolipin Antibody IgG in Pregnant and Non Pregnant Women with first Trimester recurrent Abortions"*** *by* ***Dr Sunita Kalra on page 57-58 JIMSA Issue Vol. 24, Issue 2, Apr-Jun 2011.*** *The designation of* ***Dr Sunita Kalra*** *should be read as* ***"Reader, Department of Anatomy, University College of Medical Sciences, New Delhi."***

The mistake was inadvertent and the error is regretted.

Editor, JIMSA

Sleep Disorders in Neurology: Under diagnosed and Under reported.

Sudeepta Dandapat, Kuljeet Singh Anand

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Abstract: *Sleep is a complex neurological state, with its primary function of providing rest and restoring the body's energy levels. Alterations in th quality, quantity and pattern of sleep result in sleep disorders. Persistent and repeated interruption of sleep affects the health of an individual. Undiagnosed and untreated wale/sleep complaints cause not only misery to the sufferer, but it also has socio-economic consequences. This review addresses sleep disorders commonly encountered in the neurology outpatient setting.*

Keywords: *sleep disorder, insomnia, narcolepsy, sleep symptoms*

INTRODUCTION

One of the most frequent health complaints encountered by the general physician is disordered sleep. It may vary from an occasional night of poor sleep or daytime sleepiness to chronic sleep disturbance or misalignment of circadian timing[1] These lead to serious impairment of daytime functioning and may contribute to exacerbating medical psychiatric condtions[2] Disorderd sleep has protean effects on mood, attention, memory and general sense of vigor. It is a clinical entity which if present in a patient must be addressed to allow the patient to lead a better quality of life.

A. DYSSOMNIAS

These are a group of sleep disorders associated with complaints of insufficient, disturbed, or non-restorative sleep. The sleep disturbance does not occur exclusively during the course of another mental; disorder 9e.g. major depressive disorder, generalized anxiety disorder, a delirium). The disturbance is not due to the direct physiological effects of a substance (e.g., a drug of abuse, a medication) or a general medical condition. These are sub-classified into primary Insomnia, primary Hypersomnia, Narcolepsy, breathing-related Sleep Disorder and Circadian Rhythm Sleep Disorder.

Primary Insomnia: The predominant complaint is difficulty initiating or maintaining sleep or non-restorative sleep for at least 1 month. The sleep disturbance (or associated daytime fatigue) causes clinically significant distress or impairment in social, occupational, or other important areas of functioning. The sleep disturbance does not occur during the course of narcolepsy, breathing related sleep disorder, circadian rhythm sleep disorder, or a parasomnia. Detailed history is the key to diagnosis. Patients with primary insomnia should be discouraged from using sedatives. The need to regularize their daily schedules, including bed times, and to be physically active during the day but to avoid strenuous physical and mental activity before bedtime should be emphasized. Dietary excesses must be corrected with avoidance of coffee and alcohol, especially at night (Table 1). A number of behavioral modifications may be useful[3], such as using the bedroom only for sleeping, arising at the same time each morning regardless of the duration of sleep and avoiding day time naps.

Primary Hypersomnia: The predominant complaint is excessive sleepiness for at least 1 month (or less if recurrent) as evidenced by either prolonged sleep episode or daytime sleep episodes that occur almost daily. The excessive sleepiness cause clinically significant distress or impairment in social, occupational, or other important areas of functioning. It is enhanced in situations that allow sleepiness to become manifest, such as reading or watching television in the evening. The major sleep episode may be prolonged, lasting more than 8 hours. The capacity to arouse the subject may be normal, but some patients report great difficulty waking up and experience disorientation after awakening. The excessive sleepiness is not netter accounted for by insomnia and does not occur exclusively during the course of another sleep disorder [4] (e.g., narcolepsy, breathing-related sleep disorder, circadian rhythm sleep disorder, or a parasomnia) and cannot be accounted for by an inadequate amount of sleep. Because the underlying cause of primary hypersomnia is unknown, treatment remains symptomatic in nature. Severe primary hypersomnia is a disabling problem that often leads to permanent unemployment and responds poorly to medical treatment. Modafnil, sodium oxybate, amphetamine, methamphetamine, dextroamphetamine, methylphenidate and selegiline are effective treatments for excessive sleepiness associated with primary hypersonias. Scheduled naps can be beneficial to combat sleepiness in these patients.

Table 1*.: Sleep Hygeine Tips*

1.	Do not spend much time in bed
2.	Maintain consistent sleep and wake times
3.	Get out of bed if unable to fall asleep
4.	Restrict naps to 30 min in the early afternoon
5.	Exercise regularly.
6.	Spend more time outside, without sunglasses, especially late in the day.
7.	Increase overall light exposure.
8.	Avoid caffeine, tobacco, and alcohol after lunch.
9.	Limit liquids in the evening.

Narcolepsy: The term narcolepsy is derived from Greek, "seized by somnolence." Gelineau was the first to delineate the syndrome in 1880[5] Narcolepsy is characterized by the classic tetrad of excessive daytime sleepiness, cataplexy, hypnagogic hallucinations, and sleep paralysis[6]. There are irresistible attacks of unfreshing sleep that occurs daily for at least 3 months. The presence of one or both of the following is important for the diagnosis: cataplexy (i.e., brief episodes of sudden bilateral loss of muscle tone, most often in association with intense emotion) or recurrent intrusions of elements of REM sleep into the transition between the sleep and wakefulness, as manifested by hypnagogic hallucinations or sleep paralysis at the beginning or end of sleep episode. Narcolepsy frequently is unrecognized, with a typical delay of 10 years between onset and diagnosis. This disorder may lead to impairment of social and academic performance in otherwise intellectually normal children. The implications of the disease are often misunderstood by patients, parents, teachers, and health care professional. Narcolepsy is treatable. However, a multimodal approach is required for the most favorable outcome. It includes non-pharmacologic and pharmacologic measures. Sleep hygiene, scheduled naps and avoidance of foods high in refined sugars are some of the measures patients can take to help themselves along with drugs. CNS stimulants, Modafinil[7], Sodium oxybate and few other drugs have shown some benefit in treating various aspects of narcolepsy.

Breathing-related Sleep Disorder: Sleep disruption, leading to excessive sleepiness or insomnia that is judged to be due to a sleep-related breathing condition (e.g., obstructive or central sleep apnea syndrome or central alveolar hyperventilation syndrome) fall in this category. Diagnosis is reached by eliciting history from patients' bed partner and polysomnography. Depending on etiology, various non-pharmacologic and devices are available as therapy. The management of such patients should be preferably headed by a pulmonologist.

Circadian Rhythm Sleep Disorder: A persistent or recurrent pattern of sleep disruption leading to excessive sleepiness or insomnia that is due to a mismatch between the sleep-wake schedule required by a person's environment and his or her circadian sleep-wake pattern. Circadian rhythm disturbances can be

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categorized into 2 main groups; transient disorders (e.g., jet lag, changed sleep schedule due to work, social responsibilities, and illness) and chronic disorders. The most common chronic disorders are delayed sleep-phase syndrome (DSPS), advanced sleep-phase syndrome (ASPS), and irregular sleep-wake cycle. The sleep disturbance causes clinically significant distress or impairment in social, occupational, or other important areas of functioning. Behavioral and light therapies[8] are the mainstays of treatment of circadian rhythm, disturbances. Emphasize good sleep hygiene and discourage maladaptive behaviors. Use of sedatives has been described. Melatonin has been reposted to be useful in the treatment of jet lag and I the treatment of sleep-onset insomnia in elderly patients who are melatonin deficient.

Periodic Limb Movemets in Sleep (PLMS): Previously called nocturnal myoclonus, PLMS is a disorder in which repetitive, brief, and stereotyped limb movements occur during sleep, usually about every 20 to 40 seconds. It is characterized by leg kicks every 20-40s which last for 0.5-5 seconds. Associated complaints of insomnia, excessive sleepiness, restless leg, very cold or hot feet and uncomfortable sensations in legs may also be present. PLMS is unique in that the movements occur during sleep. Most other movement disorders manifest during wakefulness. The condition is remarkably periodic, and the movements may cause poor sleep and subsequent day time somnolence. Periodic limb movement disorder may occur with other sleep disorders and is related to, but not synonymous with, restless legs, syndrome (RLS), a less specific condition with sensory features that manifest during wakefulness. The majority of patients with restless legs syndrome have periodic limb movement disorder, but the reverse is not true. Treatment involves either dopaminergic medication in an attempt to modify activity of the sub cortical motor system or, more commonly, sedative medications such as clonazepam to allow uninterrupted sleep[9]. Many new agents are proving efficacious for treatment as well.

(B) PARASOMNIAS

The parasomnias are a group of disorders characterized by disturbance of either physiological processes or behavior associated with sleep, but not necessarily causing disturbances of sleep or wakefulness. These have undesirable motor, verbal, or experimental phenomenon occurring in association with sleep, specific stages of sleep, or sleep-awake transition phases. Parasomnia may be categorized as [1] primary parasomnia, which are disorders of sleep states and are further classified according to the sleep state of origin, rapid eye movement (REM) or non-rapid eye movement (NREM) or[2] secondary parasomnias, which are disorders of other organ systems that may manifest during sleep such as nocturnal epilepsy, respiratory dyskinesias, arrhythmias, and gastro esophageal reflux. It includes nightmare disorder, sleep terror disorder, sleepwalking disorder and REM sleep behavior disorder. The disturbances are not due to the direct physiological effect of a substance (e.g., a drug of abuse, a medication) or a general medical condition.

Nightmare Disorder: Repeated awakenings from the major sleep period or naps with detailed recall or extended and extremely frightening dreams, usually involving threats to survival, security, or self esteem. The awakenings generally occur during the latter third part of the night, usually during REM sleep, but do not involve any motoric dream enactment. On awakening from the frightening dreams, the person rapidly becomes oriented and alert (in contrast to the confusion and disorientation seen in sleep terror disorder and some forms of epilepsy) and also has subsequent recollection of the dreams. The dream experience, or the sleep disturbance resulting from the awaking, cause clinically significant distress or impairment in social, occupational, or other important area of functioning.

Sleep Terror Disorder: It is characterized by recurrent episodes of abrupt awakening from sleep, usually occurring during the first third of the major sleep episodes primarily in stages III and IV of NREM sleep and beginning with a panicky scream. Intense fear and signs of autonomic arousal, such as tachycardia, rapid breathing, and sweating, occur during each episode. There is a relative unresponsiveness to efforts of other to comfort the person during the episode. No detailed dream is recalled and there is amnesia for the episode. The episodes cause clinically significant distress or impairment in social, occupational, or other important area of functioning.

Sleepwalking Disorder: It is also known as somnambulism. There are repeated episodes of rising from bed-during sleep and walking about, usually occurring during the first third of the major sleep episode. While sleepwalking, the person has a blank, staring face, is relatively unresponsive to the efforts of others to communicate with hi, or her, can be awakened only with great difficulty. On awakening (either from the sleepwalking episode or the next morning), the person has amnesia for the episode. Within several minutes after awakening from the sleepwalking episode, there is no impairment of mental activity or behavior (although there may initially be a short period of confusion or disorientation). The sleepwalking causes clinically significant distress or impairment in social, occupational, or other important areas of functioning. History is typical with polysomnography demonstrating onset of episodes during the stage3/stage4 of sleep. Reassurance, relaxation techniques, mental imagery and anticipatory awakenings are the mainstay of treatment. The benign nature of the events and subsequent disappearance in most cases should be emphasized. Medication for the treatment of sleepwalking disorder may be necessary in the following situations, when the possibility of injury is real; when continued behaviors are causing significant family disruption or excessive daytime sleepiness; and when other measures have proven to be inadequate[10].

REM Sleep Behaviour Disorder: REM sleep behavior is dream-enacting behavior that includes talking, yelling, punching, kicking, sitting, jumping out of bed, arm flailing, and grabbing. An acute form may occur during withdrawal from ethanol or sedative-hypnotic drugs. The chronic from present for evaluation following observations of bed partners. It occurs during second half of night during REM sleep. Treatment for REM behavior disorder is initiated with clonazepam at 0.5-1.5 mg taken at bedtime[11.] This medication has been shown to be beneficial in the long term. Drug discontinuation often in prompt relapse. The exact mechanism of action of clonazapam in patient with REM behavior disorder is not known, but its serotonergic properties may inhibit nocturnal motor activity in the brainstem and thus prevent arousals.

CONCLUSION

To date, more than 100 sleep disorders have been identified, affecting sexes, all races and age groups. The effects of sleep disorders range from mere annoyance to life-threatening. Sleep disorders have been found to play a role in high blood pressure, heart disease, poor work performance and strained family relationships. They affect health and interfere with a happy and productive life. It is one of the common complaints any physician comes across during his practice, be it private or in a hospital setting. Earlier it was thought of as a disorder mainly afflicting the population of western countries, but in recent times it has become increasingly visible in the Indian setting. Still very few studies have been undertaken in the Indian population regarding sleep disorders. This has led to low awareness of the great physician about the same, inappropriate use of sedatives and poor quality of life for the patients.

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Depressive Disorders in Elderly: An Estimation of this Public Health Problem.

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Abstract: *The pint prevalence of depressive disorders in the elderly population of the world varies between 10% and 20% depending on cultural situations. Objective of the study was to determine the median prevalence rates of depressive disorders in elderly population of India and various other countries in the world. retrospective study based on meta-analysis of various study reports of community based mental health surveys on geriatric depressive disorders conducted between 1955 and 2005in continents of Asia, Europe. Australia, North America and South America conducted . 74 original research studies that surveyed a total of 4,87,275 elderly individuals in the age group of 60 years and above, residing in various parts of the world were included for the final analysis. These studies were conducted on homogenous community of elderly population in the world, who were selected by simple random sampling technique. Median prevalence rate and its corresponding inter-quartile range, Chi-square test and Chi-square for Linear Trend were applied. P value < 0.05 was considered as statistically significant. The Median Prevalence rate of depressive disorders in the world for the elderly population was determined to be 10.3% [Interquartile Range (IQR) = (4.7% - 16.0%)]. The Median Prevalence Rate of depression among elderly Indian population was determined to be 21.9% [IQR = (11.6% -31.1%)]. Though there was a significant decrease trend in world prevalence of geriatric depression, but it was significantly higher among the Indians in recent years than the rest of the world.*

Keywords: *Depressive Disorders, Prevalence, Elderly, Median, Interquartile Range*

INTRODUCTION

The World Health Organization estimated that the overall prevalence rate of depressive disorders among elderly generally caries between 10% and 20% depending on cultural situations.[1,2] The community-based mental health studies in India have revealed that the point prevalence of depressive disorders in elderly Indian population varies between 10 and 25 percent.[3,4]

MATERIALS & METHODS

Study design: Retrospective study based on meta-analysis on prevalence of depressive disorders in elderly population

Setting: Community based mental health surveys on geriatric depressive disorders conducted in continents of Asia, Europe. Australia, North America and South America, were included in this analysis.

Study Period: All the studies that were conducted and published in indexed journals between 1955 and 2005 (i.e., within the last fifty one years) would constitute the sample. This is decided on the observed fact that it normally took around two to three years time for a project report to get accepted and published in an indexed journal. So, a study conducted during 2005 was expected to get published in an indexed journal by the year 2008. The sample size for this project was finalized during the year 2008.

Sample Size: All published articles on prevalence of depressive disorders in elderly population that were available, adequately analyzed and accessible from the internet, the central library of Kasturba medical College Manipal in Karnataka and the Central Library of Sikkim-Manipal Institute of medical Sciences 9SMIMS) in Sikkim, constituted the study universe.

Databases: The search engines that were utilized for electronic data from the internet were MEDLINE, PUMBED, GOOGLE, YAHOO, EMBASE, PsycINFO, and the Cochrane Collaboration Database for original human research articles in the English literature published through 1st January 1955 and 31st December 2005 using the two sets of search items. "Prevalence of Depression in Elderly" and "Prevalence of Geriatric Depression".

Sampling procedures: Only studies that either covered the total population of study area or applied simple Random Sampling Method to identify the study subjects in their corresponding research projects were included for this final meta-analysis.

Inclusion Criteria: To avoid undesired bias due to design effects from various epidemiological study designs, the researchers had included only community based cross-sectional surveys on prevalence of depressive disorders and some prospective study designs that had not excluded depression on baseline. All these studies were conducted on homogenous community of elderly population in the world, who were either selected by simple random sampling technique or covered under whole population of the study area. For determining the various correlates of depression in elderly, only those articles were included that had at studied at least one risk factor of depression.

Exclusion Criteria: all the unpublished reports and unavailable or unanalyzed or inaccessible articles from the internet as well as the Central Library of Kasturba medical College manipal in Karnataka and Central Library of Sikkim-manipal Institute of medical Sciences (SMIMS), Sikkim on studies regarding the prevalence of depressive disorders in elderly population were excluded from this study. But it was perceived by the researcher that the proportion of excluded reports on account of inaccessibility or unavailability would constitute less than 5% of the available articles on relevant topic. Hence, this was expected to have minimal impact on the final results. Studies, where the 95 %^ Confidence Interval of prevalence rate estimation exceeded more than 20 units, were excluded on account of possible improper sample size estimation. Studies conducted on migrant populations, old age homes and health care institutions were also excluded from this meta-analysis in order to avoid biasness. High prevalence rate of depression was very common among isolated groups of individuals in the community, who had migrated to some other place either due to political force or to met their physiological or financial needs.

Data Collection Procedure

The investigators were trained by the renowned psychiatrists of Kasturba Medical College Manipal, Karnataka, and Sikkim-Manipal Institute of medical Sciences 9SMIMS) on how to interpret the result from different

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community based psychiatric evaluation studies. The diagnosis generated by the questionnaires used as study instruments was strictly kept confidential and reconfirmed by consulting the senior psychiatrists for confirmation of their acceptability, content validity and reliability, before arriving at a final; diagnosis for data analysis. At the beginning. A Pilot study was conducted with randomly chosen data from 25 original research articles that surveyed elderly individuals in the age group of 60 years and above, residing in various parts of the world, some of these studies used in the pilot Study, were later include for statistical analysis in the final research project.

Data Analysis: The data was tabulated and analyzed by using the statistical package SPSS (Statistical package for social c=sciences) version 10.0 for Windows and EPI INFO version windows 2000. Findings were described in terms of median prevalence rates of depressive disorders in elderly and their corresponding Inter-Quartile range (IQR). Proportions and their 95% Confidence Intervals (CI) were used for the same purpose. Chi-square test and Chi-square for Linear Trend were applied for studying prevalence rates of elderly depressive disorders among various countries in the worlds and in India. Here, p- value <0.05 was considered as statistically significant.

RESULTS AND DISCUSSIONS

The search strategy yielded 896 potentially relevant studies, among these 143 were retrieved for more detailed evaluation. Though 77 studies met the inclusion criteria, but we could retrieve main article or structured abstract for only 74 studies which were included for the final analysis. Among these 74 selected articles, 69 (93.2%) had cross-sectional study design and 5(6.8%) had prospective study design that had not exclude d depression on baseline.

Two meta-analysis reports, one by Chen R. et al[5] (1999, China) on 10 relevant studies and another by Copeland J.R.M. et al[6] (2004, Amsterdam) on 14 relevant studies and also a systematic review report by Beekman A.T. et al[7] (1999, Netherlands) on 34relavat studies were included in this meta-analysis project. So, this study had actually taken into consideration the prevalence rates of depression in elderly from [74 + (10+14+34) = 132] survey reports from various parts of the world.

Determination of median Prevalence rate of depressive Disorders in Elderly

The 74 included studies involved 4,87,275 elderly individuals from all the parts of the world at baseline. Among these 6 studies from India involved only 2,499 (0.5%) elderly individuals at baseline for assessment of presence of depression. The mean ages of the study population were reported in 68(85.1%) articles with mean ranging from (62-71) years. Here, 68 (91.9%) articles included gender distribution and (36%-64%) of participants were men (median= 46%). The length of reported study period ranged from (3-84) months (median =9).

Only 52 (70.3%) studies used some of modern rating scales for diagnosis of depression in elderly. Among these, 14 used AGECAT/GMS-AGECAT, 4 used DIS/HDS, 8 used GMS/GDS, 11 used CSES-D and 15 used DSM/ICD criteria for the diagnosis of geriatric depression. The prevalence rate of geriatric depression was found to be higher in studies using psychiatric examination and operational definitions and studies used the geriatric depression sale 9GDS) or Geriatric mental State Schedule (GMS) alone.

The median Prevalence rate o Depressive disorders in the world for the elderly population from 74 studies was determined to be 10.3% with inter-Quartile Range varying between 4.7 5 and 16.0%. Similar findings were reported by Kirby M. Et al[8] (1997, Dublin) and Kay D.W.K. et al[9] (1985,Hobart). Studies conducted by Geerlings M.I.et al[10] [(1990-96), Amsterdam], Newman S.C. et al[11] (1998, Canada), Liu C.Y. et al[12] 91993, China), also reported the prevalence rate of depression among the elderly to be 10.5%, 11.2% and 12.9% respectively.

The comparison of median prevalence rates of depression in elderly population of India and the rest of the world was also studied. It was found that the proportion of depressed elderly population in India (18.2%) was significantly higher than the rest of the world (5.4%) and this difference was found to be statically highly significant (X^2 = 770.4 and p = 0.000000001*). Though there is an alarming increase of proportion of depressed elderly in India, but we should also keep in mind that there were only 6 relevant studies from India, covering only 0.5% of elderly participants of the world as compared to 68 studies from the rest of the world covering 993.5% of the participants.

The low prevalence of depression in elderly during recent years could be due the presence of better diagnostic instruments with optimum validity and reliability had been developed during the recent years to diagnose elderly depression in the community and ruled out cases of dementia which were often falsely diagnosed as depression in the past.

Though the proportion of elderly individuals affected with depression was significantly lower in Asia (4.2%) than Europe (10.9%) and America (8.4%), but the number of depressed elderly individuals was significantly higher in Asia which was evident from 14 studies conducted in various Asian countries covering 74.5% of the population sample. Studies from the developing countries like India had reported a very high prevalence rate of 21.9% with IQR ranging from (11.6-31.3). Care and bonding from family support systems, lesser competitive life styles and improved mental health facilities with their integration with primary health care could account for lesser prevalence rates in some of the developed Asian countries.[1, 2, 4]

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SYMPOSIUM DIABETIC FOOT: NEW DIMENSIONS

OUR GUEST EDITOR

Dr. Ashok Damir is a dedicated Diabetic Foot Care Specialist practicing in New Delhi, India having more than 20 years clinical experience. After doing his Medical Post Graduation from RNT Medical College, Udaipur he passed his USMLE (United States Medical Licensing Exam.) with more than 85 percentile. He completed his fellowship in Podiatry (Diabetic Foot Care) from Dr. Scholl College of Podiatric Medicine, at Rosalind Franklin University of Medicine & Science, Chicago, IL, USA. He has been using more advanced state of art treatment modalities like Growth Factors (PDGF, EGF etc.), Ultrasonic Debridement, Negative Pressure wound Therapy (NPWT), Hyperbaric Oxygen (HBO) Therapy and Bioengineered Skin Grafts etc. for Chronic Non Healing Diabetic Foot Ulcers. He gets Ch. Nonhealing Diabetic Foot Ulcer patients from different states of Northern India. For last 2 years he has been teaching post graduate doctors of different Medical Colleges about care of Diabetic Foot & Ch. Non healing Diabetic Foot Ulcer. (Nominated by "WDF" (World Diabetic Foundation) & DFSI (Diabetic Foot Socity of India) as Regional Co-coordinator of "National Wound Care Project"). He has been using stem cell therapy for intractable chronic non healing diabetic foot ulcers with quite encouraging results. Stem Cell Therapy is most advanced & latest in world for lower limb PAD where revascularisation is not possible. Dr. Damir is one of the few diabetic foot specialists in India & his main field of work is in diabetic wound management & pressure off loading techniques for early healing of diabetic foot ulcers with aim of preventing amputation of lower limb.

