

Abstracts

Session 1

Meet the Professor

Saturday, July 26, 1997
7-8 a.m.

1

Renal Calculi: Medical Management

RAL Sutton, DM

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Karachi, Pakistan

The main objective of medical management of stone disease is to reduce the risk of recurrences while avoiding unnecessary investigation or potentially harmful treatment. Most renal stones consist of calcium oxalate and/or phosphate. Stone analysis and other tests help to identify noncalcium (cystine, uric acid, and struvite) stoneformers who require different management. A small proportion of calcium stoneformers have underlying diseases such as primary hyperparathyroidism or renal tubular acidosis that can be identified with simple screenings, and most are idiopathic. A fairly standardized approach to the idiopathic calcium stoneformer involves the identification of accepted risk factors (hypercalciuria, hyperoxaluria, hyperuricosuria, and hypocitraturia). Such an approach recently has been shown to be cost effective in the United States, but may require modification in the developing world, where the frequency of the various risk factors differs from that in the developed world. Each of the known risk factors can be produced by dietary or intrinsic (metabolic) causes; therapy may include modification of diet, aimed at avoiding excessive intakes of calcium, salt, animal protein or oxalate, or the use of specific drug treatments such as thiazide diuretics or potassium citrate. Restriction of calcium intake below the recommended dietary allowance of 800-1000 mg per day no longer is considered advisable or beneficial as a means of stone prevention in most patients. In some parts of Asia, hypocitraturia is a major risk factor identified in calcium stoneformers, although the cause is not understood. There is a need for studies to determine the most effective and affordable therapy for stone prevention in such patients. The management of uric acid stones is easier than that of calcium stones. The first line of therapy is alkalization of the urine. For cystine stones, the most important practical decision is whether chelating agents such as penicillamine or alpha mercaptopropionylglycine are required, or whether increased fluid intake plus urinary alkalization will be effective.

2

Impact of Mediterranean Fever on Kidneys

Riyad Saed, MD

Abstract not available

3

Viral Hepatitis A-G: Global Perspective

Mohammad S Khuroo, MD

Abstract not available

4

Update in Lymphomas

Khalid L Rehman, MD

Abstract not available

Session 2 (parallel) Symposium Hypertension

Saturday, July 26, 1997
8:30-10 a.m.

5

Practical Approach to Hypertensive Crisis

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The patient under discussion, an obese 32-year-old female, presented with a headache, blurred vision, tingling in the hands, and a blood pressure (BP) of 240/130, but no objective signs of hypertensive end organ damage (normal heart size, no retinopathy). When possible, hypertensive emergencies - including hypertensive encephalopathy, CNS bleed, aortic dissection, refractory left ventricular failure, eclampsia, and (sometimes) hyperadrenergic states (such as pheochromocytoma, cocaine abuse) - prompt treatment is required to lower the blood pressure. There is a choice of effective and safe parenteral drugs for rapid BP reduction, including nitroprusside, nicardipine, or labetalol. Such patients should be monitored in an intensive care unit. The diastolic BP should be lowered promptly to 100 or by not more than 20%. A more gradual progressive reduction in blood pressure may be achieved after oral administration of rapidly absorbed drugs, including labetalol, clonidine, long-acting calcium antagonists (not nifedipine), ACE inhibitors, or prazosin. In "hypertensive urgencies," in the absence of end organ damage, rapid reduction of the BP is unnecessary and may be harmful, particularly in the patient with chronic

hypertension in whom cerebral vascular autoregulation is impaired and stroke or myocardial ischemia may be precipitated. Aggressive BP reduction with oral nifedipine or with repeated hourly doses of clonidine, is not of proven benefit. Gradual reduction of the diastolic pressure to 95 or 100 mm Hg with conventional therapy is preferable; reset and a loop diuretic may be appropriate initial therapy in the volume-overloaded patient. In the patient under consideration, long-standing hypertension appears unlikely; a hyperadrenergic state could not initially be excluded, and immediate BP lowering was undertaken. If pheochromocytoma is suspected, a beta adrenergic blocker should not be used alone since this may provoke paradoxical hypertension.



Secondary Hypertension

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Secondary hypertension is an uncommon (5-10%) but a potentially reversible and curable form of hypertension. Thus, a high index of suspicion in a subset of hypertensive patients is essential. The most common causes of secondary hypertension are renal, vascular, endocrine, and lifestyle abnormalities. Some of the clinical clues are development of hypertension before age 30 and after 55, abrupt onset of high blood pressure, and Grade 3 or 4 hypertension. The presence of hypokalemia should heighten the index of suspicion for a search of an underlying reversible etiology such as adrenal hyperplasia, primary aldosteronism, etc. Endocrine causes of hypertension account for about 1% of total cases. Besides primary aldosteronism, other causes to consider include Cushing's syndrome, thyroid disorders, primary hyperparathyroidism, and pheochromocytoma. Persistent hypertension, despite adequate drug therapy, is an indication to investigate for renovascular hypertension. Renal artery stenosis may occur without renal hypertension. Thus, it is important to determine the physiologic significance of the anatomic lesion. In patients over 55, renal artery stenosis usually is caused by atherosclerosis, while in younger patients (mostly female) fibromuscular dysplasia is the most common cause. Captopril renography, renal angiography, or magnetic resonance angiography will aid in the diagnosis. Besides the above-mentioned conditions, one must keep in mind other factors that may cause high blood pressure. Excessive consumption of alcohol and the illicit use of drugs like cocaine and anabolic steroids are some of the incriminating agents. This information may not be forthcoming. It is important to probe for such causes, especially in young people with very high blood pressure.

Patients with secondary hypertension can present with very high blood pressure. When dealing with these patients, it is important to differentiate between a hypertensive urgency versus hypertensive emergency. Severe hypertension is not synonymous with a hypertensive emergency, and the two conditions require different management. These topics will be reviewed using the case history as an example.



Long-term Follow-up and Prevention of Complications in Hypertension

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Much has been written and said about hypertension and its investigations, complications, treatment, and outcome, but little has been done about the long-term care of those patients. Hypertension is not a mere elevation of systolic and diastolic readings; it's a disease just like others e.g. diabetes mellitus, that deserves a regular follow-up not only of blood pressure level, but of other complications such as target organ disease, and other associated underlying conditions e.g. coronary heart disease risk factors. The main goals of hypertension treatment are to prevent morbidity and mortality associated with high blood pressure and to control the disease by the least intensive means possible. This should be accomplished by achieving and maintaining the blood pressure within the well-defined normal values for age and sex etc., not only this, but also by controlling other modifiable cardiovascular risk factors including hyperlipidemia, obesity, and smoking. In the long-term planning of hypertension control and patient care, it is important to include adjunctive therapy like lifestyle modifications (nondrug therapy). Since we are treating asymptomatic initial medical conditions in most patients, which makes them less compliant in taking medications when they feel quite well, this antipathy will be exaggerated if the medical regime is inconvenient or produces side effects. Special consideration should be stressed including patient education, control of isolated systolic hypertension of the elderly in order to reduce stroke incidence, and to care for other target organs. In order to accomplish this I think it is important to define the level of high blood pressure that should be treated and to identify the reasons for inadequate control of blood pressure.

Session 3 (parallel) Symposium
Airway Diseases - Asthma
Saturday, July 26, 1997
8:30-10 a.m.



**Pathogenesis of Bronchial Asthma:
The Role of Inflammation, Cytokines,
Allergy, and Occupation**

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Many definitions exist for asthma. Recently, the Global Initiative for Asthma defined it as "...a chronic inflammatory disorder of the airways in which many cells play a role, in particular mast cells, eosinophils, and T lymphocytes. In susceptible individuals this inflammation causes recurrent episodes of wheezing, breathlessness, chest tightness, and coughing particularly at night and in the early morning. These symptoms usually are associated with widespread but variable airflow limitation that is at least partly reversible, spontaneously or with treatment. The inflammation also causes an associated increase in airway responsiveness to a variety of stimuli."¹ The histologic pattern seen in airways is essentially the same whether the patients have allergic asthma or nonallergic asthma. Occupational asthma is divided into two groups depending upon whether there is latency.² Occupational asthma with latency is the most common type and includes all instances of immunologic mechanisms. In occupational asthma without latency, the mechanism of asthma induced by irritants is unknown. Though the pathological changes are similar to asthma with latency, a striking fibrosis and fewer T lymphocytes suggest the absence of an immunologic mechanism.³ Called "reactive airways dysfunction syndrome" (RADS) or "irritant-induced bronchospasm" (IIA) by some, other experts do not believe these are real clinical entities.⁴ Though occupational asthma without latency may be a possible exception, the same basic underlying immunologic mechanisms seem to be present in all asthmatics. The airway inflammation is characterized by the presence of eosinophils, neutrophils, lymphocytes, and activated mast cells, which act through a variety of mediators including histamine, bradykinin, leukotrienes, prostaglandins, chymase, PAF, reactive oxygen species, substance P, neurokinin A, and calcitonin gene-related peptide.⁵

Conclusions: Many common underlying inflammatory processes are associated with the pathogenesis of bronchial asthma regardless of etiology. Further research may show some distinguishing characteristics.

1. WHO Study Group on Global Strategy for Asthma Management and Prevention: Global strategy for asthma management and prevention. Bethesda, MD: National Institutes of Health, 1995. NHLBI publication no. (NIH) 96-3659A.

2. Chan-Yeung, M, Malo, J-L: Occupational asthma. *N Eng J Med* 1995;333:107-12.
3. Ibid.
4. Kern, DG, Sherman, CB: What is this thing called RADS? *Chest* 1994;106:1643-44.
5. Kaliner, MA: Airway inflammation and airway hyperactivity in asthma. In: Shelhamer JH, moderator. Airway inflammation. *Ann Intern Med* 1995; 123:288-304.



**Patient Education as Part of
Asthma Management**

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There appears to be widespread agreement that education of the patient with asthma is of paramount importance. In the model of medical care in the past, asthma education began and ended with the physician. However, there is a growing recognition that people with asthma who suffer significant adverse events from asthma do not always have access to appropriate continuous medical care either through their own ignorance or through failure of the health care system. Moreover, recent studies suggest that a sizable proportion of health care professionals do not have adequate skills to demonstrate the use of a metered-dose inhaler. This situation has led to the establishment of asthma education programs for patients, their families, and the medical care givers.

The main goal of asthma education is to reduce morbidity and mortality. For most asthmatics the primary aim of education is to improve the quality of life, ability to function, and control of the disease. The content of the program to achieve these goals and other goals should include:

1. General asthma education (inflammation and broncho-constriction, the disease course, etc.).
2. Rationale of therapy (goals, bronchodilators, and anti-inflammatory side effects).
3. Asthma management skills (peak expiratory flow, inhalation technique).
4. Asthma self-management plans (the recognition of unstable asthma, written guidelines for the appropriate therapeutic response).
5. Trigger avoidance (dust mite, irritants, smoker, different allergens).

Besides the goals and content, many points have to be considered in any given educational program, such as:

1. Methods (checklists, booklets, videotapes, audiovisual, intra-active computer programs).
2. How much time (few minutes to many days of teaching)?
3. Who should teach (a specialist, family physician,

health educator, or nurse)?

4. When and where to teach (physician's offices, outpatient clinics, at school, at work)?

5. How to evaluate adequacy of teaching and understanding?

6. Which materials are needed?

Such a program and other self asthma-management programs clearly lead to improved knowledge and increase self-management behavior. It is likely that there is a promising trend that self-management intervention improves outcome such as use of healthcare facilities, morbidity, and mortality.

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Bronchial Asthma in Special Circumstances

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Asthma is a common illness throughout the world with more than 10 million people afflicted in the United States alone. Despite better understanding about its basic inflammatory nature and increasing knowledge about different treatment modalities, mortality from asthma appears to be increasing.

Asthma is the most common occupational lung disease in the United States. More than 200 specific antigens that cause occupational asthma have been identified. High molecular weight agents are usually protein-containing agents that stimulate IgE production. These include animal and plant products, biological enzymes, and vegetables. Low molecular weight agents may act as haptens and cause specific IgE sensitization to a new protein. IgE and cellular immune mechanisms may be involved. Examples of low molecular weight agents include diisocyanates, wood dust, metal salts, antibiotics, and acid anhydrides. Managers and workers in all industries that handle materials known to cause occupational asthma should be educated. Medical surveillance programs are the keystone of prevention. Health care workers should have increased awareness of the disorder, and cigarette smoking should be discouraged. For sensitized persons, the best option is removal from the work environment because fatal consequences have been reported in individuals who continue to work.

Nocturnal asthma is common in poorly controlled asthmatic patients. About 70% of deaths from asthma occur during sleep-related hours. The diurnal variation in airflow obstruction, seen even in normal subjects, is exaggerated in asthmatics. Circadian changes in cortisol, epinephrine, cyclic adenosine monophosphate, and histamines may be responsible. Other potentiating mechanisms may include relative nocturnal hypoxemia, gastroesophageal reflux, airway cooling, increased secretions, and exposure to bedroom allergens. Medications for better control include long-acting

betastimulants, theophylline, and corticosteroids.

Various studies estimate between 4% and 28% of asthmatic patients as experience increased reactivity on ingesting aspirin or a nonsteroidal anti-inflammatory drug. Acute asthma may be accompanied by nasal and conjunctival symptoms and may progress to shock and respiratory arrest. Leukotrienes and other mediators/mechanisms may be involved.

Steroid-resistant asthma is rare and may necessitate the use of alternative agents like methotrexate, cyclosporin, and auranofin. Before use of these potentially toxic agents "steroid resistance" must be clearly established.

Poorly controlled asthma in pregnancy increases perinatal mortality, prematurity, and decreases birth weight. Pregnancy is not a contraindication to therapy, including bronchodilators and anti-inflammatory agents. Fetal outcomes are optimal when asthma is well controlled.

Increased awareness and understanding of etiopathogenesis of asthma in special circumstances may lead to better management in this subset of patients.

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There is a Strong Link Between Sinonasal Diseases and Asthma

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Statistics indicate that 80% of patients with bronchial asthma have rhinitis while 5-15% with perennial rhinitis have asthma. Similarly, sinusitis and asthma often coexist and impact one another at different levels. Physicians should be alert to the relationship between these conditions and their coexistence.

Current thinking is that allergic rhinitis and asthma represent a "continuum" of inflammatory processes involving one common airway. A successful therapy will include simultaneous control and treatment of both.

Similarly, proper identification of asthmatic patients with acute or chronic sinusitis should be discerned by a thorough history and physical examination and work up. Proper management of sinusitis-medical or surgical-can result in improved sinonasal and asthmatic symptoms.

Asthmatic patients with recurrent attacks, not showing expected response to adequate therapy especially with sinonasal symptoms e.g. sneezing, nasal blockage, headache, facial pain, mucopurulent discharge, fever, etc. deserve immediate attention, a thorough work up, and adequate treatment of these conditions to improve the effectiveness of asthma therapy. Another condition, which can cause asthma symptoms or precipitate the attacks is gastroesophageal reflux disease. In patients with asthma and reporting nocturnal attacks of wheezing, cough, or postprandial exacerbations, one must think of this condition and treat effectively.

Capt Angeline Lazarus, MC, USN, FACP, FCCP

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Several hormonal and physiological changes take place during pregnancy. In general, the anatomical and physiological changes of the respiratory system do not have a significant impact in normal pregnant women. However, pregnant women with pulmonary disease may experience the impact of these changes based on the severity of their underlying disease. Many studies have looked at the effects of pregnancy on the course and severity of asthma, the effects of asthma on pregnancy and the fetus, and special considerations or modification of therapy. In a study of 366 pregnancies complicated by asthma, Schatz found that asthma improved in one-third, became worse in one-third, and stayed about the same in one-third during pregnancy. When worsening of asthma was observed, it usually peaked in severity during 29-36 weeks of gestation. Asthma returned to prepregnancy levels in approximately three-quarters of patients. A similar pattern with successive pregnancies was seen in two-thirds of the patients. Other studies have shown similar findings regarding the course and severity. Early retrospective studies showed increases in premature, low birthweight infants, perinatal mortality, and increased preeclampsia in pregnant asthmatics. More recent prospective and retrospective studies where asthma was in good control demonstrated complication rates similar to that of nonasthmatic pregnant women. While many possible causes for increased complications are suggested, the most important one is related to the tenuous nature of the fetal oxygen supply. Maternal hypoxemia and hypocarbia result in reduced oxygen delivery to the fetus.

