

**Medical Research Society of Pakistan
(2003-2006)**

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University of Connecticut
United States of America

General Secretary

Dr. Faisal Sultan
Shaukat Khanum Memorial Cancer Hospital & Research Centre,
Lahore

MRSP 2006
November 18, 2006

Ayub Medical College
Abbottabad, Pakistan

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Message

I am extremely pleased to welcome everyone to the Seventeenth Annual Meeting of the Medical Research Society of Pakistan. The object of the Medical Research Society is to promote medical research in Pakistan. This cannot happen without recognising and supporting existing and potential research workers. This Society is unique in that it includes members from within Pakistan and abroad, and at each meeting welcomes new members.

One of the most important activities of this Society is this annual meeting where new research is presented, ideas are discussed, collaborations formed and worthwhile research activity recognised. Most important, it serves to stimulate younger doctors and basic scientists to involve themselves in research.

I hope that you will all enjoy this meeting and, most important of all, will be stimulated to involve yourselves in medical research - there are few things in life more satisfying than contributing to the fund of knowledge which may alleviate human disease.

Professor Nausherwan Khan Burki
Chairman
Medical Research Society of Pakistan
195 Farmington Avenue
Suite, # 201
Farmington, CT 06032
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PROGRAMME

- 09.00 – 09.30 Registration**
09.30 – 09.35 Talawat
09.35 – 09.45 Introduction of the Society by Prof. N. Burki Chair, MRSP
09.45 – 10.00 Vote of thanks by Prof. M. Ayub, Chair Local Organising Committee
10.00 – 10.20 Chief Guest
10.20 – 11.00 Tea/Poster Session

Scientific Session-I

Chairperson: Prof N. Burki

Co-Chairperson: Prof Ayub

- 11.00 – 11.30 *Invited Lecture I – “Advances in Malaria Diagnostics”.***
Dr M. Asim Beg, Associate Professor and Consultant Parasitologist
Department of Pathology & Microbiology FHS Aga Khan University
- 11.30 - 11.45 FREQUENCY OF DEPRESSION DUE TO STRESS IN FEMALE NURSES
Maqsood A, Najeeb H, Khalid M, Rasool H, Sheikh S, Abdul Razzak S and Riaz S. Karachi
Medical & Dental College.
- 11.45 - 12.00 APPENDICITIS IN PREGNANCY: EXPERIENCE OF 38 PATIENTS DIAGNOSED AND
MANAGED AT A TERTIARY CARE HOSPITAL IN KARACHI.
Syed Faraz Kazim, Inam Pal, Department of Surgery, The Aga Khan University, Karachi
- 12.00 – 12.15 RELATIONSHIP OF HCV HEPTOCELLULAR CARCINOMA AND CIRRHOSIS OF
LIVER. Asghar AS. Frontier Medical College, Abbottabad
- 12.15 – 12.45 *Invited Lecture II - “Research Ethics: Historical Context and Perspectives from Pakistan”.***
Dr. Aamir Jafarey Assistant Professor Centre of Biomedical Ethics and Culture, SIUT
Pakistan
- 12.45 – 13.00 TUMOUR THICKNESS AS A PREDICTOR OF NECK NODE METASTASIS AT
PRESENTATION IN EARLY T STAGE ORAL TONGUE CANCER
M.Bilal, R. Hussain, M A Shah, S Hameed and A Jamshed, Department of Radiation
Oncology & Department of Surgery Shaukat Khanum Memorial Cancer Hospital and
Research Centre, Lahore, Pakistan.
- 13.00 – 13.15 PREOPERATIVE MULTIMODALITY THERAPY FOR RECTAL CANCER IN
PAKISTAN
A. Rasheed, Aamer Ali Syed, M A Shah, S Hameed and A Jamshed, Department of Radiation
Oncology & Department of Surgery, Shaukat Khanum Memorial Cancer Hospital and
Research Centre (SKMCH & RC), Lahore, Pakistan.
- 13.15 – 14.15 Lunch, Prayer Break & Poster Session**

Scientific Session-II

Chairperson: Dr Faisal Sultan

Co-Chairperson: Prof. Kamran Aziz

- 14.15 – 14.40 ***Invited Lecture III- “Prevalence, Spectra and Founder Effects of BRCA1 and BRCA2
Mutations in Pakistani Breast and Ovarian Cancer Families”***
Dr Muhammad U. Rashid, Shaukat Khanum Memorial Cancer Hospital and Research Center.
- 14.40 – 14.55 MUTATIONS IN BRCA1 GENE AND THEIR RELEVANCE IN BREAST CANCER.
Aban M, Moatter T. The Aga Khan University Karachi
- 14.55 - 15.10 POLYMORPHISMS IN PARAOXONASE GENE CLUSTER AND CORONARY HEART
DISEASE IN PAKISTAN.
M.P. Iqbal, M. Saeed, F. A. Yousuf, M. Shafiq, S. Parveen, PM Frossard.
Department of Biological and Biomedical Sciences, Agha Khan University.
- 15.10 – 15.25 HEMATOLOGIC, CYTOGENETIC AND MOLECULAR RESPONSE TO
IMATINIB MESYLATE IN CHRONIC MYELOGENOUS LEUKEMIA.

- Siddiqui N, Zaigham & Anjum, FA. Shaukat Khanum Memorial Cancer Hospital and Research Center.
- 15.25 – 15.40 A STUDY OF IMMUNOLOGICAL MARKERS IN FIRST-DEGREE RELATIVES OF DIABETES MELLITUS PATIENTS
Tayyib M, Allah Ditta. Post Graduate Medical Institute, Lahore
- 15.40 – 15.55 ROLE OF ANTI VASCULAR ENDOTHELIAL GROWTH FACTOR ANTIBODIES IN TREATMENT OF RETINAL DIABETIC RETINOPATHY.
SA Haider, Shaukat Ali, Qasim Lateef, Khalid Najmi. Post Graduate Medical Institute, Lahore.
- 15.55 – 16.10 DETERMINATION OF INTEGRITY AND QUALITY OF DNA ISOLATED FROM PARAFFIN EMBEDDED TISSUE USING A MULTIPLEX PCR FOR THE HUMAN β -GLOBIN GENE.
Anwar N, Saeed M, Tahseen M, Mansoor S, Yusuf MA. Basic Sciences Research, Shaukat Khanum Memorial Cancer Hospital & Research Center
- 16.10 – 16.40 Poster Discussion
- 16.40 – 16.45 Concluding Remarks by Prof. Burki - announcement for award for best oral and poster presentations.
- 16.45 – 17.30 GBM (Members only)**