Dr. Damir has many papers published in reputated journals; he has been actively involved in research in Diabetes and Diabetic Foot management (like IDEA I , IDEA II, GIDS, NIS, DIABSITY, National Amputation Survey etc.) He is a good Medical Review Article writer & his articles got published in different reputed Journals & Medical Magazines of India. He has been part of faculty of different reputed conferences and traveled extensively in India & abroad giving lectures on Diabetes & Diabetic Foot. He has organized (Org. Sec.) 8th National, Annual Conference of Diabetic Foot Society of India, "DFSICON 2009" in New Delhi. He has also organized 3 regional Annual Diabetes Conferences of Delhi Diabetic Forum viz.DIABCON 2006, DIABCON 2007 & DIABCON 2008. Looking towards his research, social work, service to mankind & dedication for educating people he has been conferred different awards like International Medical Excellence Award 2002, Bhartiya Gaurav Samman Award 2003 & Manav Sewa Samman Award 2008. At present Dr. Damir is Head, Diabetic Foot Centre, Hyperbaric & Wound Crae Centre at Fortis C-DOC Hospital,Chirag Enclave, New Delhi. He is the Chief Consultant & Director, Podiatric services in DDC & Foot Care Research Centre and Damir Stem Cell Therapy Centre, Patel Nagar,New Delhi & is member of American Podiatric Medical Association (APMA), Diabetic Foot Society of India (DFSI), American Diabetes Association (ADA), API, RSSDI, DDF etc.

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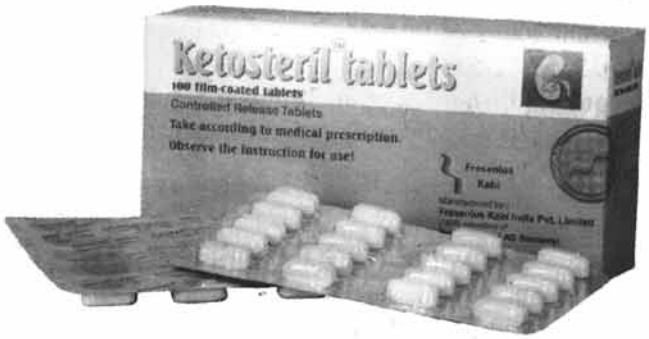

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Editorial

India is known as diabetic capital of world having around 60 million diabetics out of 300 million all over world. That means every 5th diabetic in this world is an Indian. Since cases of diabetes are increasing hence its complications are also increasing, A **diabetic foot** is a foot that exhibits any pathology which results directly from diabetes or any "chronic" complication of diabetes mellitus. Numbness, tingling, Pain in legs, Burning feet, Cramps, Claudication, Loss of hair on legs, different foot deformities, Swelling of feet & non healing diabetic foot ulcer etc. can be symptoms of Diabetic Foot.Diabetic foot is one of very important but most neglected complication of Diabetes. Most common cause of hospitalization in Diabetic patient is Diabetic Foot problems . Diabetic foot ulceration occurs in 15% of diabetic patients,once in their life time. Someone somewhere loses his leg because of Diabetes every 30 second In this world . According to Vascular Society of India (2010) the incidence of lower limb amputations are 80,000 per year in India which I think is tip of iceberg because of poor registry of medical cases in India. Ironically In 84 % of lower leg amputation cases it is small trivial foot ulcer which is found to be responsible. That means maximum number of lower limb amputations are preventable .Unfortunately even being such an important ailment there are no specific or exclusive chapters about Diabetic Foot in our Indian medical curriculum.

Being attached with this super specialty i.e. Podiatry for number of years, once Dr. P. D. Gulati requested me for writing articles on Diabetic Foot, for the benefit of JIMSA readers, we decided to bring this **symposium on Diabetic Foot: New Dimensions**. I have contributed, along with two of my colleagues, **six articles & a case report** on different important topics related to Diabetic foot.

Whenever a diabetic foot patient with or without ulcer comes in OPD most of the clinicians are always confused that how to examine & how to approach such patient. To guide clinicians I have written **"How to approach a Diabetic Foot patient?"** which tells us how to proceed & how to do systematic examination of diabetic Foot patient. Any ulcer in diabetic patient takes longer than usual time to heal but foot ulcers are more difficult to heal because of triopathy of diabetic patients i.e. poor immunity (humoral as well as cellular), poor blood supply because of micro & macro vasculopathy & neuropathy which can be sensory, motor or autonomic. In the article "**Why Diabetic Foot Ulcers donot heal?"** I have tried to give all possible reasons of chronicity of DFU. Treating infections in Diabetic foot patient is a challenging task for clinicians & it needed special mention in **"Diabetic patients: Infection in the foot"**. As far as managing difficult task of treating non healing diabetic foot ulcer is concerned lot of new researches are going on in western world, which have invented number of new gadgets & method for treating Chronic DFU like Ultrasonic debridement, Hyperbaric Oxygen therapy, O2Misly, Autologel,Ozone therapy, BATs & Low level Laser Therapy (LLLT) etc.etc..All these new modalities have been described briefly in **"Recent advances in management of Chronic Non healing Diabetic Foot Ulcer"** In recent years developments in molecular and cell biology helped to understand and treat many of the Chronic diseases including wound healing. The different events in progress of wound healing like inflammation, proliferation and remodelling needs the coordinated and sequential activation and inactivation of gene expression programmes in response to signals from the cellular environment. Stem cells are immature, un programmed cells that have the ability to grow into different kinds of tissue and can be sourced from people of all ages. In article **"New & Alternative treatments for the Diabetic Foot i.e. Stem Cells and Gene Therapy"** I tried to cover both complicated topics in a simpler way. No matter whatever difficult to difficult & costly to costly modality is used for treating Diabetic Foot Ulcer, until otherwise blood sugar is controlled meticulously the final goals i.e. closure of the wound & getting relieved of different symptoms of Diabetic Foot can't be achieved. That's why article **"Management of Hyperglycemia while dealing Diabetic Foot Ulcer"** has also been included. This compilation on "*Diabetic Foot*" is an effort to provide a comprehensive guidelines to clinicians regarding approach to diabetic foot patients. Any feedback regarding contents of different topics from the readers will be appreciated.

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Clinical Assessment of Diabetic Foot patient

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Abstract: *As the incidence of diabetes mellitus rises, so too does the number of patients at risk of diabetic foot problems, particularly ulcers. Goal of a primary care practitioner is to prevent diabetic foot complications, including amputations.*
Clinicians can do this by screening and assessing patients with diabetes at risk of developing foot ulcers and assessing and managing patients with diabetic foot ulcers.
'A minute spent on screening a foot could save a leg.'
A thorough history and physical examination is the first step necessary to determine the patient and ulcer status, establish a baseline for treatment, develop a treatment plan, determine a patient's risk status, and provide a prognosis for wound closure. Historical information should include diabetes control, current and past complications and treatments, and co morbidities. Physical examination should include information on vascular, neurological, and musculoskeletal status.
All diabetic patients must have their feet evaluated at least at yearly intervals for the presence of the predisposing factors for ulceration and amputation . If abnormalities are present, more frequent evaluation of the diabetic foot is recommended depending on risk category. It is through systematic examination and risk assessment, patient education, and timely referral to higher centres (where a multidisciplinary team can handle these problems)that a clinician may reduce the high prevalence of lower-limb amputation in diabetic patients.

Diabetic foot ulcer is a rising health problem with rising prevalence of diabetes. The most common triad of causes that interact and ultimately result in ulceration has been identified as neuropathy & or Ischemia, deformity, and trauma[1] and are frequently complicated by infection. The lifetime risk of a person with diabetes developing a foot ulcer may be as high as 25%, whereas the annual incidence of foot ulcers is <"2%[2-6]. Up to 50% of older patients with type 2 diabetes have one or more risk factors for foot ulceration[2,5]. A number of component causes, most importantly peripheral neuropathy, interact to complete the causal pathway to foot ulceration[2-4,6]. Principal contributory factors that might result in foot ulcer development could be risk factors for foot ulcers[35]

- h/o Previous foot ulcer
- h/o Previous amputation
- Peripheral neuropathy
- Foot deformity
- Peripheral vascular disease
- Visual impairment
- Diabetic nephropathy (especially patients on dialysis)
- Poor glycemic control
- Cigarette smoking

Despite the frequency of complications involving diabetic patient's lower limbs, primary care practitioners frequently neglect to examine their feet. Surveys of physicians and patient chart evaluations in USA & Canada have determined that fewer than 50% of diabetic patients receive appropriate foot evaluation as part of their annual medical checkups[7-9].

Patients themselves are often unaware of serious foot problems because neuropathy removes the pain that would normally alert them. A community study discovered that 10% of patients diagnosed with diabetic foot ulcers did not know themselves that they had ulcers until they were advised by physicians[10].

Consensus panels have recommended annual foot examinations be performed for all diabetic patients older than 15 years and even more frequent assessments if patients are at risk from peripheral ischemia or neuropathy[11,12].

Clinical examination and investigations are focused on identifying the aetiology as well as the extent of foot disease. The monofilament test is a simple, bedside test that can predict the risk of neuropathic ulceration. The majority of amputations are preventable through a combination of good foot care and appropriate education for patients and healthcare providers and appropriate footwear.

Many studies have been published proposing a range of tests that might usefully identify patients at risk of foot ulceration, creating confusion among practitioners as to which screening tests should be adopted in clinical practice.

As identification of those patients at risk of foot problems is the first step in preventing such complications, this article will focus on key components of the foot examination.

COMPONENTS OF THE FOOT EXAMINATION

History

While history is a very important component of risk assessment, a patient cannot be fully assessed by history alone; a careful foot exam remains the key component of this process. Key components of the history include previous foot ulceration or amputation. Other important assessments in the history (Table 1) include neuropathic or peripheral vascular symptoms[5,13], impaired vision, or renal replacement therapy. Lastly, tobacco use should be recorded, since cigarette smoking & Tobacco consumption in any form is a risk factor not only for vascular disease but also for neuropathy.

GAIT

In OPD as soon as patient starts walking towards you, his or her neuropathy status can be guessed.

If patient having foot ulcer is walking with a limp, that means he might be suffering from mild to moderate Neuropathy. If he walks having foot ulcer without limp, that means he has severe neuropathy. If DFU patient walks with foot drop or high stamping gait possibility

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Table 1: *Essential features of history*

Past History

- Ulceration
- amputation
- Charcot joint
- vascular surgery
- angioplasty
- Cigarette smoking- Duration,Quantity,Type(Cigarette/Beedi/Hukka)
- Consumption of Tobacco in other form (e.g.Gutka/Khainee/Paan/Jarda etc.)

Neuropathic symptoms

- Positive e.g., burning or shooting pain, electrical or sharp sensations,Tingling etc.
- negative e.g., numbness, feet feel dead, walking on 'mattress'

Vascular symptoms

- Claudication- Distance
- Rest pain
- Coolness of feet

Other diabetes complications

- Renal (Microalbuminurea /Increased Urea or Creatinine / Dialysis/ Transplant)
- Retinal (visual impairment)
- Cardio vascular(CAD, Cardiomyopathy, CHF, Stroke etc.)

of motor neuropathy can be there.
If while walking patients Slippers or "Chappals" are slipping out of his feet possibility of sensory as well as motor neuropathy can not be ruled out.

GENERAL INSPECTION

Patient should be asked to remove his shoe wear along with socks and a careful inspection of the feet in a well-lit room should always be carried out .Because inappropriate footwear and foot deformities are common contributory factors in the development of Diabetic foot ulceration[1,6], one should always inspect Shoe wear and patient should be asked about the suitability of shoe wear. Examples of inappropriate shoes include, shoes who are excessively worn off or are too small for the person's feet (too narrow, too short, toe box too low), resulting in rubbing, erythema, blister, or callus.
Features that should be assessed during foot inspection are outlined in Table 2 and are discussed below.

Table 2: *Key components of the diabetic foot exam*

Inspection

Dermatologic

- Skin status: color, thickness, Sweating/Dryness-Autonomic Neuropathy
- Turgid Veins: Autonomic neuropathy with A.V. Shunting
- Nails: Hard but brittle in neuropathy
- Loss of hair: Vasculopathy
- Any infection: Cellulitis, Boil, Abscess, check between toes for fungal infection
- Any Ulceration : Number, site, size, shape, edges, base, discharge, status of granulation tissue.
- Calluses/blistering: hemorrhage into callus?

Musculoskeletal

- Different foot deformities, e.g., Hammer toes,claw toes, prominent metatarsal heads, Charcot joint, Hallux Valgus

  Muscle wasting -guttering between metatarsals,

Neurological assessment

10-g monofilament + 1 of the following 4

- vibration using 128-Hz tuning fork
- pinprick sensation
- ankle reflexes
- VPT

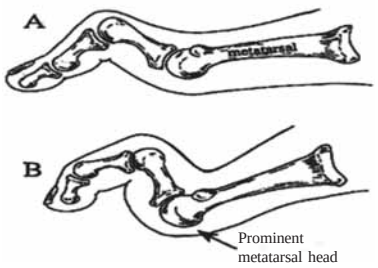
Vascular assessment

- foot pulses
- ABI, if indicated

DERMATOLOGICAL ASSESSMENT

The dermatological assessment should initially include a global inspection,(interdigitally also), for the presence of ulceration or areas of abnormal erythema. The presence of callus (particularly with haemorrhage), nail dystrophy, ingrown toe nail or paronychia should be recorded[14], Focal or global skin temperature differences between one foot and the other may be predictive of either vascular disease or Cellulitis associated with or without ulcer. Local Skin temperature can be judged crudely by back of the hand otherwise Laser Thermometer is ideal and more precise.

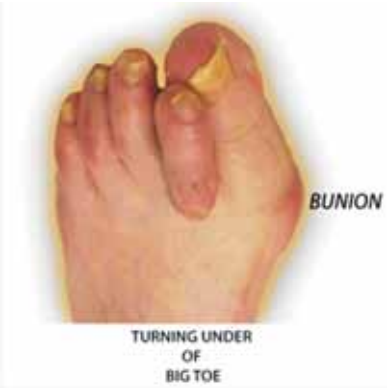
Laser Skin Thermometer



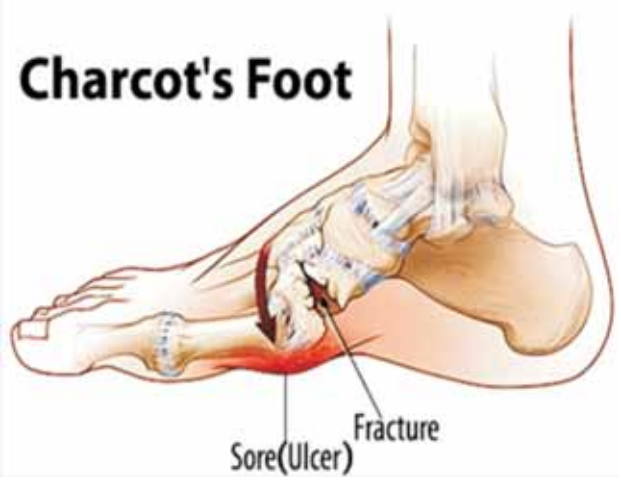
A. Hammer Toe

B. ClawToe

Musculoskeletal assessment.(Foot Deformities)



Foot deformities lead to high pressure areas leading to diabetic foot ulceration. The musculoskeletal assessment should include evaluation for any gross foot deformity[15]. Rigid deformities are defined as any contractures that cannot easily be manually reduced and are most frequently found in the digits. Common forefoot deformities that are known to increase plantar pressures and are associated with skin breakdown include claw toe or hammer toe[16-18].
An important and often overlooked or misdiagnosed condition is Charcot arthropathy. This occurs in the neuropathic foot and most often affects the mid foot. This may present as a unilateral red, hot, swollen, flat foot with profound deformity[19-21]. A rocker-bottom deformity secondary to Charcot arthropathy can cause excessive pressure at the plantar mid foot, increasing risk for ulceration at that site. A patient with suspected Charcot arthropathy should be immediately referred to a specialist for further assessment and care.



NEUROLOGICAL ASSESSMENT

Peripheral neuropathy is the most common component cause in the pathway to diabetic foot ulceration [1,3,5,6]. The clinical exam recommended, however, is designed to identify loss of protective sensation (LOPS) rather than early neuropathy. The diagnosis and management of the latter were covered in a 2004 ADA technical review[5]. The clinical examination to identify LOPS is simple and requires no expensive equipment.

Five simple clinical tests (Table3) each with evidence from well-conducted prospective clinical cohort studies, are considered useful in the diagnosis of LOPS in the diabetic foot [1-6,22]. The task force agrees that any of the five tests listed could be used by clinicians to identify LOPS, although ideally two of these should be regularly performed during the screening exam-normally the 10-g monofilament and one other test. One or more abnormal tests would suggest LOPS, while at least two normal tests (and no abnormal test) would rule out LOPS. however, identification of the patient with LOPS can easily be carried out without Biothesiometer or other expensive equipment.

Table 3 : *Simple bed side Clinical tests for LOPS*

S. No.	Clinical Tests
1.	*10-g monofilaments.*
2.	*Pinprick sensation.*
3.	*Ankle reflexes*
4.	Tuning fork test
5.	VPT(Vibration perception threshold) testing.

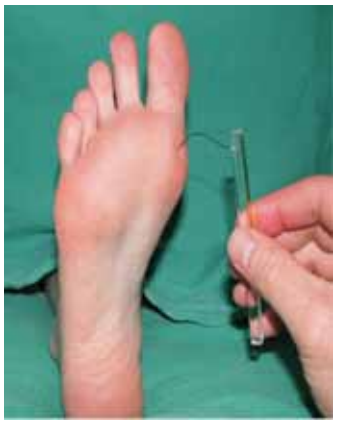
10-G MONOFILAMENTS

Monofilaments, sometimes known as Semmes-Weinstein monofilaments, were originally used to diagnose sensory loss in leprosy[23]. Many prospective studies have confirmed that loss of pressure sensation using the 10-g monofilament is highly predictive of subsequent ulceration[2,23,24]. Screening for sensory loss with the 10-g monofilament is in widespread use across the world, and its efficacy in this regard has been confirmed in a number of trials, including Seattle Diabetic Foot Study[3,23,25,26].

A prospective study published in Diabetes Care in 1992 showed the loss of sensation to the 10-g ûlament on the sole of the foot was associated with a 10-fold risk of foot ulceration and a 17-fold risk of amputation over a 32-month follow-up period[27].

The most important areas to assess are uncallused regions of the plantar surface of the metatarsal heads, although some authors advocate assessing as many as 10 spots over the sole of the foot from the toes to the heel[28].

Nylon monofilaments are constructed to buckle when a 10-g force is applied; loss of the ability to detect this pressure at one or more anatomic sites on the plantar surface of the foot has been associated with loss of large-fibre nerve function. It is recommended that six sites (1st, 3rd, and 5th metatarsal heads, plantar surface of distal hallux, Instep & Heel) be tested on each foot while the patient's eyes are closed.



For performance of the 10-g monofilament test, the device is placed perpendicular to the skin, with pressure applied until the monofilament buckles. It should be held in place for <"1 s and then released.

Caution is necessary when selecting the brand of monofilament to use, as many commercially available monofilaments have been shown to be inaccurate. Single-use disposable monofilaments or those shown to be accurate by the Booth and Young[25] study are recommended. The sensation of pressure using the buckling 10-g monofilament should first be demonstrated to the patient on a proximal site (e.g., upper arm). The sites of the foot may then be examined by asking the patient to respond "yes" or "no" when asked whether the monofilament is being applied to the particular site; the patient should recognize the perception of pressure as well as identify the correct site. Areas of callus should always be avoided when testing for pressure perception.

PINPRICK SENSATION

Inability of a subject to perceive pinprick sensation has been associated with an increased risk of ulceration[3]. A disposable pin should be applied just proximal to the toenail on the dorsal surface of the hallux, with just enough pressure to deform the skin. Inability to perceive pinprick over either hallux would be regarded as an abnormal test result.

ANKLE REFLEXES

Absence of ankle reflexes has also been associated with increased risk of foot ulceration[3]. Ankle reflexes can be tested with the patient either kneeling or resting on a couch/table. The Achilles tendon should be stretched until the ankle is in a neutral position before striking it with the tendon hammer. If a response is initially absent, the patient can be asked to hook fingers together and pull, with the ankle reflexes

then retested with reinforcement. Total absence of ankle reflex either at rest or upon reinforcement is regarded as an abnormal result.

TUNING FORK TEST

The tuning fork of 128-Hz is widely used in clinical practice and provides an easy and inexpensive test of vibratory sensation. Vibratory sensation should be tested over the tip of the great toe bilaterally. An abnormal response can be defined as when the patient loses vibratory sensation and the examiner still perceives it while holding the fork on the tip of the toe[2,3].

VPT (VIBRATION PERCEPTION THRESHOLD) TESTING

Vibration perception threshold Machine

The biothesiometer (or neurothesiometer) is a simple handheld device that gives semi quantitative assessment of vibration perception threshold (VPT). Vibration perception using the biothesiometer is also tested over the six points over plantar surface. With the patient lying supine, the stylus of the instrument is placed over the plantar point and the amplitude is increased until the patient can detect the vibration; the resulting number is known as the VPT. This process should initially be demonstrated on a proximal site, and then the mean of three readings is taken . A VPT >15 V is regarded as abnormal and higher VPT readings has been shown to be strongly predictive of subsequent foot ulceration[16,24].

CIRCULATORY ASSESSMENT

Peripheral arterial disease (PAD) is a component cause in approximately one-third of foot ulcers and is often a significant risk factor associated with recurrent wounds[1,29]. Therefore, the assessment of PAD is important in defining overall lower-extremity risk status. Assessment of peripheral circulation in diabetic patients includes the standard evaluation for pedal pulses ; however, examiner s should be aware of the possible pitfalls of using presence of pulses alone to exclude clinically signiûcant peripheral ischemia. Rivers et al[37] describe a series of diabetic patients who had sufficiently severe peripheral ischemia to warrant distal surgical bypass procedures despite the presence of readily palpable pedal pulses. Vascular examination should include palpation of the posterior tibial and dorsalis pedis pulses[30,31], which should be characterized as either “present” or “absent”[31].

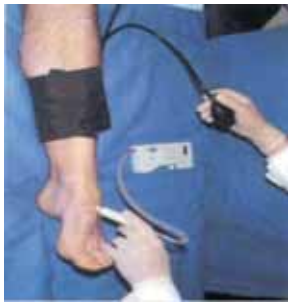
Consequently, in addition to clinical parameters, non invasive measures of circulation are frequently used to complement physical examination in assessing the degree of arterial obstruction.

More reliable methods of assessing potential for healing foot ulcers in diabetic patients suspected of having peripheral ischemia involve measurement of Ankle Brachial Index, systolic toe pressure measurements or measurement of distal transcutaneous oxygen tension(TcPo2)[32,33].

ANKLE BRACHIAL INDEX (ABI)

Diabetic patients with signs or symptoms of vascular disease(like Intermittent claudication, Rest Pains, nocturnal pain, cold feet, blanching on elevation of limb & rubor on dependency, delayed capillary filling, Impending tissue loss or established gangrene) or absent pulses on screening foot examination should undergo ankle brachial pressure index (ABI) pressure testing . The ABI is a simple and easily reproducible method of diagnosing vascular insufficiency in the lower limbs. Blood pressure at the ankle (dorsalis pedis or posterior tibial arteries) is measured using a standard Doppler ultrasonic probe. The ABI is obtained by dividing the ankle systolic pressure by the higher of the two brachial systolic pressures[13]. An ABI >0.9 to <1.3 is normal[36].ABI <0.8 is associated with claudication, and <0.4 is commonly associated with ischemic rest pain and tissue necrosis.

The ADA Consensus Panel on PAD recommended measurement of ABI in diabetic patients over 50 years of age and consideration of



ABI Measurement

ABI measurement in younger patients with multiple PAD risk factors, repeating normal tests every 5 years[13]. ABI may therefore be part of the annual comprehensive foot exam in these patient subgroups.

Although the ankle-brachial index (ABI) is used to indicate adequacy of peripheral blood flow in patients without diabetes, the ABI is less reliable in diabetic patients because calcification of the media of the distal arteries is common. This calcification makes the vessels relatively non-compressible, resulting in an artiûcially high systolic pressure in the ankle or supra-systolic ankle pressures[34].

In the presence of incompressible calf or ankle arteries (ABI >1.3), measurements of digital arterial systolic pressure (toe pressure) by photo plethysmography or transcutaneous oxygen tension(TcPo2) may be performed.

Both these latter assessments are performed in specialty diabetic foot clinics or vascular laboratories and offer an indication of potential for healing, before angiography is considered. A contrast angiogram remains the criterion standard of assessment in patients with peripheral vascular problems but has to be under taken with caution among patient s with diabetes who often already have nephropathy. Using contrast dye in patients with renal disease can result in complete renal shutdown.

CONCLUSIONS

It cannot be overstated that the complications of the diabetic foot are common, complex, and costly, mandating aggressive and proactive preventative assessments by Physicians. All diabetic patients must have their feet evaluated at least at yearly intervals for the presence of the predisposing factors for ulceration and amputation . If abnormalities are present, more frequent evaluation of the diabetic foot is recommended depending on risk category. It is through systematic examination and risk assessment, patient education, and timely referral that we may further reduce the unnecessarily high prevalence of lower-extremity morbidity & amputation in this subset of population.