Management of the pregnant asthmatic patient is remarkably similar to that of nonpregnant asthmatics. The goals are to maintain adequate maternal lung function and oxygenation. This requires monitoring of the mother with peak flow meters and PFTs and monitoring of the fetus with ultrasonography, fetal heart rate, and kick counts. Inhaled therapy is preferred over systemic therapy to minimize gastrointestinal symptoms. Avoid alpha agonists that cause uterine artery vasoconstriction. Asthma is usually quiescent during labor and delivery. Continuation of inhaled medications and stress dose steroid for those on systemic steroids are indicated. Consider epidural anesthesia. Avoid prostacyclins and histamine-releasing narcotics as they induce bronchospasm. Status asthmaticus during pregnancy is treated similar to nonpregnant patients in status. Breast feeding is not contraindicated. Theophylline appears in breast milk and it is advised to adjust the timing of medication with breast feeding to avoid infant irritability. Emphasize compliance and avoid undertreatment.

Saturday, July 26, 1997

10:15-11:15 a.m.

Mohammad Sultan Khuroo, MD

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Liver transplantation is an accepted treatment for end-stage liver disease, life-threatening complications of liver disease, and acute liver failure. Liver transplantation has shown steady growth over the years in North America and Western Europe due to the introduction of cyclosporin A. However, this therapeutic modality has shown little impetus in developing countries. Until now, only a fraction of patients who need a liver transplant can afford it and do go to the West for such treatment. A few centers in the West have recently begun to offer transplants, and the experience gained from these centers shall be of immense value to expand this treatment modality. Donor organ availability and procurement is a problem, considering the cultural, social, and religious beliefs of the population. The spectrum of liver disease demanding transplants in this population is different than in the West. Hepatitis B virus is a dominant cause of end-stage liver disease in developing countries. Transplants for hepatitis B virus-related cirrhosis is associated with high recurrence rates, loss of graft, and high mortality. Hepatitis B immunoglobulin (high doses) is effective for preventing hepatitis B virus recurrence, adding unacceptable costs to the transplant program. Lamivudine has been used recently for preventing such recurrences; however, more experience with this drug is needed for its long-term use and efficacy. Hepatitis C virus is endemic in developing countries, and hepatitis C virus-related cirrhosis is the most common indication for liver transplants in this community. Hepatitis E virus causes epidemics of jaundice and a high occurrence of acute liver failure in the Indian subcontinent. Liver transplantation, though effective, cannot be offered to these patients due to its local unavailability and high costs. Transplant centers in developing countries have to gain experience over the next few decades to formulate their own guidelines for organ procurement, patient selection listing, and the short- and long-term management of patients with transplanted livers.

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The definition of the end of human life, from a jurisprudence point of view, is a more difficult task than that encountered in definition of the beginning of human life. In the latter we have the privilege of several Qur'ānic verses and 'Aḥādīth of the Prophet (PBUH). In this regard, jurists depended heavily on opinions of professionals in biomedical sciences whenever no clear evidence exists in the Qur'ān or sayings of the Prophet. It is a combined effort, whereby jurists lay down basic principles, conditions and limitations, and Muslim medical professionals are expected to utilize and lay down the products of scientific research and progress to help jurists to formulate verdicts.

The medical profession defined death is a biological phenomenon characterized by total cessation of brain function, or brain death, according to criteria and standards that became adopted worldwide.

From the Jurist point of view, human life on this earth comes to an end by the departure of the "Rūḥ" (Soul) from the body. The "rūḥ" is from the creation and knowledge of Allāh (SWT). The main effects and manifestations of the rūḥ in the human body are knowledge, consciousness, sensation, willful movements, and choice. The complete, irreversible absence of such entities points to the departure of the rūḥ.

It became clear that jurists will not encounter difficulties in making verdicts related to death if medical professionals are able to clearly define and time the event of brain death in undisputed certainty. If that takes place, then most contemporary jurists, individually and in committees, seminars, or Fatwa bodies, have agreed on the timing of the event of brain death as defined by contemporary standards of biomedical science depending on that there is reasonable agreement on the following issues:

1. If a qualified committee of Muslim medical professionals not involved in the procedures of organ transplantation decided with undisputed confidence that the event of brain death is established in an individual then that individual can be pronounced dead.
2. Depending on the item above, the treating medical team may choose to abandon any resuscitation efforts for that individual, and the treating medical team is permitted to discontinue the use of life support systems on the individual.
3. On the same basis, and after due consents, organs from such individuals could be obtained, without mutilation, for the purpose of organ transplantation.

Sunday, July 27, 1997
7-8 a.m.

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Prostate cancer is the second most common cause of cancer death in the male population of the United States. It is estimated that about 244,000 new cases were diagnosed and 40,400 men died from the disease in 1995. From 1986-91, there has been an 82% rise in the incidence of prostate cancer in men over the age of 65, the largest single increase ever reported for cancer. This increase is related to prostate cancer screening programs.

Studies indicate that American men whose diets are rich in saturated fat from red meat have an approximately 80% greater risk of developing prostate cancer than men with a lower intake of fat. It is believed that these diets do not initiate prostate cancer, but influence androgen levels and so promote changes in the gland, leading to clinically significant and possible lethal malignancy.

Another epidemiological factor for carcinoma of prostate is a positive family history in first and second degree relatives. Genetic studies have detected a defect on the short arm of chromosome 8 that is associated with prostate cancer. African American men have a higher incidence and mortality rate from carcinoma of the prostate than Caucasians. They also develop the tumor at an earlier age. Recent reports also indicate an increased frequency of prostate cancer among relatives of women with breast cancer. Other factors include geography, prior vasectomy, and a history of venereal disease.

Screening for prostate carcinoma is a controversial topic at the present time. Both the American Cancer Society and the American Urological Association recommend an annual digital rectal examination (DRE) and prostate specific antigen (PSA) beginning at the age of 50. For high risk men, such as African Americans and those with a strong family history of carcinoma of the prostate, screening is recommended beginning at age 40. The American College of Physicians recommends a more selective approach.

Accumulated experience supports screening. Clinically significant disease may be distinguished from insignificant disease by prognostic features, such as the volume of tumor, extent of tumor, Gleason score, and DNA ploidy. Application of these criteria to the cancers detected by DRE, PSA,

and TRUS has clearly demonstrated that a majority of detected cancers are clinically significant. In isolation, DRE or PSA each have positive predictive values of 15-30%. If DRE, PSA, and transrectal ultrasound (TRUS) are positive, the chance of cancer is increased up to 60%. This low sensitivity precludes the exclusive use of PSA as a screening test for prostate carcinoma; when combined with DRE and TRUS, it can lead to greater sensitivity and specificity. If both DRE and PSA are negative, the chance of tumor is only 2%. With the addition of PSA, TRUS, and TRUS guided biopsy, significant cancers may be detected at an early stage.

The traditional DRE "gold standard" for the evaluation of prostate carcinoma has been unsuccessful in detecting prostate cancer at a sufficiently early stage for effective treatment with either radical prostatectomy or radiation therapy. No single test, PSA, DPE, or TRUS is sensitive enough to accurately detect prostate cancer or to predict the tumor's biological potential. Although serum PSA and DRE identify the men at high risk of having prostate cancer, progress in early diagnosis of prostate cancer is largely dependent on transrectal ultrasound, which improves the specificity of PSA and further allows accurate staging biopsies of nodules and hypervascular areas. A combination of DRE and PSA, followed by TRUS and ultrasound guided biopsy can detect clinically significant prostate cancers that still are confined to the gland and can be cured.

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Gastroesophageal Reflux Disease- Recent Advances

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Gastroesophageal reflux disease (GERD) is a prevalent, chronic condition that affects 7-10 % of the population in the United States. Patients most often seek medical attention because of heartburn, but various other symptoms are increasingly being associated with the disease. Primary care physicians may not be aware of the full clinical spectrum of GERD. Extra-esophageal manifestations of GERD include atypical chest pain, pulmonary symptoms such as sleep apnea and bronchospasm, and laryngeal symptoms of hoarseness and frequent throat clearing. Up to 50% of patients who do not respond to routine therapy for laryngitis, bronchitis, wheezing, and throat clearing have evidence of acid reflux. The diagnosis and the assessment of response to therapy may require the use of sophisticated, invasive tests including endoscopy, ambulatory pH monitoring, and manometry. "Red flags" such as weight loss, dysphagia, and pain must be recognized and evaluated promptly. Therapeutic considerations must be based not only on cost effectiveness but on efficacy in preventing complications such as bleeding, stricture, and carcinoma. Treatment regimens are often empiric and may be based entirely on the presenting

complaint of heartburn without discrimination as to severity or cause of other complaints. Managed care organizations prescribing guidelines may "mandate" inappropriate therapy, which can lead to inadequate acid suppression and inefficiency in rapidly instituting the correct therapy. This session will focus on the pathophysiology of GERD in relationship to the clinical syndromes associated with reflux. A cost-effective diagnostic and therapeutic decision analysis approach will be developed based on evidence-based studies. Case histories will be presented to illustrate certain aspects of this disease. A GERD activity index will be presented as an aid to objectively quantitate the severity of GERD and to recognize and manage its complications.

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Echocardiography in Clinical Practice

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Echocardiography is a commonly employed imaging and hemodynamic technique for evaluation of cardiovascular diseases. The basic components include image acquisition, assessment of cardiac function, measurement of hemodynamics, and visualization of blood flow.

This technique can be applied to any age group from fetus to elderly and is a portable technique. Echocardiography initially began as a noninvasive screening procedure for cardiac disease. With advancement, it now is also an invasive technique for some of its components. It had a modest beginning and now has invaded the emergency room, cardiac cath lab, and the operating room. The devices in use at the present time include precordial, transesophageal, intravascular, and intracardiac. The frequency of ultrasound beam used varies between 1.9 to 40 mhz, depends on the size of the object and depth of penetration. For deeper penetration of the beam, the lower frequencies are used, including those for surface echoes, while higher frequencies are used for intravascular ultrasound. A number of procedures in addition to routine screening and evaluation can be performed by echocardiography guidance. They include contrast echocardiography, transesophageal, exercise (both pharmacological and physical exercise), intraoperative (epicardial and TEE), interventional procedures, and pericardiocentesis under ECHO guidance.

The major impact of echocardiography has been on the evaluation of valvular heart diseases, specifically mitral and aortic, cardiomyopathies, congenital heart diseases, coronary artery diseases and its complications, endocarditis, pericardial diseases, prosthetic valves evaluation, pulmonary hypertension, tumors, and masses. Two-dimensional echocardiography remains the main modality of imaging. Mode Doppler (pulsed and continuous wave) and color flow imaging are added to define the hemodynamic parameters

and other pathological findings to complete a comprehensive echocardiographic exam.

The newer modalities of echo that are being evaluated at the present time include 3-D, 4-D echocardiography, color kinesis, and harmonic imaging. These will be discussed in this presentation.

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Critical Review of Treatment Options in Cerebral Arteriovenous Malformations

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The treatment of cerebral arteriovenous malformations has gone through revolutionary changes over the last three decades. Initially, as angiography became widely available, the malformations were easily diagnosed; but the majority were considered inoperable. It also was presumed that with advancing age (50 and older) the risk of hemorrhage was extremely low. With the introduction of computed tomography and the MRI later in the last decade, the diagnosis of asymptomatic and minimally symptomatic arteriovenous malformations has become easy.

At the same time, natural history studies have shown a much worse prognosis of untreated patients compared to what was believed earlier. The treatment similarly has paralleled the advances in technology and surgical experience. At the present time, three modalities are available for the management of cerebral arteriovenous malformations, (i.e. surgery, embolization, radiosurgery or combinations thereof), each having pros and cons. The approach in arriving at a management decision can best be made with an interdisciplinary team in place. This will be discussed in light of personal experience in the management of more than 450 patients with cerebral arteriovenous malformations.

Session 6 (parallel) Symposium Cardiovascular Diseases

Sunday, July 27, 1997
8:30-10:15 a.m.

19

Thrombolytic Therapy in Acute Myocardial Infarction

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Acute myocardial infarction is precipitated by the disruption of an atherosclerotic plaque in an epicardial coro-

nary artery with subsequent thrombosis occluding the vessel. If the vessel becomes totally occluded, a wave-front of myocardial necrosis begins within 30 minutes and spreads from the endocardium towards the epicardium. The major goal of therapy is to restore blood flow as quickly as possible to prevent lethal consequences of necrosis.

Thrombolytic agents decrease mortality, improve left ventricle function, reduce the occurrence of congestive heart failure and generally reduce the complications of infarction emanating from extensive left ventricular damage. The mechanism of these beneficial effects is restoration of coronary blood flow, and the benefit is specifically related to the occurrence of TIMI grade 3 flow. Thrombolytic agents act by converting plasminogen to plasmin, which then lyses the fibrin clot. Reperfusion early after an acute myocardial infarction will decrease infarct size, while reperfusion at a later time will benefit patients by preventing infarct expansion.

Eligible patients for thrombolytic therapy are those with a history of chest pain presenting within 12 hours from the onset of symptoms, an EKG showing ST-segment elevation or left bundle branch block, and who have no contraindications to the use of thrombolytic agent. Studies demonstrate a 25% reduction in the short- and long-term mortality. Earlier administration results in the greatest benefits. Equivalent risk reductions are seen in all types of patients (i.e., inferior MI, females, diabetics, and elderly patients.)

In the GUSTO trial, an accelerated dosing regimen of alteplase was associated with an additional 14% relative risk reduction in mortality when compared to streptokinase. Heparin should be administered intravenously when using a fibrin specific lytic agent like alteplase, and it may not be indicated when using a fibrin nonspecific lytic agent like streptokinase. Since different thrombolytic regimens have different costs and outcomes, the trade off between cost and expected benefit should be considered.

Unless contraindicated, concomitant administration of aspirin is mandatory with all thrombolytic agents. Its use has led to an additional 23% reduction in the risk of death, reinfarction, and stroke in acute myocardial infarction may be related to improved microvessel patency in the infarcted segment, resulting in less infarct expansion.

New thrombolytic agents are more fibrin specific. They may provide faster and higher rates of coronary reperfusion, resulting in better outcomes.

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Congestive Heart Failure in Myocardial Infarction

Qamar Zaman, MD, FACC

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Rockville Center, New York

The onset of congestive heart failure in a patient with acute myocardial infarction poses a serious therapeutic challenge for the physician and has a direct impact on the patient's

outcome. While mild forms of congestive failure may respond to conventional therapy, in its worst form, cardiogenic shock (CS), it is a harbinger of grave outcome. Despite improvements in the management of acute myocardial infarction (AMI), the incidence of CS and mortality from CS have emerged following aggressive revascularization strategies. Thus, therapeutic options based on early diagnoses may have a positive impact on prognosis and recognizing important predictors of CS in patients with AMI is critical. These include: age >65 years, EF<35%, large MI, diabetes, prior MI, and history of prior CHF or angina. Besides pump failure, it is important to exclude correctable mechanical causes of CS: papillary muscle rupture (10%), ventricular septal rupture (5.1%), LV free wall rupture with tamponade, right ventricular infarction, and hemopericardium with tamponade following thrombolysis. Despite a variety of compensatory mechanisms, a vicious cycle of repetitive myocardial injury leads to a decreasing cardiac output. Invariably, all patients with CS have multivessel coronary artery disease, including thrombotic occlusion of LAD (left anterior descending artery). Clinical signs of hypoperfusion (falling BP, clammy skin, decreased mentation and urine output) and lung congestion may be present to a varying degree. However, it is important to bear in mind that an EKG may remain nonspecific and heart size on chest X-ray may remain normal. Noninvasive assessment of LV function by echocardiography and hemodynamic monitoring allow for rapid assessment of hemodynamic subsets. In the face of a large infarct, elevated filling pressures and falling cardiac output, may respond to aggressive use of vasodilators, inotropes with judicious use of diuretics and ace-inhibitors. These measures are only palliative; however, and precious time should not be lost in the hope of allowing the patient's condition to "stabilize." The use of intra-aortic balloon counter pulsation (IABP) provides a useful increment in cardiac output (20%) by decreasing afterload and augmenting diastolic coronary perfusion. IABP, too, however provides only a temporary palliation. Without specific reperfusion strategies-angioplasty or revascularization, the use of IABP, (with or without vasopressors and inotropic agents) has no effect on mortality or survival. Successful revascularization of the infarct vessel with angioplasty or bypass surgery when performed early (within 24 hours from onset of shock) may improve the short-term and long-term survival of patients after AMI.