POSTER PRESENTATIONS

1. CAUSES OF INITIATION AND PROMOTION OF CANNABIS AMONG LOCAL TRANSPORT DRIVERS IN PESHAWAR. Hamzullah Khan, Mir Hassan Khan. Khyber Medical College, Peshawar
2. HIV/AIDS: EXPERIENCE AT TWO TERTIARY CARE HOSPITALS OF PESHAWAR. Hamzullah Khan, Nadim Jan, Miraj Muhammad Khan Khattak. Khyber Medical College, Peshawar & Hayatabad medical complex, Peshawar,
3. COMPARTMENT SYNDROME, AN UNUSUAL PRESENTATION. K Aziz, M A U Haq, N Yousaf. Pilgrim Hospital Boston UK.
4. USE OF HALOTHANE FOR ACUTE EXCEREBATION OF ASTHMA IN INTENSIVE CARE UNIT. Faraz Shafiq*. Department of Anaesthesia, Aga Khan University Hospital.
5. CASE OF A 65 YEARS MALE WITH ANEMIA. A. Azhar, K. Ehsan. Shaukat Khanum Memorial Cancer Hospital & Research Centre.
6. IMPACT OF OVERALL RADIOTHERAPY TREATMENT TIME ON LOCAL CONTROL AFTER CONCURRENT CHEMORADIATION (CRT) FOR T3/4 GLOTTIC CARCINOMA. M Fareed, R Hussain, M A Shah, S Hameed and A Jamshed. Department of Radiation Oncology & Department of Surgery. Shaukat Khanum Memorial Cancer Hospital and Research Centre, Lahore, Pakistan
7. PATHOLOGICAL PATTERNS OF CERVICAL LYMPH NODE METASTASIS AT PRESENTATION IN EARLY (T1 –T2) ORAL TONGUE CANCER. S Magsood, R. Hussain, M A Shah, S Hameed and A Jamshed. Department of Medical Oncology, Department of Surgery & Department of Radiation Oncology. Shaukat Khanum Memorial Cancer Hospital and Research Centre, Lahore, Pakistan.
8. CORRELATION OF PREOPERATIVE CLINICAL STAGE WITH PATHOLOGICAL FINDINGS IN CARCINOMA ORAL TONGUE. Mutahar Ali, R Hussain, M A Shah, S Hameed and A Jamshed. Department of Radiation Oncology & Department of Surgery. Shaukat Khanum Memorial Cancer Hospital and Research Centre, Lahore, Pakistan.
9. INDUCTION COMBINATION CHEMOTHERAPY WITH GEMCITABINE AND CISPLATIN IN LOCALLY ADVANCED HEAD AND NECK CANCER. K. Shahzad, R. Hussain, M A Shah, S Hameed and A Jamshed. Department of Radiation Oncology & Department of Surgery. Shaukat Khanum Memorial Cancer Hospital and Research Centre, Lahore, Pakistan.
10. EFFECTS OF NOISE ON RICKSHAW DRIVERS OF KARACHI. Fatima Abbasi, Humera Khan, Ayesha Ahmad, Javeria Zaheer, Saana Saifuddin, Rahda Mahmood. KARACHI MEDICAL AND DENTAL COLLEGE
11. MOLECULAR EPIDEMIOLOGY OF HEPATITIS C VIRUS (HCV) IN PUNJAB. Nousheen Iram, Mohsan Saeed, Kiran Khawaja, Saira Saleem, Fatima Khwaja and Natasha Anwar. Basic Sciences Research, Shaukat Khanum Memorial Cancer Hospital and Research Centre, Lahore.
12. DURATION OF LACTATIONAL AMENORRHEA: A SURVEY CONDUCTED AT AYUB TEACHING HOSPITAL ABBOTTABAD. Aqeel Subhani, Department of Physiology, Ayub Medical College, Abbottabad
13. CERVICAL CARCINOMA IN A TERTIARY CARE SETTING. Farhana Badar, Natasha Anwar, Fouzia Meerza, Faisal Sultan. Shaukat Khanum Memorial Cancer Hospital and Research Center, Lahore, Pakistan.
14. CARCINOGENISITY OF HEAVY METALS – PRESENTATION OF A MODEL YEAST BIOREACTOR TO CLEAN UP OUR WATER RESOURCES OF METAL CARCINOGENS. Farooq H, Department of Pathology, Shaukat Khanum Cancer Hospital & Research Centre
15. TO IDENTIFY BYSSINOSIS REPORTED BY COTTON SPINNING MILL WORKERS. Mohammed Irfan, Bushra Khan, Erum Aziz, Mehreen Moosa, Mohammed Raheel, Santosh Kumar. Karachi Medical and Dental College.
16. HAZARDOUS EFFECTS OF NOISE POLLUTION ON THE HEALTH OF TRAFFIC POLICE PERSONNEL. S. Qadeer, T. Feroz, S. Rashid, F. Siddiqui, M.A Usmani, M. A Adnan. Karachi Medical and Dental College.
17. ANTIMALARIAL ACTIVITY OF TRADITIONAL MEDICINAL PLANTS INVITRO. S I Khokher. Institute of Biochemistry and Biotechnology. University of Punjab.

18. FREQUENCY OF MUSCULOSKELETAL DISORDERS IN RAILWAY STATION PORTERS. Aasma Saleem, Aniq Jabeen, Kiran Wahab, Mahwish Naim, Sadaf Hussain, Saiqa Majeed, Shaiwah Zain, Sheeza Imtiaz. KARACHI MEDICAL AND DENTAL COLLEGE.
19. ON THE ROAD TO AN ESOPHAGEAL CANCER VACCINE. C.M.Shahbaz Sarwar, MD. Tomoharu Miyashita, MD PhD. John William, MD. Johns Hopkins University.
20. THE VALUE OF BONE MARROW BIOPSY IN INITIAL STAGING OF NEWLY DIAGNOSED HODGKIN'S LYMPHOMA PATIENTS. N Siddiqui, A Sattar, F Badar, F.A Anjum. Shaukat Khanum Memorial Cancer Hospital and Research Center, Lahore.

KEYNOTE LECTURES

Lecture 1
Advances in Malaria Diagnostics

Dr M. Asim Beg
Associate Professor and Consultant Parasitologist
Department of Pathology & Microbiology FHS
Aga Khan University

Recent advances in technology have had an impact on diagnostic parasitology both in hospital practice and in the field.

Empirical diagnosis of malaria made in areas without laboratory facilities leads to error in the diagnosis and treatment of malaria. Rapid diagnostic tests (RDTs) provide sensitive and specific diagnosis of *Plasmodium falciparum* and mixed malaria infections. RDTs have been a useful addition in our laboratory in support of microscopy.

Molecular diagnostic tools have dramatically changed the laboratory diagnosis of malaria and with leishmaniasis; polymerase chain reaction (PCR) is now the gold standard test and offers greater accuracy in diagnosis. However, microscopy remains fundamental to diagnostic parasitology and using trained technologists is still cost effective in a modern hospital laboratory.

Lecture 2
Research Ethics: Historical Context and Perspectives from Pakistan

Dr. Aamir Jafarey
Assistant Professor
Centre of Biomedical Ethics and Culture, SIUT Pakistan

The Nuremberg Tribunals are seen as the turning point for research ethics regulation in modern times. Out of these tribunals emerges the Nuremberg Code in the Post World War II era followed by the Declaration of Helsinki in 1964. Other codes and guidelines, national and international have been formulated since then, and existing ones have undergone major revisions to keep them current. Institutional Review Boards (IRB's, also termed Ethical Review Committees) emerged on the scene in the early 1970's in the US and then gradually spread across the world as committees entrusted to ensure the protection of the rights of the research participants. The seminal events that helped shape contemporary research ethics as the world knows it today will be discussed.

The ethical review process in Pakistan remains rather patchy and underdeveloped. This is because there is a dearth of capacity in bioethics in general and research ethics in particular in the country. Up till very recently, there were no opportunities anywhere in the country to acquire comprehensive training in bioethics except for sporadic workshops taking place primarily in Karachi. However, a countrywide survey of 68 medical institutions conducted in 2004 surprisingly revealed 65% claiming to have such committees. One can only speculate on the quality of review taking place by these committees. There is a nationwide need for institutions to enhance their capacity in bioethics and there are several ways in which institutions can further improve and enhance their IRB's.

The review process is not infallible. Even in developed countries where the process is well established for several decades now, serious ethical breaches do come to light periodically. A brief example of research being hijacked from our very midst, highlighting how easily our ethical review system can fall prey to derailing influences will be discussed. We also need to strengthen the process of safeguarding the research community's rights.

Lecture 3

Prevalence, Spectra and Founder Effects of *BRCA1* and *BRCA2* Mutations in Pakistani Breast and Ovarian Cancer Families

Dr Muhammad U. Rashid,
Shaukat Khanum Memorial Cancer Hospital and Research Center, Lahore, Pakistan

Excluding Jews in Israel, Pakistan has the highest rate of breast cancer and the highest rate of ovarian cancer in Asia. Since little is known about the contribution of the *BRCA1* and *BRCA2* genes to hereditary breast and/or ovarian cancer in this population, we performed the first comprehensive mutation analysis of both genes in 176 breast and/or ovarian cancer patients, selected on family history and on age of diagnosis. Comprehensive *BRCA* mutation screening was done using combined denaturing high-performance liquid chromatography (DHPLC), single strand conformational polymorphism (SSCP), protein truncation test (PTT) and DNA sequencing analysis.

Thirty deleterious germline mutations were identified in 176 families (30/176, 17.0%; 95% CI 12.2%-23.3%), including 23 in *BRCA1* (23/30, 76.6%; 95% CI 59.1%-88.2%) and seven in *BRCA2* (7/30, 23.3%; 95% CI 11.8%-40.9%). Thirty-three percent of mutations in *BRCA1* and 71% in *BRCA2* were unique to Pakistan. Four mutations, 185delAG, 185insA, S1503X and R1835X, were recurrent accounting for 52% of all *BRCA1* mutations. Haplotype analyses suggested founder effects for three of these. The prevalence of *BRCA1* or *BRCA2* mutations was 42.8% in families with multiple cases of breast cancer, 50.0% in families with breast and ovarian cancer; 11.9 % in families with one breast cancer case (≤ 30 yr) and 9.0% in families with one ovarian cancer case (≤ 45 yr).

Our findings show that *BRCA1* and *BRCA2* are implicated in a substantial fraction of Pakistani breast/ovarian cancer families. Further, they provide evidence for other predisposing gene(s) contributing to breast and ovarian cancer development. The presence of founder and recurrent mutations in *BRCA1* may facilitate carrier detection in Pakistani breast and/or ovarian cancer families.