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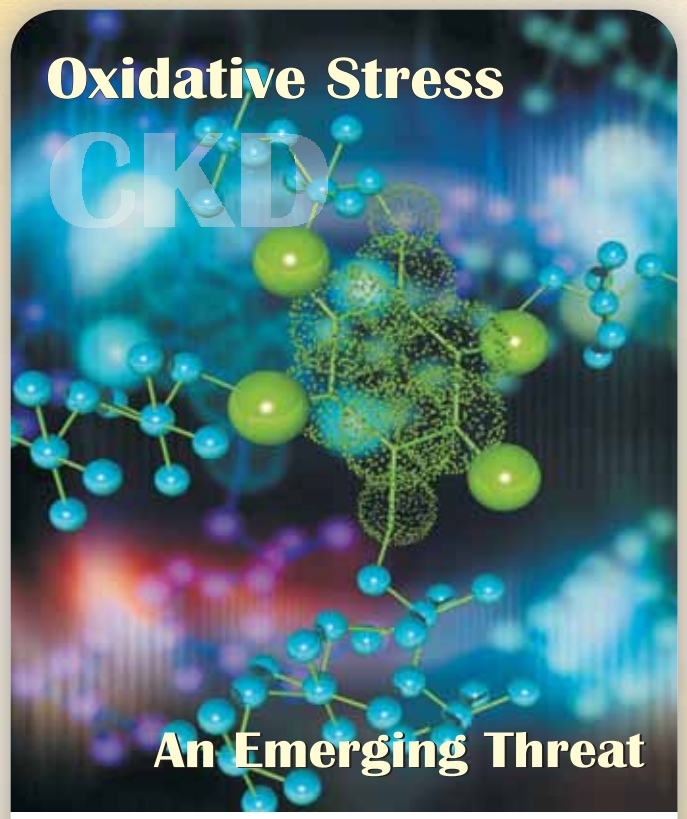

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Why Diabetic Foot Ulcers do not heal?

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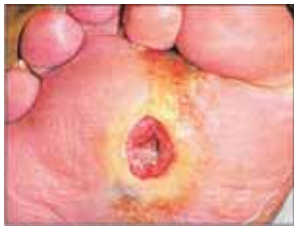
Abstract: *Diabetic foot ulcers are known for their chronicity and they pose challenges to even the most experienced health care professionals. Three basic reasons of chronicity of Diabetic Foot Ulcers are Diabetic Triopathy (neuropathy, vasculopathy & immunopathy),inadequate levels of growth factors & presence of biofilm. Following an injury to the skin, a set of complex biochemical events take place in a closely orchestrated cascade in order to repair the damage. The natural healing process can be divided into four stages: inflammation, granulation, epithelialisation and maturation. However, when a wound becomes delayed in healing, these four stages are interrupted and a large number of changes occur that result in the wound becoming chronic, lasting sometimes for years without healing. Unstable diabetes and colonization of bacteria are two of the primary causes of this chronicity.*
The decisions of when to use antimicrobials, offloading and antibiotics, are not always straightforward and inexperienced assessors can choose inappropriate and unnecessarily expensive dressings. Infections with methicillin resistant Staphylococcus aureus have been increasing worldwide and they are difficult to treat. Diabetic Foot Ulcers carrying drug resistant bacterial strains such as methicillin resistant Staphylococcus aureus (MRSA) have more chronic wounds and Wound Chronicity. Inpatient Care, and Chronic Kidney Disease Predispose to MRSA Infection in Diabetic Foot Ulcers. In diabetic patients there is failure of fibroblasts to produce adequate ECM proteins and keratinocytes to epithelize the wound. Fibroblast gene expression is different in chronic wounds than in acute wounds. Localized Pressure also plays a major role in the formation of non healing diabetic foot ulcers that's why off-loading of the DFU is mainstay of treating DFU.
Diabetic patients are always under emotional stress which can negatively affect the healing of a wound, possibly by raising blood pressure and levels of cortisol, which lowers immunity . Co morbid ailments that may contribute to the formation of chronic wounds include vasculitis, immune suppression, pyoderma gangrenosum, and diseases that cause ischemia.

INTRODUCTION

60–80% of all human infectious diseases comprise of Chronic human infections, including chronic wounds[1].
Diabetic extremity ulcers develop in approximately 15 percent of people with diabetes and are a leading cause of hospitalization and amputation among such patients[2]. Wound infection, faulty wound healing, and ischemia in combination with a foot ulcer are the most common precursors to diabetes-related amputations; and eighty-five percent of lower-limb amputations in patients with diabetes are preceded by biofilm infected foot ulceration[3-5].
More than 80,000 amputations were performed on the United States' diabetic population each year(National Diabetes Statistics 2005)[6]. According to vascular Society of India (2010) no. of amputations in India are 80,000 to 100,000 every year,which are tip of Iceberg because of poor registry in India. Diabetic foot ulcer infection followed by amputation contribute dramatically not only to the morbidity among persons with diabetes[7] but are also associated with severe clinical depression and dramatically increased mortality rates[8]. Such infected ulcers resulting in amputation account for a threefold increased risk of death within 18 months. Additionally, the psychological impact of an amputation dramatically increases this risk of mortality within a similar time period. As such, diabetic foot ulcers are the most common, disabling,Chronic and costly complications of diabetes[9,10].

CHRONIC NONHEALING METATARSAL DIABETIC FOOT ULCER

Following an injury to the skin, a set of complex biochemical events take place in a closely orchestrated cascade in order to repair the damage. The natural healing process can be divided into four stages: inflammation, granulation, epithelialization and maturation[11].
However, when a wound becomes delayed in healing, these four stages are interrupted and a large number of changes occur that result in the



wound becoming chronic,lasting sometimes for years without healing. Unstable diabetes and colonization of bacteria are two of the primary causes of this chronicity[12].
Diabetic foot ulcers pose challenges to even the most experienced health professionals[13].
The decisions of when to use antimicrobials, offloading and antibiotics are not always straightforward and inexperienced assessors can choose inappropriate and unnecessarily expensive dressings.

CAUSES OF CHRONOCITY OF DIABETIC FOOT ULCERS CAN BE

A. Triopathy of Diabetes
B. Inadequate levels of Growth Factors
C. Biofilm
D. Miscellaneous causes

A.Triopathy of Diabetes

DURING the observation of patients whose diabetes has been for no. of years, a triad is being recognized with increasing frequency; It is well established that poorly controlled diabetes mellitus leads to vasculopathy, immunopathy and neuropathy[14]. This triopathy collectively & individually is responsible for chronicity of Diabetic Foot Ulcers.
1.Immunopathy: Diabetic patients have Impaired Poly Morpho Nuclear Function. Their polymorps have reduced capacity to migrate at infective

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site and have decrease capability to engulf micro-organisms. There is reduced chemo taxis & intracellular killing. These defects in Immune system are more so when patient has ketosis.
Because of poor Immune response & abundant food(i.e. sugar) in blood & wound, bacterias flare up & wound gets infected which is usually Polymicrobial ,difficult to treat hence chronicity of wound.
2. Neuropathy : Diabetes causes neuropathy, which inhibits nociception and the perception of pain. Thus patients may not initially notice small wounds of legs and feet, and may therefore fail to prevent infection or repeated injury.
Galkowska H et al from Poland observed reduction of foot skin innervation and neurogenic factors expression in Diabetic Foot Ulcers and they correlated low inflammatory cell accumulation and subsequent chronicity of diabetic foot ulcer healing process in both neuropathic and non-neuropathic patients[15].
3. Vasculopathy: Almost all Diabetic patient have Micro & or Macroangiopathy causing decrease oxygenation of tissue.Ischemia causes tissue to become inflamed and cells to release factors that attract neutrophils.While they fight pathogens, neutrophils also release inflammatory cytokines and enzymes that damage cells. They also produce ROS (**Reactive oxygen species)** to kill bacteria, for which they use an enzyme called myeloperoxidase. The enzymes and ROS produced by neutrophils and other leukocytes damage cells and prevent cell proliferation and wound closure by damaging DNA,lipids, proteins,the ECM, and cytokines (who speed healing).
Neutrophils remain in chronic wounds for longer than they do in acute wounds, and contribute to the fact that chronic wounds have higher levels of inflammatory cytokines and ROS[16].

B.Inadequate levels of Growth Factors

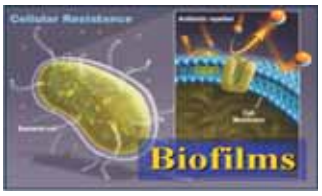
Chronic wounds also differ in makeup from acute wounds in that their levels of proteolytic enzymes such as elastase. and matrix metallo proteinases (MMPs) are higher, while their concentrations of growth factors such as PPDGF and Keratinocyte Growth Factor are lower.As we knowGrowth factors (GFs) are imperative in timely wound healing hence ***inadequate GF levels*** may be an important factor in chronic wound formation[17].

C. Biofilm

Legwound with (Rt. Side) & without (Lt. side) Biofilm
Biofilms are bacterial cities clinging to wound .Bacterial biofilms,or sessile communities of bacteria that reside in a complex matrix of exo polymeric material, contribute to the severity, chronicity and refractoriness of diabetic wounds.
Biofilms are highly resistant to both phagocytes and antibiotics
The NIH has estimated that more than 80% of chronic bacterial infections involve biofilms, and it has been demonstrated that bacterias residing in biofilms can be up to 1000 times more resistant to antibiotic s than free floating planktonic bacteria.
P. aeruginosa forms biofilms more readily in the diabetic wound environment, which leads to increased resistance to antimicrobial agents, and could help explain why diabetic wounds are typically slower to heal, and more difficult to treat than non-diabetic wounds[18].

D. Miscellaneous Causes

Infections with methicillin resistant Staphylococcus aureus (MRSA) have been increasing worldwide and they are difficult to treat. Diabetic Foot Ulcers carrying drug resistant bacterial strains such as methicillin resistant Staphylococcus aureus (MRSA) have more chronic wounds[19] and Wound Chronicity, Inpatient Care, and Chronic Kidney Disease Predispose toMRSA Infection in Diabetic Foot Ulcers[20].
In diabetic patients there is Failure of fibroblasts to produce adequate ECM proteins and keratinocytes to epithelize the wound. Fibroblast



Leg wound with (Rt. Side) & without (Lt. side) Biofilm

gene expression is different in chronic wounds than in acute wounds[21].
Localized Pressure also plays a major role in the formation of diabetic ulcers.
Diabetic patients are always under tremendous emotional stress. Emotional Stress can also negatively affect the healing of a wound, possibly by raising blood pressure and levels of cortisol, which lowers immunity[22].
Co morbid ailments that may contribute to the formation of chronic wounds include vasculitis, immune suppression,pyoderma gangrenosum, and diseases that cause ischemia.

Clinical Causes of Delayed/Non Healing DFU

Primary Causes	**Secondary Causes**
Inadequate Off Loading	Inadequate Antibiotic Therapy
Incorrect Vascular assessment	Incorrect Method of Dressing
Inadequate Debridement	Associated Tuberculosis/ Nephropathy Drugs

Agents which Delay Wound Healing In Diabetes

Corticosteroids	Povidone Iodine
Nitrofurantoin	Eusol Solution
Liquid Detergents	Chlorhexidine 2%
Neomycin Sulphate	Hydrogen Peroxide

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Diabetic Foot Infections.

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Abstract: *Diabetes is known for it's complications & Diabetic Foot infections are one of the most common problems in Diabetics. They are predisposed to foot infections because of a compromised vascular supply secondary to diabetes. Local trauma in association with lack of sensation because of neuropathy & microvascular disease, may result in various diabetic foot infections that run the spectrum from localised simple, superficial* ***Cellulitis to chronic osteomyelitis.***

Infections in patients with diabetes are difficult to treat because they have impaired microvascular circulation, which limits the access of phagocytic cells to the infected area along with poor concentration of antibiotics in the infected tissues. In addition, diabetic individuals can not only have a combined infection involving bone and soft tissue called fetid foot, a severe and extensive, chronic soft-tissue and bone infection that causes a foul exudate, but they may also have peripheral vascular disease involving large vessels, as well as microvascular and capillary disease that results in PVD with gangrene.

Normal Commensals of skin who are harmless in non diabetics can cause severe life threatening infections in Diabetic patients leading to loss of limb or life. Gas gangrene is conspicuous because of its low incidence in patients with diabetes, but deep-skin and soft-tissue infections, which are due to gas-producing organisms, frequently occur in patients with these infections.

In general, foot infections in persons with diabetes become more severe and take longer to cure than do equivalent infections in persons without diabetes.

INTRODUCTION

Diabetes is known for it's complications & Diabetic Foot infections are one of the most common problems in Diabetics. They are predisposed to foot infections because of a compromised vascular supply secondary to diabetes. Local trauma in association with lack of sensation because of neuropathy & micro vascular disease, may result in various diabetic foot infections that run the spectrum from localised simple, superficial Cellulites to chronic osteomyelitis.

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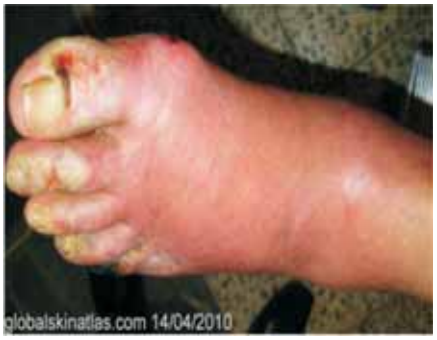

Normal Commensals of skin who are harmless in non diabetics can cause severe life threatening infections in Diabetic patients leading to loss of limb or life. Gas gangrene is conspicuous because of its low incidence in patients with diabetes, but deep-skin and soft-tissue infections, which are due to gas-producing organisms, frequently occur in patients with these infections.

In general, foot infections in persons with diabetes become more severe and take longer to cure than do equivalent infections in persons without diabetes.

EPIDEMIOLOGY

Globally, diabetic foot infections are the most common skeletal and soft-tissue infections in patients with diabetes. The incidence of diabetic foot infections is similar to that of diabetes in various ethnic groups and elderly patients are more commonly affected. There are no significant differences between the sexes.

In USA incidence of Amputation was 40,000 per year (Lancet, 2005) & in India the Incidence rate is @ 80,000 to one lakh amputations per year (2010 data of Vascu.Society of India) which can be tip of the Iceberg because of poor registry in india and it is well established fact that more than 85% of amputations are preceded by trivial DFU which get infected.

The mortality risk is highest in patients with chronic osteomyelitis and in those with acute necrotizing soft-tissue infections.

PATHOPHYSIOLOGY

Patients with diabetes are particularly susceptible to foot infection primarily because of Neuropathy, Vasculopathy (vascular insufficiency), and Immunopathy (diminished neutrophil function).5 Peripheral neuropathy has a central role in the development of a foot infection and it occurs in about 50 to 70 percent of patients with diabetes. Patients with diabetes lose the protective sensations for temperature and pain, impairing awareness of trauma such as abrasions, blistering, or penetrating foreign body. Bare feet walking is very common in Indians particularly those of rural areas & with insensate foot diabetic patients donot come to know various local injuries made by small pebbles,thorn,Splinters,nails etc.Motor neuropathy can

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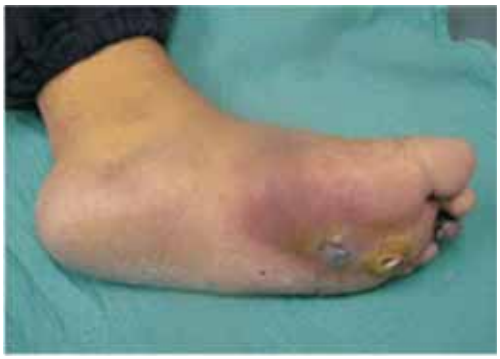
result in foot deformities (e.g., Hammer & claw toe etc.) that contribute to increase local pressure from footwear, leading to corn or callus formation with s.c. haemorrhage making skin ulceration even more likely.

Once the skin is broken (typically on the plantar surface), the underlying tissues are exposed to colonization by pathogenic organisms. The resulting wound infection may begin superficially, but with delay in treatment and impaired body defence mechanisms, it can spread to the contiguous subcutaneous tissues and to even deeper structures(deep Plantar spaces)[5,6].



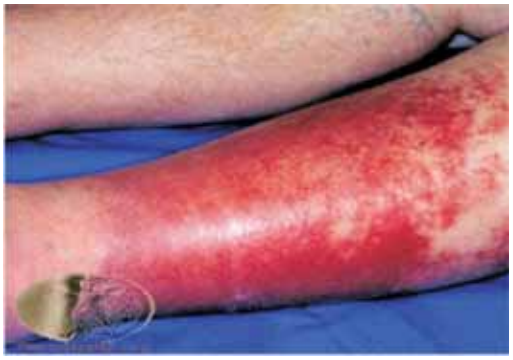
Plantar foot ulcers with a deep space infection.

Although most diabetic foot infections begin with an ulcer, localized cellulites and necrotizing fasciitis can develop in the absence of an ulcer or traumatic injury. Most diabetic foot infections occur in the setting of good dorsalis pedis pulses; this finding indicates that the primary problem in diabetic foot infections is micro vascular compromise.

If chronic osteomyelitis is left untreated for years, it may lead to complications such as amyloidosis or squamous cell carcinoma at the site of drainage through the skin.

MICROBIAL CHARACTERISTICS

The microbiologic features of diabetic foot infections vary according to the tissue infected. In patients with diabetes, superficial skin infections, such as cellulitis, are caused by the same organisms as those in healthy hosts, namely group A streptococci and Staphylococcus aureus. Group B streptococcal cellulitis is uncommon in healthy hosts but not uncommon in patients with diabetes. In diabetic individuals, group B streptococci may cause urinary tract infections and catheter-associated bacteriuria in addition to cellulitis, skin and/or soft-tissue infections, and chronic osteomyelitis. Such infections may be complicated by bacteremia.



Cellulitis of Leg

Furthermore, as previously mentioned, deep soft-tissue infections in diabetic persons can be associated with gas-producing, gram-negative bacilli. Clinically, these infections appear as necrotizing fasciitis, compartment syndrome, or myositis. Gas gangrene is uncommon in persons with diabetes.

Acute osteomyelitis usually occurs as a result of foot trauma in an individual with diabetes. The distribution of organisms is the same as that in an individual without diabetes who has acute osteomyelitis. In chronic osteomyelitis, however, the pathogens include group A and group B streptococci, aerobic gram-negative bacilli, and Bacteroides fragilis.

Other pathogens implicated in chronic osteomyelitis in patients with diabetes include *B fragilis*, Escherichia coli, Proteus mirabilis, and Klebsiella pneumoniae.

Pseudomonas aeruginosa is generally not a pathogen in chronic osteomyelitis in these individuals. Although P aeruginosa is frequently cultured from samples obtained from a draining sinus tract or deep penetrating ulcers in patients with diabetes, these organisms are superficial colonizers and are generally not the cause of the bone infection.

Because Pseudomonas organisms are water-borne, superficial ulcers may be contaminated by bacteria in wet socks or dressings or walking bare feet in religious places (a common practice adopted by Indians washing their feet in common water trough while going inside Gurudwara /Temple or Mosque) or common bathing places or swimming pool.

Fetid foot usually represents a combined deep-skin and or soft-tissue infection caused by anerobic micro-organisms. Anaerobic bacteria are usually part of mixed infections in patients with foot ischemia or gangrene.

The most common pathogens in acute, previously untreated, superficial infected foot wounds in patients with diabetes are aerobic gram-positive bacteria, particularly *Staphylococcus aureus* and beta-hemolytic streptococci (group A, B, and others).[5] Infection in patients who have recently received antibiotics or who have deep limb-threatening infection or chronic wounds are usually caused by a mixture of aerobic gram-positive, aerobic gram-negative (e.g., *Escherichia coli*, *Proteus* species, *Klebsiella* species), and anaerobic organisms

(e.g., *Bacteroides* species, *Clostridium* species, *Peptococcus* and *Peptostreptococcus* species).[8]

Picture of MRSA bacteria greatly magnified.

Methicillin-resistant *S. aureus* (MRSA) is a more common pathogen in patients who have been previously hospitalized or who have recently received antibiotic therapy. MRSA infection can also occur in the absence of risk factors because of the increasing prevalence of MRSA in the community[9,10].

CONFIRMING THE DIAGNOSIS

Diabetic foot infection must be diagnosed clinically rather than bacteriologically because all skin ulcers harbour micro-organisms . The clinical diagnosis of foot infection is based on the presence of purulent discharge from an ulcer or the classic signs of inflammation (i.e., erythema, pain, tenderness, warmth, or induration). Other suggestive features of infection include foul odor, the presence of necrosis, and failure of wound healing despite optimal management[11]. Local inflammatory findings may be less prominent or absent in some diabetic foot infections. For example, pain and tenderness may be reduced or absent in patients who have neuropathy, whereas erythema may be absent in those with vascular disease[12].
Acute Charcot's foot is characterized by a progressive deterioration of weight-bearing joints, usually in the foot or ankle. It can clinically mimic cellulites and presents as erythema, edema, and elevated temperature of the foot. Most patients with diabetic foot infection do not have systemic features such as fever or chills. The presence of systemic signs or symptoms indicates a severe deep infection[13].

OBTAINING CULTURES

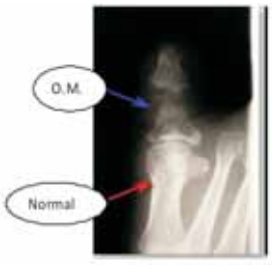
Never take a superficial swab for Culture. Before an infected wound is cultured, any overlying necrotic debris should be removed by scrubbing the wound with saline-moistened sterile gauze to eliminate surface contamination[5,14].
For wound culture, tissue specimens should be obtained by scraping the base of the ulcer with a scalpel or curette, or by a biopsy of the wound or bone. The specimen should be processed for a Gram-stained smear and aerobic and anaerobic cultures.

ASSESSING VASCULAR STATUS

One should always palpate peripheral pulses (Dorsalis Pedis artery, Posterior Tibial artery, popliteal artery & Femoral artery) in case of diabetic Foot. Peripheral artery disease (PAD) can be diagnosed by absence of foot pulses , reduced ankle-brachial index (ABI) or ischemic flow pattern on Peripheral arterial Vascular Doppler followed by Angiography,if need arises. If a PAD diagnosis is confirmed and revascularization is planned, magnetic resonance angiography, computed tomography angiography, or contrast angiography can be performed for anatomic evaluation[15].
Venous insufficiency can be diagnosed clinically by the presence of tortous & engorged veins, edema and skin changes and confirmed by duplex ultrasonography.

ASSESSING NEUROPATHY

Touch, vibration, and pressure sensations should be checked routinely using cotton wool, tuning fork, and 10-g nylon monofilament, respectively.



Diagnostic Imaging

Diagnostic imaging is not necessary for every patient with diabetes who has a foot infection. Plain radiography of the foot is indicated for detection of osteomyelitis, foreign bodies, or gas in soft tissue. Bony abnormalities associated with osteomyelitis may be indistinguishable from the destructive effects of Charcot's foot and are usually not evident on plain radiography until two to four weeks after initial infection[17].
When plain radiography is negative but osteomyelitis is clinically suspected, radio-nuclide scan or magnetic resonance imaging should be performed. Combining Technetium Bone Scan with Gallium Scan or white blood cell scan may improve the diagnostic yield for osteomyelitis[16,17]. Magnetic resonance imaging provides more accurate information regarding the extent of the infectious process[18]. Ultrasonography and computed tomography are also helpful in evaluating abnormalities in the soft tissue (e.g., abscess, sinus tract, cortical bone involvement) and may provide guidance for diagnostic and therapeutic aspiration, drainage, or tissue biopsy[19].

ESTABLISHING SEVERITY OF INFECTION

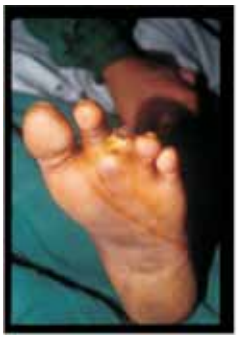
The severity of the infection determines the appropriate antibiotic regimen and route of administration. It also is the primary consideration in determining the need for hospitalization and the indications and timing for any surgical intervention. A practical and simple approach to classifying diabetic foot infection is provided.

CLINICAL CLASSIFICATION OF DIABETIC FOOT INFECTION

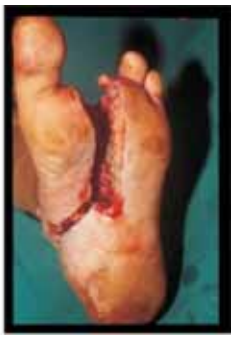
IDSA (**Infectious Diseases Society of America**) Diabetic Foot Infection Classification[20].