21

Atrial Fibrillation in Myocardial Infarction

Abdul Ali, MD, MRCP, FACC, FSCAI

University of Texas Health Science Center
Hermann Hospital
Houston, Texas

In the setting of acute myocardial infarction or following cardiac surgery, atrial fibrillation is a common, but usu-

ally self-limiting, problem. Most patients experience palpitations, but presyncope, dizziness, fatigue, and dyspnea are not uncommon. It is important to control ventricular response during a trial fibrillation to decrease the patient's symptoms as well as prevent a tachycardia-induced cardiomyopathy. Acute rate control is most effective with intravenous verapamil, diltiazem, or beta-blockers. In patients who are hemodynamically unstable, direct-current cardioversion is the treatment of choice. For long-term rate control, verapamil, diltiazem, and beta-blockers are more effective than digoxin and should be the initial drugs of choice. Digoxin should be considered as first-line treatment only in patients with congestive heart failure secondary to impaired systolic ventricular function. In some patients, the combination of digoxin, calcium channel blockers, and beta-adrenergic blockers may be needed to control ventricular response.

Proarrhythmia is the most important risk associated with antiarrhythmic drug therapy in patients with atrial fibrillation. Both bradyarrhythmias, especially sinus bradycardia, and ventricular tachyarrhythmias, especially torsade de pointes, can occur. Proarrhythmia is relatively rare in patients without heart disease, and outpatient initiation of antiarrhythmic treatment is reasonable. Patients with heart disease are most at risk for proarrhythmia, especially those with a history of congestive heart failure. Inpatient initiation of antiarrhythmic therapy is recommended for these patients. The results of the Cardiac Arrhythmia Suppression Trial (CAST) indicate that flecainide should be avoided in the post-myocardial infarction setting. Because of its vagolytic effect and resultant rapid ventricular response, quinidine should not be given without prior administration of agents that slow AV nodal conduction. Many antiarrhythmic agents, especially flecainide and propafenone, may slow the atrial rate, allowing more atrial impulses to be conducted through the AV node, which results in a faster ventricular rate. This situation can be prevented or treated by the addition of agents that slow AV nodal conduction, for example, digitalis, beta adrenergic blockers, or calcium channel blockers. The most common proarrhythmic event reported with antiarrhythmic drug therapy for atrial fibrillation is torsade de pointes, a rapid polymorphic ventricular tachycardia that occurs with agents that prolong ventricular repolarization (QT interval) (e.g., quinidine). Torsade de pointes usually occurs after sinus rhythm has been restored. Thus, for patients at risk, it is recommended that therapy be initiated in the hospital and the patient observed for 24 to 48 hours in sinus rhythm. Low risk atrial fibrillation patients may be given 325 mg aspirin daily to prevent stroke and may be carefully followed unless high-risk criteria develop. This can be strongly recommended for low-risk atrial fibrillation patients younger than 65. For high risk atrial fibrillation patients 75 or younger, an INR range of 2.0 to 3.0 is safe and effective.

22**Prevention of Coronary Artery Disease***Tajuddin Ahmed, MD*

Abstract not available

23**The Middle East and Coronary Artery Disease***Yusuf Goussous, MD*

Abstract not available

Session 7 (parallel) Symposium**Diabetes - Recent Advances in Management**

Sunday, July 27, 1997

8:30-9:45 a.m.

24**Advances in Therapy of Noninsulin Dependent Diabetes Mellitus (NIDDM)***KMM Shakir, MD*

Department of Endocrinology
National Naval Medical Center
Bethesda, Maryland

Although there is a strong genetic component in the causation of noninsulin dependent diabetes mellitus (NIDDM), the genes responsible for this disorder have not been clearly delineated, except for inpatients with maturity onset diabetes of the young (MODY). Glucokinase gene mutations account for more than 50% of all cases of MODY. Mutations involving chromosome 20 q and 12 q also have been described in MODY. In selected families, genetic defects in the insulin receptor, defects in the insulin molecule leading to generation of mutant insulin or a failure to process proinsulin have been described. A variant type of NIDDM characterized by a maternal inheritance has been described. This disorder is associated with a point mutation in the gene encoding tRNA for leucine. This gene is present in the mitochondrial DNA. However these identified mutations account for a small percentage of NIDDM patients.

In obese NIDDM, weight reduction is essential since a major cause of insulin resistance in these patients is increased body fat. Pharmacologic agents such as dexfenfluramine reduce appetite and have some beneficial effects on glycemic control. Leptin, a polypeptide made by adipose tissue, binds to a receptor in the hypothalamus and decreases appetite. Clinical trials with administration of exogenous leptin or analogs of leptin are underway. Regular exercise should be an important part of diabetic management since exercise can increase insulin sensitivity, significantly more than drugs.

Currently available drugs for managing NIDDM include insulin, α -glucosidase inhibitors, sulfonylureas, biguanides

and thiazolidinediones. The α -glucosidase inhibitors (Acarbose) slow the digestion of carbohydrates and are useful to lower the postprandial plasma glucose. Acarbose monotherapy reduces HbA_{1c} levels between 0.5 to 1%. GI side-effects are often bothersome. Sulfonylureas act on the beta cell through a plasma membrane receptor. Sulfonylurea drugs provide adequate control in 50% of newly diagnosed NIDDM and can lower HbA_{1c} by 1.0 to 1.5%. Biguanides (metformin) lower blood glucose by decreasing hepatic glucose production and by potentiating insulin action in peripheral tissues. Biouanides do not stimulate insulin release and are contraindicated in patients who abuse ethanol or with congestive heart failure, renal failure, hepatic or respiratory failure. Thiazolidinediones reduce insulin resistance and decrease hyperinsulinemia. These drugs bind to a nuclear receptor (PPARS) that regulates gene transcription. These drugs lower HbA_{1c} by 0.5 to 0.8% and are most effective in NIDDM associated with insulin resistance states.

The α -glucosidase inhibitors, sulfonylureas, and biguanides require significant endogenous insulin secretion. Since the drugs work through different mechanisms, these drugs can be given in combination. As endogenous insulin decreases in NIDDM patients it may be necessary to eventually initiate insulin therapy. Insulin pumps also have been used recently in selected NIDDM patients. Insulin therapy has the disadvantage of weight gain. Preliminary studies have shown nasal insulin may be useful in selected patients. Lispro insulin is a rapid-acting insulin analog that offers the benefit of a shorter interval between injections and meals and the potential advantages of better postprandial glucose control. The Diabetes Control and Complication Trial demonstrated that compared conventional diabetes therapy with intensive therapy reduced the development and progression of the long-term complication of IDDM by 35 to 75%. Improving glucose control in NIDDM patients to levels similar to those in DCCT may decrease long-term microvascular and neurological complications. Although some preliminary studies show fewer cardiovascular events and diminished mortality in better controlled NIDDM patients, there are currently no randomized studies to support these findings.

25**Management of Stable Type 2 Diabetes (NIDDM) During Ramadan Fasting***Shahid Athar, MD*

Department of Medicine Endocrinology
St. Vincent Hospital and Indiana University
Indianapolis, Indiana

Many adult Muslims suffer from noninsulin dependent diabetes mellitus (NIDDM), the most common form of diabetes mellitus. We consider a NIDDM patient stable when he or she is free of infection, has fasting blood glucose under 150, and a glycohemoglobin (A1C) under 7 (n<6).

We encouraged our Muslim NIDDM patients who weigh 20% above their ideal body weight, whose diabetes is stable, and do not have severe complications like coronary artery disease to fast during Ramadan.

We advised them to be on a 1200 kilocalorie American Diabetes Association diet for their Iftar and Sahoor, to take their oral agent or insulin with Iftar only, and check blood sugar before Isha and Sahoor.

Using this regime our patients were able to fast without any adverse effect on diabetes, with improvement in their blood glucose, HbA1C, cholesterol, and blood pressure with minimum weight loss (< 5 lbs).

26

Prevention of Premature Atherosclerosis in Diabetes

Gildred Colon, MD, FACP, FRCP-C

San Juan City Hospital
San Juan, Puerto Rico

Atherosclerotic vascular disease is a major cause of morbidity and mortality in noninsulin-dependent diabetes mellitus (NIDDM). Cardiovascular (CV) complications in NIDDM are two to six times more frequent than microvascular complications, and more than half of all deaths in NIDDM are due to CV disease.

Intensive management of CV risk factors are the most promising strategies to reduce premature atherosclerosis in NIDDM.

In the case history no. 3, we have a 57-year-old female with six CV risk factors: age, diabetes, obesity, hypertension, high LDL, and low HDL. Despite compliance with diet and exercise, she has gained six pounds. A drop in calories from 1,800 to 1,200 calories per day with a decrease in saturated fats to less than 7% can promote further weight loss. A very low calorie diet (VLCD) might also be tried under medical supervision. Stepping up on her exercise program can also promote more weight loss, emphasizing regular sustained aerobic exercise, which has been identified as one of the factors that can help improve lipoprotein profiles and thus decrease the risk of premature CHD.

Despite the ACEI, the patient's blood pressure still is not optimally controlled (160/90). Optimizing the ACEI and/or adding a Ca⁺⁺ channel blocker would be in order to prevent the risk of cardiovascular accident and also to prevent or delay the microvascular complications of retinopathy and nephropathy. Ideally, the blood pressure should be brought down to 120/80 if the patient can tolerate it or there are no contraindications.

Her LDL cholesterol is dangerously high (120), with a drop to 70 after lovastatin 40 mg qd. According to the National Cholesterol Education Program, the goal LDL in this patient is less than 130. Therefore, more aggressive therapy is mandatory. The saturated fat in the diet can be further dropped as noted above. If a bile acid sequestrant is added

to the regimen, serum triglycerides can further decrease and HDL can drop even further. Instead, due to the fact that this patient has dangerously low HDL, adding gemfibrozil can increase HDL, besides normalizing the mildly elevated serum triglycerides and dropping somewhat the LDL. The mild hypertriglyceridemia also can improve with better glycemic control. Adding metformin to the sulfonylurea can further improve glycemic control, promote weight reduction, and have a positive effect on lipids.

Considering the patient's age and menopausal status, consideration should be given to hormone replacement therapy, keeping in mind the favorable lipid profile and cardiovascular protection induced by estrogen therapy.

Finally, a TSH should be ordered to rule out hypothyroidism, which could explain further the weight gain in this patient compliant with diet and exercise and could explain a secondary hyperlipidemia resistant to conventional therapy.

27

Prevalence of Diabetes Mellitus and Impaired Glucose Tolerance in Jordan

*Kamel Ajlouni, MD; Hashim Jaddou, MD;
and Anwar Batiehah, MD*

The National Center for Diabetes, Endocrine
and Genetic Diseases
Amman, Jordan
University of Science and Technology
Irbid, Jordan

Objectives: To study the prevalence of diabetes mellitus and impaired glucose tolerance and their risk factors in Jordan.

Design: A random sample of 2,836 subjects, aged ≥ 25 years, were studied, applying WHO criteria for the diagnosis of DM (fasting blood glucose more than 7.8 mmol L⁻¹, or 2h PP glucose concentration ≥ 11.1 mmol L⁻¹ after an oral glucose load of 75 gm) and impaired glucose tolerance (fasting blood sugar less than 7.8 mmol L⁻¹, 2h PP glucose concentration between 7.8 mmol L⁻¹ and 11.1 mmol L⁻¹ with normal fasting blood sugar < 7.8 mmol L⁻¹).

Setting: Four Jordanian communities - Sarih in the north, Sikhra in the middle, Mazar in the south, and Subha-Subhieh in the eastern region - were selected.

Results: Prevalence of DM was found to be 13.3%; 14.9% among males and 12.5% among females. IGT was found to be 9.8%; 9.0% among males, and 10.3% among females. Factors independently related to diabetes mellitus, using stepwise logistic regression analysis, were sex, age, family history, hypertension, hypercholesterolemia, and obesity.

Conclusion: Diabetes mellitus and IGT are common among Jordanians. Considering the high prevalence rate makes it mandatory to have a national plan to face this disease and its complications.

Session 8
Al-Rāzī Memorial Lecture
Sunday, July 27, 1997
10:15-11 a.m.

28

**Diabetes and Obesity:
From Genotype to Environment**

Aly A Mishal, MD, FACP

Department of Environment
Islamic Hospital
Amman, Jordan

Diabetes and obesity are serious and costly conditions that extract high tolls on morbidity, mortality, and national expenditures. In countries of the middle east and southwest Asia, the dimensions of these problems have escalated to epidemic dimensions. As more communities acquire urbanized, western-type lifestyles, the prevalence of diabetes, obesity and related ramifications is expected to proliferate, as indicated by many epidemiologic studies over the past decade.

Two recent studies in Jordan showed the prevalence of diabetes and glucose intolerance to be as high as 40% of the adult population, and the prevalence of obesity to be 55% in general adult population, and 75% among adult diabetics. This is not significantly different from epidemiologic studies conducted in other countries in the region or among Asian immigrant minorities in western countries; and is not far away from prevalence reported in the Pima Indian Americans of Arizona. Members of the same tribe living across the borders in Mexico, who have not changed their traditional ways of life, are still protected from the ravages of diabetes and obesity.

Interplay of environmental, socioeconomic, and genetic factors is believed to underlie this growing problem. Evolution of a "thrifty genotype" is postulated to have resulted in a selective survival advantage in times of fluctuating feast and famine. It is thought to allow highly efficient storage of calories in times of plenty. When food supplies become abundant and constant, this genotype becomes detrimental, leading to increased prevalence of diabetes and obesity in certain populations. This hypothesis is applicable to rural and nomadic communities in the middle east and southwest Asia where millennia of poverty and chronic food shortages were followed recently by urbanization, plentiful westernized diets, and sedentary lifestyle.

The dimensions of this problem should make it mandatory to organize major integrated efforts by all health care institutions towards promoting public awareness, and diligent work to curb the alarming trends of westernization in dietary habits and sedentary lifestyles in these communities. The time-honored golden rule in this strife should be: Protection is better than cure.

Session 9 (parallel)
Scientific Papers
Sunday, July 27, 1997
11 a.m. - 12:30 p.m.

29

Brucellosis in Jordan University Hospital

Yousef Ajlouni, MD
Kandil Shaker Shubair, MD, FRCP (ed), M Ed

Jordan University Hospital
Amman, Jordan

Human brucellosis was not recognized as a public health problem prior to 1985, and the number of cases notified yearly was fewer than 10. Awareness of human brucellosis began in late 1985 and after that notification increased from 17 cases during 1985 to 531 cases in 1986, 503 cases in 1987, 463 cases in 1988, and 399 cases in the first seven months of 1989. Most cases occurred during the spring and early summer. This coincides with the breeding season for goats and sheep, the main domesticated animals in the country and with increased consumption of homemade dairy products. More than 70% of the cases occurred in the age group 5-34.

Brucellosis is a major health problem especially in developing countries. *Brucella* species are facultative intracellular microorganisms (coccobacilli). Complete eradication is difficult to achieve and relapses are common. The best regimen for the treatment of brucellosis has not been clearly determined. Common routes of infection include inoculation through cuts and abrasions in the skin or via the conjunctival sac of the eye, ingestion via gastrointestinal tract, and inhalation of infectious aerosols. Brucellosis is a multisystem disease with protein clinical manifestation and can simulate any other disease (it mimics all diseases).

Diagnosis of brucellosis is sometimes very difficult and in endemic areas like Jordan where antibiotics are used inappropriately causing negative serology, physicals have to rely on bedside diagnosis.

We studied prospectively 291 patients between 1986-1996 admitted to Jordan University Hospital in order to find the best way to diagnose and treat brucellosis and to study the presentation and complications of the disease in Jordan. In the presence of symptoms and signs, a titre more than 160 is diagnostic. When the titre is higher the possibility of a positive blood and bone marrow culture is more likely. A titre of more than 2560, noncaseating granuloma of the bone and liver is likely to appear and usually it is diagnostic in cases where the serology is negative.

Serological tests may remain negative despite bacteriological proof of infection.



Appna Sehat - Primary Health Care Model for Developing Countries

Nasim Ashraf, MD

Appna Sehat

Pakistan Rural Health Care Project of the Association of Pakistani Physicians of North America
Roseburg, Oregon

Health care problems in developing countries emerge from inappropriate health behavior. Poor sanitation, lack of safe drinking water, and inadequate disease prevention services such as immunization result in 80% of total morbidity and mortality in these societies.