ORAL PRESENTATIONS

FREQUENCY OF DEPRESSION DUE TO STRESS IN FEMALE NURSES

Aafia Magsood, Hiya Najeeb, Mahvish Khalid, Humaira Rasool, Salma Sheikh, Sabeen Abdul Razzak, Sumera Riaz

Karachi Medical and Dental College

Objectives/Aims:

Nurses are an integral component of the health care delivery system. Depression among nurses affects the quality of health care. Stress and depression are the most important factors influencing individual efficacy and satisfaction in a modern day occupational setting. The objectives of the following study were to:

- To determine the level of stress and depression in female nurses.
- List problems encountered by nurses in relation to their job.
- Recommend possible solutions and strategies to deal with the problem of job related stress.

Methods:

A cross-sectional study was conducted at ABBASI SHAHEED HOSPITAL. Seventy nurses who fulfilled the inclusion /exclusion criteria were recruited in the study. Depression was assessed with the help of the Hamilton Rating scale .The data was entered and analyzed by Statistical Package for Social Sciences SPSS (version 11.0)

Results:

The frequency of depression was as follows; 30% showed mild symptoms of depression, 42.9% mild-moderate, 8.6% moderate-severe and 18.6% had no symptom of depression. Work experience and age was significantly associated with anxiety and depression (P value < 0.01). The major problems faced by the nurses were, poor environment (27.1%), workload (21.4%), abusive behavior (15.7%), transport problem (14.3%) and occupational hazard (12.9%). The majority of the nurses enrolled in the study suggested improving the working environment of the hospital.

Conclusion:

The presence of depression among nurses is high. Prolonged exposure to such depression, without correct coping strategies, may emerge as a potential risk factor for other diseases. Immediate steps should be taken for their control and management. This study invites further research to explore, implement and evaluate intervention strategies for prevention of depression in nurses as well as other healthcare workers.

APPENDICITIS IN PREGNANCY: EXPERIENCE OF 38 PATIENTS DIAGNOSED AND MANAGED AT A TERTIARY CARE HOSPITAL IN KARACHI.

Syed Faraz Kazim, Inam Pal

The Aga Khan University College, Karachi.

Objectives/Aims:

The purpose of this study was to evaluate the incidence, clinical presentation, diagnosis, management, and outcome of acute appendicitis in pregnant patients.

Methods:

A retrospective review of records from patients who presented with acute appendicitis during pregnancy at Aga Khan University Hospital (AKUH), Karachi from January 01, 1990 to July 31, 2006 was conducted.

Results:

Between January 1990 and July 2006, there were 43,134 deliveries at AKUH and the incidence of acute appendicitis was 0.08% (38 cases). Appendectomy was performed in 37 (97.4%) cases. Ultrasound abdomen confirmed the diagnosis in 15(39.5%) cases. Thirty-six (97.4%) patients had pathologically proven appendicitis. Gestational age at diagnosis was first trimester in 11, second trimester in 14, and third trimester in 13 patients. Abdominal pain and tenderness were observed in almost every patient, with right lower quadrant being the most common location, irrespective of the gestational age. Rebound tenderness and vomiting were other common presenting signs and symptoms. Leukocytosis was found to be reliable a laboratory parameter for diagnosis of appendicitis in pregnancy. A perforated appendix was identified in 6 (15.8%) cases. Non effect of tocolytic agents could be demonstrated. Six patients (15.8%) developed post operative complications. Preterm contractions developed in 5 (13.2%) patients and 3 (7.9%) patients had preterm delivery. There was no maternal mortality; however 2.63% (1 case) fetal mortality was noted.

Conclusion:

Diagnosis of acute appendicitis in pregnancy is difficult. Any delay in diagnosis and surgical intervention results in an increase in complication rates. Urgent surgery should be done when appendicitis is suspected in a pregnant patient.

RELATIONSHIP OF HCV HEPATOCELLULAR CARCINOMA AND CIRRHOSIS OF LIVER

Prof. Abdul Shaheed Asghar

Frontier Medical College Abbottabad

Objectives/ Aims:

The aim of the following study was early HCV detection for prompt management of hepatocellular carcinoma and cirrhosis of liver, with the objective to determine the prevalence of anti- HCV antibody and HCV RNA in patients with hepatocellular carcinoma with cirrhosis of liver.

Methods:

Sera from biopsy proven patients of hepatocellular carcinoma (n=75) and from clinically healthy subjects (n=20) were collected. The subjects included had no history of autoimmune disease and all are rheumatoid (RA) factor negative. All samples were analyzed for alanine transaminase (ALT) levels, anti-HCV and HCV-RNA. Ultrasonography was also performed to determine current liver status.

Results:

Mean ALT level was 74.38 ± 8.54 IU/L in hepatocellular carcinoma patients and 17.59 ± 1.07 IU/L in healthy subjects. Overall prevalence of HCV was 45.33% (34 of 75) in hepatocellular carcinoma patients. Among these, seven (9.33%) were anti- HCV reactive, 13 (17.33%) were HCV- RNA positive and 14 (18.66%) were having both anti- HCV and HCV- RNA. Among 34 hepatocellular carcinoma patients; 25 (73.52%) patients also had histological features of cirrhosis of liver. In healthy subjects no case was found to have anti-HCV antibodies or and HCV- RNA.

Conclusion:

HCV infections often progress to chronic carrier state and liver cirrhosis, which can be considered as a precancerous condition (hepatocellular carcinoma). It is suggested to adopt all necessary measures for prevention and spread of HCV infection.

TUMOUR THICKNESS AS A PREDICTOR OF NECK NODE METASTASIS AT PRESENTATION IN EARLY T STAGE ORAL TONGUE CANCER

M.Bilal, R. Hussain, M A Shah, S Hameed and A Jamshed

Department of Radiation Oncology and Department of Surgery

Shaukat Khanum Memorial Cancer Hospital and Research Centre, Lahore, Pakistan

Objectives/ Aims:

Twenty to thirty percent of patients with oral tongue carcinoma have occult neck nodal metastasis at presentation. Elective treatment of neck in early T stage tongue cancer is controversial. This study was conducted to determine the risk of neck node metastasis in patients with T1 or T2 carcinoma tongue on the basis of pathological tumour thickness.

Methods:

The study group consisted of 20 patients with early T stage carcinoma oral tongue treated at Shaukat Khanum Memorial Hospital and Research Centre, between December 2003 and October 2005. All patients underwent partial glossectomy with modified neck dissection. Nine patients (45%) had pT1 and 11 patients (55%) had pT2 disease. Patients were divided in to three groups based on tumour thickness; Group I (tumor \leq 3 mm), Group II ($>$ 3 mm but \leq 9 mm) and Group III ($>$ 9 mm).

Results:

In patients with pT1 lesions there were 2, 3 and 4 patients in group I, II and III respectively. Pathological neck nodal metastasis were seen in 0/2 patients in group I, 1/3 patients in group II and 1/4 in group III. With pT2 lesions there were 0, 4 and 7 patients in group I, II and III respectively. Neck nodal metastasis were found in 3/4 and 3/7 in group II and III patients. The risk of neck node metastasis in patients with tumor thickness more than 3 mm was 28% (2/7 patients) for pT1 patients and 55% (6/11 patients) for patients with pT2 disease.

Conclusion:

Tumor thickness more than 3 mm in patients with early T stage squamous cell carcinoma oral tongue carries a high risk of neck nodal metastasis. Elective neck treatment should be considered for this group of patients.

PREOPERATIVE MULTIMODALITY THERAPY FOR RECTAL CANCER IN PAKISTAN

A. Rasheed, Aamer Ali Syed, M A Shah, S Hameed and A Jamshed

Department of Radiation Oncology Department of Surgery

Shaukat Khanum Memorial Cancer Hospital and Research Centre, Lahore, Pakistan

Objectives/Aims:

The efficacy of preoperative chemoradiation (CRT) in reducing local recurrence in rectal cancer has been demonstrated in randomized trials. The data on preoperative CRT in Asian population is limited. This study was performed to document the effect of preoperative CRT and recurrence among patients with locally advanced rectal cancer, treated in Pakistan

Methods:

Fifty three medical records of rectal cancer patients treated between January 2001 and December 2005 at SKMCH & RC were retrospectively analyzed. Pre treatment stage as assessed on MRI pelvis: cT2N+ 4%, cT3 83%, cT4 13%. The site of tumor within the rectum was upper 15%, middle 21% and lower 64%. Pelvic radiation therapy was 50.4Gy with 5FU as bolus IV injection during week 1 and 5 of radiation treatment. Total mesorectal excision was planned 6 to 8 weeks after completion of CRT. Pathological complete response (pCR) was defined as either no evidence of viable malignant cells in specimen or scattered isolated malignant cells without gross residual disease.