- Uninfected: lacking purulence or signs of inflammation
- Mild: infection limited to superficial tissue, cellulites < 2 cm around ulcer, no systemic signs
- Moderate: Systemically well & metabolically stable, more than one of -Cellulites > 2 cm from ulcer, deep tissue involvement, abscess, gangrene, involvement of muscle, tendon, joint or bone
- Severe: foot infection and systemic toxicity and/or metabolic instability
- Fever or chills
- Confusion, vomiting
- Tachycardia, hypotension
- Leukocytosis
- Severe hyperglycemia, DKA or azotemia

ESTABLISHING EXTENT OF INFECTION



ICEBERG Phenomenon of DFI



Small Abscess at base of III toe *Same case after Surgery*

Diabetic Foot infections are like Iceberg, Most of the time only small part is visible.

Early recognition of the area of involved tissue can facilitate appropriate management and prevent progression of the infection. The wound should be cleansed and debrided carefully to remove foreign bodies or necrotic material and should be probed with a sterile metal instrument to identify any sinus tracts, abscesses, or involvement of bones or joints.

Osteomyelitis is a common and serious complication of diabetic foot infection that poses a diagnostic challenge. A delay in diagnosis increases the risk of amputation.[21]

Risk factors associated with osteomyelitis are summarized in *Table1*.Visible bone and palpable bone by probing are suggestive of underlying osteomyelitis in patients with a diabetic foot infection.[22] Laboratory studies, such as white blood cell count and the erythrocyte sedimentation rate (ESR), have limited sensitivity for the diagnosis of osteomyelitis. Osteomyelitis is unlikely with normal ESR values; however, an ESR of more than 70 mm per hour supports a clinical suspicion of osteomyelitis.[21] Definitive diagnosis requires

Table: *Risk Factors for Osteomyelitis in Patients with Diabetic Foot Infection*

Appearance of a swollen, deformed red toe (also called sausage toe)
Bone visible or palpable on probing
Infected ulcer with an erythrocyte sedimentation rate of more than 70 mm per hour
Nonhealing ulcer after a few weeks of appropriate care and off-loading of pressure
Radiologically evident bone destruction beneath ulcer
Ulcer area greater than 2 cm^2 or more than 3 mm deep
Ulceration presents over bony prominences for more than two weeks
Ulceration with unexplained leukocytosis

Information from references[5,21-25]

percutaneous or open bone biopsy. Bone biopsy is recommended if the diagnosis of osteomyelitis remains in doubt after imaging[24].

CLINICAL EVALUATION

Treatment

Effective management of diabetic foot infection requires

-Appropriate antibiotic therapy,

-Surgical drainage, debridement and resection of dead tissue,

-Appropriate wound care and

-Correction of metabolic abnormalities.

ANTIBIOTIC THERAPY

The selection of antibiotic therapy for diabetic foot infection involves decisions about choice of empiric and definitive antibiotic agent, route of administration, and duration of treatment

Table 2: *Principles of Antibiotic Therapy for Diabetic Foot Infection*

- Empiric antibiotic regimen should include an agent active against *Staphylococcus aureus*, including methicillin-resistant *S. aureus* if necessary, and streptococci.
- Coverage for aerobic gram-negative pathogens is required for severe infection, chronic infection, or infection that fails to respond to recent antibiotic therapy.
- Necrotic, gangrenous, or foul-smelling wounds usually require ant anaerobic therapy.
- Initial empiric antibiotic therapy should be modified on the basis of the clinical response and culture or susceptibility testing.
- Virulent organisms, such as *S. aureus* and streptococci, should always be covered in polymicrobial infection.
- Coverage for less virulent organisms, such as coagulase-negative staphylococci, may not be needed.
- Parenteral antibiotics are indicated for patients who are systemically ill, have severe infection, are unable to tolerate oral agents, or have infection caused by pathogens that are not susceptible to oral agents.
- Using oral antibiotics for mild to moderate infection and switching early from parenteral to oral antibiotics with appropriate spectrum coverage and good bioavailability and tolerability are strongly encouraged.
- Although topical antibiotics can be effective for the treatment of mildly infected ulcers, they should not be routinely used.
- Discontinuation of antibiotics should be considered when all signs and symptoms of infection have resolved, even if the wound has not completely healed.
- Cost should be considered when selecting antibiotic therapy.

Information from references[5,25]

Initial empiric antibiotic therapy should be based on the severity of the infection, history of recent antibiotic treatment, previous infection with resistant organisms, recent culture results, current Gram stain findings, and patient factors (e.g., drug allergy). A Gram-stained smear of an appropriate wound specimen may help guide therapy. The overall sensitivity of a Gram-stained smear for identifying organisms that grow on culture is 70 percent.[9] The empiric antibiotic regimen for diabetic foot infection should always include an agent active against *S. aureus*, including MRSA if necessary, and streptococci.[5,26,27,28]

The patient should be reassessed 24 to 72 hours after initiating empiric antibiotic therapy to evaluate the response and to modify the antibiotic regimen, if indicated by early culture results. Several antibiotics have been shown to be effective, but no single regimen has shown superiority.[1,2,3,5,29-32] Antibiotic therapy should not be used for foot ulcers without signs of infection because it does not enhance wound healing or prevent infection.

Clinical failure of appropriate antibiotic therapy might be because of patient nonadherence, antibiotic resistance, superinfection, undiagnosed deep abscess or osteomyelitis, or severe tissue ischemia.

SURGICAL TREATMENT

Surgery is the cornerstone of treatment for deep seated diabetic foot infection. Timely and aggressive surgical debridement or limited resection or amputation may reduce the need for more extensive amputation.[34] Procedures range from simple incision and drainage to extensive multiple surgical debridements and amputation. Indications for emergent surgery are severe infection in an ischemic limb, necrotizing fasciitis, gas gangrene, and an infection associated with compartment syndrome. Surgical excision of affected bone has historically been the standard of care in patients with osteomyelitis. Nevertheless, successful therapy with a long course of antibiotics alone has been achieved in two thirds of patients with osteomyelitis. Outcome of diabetic foot infections treated conservatively: a retrospective cohort study with long-term follow-up.[35] As infection is controlled and the wound starts to granulate, delayed primary closure may be successful. The wound may also be treated surgically with a flap or graft, left to heal by secondary intention, or managed with negative pressure dressings,NPWT or VAC(Vacuum Assisted Closure).[36] If the infected limb appears to be ischemic, the patient should be referred to a vascular surgeon. Although noncritical ischemia can usually be treated without a vascular procedure, early revascularization within a few days of the infection is required for

TABLE
Empiric Antibiotic Regimens for Treatment of Diabetic Foot Infection

Severity or extent of infection	*Recommended therapy*	*Comments*
Soft tissue infection		
Mild (duration of treatment is one to two weeks)	Dicloxacillin 500 mg orally four times per day	Oral agent of choice for MSSA
	Cephalexin (Keflex) 500 mg orally four times per day	For penicillin-allergic patients, except those with immediate hypersensitivity reactions
	Amoxicillin/clavulanate (Augmentin) 875/125 mg orally twice per day	Good option for polymicrobial infection
	Clindamycin (Cleocin) 300 to 450 mg orally three times per day	Potential cross-resistance and emergence of resistance in erythromycin-resistant *Staphylococcus aureus;* inducible resistance in MRSA
	Doxycycline (Vibramycin) 100 mg orally twice per day *or* Sulfamethoxazole/trimethoprim (Bactrim) 160/800 mg orally twice per day	Effective for MRSA
Moderate (duration of treatment is two to four weeks, depending on response; administer orally or parenterally followed by orally)		
Risk factors for polymicrobial infection absent*	Nafcillin 1 to 2 g IV every four hours	Parenteral drug of choice for MSSA
	Cefazolin 1 to 2 g IV every eight hours	For penicillin-allergic patients
	Vancomycin 30 mg per kg IV twice per day	Parenteral drug of choice for MRSA
Risk factors for polymicrobial infection present*	Ampicillin/sulbactam (Unasyn) 3 g IV four times per day	—
	Ceftriaxone (Rocephin) 1 to 2 g IV once per day plus clindamycin 600 to 900 mg IV or orally three times per day or metronidazole (Flagyl) 500 mg IV or orally three times per day	—
	Or	
	Levofloxacin (Levaquin) 500 mg IV or orally once per day plus clindamycin 600 to 900 mg IV or orally three times per day	
	Moxifloxacin (Avelox) 400 mg IV or orally once per day	—
	Ertapenem (Invanz) 1 g IV once per day	—
Severe (duration of treatment is two to four weeks, depending on response; administer parenterally, then switch to orally)	Ciprofloxacin (Cipro) 400 mg IV twice per day plus clindamycin 600 to 900 mg IV three times per day	—
	Piperacillin/tazobactam (Zosyn) 3.375 to 4.500 g IV every six to eight hours	—
	Imipenem/cilastatin (Primaxin) 500 mg IV four times per day	—
	Vancomycin 30 mg per kg IV twice per day plus ciprofloxacin 400 mg IV twice per day plus metronidazole 500 mg IV or orally three times per day	Vancomycin is the parenteral drug of choice for MRSA; linezolid (Zyvox) 600 mg IV or orally twice per day or daptomycin (Cubicin) 4 mg per kg IV once per day can also be used for MRSAUse vancomycin for penicillin-allergic patients
	Tigecycline (Tygacil) 100 mg IV loading dose then 50 mg IV twice per day	Should be used when suspected polymicrobial infection, including MRSA
Bone or joint infection		
No residual infected tissue	Use the above parenteral or oral antibiotic regimens for two to five days	—
Residual infected tissue only	Use the above parenteral or oral antibiotic regimens for two to four weeks	—
Residual infected viable bone	Initially use the above parenteral antibiotics followed by oral antibiotics for four to six weeks	—
Residual infected dead bone	Initially use the above parenteral antibiotics followed by oral antibiotics for eight to 12 weeks	—

IV = intravenously; MRSA = methicillin-resistant Staphylococcus aureus; *MSSA = methicillin-susceptible* S. aureus.

**— Risk factors for polymicrobial infection include chronic ulcers, recent antibiotic use, and foot ischemia or gangrene.*

*Information from references*1,2,3,5,29-32

successful treatment of an infected foot with critical limb ischemia.[37]

WOUND MANAGEMENT

The wound should be dressed to allow for careful inspection for evidence of healing and early identification of new necrotic tissue. Necrotic or unhealthy tissue should be debrided, preferably surgically or with topical debriding agents. Removing pressure from the foot wound (i.e.Off-loading) is crucial for healing[38]

Which can be achieved through total contact casting, removable cast walkers, and various ambulatory braces, splints, modified half-shoes, and sandals.[39] Edema of the legs can delay wound healing; controlling edema with leg elevation, compression stockings, or a pneumatic pedal compression device enhances the healing process.[40]

Evidence of resolution of infection includes formation of granulation tissue, absence of necrotic tissue, and closing of the wound. If osteomyelitis is present, signs of healing include a drop in ESR & CRP and loss of increased uptake on nuclear scan.

INDICATIONS OF HOSPITALIZATION

A clinician should remember certain indications of Hospitalization in Diabetic Foot Infections like-

- Serious Infection like Necrotising Fasciitis/Gas gangrene
- Patients who need Parenteral Therapy or fluid resuscitation
- Patients who require Surgical intervention

- To control metabolic derangements e.g. Diabetic Keto Acidosis
- Patient who is unable or unwilling to perform proper wound care
- Patient who can or will not be able to offload the Wound.

METABOLIC STABILITY

Good glycemic control may help eradicate the infection and promote wound healing.[41] All patients should have blood glucose and A1C levels measured at initial presentation and then at regular intervals. Frequent home blood glucose monitoring is strongly encouraged. Other than Blood sugar control correction of fluid and electrolyte imbalances, acidosis, and azotemia is essential.Patient's nutrition should be taken care of particularly high protein diet(If no renal problem).

PROGNOSIS

The prognosis for cases of cellulitis, skin and/or soft-tissue infections, and acute osteomyelitis depends on the adequacy of antimicrobial therapy and surgical debridement. For cases of chronic osteomyelitis, the prognosis is directly related to the vascular supply in the affected limb and the adequacy of surgical debridement along with adequate off loading.

PREVENTION

Prevention of diabetic foot ulcers begins with identifying patients at risk. All patients with diabetes should have an annual foot examination that includes assessment for anatomic deformities, skin breaks, nail disorders, loss of protection sensation, diminished arterial supply, and inappropriate footwear. Patients at higher risk of foot ulceration should have examinations more often.[42] Educating patients and caretakers about proper foot care and periodic self-foot examinations are effective interventions to prevent ulceration. Other effective clinical interventions include optimizing glycemic control, smoking cessation, debridement of calluses and certain types of prophylactic foot surgery.[43]

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Managing Hyperglycaemia in Diabetic Foot.

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Abstract: *Type 2 diabetes has gained epidemic proportions and its complications pose a major health burden to all segments of the society. Diabetic foot ulcers are common in diabetic patients, having a cumulative lifetime incidence rate as high as 25% and are the harbingers of lower extremity amputations. The triad of neuropathy, ischaemia and infection is involved in the pathophysiology of diabetic foot ulcers. It is imperative that chronic hyperglycaemia which predisposes to this triad is addressed to prevent and manage diabetic foot ulcers effectively. Insulin therapy is the cornerstone in managing hyperglycaemia in diabetic foot patients in view of their long duration of diabetes and co-existent microvascular complications and other co-morbidities. Insulin-sensitising drugs (metformin and pioglitazone) and other oral antihyperglycaemic agents can be used as an adjunct. Achieving euglycaemia is one of the cornerstones of effective management of diabetic foot ulcer.*

India faces a mammoth burden of type 2 diabetes and its complications with prevalence of diabetes being around 10% reported from several parts of the country. Unfortunately, the epidemiology of type 2 diabetes in Indians has shown a demographic transition as well, with rising prevalence observed in the young and also the adolescents and children [1].

Apart from the microvascular complications, the loss of a limb or foot is the most feared complications of diabetes and still, the foot problems are neglected and remain one of the commonest reasons for diabetic patients to be hospitalised[2]. Diabetic foot ulcers are common in diabetic patients, having a cumulative lifetime incidence rate as high as 25% and frequently become infected[3]. This is apart from the corns and calluses which are routinely seen in our day-to-day practice and in diabetics these minor routine lesions can be the harbinger of infections and diabetic foot ulcers and eventually lead to complications. Diabetic foot ulcers precede almost 85% of amputations.

The foot complications occur in both types of diabetes and is more related to the duration of diabetes rather than the age of onset of diabetes. Protracted hyperglycemia has a number of deleterious effects on the body, the major complications include accelerated peripheral atherosclerosis, complicated coronary artery disease, obesity, renal insufficiency, visual deterioration and peripheral neurologic degeneration inevitably compromising on the quality of life of diabetics and shortening the life span[4].

The two main pathologies contributing to a diabetic foot are diabetic neuropathy (microvascular complication of diabetes) and peripheral vascular disease (macrovascular complication of diabetes). Diabetic neuropathy especially sympathetic autonomic neuropathy results in reduced sweating and dry skin which results in cracks and fissures, especially in the lower limbs. Sensory neuropathy results in decreased pain and position sense and motor neuropathy results in intrinsic muscle wasting and foot deformity. Hence, **diabetic neuropathy** is the single most important determinant for development of diabetic foot ulcers. **Peripheral vascular disease** is another component which predisposes to diabetic foot. Hypertension and smoking are known risk factors for development of peripheral vascular disease. **High plantar pressures**, especially in the presence of diabetic neuropathy, is known contributor to development of diabetic foot ulcers. **Limited joint mobility** is another factor which contributes to abnormal mechanics in the diabetic foot and predisposes to diabetic foot ulcers. Glycosylation of collagen in tendons and ligaments results in limited motion of foot joints. **Abnormal footwear** obviously also contributes. **Chronic infection**, which in the setting of uncontrolled hyperglycaemia continues unabated and causes a chronic diabetic foot ulcer may go on to amputation.

The **triad of neuropathy, ischaemia and infection**; resulting from chronic hyperglycaemia and contributing to the pathophysiology of diabetic foot has consistently been emphasised[5]. Incidentally, a Jamaican study also reported high prevalence of peripheral vascular disease (66.6%), peripheral neuropathy (50%), hyerglycaemia (75.6%) and increased duration of diabetes (17.5 years) among the diabetic foot patients studied[6].

The management of diabetic foot disease is focussed primarily on prevention of development of diabetic foot ulcers and on avoiding amputation of lower extremities. The main strategies include-identification of "at-risk" foot, treatment of acutely diseased foot and prevention of further problems.

The various pathophysiologic determinants of diabetic foot ulcer are all related to hyperglycemia as is shown in Figure 1.

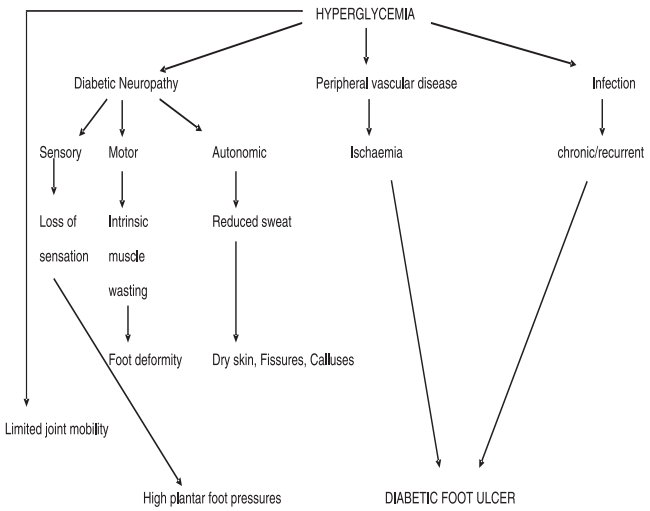

Figure 1- Role of Hyperglycemia in pathogenesis of diabetic foor ulcer.

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Hyperglycemia plays a pivotal role in the genesis of diabetic foot ulcers, in its recurrence, chronicity, and worsening of diabetic foot ulcers and eventually contributing to amputations. It has been shown recently that careful glucose control can significantly decrease the complications of diabetes[4]. Much effort has gone into trying to help diabetics maintain near-normal glucose levels and those patients who have been successful in achieving euglycaemia definitely have better outcomes. It has been conclusively proved as well that patients with chronic diabetic foot ulcers with better glycaemic control had much better wound healing than those with poor glycaemic control[7]. Marston et al in 2006[7], reported for the first time that patients whose HbA1c increased during their study (n=101), 20.7% of all wounds and 21% of dermal substitute-managed wounds (n=105) healed; whereas, in patients whose HbA1c levels remained stable or decreased, 26.3% of all wounds and 47% of dermal substitute-managed wounds healed ($p < 0.05$).

However, in a majority of diabetic patients, for a variety of reasons, good blood glucose control is not easily obtained. Therefore, the management of diabetic complications still remains a major area of focus. Well-controlled diabetes is also reported to decrease the prevalence of diabetes-specific cutaneous disorders associated with chronic hyperglycaemia[8]. In fact, among diabetic patients with an initial complication also, tight glycaemic control has been associated with reduced risk of additional complications in other organs[9].

Control of hyperglycaemia and achieving euglycaemia in a patient with diabetic foot ulcer is of paramount importance because hyperglycaemia can predispose to new infections, delayed wound healing and spreading of existing infections, septicaemia and its attendant complications. In fact, foot infections are common in patients with diabetes and are associated with high morbidity and risk of lower extremity amputation[10]. Apart from aggressive surgical debridement, wound management, effective antibiotic therapy, achieving euglycaemia ranks foremost among the other measures.

Glycaemic control has been enunciated as the foremost principle in effective management of diabetic foot ulcers and preventing amputations[11]. A target HbA1c of < 7% is acceptable in diabetic patients and is applicable for diabetic foot ulcer patients as well[12].

Despite the advent of newer therapies the average level of glycaemic control remains unsatisfactory. Failure of individual therapies to achieve adequate glycaemia with a single oral agent, has lead to a search for various permutations and combinations. Combination therapy offers the physician an opportunity to tailor a pharmaceutical regimen to individual patient needs-improving compliance, facilitating weight loss or reducing cardiovascular risk factors.

Euglycaemia is best achieved by prescribing insulin therapy to these patients. Patients with diabetic foot ulcers usually have had long-standing diabetes and have microvascular complications. Not only is diabetic neuropathy, sort of since qua non, but co-existent retinopathy and nephropathy and occult/overt coronary artery disease make insulin therapy the ideal regimen for treating hyperglycaemia in these patients and achieving euglycaemia. Besides, diabetic foot ulcer patients do harbour infections and insulin is the recommended agent to control glycaemia during an intercurrent illness or to control and eliminate infections. Moreover, insulin regimens can be tailor-made to suit the needs of an individual patient. Some possible ones are outlined:

1) Single dose regimens:
   a.) Single daily injection of intermediate acting insulin before breakfast.
   b.) Single daily injection of biphasic (regular + intermediate acting insulin) before breakfast. Mixed regular & NPH (or premixed, such as 70/30, 75/25, 50/50) insulin can be used for the purpose.
   c.) Control of Fasting plasma glucose is critical; bedtime NPH insulin treatment for this purpose is specially useful.
   d.) For control of the post-prandial glucose excursions, insulin lispro has been shown to be effective.
2) Twice daily regimens:
   a. Twice daily NPH insulin
   b. Mixed regular & NPH (or premixed) insulin twice daily.
   c. Biphasic insulin before breakfast and Lente/NPH insulin before dinner/bedtime.
3) Basal-bolus regimens: With advent of basal insulins- glargine and detemir, which can be administered once a day, the prandial glucose excursions can be controlled with short-acting insulin analogues.
4) More intensive regimen of daily multiple subcutaneous insulin injections (MSII), e.g. premeal regular (or lispro) with bedtime NPH.
5) Continuous subcutaneous insulin infusion (CSII) pump therapy.
6) Implantable intraperitoneal pumps.
7) Subjects with erratic food intake like elderly patients, may benefit particularly with insulin lispro since it can be given immediately after the patient has eaten. Alpha glucosidase inhibitors (acarbose, voglibose and miglitol) can also be used as oral agents for the purpose.
8) For patients inadequately managed with large doses of insulin, addition of an oral agent may improve control (specially the insulin sensitisers- metformin and pioglitazone).
9) Those patients who are on oral hypoglycaemic agents can be started on single daily dose of an intermediate acting insulin, the classically know bedtime insulin and day-time sulphonylurea (BIDS) regimen can be used. Even a single morning dose of insulin may be beneficial. Alternatively, a basal insulin injection shot can be given viz. insulin detemir or insulin glargine.
10) Patients who have secondary sulphonylurea failure, should be started on a split-mix regimen as already outlined above. Alternatively, a basal-bolus regimen can also be initiated.

Use of oral antihyperglycemic agents is not contraindicated and a plethora of such agents are available viz. sulphonylureas, glinides, metformin, thazolidinediones (pioglitazone), alpha-glucosidase inhibitors, DPP-IV inhibitors/GLP-1 analogues. However, the treating physician should be careful in this regard because patients with diabetic foot ulcers, having long-standing diabetes may not respond to oral antihyperglycaemic agents so effectively. Moreover, these patients harbouring infections do have an insulin resistant state wherein even insulin may be required in high dosages. Sulphonylureas have been in use for decades and have the largest experience associated with them. The newer generation sulphonylureas like glimepiride (1-8 mg/day in 1-2 divided doses) or gliclazide (40-320 mg/day in 1-2 divided doses) have lower risk of hypoglycaemia associated with them. Glipizide (5-20 mg/day in 2-3 divided doses) has an additional advantage since it has a short half-life and so can be given immediately before meals minimising chances of hypoglycaemia. Weight gain and hypoglycaemia are the two main side-effects with suphonylurea drugs. Metformin (500-2500 mg/day in 1-3 divided doses) is the biguanide which has stood the test of time with minimum of side-effects and has the

benefit of reducing appetite and weight gain and is also in vogue because of its insulin-sensitising effect. However, caution needs to be exercised in patients with renal failure and those with septicaemia or heart failure because in such patients tissue hypoxia or acidosis can precipitate or mask development of metformin-induced lactic acidosis. Gastro-intestinal disturbances are commonly witnessed with metformin use. Thiazolidinediones are also insulin-sensitisers, but have been bogged down by controversies one after the other. Troglitazone, the first thiazolidinedione had to be withdrawn because of cases of hepatic failure while rosiglitazone was withdrawn because of cases of heart failure/sudden death. Pioglitazone is presently considered safe and can be used (15-45 mg single daily dose) but the glycaemic effect takes up to 3 weeks to establish because of its mode of action on the cellular transcription process. Also fluid retention of 1.5 kg to 12 kg may be witnessed and could be problematic in some patients. Pioglitazone may be used for achieving euglycaemia in the long run in cases of diabetic foot ulcer, but because of its delayed action and fluid retention, would seem improper to initiate in the patients of diabetic foot ulcer who require an early control of their hyperglycaemia. Thiazolidinediones also cause reduction in bone mineral density and consequently increase fracture risk. Alpha-glucosidase inhibitors like acarbose, miglitol and voglibose do not cause a very great decline of HbA1c; 0.6% as compared to 1-1.7% with sulphonylureas and metformin. Alpha-glucosidase inhibitors inhibit alpha-glucosidase enzyme in the gut and thus, reduce absorption of glucose from the gut in to the blood stream. These agents need to be taken with the first bite of each meal and the anti-hyperglycaemic effect is meal-related, and so theoretically there are virtually no chances of hypoglycaemia with these agents. Glinides (repaglinide and nateglinide) are non-sulphonylurea insulin secretagogues and do carry a risk of hypoglycaemia because of their very nature of causing insulin release. However, their duration of action is short and so need to be administered before a meal and can be used as effective prandial glucose regulators like alpha-glucosidase inhibitors.