Appna Sehat is an innovative primary health care model based on community participation, launched in 1989 in four regions of Pakistan. The principal goals of this project are fivefold:

1. To have people improve their health behavior through extensive health education;
2. To reduce morbidity and mortality for the population group at greatest risk;
3. To have villagers identify and solve, to the maximum extent possible, their health problems, utilizing existing resources;
4. To demonstrate how affordable collaboration between public and private sectors can result in marked reductions in serious health problems;
5. To successfully demonstrate a model of sustainable primary health care that could be replicated by institutions and organizations working to improve the quality of life in rural areas of the developing world.

At the very core of Appna Sehat projects is the optimal utilization of local sources. The focus is on preventive and promotional aspects of health care and the creation of health awareness in the community. Since its inception in 1989, this project now serves more than 150,000 people in 35 villages in Pakistan. We have been pleased with the results achieved so far. Some of the highlights are:

Indicators	Appna Sehat	Pakistan
Crude birth rate	28	41
Infant mortality rate (per 100,000)	75	95
Percentage of children under 5 fully immunized	90	65
Percentage of children under 5 moderately or severely malnourished	30	40

Under 5 mortality due to diarrhea as a percentage of total mortality of children under 5 7 30

In conclusion, we believe that the Appna Sehat model can be replicated to achieve similar results obtained in rural Pakistan.



Gene Therapy

Rafil A Dhafir, MD

Clinical Assistant Professor
SUNY Health Science Center
Syracuse, New York

The discovery of the molecular origins of both acquired and inherited disease states and the development of vector systems for the delivery of genetic material into somatic cells have opened the door to the use of bone marrow transplantation for the genetic therapy of human disease. In order to ensure that the genetic modification will be durable in its therapeutic effect on the disease, it is necessary to evaluate the feasibility of modification of the population of cells that have the capability of indefinite self-renewal. In this review, we will summarize the approaches being undertaken to determine if it is feasible to introduce genetic information into such self-renewal cells in the population of bone marrow cells, and if such genetically modified cells can be maintained for long periods of time following transplantation back into the donor. The technology and clinical applications will be briefly reviewed as well as safety issues.



Pros and Cons of Genetic Engineering

Najim A Abdulwahid, MD, PhD

Reproductive Endocrinologist
Islamic Hospital
Amman, Jordan

In this paper I will briefly explain genetic engineering (GE) and how it is done. Accordingly, I will discuss advantages and disadvantages of GE. Some examples of GE advantages include the use of recombinant DNA in the pharmaceutical industries, cancer diagnosis and treatment, and the treatment of the previously untreatable genetic disorders (such as thalassemia). Examples of the GE disadvantages include human research on normal individuals and cloning of human embryos.

It is clear that ethics in this medical practice have to pay attention to the advantages and disadvantages of GE. Moreover, Islam should have its word towards the acceptable advantages in the medical practice. Otherwise, the disadvantages of GE must be known and disregarded.



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33

Hepatitis E Virus: New Insights into Molecular Biology, Diagnostics, and Vaccine Development

Shahid Jameel, MD

Centre for Genetic Engineering and Biotechnology
(ICGEB)

Aruna Asaf Ali Marg
New Delhi, India

Infection by the hepatitis E virus (HEV) is the major cause of acute viral hepatitis in much of the developing world, including India, and results in high morbidity and mortality. A thorough understanding of the molecular biology of HEV as well as the host response to infection will be essential for developing effective diagnostics, vaccines, and therapeutics. I will outline our efforts in these directions.

In the absence of a culture system for HEV, we have expressed the viral structural proteins in COS cells and have studied their properties. The major structural protein, pORF2 is a 88 kDa glycoprotein. PORF2 assembles into high order structures, perhaps aided by the minor structural protein, pORF3. The two viral proteins interact, in their nascent forms. I will present a model of HEV capsid biogenesis.

The diagnosis of HEV infection has moved rapidly since the cloning and epitope analysis of the virus. Still, there are problems of the sensitivity, specificity, and utility of diagnostic tests that should be worked out in the context of endemic areas. I will summarize the available technology, including the one developed by us at ICGEB and discuss some of the practical problems that require attention.

A vaccine against hepatitis E will benefit travelers from nonendemic areas and pregnant women and health care workers in endemic areas. While it may be possible at the present time to develop a short-lasting antidisease vaccine, a better understanding of the system is needed to develop a long-lasting antiviral vaccine. I will present our data on whole virus, recombinant protein, and naked DNA immunization studies.

34

Additive Effects of Inhaled Prostacyclin and Inhaled Nitric Oxide in Reducing Experimental Pulmonary Hypertension in Rats

I Mirza, MD; J Nagamine; and RG Pearl

Stanford University
Stanford, California

Introduction: Inhaled prostacyclin (PGI₂) decreases pulmonary hypertension and reverses hypoxic pulmonary vasoconstriction without adversely decreasing systemic pressures in normal sheep.¹ Inhaled nitric oxide (NO) also pro-

duces selective pulmonary vasodilation. We have previously demonstrated that the effects of intravenous prostacyclin and inhaled NO are additive during experimental pulmonary hypertension. The current study investigated whether the effects of inhaled PGI₂ were additive to those of inhaled NO during pulmonary hypertension in rats.

Methods: Anesthesia was induced in Sprague-Dawley rats with subcutaneous sodium pentobarbital and intramuscular ketamine. Anesthesia was maintained with subcutaneous pentobarbital. A pulmonary artery catheter, carotid artery catheter, and aortic thermistor were placed by neck cutdown. Tracheostomy was performed. Rats were initially ventilated with a neonatal ventilator utilizing continuous gas flow, 40 % FiO₂ 12 cm H₂O inspiratory pressure control, 2 cm H₂O PEEP, and a rate of 35 breaths per minute. Ventilation was adjusted to maintain normal carbon dioxide tension. Following baseline measurements, pulmonary hypertension was produced by the continuous intravenous infusion of the thromboxane mimetic U46619 at a rate titrated to increase pulmonary artery pressure (PAP) to 25-30 mm Hg. During stable pulmonary hypertension, prostacyclin was nebulized into the inspiratory limb of the circuit for one minute using a neonatal Whisper jet nebulizer system with oxygen flow at 8 l/m. Inhaled prostacyclin solution for nebulization was prepared in four concentrations (10, 20, 40, 80 µg/cc) and delivered in random order. Hemodynamic measurements were recorded 5 minutes after PGI₂ administration. After a recovery period of 20 minutes, the same concentration of PGI₂ was studied during INO administration at 100 ppm (verified by a chemiluminescence analyzer). Measurements were made 5, 10, 15, 20, and 30 minutes after administration of nebulized PGI₂ and INO. Statistical analysis was by ANOVA.

Results: Prior to PGI₂, inhaled NO decreased PAP with no effect on systemic arterial pressure, cardiac output, or oxygenation. PGI₂ produced dose-related decreases in PAP with a maximal effect at the 40 and 80 µg/mi concentrations. PGI₂ did not affect systemic arterial pressure, cardiac output, or oxygenation. PAP returned to baseline values within 15 minutes of each PGI₂ dose with no additional prolongation at higher doses. The effects of INO and nebulized PGI₂ were additive at each PGI₂ concentration.

Discussion: INO is increasingly being used to treat pulmonary hypertension, either primary or secondary to various conditions such as ARDS. INO administration is complicated by the need for special equipment for gas administration and scavenging of exhaled gas. In contrast, nebulized PGI₂ administration requires no special equipment and recently has been shown to be of benefit in a small clinical trial.² In the current study, both INO and nebulized PGI₂ were equally effective and selective in decreasing PAP. The combination of INO and nebulized PGI₂ decreased PAP to a greater extent than either drug alone. These additive effects are similar to the those seen in our laboratory when INO is combined with intravenous vasodilators, which act via CAMP (PGI₂ and adenosine but not nitroprusside). The

use of nebulized PGI₂, either alone or in combination with INO, may be effective in the treatment of pulmonary hypertension.

References:

1. Crit Care Med 1996; 24:1841-8.
2. Ann Intern Med 1996; 124:820-4.



Anemia as a Cause of Intolerance to L-Thyroxine Therapy

JC LaRocque, LT Jackson, SA Brietzke, SFW Cavanah, KMM Shakir, MD

Endocrine Division
National Naval Medical Center
Bethesda, Maryland

L-Thyroxine (L-T₄) therapy is generally well tolerated by patients. Patients rarely develop allergy to the coloring agents present in the tablet. Patients with severe hypothyroidism, heart disease, or of advanced age are sensitive to L-T₄. Patients with severe anemia demonstrate increased cardiac output and compromised O₂ delivery. These patients may not be able to tolerate further augmentation in cardiac output when treated with L-T₄. In this regard, we have observed intolerance to L-T₄ therapy in four female patients with anemia. All four patients had an iron deficiency.

Patient Number	1	2	3	4
Age (years)	28	36	21	33
HCT at Presentation (%)	29	26	25	23
TSH (mU/L)	52	68	109	42
Total T ₄ (µg/dl)	3.1	2.6	1.9	2.9

Normals: HCT 34-47, TSH 0.9-4, Total T₄ 4-10

In three patients, the anemia was 2° to menorrhagia, whereas in one patient the cause of anemia could not be ascertained. In patient #1, L-T₄ therapy was initiated at 50 µg qd and three days following therapy, the patient developed severe palpitations and feelings of restlessness. HR at this time was 120/min, and although the L-T₄ therapy was reduced to 25 µg, the patient still refused to take L-T₄ due to symptoms. L-T₄ was discontinued and the patient was treated with ferrous sulfate (FESO₄) for six weeks; then the patient could tolerate L-T₄ (25 µg/day). At the time of reinitiation of L-T₄ the patient's HCT had improved to 33%. Two months later, the patient could tolerate 112 µg L-T₄ with subsequent normal thyroid functions. Patients 2, 3, and 4 although L-T₄ was initiated at a 25 µg daily dose, could not tolerate the hormone because of palpitations and a sense of restlessness. These three patients self-discontinued the L-T₄. Two of these patients could tolerate L-T₄ (25

µg/day) after four weeks of FeSO₄ therapy, whereas patient #4 could tolerate 12.5 µg/day of L-T₄ after three weeks of FeSO₄ therapy. None of these four patients had any evidence of hypoadrenalism. In conclusion, patients with significant anemia may demonstrate intolerance to L-T₄ even in relatively small doses, and this fact should be kept in mind when a patient complains of intolerance to L-T₄.

Session 10 (parallel)
Scientific Papers
Sunday, July 27, 1997
11 a.m. - 12:30 p.m.



The Last Great Race 1,049 Miles Across Alaska by Dog Sled

Norman J Wilder, MD, FCCP, FACP

Internal Medicine Associates, Inc.
Anchorage, Alaska

In 1925, an outbreak of diphtheria occurred in Nome, Alaska. How to transport the lifesaving serum over 1,100 miles of roadless wilderness from Anchorage to Nome? The answer was by dog sled. Now in its 25th running, the Iditarod Sled Dog Race commemorates this historic feat. In 1973, the winner took just a little more than 20 days and won \$1,000. The fastest race was in 1995 with a time of 9 days, 2 hours, and 39 minutes, including a mandatory 24-hour period of rest. The prize was \$50,000. The last musher to cross the finish line receives the "red lantern award." Today it takes \$15,000-20,000 to just run the race. The exact distance is unknown and two slightly different routes are taken on alternating years. It is considered to be about 1,100 miles, but the official distance of 1,049 miles reflects the fact that Alaska was the 49th state admitted to the United States.

The scenery is breathtaking and the challenges immense. Imagine the thrill of crossing one of the last great, isolated frontiers of the world behind a team of dogs pulling a sled with your equipment for sustenance and survival strapped inside. But consider the hours of loneliness and the fatigue. The musher prepares all the food and doesn't eat until the dogs are fed and bedded down. Small amounts of sleep and endless chores are the musher's lot. Think of putting on and taking off many times over the course of the race the individual booties for up to 80 paws! For the racer and the organizational and support personnel, the planning is daunting. How do you prepare for racing checkpoints, food drop-offs, trail preparation, transportation of the many support personnel, and assure the health and safety of the key ingredient of the race ... the sled dogs? How much food is needed daily for up to 1,200 dogs? How are the supplies transported? Of the 1,100 miles of the race, less than 100 are

reached by a connecting road system and that is on the first day of the race! Coordinating all these aspects during the running of the race with the endless number of minor crises keeps a large staff hopping. Planning is a year-round process, however.

Medical problems vary from the mundane to the life-threatening. Sleep deprivation and fatigue are suffered by all the mushers. These effects may lead to poor judgment, which in the context of severe cold (-50 degrees F) and isolation easily can lead to frostbite and hypothermia. Attesting to these severe conditions is the fact that mushers have quit with fewer than 100 miles to go. Carbon monoxide poisoning almost killed several mushers sleeping in a very well-insulated tent in the 1994 race. The dogs are inspected by veterinarians at the start and end of the race and at every checkpoint along the way. Blood samples and urine samples are taken to monitor the general health of the dogs and to check for the possible use of illegal drugs to enhance performance. EKGs are even done! Despite the maximum effort aimed at the health of the dogs, there are occasional deaths. Moose not wanting to give up the trail have resulted in the stomping deaths of several dogs over the years. Heart attacks and congestive cardiomyopathy have led to the deaths of others. Infectious diarrhea and problems with the dog's feet make up the majority of the health problems. The bond between musher and dog is great and any illness or death is mourned like that for a family member. The sled dogs will give their all for a musher they like and know. Several mushers have rented "world-class" teams for the race and discovered that after awhile the dogs refused to obey their commands.

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Can Somatosensory-Evoked Potentials Predict Outcome from Coma?

Iftekhar Ahmed, MD

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Trinity Lutheran Hospital
University of Missouri, Kansas City
Kansas City, Missouri

We report a long-term somatosensory evoked potential recording for two and half years in a patient rendered comatose from hypoxic encephalopathy. We also compared previously published reports on poor outcome associated with bilateral absent cortical responses. In the present case, the patient was admitted with poor neurological status but has preserved cortical responses bilaterally throughout his course until his final recovery back to previous employment. Somatosensory cortical responses when bilaterally absent are universally associated with poor outcome; however, when persistently present can indicate hope of recovery despite poor clinical status on admission.

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Regulation of Angiotensin-I Converting Enzyme Expression in Vascular Endothelial Cells

Khaja Basheeruddin, MD; John Lee

Division of Molecular Diagnostics
Department of Laboratories
Cook County Hospital
Chicago, Illinois

The endothelial cell injury and smooth muscle cell proliferation are implicated as critical events in vascular atherosclerotic and restenotic lesions. Several lines of evidence suggest that the generation of angiotensin II by angiotensin-I converting enzyme (ACE) activity contributes to the vascular response to injury in animals after balloon injury. To gain insight in the regulation of ACE levels and function, we examined expression of ACE after cell injury *in vitro* in cultured human coronary artery endothelial cells. Cells were cultured under normal conditions and injured mechanically by scraping, from the substratum. A reverse transcriptase-PCR analysis was performed to estimate the ACE mRNA levels and corrected with the amplified signal of an internal standard, glyceraldehyde-3 phosphate dehydrogenase. Injuring endothelial cells *in vitro* causes the release of a basic fibroblast growth factor (bFGF)-like activity and increases endothelial ACE mRNA levels two-to-three-fold. Using a bFGF-antibody in the conditioned medium from injured cells blocks the increase in the ACE mRNA, suggesting that the increase is mediated by BFGF. In addition, human recombinant BFGF also increases endothelial ACE mRNA levels two-fold in a concentration and time dependent manner. These data indicate that BFGF-stimulated ACE expression in vascular endothelial ACE and such regulation could significantly increase the amount of ACE in mechanically injured arterial endothelial cells.

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Treatment of Post-Transplant Erythrocytosis with Enalapril

N Akash; I Smadi, MD; M El-Lozi

Nephrology Department
King Hussein Medical Center
Amman, Jordan

Objectives: This study was carried out to estimate the efficiency and safety of Enalapril therapy of post-transplant erythrocytosis and to establish the mechanism by which Enalapril reduces red cell mass.

Materials and Methods: 13 long-term renal allograft recipients with increased hematocrit values (>51%) and elevated red cell mass were treated with Enalapril for 12 weeks. There were 11 males and 2 females aged from 18-54 years.

Results: After 12 weeks of therapy, mean hematocrit values decreased from 53.9% to 46.7% and red cell mass significantly decreased from 50.8 ml/kg to 40.5 ml/kg. During the following six months without Enalapril treatment, an increase to hematocrit was noted reaching 47.5%.