Results:

Post treatment tumor stages were ypT1-2 ypN0 in 24%, ypT3 ypN0 in 22%, ypT1-2 ypN+ in 6%, ypT3 ypN+ in 42% and unknown in 6% of cases. A PCR was evident in 18% (complete response 6%, microscopic foci 12%), pathological tumor regression $\geq 50\%$ regression occurred in 51% and $< 50\%$ regression or no response in 38%. To date 28% have recurred; isolated pelvic recurrence 8% and distant metastases 20%. The median overall survival was 3.17 years (95% CI: 2.74 – 3.60) with a 50% 5 year survival. The median disease free survival was 3.43 years (95% CI (1.67 – 5.18) with a 40% 5 year survival.

Conclusion:

Pathological response to preoperative 5FU based CRT and survival following total mesorectal excision in our population is similar to other reported series.

MUTATIONS IN BRCA1 GENE AND THEIR RELEVANCE IN BREAST CANCER

Muniba Aban, Tariq Moatter

The Aga Khan University Karachi

Objectives/Aims:

To identify BRCA1 mutations in breast cancer patients of familial origin and relate it to disease outcome.

Methods:

Fifty patients of breast cancer having positive family history of breast cancer were screened for germline mutations in BRCA1 gene. We analyzed BRCA1 exon 11 by the protein truncation test. It was amplified in three fragments using a modified primer containing T7 promoter sequence. SSCP was used for screening mutations in exons 2, 5, 6, 16, 20 and 22 of BRCA1 gene of patients amplified by PCR under optimized condition.

Results:

In this study, the most common breast cancer type identified was invasive ductal carcinoma. Out of 50 patients 3 patients were positive for mutations in exon11. Their sequences were conformed by automated DNA sequencing technique. In one patient a novel germline mutation T>G at position 1123 was detected by protein truncation test which was confirmed by DNA sequencing. Gel Mobility shift was observed in exon 6, 16, 20 and 22 of 6 patients using SSCP assay. All patients who showed sequence variation on SSCP were disease free on follow-up.

Conclusion:

In breast cancer patients' identification of mutations in BRCA1 gene would help in predicting disease progression whereas their family member will benefit from precautionary measures made possible by early screening. Moreover, mutation screening can be used to develop better diagnostic strategies, targeted therapies and management of patients and their families.

POLYMORPHISMS IN PARAOXONASE GENE CLUSTER AND CORONARY HEART DISEASE IN PAKISTAN

M.P. Iqbal, M. Saeed, F. A. Yousuf, M. Shafiq, S. Parveen, PM Frossard.

Department of Biological and Biomedical Sciences, Agha Khan University, Karachi

Objectives/Aims:

Paraoxonase gene family consist of three 3 genes, PON1, PON2 and PON3 located on long arm of chromosome 7. A number of case-control studies have shown associated between single nucleotide polymorphisms (SNPs) in PON genes and coronary heart disease (CHD). The objective of this study was to assess the combined contribution of six polymorphisms (Q192R, L55M, C – 108T, G – 909C, A148G, S311C) to the risk of CHD in a Pakistani population.

Methods:

A case-control study involving 211 myocardial infarction(MI) patients and 370 control subjects from the Armed Forces Institute of Cardiology, Rawalpindi and the Agha Khan University, Karachi was carried out to investigate the association of PON gene cluster polymorphisms with MI. Genotyping was performed by PCR-RELP based assays.

Results:

All genotype distribution of dimorphisms were in Hardy-Weinberg proportions in both patients and control groups. The Q192R, C-108T and A148G polymorphisms were found to be associated with MI in this sample population (Odds ratios-1.154 for QQ vs QR + RR, 1.72 for CC vs CT + TT and 1.69 for AA vs AG + GG, respectively).

Conclusion:

These results point towards the important role PON genes appear to playing in the development of CHD in the Pakistani population.

HEMATOLOGIC, CYTOGENETIC AND MOLECULAR RESPONSE TO IMATINIB MESYLATE IN CHRONIC MYELOGENOUS LEUKEMIA

N. Siddiqui , Zaigham , F. A. Anjum

Shaukat Khanum Memorial Cancer Hospital & Research Center

Objectives/Aims:

Chronic Myelogenous leukemia (CML) is caused by the BCR-ABL tyrosine kinase, the product of the Philadelphia chromosome. Imatinib Mesylate, is a selective inhibitor of this tyrosine kinase. We studied the efficacy of Imatinib in patients with CML. The primary end points were complete hematological (CHR), cytogenetic (CCR) & molecular response (MR), with secondary end points of time to average response (ATR) and duration of response.

Methods:

Retrospective data of all registered CML patients (total: 163) from 2001 to 2005 treated at Shaukat Khanum Memorial Cancer Hospital & Research Center (SKMH & RC) with oral Imatinib, was collected and analyzed. Patients were evaluated for hematological, cytogenetic and molecular response. The ATR & duration of response was also recorded.

Results:

In patients with Chronic phase CML, Imatinib produced CHR in 95% patients, CCR in 41% patients and MR in 17% patients. Average time to response was 29 days, 10.5 months & 15.5 months respectively. In accelerated phase 87% CHR (ATR 61 days), 15% CCR (ATR 9.3 months) and 4. 5% MR (TR 13 months) were observed. None of the patients with blast phase achieved a cytogenetic or molecular response.

Conclusion:

Imatinib induces early and high rates of hematological and cytogenetics responses in patients with chronic phase CML with decrease in likelihood of progression to accelerated phase & blast crisis.

A STUDY OF IMMUNOLOGICAL MARKERS IN FIRST-DEGREE RELATIVES OF DIABETES MELLITUS PATIENTS

Prof. Muhammad Tayyib, Dr. Allah Ditta

Post Graduate Medical Institute, Lahore

Objectives/Aims:

To detect serum islet cell (ICA), glutamic-acid decarboxylase (GAD) and insulin autoantibodies (IAA) in first degree relatives of patients with type-I diabetes mellitus (DM)

Methods:

Fifty first degree asymptomatic relatives of patients with type-I DM were selected from Diabetic Clinic, Mayo Hospital, Lahore. Both male and female subjects aged upto 21 years were included. The sera from subjects were tested for ICA, GAD and IAA using the commercially available kits based on ELISA technique.

Results:

The results of serum ICA were inclusive. The serum GAD and IAA were found to be positive in 28 (56%) and 23 (46%) first degree relatives of DM patients.

Conclusion:

Detection of immunological markers (ICA, GAD & IAA) are clinically useful for early detection of subject supposed to be future candidate of diabetes mellitus.

ROLE OF ANTI VASCULAR ENDOTHELIAL GROWTH FACTOR ANTIBODIES IN TREATMENT OF RETINAL DIABETIC RETINOPATHY.

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Post Graduate Medical Institute, Lahore.

Objectives/Aims:

Retinopathy due to diabetes mellitus consists of both vasoproliferation and vascular permeability. Current treatment by laser photocoagulation aims to reduce oxygen demand by ablation of ischemic retina. It fails often in cases of severe retinopathy. We aimed to find out whether adjunctive treatment with an anti-vascular endothelial agent (Behvacizumab) would be helpful in inhibiting neovascularisation and reducing vascular permeability.

Methods:

Patients with proliferative diabetic retinopathy or macular oedema were given a single injection of 1.25 mg of intravitreal Avastin either in conjunction with laser photocoagulation or after maximum laser photocoagulation.

Results:

Vitreous haemorrhage resolved and neo-vascularisation regressed in almost all patients. Macular oedema regressed more slowly.

Conclusion:

In patients with severe diabetic retinopathy, intravitreal Behvacizumab (Avastin) is a very useful adjunct to conventional treatment.

DETERMINATION OF INTEGRITY AND QUALITY OF DNA ISOLATED FROM PARAFFIN EMBEDDED TISSUE USING A MULTIPLEX PCR FOR THE HUMAN B-GLOBIN GENE.

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Basic Sciences Research Department, Shaukat Khanum Memorial Cancer Hospital & Research Center (SKMCH & RC).

Objectives/Aims:

Development and optimization of a rapid method to screen for the integrity and quality of DNA isolated from paraffin embedded tissue.

Introduction:

Conditions of fixation (time, temperature and fixative) are quite variable for many biopsies. The fixation of tissue samples in formaldehyde leads to extensive cross-linking of all tissue components. As a consequence of this cross-linking, the nucleic acids isolated from these specimens are highly fragmented. The extent of fragmentation (the average fragment size) depends on the tissue type and the condition of fixation. The human β -globin gene has been used extensively to determine the integrity and quality of DNA isolated from formalin fixed paraffin embedded tissue specimens. However several reactions with individual primer pairs are required to screen extracted DNA, utilizing considerable amount of DNA and reagents. In order to minimize the amount of DNA used and to reduce costs, a multiplex PCR was developed to determine the integrity of DNA in a single reaction.