These oral agents address various aspects of the pathophysiology of diabetes, but the concomitant hyperglucagonaemia associated with insulin deficiency was never addressed. In the last decade, incretin-based therapies (dipeptidyl peptidase-4, DPP-4 inhibitors and glucagon like peptide-1, GLP-1 analogues) have evolved and are increasingly finding a place in the management of diabetes[13]. However, advocating their role in management of hyperglycaemia in diabetic foot ulcer will be too premature. The experience with them is limited and is gradually building up and primarily their role can be advocated for controlling hyperglycaemia. Incretins exert their effects in a variety of different target tissues- glucose disposal is facilitated in peripheral tissues such as muscle due to improved insulin secretion; directly reduce hepatic glucose production by decreasing glucagon, increasing insulin secretion and eventually suppressing fasting hyperglycaemia; directly inhibit gastric emptying; exert effect on hypothalamus to reduce appetite and eliminate cravings. Additionally, incretin-based therapies are vasodilators and so increase cardiac output slightly by improving endothelial dysfunction in the arterial tree. In fact, GLP-1 receptor agonists cause acute significant drops in systolic pressure with some reflex increase in cardiac output. The incretin-based therapies hold great promise and their exact place in the armamentarium of diabetes apart from management of hyperglycaemia, especially in situations wherein complications of diabetes have set in will unfold in the coming years.

It is important to realise that achieving euglycaemia at the earliest possible is of foremost importance in diabetic foot ulcer patients and insulin does fit the bill in its prowess of achieving euglycaemia in a couple of days under expert hands; and fares much better over oral agents which take days to weeks to achieve euglycaemia. Also titration of drug can be done easily in case of insulin and can be done rapidly, wherein with oral agents, that is not the case. There are a number of side-effects and contraindications and care which needs to be exercised with oral agents, while with insulin it is only hypoglycaemia which in a case of overt hyperglycaemia indicates achievement of target rather than a side-effect. Additionally, it is important to realise that patients with diabetic foot will have other micro- and macrovascular complications and in most cases would be heading for secondary oral hypoglycaemic agents failure; and herein also achieving control with insulin would be more feasible and prudent. The role of oral agents specially insulin sensitisers can not be totally ruled out since they may act in concert to address insulin resistance and thus reduce insulin requirement. Prandial regulators (alpha-glucosidase inhibitors and glinides) can be used to achieve control of post-prandial hyperglycaemia as an adjunct to insulin therapy, once fasting hyperglycaemia has been brought under control. Incretin-based therapies are the new drugs in their infancy, and their place is also likely to settle down soon.

It is important to understand that chronic hyperglycaemia is at the centre-point of diabetic complications and predisposes to the triad of neuropathy, iscahemia (peripheral vascular disease) and infections, which variably combine together to produce a diabetic foot ulcer, which in turn is the harbinger of lower extremity amputations. It is pertinent to address hyperglycaemia and achieve euglycaemia to prevent diabetic foot ulcer, manage diabetic foot ulcer effectively, and prevent complications of diabetic foot ulcer including gangrene, septicaemia and lower extremity amputations.

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Importance of Diabetic Foot Education-A Case Study.

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Clinical Director Special Olympics International 'Fit Feet' Program

CASE SUMMARY

30/01/2011(DAY 1ST ON ADMISSION)

HISTORY

On 30/01/2011 at 10.00 A.M., 56 years old male known case of diabetes for 15 years presented with history of fever, discoloration of skin with foul smelling discharge from right foot since 5 days. Patient gave history of soaking feet in hot water 8 days back. Patient was taking treatment from physician in neighbourhood who advised alternate day dressing and patient had visited doctor 3 days back.

ON EXAMINATION

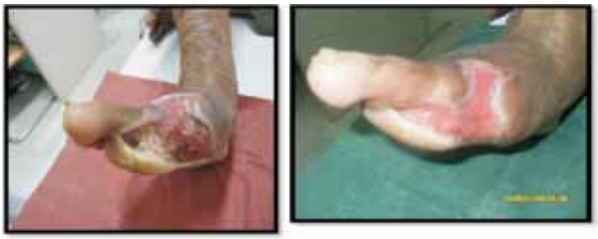
General condition poor, patient was toxic. Temperature - 103.4^0 degree F, B.P.-142/94mm of Hg. There was complete loss of sensation in ankle and foot area for vibration & fine touch (peripheral neuropathy). Doralis pedis & Posterior tibial artery were palpable. Capillary refill was good in rest of the toes in both feet. On examination of wound: foul smelling discharge was oozing out from wound at the dorsum of right foot with gangrenous necrotic Rt. Big toe.

Investigations

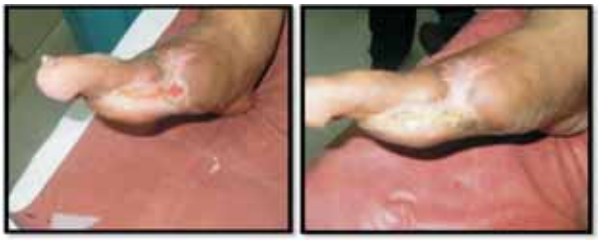
TLC: 25600, DLC: P90, L08, E02, blood urea: 100, S.Creatinine: 1.6, RBS: 256 mg% , Pus C/S growth was staph. Aureus, sensitive to amoxy + clavunic acid, plan of treatment: patient was posted for immediate debridement and removal of necrotic tissue alongwith partial amputaion of 1st metatarsal at 2.00 p.m. (photographs after surgery given). Imperical intravenous antibiotics amoxy + clavulanic acid with metronidazol started, blood sugar charting and insulin was given for blood sugar control. On 02/02/2011 patients general condition improveddrastically, TLC came down to 10700, blood urea was 57, s. Creatine was 1.1. Patient was dischage on 03/02/2011 with future plan of treatment for wound care (including advice of daily dressing in OPD, offloading by front wedge shoes) and secondory closure by SSG, but after 4 weeks of wound care when the wound bed was ready for SSG patient did not agree for superficial skin grafting (SSG) and wound closure was achieved by secondary intention of regular dressing with Recombinent PDGF.

(DAY 2, ONE DAY AFTER SURGERY)

AFTER 4 WEEKS AFTER 8 WEEKS



AFTER 10 WEEKS AFTER 12 WEEKS



SUMMARY

OBJECTIVE OF THE TREATMENT WAS

1. To bring out the patient from septicaemia.
2. Minimal cost of treatment by short duration of hospitalisation.
3. Plan to achieve complete wound closure.
4. Give patient a functional limb with minimal amputation.

POINTS TO REMEMBER

- All diabetic patients must have regular screening for risk assesment for neuropathy & vasculopathy at least once in a year even if there are no complaints.
- General physicians should take diabetic wound more seriously, either review them daily or send to specialist.
- Diabetic foot education is an integral part of diabetes management for doctors and for patients.

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Biomyf
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Recent Advances in Management of Chronic Non healing Diabetic Foot Ulcers

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Abstract: *As number of Diabetic patients are increasing, different chronic complications of diabetes are also increasing, Chronic Diabetic Foot Ulcer is one of the very important but most neglected complication of Diabetes.*
Foot ulcers in diabetic patients are not uncommon. Approximately 14% of diabetic ulcers lead to amputation & in most of the cases it is trivial foot ulcer which ultimately leads to amputation .
More than 80,000 amputations are performed each year on diabetic patients in the United States, and around 50% of the people with amputations will develop ulcerations and infections in the contra lateral limb within 18 months. An alarming 58% will have a contra lateral amputation 3-5 years after the first amputation. In addition, the 3-year mortality after a first amputation has been estimated as high as 20-50%, and these numbers have not changed much in the past 30 years, despite huge advances in the medical and surgical treatment of patients with diabetes.
But prompt treatment of chronic non healing Diabetic Foot Ulcer with multidisciplinary approach can overall change the clinical outcome in nonhealing DFU.
Recent technological advanced combined with better understanding of the wound healing process have resulted in a myriad advanced wound healing modalities in the treatment of diabetic foot ulcers.
A wide variety of advanced treatments for diabetic foot ulcers, such as Ultrasonic debridement,Topical growth factors, Bioengineered skin grafts(BATs), VAC(Vacuum Assisted Closure) Therapy, and hyperbaric oxygen therapy(HBOT), are available commercially now in India, and clinical studies of these products have shown some evidence of improved wound healing compared to standard wound care.
During the prolonged healing process of a chronic wound, rapid and accurate evaluation of the healing progress is critical so that unsuccessful treatments can be discontinued and alternate treatments be initiated as soon as possible.
Though recent advances in the management of Diabetic Foot Ulcers have increased our abilities to salvage the lower limb, the best management still remains prevention. This can only follow with intense patient education about foot care and a proactive role in treating the factors which lead to these foot problems.

INTRODUCTION

Foot ulcers in diabetic patients are common. It is estimated that 15% of diabetes patients will develop Diabetic foot ulcer once in their life time, and approximately 14% of diabetic ulcers lead to amputation[1] unless a prompt, rational, multidisciplinary approach to therapy is taken.

Factors that affect development and healing of diabetic patient's foot ulcers include the degree of metabolic control, the presence of ischemia or infection, and continuing trauma to feet from excessive plantar pressure or poorly fitting shoes. Appropriate wound care for diabetic patients addresses these issues and provides optimal local ulcer therapy with debridement of necrotic tissue and provision of a moist wound-healing environment.

A wide variety of advanced treatments for diabetic foot ulcers, such as topical growth factors, bioengineered skin grafts, VAC(vaccum Assisted Closure) Therapy, and hyperbaric oxygen therapy(HBOT), are available commercially now in India, and clinical studies of these products have shown some evidence of improved healing compared to standard wound care[2].

During the prolonged healing process of a chronic wound, rapid and accurate evaluation of the healing progress is critical so that unsuccessful treatments can be discontinued and alternate treatments be initiated as soon as possible[3,4].

MANAGEMENT OF DFU CAN BE DISCUSSED BY FOLLOWING HEADINGS

A. Microbiological Control
B. Wound Control
C. Metabolic Control
D. Vascular Control
E. Mechanical Control
F. Educational Control

A.Microbiological Control

Certain principles should be followed while giving antibiotics when diabetic foot infection cases are suspected. Most of the Diabetic Foot Infections are poly microbial[5].

So broad spectrum Antibiotic are to be used for longer duration.Because of Immunopathy there is a Poor immune response in diabetics hence normal skin commensals can cause serious infection.Wide spectrum of antibiotics should always be used even at initial presentation because it is Imposible to predict type & no. of microorganisms clinically, there is no way of predicting-rapidly ascending or Life threatening Diabetic Foot Infection and Triopathy of DM reduces local resistance to invading bacterias[6].

B. Wound Control

After exposing the wound you should irrigate the wound with saline or diluted solution of Povidone iodine. Never use concentrated solution of Povidone iodine who damages normal granulation tissue to grow.

VASHE WOUND CLEANSING SOLUTION

VASHE is solution of Hocl (Hypochlorous Acid) .It Kills important wound pathogens like Gram +ve, Gram -ve bacterias, Anaerobes &Fungi.

A gauze soaked in VASHE solution is wrapped around wound for 10-15 mnts. which cleans, irrigates, moistens & debrides the wound

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Vashe Generator

and removes bacteria & fungus along with bed odor from wound[7].

DEBRIDEMENT(REMOVAL OF DEVITALIZED TISSUE FROM ULCER)

Once you have cleaned the wound, it should be debrided thoroughly. There are different ways of debridement likeSharp,blunt, Surgical,Chemical & Auto debridement but I'm going to discuss here only two new modalities i.e.Ultrasonic debridement & Biodebridement (also known as Maggot Rx).

ULTRASONIC DEBRIDEMENT

With ultrasonic debrider there is Ultrasonic formation & collapse of Vapor Bubbles who fragments & emulsify the necrotic tissue without disturbing the viable tissue.

Ultrasonic debridement is effective in removal of particulate matter and reduction of bacterial counts. Good thing about this modality of

Leg wound before & after Ultrasonic debridement

debridement is that there is hardly any blood loss.

This type of debridement is particularly useful in handling deep and tunnelling wounds where debridement with other technique is difficult[8].

BIODEBRIDEMENT OR MAGGOT Rx

Medicinal maggots of Lucilia sericata (Green Bottle fly) are used for debriding the dead necrotic & infected tissue of wound. Beuty of


Lucilia sericata (Green Bottle fly)

Indications for Maggot's Rx

S.No.	**Indications**
1.	Infected or sloughy wounds
2.	Necrotic area on diabetic foot
3.	Necrotizing fasciits
4.	Infection with MRSA

Contraindications for Maggot's Rx

S.No.	**Contraindications**
1.	Fistulae
2.	Wounds that connect with vital organs such as Brain
3.	Wounds near cavities eg. Abdoman,Thorax
4.	Wounds near large blood vessels

these maggots is that they donot eat or disturb normal host tissue. Benefits of Maggot's therapy are good debdridement with removal of dead necrotic tissue and elimination of infection[9].

Shortcomings of Maggot's therapy are that Medicinal maggots are costly & difficult to get. They have short shelf life, pt. can have uncomfortable crawling sensation & once move out of dressing


Author applying VAC dressing to a patient

Maggots can create lot of neusense.

VAC (VACCUM ASSISTED CLOSURE)/ NPWT (NEGATIVE PRESSURE WOUND THERAPY)

VAC or NPWT device comprises

1. Granufoam Dressing
2. Plastic Tubing
3. Canister

4. Computerized Rx Unit

After cleaning & debriding the wound a special granufoam dressing is applied over wound which is connected to special Computerized Rx Unit with a plastic tubing. This Computerized Rx Unit applies 125mmHg negative pressure to wound which draws exudates etc. into a special canister attached to Unit.

VAC therapy helps in reducing oedema, exudates and bacterial load & also helps in regeneration of granulation tissue & neo vascularisation[10].

AUTOLOGEL-AUTOLOGUS PLATELET RICH PLASMA (PRP) GEL

This new modality for wound healing is based upon principle of Platelets containing components & properties for wound healing & Plasma containing fibrin matrix.

Procedure- Depending upon the size of ulcer, around 5 to 30 ml patient's blood is centrifuged & Platelet Rich Plasma is separated. This PRP is taken into a syringe having different reagents [Thrombin(CaCl2) & Vita C], who activate platelets & make gel consistency. This is known as Autologel.

This gel like material is applied over wound twice a week for 12 weeks & it was observed by Vickie R. Driver etal. that 68.4% of those wounds which were treated with Autologel healed in comparison to 42.9% of Control wounds[11].

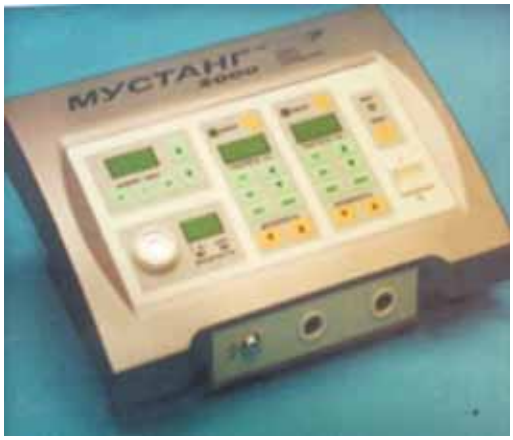
O2 MISLY

After Cleaning & Debriding the wound pt. puts his lower limb in a canister of O2 Misly machine & wound is exposed to 4 Cycles of 100% O2(5 mnt.each) alternatively with Vapor of water & antibiotic(10 mnt.each).

This therapy is given Twice a week for 12 to 20 weeks. Ubbink DT et al found that in comparison to standard wound care proportion of healed Wounds with use of **O2 Misly** were 200% better at 12 to 20 week[12].

LLLT(LOW LEVEL LASER THERAPY)

LASER is Light Amplification by Stimulated Emission of Radiation. There have been lot of medical indications of using Laser & one



LLL unit

indication is nonhealing Diabetic Foot Ulcer.

Wound is exposed to Low Level Laser Therapy which activates Microcirculation & Macrophages leading to Anti-inflammatory, Analgesic, Regenerative, Bacteriostatic & Bactericidal clinical effects on wound. Martinez-Sanchez G et al. Found Low Level Laser Therapy very effective in healing of Chronic Nonhealing diabetic Foot Ulcer[13].

GROWTH FACTORS

The term growth factor refers to a naturally occurring protein capable of stimulating cellular proliferation and cellular differentiation .There are different types of Growth Factors which are involved in wound healing.

Growth Factors involved in wound healing

S. No.	Growth Factors
1.	Epidermal growth factor (EGF)—US FDA approved
2.	Platelet derived growth factor (PDGF)—US FDA approved
3.	Hepatocyte growth factor (HGF)
4.	Vascular endothelial growth factor (VEGF)
5.	Fibroblast growth factor1 and 2 (FGF-1, -2)
6.	Transforming growth factor alpha (TGF-α)
7.	Transforming growth factor- β (TGF-β)
8.	Keratinocyte growth factor(KGF)

US FDA has so far approved only two types of growth factors for use in Chronic Wounds. They are Platelet derived growth factor (PDGF) and Epidermal growth factor (EGF). Most commonly used plermin (rh PDGF BB,Recombinent human Platelet derived growth factor) has Chemo tactic, mito genic, angio genic, and stimulatory effects and helps in wound healing if used in noninfected superficial wounds[14].

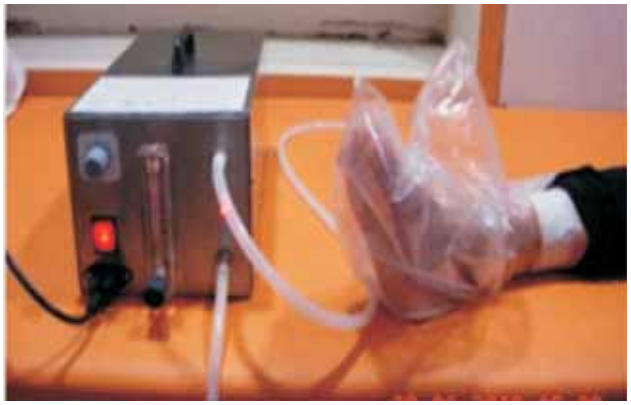
OZONE THERAPY

Ozone is "active oxygen".It is triatomic allotrope of oxygen formed by recombination of oxygen atoms. It is a Colourless pungent-odor gas.

Ozone disinfects, oxidizes, deodorizes and decolorizes.

Ozone is very strong oxidant and is found to be more than 3000 times powerful disinfectant than chlorine.

Peripheral Ozone Therapy is very effective for badly-infected and non-healing Ulcers like chronic Diabetic foot ulcers .Technique of giving Peripheral Ozone Therapy is known as "Bagging" .That means after preparing the wound, limb is covered with a plastic bag & a tube from Ozone generator is tightly secured in upper portion of bag. Wound is exposed to Ozone for 20 to 30 mnt.



Ozone Therapy

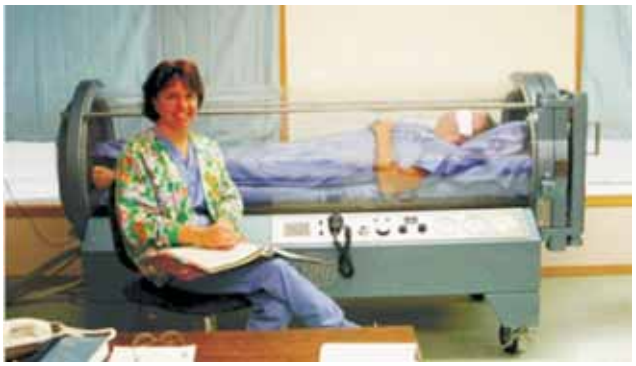
Initially higher concentration (60-90ug/ml)is used to control infection and lateron lower conc. (30-40ug/ml) is used for wound healing[15].

HYPERBARIC O2 (HBO) THERAPY

Hyperbaric oxygen therapy means exposing pt. to 100% oxygen under increased atmospheric pressure.

Indications of HBO Therapy

S. No.	**Podiatric Indications**
1.	Ch. Non healing wound of >30 days (Wagner Gr. 3 or more)(16-19)
2.	Gas Gangrene(20,21)/Embolism
3.	Necrotizing Fasciitis (22)
4.	Refractory Osteo Myeliitis(23-25)
	General Indications
5.	CO Poisoning (Carbon Mono-oxide Poisoning)(26)
6.	Decompression Syndrome(27)
7.	Intracranial Abscess,Stroke(28),Multiple Sclerosis(29,30)
8.	Skin grafts and flaps (compromised)(31)



Monoplace HBOT Chamber

Two types of HBO chambers are available. Monoplace & Multiplace Chambers. In Monoplace chamber one person can lie down inside glass chamber and he is exposed to pressurised oxygen for a prescribed limit of time.While Multiplace chamber is like a big Oil-tanker in which number of patients can simultaneously be exposed to HBO . Pt. is placed in Monoplace / Multiplace HBO Chamber & he breaths 100% oxygen under increased (2 to 3 times) atmospheric pressure for 90 to 120 mnts. This Increases tissue oxygen tension, angiogenesis, fibroblast proliferation, collagen deposition and enhanced bacterial killing[32].

This Rx is given for 5 days a week & total such 20 to 40 treatments are given depending upon size & severity of wound.

Improved wound healing & reduced rate of amputations were observed in significant no. of cases of DFU by Stone JA et al.[33]

SKIN GRAFTS –APLIGRAF

Whenever size of wound is large & it is superficial & well granulated, it needs skin grafting. Skin graft can be natural skin grafts or Bioengineered grafts

Apligraf

Apligraf is Bioengineered Epidermis & Dermis Graft ,developed from foreskin of Newborn.Indication of using Apligraf are Ch. Non healing (non infected) DFU[34] or Superficial Venous Ulcers[35].

C. METABOLIC CONTROL

Controlling Blood sugar and other general parameters are equally important for comprehensive management of Ch. Non healing Diabetic Foot Ulcer.

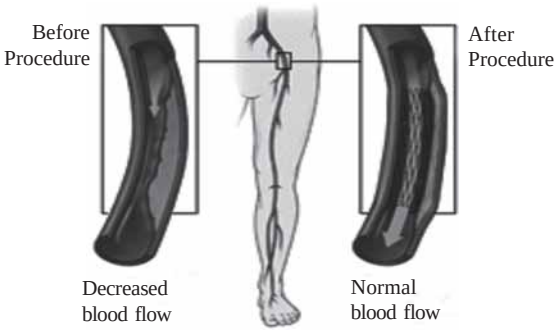
If wound is small & superficial one can use OHAs (Oral Hypoglycemic Agents) for controlling Blood sugar in Type II DM. Pt. should be put on Insulin if wound is large, Infected ,necrotic & patient has septicaemia, looks toxic and or has Diabetic Keto acidosis. DKA should be treated & hydration should be maintained. Take care of pt's nutrition ,if hypo proteinemia, treat it.

D. VASCULAR CONTROL

Whenever pt of DFU comes always put your fingers on peripheral arteries like DP,PT,Pop & femorals. If two or more than 2 arteries are impalpalpable & or ABI (Ankle Brachial Index) is low get Peripheral Vascular Doppler & Angiography done , if need arises.

If arterial occlusion is less than 10 cm then different options available are-Intraarterial Thrombolysis, Endarterectomy & Angioplasty which can be conventional Balloon Angioplasty with or without Stents, Sub intimal angioplasty, Lasers Angioplasty and Rotablaters for Hard Plaque .