Conclusion: Erythrocytosis after kidney transplantation is relatively common, occurring in up to 15% of patients. It is a heterogeneous condition and several mechanisms are involved in its pathogenesis.

Enalapril can be safely and efficiently used to treat post-transplant erythrocytosis.



A Comparison of Different Cytopreparatory Microscopic Slides and Fixation for Fine Needle Aspiration Biopsy Optimization

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Russell M Fiorelia, MD, MBA*

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Fine needle aspiration has proven efficacy in the evaluation of palpable and nonpalpable lesions in many anatomic locations. Variable factors regarding optimization for accurate diagnosis include operator educational training, cytopreparatory technique, and cytopreparatory supplies, including microscopic slides and fixatives.

We performed 100 fine needle aspiration biopsies from autopsies and surgical pathology specimens in order to compare cell retrieval using plain, charged, fully frosted, and albumin coated microscopic slides. Optimum cell preservation was determined using alcohol, spray and Carnoy's fixatives. All cases were stained with Papanicolaou stain except air dried smears that were stained with Diff-Quick. Each case was evaluated on a scale of 0-3+ in regards to cellularity, nuclear and cytoplasmic preservation, and smear background.

From our data, it appears that cellularity was maximized for air-dried and albumin-coated slides. Cytoplasmic preservation was maximized using charged slides that were alcohol-fixed or air-dried. Nuclear preservation was maximized with charged slides that were alcohol-fixed. Smear background was best assessed with slides treated with Carnoy's fixative. Lastly, cell retrieval for fatty aspirations was maximized using albumin-coated slides.



Adult Respiratory Distress Syndrome in AIDS Patients

*Abida K Haque, MD; Patrick A Adegboyega, MD;
Adekunle Adesokan, MD*

Department of Pathology
University of Texas Medical Branch
Galveston, Texas

Adult Respiratory Distress Syndrome (ARDS) is characterized by acute, sudden respiratory failure associated with diffuse lung infiltrates on chest roentgenogram. ARDS is reported to be one of the leading causes of death in HIV-infected patients. The prevalence and clinicopathologic correlations of ARDS in AIDS are, however, not well studied.

Study Design: We retrospectively reviewed the medical records, autopsy protocols, and glass slides of 196 consecutive HIV-infected/AIDS patients who were autopsied at our institution between January 1987 and December 1992. The results of antemortem broncho-alveolar lavage (BAL), antemortem sputum and blood cultures, postmortem lung and other cultures were examined. The incidence of pulmonary infections and ARDS was documented and all special stains on the antemortem and postmortem pathology material were reviewed as necessary.

Results: ARDS was present in 63 (34%) of the 196 patients. There were 60 males, 3 females; 24 were black, 32 were Caucasian, and 7 were Hispanic. The patients ranged from 21 to 63 years. The most common lesion in the lungs with ARDS was an infection with *Pneumocystis carinii* pneumonia (PCP). This was seen in 37 of 63 patients (55%). In nine of these patients, PCP was the only pathogen. Other infective agents included Cytomegalovirus (20/63; 30%), fungi (16/63; 24%), gram-negative bacilli (14/63; 20%), and mycobacteria (12/63; 18%). *Pseudomonas* species were the most common gramnegative bacilli, while candida was the most common fungus cultured. Some patients had more than one pathogen.

Conclusions: ARDS is a frequent pulmonary complication in HIV-infected/AIDS patients and thus responsible for the terminal respiratory failure seen in a large number of these patients. While ARDS in immunocompetent patients is usually secondary to noninfectious acute lung injury, ARDS in AIDS patients is almost always of infectious etiology. *Pneumocystis carinii* is the most frequent etiologic agent, followed by cytomegalovirus. Then findings have therapeutic implications in AIDS patients.

42**Cardiac Echinococcosis***Sami Kabbani, MD; Aref Sandouk, MD;
Fawzi Nabhani, MD; Hisham Jamil, MD*

Damascus University Cardiovascular Surgical Center
Damascus, Syria

Between Jan. 2, 1989, and July 13, 1996, nine patients with cardiac echinococcosis were surgically treated at Damascus University Cardiovascular Surgical Center. Five were female; ages ranged between 8 and 57 years. Diagnosis was suspected or established before operation by serology, echocardiography, and cardiac catheterization.

The cysts were located in the right atrium (1), left atrium (1), left ventricular wall (3), interventricular septum (2), right ventricular outflow tract (1), and pericardium (1).

All cysts were successfully removed under cardiopulmonary bypass. Two cysts were infected; one cyst was managed by injection of hypertonic saline and evacuation of contents; and six cysts were enucleated intact.

Patients with systemic hydatidosis were discharged on mebendazole.

We believe where hydatid disease is endemic, cardiologists and cardiac surgeons should retain a high index of suspicion with regard to cardiac echinococcosis, which is a potentially fatal disease. Early surgical removal under cardiopulmonary bypass is recommended for cure or palliation, especially now that effective anthelmintic therapy is available.

Session 11 Symposium**Medical Education**

Monday, July 28, 1997
7:30-10 a.m.

43**Postgraduate Medical Education
in a Developing Country
with Limited Resources***Zarina Muzaffar, MD*

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Islamabad, Pakistan

Pakistan is a developing nation with a population of 140 million people. The rural-to-urban ratio is 70:30, and the per capita income is \$500. Medical care is primarily available in the cities with big hospitals. All of the care centers and hospitals affiliated with academic medical institutions are owned and run by the government of Pakistan; the Aga Khan University Hospital is the only notable exception in the private sector. Since medical care is free at these government institutions, the hospitals are overcrowded and underfunded. Eighteen undergraduate and seven postgraduate institutions are registered with the Pakistan Medical and

Dental Council (PMDC), which is the regulatory body overseeing licensing and credentialing. There are 7,000 physicians registered with the PMDC as specialists. Of these, 30% have a major postgraduate qualification obtained either in Pakistan, the United Kingdom, or the United States. The College of Physicians and Surgeons of Pakistan has certified 1,543 specialists during the last 30 years. The majority of these specialists are working at the teaching institutions, a far smaller number at the secondary health level, and none in the rural areas.

Though some of the academic institutions are more than a hundred years old with a rich tradition in undergraduate education, the concept of structured postgraduate training culminating in a unified certifying exam is new and has evolved only in the last decade. The volume of clinical material in the busy tertiary care centers is tremendous, and trainees are exposed to an extraordinary variety of medical problems. Communicable diseases, infections, nutritional disorders, hereditary and metabolic diseases, along with maternal and child health problems, constitute the bulk of patients seeking care. The teaching faculty at most institutions is well trained and highly qualified in the primary clinical fields, but there is a definite paucity of physicians in the subspecialty fields and a glaring deficiency in the fields of diagnostics and the basic sciences. Several of these fields could use help from abroad to train and develop them. As medical technology advances and become more expensive, the centers lag behind not only in acquiring the equipment but in attaining the technical skills to use it.

Working in these circumstances is extremely challenging. One sees patients at all stages of the natural history of disease, with all the ramifications of the ensuing complications. One learns to be cost effective due to the financial limitations; clinical diagnostic skills are perfected to counter the lack of sophisticated technological aids. Legal issues are nonexistent, and yet one teaches medicine to be practiced professionally and ethically. Training programs must, therefore, be developed within these constraints. The vast difference between the two worlds of West and East affords a unique opportunity. We have much to learn from each other, and an exchange at all levels of medical education will be mutually beneficial and intellectually stimulating. For indeed, the ultimate goal in the practice of medicine is the same everywhere: to heal and to comfort the sick and the suffering.

44**Clinical Postgraduate Training Programs
The Aga Khan University Experience***F Moazam, MD*Postgraduate Medical Education
Aga Khan University
Karachi, Pakistan

Background: Pakistan, with a population of about 130 million people, mostly rural, graduates approximately 4,000 students from its 18 medical colleges each year. Several hundred leave for the United Kingdom and the United States, and many do not return. One of the factors contributing to this is a dearth of high standard postgraduate training programs in the country. The Aga Khan University (AKU) and its Faculty of Health Sciences was the first private university in Pakistan to be awarded an independent charter in 1983. In 1986, the Aga Khan University Hospital (AKUH) initiated the first structured residency program in the country in general surgery, based on a North American model with appropriate modifications to make it relevant to the needs of Pakistan. In 1995, following approval by the Board of Trustees, all residency programs were shifted from AKUH to the purview of AKU to strengthen their educational components. The programs now are overseen by a Postgraduate Medical Education Committee (PGMEC) of the university.

Current Status: At this time, AKU offers training programs in the clinical disciplines of anesthesia, community medicine, family medicine, neurology, pathology, radiology, urology, general surgery, internal medicine, obstetrics and gynecology, orthopedics, adult cardiology, and pediatric surgery. Approximately 120 young men and women currently are enrolled in these programs. Training programs are anticipated in neonatology, gastroenterology, psychiatry, and gynecological oncology. All residency programs are approved by the College of Physicians and Surgeons of Pakistan and some by the Royal Colleges of the United Kingdom.

Early Results: Since 1991, AKU has graduated 118 residents from its programs. A significant number (68.6%) are practicing in Pakistan. Some are on the faculty of AKU and others are on the staff of various teaching institutions in the country. The first formally trained anesthesiologist in a small town in Punjab and the first gynecologist in the remote northern areas of Gilgit and Chitral are graduates of AKU. There is evidence therefore that AKU is beginning to make an impact on the health care systems of Pakistan.

Future Challenges: These include: 1. raising the standard of programs to international levels to attract top graduates and prevent brain drain. 2. Ensuring a balance between educational and service components of training. 3. Providing an atmosphere that fosters and assists research and scholarly work. 4. Instituting linkages with national and international programs of repute for mutual benefit.

45**Educational Needs in Jordan***Lekha Pathak, MD*

Abstract not available

46**Overview of Medical Education in Jordan***Kandil Shaker Shubair, MD, FRCP(Ed), M Ed*Jordan University Hospital
Amman, Jordan

This paper is primarily descriptive and aims to set the stage for a mutually beneficial collaboration with the American College of Physicians, the Islamic Medical Association in America, the Jordan Medical Council, and the two medical schools in Jordan. It will present a brief overview to the social, economic, and medical education in Jordan and will describe the existing medical agencies in the country that provide the population, including the private sector, with the needed health care.

The possible areas of cooperation will be highlighted in terms of undergraduate and postgraduate medical education. The existing limitations, difficulties, and handicaps of medical education and practice will be discussed, and personal proposed solutions will be presented, based on many years of involvement in medical education, practice, and a general Jordanian perspective.

47**International Physician Exchange Program***Shahid Siddiqui, MD*

Abstract not available

48**Preparing Medical Students for a
Rapidly Evolving Diverse Ethnic Population
in the United States:
Experience of a Unique Curriculum
at Ohio State University, College of Medicine***Malika Haque, MD, FAAP*Pediatrics and International Health
College of Medicine
Ohio State University
Columbus, Ohio

Islam is a rapidly growing religion in the United States, with a population estimated at more than 8 million. For understanding Islam and Islamic culture, removing misconceptions that prevail, acquiring knowledge, developing cultural awareness and sensitivity with appropriate skills in the management of Muslim patients, a course titled "Islam and

Medicine" was successfully introduced to first year medical students in the Behavioral Science Program at Ohio State University, College of Medicine, in 1996. It is a three-hours a week, four-week course in the following format:

Week 1: General discussion on Islam, distribution of Muslim population in the United States and across the world, definition of Islam, Islamic greetings, glimpses of mosques as places of worship in the United States and across the world, and the relationship of science and Islam.

Week 2: Discussion of basic beliefs, the five pillars of Islam, moral values in Islam, impact of Islam on physical, spiritual and emotional health, and social well being of an individual.

Week 3: Discourse on Islamic Law, Islamic beliefs in raising children and family values, marriage, divorce, and what is prohibited in Islam. How does Islamic culture vary in different parts of the world?

Week 4: Expectations of Muslim patients from the physician, skills useful in the management of Muslim ambulatory, hospitalized and critically ill patients, and Islamic perspectives on euthanasia and medical ethics. Lectures, guest speakers, slides, and videos are modes of presentation ensuring lively discussions. Student evaluation was excellent and the course is now an ongoing part of the curriculum. The successful introduction of this course at Ohio State University, College of Medicine, should clearly provide sufficient incentive to physicians and other health professionals to make similar efforts in their respective universities and hospitals for students and staff education. It is a much needed course at the professional level, resulting in better management of Muslim patients.



Internal Medicine Training in a University-Affiliated Residency Program in the United States

Robert B Gibbons, MD, FACP

Denver, Colorado

The Saint Joseph Hospital Residency in Internal Medicine is a medium-sized training program that utilizes the resources of a large tertiary community referral center (Saint Joseph Hospital), a university medical center (University of Colorado Health Sciences Center), a large health maintenance organization (Kaiser Permanente), and private physicians' offices. The program includes two tracks: a one-year preliminary track, which prepares 10 residents for further training in other specialties requiring an internship and a three-year categorical track that prepares eight residents to practice general internal medicine or continue into subspecialty fellowship training. All first year residents are selected through the National Residency Matching Program and must have graduated from a medical school in the United States or Canada or have been a student or resident teaching hospitals in the United States. The institution also trains

residents in general surgery, obstetrics and gynecology, family medicine, and emergency medicine.

During their first year, residents spend nine months on inpatient services, which include general medicine, oncology, coronary care, and intensive care units. One month is spent in a large metropolitan emergency room, and two months are allowed for electives in any discipline. The elective time may be spent in research or in locations outside the city or the country. Each resident also works one half-day each week in a general medicine continuity care clinic.

During years two and three, residents spend approximately half of their time supervising interns and medical students in the inpatient services noted above. The remaining 50% of the time is spent on subspecialty and primary care electives, which are primarily devoted to outpatient and consultative care of patients. These rotations are conducted at both Saint Joseph Hospital the University of Colorado Health Sciences Center and Kaiser Permanente clinics. For additional general medicine/primary care training, residents may select sites at Indian Health Services, rural offices, inner city clinics, or managed care clinics. Residents have also had overseas experiences in England, Switzerland, Russia, Central America, and Africa. In inpatient services, second and third year residents supervise first year residents and third and fourth year medical students. These services or teams are supervised by full-time or volunteer faculty members at Saint Joseph Hospital. Third year medical students are restricted to those from the University of Colorado Health Sciences Center, but fourth year students come from throughout the United States and Canada.

Didactic conferences include a daily morning report and a primary care or subspecialty curriculum conference. Grand rounds, Clinicopathologic Correlation Conference, Morbidity/Mortality Conference, Tumor Conference, EKG training, and Journal Club also are conducted throughout the month. Categorical residents are expected to present a seminar and are encouraged to conduct a clinical research project during their training. Residents are expected to take the certifying examination of the American Board of Internal Medicine immediately following their training. All faculty members are certified by the American Board of Internal Medicine and its subspecialty boards where appropriate. These physicians also serve on the clinical faculty at the University of Colorado School of Medicine. All full-time faculty members are members or fellows of the American College of Physicians.



Residency Training of Internists in the Military

Capt Angeline Lazarus, MC, USN, FACP, FCCP

Department of Internal Medicine
National Naval Medical Center
Bethesda, Maryland

The mission of the medical command of the U.S. De-

partment of Defense is to ensure the health of our active duty forces so that they are physically and mentally ready to carry out their worldwide mission. This we accomplish with a comprehensive health program and, when illness or injury intervenes, restore optimal health. We also provide this same level of quality health care services to the families of active duty members, retirees, and to all others entrusted to our care. Hence the goal of the military medicine curriculum for physicians in graduate medical education programs is to make the military physician aware of those aspects of practice that are unique to the military both in combat and peace time and to keep their medical readiness enhanced for combat deployment and humanitarian mission. The curriculum should enhance the knowledge, skill and attitude of military physicians preparing them to function in the field during war and humanitarian missions with high proficiency and efficiency. Physicians, irrespective of specialty, are vital members of the combat casualty care team. The curriculum will prepare primary care specialists to accept responsibility for the nonsurgical aspects of combat deployment and the surgical specialists to acquire the knowledge and skills required for wartime. The curriculum of internal medicine residency training in the military has three components casualties: 1. a basic military medicine course, which is given to all the physicians in the military. 2. specialty-based training, which contains the specialty curriculum as outlined by the residency review committee and military specific internal medicine, and 3. Unit-based medicine, which includes site-specific medical unit training such as hospital ship, field hospitals, and clinics. The training in military hospital provides population-based training.