Methods:

Sixty-eight esophageal cancer tissue samples, collected over a period of seven years (1997-2003) were screened. DNA was extracted from tissue sections and used as a template for the amplification of human β -globin DNA fragments that ranged from 110-599bp in length. Optimal conditions including primer and $MgCl_2$ concentrations were determined for each primer pair in individual reactions and as constituents of a multiplex PCR. Amplicons were analyzed on 1% agarose gels and visualized by ethidium bromide staining.

Results: The multiplex PCR yielded 4 fragments of different lengths. The 110 bp fragment could not be amplified in 4 DNA samples, whereas the 410bp fragment was amplified in 69% of the samples and only 50% of the samples were positive for the 599bp fragment. The effect of age of the tissue samples, on the extent of DNA fragmentation was reviewed. Fragmentation of DNA appeared to increase over time. Forty percent of the samples from 2000-2003 amplified a 536bp fragment whereas only 19% of the samples from 1997-1998 were positive. Similarly, 50% of the tissue samples from 1999-2000 were positive for a 410bp fragment, this increased to 75% when samples from 2001-2003 were analyzed.

Conclusion:

A multiplex PCR enabled the rapid determination of DNA integrity in a single reaction. DNA isolated from paraffin embedded esophageal cancer tissue samples analyzed in this study contained fragmented DNA. The majority of the samples had an average fragment length of around 400bp. A greater degree of fragmentation was observed in older tissue samples, this information will aid the future selection of tissue samples for molecular studies.

POSTER PRESENTATIONS

CAUSES OF INITIATION AND PROMOTION OF CANNABIS AMONG LOCAL TRANSPORT DRIVERS IN PESHAWAR

Hamzullah Khan, Mir Hassan Khan

Khyber Medical College, Peshawar, PMRC, KMC, Peshawar .

Objectives/Aims:

To determine the causes of initiation and promotion of cannabis smoking among local transport drivers of Peshawar.

Methods:

A descriptive observational study was conducted in a main wagon and bus stop in the city; Haji camp bus stop and roadway Hashtangri, from October 2004 to September 2005. Relevant information's were recorded from the respondents on a pre-designed questionnaire.

Results:

A total of 400 smoker drivers were included. Of these, 181(45.25%) were cannabis smokers. The age range of the cannabis smokers was from 16 years to 65 years of age with a mean age of 35.5 years. The distribution of smoking habits recorded was: cigarette smoking alone 19%, snuffing 23%, cannabis smoking 42.25%, heroin and cannabis smoking 3% etc. Out of total cannabis smokers 43% were illiterate. The exposure state of the respondents was: to compensate fatigue 39.21%, inspiration from friends 31.49%, parents were smokers 11.6%, pleasure to smoke 8.83% etc. Ninety percent were agree that cannabis is easily available to them. Fifty seven percent had poor social background. Thirty four percent had faced road accidents. The effect of cannabis on respondents was: lack of interest 36.46%, decreased memory 19%, depression 16%, sedation 5.52% etc. Maximum number of the respondents (19.33%) wanted to quit cannabis smoking.

Conclusion:

The major causes that are involved in the initiation and progression of cannabis smoking are; driving in young age, poverty, lack of education, easy availability of cannabis, inspiration from colleagues and smoking parents.

HIV/AIDS: EXPERIENCE AT TWO TERTIARY CARE HOSPITALS OF PESHAWAR.

Hamzullah Khan, Nadim Jan, Miraj Muhammad Khan Khattak

Khyber Medical College, Ibn-e-sina foundation, Dermatology unit, Hayatabad Medical Complex, Peshawar, Pakistan

Objectives/Aims:

To determine the experience of physicians posted in two tertiary care hospitals of Peshawar, regarding HIV/AIDS.

Methods:

A descriptive observational survey was conducted at the Khyber Teaching Hospital (KHT) and Postgraduate Medical Institute Hayatabad Medical Complex Peshawar (PGMI, HMC) from 12th September to 21st December 2005. Relevant information's were recorded with the help of a pre-designed questionnaire prepared in accordance with the objectives of the study.

Results:

A total of 50 health staff including physicians, pathologists, gynecologists and dermatologists were selected. Only 2% of physicians were claiming themselves volunteers for management of HIV cases. Main referral center for treatment and diagnosis was National Institute of Health (NIH) for 72% of physicians. Of total, 74% of physicians had recorded only 0-5 cases during their carrier. No outreach counseling or advertising VCT recorded. Opportunistic infections recorded by physicians were: Tuberculosis (18%), Oral/esophageal candidiasis (14%), STIs (6%), Herpes simplex, CMV Infection & Pneumocystic cranii (4% each) and septicemia (2%). Malignancies recorded were: Kaposi's sarcoma (6%) and Non-Hodgkin's Lymphoma (2%).

Conclusion:

The knowledge and attitude of the medical staff was satisfactory, however the majority of physicians had recorded only few HIV/AIDS cases. There is need for more awareness through advertisement, workshops and seminars on HIV/AIDS.

COMPARTMENT SYNDROME, AN UNUSUAL PRESENTATION.

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Pilgrim Hospital Boston UK.

Objectives/Aims:

Compartment syndrome can present in atypical way.
Clinicians must not delay in its care.

Introduction:

38 years old, chronic alcoholic, presented to Accident and Emergency with abdominal pain and vomiting for the last 24 hours. At the same time, he complained of severe pain in the legs particularly worst in the left. There was no history of injury or trauma to the legs.

Methods:

Initially, he had routine bloods taken and on examination he had tenderness in both his legs and his leg pulses were absent bilaterally but were found on Doppler. His blood results showed renal failure. Patient was referred to the medical team. There was a delay of 8-10 hours in involving the orthopaedic team.

Results:

Finally, being assessed by the orthopedic team, patient went to theatre 13 hours following admission, for compartment syndrome. In theatre, he had confirmed compartment syndrome and muscle necrosis.

Conclusion:

Compartment syndrome is an orthopaedic emergency, and diagnosis should be made only on clinical grounds. The delay in the care could have been avoided by clinicians being more observant and aware of the diagnosis.

USE OF HALOTHANE FOR ACUTE EXCERBATION OF ASTHMA IN INTENSIVE CARE UNIT.

Dr. Faraz Shafiq, Hameed Ullah

Department of Anaesthesia, Aga Khan University Hospital Karachi, Pakistan.

We report a case of a middle-aged women, who presented to our intensive care unit (ICU) for the management of acute severe asthma (ASA) including ventilatory support. She was unresponsive to the conventional modalities used for the treatment of ASA, but responded very well to Halothane, an inhalational anaesthetic agent, with favorable outcome.

ON THE ROAD TO ESOPHAGEAL CANCER VACCINE.

C.M.Shahbaz Sarwar, Tomoharu Miyashita, John William,

Johns Hopkins University, Baltimore, Maryland.

Objectives/Aims:

Developing a successful whole cell cancer vaccine.

Methods:

We have established three adeno-squamous rat cancer cell lines from reflux induced esophageal cancers. These cell lines share molecular characteristics of human esophageal cancer cells including expression of the EGF receptor, and activation of the Sonic Hedgehog pathway. To use the cells to make a vaccine, we heightened their immunogenicity by transfecting the cells to express Granulocyte Macrophage Colony Stimulating Factor (GM-CSF). The cells (55 ng/24 hours/ 1×10^6 cells). We then radiated the cells with 50 GY to prevent propagation of the cells. To test the efficacy of the vaccine, we compared the growth of 1.5×10^7 cultured tumor cells injected 1-1 with matrigel into the subcutaneous tissue of the back of normal Sprague Dawley rats with vaccinated animals which were injected with radiated/GMCSF transfected cells one week prior to tumor implantation.

Results:

In the vaccinated animals the tumors either regressed or disappeared entirely while in the control group tumor growth was progressive

Conclusion:

We conclude that this esophageal cancer vaccine has the potential to inhibit the growth of subcutaneously implanted tumor cells in rats.

DURATION OF LACTATIONAL AMENORRHEA: A SURVEY CONDUCTED AT AYUB TEACHING HOSPITAL ABBOTTABAD.

Aqeel Subhani

Department of Physiology, Ayub Medical College, Abbottabad

Objectives/Aims:

To determine the duration of lactational amenorrhea in female population of Hazara Division, NWFP, Pakistan

Methods:

A survey was conducted at Ayub Teaching Hospital from June to August 2006. Female patients admitted and their attendants were selected at random and subjected to a questionnaire and interview to collect relevant data. The sampled females belonged to different districts of Hazara division.