If arterial occlusion is more than 10 cm then different types of Vascular Grafts (Natural or Synthetic) are applied to bypass the occlusion & to achieve good circulation distal to occlusion leading to healing of ulcer.



E. MECHANICAL CONTROL- OFF LOADING

Offloading is cornerstone of managing Chronic Nonhealing diabetic foot ulcer[36] which is most of the time overlooked by clinicians.

No matter what ever modalities so far I have mentioned (Old or New) are used for treating Ch. Nonhealing Diabetic Foot Ulcer, if proper offloading of the wound is not done, one will not be able to achieve ultimate target that is complete healing of Diabetic Foot Ulcer .

Depending upon site,size & severity of wound pt. may be advised for complete bed rest or may be advised of using different offloading devices.Pt. should be asked not to bear weight until wound is healed up. Every step which is taken will delay the wound healing until otherwise optimal offloading is instituted.

Different offloading devices could be Crutches,Wheel Chair, different types of ffloading Shoes,Scotch Cast boot,Removable Cast Walker(RCW) & Air Cast walker which is latest in armamentarium.

TCC (Total Contact Cast) is just like applying plaster around fracture of foot or leg.TCC can be made of Plaster of Paris(POP) or Fibreglass.

Although best offloading is achieved by TCC(37) but it is cumbersome, time consuming & needs expertise & one can not follow the growth of wound.

Most of these shortcomings of TCC can be overcome by using ITCC i.e. Instant Total Contact Cast which was developed by Dr. David G. Armstrong et al. of Chicago[38].

SUMMARY

Most Common Cause of hospitalization in Diabetics is Diabetic foot Problems. Since no.of Diabetics is increasing hence different complications related to diabetes are also increasing including non healing diabetic foot ulcers.

Minor ulcer can lead to Amputation so one should be cautious since beginning. Newer & more advanced techniques are now available for better wound care including VAC therapy, Hyperbaric Oxygen Therapy, Growth Factors, Bioengineered Skin grafts,Maggot's therapy etc.

If Diabetic Foot Ulcer is not improving one should refer case to Podiatrist or specialist.

The holistic care of diabetic foot ulcer requires a multidisciplinary team approach. Apart from blood sugar control, treatment of ulcer involves debridement, offloading, appropriate dressings, vascular maintenance and infection control.

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Gene Transfer & Stem Cells: Recent advances for treating Diabetic Foot.

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INTRODUCTION

Latest developments in molecular and cell biology help to understand and treat many of the Chronic diseases including wound healing. The different events in progress of wound healing like inflammation, proliferation and remodeling needs the coordinated and sequential activation and inactivation of gene expression programmes in response to signals from the cellular environment. There are few genetic defects that are directly linked to altered wound healing. The reverse genetic approach in recombinant mice and other species has identified many genes whose over or under expression leads, in part, to a wound healing phenotype. These studies, together with detailed, descriptive studies of patterns of gene expression in normal and abnormalhealing,[1] have lead to the selection of leading candidates for potential therapeutic application.

Stem cells are immature, unprogrammed cells that have the ability to grow into different kinds of tissue and can be sourced from people of all ages. The first mammalian stem cells to be studied in detail were those of the hematopoietic system, and much is understood about conditions that cause these marrow precursors to differentiate along different pathways in order to maintain appropriate concentrations of a variety of cell populations in circulating blood. Characteristi-cally, these marrow stem cells, divide much more slowly than their surrounding, derived cell population, and they remain in a relatively undifferentiated state as long as they reside in an appropriate environment (niche).2 The third type of precursor cell to be considered is the marrow-derived tissue progenitor that circulates in the bloodstream, waiting to be called into sites of injury to participate in the repair process.[3]

GENE TRANSFER TO WOUNDS

Many investigators had clearly established by 1990,both an intrinsic and a therapeutic role for peptide growth factors in wound healing, and many biotechnology groups had succeeded in expressing the recombinant proteins as potential therapeutic agents.[4] However, as clinical trials with agents such as epidermal growth factor, fibroblast growth factor 2,platelet-derived growth factor, and transforming growth factor proceeded, it was quickly appreciated that very high levels of exogenous peptides would be needed in chronic, human-wounds to mimic the effects of very small amounts of similar or identical proteins expressed by the resident cells.[5-7] Thus, several groups developed strategies to augment the putative deficiencies of peptide growth factors by introducing cDNA copies of the growth factor genes into target cells at the wound site.

HOW TO TRANSFER GENES ?

There are several potential methods, to. transfer genes into skin or wounds[8,9] **Physical methods** involve driving the DNA vector (a purified bacterial plasmid) into tissue cells with mechanical electrical for Successful introduction of biologically active DNA into wounds has been achieved with the "gene gun", a device that propels small, DNA-coated gold/ tungsten particles into the tissue in a shotgun pattern[10] a needle array that functions much like a tattooing instrument and an electrode array that uses a train of high-voltage pulses to create temporary pores in nearby cells [11,12] **Chemical methods** of DNA delivery are less efficient but less expensive and they have included liposomes, nano particles, dried methylcellulose discs and collagen gels or scaffolds. Viruses are **natural** gene delivery systems.[13] DNA viruses. such as adenovirus do not insert viral DNA into the host genome, and so they act as transient gene delivery-systems. Adenovirus does express proteins that can incite an inflammatory response, and newer vectors have been engineered to minimize this reaction, albeit a minor consideration for wound infection. Adeno-associated virus produces less inflammatory response, although it has limitations in the amount of genetic material it can carry and the cell types that can be infected[14,15] RNA viruses (retroviruses) such as Moloney sarcoma virus and the lenti viruses act by stable insertion of their genome into the host genome; thus they are more useful for gene therapy applications, in combination with a tissue engineering substitute that has a limited lifespan in the host, or by placing the gene under regulation of a drug. Traditional retroviruses infect only dividing cells, but derivatives of HIV-like lenti viruses are able to infect a wide variety of cell types.[16] Transient transformation of wounds with candidate genes can result in 1-3 weeks of expression, depending on the delivery method and the choice of DNA regulatory sequence. In practice, most current protocols for wound gene transfer employ a strong, promiscuous promoter of gene expression that is derived from cytomegalovirus (CMV). Greater selectivity of gene, action can readily be achieved by using gene regulation sequences that are tissue specific or that respond to a drug/hormone such as RU-486 or tamoxifen[17-19].

Gene transfer has achieved a successful outcome in many pre-clinical models, using cDNAs for EGE-TGF-Bl, PDGF, FGF-2 vascular endothelial growth factor (VEGF) hepatocyte growth factor (HGF) and other peptidesin the delivery-systems descrihexlabove.[9] A potentially attractive aspect of gene transfer is the ease of combining two genes into one DNA vector This may be a way to develop, with a less complicated regulatory pathway, a therapy that capitalises upon the synergistic effects of growth fartor or cytoking combinations.[20-22] AS another strategy, gene transfer studies have also shown that (wound) cells may benefit from added expression of not only the stimulus, but the receptor for that stimulus and the machinery that transmits signals from the receptor to other cellular machinery.

Gene transfer has recently taken on a role in drug development, since it is a relatively efficient method to screen for genes that have wound-healing properties, independent of a requirement that they act on cells from the outside. Indeed, nuclear transcription factors such as HoxA3,[23] Smads 3 and 7,[24-25] Egr-1,[26] engineered zinc finger proteins[27,28] and cardiac ankyrin repeat protein (CARP)[29] as well as signal transduction molecules such as

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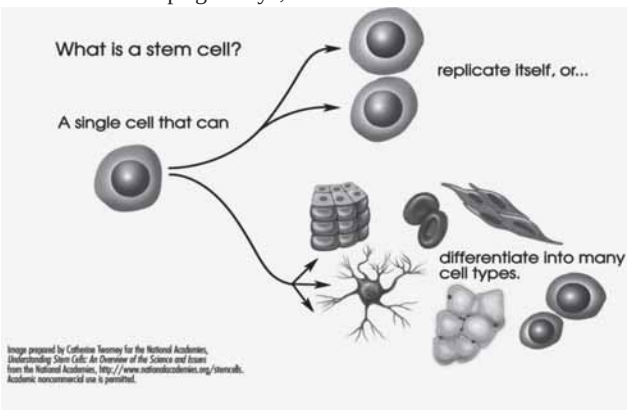
eps8, which act inside of cells are active in wounds of either normal or diabetic animal, after gene transfer. Gene transfer is thus a powerful screening method for the most effective therapeutic genes.

I would like to mention Two gene therapy clinical trials for wound healing. One is a National Institute of Health sponsored trial of PDGF-BB delivered by an adenovirus in diabetic foot ulcers[30]. A **second,** trial completed by Tissue Repair Company, which administers adenoviral PDGF to diabetic foot ulcers. Positive findings of the latter trial were reported at the 2005 annual meeting of the Wound Healing Society. There are also many efforts to use EGF-2 andJVEGF28,31 in gene transfer experiments to improve (lower extremity) circulation. It is likely that success in these trials would have an important influence on the management and prognosis of the diabetic foot ulcer. Additional trials with FGF-2 and Vascular Endothelium Growth Factor genes or proteins for the development of collateral circulation (usually cardiovascular) may eventually have an impact on improving collateral circulation in the diabetic limb also.

STEM CELLS

In 1908 - The term "stem cell" was proposed for scientific use by the Russian histologist Alexander Maksimov (1874–1928) at congress of hematologic society in Berlin. It postulated existence of haematopoietic stem cells.

Stem cells are basic cells that can divide and differentiate into diverse specialized cell types and can self-renew to produce more stem cells. In mammals, there are two broad types of stem cells: embryonic stem cells, which are isolated from the inner cell mass of blastocysts, and adult stem cells, which are found in various tissues. In adult organisms, stem cells and progenitor cells act as a repair system for the body, replenishing adult tissues. In a developing embryo, stem cells can differentiate into all the



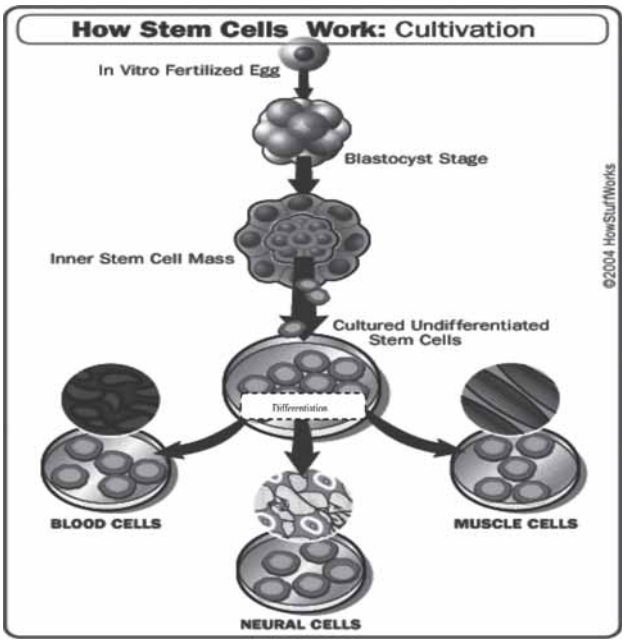
specialized cells, but also maintain the normal turnover of regenerative organs, such as blood, skin, or intestinal tissues.

There has been an explosive growth of information and speculation regarding the therapeutic potential of stem cells derived from adult and embryonic tissues.[32]

A more conservative perspective focuses on the role of adult stem cells in wound repair. The present concept of stem cell differentiation is evolving, however, since progenitor cells from any tissues seem to be able to trans differentiate into other cell types when place in an appropriate environment. DNA transfer must be carefully ruled out to validate these findings.

There are three categories of bone-marrow-derived cells that participate in the repair of connective tissue: (1) the angioblast or endothelial precursor cell (EPC): (2) the fibrocyte; (3) the marrow/mesenchymal stem cell (MSC). Epithelial layers, in general, harbour resident stem cells.

1.EPC-The Endothelial precursor cell is derived from a primitive haematopoietic cell in the bone marrow, prior to differentiation into the leucocyte lineage. It was first reported in 1997 as a cell type that could be



isolated from circulating blood, cultivated in vitro, transplanted in into syngenic host and localised to vascular structures.[33] Further work has decisively demonstrated that EPCs are recruited from the bloodstream at many sites of vasculogenesis, that is the de novo formation of new capillaries. Endothelial precursor cell are recruited to sites of repair or vessel growth by Vascular endothelial growth factor[34] and stromal-cell-derived factor (SDF).[35] These factors may also be involved in the mobilisation of the precursors from the marrow.[36] EPCs are not true stem cells, since they are apparently committed to the endothelial lineage while in circulation. For this reason, such cells can be purified from whole blood, based on their expression of the VEGF receptor 2 (flk-1) and the angiopoietin 1 receptor (tie-2). The haemangio blast and a more primitive progenitor, the multipotent adult progenitor cell (MAPC) have been suggested as the marrow-based precursors.[37]

2.The Fibrocyte- First, described in 1994, is a leucocyte-like cell from bone marrow ,that infiltrates wounds during the inflammatory phase, produces collagen and has many characteristics of the antigen-presenting, dendritic cell.[38] This cell type can produce many cytokines, collagen and growth factors, and its presence has been associated with fibrotic conditions.

3.The Marrow/mesenchymal stem cell (MSC)- The MSC is another circulating, marrow-derived cell which is a pluripotential stem cell in that it can be isolated from marrow and grown for many generations in vitro, and MSC can be induced to differentiate into many types of mesodermal derivatives, including bone, cartilage, skeletal muscle and adipose tissue.[39] MSCs traffic to many different connective tissues and recent studies in a mouse model from this laboratory have shown that MSCs constitute a significant proportion of the collagen producing, fibroblastic population in a healing wound.[40]

At present, it is not known whether these circulating sources of stem/precursor cells may be rate limiting for wound-healing processes. Patients undergoing immunosuppressive therapy are certainly at risk for healing problems due to infection, but marrow-derived mesenchymal cells may be more resistant. Ageing may affect the availability and regenerative capacity of stem cells. It is conceivable that we will be able to identify the factors that mobilize stem/precursor cells from the marrow and that stimulate their recruitment to sites of injury.[41] There is not a great deal of

evidence that these marrow-derived cells take up permanent residence in tissues. They may be largely important during phases of acute repair where local proliferation cannot meet tissue needs.[40] It has recently come to light that many connective tissues do harbour pluripotential stem cell populations, including dermis.42adipose [43] and skeletal muscle.[44] These may be alternative sources of stem cells for therapeutic applications.

Many epithelial tissues have much higher rates of cellular turnover and renewal, and resident stem cells are localised to specific areas. In, the epidermis, stem cell populations have been identified in the bulge region of the hair follicle[45] and in the inter follicular zone.[46] The interfollicular cells represent a subset of the epidermal basal cells that undergo differentiation as they detach from the basal lamina and move towards the stratum corneum. While it has been difficult to identify specific surface characteristics that could aid in epidermal stem cell purification,[47] It is likely that these cells provide a significant fraction of the dividing keratinocytes in cultures that have been used to generate skin substitutes. There are several reports that indicate that these stem cells may be multipotent, and there are also reports that marrow-derived cells can he recruited through the bloodstream and participate in epidermal structure.[48]

The clinical application of stem cells is well advanced for the treatment of corneal stem cell deficiency, chemical burns and several disease states.[49,50] Both unfractionated bone marrow as well as purified MSC from marrow and connective tissue sources have been evaluated in many forms of tissue repair: skin, bone, teeth, cartilage and tendon. There have been attempts to apply MSC to wounds: one study simply used whole marrow populations on three non-healing wounds with a favourable outcome[51]; another study reported improved healing on systemic injection of a dermal MSC population[42]; there is also a report of MSC effects in deep burn wounds in rats. Favourable repair results have been obtained in bone and cartilage, and there is every reason to expect that living skin equivalents so engineered could enhance wound healing. Strategies that improve recruitment or growth of MSC may be effective.

Since the vascular supply is often rate limiting for repair, Endothelial Precursor Cells(EPC) also offer therapeutic potential.[52] Agents that recruit Endothelial Precursor Cells, such as VEGF,[32] also increase vascularity and other aspects of wound healing.[34] EPCs are readily purified from whole blood by apheresis techniques. Studies suggest that these cells and the factors that recruit them can reverse tissue ischemia. A study reports that purified human EPCs enhanced wound repair in the athymic nude mouse, increased vascularity and macrophage influx and occasionally became incorporated into patent, hCD-31 positive vessels.[53]

SUMMARY

Gene transfer and applications of progenitor stem cells are two advanced technologies with great promise in wound healing and tissue repair applications. Safety issues have slowed the commercial development of gene transfer, but active trials are underway. This strategy is likely to overcome many of the drawbacks of recombinant proteins at potentially lower cost. Stem cell therapies with autologous grafting are likely to be accepted more easily by the medical and regulatory communities. Factors that regulate the mobilization, recruitment and differentiation of progenitor cells will also play an important role. Many of these findings will find their way into the development of more effective tissue engineering devices. The combination of gene transfer and applications of stem cells has even greater potential, since it lead to the design of medical devices that contain multipotential cells that are capable of delivering specific gene products.

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IMSACON 2011: ABSTRACTS OF SCIENTIFIC PAPERS
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Role of CT angiography and color doppler Sonography in evaluation of peripheral arterial disease.

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The advent of multidetector helical CT technology during the last decade has seen CT angiography emerge as a comparable modality to conventional angiography in the assessment of aorta, renal, iliac, lower limb and upper limb arteries. The technological leaps have enabled imaging of long segments of the vascular tree from the renal arteries upto the toes with a single contrast injection, in a short time, acquiring thinner sub millimeter slices. CT angiography has proved highly accurate in detection and grading of peripheral artery disease providing all the information needed by the surgeon for planning revascularization procedures. It has replaced DSA which stood as the gold standard in vascular imaging for decades, allowing volumetric vascular imaging and anatomical mapping, thereby becoming a noninvasive alternative to DSA. Duplex Doppler Sonography which integrates the real time B mode image and Doppler image to detect presence or absence of flow and analysis of flow characteristics is also an excellent noninvasive modality for evaluation of peripheral arterial disease. It provides information on flow homodynamic within the vessels. Color flow imaging is an important adjunct of Doppler sonography allowing a global depiction of blood flow in vessels, localization of normal arteries as well as identification of abnormal vessels. The role of these noninvasive diagnostic radiological modalities along with a detailed discussion of peripheral arterial disease quantification and detection will be presented. The result of CT angiography and Duplex Doppler Sonography in 40 patients, who underwent these studies in our department over the last two years for evaluation of peripheral vascular disease, will be discussed.

Impotance of fetal suprarenal gland volume

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In this study, twenty five aborted fetuses of various gestational ages were observed. Fetal autopsy specimens were provided by the department of Obstetrics and Gynaecology, Government Medical College & Hospital, Chandigarh. The fetuses with any obvious gross Congenital Malformation or deformity of genitourinary system were excluded from the study, these were arranged into four groups <15 weeks, 16-20 weeks, 21-25 weeks and 26-30 weeks. Weight and Crown to Rump length of the fetuses were the gland was removed with intact kidney on both sides and volume was measured by water displacement method.

The study showed a direct relationship between the fetal adrenal gland volume and fetal weight. The volume of the left Suprarenal glands were higher than those on the right side. It was also found that the volume of suprarenal glands were increasing with gestational age as well as with fetal weight till 20 weeks after that there was no change in volume. These findings are discussed in light of its clinical significance.

Clinical relavance of pharmacokinetics in the chemotherapy of tuberculosis

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Several pharmacokinetic drug interaction studies with anti-TB drugs in patients with pulmonary tuberculosis, intestinal tuberculosis and also in patients undergoing peritoneal dialysis have been carried out and important guidelines to the clinicians have been evolved based on these studies. Studies carried out in healthy volunteers on pharmacokinetic drug interactions of anti-TB drugs when given alone and in combinations and also bioavailability of anti-TB drugs from a triple drug formulation containing rifampicin, isoniazid and pyrazinamide, have generated important findings such as "Non-invasive" – sampling techniques using either saliva or urine could replace invasive blood collections.

Drug interactions could lead to toxicity and detailed investigations undertaken to study the mechanisms and biochemical aspects of adverse reactions namely arthralgia, hepatitis and peripheral neuropathy to anti-TB drugs, had contributed in terms of reducing the toxicity and the best effective combinations to be given to patients without any therapeutic penalty. The results and implications of these findings will be discussed.

Clinical-epidemiological profile of laboratory confirmed cases of influenza a H1N1,At government medical college and hospital (GMCH), Chandigarh

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Methodology: A retrospective study of epidemiological characteristics were descriptively analysed using data of influenza AH1N1 screening center and isolation ward from May 2009 to April 2010 at Government medical College and Hospital, Chandigarh. Data was collected using Performa which was used in influenza A H1N1 screening center to record patient information and presentation. Results: In, GMCH a total of 365 patients were sampled, out of which 29.58% (108) were found to be positive and there were 54 admission in influenza A H1N1 isolation ward out which 54.9% (28) succumbed to it. Influenza A H1N1 cases gradually increased starting from the month of July to maximum in moth of December. Maximum cases were detected in patients' less than 40 years of age which accounted for 81.4% (44 cases). Most common symptom was fever (87.6%), cough (49.77%), sore throat (27%) and breathlessness (23.9%). 28(77.7%) deaths were reported in influenza A H1N1 patients. 46% (12) deaths occurred within 48 hours of admission, of which 7 deaths occurred within 24 hours. Singe death was reported in pregnant female.

Ayurvedic outlook in neurological regeneration of myelin

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Methodology: The detailed study of the patients with MS over various locations, through the databases shows that the initial attack few years before the onset of the disease which shows the acceptance of MS theory. Through the assay and the studies conducted with the real cases, we could find that a particular course of treatment methodology named as DATMS, it is the treatment aimed mainly on four types treatments which prolongs as the case of the patient differs. The successful case studies are the real testimonies for the success of the treatment.

Results & discussion: Through the analysis and the real time study and the basis of treatments done and the medical reports done after the course of treatment, it is seen that the regeneration of myelin is reported. This treatment method could be a promising one for the huge number of MS reported cases.

An experience of 400 cases of total replacement of knee joints

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Osteoarthritis and rheumatoid arthritis afflicts the knee joint quite frequently. With increasing longevity, the [problems of instability, deformity, pain and locking has become very common. Added to this is the attitude of patients to delay the surgery of the replacement of knee joint as much as possible. Hence in this country we have to deal with patients who have very advanced osteoarthritis with deformities and instability.

In this paper we wish to deal with the clinical profile, difficulties in the surgery, the complications and rehabilitation.

A novel approach to trochanteric fracture

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Trochanteric fractures are a very common problem particularly in the aged population who have a tendency to fall and are osteoporotic also. The conventional treatment of open reduction and internal fixation with DHS has two drawbacks.

a) Mobilization can be given only after 10-12 WEEKS
b) The implant has a tendency to cut through the head and neck of the femur.

To obviate these problems we have started fixing the loose fragments with stainless steel wires and then performing a bipolar orthoplasty fixing the femoral stem with cement. The result of this surgery have been very encouraging as it helps in early mobilization and rehabilitation, thus improves the morale of the patient.

The patient satisfaction study in a multispecialty teritiary level hospital of north india

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A pre- designed and pre- tested structured questionnaire was given to the patients (n=1420), as exit interviews, after the patients had undergone consultation. The average registration time was found to be 33 minutes. Satisfaction levels with respect to their doctor's professional communication and behavioural aspects were more than 80%. With regard to the interaction with paramedics, it was 78.4% nursing and 75.0% with other paramedical staff. The satisfaction level with facilities was (drinking water and cleanliness 90%, cleanliness of toilets 62.8% etc.).40.0% responded that found the services costlier and had to spend more money.

Overall 77.2% respondents were satisfied with the type of medical care and services. To conclude infrastructure and architectural corrections need to be made to enhance the comfort and satisfaction of the patients, especially at reception and registration counters. Certain improvements are also needed in the waiting area by making it informative and comfortable.