The basic military medicine course will include training to provide knowledge and management skills in: 1. Combat-related injuries. 2. Field laboratory and X-ray procedures. 3. The principles and decision-making on returning casualties to duty. 4. Common infectious diseases worldwide and prophylaxis, immunizations, and sanitation in the field. 5. Lightning-related injuries, drowning, near-drowning, injuries of snake, insect, marine and animal bites and stings. 6. Stress in combat and support units. 7. Echelons of medical care, patient evacuation, and transportation and 8. Ethics of combat casualty care, triage of war casualties, communication with operational commanders. The internal medicine resident should demonstrate knowledge and skills in managing critical care units, nonacute common and combat-related illnesses, communication skills with local medical authorities, initial psychiatric evaluation and treatment, hypo- and hyperthermia-related illnesses, blunt trauma injuries, and nuclear, biological and chemical (NBC) warfare-related injuries. They will acquire technical skills such as intubation, peritoneal dialysis, tube thoracostomy, vascular access, thick and thin blood smears, identification of malarial infection, and minor orthopedic injury management skills. They will require certification in advanced trauma life support, training in tropical medicine, and NBC medicine course. Unit-based training includes orientation to the medical unit,

equipments, communication channels, and policies unique to their platform.

The uniform worn, individual physical fitness, the camaraderie during training and beyond, the discipline of observing authority and leadership, and the skills to effectively interact with local health authorities distinguish the military residents from their civilian counterparts. The effectiveness of our training is readily assessed by observation of their performance after graduation, being assigned to various military platforms and hospitals both within and outside United States. Their performance in American Board of Internal Medicine boards reflects the strength of their clinical competency. The nonmedical and medical military medicine training woven with internal medicine residency training prepare them to function as a team in the combat medical units with courage and confidence and carry out the mission to preserve the wellness and morale of deployed force.



International Health and Medical Education

John Noble, MD

Abstract not available

Session 12

Ibn Sīnā Memorial Lecture

Monday, July 28, 1997

10:15-11 a.m.



Ibn Sīnā and the 21st Century

John Noble, MD

Boston University School of Medicine and
Center for Primary Care
Boston, Massachusetts

Change has been present throughout medical history. There are certain times, however, when changes have occurred at an accelerated rate. Cultural, political, and scientific revolution have introduced sudden and dramatic changes in the knowledge and practice of medicine. Such changes took place during the times of Aristotle, Ibn Sīnā, and William Osler, roughly 2,000, 1,000, and 100 years ago, respectively. Each of these men was a physician, an observer, and a scholar who studied and interpreted nature, the institutions, and traditions of their times. Their contributions have served as the foundation of modern society, science, and medicine.

Standing on the threshold of the 21st century and third millennium, we, too, are confronted by challenges of transition, creation, the interpretation of new medical knowledge, and the preservation of the traditions of professional service and excellence.

The forces raged against us, outside of the domain of the profession; politics and wars, strife, and natural disaster

are unchanging. It is the forces within the professional domain on which we must focus most intensively. The three major forces reshaping medicine at the present time are:

1. The discovery of the molecular and genetic basis for pathophysiology,
2. The corporatization of medical practice
3. Global informatics and the world wide web.

In the midst of these changes, will we be able to continue the traditions of quality in health care for all who will soon be living in the global village of the internet? Or as Umberto Eco presaged, will medicine languish in the coming of a new middle ages dominated by the politics of the revolutionary right, geographic isolation, unstable economics, regional conflicts, and intolerance?

Ibn Sīnā (980-1038), the physician, poet, codifier of medicine, and scholar lived in a time of major geographical upheaval. He strove to preserve the knowledge and medical traditions of Greece, Rome, Mesopotamia, and Egypt. His canon entitled *Principles of Arabic Medicine* was intended to serve as an 11th century *Index Medicus*. His definition of the profession included not only the pursuit of science and of the practical art, but also encompassed worldly motives, devotion to fellowman, and devotion to God.

The religious and cultural tolerance of the Arabic renaissance was critical to Ibn Sīnā's success. Scientists did not perpetuate science alone in the following centuries. During the counterreformation, Thomas Aquinas, Erasmus, Milton, and artists including Leonardo de Vinci and Michelangelo opened up discourse on rational scientific topics and ensured the publishing of science and anatomical studies all within the contest of conservative Christian beliefs.

In 1997, it is our responsibility to meet the challenges of the current day and build a foundation for medicine in the 21 century by synthesizing the best of medical knowledge and clinical practice to ensure the continuation of quality care and the highest of ethical standards. In the traditions of Aristotle, Ibn Sīnā, and Osler, we must delineate principles for the care of the patient, the conduct of practice, and the integrity of the profession. To attain their levels of success, we must advocate for access to care for all, the empowerment of the individual, and the incorporation of the best evidence into world wide clinical practice. Our success will be determined by our tolerance and inclusiveness of all people, by our caring for our patients as individuals, and our ethical conduct.

Session 13
Scientific Papers
Monday, July 28, 1997
11-12:30 a.m.



Medical Ethics - An Islamic Perspective

Shahid Athar, MD

Indiana University School of Medicine
Indianapolis, Indiana

With the advancement of medical technology, new questions and issues are being raised in the areas of artificial life support, brain death, euthanasia, assisted suicide, abortion, assisted reproduction, surrogate parenting, and care of AIDS patients.

Muslim patients and physicians cannot remain aloof in such issues affecting general population. Even if they are not involved, they may be asked to give an Islamic perspective. All these issues are discussed in the light of Qur'ān, the Sunnah, and contemporary knowledge of medicine.



Medical and Scientific Verses ('Āyāt) in the Glorious Qur'ān

Mohammad Jamil Al-Habbal, FRCP (London)
Mekdad Al-Juwarey, PhD (Wales)

Mosul Teaching Hospital and College of Science
Mosul University
Mosul, Iraq

There are many 'Āyāt (verses) in al-Qur'ān Al-Karīm that deal with different branches of medicine and cosmic sciences. In this work, we have reviewed and classified them according to their topics and also studied the rationale behind their recurrence in this glorious book. The results were as follows:

1. The number of 'Āyāt that refer to medical and cosmic sciences are about 1200 'Āyāt (nearly 20% of the total number of 'Āyāt in al-Qur'ān al-Karīm, which are about 6236 'Āyāt. The majority of the studied 'Āyāt (about one-third) refer to different medical themes.

2. There are about 70 'Āyāt that praise science and scientists and encourage them to be involved in discovering the universe for the good of humanity. As a matter of fact, the first five 'Āyāt revealed to the Prophet Muḥammad (PBUH) ordered him to read and learn ('Āyāt 1-5/al-'Alaq).

3. The 'Āyāt studied were categorized according to their scientific topics - medicine, physics, biology, astronomy, geography, agriculture, mathematics, statistics, geology, seas and rivers, transportation, origin of man and others, engineering, chemistry, language of birds and animals - and numbered. Finally, there were more than 20 'Āyāt that are applicable to all mentioned and/or other sciences. These are about

170 'Āyāt mentioned repeatedly in more than one scientific topic as they include more than two scientific subjects. For example, 'Āyah No. 164/al-Ḥagarh and 'Āyah No. 5/al-Ḥajj.

4. It was understood from the above study (Allāh knows best) that the reasons for the recurrence of those 'Āyāt are to achieve the following:

a. To support the six principles of 'Īmān (faith), especially the 'Īmān in Allāh-almighty (SWT) and the Day After ('Āyah 136/al-Nisā'). It was found that there is a strong correlation (about 92%) between such 'Āyāt and these principles of 'Īmān as follows: 'Īmān in Allāh (SWT), 738 'Āyāt; 'Īmān in Angels, 24; 'Īmān in Holy Books, 53; 'Īmān in Messengers, 100; 'Īmān in the Day After, 120; 'Īmān in Destiny, 30 'Āyāt.

c. The scientific unprecedent: to stimulate thinking and research in order to discover more about the universe ('Āyah-114/Tāhā).

d. To express the power and the mercy of Allāh (SWT) and his unique creations and numerous favors to mankind, 'Āyāt 20-24/al-Mu'minin, 'Āyah 18/al-Nahl).

This study showed that the Qur'ān is mainly a book of faith and guidance. It also encourages science and research. We recommend that this approach can be taken in consideration as a useful practical outline to be followed in designing future programs in education, teaching, and research.

Two computer diskettes are available for demonstration to show the studied verses and the above-mentioned results.



Sufism and Modern Psychotherapy: A Comparison

Abdul Basit, MD

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Though during the past two decades a massive amount of research has been done on the efficacy of psychotherapy, the recent CR Study (1995) is considered most exhaustive and unimpeachable. Unfortunately, the results of this study raised more questions than answered. In his review, Hans H Strupp (1996) stated: "The problem of evaluating outcomes from psychotherapy continues to bedevil the field as it did a century ago when modern psychotherapy came into being." But in our search to have well qualified healers to help the "disturbed" people, we forgot that for thousands of years religious mystics have successfully used various techniques to modify peoples' behavior. This presentation will focus only on sufis (Muslim mystics). Sufism is little known in the Western world, especially in the field of psychiatry, and what is known is a rather distorted version of sufism. Sufis gained worldwide recognition by showing how to gain peace and tranquility and attain deeper insights by "unsealing the soul." With the help and guidance of these sufis, many criminals, drug addicts, and people riddled with guilt, anxiety,

and depression have gained peace by purification of the soul and untying of spiritual knots. Any technique that helps individuals to ease pain, gain peace and tranquility, unlock the secret doors of the inner self and empower themselves to achieve their potentials must be compared with modern techniques that claim to unlock complexes, untie psychic knots, and change maladaptive behavior patterns. Exposure to nontraditional methods and techniques, such as sufism, provides us with valuable information that for centuries has been the occupation of the best minds of the East. The comparison of these approaches brings out many hidden and important aspects of both, and it also reveals how Eastern and Western psychotherapies can fertilize each other. It may compel us to reexamine current methods and systems and develop, if possible, new and creative ways of helping "disturbed" people.



Current Ethics in Medical Practice and Islam

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Ethics have been changing with the advancement of medical knowledge. The ethics applied in the western society are far more extreme than in the Islamic world. In this paper, I will discuss two issues: The first concerns the real practice in the Islamic world of many medical procedures, in which Islam opposes without being noticed. Examples of such procedures include tubal ligation, freezing sperm, and freezing embryos. The second issue concerns many other medical procedures that Islam prohibits, yet have been practiced in the non-Muslim world. The said procedures are commonly exercised on Muslims without their knowledge or consent. Examples of these procedures include sperm, ovum, and embryo banking, which are subsequently used as a commercial business.



Historical, Socioreligious, and Medical Aspects of Clitoridectomy

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and Musa H Awan*

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Purpose: Referring to ritual clitoridectomy, known as female circumcision or female genital mutilation (FGM) in the popular media, an author stated in a recent issue of the *New Physician*, the official publication of the American Medical Students Association, that "the reasons for the practice's endurance include Islam...." Out of concern for the anti-Islamic effect this erroneous assertion in a publication aimed at the medical students could have on the would-

be physicians prompted a study to establish historical facts about the female circumcision.

Materials and method: The historical, medical, and religious literature related to the subject, some dating as far back as 12th century, was carefully reviewed. The views and, where possible, formal decrees of modern Islamic scholars concerning female circumcision were collected for overall analysis and conclusion.

Results: Female circumcision was practiced by the ancients, Egyptians, Abyssinians, etc., thousands of years before the emergence of Islam. Also, according to at least one source from the 12th century, it was practiced by the ancestors of the Jews and, according to a more than hundred-year-old American source, circumcision also is imposed on women by some Christian churches. Of all the material reviewed or sources consulted, none confirmed or even suggested that ritual clitoridectomy, unlike male circumcision, is or has ever been a required practice in Islam. On the contrary, the evidence is present that Prophet Muḥammad (PBUH) advised those few tribes who had been practicing it as a cultural and ancestral tradition since pre-Islamic times to avoid cruelty and mutilation.

Conclusions: 1. Female circumcision is an ancient custom that began and was practiced thousands of years before the appearance of Islam. 2. There exists at least some literary evidence that the ancestors of the Jews practiced it. 3. Some earlier American sources categorically declare that some Christian churches imposed it on women. 4. Although male circumcision is practiced by Muslims, female circumcision is not and has never been required in Islam. 5. Wherever it is practiced in the isolated patches of some Muslim countries, it actually is practiced because of the local customs and cultural traditions of the people of that area. 6. If one is, nonetheless, determined to seek a religious connection for it, one is likely to find a firmer support for this in Christianity and the Jewish traditions than in Islam. 7. However, therapeutic clitoridectomy for hyperplasias and tumors of the clitoris was, indeed, described in 10th century by the famous Muslim surgeon 'Abul-Qāsim al-Zahrāwī (Abulcasis). 8. Associating of ritual clitoridectomy with Islam is unfounded, and any continued publication of this assumption a disservice to ethical reporting.



**Investigation of Human Rights Violation:
Genocide in Bosnia**

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Pathology (Forensic Pathology)
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The paper will present a succinct definition and concept of human rights as understood by the United Nations and will relate these to the Islamic concept of human rights

and their violation.

It also will discuss the overall role of physicians in both monitoring and evaluating physical violations of human rights when they occur as well as present the concept of team approach in studying genocide. Finally, it will provide scientific evidence to support the occurrence of genocide in Bosnia and will discuss the findings of a mass grave at Ciserska for the victims of the fall of city of Srebrenica, a United Nations "Safe Haven," in July 1995.



**The Effect of Economic Sanctions on
Operative Complications in Iraq**

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Factors associated with the development of postoperative complications are well documented in the literature. However, national and international factors also can be important in this aspect. The economic sanctions on Iraq, which have been exposed since 1990, have greatly raised the incidence of operative and postoperative complications in Iraq.

In this paper, I am going to discuss the different complications we faced mainly due to the economic sanctions from January 1992 to January 1997 and compare the results with the presanction era, as well as factors affecting these complications that were documented in this literature.

**Session 14 (parallel)
Scientific Papers**

Monday, July 28, 1997
2:45-4:15 p.m.



**Botulinum Toxin A:
A Blessing for Patients with Dystonias**

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Michigan State University
College of Human Medicine
Kalamazoo, Michigan

Botulinum Neurotoxin Type A (BTx) recently has emerged as an effective and safe treatment for focal and segmental dystonias including graphospasm (writer's cramps). Until its advent, most of the dystonias were refractory to medical therapy. This is yet another testimony to the Prophet's (SAS) saying:

"Allāh has sent down both the disease and the cure and He has appointed a cure for every disease."

In an office setting, 24 consecutive patients with dystonias and other muscle spasms (cervical dystonia, dystonic writer's cramps, blepharospasm, hemifacial spasm, and spasticity from multiple sclerosis) received lyophilized Btx after careful selection of muscles, some requiring electromyographic guidance. The response to treatment with relief of dystonia/spasm and associated pain varied from immediate to a peak effect at two weeks after injection. There were no untoward effects noted. The current experience regarding the dramatic response of dystonias and other muscle spasms to this treatment modality will be discussed.

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Malignant Lymphomas in Al-King Hussein Medical Center

Khalifeh Omari, MD; Marwan Akasheh, MD; Feik Madanat, MD; Ahmed Othman, MD; Naeif Hababben, MD; Yousef Fraihat, DN; Ali Zgoul, DN

Department of Medicine, Hematology/Oncology Division
King Hussein Medical Center
Amman, Jordan

Objectives: The aim of this study was to analyze the pattern of malignant lymphomas in Jordan.

Material and Methods: A prospective study of 93 patients with malignant lymphomas, who were diagnosed between the period of January 1996 and January 1997 at King Hussein Medical Center (KHMC) Hematology/Oncology Clinic in Amman.

Results: Non-Hodgkins lymphoma (NHL) was the most common type of lymphoma (52 cases vs. 41, 55.9% vs. 44.1%), with a higher median age at presentation (54 years vs. 30 years) than Hodgkin's disease (HD). The male-to-female ratio showed a male preponderance in NHL (1.36:1), and was equal for HD. The most common NHL was diffuse large cell (42.3%), followed equally by large-cell immunoblastic (15.4%), and small lymphocytic (15.4%). The histopathologic pattern was diffuse in (90.4%) and follicular in (9.6%). Extranodal lymphomas (ENL) were present in 25 cases (48%), with gastrointestinal tract being the most common site (44%).