Results:

Fifty-nine (59) mothers of parity 1–5 were included in the study. The mean duration of lactational amenorrhea for different pregnancies ranged from 16.92 ± 20.18 weeks to 22.59 ± 24.72 weeks. The frequency of breast feeding ranged from 2 to 12 months, with the mean weaning time ranging from 4.85 ± 1.50 to 5.10 ± 1.85 months.

Conclusion:

The coincidence of similar times of breast feeding, amenorrhea and weaning may indicate the role of lactation in maintaining postpartum amenorrhea.

EFFECTS OF NOISE ON RICKSHAW DRIVERS OF KARACHI

Fatima Abbasi, Humera Khan, Ayesha Ahmad, Javeria Zaheer, Saana Saifuddin, Rahda Mahmood
Karachi Medical and Dental College

Objectives/Aims:

Hearing loss is the most obvious threat posed by noise pollution. Road noise is a major contributor to perceived environmental noise. The objective of this study was to assess hearing loss in rickshaw drivers of Karachi due to rickshaw noise and to analyze the non-auditory effects of noise that is hypertension and mood changes.

Methods:

STUDY DESIGN: Descriptive study design, cross-sectional study.

SETTING: The study was conducted at Patel Paara, Karachi.

SUBJECTS: 51 rickshaw drivers who had been driving for at least past 5 years and were below 50yrs of age were selected. The mean age of rickshaw drivers was 35 years. Questionnaire was filled which was translated into Urdu. Blood pressure was recorded, tuning fork tests, and proper audiometry was performed on all study subjects.

Results:

Interviews of 51 rickshaw drivers were completed. All subjects were male. The following areas were investigated in some detail; sensorineural and conduction hearing loss, blood pressure, effect of duration of driving on hearing and tinnitus. Audiometry results clearly showed that hearing of most of the rickshaw drivers was affected. The hearing loss observed in most of the study subjects was sensorineural in type, although some of the subjects also showed conduction loss. Majority of the subjects were found to be hypertensive on examination.

Conclusion:

There was loss of hearing and tinnitus among rickshaw drivers that seems to be most probably a result of their noisy occupation. Noise was also found to be a risk factor for developing mild to moderate hypertension. Suggestion: Use of silencers by rickshaw drivers and proper legislation by the government can result in less hearing loss and less noise pollution in the environment.

FREQUENCY OF MUSCULOSKELETAL DISORDERS IN RAILWAY STATION PORTERS

Aasma Saleem, Aniq Jabeen, Kiran Wahab, Mahwish Naim, Sadaf Hussain, Saiqa Majeed, Shaiwah Zain, Sheeza Imtiaz.

Karachi Medical and Dental College

Objectives/Aims:

- To determine the frequency of musculoskeletal disorders (MSDs) in railway station porters.
- To determine association between various risk factors and MSDs in porters.

Methods:

Study design: Cross sectional comparative study.

Subjects and Setting: 100 Porters of Cantonment Railway Station in Karachi were interviewed and a questionnaire was filled.

Main outcome measures: Age, addiction, years in occupation, working hours, nature of work and number of trips made by the porters per day.

Results:

According to our research, 44 % of the railway station porters were diagnosed as MSD positive on the basis of negative family history of MSD and any accidental injury, positive history of pain and physical tests. An association was identified between MSD and various risk factors namely **addiction** (68.18% of the porters were found to be addicted to smoking, pan or niswar), **working hours** (70.45 % of the porters worked for more than 10 hours per day), **nature of work** (70.45% of porters generally pulled and lifted heavy loads), **number of trips** (75% of the porters took more than 10 trips per day), **years in occupation** (72.72% of the porters were in this occupation for more than 10 years).

Conclusion:

The study revealed that MSDs were prevalent among the railway station porters. Significant influence of risk factors on the porters was seen, addiction (p-value < 0.002), working hours (p-value < 0.002), nature of work(p-value < 0.003), number of trips(p-value < 0.001) , years in occupation(p-value < 0.001).

TO IDENTIFY BYSSINOSIS REPORTED BY COTTON SPINNING MILL WORKERS

Mohammed Irfan, Bushra Khan, Erum Aziz, Mehreen Moosa, Mohammed Raheel , Santosh Kumar
Karachi Medical and Dental College

Objectives/Aims:

The objective of this study was to identify Byssinosis in cotton spinning mill workers, to identify probable associations of disease with factors such as different work areas, safety gadget usage, and overtime and to ascertain proportions of byssinosis to accidental injuries.

Methods:

The study was conducted at a spinning mill conveniently selected in Karachi in June 2006. Mill workers who had worked for a minimum 5 years, were enrolled in the study. A sample size of 83 randomly selected workers participated in the research study. Data collection was done via 1) questionnaire 2) pulmonary function tests.

Results:

The mean age of the workers was 30 years \pm 7 years. Seventy-two percent of the workers used safety gadgets (masks) while working, 50% of the workers availed overtime. Smokers amounted to 31% of the total subjects. Around 35% of the workers complained of having respiratory ailments of which 19% (16 workers) closely matched byssinotic symptoms. Pulmonary Function Tests (PFTs) confirmed 13 of 16 workers to be byssinotics, with the remaining being labeled as Probables. The overall proportion of byssinotics in the mill was 19.28% (95% C.I. 11-27) and that of accidental injuries was 22.9%. The association of byssinosis with respect to work areas was significantly high in a Ring area (O.R.= 2.04) followed by carding (O.R. = 1.3). The association of byssinosis was also high in workers who did not use safety gadgets, e.g. dust masks (O.R = 4.89) and in people who worked overtime (O.R. = 1.25). Associations with respect to duration of employment and smoking could not yield significant results.

Conclusion:

Results indicate a very high probability of association of disease to non-safety gadget usage and overtime work. Studies comprising of a greater sample size would show precisely the overall prevalence of the disease.

HAZARDOUS EFFECTS OF NOISE POLLUTION ON THE HEALTH OF TRAFFIC POLICE PERSONNEL.

Sadaf Qadeer, Tahmina Feroz, Sadia Rashid, Farhan Siddiqui, Mohsin Ali Usmani, Mohammad Ali Adnan

Karachi Medical and Dental College, Karachi.

Objectives/Aims:

To compare the effect of noise pollution on health of traffic police personnel exposed and not exposed to road traffic noise in Karachi working for five years or more.

Introduction:

Noise pollution is a serious health problem and steadily increasing over the years. This has direct and indirect effect on people that can lead to health hazards.

Methods:

One hundred traffic police personnel were questioned for comparing the effect of noise pollution in them. We divided these hundred police personnel into two groups (exposed and non-exposed) of fifty each. Data was collected from different areas of Karachi according to our feasibility. Rinnie's and Weber's tests were performed by using tuning fork of 512 frequencies. Blood pressure readings were recorded using a sphygmomanometer. T-test and chi-square were applied and 95% confidence interval was estimated.

Results:

The exposed traffic police personnel are found to be 13 times more at a risk of having impairment in the right ear. Significant difference was also observed in mean diastolic blood pressure reading among exposed and non-exposed (95% C.I. 2.256, 8.264; P-value < 0.01)

Conclusion:

This study shows that exposure to noise causes wide range of effects on hearing, blood pressure and headaches of traffic police personnel. The exposed individuals are at higher risk of having hearing impairment as compared to non-exposed individuals.

ANTIMALARIAL ACTIVITY OF TRADITIONAL MEDICINAL PLANTS INVITRO

Saba Irshad Khokher

Lecturer in Institute of Biochemistry and Biotechnology, University of the Punjab.

Objectives/Aims:

- To evaluate antimalarial activity of traditional medicinal plants invitro, which are reported to have antimalarial effects, reported in traditional systems.
- To establish invitro antimalarial test systems.

Methods:

Three medicinal plants, *Artemisia absinthium*, *Ceasalpinia bonducella*, and *Picrorhiza kurrooa* were selected and identified. Their plant parts were extracted in three different solvents and 3 types of extraction methods were used. Various concentrations were used in a 24 well plate, each well contained Plasmodium falciparum in blood and RPMI 1640. The plant extracts and parasites were incubated for 24 hours, slides were prepared in Geimsa stain to determine if growth was inhibited or not.

Results:

The least antimalarial effect was seen with *Ceasalpinia bonducella* and *Artemisia absinthium in vitro*. The highest antimalarial effect was seen when hot alcoholic extract of *Picrorhiza kurrooa* was incubated with the blood containing the parasit, which showed 100 % growth inhibition, *in vitro*. While hot alcoholic extracts of other plants showed 90 % and 50 % growth inhibition.