Padiatric femaral neck fractures: our 10 years of experience

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Methods: The study included 36 children (20 boys and 16 girls) who sustained femoral neck fracture and completed a minimum follow up of 1 year. The children were treated either conservatively, or by open reduction and internal fixation(ORIF) or closed reduction and internal fixation (CRIF). The oputcomes were analyzed using Ratliff critirea and a detail record of complications kept for all the patients. Results: The mean age of included patients was 10 yrs(range3-16 yrs) and the average follow up was 3.2 years (1.1-8.5 years). According to Delbet's classification system, there were no type1,(transepiphyseal) fractures and 16 type II,11 type III,and 9 type IV fractures. There were 8 undisplaced after being managed initially in a hip spica. A satisfactory outcome was obtained in 27 (75%) children. Avascular necrosis (AVN) was the commonest complication, seen in 7 of our patients and all these patients had an unsatisfactory outcome. Other complications included three cases each of coxa-vara, non union and arthritic changes;and one case each of infection, primary screw perforation of head and premature epiphyseal closure. Complications were least in the group treated by ORIF while only 2 [patients managed exclusively by conservative treatment ultimately achieved a satisfactory outcome. Conclusion: We believe that internal fixation of pediatric femur neck fractures should be preferred whenever feasible as conservative treatment carries a high risk of failure of reduction. Aggressive operative treatment aimed at anatomical reduction should be the goal and there should be no hesitation in choosing ORIF over CRIF.

Outcome of patients is primarily influenced by development of AVN which occurs as an independent entity without much relation to the mode of treatment carried out.

Clostridium difficle infections- an emerging menace among elderly patients in ICUs

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Clostridium difficile (CD) is an anaerobic bacteria causing healthcare associated diarrhea on hospitals, especially among the patients above 65 years of age. Is causes pseudo membranous colitis (PMC) often with preceded antimicrobial therapy. The eradication or reduction of bowel bacteria flora amplifies the multiplication of CD due to ample nutrition found, leading to toxin associated leading to PMC are II and III generation Cephalosporins, broad spectrum penicillins and Clindamycin. Fluoroquinolones are also implicated in the genesis of CD associated PMC. Though most of the CD infections are asymptomatic, in some persons it can cause mild self limiting diarrhea or severe symptoms like PMC, toxic mega colons and sometimes even bowel perforation leading to death. Antimibrobial exposure is the most leading high risk factor for many CD associated PMC. The other risk factors are old age, prolonged hospital stay and highly resistant CD spores. The carrier rate of CD is 1-3% among the healthy adults and 20-25% among the hospitalized patients. Recently a hyper-virulent CD-ribotype 027 emerged in Canada, USA and Europe causing severe diseases.
The laboratory diagnosis of CD infections depends upon isolation and identification of CD, detection of Toxin-A and B by cytoxic assay or ELISA technique. For Toxin-A negative patients, culture and PCR methods are useful. Besides detection of enzyme Glutamate dehydrogenase also indicate the CD infections even when Toxin A or B is absent. Culture of CD from children below one year is not recommended as many of them may be carriers. Environmental screening and hospitalized patients below 65 years are also not recommended for surveillance. The treatment of CD associated diarrhea or PMC is Oral Vancomycin or metranidozle. The preventive methods of CD infections are restricted use of antibiotics, high degree of disinfection in hospital environments, improved hand hygiene, isolation of infected patients and occasionally even closure of the affected unit and education of both patients and HCWs. Hand washing is the most important precaution in preventing spread of CD infections within the hospital. Use of disposable rectal thermometers and single person use of toilet also help in further prevention of CD within in the hospital. Alcohol based gels are less effective than the chlorhexidine and 4% polyvidone is also more effective than iodophores or other chlorine based disinfectants.

Role of iron in persistence of goitre in post iodization phase

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Methods: A two phase study was conducted. In the first phase, 2700 school going children of 6 to 12 yrs of district Ambala were examined as per standards laid by National iodine deficiency disorder and control programme. In the second phase, a case-control study, 270 children with goiter and 270 children without goiter were compared with respect to urinary iodine, iodine content of salt and hemoglobin level.
Results: Prevalence of goiter in the studied subjects was 12.6%. Median urinary iodine excretion in both the groups was sufficient and comparable. 82(30.7%) of the goitrous children had anemia (Hb<12g/dl) as compared to 48 (17.7%) of the control group also not significantly (p=.98) different in both the groups. Hemoglobin level negatively correlated with the presence of goiter (r=-0.18, p=0.008) and had an OR of 3.2 (Cl 1.28 – 6.84, p=0.017).
Conclusion: There was a high prevalence of goiter in young children despite iodine repletion. Concurrent iron deficiency correlated with the presence of goiter. However, more evidence based research is required to establish a cause and effect relationship between iron deficiency state and goiter.
Keywords: Goitre, Anemia, Iodine, Haemoglobin.

Evaluating the utility of bactec micro mgit 960 and lowenstein jensen media in the diagnosis of endometrial tuberculosis

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Material & Methods: A cross sectional study was conducted on 300 suspected cases of endometrial tuberculosis and endometrial tissue biopsy were taken. Direct AFB smears were prepared and cultures were done on MGIT 960 vial and L.J medium. Results: Out of the total 300 samples, 30 (10%) came positive for mycobacteria. Out of these 24 isolates (80%) were positive by MGIT 960 system and 8 (26.6%) by L.J media. The average detection time for detection was 9 days with MGIT 960 and 38 days with L.J medium. Conclusion: Bactec MGIT is sensitive enough to detect mycobacterium even from paucibacillary samples especially in extra pulmonary cases.

An outbreak of enterovirus virus-71 meningitis in calicut

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Ever since it was recognized in California (1969), enetrovirus-71 infection appears giving rise to large epidemics with much fatality among children. Entervirus-71 infections, like other enteroviruses are usually asymptomatic or may be associated with various clinical syndromes like diarrhoea, rash, hand-foot mouth disease, herpangina, aseptic meningitis, encephalitis, myocarditis, acute flaccid paralysis, bulbar and brain stem encephalitis, Gullain-Barre syndrome and pulmonary haemorrhage/edema. It was Ihimaru et al who described two outbreaks in Japan with involvement of central nervous system like acute flaccid paralysis, bulbar and brainstem encephalitis and Gullain-Barre syndrome. Increasing attention is now being paid to the study of this virus. There is continuing activity of this virus in our neighborhood for the last 3 decades. Its invasion into India caused Hand-foot and mouth disease in Calicut 2005. We were in search of this virus and as expected, we came across children with aseptic meningitis caused by the same virus, which is the subject of this paper. This is for the first time Entero-virus-71 meningitis being reported from India and probably as years go by, the severity and the variety clinical spectrum may be on the increase. The results will be presented in the Conference.

Prevalnce of metabolic syndrome in rural haryana: a community based cross sectional study.

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Background & objectives: A total of 57 million deaths occurred in the world during 2008; 36 million (63%) were due to NCDs. In India, NCDs are responsible for 53 percent of deaths and 44 percent of disability adjusted life years lost.
Material & Methods: A total of 1200 individuals more than 20 years of age, stratified by age group, sex and place of residence were selected using stratified random sampling. International Diabetes Federation criterion for diagnosing metabolic syndrome was employed. WHO STEPS proforma was used to collect information on behavioural risk factors: tobacco use, diet, physical activity, alcohol use, measured anthropometry and blood pressure. Fasting blood samples were analysed for blood glucose, total cholesterol and triglycerides.
Results: The prevalence of metabolic syndrome was found to be 8%. Burden of NCDs was high (15%) in the study population. Prevalence of NCD risk factors was also high. Prevalence of behavioural and each of the biochemical risk factors increased with age, adjusting for other factors including sex and the place of residence. The odds ratios relating anthropometric variables to biochemical variables was not significant (p=0.843) suggesting that anthropometric variables may not be useful surrogates for biochemical risk factors for population screening purposes.
Conclusions: In this large study of community-based sample in Haryana, high burden of NCD risk factors was observed, comparable to that in the developed countries. These data may serve to propel multi sectoral efforts to lower the community burden of NCD risk factors in India.

Values in healthcare

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Thrive and Survive? With today's emphasis on quality of service, how can healthcare professionals deliver the best possible care to patients and at the same time, feel enriched and supported by their work? How can they thrive, rather than just survive? Values in Healthcare a spiritual approach address an important gap in personal and team development for healthcare professionals today by taking a fresh, value-based approach to their learning and practice.
Values in a pack? Values in healthcare is a modular development programme which will help healthcare professional and teams to support themselves and their patients. Through experiential exercises and opportunities for reflection and self-enquiry participants can identify their own core values and discover how their insights can enhance and revitalize their work. The programme is delivered via a pack of materials which introduce values such as compassion, co-operation, peacefulness and self-care and encourage participants to explore using them in their personal lives and professional practice. This learning outcomes will enable professionals in all settings to cope better with their work, raise morale and restore a sense of purpose, helping to prevent problem of burnout, sickness absence, and staff retention. A spiritual approach: Today sees a new emphasis on meeting the spiritual needs of patients as part of effective, whole-person health care. In order to do this, healthcare practitioners need opportunities to recognize and address their own spiritual needs. Values in Healthcare emphasizes this essential relationship through a number of learning tools. These include reflection, listening, appreciation, meditation, visualization, creativity, and play. Contents: Values in Healthcare comprises seven one-day modules, each of which will help groups of healthcare professionals to explore values in depth, as they relate to their personal lives and professional practice:
Module 1: Values- gain strength through motivation
Module 2: Peace- benefit from being calm
Module 3: Positivity- harness the power of thoughts
Module 4: Compassion- release healing energy
Module 5: Co-operation- appreciate the wisdom of teams
Module 6: Valuing yourself- sustaining the Career
Module 7: Spirituality in healthcare- spiritual care in practice
Who can benefit from the programme?

- Practicing professional at all levels, including doctors, nurses, professions allied to medicine, social workers, managers, support and administrative staff.
- Practitioners in a wide range of setting including hospitals, hospices, general practices, health centres, clinics
- Staff groups and teams, including multidisciplinary teams, primary health care teams, outpatient teams, departmental teams
- Qualifying and undergraduate teaching programme as part of, or as elective elements of, curricula
- Postgraduate and post qualifying courses
- A range of professionals on their Continuing professional Development

The module to train 25-30 people in a group is the facilitating experience preogramme.
This preogramme is introduced in RMMCH and Nursing College,Annamalai University and also Chettinad Hospital, Chennai
Its aim is giving healthcare to the professionals to thrive rather than survive
It is acknowledged that this programme is prepared and done by Janki Foundation, UK

Polumeric alginate beads for the controlled deleivery of therapeutic macromolecules and their in vivo tissue reaction

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Several life saving drugs which are offsprings of biotechnology industry are not without disadvantages like short plasma half lives, low bioavailability and are also difficult to administer by conventional routes. Developing novel drug delivery systems will help to ameliorate these factors, obviate the need for repeated drug administration and consequently improve their therapeutic index and patient compliance. With this aim in this work calcium cross linked polymeric alginate beads entrapping macromolecules like human recombinant insulin and double stranded DNA were prepared by ionic gelation method and their in vitro drug release profiles were estimated spectrophotometrically. Their drug release characteristics showed that about 60% and 20% of (hr) insulin and (ds) DNA respectively were released within 14 days

in PBSpH 7.4, in a controlled near zero order fashion. The tissue reaction to subcutaneously implanted alginate beads in male albino Wistar rats was evaluated by histological examination. The alginate beads evoked only a mild to moderate inflammatory reaction which subsided by the fourth week at the site of implantation and healing response was seen. The beads completely dissolved and degraded within 35days without causing any fibrous capsule formation, calcification, and tumorogenesis. It can be concluded that the polymeric alginate beads developed in this study show promise as biocompatible and bioresorbable implants for the long term in vivo controlled delivery of biotechnology based therapeutic macromolecules like recombinant hormones and genes. They also favor the biochemical processes that promote growth and regeneration of tissues.

Current status of the stomatological education and practice in China

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In 1917, the first department of dentistry was founded by American and Canadian Christian church in Chengdu, which is the precursor of West China College of Stomatology, Si Chuan University. This indicates the beginning of the modern dental education system in China. In early 1950s, following the medical system of the former Soviet Union, the terminology "Dentistry" was changed into "Stomatology" in China. The foundation of Stomatology made this discipline more closely related to clinical medicine, promoted the development of oral & maxillofacial surgery and plastic surgery in China. There were only 5 dental schools or faculties in China when the new China was established in 1949, thenumber increased drastically during the 1970s and the past 10 years, there are totally 83 dental schools/faculties in China now, distributing in the 26 provinces all over the country. So far, all the dental schools in China are public schools. The administrative management, financial usage, student intake, and staff appointment are all supervised by the government. Dental education system in China currently includes the following programs: college education, 5-year undergraduate program, 7-year bachelor-master combined program, 8-year bachelor-doctor combined program, postgraduate education, as well as continuing education. China is a developing country with a large number of populations. According to the Second National Dental Survey in 2005, prevalence of dental caries in Chinese population is as follows: 5 year group is 66%, 12 year group is 29%, 35-44 year group is 88%, 65-74 year group is 98%; the incidence of periodontitis are as follows: 5 year group is 57.7%, 35-44 year group is 77.3%, 65-77 year group is 68%; the average number of lost teeth is 2.6 in middle-aged group, 11 in the elderly group. Therefore, the need for dental health care is tremendous, and the task of dental service is demanding. With the development the development of China's economy, the number of dentists has increased from less than 6 thousand (5,741) in 1978, to more than 182 thousand (182100) in 2009. The ratio of the number of dentist to population keeps increasing, but compared with developed countries there are still serious imbalance problem. After nearly a decade of development, Guanghua School of Stomatology, Hospital of stomatology, Sun Yat-sen University has made remarkable achievements in oral medicine education, medical treatment and oral scientific research. This is a concentrated expression of rapidly development of oral medicine in China.

Bigger microbes hit big time!!!

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Retrospective study of 295 candidal isolates (from September 2009-june 2011) from patients admitted in intensive care units were included in the study. Vitek 2 was used for identification and antifungal suspectibilty testing.

Candida was isolated from 295 clinical isolates. C.tropicalis was the most frequent isolate(39.3%). Suspectibility to 4 antifungals(i.e.Amphoterecin B, Fluconajole, 5 flucytosine, voriconazole) was done. Almost 92% of the isolates ware suspectible to voricanazole while sensitivity to Amphoterecin B, fluconazole and % fluctosine was 86.4%, 82.03% and 93% respectively with variable sensitivity according to species. All C.krusei were resistant to fluconazole and 90% were resistant to 5 flucytosine.

Candidal infections were more common in men, patients more than 45 years, those with hospital stay more than 9 days and patients from gastroenterology deptt.

Conclusion: Emergence of Candidal infections in the immunosuppressed/ hospitalized patients compounded by the high morbidity and mortality of these isolates makes early diagnosis and treatment mandatory for these isolates. Knowledge of epidemiology/ known risk factors for these fungal isolates help in prompt initiation of empirical antifungals against the suspected fungal isolates significantly reducing morbidity and mortality in these infected patients.

Scope of alternative medicine in health care

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Alternative Medicine is any healing practice, "that does not fall within the realm of conventional medicine". In some instances, it is based on historical and cultural traditions, rather than a scientific (i.e. evidence-based) basis and varies from country to country Alternative medicine methods are diverse in their foundations and methodologies. National centre for Complimentary and Alternative Medicine (NCCAM) defines CAM as group of diverse medical and health care systems practices that are not generally considered as part of conventional medicine, also called Western Allopathic Medicine. Integrated medicine is a practice that combines both conventional and CAM treatments. Methods may incorporate or base themselves on traditional medicine, folk knowledge, spiritual beliefs, or newly conceived approaches to healing. The use of Alternative medicine is noticed to be increasing at a rapid pace and is estimated to have a market of $340m by the end of 2011 in Britain alone. Around the world, according to an estimate made in 2008, the industry's value is about $60 billion for alternative medicine. NCCAM in America has developed one of the most widely used classification systems for the branches of complementary and alternative medicine and it includes Traditional Chinese medicine, Naturopathy, Homeopathy, Ayurveda, Acupuncture, Chiropractic as a few examples. The International Centre for holistic Healing and Allied Research (ICHHAR) is an alternative medicine institute in Kolkata, India which imparts training in various branches of alternative medicine. Although heterogenous, these systems have many common characteristics, including a focus on individualizing treatments, treating the whole person, promoting self-care and self-healing, recognizing the spiritual nature of each individual and focus on good nutrition and preventive practices. However, Alternative medicine often lacks or has only limited experimental and clinical study. This paper focuses on various alternative medicine forms presently adopted in the world and their application towards health care. It also discusses the importance of Alternative Medicine over Conventional Allopathic Medicine including its limitations.

Informed consent and risk of medical negligence litigation-A comparative analysis of law in the UK and USA

Srinimmagadda Seshagiri Rao

Thornford Park Hospital

This talk examines the ethical and legal aspects of the concept of informed consent with relevant discussion on up to date case law on the legal standard for medical negligence litigation in common law countries. It examines the changing professional standards in relation to informed consent, their implications for negligence litigation in English law and highlights the steps aimed to decrease the litigation potential in one's clinical practice. It further discusses the differences between the English and the American systems with regard to informed consent and examines whether the English system is moving towards the American direction, which is known to be associated with increased risk of medical negligence litigation. This talk is developed based on my legal research for my Masters degree (LL.M) in Law.

An ounce of public health is worth a pound of health care

G Samaram

Imm. Past National President, IMA

Public Health is for Everyone, Everywhere & Everyday: Protect Promote, Prevent & provide. Rural India bears three-fourth of the ailments burden of India, but has only one-fourth of the human resources for health and one-ninth of hospital beds. One million Indian die every year due to inadequate health care facilities and 70 crore people have no access to specialist care because of social inequality, poor sanitation facilities & shortages in primary healthcare facilities in addition to financial constraints and shortage of human resources. Political will is not strong enough and in addition Corruption drains excellently planned programs. Science discovers, technology develops and health care delivers and availability and application of technology helps easy accessible quality health care services to all. Empowering the skilled women health worker promotes safe motherhood practices at the house hold and at community levels in the slum. Establishment of an ideal PHC with good referal system & periodic specialist services is very much needed for the improvement of health indicators.

Towards achievement of universal health care in India by 2020 A call for Action

-Securing the right to health for all in India

-Gender equity and universal health coverage

-Accessibility to all healthcare facilities and affordability of drugs

- Financing healthcare for all

-Good Governance in healthcare.

Autonomic disorders

Paola Sandroni

Mayo Clinic, Rochester, MN, USA

Autonomic symptoms are relatively common complaints that prompt patient to search medical attention. They can be caused by either primary autonomic disorders (due to pathology of the central and /or peripheral nervous system) or be secondary to other disorders or be iatrogenic (due to medications, post RT etc.). Most common symptoms includes: orthostatic intolerance, bladder/ bowel dysfunction, altered thermoregulation, sicca complex. Symptoms recognition is generally easy, although in the elderly orthostatic hypotension may manifest with very non specific complaints and the diagnosis should be always considered. The next step is to search for potentially treatable causes, the most common one being medication side effects. Medical condition can cause autonomic dysfunction either directly (i.e. cardiovascular or gastrointestinal disorders,) or indirectly (i.e., resulting in prolonged immobilization, dehydration or debility). Autonomic disorders can be grossly divided in dysfunctional syndromes and in autonomic failures, the first portending much better prognosis than the latter. The physician needs then to identify which pathology may be present looking for central and peripheral causes. Autonomic neuropathies are relatively common and may be pure or associated with somatic forms. The most common autonomic neuropathies are caused by diabetes, amyloidosis, autoimmune disorders (such as Sjogren's, paraneoplastic syndromes etc.), heridatery neuropathies and toxic forms. Severity can vary quite widely both in different forms and in different patients. Some forms may be very selective and affect omly one system such as the sicca syndrome, idiopathic orthostatic hypotension or chronic idiopathic anhidrosis. Others can cause generalized autonomic failure (diabetes, amyloid, pure autonomic failure). Limited small fiber neuropathies may manifest with erythromelagia. Dysfunctional, non lessional syndromes include disorders of reduced orthostatic tolerance due to excessive tachycardia (POTS), irritable bowel syndrome and probably visceral hypersensitivity syndromes. Central autonomic disorders are more complex and can be degenerative in nature (multiple system atrophy, parkinsonism etc.) or due to autoimmune syndromes, multiple sclerosis, trauma, hypothalamic mass etc. Autonomic evaluations can be done at beside, but more detailed assessment can only be achieved with proper testing equipment. Multidisciplinary approach may be necessary. Various symptomatic treatment strategies are available if there is no specific cure.

An outbreak of enterovirus virus-71 meningitis in Calicut

C.K. Sashidharan

Senior Consultant in Paediatrics & Neonatology, Baby Memorial Hospital, Calicut, Kerala, India

Ever since it was recognized in California(1969), enterovirus-71 infections appears giving rise to large epidemics with much fatality among children. Entrovirus-71 infections like other enterovirus are usually asymptomatic or may be associated with various clinical syndromes like diarrhea, rash, hand-foot mouth disease, herpangina, aspeticmeningitis, encephalitis, myocarditis, acute laccid paralysis, bulbar and brain stem encephalitis, Gullain- Barre syndrome and pulomanary haemorrhage/edema. It was Ihimaru et al who described two outbreaks in japan with involvement of central nervous system like acute flaccid paralysis, bulbar and brainstem encephalitis and Gullain-Barre syndrome.

Increasing attention is now being paid to the study of this virus. There is continuing activity of this virus in our neighbourhood for the last 3 decades. Its invansion into India caused Hand-foot and mouth disease in Calicut 2005. We were in search of this virus and as expected, we came across children with aseptic meningitis caused by the same virus, which is the subject of this paper. This is for the first time Enterovirus-71 meningitis being reported from India and probably as years go by, the severity and the variety clinical spectrum may be on the increase. The results will be presented in the Conference.

Flow CT-Fometry Myelodysplastic Syndrome: Diagnostic Utility

Har Prasad Pati, Anita Chopra, R. Kumar
PGIMS, Rohtak, Haryana, India

Methods bone narrow aspirates of 57 suspected or known MDS and 31 normal controls were studied farm maturation pattern, quantitative FCM with multiple antigens & for CD71 on erythroblasts.
Results: Patients (n=57) Included proven MDS (n=14), suspected MDS (n=13) and non-MDS (n=30) By em-based approach, all proven cases were FCM positive. Insuspected MDS 11/13 (84.6%) including morphology negative cases, were positive and 2/13s (154%) cases were FMC mdermmate In non MDS cases,37/30 (90%) were FCM negative, and 2/30 (6.7%) were indeterminate. Quanhtatve analysis showed that an FMC score of and percentage of CD34= 0 cells and expression of COI lb, CDI5 and CD56 on myeloblasts were characteristic of M.CD71 MFI on erythroblasts and CD38 MFI on myelohlasts were significaMly lower m MDS.
Conclusions: Both the Maturation patter-recognition and quantitative approaches are sensitive methods of diagnosing MDS Their value in Morphology negative AND cytogenetic negative cases must await better definition of the speafiaty f FCM through a more extensive study.

Operative Management of Type II and Type IIIA Open Tibial Fractures Presenting from 6 to 24 Hours after Injury : An Indian Experience

Vishal Kumar, Sameer Aggarwal, Mandeep Singh Dhillon
PGILER, Chandigarh

METHODS: 142 open (type 2 and type 3a) fractures of the tibial shaft in the age group 16-40, presenting with treatment delays (between 6 to 24 hours of injury) were alternatively manged with external fixator (EF) and undreamed tibial nail (LTN). Exclusion criteria included patients with fracture extending into the articular surfaces of either end of the tibia, pallets with open Type 1 or Type 3b/c fractures where we universally used UTN and EF respectively, patients with communicated fractures (Win quist Hansen type 3 or type 4), time of injury <6 hours or >24 hours and polytraurri a patients. A total of 114. Patients (who completed a minimum follow up of 1 year) were assessed at a mean foil Ow up of 64.5 weeks. Evaluation was based on time to union, evidence of nounion. Presence of nn alun ion or malalignment or osteomy-elitis.
RESULT: Union time and infection rates were less for EF grcu p (p value: 0.047 and 0.000 respectively) while malunion and nounion was lesser in UTN group (p value: 0.013 and 0.012 respetively). After repeated surgeries. All these fractu res ultimately united, but 4 patients in the UTrit group were left with a persistent discharging sinus.
CONCLUSIONS: We conclude that UTN may not be the implant of choice for patients presenting after 6 hours of injury. EF is a better alternative in developing countries when patients reach date to the hospital. Although initial union rates may be lower with EF as compared to UTN, these fractures ultimately unite if a second staged reamed nailing is carried out.