Immunoproliferative small intestinal disease (IPSID) was diagnosed in a single case.

In HD, nodular sclerosis was the most common type (51.2%), followed by mixed cellularity in 26.8%.

Advanced disease (stage III or IV) was present in 58.5% of HD patients, and 48.1% of NHL patients.

B-symptoms were present in 53.6% of HD patients and 34.6% of NHL patients.

Bone marrow was involved in 19.5% of the HD patients and 32.7% of NHL patients.

Conclusion: This study delineates the following special features of malignant lymphomas in Jordan:

1. The high incidence of extranodal lymphomas
2. The virtual absence of IPSID

3. The rarity of follicular lymphomas
4. Only a few patients underwent staging or diagnostic laparotomies
5. Our results were discordant with other studies done in the area.

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Retrospective Analysis of 699 Ca-Lung Cases Seen at the Radiotherapy Department, Al-Basheer Hospital, from 1992-1996

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Despite the recent advances in oncology treatment, lung cancer still is the leading cause of cancer death in males and the second most common in females. Most of the patients (80-90%) die within the first year of registration.

Purpose: to study the relationship between Ca-lung and nationality, sex, age, place of residence, place of referral, profession, smoking, side of lung affected, incidence of SVCO at first presentation, histopathology, sites of distant metastasis, staging, and treatment given.

Materials and Method: We analyzed 699 Ca-lung cases seen at the radiology department, Al-Basheer Hospital from 1992-1996.

Results and Conclusion: Median number of Ca-lung cases seen was 139.8 cases per year, which constituted about 10.6% of the total cancer cases seen at the department during this period. Ninety-two percent of the cases were Jordanian and only 8% were non-Jordanian. The male-to-female ratio was 5.7:1. The median age according to age grouping was 0.7% (20-29 years), 3% (30-39 years), 12.3% (40-49 years), 28.6% (50-59 years), 36.2% (60-69 years), 14.6% (70-79 years), and 9% (>80 years). Place of residence: Amman was the most common, 52%; Trbid, 17.2%; Zarka, 10.8%; Balka, 8.2%; Karak, 2.1%; Mafraq, 2.1%; Ma'an, 1.5%; Jerash, 1.4%; Madaba, 1.3%; Aqaba, 0.8%; Tafila, 0.4%; and AjJoun, 0.2%. Most of the patients were referred from the private sector, 32.8%, King Hussain Medical Center, 30.8%, MOH, 27.2%; and the university sector, 8.9%. Profession of patients: 29.4% employees and workers, 17.1% not known, 15.4% farmers, 15.02% business, 13.5% homemakers and retired, 7.26% military personnel. Most of the patients were smokers, 91.8%; and only 8.2% were non-smokers. The right side of the lung was most affected in 61.4% of the cases, while the left side was affected in 38.6% of the cases. SVCO was seen at presentation in 5.9% of the cases. Histopathology: NSCLC was seen in 89.2% of the cases, while SCLC was seen in 10.8% of the cases. Out of NSCLC, 55% was squamous cell cancer, 38.3% was adeno

cancer, 4.2% was large cell cancer, 0.6% was bronchio-alveolar cancer, 0.6% was carcinoma cancer, 0.2% was adenoid cystic, and cases referred as NSCLC without subtyping were 12.8%. Distant metastasis was seen in bone, 22.8%; brain, 16.8%; liver, 5.2%; pulmonary, 2.5%; adrenal, 1.7%; and 0.7% in other sites. Out of the bone metastasis, 59% was in the spine and pelvis, 18.4% widespread bony metastasis, and 23.2% other bony sites. Most of the referred cases were stage III and IV. Treatment given: 9.7 underwent surgery out of which 33.8% underwent only thoracotomy and biopsy and 66.2% underwent lobectomy or pneumonectomy. All of the SCLC patients received cisplatin-based chemotherapy and only 7.38% of the NSCLC patients received chemotherapy. Most of the patients received palliative radiotherapy, and only 4% received radical radiotherapy. No treatment was given in 9% of the cases.

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**Association of Cerebral Arteriovenous Malformations and Occlusion of Major Feeding Vessels:
Clinical and Therapeutic Implications**

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Spontaneous occlusion of an arteriovenous malformation (AVM) is a known but rare occurrence. Occlusion of a major feeding vessel to the AVM is even more rare. We report three cases of AVM with occlusion of a major feeding vessel to the AVM, without occlusion of the nidus. These cases were identified from a review of approximately 500 cases of cerebral AVMs presenting for surgical or nonsurgical management. The incidence of such occlusions in our series is thus less than 1%. Two of the three cases were similar angiographically, consisting of a right (R) hemispheric AVM with occlusion of the R internal carotid artery (ICA). The distal portion of the ICA and its major branches reconstituted via a moyamoya pattern of anastomoses. Pial collaterals developed from the posterior circulation, extracranial circulation, and the left (L) anterior circulation. All segments of R and L anterior cerebral arteries (ACA) in both these cases were either hypoplastic or absent. The third case consisted of a L cerebral AVM with occlusion of the L middle cerebral artery (MCA). Pial anastomoses fed by ACA and posterior cerebral artery (PCA) reconstituted distal MCA. The patient with L MCA occlusion had a history of oral contraceptive use, but in the other two cases neither their history nor investigation suggested any condition predisposing to arterial occlusion. Although association of infarcts with AVM is unusual, two of the three cases developed infarcts. One case with the R ICA occlusion developed a large R frontal infarct, and the case with the L MCA occlusion developed a L basal ganglia infarct. Two of the AVMs

were classified as giant, and the third was medium-sized. The pathogenesis of the occlusions is not known but is probably related to endovascular injury and platelet aggregation due to high flow and turbulence or endovascular type proliferation seen in Moya Moya disease.

Surgical management of AVMs with major arterial occlusions is controversial. Only two such surgically treated cases have been reported. Both developed complications of either intracerebral hemorrhage or massive brain swelling. Our three cases were managed by surgical excision without any postoperative complication. Although caution is imperative in the surgery of such AVMS, we consider that development of collaterals provides more reasons to intervene surgically. Embolization by interventional endovascular techniques is not feasible for these AVMS. Moyamoya anastomoses in the pial bed tend to bleed. High flow due to AVM through these collaterals may further increase the risk of hemorrhage. Furthermore, development of collaterals from other circulation may lead to a cortical steal in regions away from the AVM. Two other cases (separate from the three cases reported above) support this argument in which a component of the circle of Willis was interrupted to reduce the risk of hemorrhage. These cases developed signs and symptoms localized to the hemisphere contralateral to the AVM when collaterals from the other side of the cerebral circulation opened. Thus occlusion of a major artery associated with AVM is an extremely rare occurrence, and these AVMS should be considered for careful surgical management to prevent collateral flow-related complications as well as usual risk of hemorrhage.

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Cerebrospinal Fluid Aluminum in Patients with Dementia

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Sudhir Batchu, MD; William J Crowle, Jr, MD

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Using atomic absorption spectrophotometry, cerebrospinal fluid (CSF) aluminum levels were estimated in patients with primary dementia (Alzheimer's type: n=15) and compared with CSF aluminum levels in patients with other dementias (OD) and neurological disorders (n=X). Patients in the other dementia group consisted of those with multi-infarct dementia, dialysis dementia, dementia associated with progressive supranuclear palsy, and pseudodementia secondary to depression. The patients ranged in age from 39-93 years. Mean age of the patients with primary dementia was 67.5 years. None of these patients were on aluminum-con-

taining medications such as antacids. Mean CSF aluminum concentration in primary dementia was 10.00 ± 5.237 mcg/dL and in the OD group was 10.6 ± 7.797 . The mean CSF aluminum level in patients with other neurological disorders was 9.75 ± 2.517 mcg/dL.

Statistical analysis using multiple range tests and analysis of variance demonstrated no significant differences in CSF aluminum levels in the dementia compared to the same in other neurological disorders. This study concludes that a change in CSF aluminum concentration in patients with dementia most likely represents an epiphenomenon rather than the cause of the dementia.

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Superiority of Phenytoin Sodium in Severe Pre-eclampsia and Eclampsia Compared with Magnesium Sulfate and Menon's Lytic Cocktail Regimen (Pethidine, Chlorpromazine, and Promethazine)

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East Meadow, New York
State University of New York at Stony Brook
Stony Brook, New York

Background: Pre-eclampsia and eclampsia are associated with significant material and perinatal morbidity and mortality. The mainstay of treatment usually consists of a combination of anti-hypertensive and anticonvulsant drugs. While the mode of delivery or the choice of anti-hypertensives are not contentious issues, conflicting opinions exist over the choice of anti-convulsants.

Methods: We conducted a clinical trial in a tertiary care hospital in India from August 1992 to December 1993 to study the efficacy of phenytoin in patients with severe pre-eclampsia and eclampsia. Twenty-eight patients with severe pre-eclampsia (with diastolic blood pressure of 110 or more, edema and proteinuria and a history of premonitory signs of headache, visual disturbances, nausea, vomiting, epigastric pain, oliguria) or frank eclampsia (the above plus seizures) admitted between August 1992 to December 1993 were treated with intravenous phenytoin infusion. Patients were monitored during the infusion and for late side effects. This group was compared with the historical controls of 20 patients who had received parenteral magnesium sulfate and 30 patients who received Menon's lytic cocktail regimen. Though patients were selected randomly to the two groups, the preferences of the attending physicians led to a greater number of patients being allocated to Menon's group.

Results: Maternal mortality in the three groups was nil. Maternal morbidity (aspiration pneumonia, urinary tract infection, thrombophlebitis) was less common in the phenytoin group:

Conclusion: Our study evaluated patients with severe preeclampsia and eclampsia. We demonstrated that phenytoin is equally efficacious as magnesium sulfate in prevention of seizures. It significantly lowers perinatal mortality. Apgar scores are the best in phenytoin group babies. The above are due to phenytoin having no sedative effect and no effect on fetal heart rate variability and neonatal tone. There is improved patient tolerance of the drug and its minimal side effects. Added advantages are its lack of tocolytic effect, long half life, ease and convenience of administration with the possibility of oral dosing. Our study thus strongly suggests the superiority of phenytoin over magnesium sulfate and Menon's regimen.

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Case Presentation of Ellis Van Creveld Syndrome and the Dilemmas and Implications of Prenatal Diagnosis of a Congenitally Malformed Baby

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This paper highlights characteristic features of Ellis Van Creveld syndrome, the dilemmas in its prenatal diagnosis, and its implications in the management of a congenitally malformed baby born to Muslim parents who were second cousins before they were married.

Following an ultrasound in the third trimester, the parents were told by their obstetrician that the baby had a severe congenital malformation called short rib polydactyly syndrome that would cause death soon after birth. Do not resuscitate (DNR) procedure was discussed with the parents who consented to it.

Baby boy weighing 2888 gms was born on October 23, 1996, with Apgar of 1 at 1 minute, 5 at 6 minutes, and 8 at 10 minutes. DNR orders were maintained both in the delivery room and the newborn nursery. Baby continued to do well in the newborn nursery and was discharged in stable condition on October 25, 1996. The baby was later diagnosed to have Ellis Van Creveld syndrome, which closely resembles short rib polydactyly syndrome, but has a better prognosis with about 50% survival rate to adulthood.

The infant had a short stature, narrow thorax, polydactyly six fingers in each hand with nail hypoplasia, short upper lip bounded by frenula to alveolar ridge, and cardiac evaluation indicated a small PDA and ASD. Also, the baby had a lack or absence of voice when he cried.

After an uneventful first 2 1/2 weeks, the baby developed respiratory problems, feeding difficulties, and respiratory infections needing four hospitalizations. Despite all the efforts and help from modern medical technology, the baby expired on December 29, 1996.

Session 15 (parallel)
Scientific Papers
Monday, July 28, 1997
2:45-4:15 p.m.

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**Significance of Free vs. Total PSA Ratio
in the Detection of Prostate Cancer at
its Early Stage**

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and Khursheed Mallick*

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Prostate cancer is the most common visceral cancer and the second leading cause of cancer deaths in American men. This asymptomatic malignancy kills more than 35,000 men and more than a quarter million cases are diagnosed annually. The prognosis is poor and the treatment options are limited because a large number of cases are detected when the cancer has spread beyond the gland. Therefore, detection of prostate cancer at early stage is crucial in improving the prognosis. Prostate specific antigen (PSA) has improved early detection of prostate cancer and helped in monitoring response to therapy, but it is unable to distinguish between benign prostatic hypertrophy (BPH) and early prostate cancer. Using Hybritech's immunoradiometric assays, we measured total PSA and free PSA (not completed to alpha-1-antichymotrypsin), in untreated prostate cancer patients and those on therapy in all stages of prostate cancer, BPH, and patients with cancers other than that of prostate (controls) to see if the free vs. total PSA ratio has any clinical significance. Our data revealed that this ratio in all stages of untreated prostate cancer patients was 1:10. However, free vs. total PSA ratio dropped to 1:5 in BPH, controls, and prostate cancer patients on lupron with flutamide therapy. This seems to suggest that this difference may have diagnostic/screening potential. The difference in free PSA level between untreated prostate cancer patients with stage D vs. untreated prostate cancer patients with stage A or B was statistically significant. Also, the difference in free PSA level between untreated prostate cancer patients with stage D vs. those on therapy was statistically significant ($P < 0.01$). However, there was no significant difference in free PSA level between untreated prostate cancer patients with stage A/B or BPH. There was no significant difference in free PSA level between fresh and frozen samples.

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**Single AM Serum Testosterone Level
Can Replace Pooled Serum Testosterone
for Evaluation of Hypogonadism**

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Clinical diagnosis of hypogonadism is confirmed by determination of serum testosterone (T) by a pooled sample collection, multiple determinations, or one sample collection. To evaluate whether a 0800-hour serum T level can replace the time-consuming collection of pooled samples, we studied 26 male patients (age 25-60 years), with normal serum T in 15 and low serum T in 11. The 15 eugonadal patients had normal libido and sexual potency with normal semen analysis obtained in six. Of the hypogonadal patients, seven had decreased sexual potency and the five with semen analysis had decreased sperm count. Pooled T were determined by combining serum obtained at 0800, 0830, and 0900. On three separate days, pooled T were performed in 25 patients, whereas only two pooled T were obtained in one patient. Morning samples were collected at 0800 on three separate days in all patients. Both pooled and morning collections were performed on each of the patients over eight weeks. There were no differences between the pooled and single morning serum T groups when analyzed by repeated measures of ANOVA.

There was significant correlation between the free T and total T in the whole group ($r=0.80$, $p<0.0001$). Between patients, there were no significant differences in the pooled or 0800 T values. In conclusion, serum total T performed at 0800 hours provides the same information as pooled serum samples.

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**Syndrome of Recurrent Sinopulmonary
Infections, Mental Retardation, and
Hydrocephalus in Four Jordanian Male
Siblings: Khalil Syndrome**

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We have followed a Jordanian family of 15 siblings since 1985. In this large family, there are four males aged 29, 23, 21, and 19, who have recurrent pulmonary infections, sinusitis, bronchiectasis, low IQ-(between 30-60), and height and weight below the fifth percentile. We have studied the

chromosomal patterns and nasal ciliary biopsies of these patients.

Based on the results of our analysis, we believe this unique syndrome is an X-linked disorder with resulting abnormalities in ciliary activity in the brain and respiratory tract. The 11-year follow-up has revealed 100% survival, but with an increasing incidence of sinopulmonary infections. The healthy siblings of the family, who were fast-studied, were married to nonrelatives, and no evidence of this syndrome was found in their offspring. This syndrome differs from similar entities, like Kartagener's, immotile cilia, fragile X, and Wischott-Aldrich syndromes in that the respiratory tract and the central nervous system involvement come in combination with an X-linked pattern of inheritance.

In conclusion, we describe a new syndrome as an etiology of recurrent sinopulmonary infections. The association of ciliary dysfunction, mental retardation, and hydrocephalus is unique, and we would like to name this entity Khalil syndrome (after the city where this family originated). Genetic counseling is an important aspect in the management of such patients, in addition to pneumococcal and influenza vaccinations.

Currently, we are evaluating the genetic pattern in the affected members of the family.