Conclusion:

Picrorhiza kurrooa was seen to be the most effect inhibitor (100 % growth inhibition) of plasmodium falciparum with its hot alcoholic extract.

PATHOLOGICAL PATTERNS OF CERVICAL LYMPH NODE METASTASIS AT PRESENTATION IN EARLY (T1 –T2) ORAL TONGUE CANCER

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Department of Medical Oncology, Department of Surgery, Department of Radiation Oncology
Shaukat Khanum Memorial Cancer Hospital and Research Centre, Lahore.

Objectives/Aims:

The study was conducted to determine the histological distribution of neck node metastasis in early oral tongue squamous cell carcinoma (SCC) and improve the rationale for optimum neck treatment.

Methods:

Between November 2003 and June 2006, 30 patients with oral tongue SCC (pT1 and pT2) were treated with curative surgery at Shaukat Khanum Memorial Cancer Hospital and Research Centre. Records of these patients were analyzed retrospectively. All patients underwent partial glossectomy with neck dissection. Neck dissection was ipsilateral in 28 patients (93%) and bilateral in 2 patients (7%). Sixteen patients (47%) had pT1 and 14 patients (53%) had pT2 tumours. A total of 1056 cervical lymph nodes were analysed. The number of nodes in level I, II, III, IV and V were 261, 295, 230, 250 and 20 respectively.

Results:

Fifty three percent (16/30) of the patients had positive cervical nodes at presentation. The distribution of positive nodes in neck was 40%, 40%, 20%, 10% and 0% in level I, II, III, IV and V respectively. Skip metastasis in level III and IV were seen in 10% (3/30) of the patients. No patient had isolated level IV involvement. With pT1 44% (7/16) and in pT2 64% (9/14) had neck node metastasis; involvement in level I, II, III, IV and V for pT1 was 25%, 31%, 19%, 12% and 0% and for pT2 was 57%, 50%, 21%, 7% and 0% respectively.

Conclusion:

Risk of cervical nodal metastasis at presentation in early tongue cancer is high (> 50%). Level I and II are the most frequently involved nodal sites in the neck. Treatment of upper neck should be considered in these patients.

IMPACT OF OVERALL RADIOTHERAPY TREATMENT TIME ON LOCAL CONTROL AFTER CONCURRENT CHEMORADIATION (CRT) FOR T3/4 GLOTTIC CARCINOMA

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Shaukat Khanum Memorial Cancer Hospital and Research Centre, Lahore.

Objectives/Aims:

There is sufficient evidence to support that prolonged overall time of fractionated irradiation has a negative influence on local control and survival in head and neck cancer. The effect of concurrent CRT in compensating for prolonged radiotherapy treatment time is unclear. This study was performed to determine whether definitive concurrent chemotherapy offsets prolonged overall radiotherapy treatment time in advanced glottic carcinoma.

Methods:

Twenty five patients with locally advanced glottic cancer (T3/T4 N0/N+ M0) received definitive concurrent chemoradiation at Shaukat Khanum Memorial Cancer Hospital and Research Centre between November 2003 and December 2005. Ten (40%) had T3 and 15 (60%) patients had T4 tumors. Cartilage invasion on CT/MRI scan was seen in 12 (48%) patients. Radiation therapy dose was 70 Gy with concurrent cisplatin 75 mg/m² was given on day 1, 22 and 43.

Results:

Fifty-two percent (T3 7 and T4 6 patients) completed CRT treatment in ≤ 50 days. The CRT treatment time was > 50 days due to unscheduled interruptions in 48% (T3 3 and T4 9 patients). Two year local control for the group was 65%. Two year local control rates for patients completing CRT ≤ 50 and > 50 days were 90% and 36% ($p=0.02$) respectively.

Conclusion:

This study demonstrates the negative impact of protracted overall radiotherapy treatment time on local control in patients with advanced glottic carcinoma, even when concurrent chemotherapy is used. Further study of novel radiation-chemotherapy dose/fractionation regimens is warranted.

CORRELATION OF PREOPERATIVE CLINICAL STAGE WITH PATHOLOGICAL FINDINGS IN CARCINOMA ORAL TONGUE

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Shaukat Khanum Memorial Cancer Hospital and Research Centre, Lahore.

Objectives/Aims:

To determine the accuracy of clinical examination and MRI in staging carcinoma oral tongue.

Methods:

Between November 2003 and October 2005, 21 patients with oral tongue carcinoma underwent primary excision with modified neck dissection at Shaukat Khanum Memorial Cancer Hospital and Research Centre. All patients were assessed and staged (AJCC 2002) preoperatively in the joint head and neck clinic by an experienced oncologist and head and neck surgeon. MRI scan head and neck was done in all patients. Radiology was reviewed in the multidisciplinary meeting by a head and neck radiologist to assign an MRI stage. Twenty patients had partial glossectomy with ipsilateral neck dissection and one patient had bilateral neck dissection with primary excision.

Results:

Clinical T stage correlated, under or over staged with pathological T stage in 90%, 5% and 5% of the patients respectively. Clinical N stage correlated, under or over staged patients with pathological N stage in 52%, 33% and 15% respectively. MRI staging for T stage showed correlation with pathological T stage in 76%, under staging in 5% and over staging in 19% of the patients. MRI nodal stage correlated with pathological nodal stage in 62% and under or overestimated in 19% each.

Conclusion:

MRI may over stage the primary tumour as signal abnormality may be due to local oedema. MRI is more accurate than clinical staging for neck nodal disease.

INDUCTION COMBINATION CHEMOTHERAPY WITH GEMCITABINE AND CISPLATIN IN LOCALLY ADVANCED HEAD AND NECK CANCER

K. Shahzad, R. Hussain, M A Shah, S Hameed and A Jamshed

Department of Radiation Oncology and Department of Surgery
Shaukat Khanum Memorial Cancer Hospital and Research Centre, Lahore.

Objectives/Aims:

To evaluate the activity and toxicity of combination of cisplatin and gemcitabine in previously untreated patients with locally advanced head and neck cancer.

Methods:

Twenty patients with previously untreated advanced head and neck cancer (AJCC Stage IVB) were treated between August 2005 and January 2006. The site of disease was oral cavity; 35%, paranasal sinuses; 30%, hypopharynx; 25%, oropharynx; 5% and larynx 5%. Histologically, 95% were squamous cell carcinomas and 5% had adenocarcinoma. The decision on unresectable disease was in conjunction with head and neck surgeon. TNM stage was; T4bN0M0 40%, T4bN1M0 5%, T4bN2M0 45% and T4bN3M0 5%. Two 3 weekly cycles of cisplatin 75 mg/m² day 1 and gemcitabine 1000 mg/m² day 1 and 8 were given to all patients. Toxicity was scored after each cycle and response assessed following completion of second cycle.

Results:

All patients were available for assessment of toxicity and response. No grade 3 – 4 haematological, renal or hepatic toxicity was seen. Response at the primary site was complete (CR) 25%, partial (PR) 60% and no response/progression was seen in 15% of the patients. The overall response at primary site was 85%. In 12 patients with node positive disease complete, partial and no response/progression of lymph nodes was seen in 9%, 58% and 33% respectively. The overall response in cervical lymph nodes was 67%. Patients with complete or partial response went on to receive radical chemoradiation.

Conclusion:

Cisplatin and gemcitabine combination is well tolerated with low toxicity and high anti tumour activity in untreated head and neck cancer. Forthcoming studies focusing on induction chemotherapy in head and neck cancer should include arms with cisplatin gemcitabine combination regimens.

CERVICAL CARCINOMA IN A TERTIARY CARE SETTING

Farhana Badar, Natasha Anwar, Fouzia Meerza, Faisal Sultan.

Shaikat Khanum Memorial Cancer Hospital and Research Center, Lahore.

Objectives/Aims:

The aims of the research were to conduct an epidemiologic study to review the distributions of age, stage at presentation, morphology, and overall survival of the patients presenting with carcinoma of the cervix at the the Shaikat Khanum Memorial Cancer Hospital and Research Center, situated in Lahore, Pakistan, by retrospectively reviewing the medical records of the patients.

Methods:

Patients and methods: Four-hundred and twenty cervical cancer patients were registered at the hospital during a nine-and a half year time period extending from December 1994 to June 2004. Histology was confirmed by exfoliative cervical cytology typically by means of Papanicolaou smear. The International Federation of Gynecology and Obstetrics classification was used to stage the disease. Univariate analysis on factors as age, stage at presentation, and morphology was conducted. The outcome of interest for overall survival was death. Sixty-four patients with only visit were removed from the survival analysis. The overall survival estimates were determined on 356 remaining patients by constructing life-tables through the Kaplan-Meier procedures.