Prevalence of Hyperhomocyteinemia in Chronic Kidney Disease Effect of Supplementation of Folic Acid Vitamin B12 Cardiovas-cular Mortality

N.Nand, M Sharma & N Mittal
Professor & Head Nephrology, Department of Medicine, PGIMS, Rohtak , Haryana, India

A randomized placebo controlled Mal on HO cases was earned out at terhary care hospital. N May 2009 to Novell]." MO Adult patient of CKD having glomendar filtrahon rate (GFR) <60m11 min were enrolled for the study Patients were randomly assigned Into two groups. Control group was gven fohc acid and vdamin B12 supplementation for 6 months
Mean baseline hoocysteme levels were similar m two groups It was 3261 umol, m the mtervenhonal group and 29 8 umolfi. In the placebo group (p>0.05) The level decreased signcantly to 19 69 umold. (pe0 001) the interventional group and it increased to 34 41 umon (p>01 05) m the placebo group 6 moMhs The homocysteme level had a negative co-relahon with haemoglobin (r=19) and vitamin (r+-0 16), folic acid (r=-019) and vitamin B12 (r=,35) There uas no signify.nt effect on total mortality, [lea. Due to CVD, to.1 mchemic eve., hospitalization due to unstable angma, heart failure or venous thrombotic events after 6 months of supplementation therapy
Serum homocysteme elevated pahents of CKD Folic acid and vitamin supplementation lowered homocysteme, but it did not reduce cardiovascular Msease mortality. B12

Pattern Of Renal Diseases In The Elderly: Experience From Aa Teritiary Care Hospital

H.K. Aggarwal, Deepak Jain
Rohtak

The present study included retrospective analysis of 212 elderly above 60 years of age hospitalized for symptomatic renal diseases over a period of 5 years (January 2005 to December 2009). The mean age was 68.72=5.44 years and 65% of these were male. ARF was seen in 34 (16.03%), CRF in 154 (72.6%) and nephritic syndrome in 18 98.49%). Four patients had renal artery stenosis, the other two had renal cell carcinoma.
58.8% had medical cause of ARF, whereas 41.7% had surgical causes. Volume loss due to gastroenteritis was the commonest medical cause 940%). Other common medical causes were septicemia, drugs and CHF. Benign prostate hypertrophy was the commonest surgical cause (57.14%), followed by post-operative complications (42.85%)
154 patients had CRF (72.64%), the common causes of CRF included diabetic Nephropathy, renal stone disease, benign nephrosclerosis and benign prostatic hypertrophy together accounting for 82% of all cases of CRF. The common cause of nephritic syndrome was idiopathic membranous nephropathy (50%)
With increase in life expectancy and ever increasing geriatric population, this group of patients needs specific categorization as the management strategies and further course of disease may differ.

Glycated Hemoglobin A Better Diagnostic Parameter Than Faster Plasma Glucose Levels In Patients Undergoing Dental Surgery: A Comparative Study.

Qazi N, Singh J, Pandey R, Bhaskar N, etal.
MMIMSR, Mullana, Ambala, Haryana, India

100 non-diabetic participants were included in this prospective study, diabetes was defined as an FPG level?126 mg/dl or an HbAlc level >6.5%. data was collected from the baseline and second examination conducted at 6 months
The screening model using FPG>126 mg/dl had sensitivity of 68% while that of HbAlc.6.5% was 100% and specificity of FPG>126mg/dl and HbAlc>6.5% was 95% and 100% respectively for detecting undiagnosed diabetes.
FPG and HbAlc criteria do not identify identical groups of individual from a population-based sample as having diabetes. Using HbAlc alone to conduct an initial diabetes screening in undiagnosed participants detects more cases of prevalent diabetes than FPG alone. Keywords: Diabetes, fasting plasma glucose, glycated haemoglobin.

Ultrasonography In Maxillofacial Pathologies

Pramod
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Ultrasonic Echography has been used as an instant, non-invasive method for the observation of relatively deep areas. Diagnostic ultrasound uses a very lugh frequency (15-10Hz) pulsed ultrasound beam directed into the body from a transducer placed in contact with the body. By using absorption, reflection, refraction and diffusion, sonic waves are reflected, which in turn produces electric signal that is amplified and processed and ultimately displayed as an image. Changes in the echo pattern determine the changes in tissue. Recent advancements in ultrasound like Color Doppler are used to detect the moving content like blood with addition of color to the echo This papers focuses and the Ultrasound as diagnostic tool for evaluation of maxilla facial fractures and pathologies like salivary gland disorders, head and neck swell-ings, determination of vascular structures and their relationship, lymphnode disorders, ultrasound- guided fine needle aspiration (FNA) biopsy. This paper also details the limited use in head and neck with a real-time imaging technique which requires the presence of radiologist during the investigation.

A Study to Assess the Perception of Health Insurance among Urban and Rural Popultion of Haryana

Sachin Singh Yadav, SK Ahluwalia, Rambha Pathak, et.al.
Deptt. of Community Medicine, M.M. Medical College, MMIMSR, Maula, Ambala, Haryana, India

Material methods: A community-based cross-sectional study was carried among rural and urban popu-lation of Haryana. Systematic random sampling technique was used to select the respondents. A total of 500 household were taken for the study purpose. A self designed, pretested, semi structured questionnaire was developed to assess the perception of community regarding health insurance.
Results: Overall, 56% of the residents had knowledge regarding health insurance, while 17% had not heard about it. Individuals residing in urban area had higher (68%) level of knowledge and were willing to get their health insured than rural areas (43%). Around 45.0% of the respondents came to know about health insurance schemes from media which played an important role in the dissemination of information. The mean premium amount agreeable to be paid by the respondents for health insurance was found to be Rs 1000, even the low socio-economic group of people were also willing to part with a reasonable amount of Rs. 500 annually for health insurance. The middle and low socio-economic groups favored government health insurance compared to private health insurance.
Conclusion: There is a need to improve level of awareness regarding health insurance. It is a necessity of life as all individuals suffer from any disease or health related problem at any time of their life. Therefore it should be acquired by all for future security as it reduces the burden of high medical expenses.

Clinico-Epidemiological Investigation Of An Epidemic Dropsy Outbreak In A Village Of Haryana, India

Ramesh Verma, Pardeep Khanna, Sandeep Sachcdeva, etal.
Associate Professor, Department of Community Medicine, Pt BDS Postgraduate Institute of Medical Sciences, Rohtak, Haryana, India

Method: This is a cross-sectional, community-based study, undertaken on 46 rural patients aged 4-65 years.' Results: Forty-six cases of Epidemic dropsy were detected from an epidemic in a village in Haryana, of all affected patients 19(41.3%) were males and 27 (58.69%) were females. The age group of the affected individuals varied from 4 years to 65 years. The clinical manifestations and epidemiological factors were studied GIT symptoms were present in 86.3% of the cases. Sanguinarine was detected in all mustard oil samples collected from the homes of affected families
Conclusion: Adulteration of mustard oil with agremone oil, either deliberate or accidental is the main cause of the disease.

Breast feeding practices in urban slums of Rohtak district, Haryana.

Suraj Chawla, Ramesh Verma, Pardeep Khanna
Associate Professor, Department of Community Medicine, PT BDS Postgraduate Institute of Medical Sciences, Rohtak, Haryana, India

To study the breast feeding practices in urban slums & to know the influence of socio-cultural factors on breast feeding practices. Cross-sectional study was conducted in urban health centre field practicing area of Deptt. Of community medicine, Pt BD Sharma PGMIS, Rohtak, Haryana. The study included 325 mothers having children upto the age of 2 years were interviewed using pre-tested proforma. It was found that 52.2% of mothers initiated breast feeding within first 24 hours of delivery. Short duration of breast feeding was observed among mothers with higher socio-economic status. 89.5% of the mother gave pre lacteal feeds and 42% mother gave colostrum.

Application of Nanocopper in Bioprocess and Industry

J. Tracy Tina Angelina

K.J. Hospital Research & Post Graduate centre, Chennai

Biofouling is one of the major concerns in the use of Titanium, an excellent material with respect to corrosion resistance and mechanical properties, for sea-water-colled condensers of power plants. An additional problem reported to develop as a consequence of biofouling is that of biomineralization. Fouling control strategies in condensers include a combination of mechanical and chemical treatments like sponge ball cleaning, backwashing and chlorination. In general, innumerable studies have shown that no routine treatment regime can be successfully keep the condenser tube over a period of years. Since, surface properties of the substratum influence initiate adhesion and growth of bacterial cell on materials, modification of the surface of condenser material like titanium etc., in order to reduce microbial attachment is the need of the hour. Metal nanoparticles are known to exhibit enhanced physical and chemical properties when compared to their bulk counterparts because of their high surface to volume ratios. Metals like copper are very toxic to microorganisms and effectively kill most of the microbes by blocking the respiratory or a fungus survives. Therefore, nanostructured Cu Thin films will be grown on titanium substrate to enhance its antibacterial properties by reducing adhesion. Cu thins films are deposited on different substrate using Pulsed DC Magnetron Sputtering system. Both the GIXRD (Glance Incidence X-ray Diffraction) and AFM (Atomic Force Microscopy) studies confirmed that the copper thin films obtained in the present study were smooth and within the dimensions of a nanofilm consisting of small clusters of copper nanoparticles. The two order decrease in the bacterial density on copper coated surface and Epifluorescence micrographs depicting very few fluorescing cells clearly demonstrate the superior antibactericidal capacity of nanocrystalline copper thin films.

Sacrococygeal Teratoma

Ashutosh Talwar, Neerja Puri, HPS Sandhu

Sacrococygeal teratoma is a tumour of the newborn seen in 1 out of 35,000 to 40,000 live births. We presented to the department of surgery with swelling in the sacrococygeal region since birth. After ultrasound confirmation of the diagnosis, the swelling was excised along with coccyx.

Breast Imaging: Comparaioson of Mammography, Ultra Sonography and Dynamic Contrast Enhanced MRI in the Diagnosis of Benign 7 Maligent Breast Lesions

Shibani Mehra

Breast cancer is the most common malignancy in women and the second most common cause of cancer related mortality. Benign breast lesions though less common, are also encountered. Early treatment of nanpalpable breast cancer reduces mortality rate. Radiological imaging is extremely important in early detection, accurate diagnosis and obtaining biopsies to differentiate benign from malignant lesions.

Mammography continues to be the primary modality for breast imaging and is routinely used for screening and lesion detection. It has a good sensitivity of 80% in Grade 1 and 2 breats. Microcalcifications associated with ductal carcinoma in situ are best demonstrated on mammography and classification of various types of classification is best achieved using mammography. The major limitations of mammography are dense Grade 3 and 4 breasts where lesion detection becomes difficult.

Sonography has the ability to detect clinical and mammographically occult breast cancer with a sensitivity of 88%, the higher sensitivity is attributed to the fact that sonography lesion detection is independent of breast density. It provides goos distinction of cystic from solid lesions and better appreciation of margins as well as the surrounding breast parenchyma. The drawback of sonography is that microcalcifications which are associated with both infiltrating carcinomas and ductal carcinoma in situ, cannot be detected by this modality. Nonetheless, both mammography and sonography used together increase the sensitivity for detection of breast cancer and both these are currently most sensitive for breast lesion detection.

Dynamic contrast enhanced MRI of the breast is indicated for detection of occult lesions, for characterization of lesions inconclusive on US, mammography and for evaluation of those lesions that could not be biopsied. It provides proper assessment of local extent of disease and is used prior to surgery for evaluation of margins of lesions, extent of disease and ruling out chest wall involvement.

A discussion of all the three modalities and a comparison of their diagnostic efficacy in breast pathology will be presented.

Breast Reconstruction After Mastectomy

Kulwant S. Bhangoo

Certified Surgeon, Buffalo, NY, USA

The loss of a breast has a devastating effect on a woman. This is because the female breast has profound social, sexual and sensual connotations. This is manifest from the prominent role that the female breast has played in art, paintings, sculptures and statues since the dawn of history.

I this presentation, Indications, timing and techniques of breast reconstruction after mastectomy are discussed. The issue of immediate versus delayed reconstruction is concerned, various methods are discussed. These include:

- Direct placement of an implant if there is sufficient available local tissue. If the local tissue is inadequate then other methods of recruiting tissue, such as tissue expansion, is described.
- Local flaps are discussed although they have very limited application. A latissimus dorsi myocutaneous flap with and without an implant is also discussed.
- The state of the art method of breast reconstruction with autologous tissue in transverse rectus abdominis myocutaneous flap is discussed in detail.
- Planning operative details and results are discussed. The issue of opposite breast to obtain balance between the reconstructed and the normal breast is also discussed.
- Various methods of nipple areolar reconstruction are described.

Clinical cases are demonstrated to illustrate the various reconstructive techniques.TMA PAI Oration Hyperparathyroidism-The Indian Scenario

M. Chandrasekaran

Professor & Head, Dept. of Endocrine Surgery, Madras Medical College, Chennai, Tamil Nadu, India

Hyperparathyroidism is suspected and diagnosed only when there is hypercalcemia. The western world talks about the usefulness of estimating serum calcium as a routine to detect hyperparathyroidism. Unfortunately serum calcium alone cannot be used to detect patients with hyperparathyroidism in India have normocalcemia and not hypercalcemia.

This is primarily because of the Vit.D deficiency and inadequate intake of calcium. Though sunlight is available in plenty the incidence of hyperparathyroidism due to Vit.D deficiency is increasing in India. Surgeons in India should be aware of the fact that three and a half parathyroidectomy is not the treatment of choice for hyperparathyroidism due to Vit.D deficiency.

However, these patients can develop an adenoma at a later stage which is an indication for surgery. Hence, patients with adenoma should be identified in order to suggest surgical treatment. I have designed a very simple test called “Calcium Challenge test” to identify patients with parathyroid adenoma so that a definitive surgical procedure can be carried out with utmost confidence.

Calcium Challenge test: Give 1gm of oral calcium along with 25 mcg of 1-25 vit D for a period of 14 days for patients with elevated serum PTH and Normal serum calcium. Repeat the serum PTH after 14 days. If there is a fall in the serum PTH (Calcium Challenge test-positive) it means the feedback mechanism is intact and it is a case of hyperplasia which requires only a medical management. If there is no fall in the serum PTH level or serum PTH increases (Calcium Challenge test-negative) it is a case of parathyroid adenoma which requires surgical removal after localization studies.

The Indian scenario of hyperparathyroidism is totally different from the western scenario and my experience with it, in the last 24 years at the Department of Endocrine Surgery of madras medical College is presented to the distinguished delegates of the International Medical Sciences Academy.

Symmetry States Of The Physical Space: An Expanded Reference Frame For Understanding Human Consciousness

Nisha Manek

Mayo Clinic, Rochester, MN, USA

The last decade has seen an impressive amount of research in the medical sciences regarding the relationship between spirituality and health. From this vast body of research emerges a neurologically-based rationale for the development of self-awareness through meditation and released techniques. The neuro-sciences have enriched our understanding of the benefits of meditation. On a more fundamental level research in intention has conclusively shown that human consciousness can have effects on physical properties of materials and that a change in the symmetry states of the physical space is a necessary condition. This work expands our frame of reference for understanding human consciousness from a neuro-science perspective. The data of the intention experiments, characteristics of the symmetry states of the physical space and the pragmatic clinical applications in medicine will be discussed.

A necessary future- the integration of health and healthcare

Kerry D. Olsen

Mayo Clinic, Rochester, MN, USA

The world is facing a global obesity pandemic. The sequelae of obesity and many other rapidly increasing diseases can be largely attributed to adverse lifestyle behaviours. The resultant health care costs are taking our health and economic systems to the breaking point. Interventions to reverse these trends must come from individual behavior change, school and work place intervention, sector changes in agriculture, food services, education, and urban planning, and government policy changes. The health care sector must also appropriately respond. Too often physicians view adverse life style change as the moral failure of their patient, revert to therapeutic nihilism, or have too little time or training to adequately address these problems. Doctors simply recommend pursuing diet and exercise, revert to pharmacotherapy, or suggest bariatric surgery. There must be a new model of health care to address adverse individual health behaviors. At mayo clinic, we are introducing a new member to the health care team, the health and wellness specialist. This person can most cost effectively and skillfully assess and manage health, lead life style change programs, provide ongoing health coaching, and better understand and impact sustainable behavioral change. These interventions are a key factor in disease prevention, disease prediction, disease mitigation, health promotion, and health potentiation. This presentation will describe the use and early results of a new transformative model for the care of a local population. That model is the integration of health and health care. Physicians refer their patients directly to a health and wellness specialist and many medical programs are now directly integrated with healthy living programs. Changing adverse lifestyle behavior should significantly reduce health care costs.

A Study On Infantile Hemangiomas.

NEERJA PURI, ASHUTOSH TALWAR

METHODS: A prospective study of 50 children with infantile hemangiomas who were below 12 years of age were taken up for the study. RESULTS: In our study, 66% of hemangiomas were present at birth, 22% were seen between 1-5 years of age, 10% appeared by first month of life and 2% appeared after 5 years of age. Also, it was seen that 90% of hemangiomas were of superficial type and 10% were of deep type. Regarding the number of hemangiomas, 84% of children had single hemangioma, 10% had 2-5 lesions, 4% patients had 6-10 lesions and 2% patients had more than 10 lesions. Positive family history was seen in 8% children. The commonest site of involvement was head and neck seen in 56% patients, trunk involvement was seen in 28% patients and extremities were involved in 16% of children. The commonest complication was ulceration seen in 12% patients. CONCLUSION: Because hemangiomas proliferate rapidly in the first few weeks to months of life, there may be a window of opportunity to intervene in high-risk hemangiomas, in an attempt to prevent complications, including permanent scarring.

Study Of Sociodemographic Factors Affecting Level Of Physical Activity Among School Children In Urban And Rural Areas Of Ambala (Haryana).

Sanjeev Sharma, Jagjeet Singh, SK Ahluwalia, Anshu Mittal

Physical activity is decreasing among children with the emergence of newer ways of entertainment viz television, computer, electronic gadgets etc. decrease in physical activity leads to increased BMI and thus leading to increased risk of cardiovascular diseases, diabetes and others. Objective: To study the sociodemographic factors affecting physical activity and its effect on Body mass Index. Methodology: Cross-sectional study conducted in the government and private schools of District Ambala among 500 adolescent students of age 11-19 years. A pretested, self designed questionnaire based on INDIA (CBSE) GSHS Questiobnaire-2006 was used. The data thus collected was complied, analysed and statistically tested using appropriate statistical tests using Epi info 6 or SPSS-17 software. Conclusion: Level of physical

activity was found to be low among both rural and urban students. Prevalence of overweight was found to be more than 20% among boys and more than 15% among girls. Physical activity like exercise, sports etc. had remarkable effect on the prevalence of overweight and obesity.

Survival Curves

Murali Duggirala
Mayo Clinic, Rochester, MN, USA

In many studies, especially in cancer research, the primary outcome under assessment is time to event. In survival studies, by the end of study follow up some individuals have not had the event of interest. In addition, survival data are not normally distributed. So, the survival data need special methods called survival analysis. In medical literature, Kaplan-Meier plots are most commonly used to analyze survival data. Basic concepts of survival, how to construct and interpret survival curves, and testing the survival difference will be discussed.

Robotic In Gynecology

Neena Desai/ Savitha Desai

Robotic Surgery is a revolution in the medical field and changed the standards of the minimally invasive surgery. It has been just a decade since Robotic Surgery has been introduced the surgical field in all specialties Robotic Gynecology surgery has enormous growth in Gynaecology. Robotically Assisted Surgery was developed to overcome both the limitation of MIS (Minimum Invasive Surgery) or to enhance the capabilities of surgeons performing open surgery. In comparison with other conventional laparoscopic surgeries RAS 9Robotic Assisted Surgery) gives the surgeon better control over the surgical instruments, better view of the surgical site. There advantages are due to the high definition 3Dvision systems, wristed instruments, better surgical result like lesser intra operative blood loss, quick post operative recovery and less pain. The disadvantages are due to its steep learning curve, its high cost and huge size of the equipment. All the conventional surgeries like Hysterectomy, Myomectomy, Endometrosis Tubal Canalization, Sacrocolpopexy are done with greater accuracy and easy. Conclusion: However with further improvement in the present technology and more Surgeon being trained in the technologies, more patients seek MIS (Minimal Invasive Surgery). Well designed prospective long term studies in the assessment of different parameters of quality of life in patients following RAS (Robotic assisted surgery) is needed to assess the value of this technology. In conclusion, Robotic is the future and here to stay.

Mouth Breathing – Health Hazards: Role In OSA, GERD, COPD

Sheo Kumar Prasad
Patna Medical college & Hospital.

Nasal blockage is common with presence of adenoids, excessively hertrophied tonsils, high arched palate, elongated narrow face, hypertrophied turbinates, deviated nasal septum, nasal polypi, recurrent rhino sinusitis, nasal tumours etc. besides contributing to crowding of teeth, otitis media, sinusitis, snoring-sleep apnea, SIDS, this may in longterm lead to pulmonary diseases.

Mouth breathing from infancy through adolescence to adult life is quite common. Most of the time, mouth breathing is not taken seriously both by sufferer as well as by clinicians. Mouth breather swallows lot of dry air, bypassing nose & sinuses. Eventually bloating of stomach will push against esophageal sphincter leading to acid reflux. If not detected & treated early, continuous assault of stomach contents on pharyngeal lining will cause loss of its elasticity with increased chances to cause it to collapse. Aspiration of foreign particles & fluid into lungs, as happen in GERD is likely to explain the loss of elasticity in lungs as found in COPD.

With advanced tools in hand like LASER, Fibre optic rigid & flexible endoscopes, sophisticated power micro debriders, those cause of nasal blockage not relived by medical treatment, can be managed well by surgery, improving airway. The presentation entails relevant details.

Probiotics – A Preventive Measure Against Ventilator Associated Pneumonia

Avneet Soodan, Varsha A Singh
M M Institute of Medical Sciences & Research.

Probotic bacteria are live microorganisms which when administered in adequate amount confer a health benefit on the host. They are perceived to exert such effects by changing the composition of the gut micro biota. Several probiotic preparations seem to have promise in prevention or treatment of various conditions. Ventilator associated pneumonia (VAP), a life-threatening complication the course of incubated and mechanically ventilated critically ill patients. Probiotics reduces the incidence of VAP via a combination of local and systemic effects resulting in decreased colonization. Administration of probiotics is not expected to eradicate the pathogenic bacteria as antibiotics would do, but delaying the time to colonization while the patients are intubated. In Ventilator-associated pneumonia patients, the normal flora disappears and is replaced by an overgrowth of potential pathogenic microorganisms which is further followed by aspiration of pathogenic microorganisms (Staphylococcus aureus, Pseudomonas aeruginosa and Enterobacteriaceae) which could finally result in VAP. Prevention of colonization of the upper and/or lower digestive tract is a approach for the prevention of VAP.

Advanced Technology Radiation Therapy

T. Pratap Reddy
KIMS, SEC-BAD

The goal of radiation treatment has always been to destroy the cancer without harming normal structures and cells. Normal structure tolerance is the greatest limitation of successful treatment.

Advanced Technology Radiation is the most dramatic advance in the past 10 years of clinical oncology. It gives better results of treatment, involves accurate delivery of effective radiation to produce cancer control. It limits the side effects and complications associated with less sophisticated methods of radiation and the ability to perform salvage treatment for recurrence in a much safer manner than previously. There are several methods of Advanced technology Radiation like IMRT, Rapid Arc, SRS, SRT, SBRT, Adaptive radiation treatments. The more advanced the technique, the better result of treatment.

Advanced Technology radiation paves the way to precise treatment delivery.

The application of a radiation plan must for verification of each treatment to assure proper targeting over the entire course of therapy. The ability to reliably reproduce the planned treatment is a mandatory function of any radiation delivery system. The application of advanced imaging to radiation therapy planning and delivery has made these advances possible.

Not only is the main goal of tumor eradication closer than it has ever been before, but treatment without side effects and complications has opened new doors for victims of cancer.

GUIDELINES FOR AUTHORS

The Journal of the International Medical Sciences Academy (JIMSA) is published quarterly on behalf of the International Medical Sciences Academy in the last week of January, April, July and October.

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The authors should provide a written undertaking signed by the senior author / authors that article submitted has neither been published elsewhere nor sent for publication at the time of submission.

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The manuscript of the article should be submitted in triplicate, typed in double space on standard A-4 size with 3 cm margin all around and should be sent to the **Editor JIMSA, 2nd Floor, National Medical Library Building, Ansari Nagar, Ring Road, New Delhi -110029 India.** Update/Review article, Original article should not exceed 10-12 typewritten pages; case report, brief communication, procedure, current drug therapy-6 pages. The article should be preceded by an **abstract** not exceeding 350 words; keywords, where ever relevant, should be given below the abstract. The original manuscript should be arranged in the following sequence: title page with address for correspondence, abstract, introduction, material and methods, results (or case report) discussion, table, legends to figures.

CD with complete write up as given above including figures and legends, must accompany the article.

References

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Fulphus SW, characterization, isolation and purifications at chollnergicreceptors in motor Innervations of muscle: edited by Sloff S, Academic Press London 1976; page 1-26.

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