Results:

1) Of the 420 registered patients, 308/420 (73%) were diagnosed with squamous-cell carcinoma, 33/420 (8%) with adenocarcinoma, and 77/420 (19%) with unspecified carcinoma; 2) The age distribution of the 420 patient cohort was recorded to be as follows: mean 49.2 years, standard deviation 11.7, median 50 years, mode 50 years (37 patients), and age range 11-85 years; 3) Only two patients (0.5%) were identified as being in stage 0, 49/420 (11.7%) in stage I, 140/420 (33.3%) in stage II, 90/420 (21.4%) in stage III, 52/420 (12.4%) in stage IV, and 87/420 (20.7%) as not being evaluable; 4) In 356 patients, 31 (8.7%) deaths were recorded; the average overall survival time was 86.24 months; 115/356 (32.3%) patients were still on follow-up when the study concluded whereas, 210/356 (59%) were either discharged on treatment, sent home on palliative care, referred back to the referring facility, or lost-to-follow-up.

Conclusion:

There seems to be a lack of awareness about early detection and prevention of the disease. The importance of detection of the pre-clinical stage of the disease by considering the possibility of initiating a cost-effective measure needs to be emphasized in our setting.

CARCINOGENISITY OF HEAVY METALS” PRESENTATION OF A “MODEL YEAST BIOREACTOR” TO CLEAN UP OUR WATER RESOURCES FROM METAL CARCINOGENS

Humairah Farooq

Department of Pathology, Shaukat Khanum Cancer Hospital & Research Centre, Lahore.

Objectives/Aims:

Transition or heavy metals are highly **genotoxic and carcinogenic** in nature and cause immense damage to important biological molecules like proteins, enzymes and DNA when enter into human body. The DNA damage is mainly caused due to ‘*free radical*’ nature of transition elements *strongly attracted by negatively charged DNA*, binding its PO_4^- groups or replacing one or two H^+ ions of H-bonding. This causes various major cancerous mutations and other genetic defects, which are often transferred generation to generation. A considerable number of Pakistani people are affected by these “**hidden human killers**” due to increased industrial and agricultural practices. Physiochemical and other mechanical procedures used worldwide seem to be failures or non-ideal for third world countries like Pakistan, because of additional side effects and disposal costs. Therefore, the ultimate goal would be to produce a ‘*treatment plant*’ that is cost effective as well as non-toxic. Microorganisms such as bacteria and yeast especially **baker’s yeast** *Saccharomyces Cerevisiae* have proven to be “**Excellent Natural Cleaners**” of waste water resources worldwide, without causing any toxic side effects and extra burden on economy. This study proposes an easy, simple and cheap “**Model Yeast Reactor**”, designed and proposed to clean up our waste water resources from the heavy metal pollution, based on the process of bioremediation by using edible baker’s yeast *Saccharomyces Cerevisiae*.

Methods:

Various yeast strains were isolated from industrial wastewater (Lever brothers & Kasur tanneries etc). Each yeast strain was incubated with the optimal growth conditions (with known pH & temperature). The effect of **metals** on the protein pattern was analyzed by using **PAGE** (Polyacryl amide gel electrophoresis). The efficiency of each yeast strain to remove heavy metals from medium was analyzed by using **Atomic absorption spectrophotometer (AAS)**.

Results:

All yeast strains showed excellent results with high capability (range from 40 –90%) of removing different metals from the medium.

Conclusion:

The proposed “Yeast Rector” can be an effective, non toxic and low cost solution towards the water –borne diseases. Such thought should be promoted not just on scientific grounds but also on governmental and social levels for its implication as a natural treatment plant in every industry, every ‘*ganda nalla*’ and every waste water resource to protect water and life.

THE VALUE OF BONE MARROW BIOPSY IN INITIAL STAGING OF NEWLY DIAGNOSED HODGKIN'S LYMPHOMA PATIENTS.

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Shaukat Khanum Memorial Cancer Hospital and Research Center, Lahore.

Objectives/Aims:

Bone marrow biopsy is routinely performed in staging workup of newly diagnosed Hodgkin's lymphoma patients (HL). We undertook this study to re-evaluate the role of bone marrow biopsy in this setting. Our aim was to determine the predictive factor(s) of bone marrow involvement in HL patients and to categorize the patients on the basis of these risk factors

Methods:

Data of 246 adult HL patients seen at Shaukat Khanum Memorial Cancer Hospital and Research Center (SKMCH & RC) during years 1994 and 2003 was evaluated, and association between bone marrow involvement and various clinical and laboratory factors was analyzed by applying chi-square test using statistical package for social sciences (SPSS) software.

Results:

Age greater than 40 years, fever, night sweats, histological subtypes mixed cellularity and lymphocyte depleted, hemoglobin less than 10g/ dl, Total leukocyte count (TLC) less than 4000/ ul, alkaline phosphatase level greater than 126 U/ L and clinical stages III and IV were found to be associated with bone marrow involvement.

Conclusion:

Bone marrow biopsy is of value in detecting marrow involvement in certain high risk categories of HL patients. Routine use of bone marrow biopsy in low risk, young patients with favorable histological subtypes and early stage (IA & IIA) disease may be unnecessary.

CASE OF A 65 YEARS MALE WITH ANEMIA

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Objectives/Aims:

In an otherwise healthy male, incidental finding of anemia demands thorough investigations. Differential microcytic anemia includes iron deficiency, thalassemia, anemia of chronic disease and sideroblastic anemia, with the first two being the most common. Diagnostic workup to rule out underlying cancer is of utmost importance. This vignette describes a male of 65 years with incidental finding of anemia.

Methods:

He presented to the comprehensive health check clinic with no complaints and an unremarkable past medical history. He was found to have microcytic anemia with hemoglobin (Hb)-10.8g/dl, hematocrit-36.2, MCV-64.6 with high normal red blood cell (RBC) counts. Other routine tests were normal. He was further investigated with fecal occult blood testing (FOBT), repeated thrice, RBC morphology and Hb-electrophoresis.

Results:

FOBT was negative. Hb-electrophoresis suggested elevated Hb-A2 of 5.9 % (1.5-3.2), which in the presence of hypochromic anemia is suggestive of a beta thalassemia trait. RBC morphology revealed hypochromia, microcytosis and anisocytosis.

Conclusion:

Incidental finding of anemia in a male mandates cancer screening. Our patient had no awareness of his underlying condition, hence reinforcing the benign nature of the thalassemia trait. Such individuals should be counseled about family screening as well. Nevertheless a screening work up for underlying intestinal malignancy should also be emphasized especially in this age group. Supplementation with iron therapy should be avoided.

MOLECULAR EPIDEMIOLOGY OF HEPATITIS C VIRUS (HCV) IN PUNJAB.

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Objectives/Aims:

To describe the frequency and distribution of various HCV genotypes in the province of Punjab.

Introduction:

It has been almost ten years since the last report on the frequency of different HCV genotypes in Pakistan. Monitoring HCV genotypes provides evidence based data to help understand the transmission, pathogenesis and the etiology of a disease in our population. In order to monitor such patterns it is important to review data on a regular basis to detect shifts. Here we present an analysis of genotypes, from samples accumulated during the year 2006.

Methods:

Total ribonucleic acid (RNA) was extracted from serum samples received at the diagnostic laboratory for HCV Genotyping between Jan and Sept 2006. Genotyping was performed on these samples using two different methods; a restriction fragment length polymorphism (RFLP) method based on heterogeneity in the 5'-UTR of the HCV genome, and a type specific PCR method described based on differences in the core region of the HCV genome.

Results:

In a total of 1231 samples analyzed, HCV genotype 3 was found to be the predominant genotype (89%) in the Punjab population. This was followed by genotype 1 (9.75%) and 4 (0.89%), with 2 being the most rare HCV genotype (0.24%). Mixed infections were detected in 0.24% of the samples. Within this set of data the male to female ratio was about equal. However, the mean age at diagnosis was slightly higher for female patients (46 years) as compared to males (38 years). There was no difference in genotypes 3 and genotype 1 in terms of age and sex of the patients. Interestingly males were found to be three times more likely to be diagnosed with type 4 infection than females (8 vs. 3; 1.23% vs. 0.4). Furthermore, while the age distribution was quite large for the patients in the other genotypes (7-76 for males and 15-70 for females); the males with type 4 infection were all between the ages of 28-50.

Conclusion:

There is a skewed distribution of genotypes amongst patients in Punjab. This may suggest a common route of transmission. The fact that women on average are older when they present with disease may also have underlying implications in terms of differences in symptoms between men and women. It may also reflect a difference in the lifestyle of men and women in this part of the world and hence mode of acquisition of the disease. Genotype 4 HCV infections are rare in Pakistan; however it is the predominant type in Middle East.