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Attention Deficit Hyperactivity Disorder

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Attention deficit hyperactivity disorder (ADD) is the most common psychiatric disorder in childhood. Approximately 3-5% of all American children, up to 3.5 million, have an attention deficit disorder. It is a leading cause of school failure and underachievement. Attention deficit hyperactivity disorder is a neurobiological disability. There also is an adult version of ADD, and it is an important cause of unrecognized and untreated distress. On the other hand, it is a diagnosis that has been criticized in the lay press and in professional journals. Given its continuous nature, it seems appropriate to review the status of the disorder. The psychostimulant treatment of ADD presents a major public policy problem. The psychostimulants are highly abusable. An educational approach to the use of medications and the development of less practices for ADD have not changed much in the last 25 years in the United States. Nonetheless, some new and modified treatment approaches that have been added to the medical literature in the last few years are deserving of consideration.

Parenting a child who has ADD can be an exhausting

and at times frustrating. Parents play a key role in managing the disability. They usually need specialized training in behavior management and benefit greatly from parent support groups.

My talk will review the current status of this disorder, and present a historical perspective pathogenesis, and discuss disorder's effect upon academic performance of the children and peer relationship and the challenge it poses to the parents at home.

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Depression in Women

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Transient feelings of sadness and depression are a fairly universal phenomenon and almost everyone experiences it with some frequency. This is different from the illness of depression (called major depression), which carries a high degree of morbidity and mortality, and will be the topic of my talk this morning.

Depression is the most common of psychiatric disorders. It is also very common in the general practice of medicine. A general practitioner sees more patients with depression than hypertension. According to one study, 20% of all patients seen in a large diagnostic hospital clinic suffered from depression. Other estimates vary from 15-35%. Lifetime prevalence of depressive illness is 15%, and point prevalence is 4-5%. These figures generally hold true across countries, cultures, and religions.

Even though the depressive illness now is very much a treatable illness, most cases are either undiagnosed or misdiagnosed, and therefore go untreated. This causes untold and unnecessary suffering and misery not only to the patients but to their families.

With the help of slides and tables, I will discuss some factors that may explain why depressive illness is 2-3 times more common in women than in men. These include socio-cultural, socioeconomic, and biological factors. This paper will also discuss the recognition, diagnosis, and treatment of depression, offering a simple rational approach easily usable by primary care physicians.

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Recognition and Treatment of Depression in Elderly

M Basheer Ahmed, MD

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Health Science Center, Fort Worth

The world population is increasing steadily, however,

there is a disproportionate increase in elderly population. One of the issues related to aging population is mental health. Potentially, a large number of elderly people are in need of mental health services and it is becoming a challenge for developing countries.

Depression in the elderly is a serious public health problem. It is associated with increased morbidity and mortality. It complicates the treatment of coexisting medical illnesses causing depressed patients to use relatively more health care resources.

It is noted that depression in the elderly, which is a treatable disease, is left untreated due to difficulty in diagnosis, resulting in more serious consequences. The diagnostic approach and the new treatment options will be discussed during the presentation.

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Unusual Cardiac Manifestations of Tuberculosis

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An unusual case of pulmonary fibrocavitary tuberculosis with massive hemoptysis and a continuous murmur in the left infraclavicular region in a 28-year-old male is presented. An acquired communication between the left subclavian artery and left pulmonary artery was demonstrated by pulmonary arteriography, which revealed a reversal of blood flow. The diagnosis was confirmed by aortography, which showed a tortuous branch of the left subclavian artery draining into the left pulmonary artery through the pulmonary parenchyma. Surgical cure was affected by a left upper lobectomy during which the procedure severe intraoperative bleeding was encountered despite adequate extra-thoracic ligation of the tortuous vessels. The postoperative course was uneventful.

Session 16

Meet the Professor

Friday, August 1, 1997
7-8 a.m.

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Radiology Update - Spiral Computed Tomography

Arfa Khan, MD

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Spiral computed tomography (CT) represents the state-of-the-art for CT scanning. It has radically changed the way in which we are able to image the body. Spiral CT scanners were introduced in 1991. This technique is based on a slipping technology and, depending on the manufacturer, is called spiral, helical, or volumetric scanning. The basic CT-equipment required for this technique is a CT scanner that acquires data continuously while the patient is advanced through the gantry. This allows for true volumetric acquisitions without arbitrary divisions between "slices" and with elimination of interscan delay. The X-ray focus performs a spiral motion relative to the patient, thus, this technique is often defined as spiral CT. Some of the advantages of spiral CT over conventional CT are:

1. Dramatically shortens scan times so that the entire thorax or abdomen can be scanned in a single breath hold, usually in 25-30 seconds as compared to conventional CT, which takes 12-15 minutes.
2. Better delineation of small lesions due to elimination of respiratory misregistration.
3. With rapid scanning techniques, one can scan a volume of tissue during peak contrast enhancement using only a moderate amount of intravenous contrast.
4. The raw data can be analyzed retrospectively and axial as well as multiplanar, and three dimensional (3D) images can be generated. The 3D images display the vascular anatomy similar to conventional angiography. Completed tomography angiography is being increasingly utilized for evaluation of cerebral circulation, carotid stenosis, pulmonary embolism, aortic diseases, renal stenosis, etc.

Some other uses of 3D imaging are for evaluation of airways and for presurgical planning.



Training Opportunities in the United States

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Introduction: The changing millennium will bring about significant changes in graduate medical education opportunities in the United States. This will have enormous impact on candidates applying for training positions in this country. The nation's supply of physicians increased by 125,000 over the past decade. The total number of allopathic and osteopathic physicians engaged in patient care, teaching, research, and administration has more than doubled from 308,487 in 1970 to 627,723 in 1992. In terms of physician-to-population ratios, the supply ratio has increased from 151 to 245 per 100,000 population. Estimations and projections vary, but there is a growing consensus whether projections are made based on marketplace demand, health maintenance organization staff-models, physician-to-population ratios, or disease-specific estimates of need. The overall supply of physicians is soon or will be more than necessary to meet the healthcare needs of the country. With the advent of telemedicine, consultations and expertise would be available on line. Evidence-based medicine will change the utilization patterns of services and the need for subspecialists. With the aging of the American population, an increased need for geriatricians will be in keeping for the current projection of 22% of the population being over 65 years of age by the year 2020. The marketplace for physicians' services has been increasingly affected by the growth of managed care and capitation plans that require fewer physicians than traditional fee-for-service plans. There is a surplus of subspecialists as compared to generalists. Many graduating internal medicine subspecialists and noninternal medicine specialists such as anesthesiologists and radiologists are finding it hard to find employment. Under managed care, the earnings of the subspecialists will fall and there will be fewer subspecialty jobs.

Suggested Policy: Currently, training positions in subspecialties such as gastroenterology, cardiology, and pulmonary diseases are being reduced due to lack of reimbursement to programs that train these subspecialties. Establishing a nationwide goal that at least half of all residency graduates begin generalist careers seems prudent. The Pew commission, Council on Graduate Medical Education (COGME) has proposed a 25% reduction in the total number of all training positions in the country. Institutions that do not reduce the number of trainees by 25% may lose all funding for graduate medical education. At this time, the total number of US medical school graduates also is being critically reviewed. All the healthcare policymakers suggest no new medical schools be opened and the number of enrollees in

all medical schools be limited to the present numbers (17,000). Also, the number of international medical graduates entering training in the US is being studied and will be restricted to short-term advanced training in the US with return to the country of origin after completion of training. The exchange-visitor program will limit extraordinary candidates only to receiving J-1 or H-1 visas based on their accomplishments in areas of medical research, education, and patient care. At the present time, the pool of IMGs competing for a diminishing number of positions is growing; in 1995, 5500 IMGs and in the 1996 NRMP more than 7,000 IMGs remained unmatched. With increasing numbers of medical graduates taking USMLE worldwide, the numbers have increased in 1997 and will continue to rise.

The Future: Suggestions of changing residency training to the outpatient setting from the traditional hospital-based medicine is in place. The increased need for primary care physicians to learn most, if not all, aspects of medicine is essential in the HMO era. The reduced need for the subspecialists as determined by the market forces has led to a de-emphasis of training in the procedure-related specialties. Medical informatics, occupational health, epidemiology, geriatrics, population-based and evidence-based medicine are areas that will flourish. With the advent of on-line technology, all physicians will be expected to learn the technology involved. Physicians will have to work in the underserved areas to provide care for the populations with limited access to healthcare.



The Epidemiology and Prevention of Hepatitis A Virus Infection in the Middle East

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Control strategies against viral hepatitis infections require elucidation of epidemiology relevant to the area. The socioeconomic development of the country over the recent past may have affected the epidemiology of hepatitis A infection. The effect of a 15-year observation period on age of infection, with particular reference to socioeconomic factors has been studied. One hundred and sixty-four patients with acute hepatitis A and 1,900 people without evidence of acute hepatitis, were included.

Results: A shift to the right in age-prevalence of acute hepatitis A was found over the study period, such that peak prevalence of acute hepatitis A in children now is at 5-10 years, compared to 0-5 years in the first half of the study period. A similar age-shift has occurred in adults so that peak age of hepatitis A in adults now is at 20-30 years, compared to 15-20 years before. No comparable change was

detected for hepatitis B infection. In children, 58% of acute hepatitis A was in persons in the lower socioeconomic category, compared to 1% in the higher category ($p < 0.05$). However, in adults a markedly different picture has emerged: 52% of acute hepatitis A cases was in patients of higher socioeconomic status, as compared to 6% in persons with lower status. Again, no comparable effect was noted in hepatitis B infection. Similarly, a shift in age-prevalence of infection was also strongly related to socioeconomic status.

Conclusion: Infection with hepatitis A is becoming delayed, and this seems to be related to socioeconomic status. This will result in a greater clinical hepatitis disease load. These changes, due to rapid socioeconomic developments taking place in Jordan, are important considerations in the development of a national strategy for the control of hepatitis A.



Androgen Supplementation in the Male and Female

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Androgens have many important physiological actions, including effects on muscle, bone, prostate, bone marrow, and sexual function. Androgens increase nitrogen retention, lean body mass, and body weight. They also stimulate the proliferation of bone cells *in vitro* and increase bone density. These hormones increase erythropoietin production in the kidneys, thereby increasing hemoglobin concentration. Androgens also have a role in stimulating and maintaining sexual function in men and probably in females.

Men with documented testosterone deficiency are candidates for androgen replacement therapy. Prior to embarking on therapy, it is important to differentiate between primary and secondary hypogonadism in these patients. The patient's clinical status is the best indication of the effectiveness of androgen therapy. Increased libido, energy, and strength are noticed within days to weeks after therapy is initiated.

Testosterone preparations are available as oral, parenteral, or transdermal preparations. Testosterone undecanoate, an oral preparation, must be taken more than once daily for optimal use. Testosterone esters are available for parenteral use. Recently, testosterone patches that can be worn on the scrotum or non-scrotal skin have become available. These patches are more expensive. The side-effects of testosterone administration for hypogonadism include polycythemia, lowered plasma high-density lipoprotein cholesterol levels, sleep apnea, and stimulation of an occult prostate cancer into clinical disease. Prostate specific antigen (PSA) should be measured before the start of therapy along with a careful prostate examination. PSA mea-

surement and prostate examination should be repeated during therapy. A recent report demonstrated a high prevalence of biopsy-detectable prostate cancer in men with low serum testosterone level despite normal prostate examination and a normal PSA level.

The decline in serum testosterone level in aging men may contribute to a decrease in libido, muscle strength, and mass. Testosterone treatment in elderly men may restore body weight, improve hematocrit, bone density, and lean body mass, although more studies are needed before this can be widely recommended. A recent study has also shown that supraphysiologic doses of testosterone, especially when combined with strength training, increases muscle mass and strength. These studies, although not justifying the use of testosterone therapy in sports, support the fact that short-term administration of androgens may have beneficial effects in patients with career-related cachexia, chronic wasting disorders (such as human immunodeficiency virus infection), and immobilized patients. Significant side effects can occur with supraphysiologic doses of androgens. These include decreased serum HDL cholesterol, elevated LDL cholesterol, myocardial infarction, and stroke. Psychotic symptoms may develop.

Postmenopausal estrogen-androgen replacement therapy improves libido, sexual enjoyment, sense of well-being and certain other symptoms of menopause such as depression and lack of energy.

Session 17 Symposium
Women's Health
Monday, July 28, 1997
8:30-10:30 a.m.



Hormone Replacement Therapy: Benefits and Risks

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Women approaching menopause should be counseled about the benefits and risks of hormone replacement therapy. With the increase in life expectancy, a significant number of women will spend one third or more of their lives in postmenopausal years. It appears that the most important benefit of estrogen replacement is the reduction of coronary artery disease and prevention of osteoporosis. Osteoporosis, which is characterized by a loss of bone mass and greater susceptibility to fractures, is a major concern of millions of postmenopausal women. Estrogen is the therapy of choice

for prevention and treatment of osteoporosis. It has been seen that the maximum loss of bone density occurs within 5-6 years after menopause. The greatest benefit of hormone replacement is obtained when it is started within first 5 years of menopause. However, it is never too late to start hormone replacement therapy to prevent further bone loss. Recent data indicates that bone restoration may occur in elderly women also.

Coronary artery disease kills nearly as many postmenopausal women as all cancers combined. Recent studies show that hormone replacement therapy reduces the risk of heart disease and can be safely taken by an increasing number of women. Estrogen-associated changes in lipid metabolism, and other effects of estrogen such as direct vasodilatation, altered production of prostacyclins, and estrogen's antioxidant properties may be responsible for the cardioprotective effects of estrogen.

Estrogen replacement remains a major component in treatment of conditions associated with menopause. It is effective in reversing vaginal atrophy, which is responsible for vaginal itching, vaginismus, and pelvic pressure seen in menopause. It is helpful in vasomotor symptoms and urinary incontinence seen in these women. There is some evidence to support that women on hormone replacement therapy have lower incidence of large bowel cancer.

The fear of cancer with hormone replacement therapy continues to be a major hurdle for both the physician and patient. Clinical and epidemiologic studies suggest that the risk of endometrial cancer is greatly reduced by combined estrogen/progestin preparations. The effect of the therapy on breast cancer remains controversial. Data regarding this is conflicting. The risk, if any, is small. Patients should be fully informed about the status of the current knowledge on this subject. For the majority of women the benefits outweigh the risks.

Side effects like vaginal spotting and bleeding can be reasons for discontinuance of therapy. In depth counseling by physician is crucial to ensure patient compliance. Quality of life remains a major issue for elderly women.



Domestic Violence and its Effects on Social Behavior of the Society

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“O you who believe! Truly among your wives and your children are some who are enemies to yourselves, so beware of them, but if you forgive and overlook and cover up their faults, surely Allāh is forgiving, merciful. Your riches and your children may be a test, but in the presence of Allāh is the highest reward (The Glorious Qu’rān, Chapter 64, Verses 11-15).”

Domestic violence has become the most social evil of the 20th century and it is increasing with great frequency. Just to look at some of the statistics in 1992, the AMA predicted that as many as one in three women will be assaulted by a domestic partner in her lifetime, four million per year.

Most physicians lack the training to deal effectively with battered women. Yet, they are in the ideal position to intervene. With a few straight forward questions, they may be able to detect a volatile situation before it escalates to violence. When abuse does occur, they can take a key role in management by becoming patient advocates, making referrals, and coordinating team care.

Every Islamic community must establish a resource to deal with this problem in their community. A team of well-trained advocates must be available for intervention. Not accepting this problem has a far-reaching consequence on the family, including children.



Pap Smear Diagnosis of ASCUS and its Implications

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The management of patients whose pap smears show atypical squamous cells of undetermined significance (ASCUS) is a complex challenge for physicians. The term ASCUS was introduced in 1989 when the Bethesda System was introduced to standardize pap smear reporting. The preinvasive lesions of cervix were designated squamous intraepithelial lesion (SIL) to avoid potential misunderstandings as to the definitions of dysplasia, carcinoma in situ, or frank neoplasia. The preinvasive lesions were further divided into low grade and high grade types, since most low grade lesions (condyloma/CIN 1) had relatively uneventful follow up, and most high grade lesions (CIN II/III) were associated with high risk human Papilloma virus (HPV 16) infections. The Bethesda system also recommended a special format for the cytology report to include an explicit statement on the adequacy of the specimen, followed by the general categorization and a descriptive diagnosis.

Patients with ASCUS need a careful evaluation and a management plan that depends on the qualifier statement accompanying the ASCUS diagnosis. The diagnosis of ASCUS is a challenge for cytologists also, since the decision to classify a pap smear in the ASCUS category implies that the nature of alterations in the pap smear are not fully explainable, and may be due either to inflammation, repair, metaplastic changes, human Papilloma virus infection, or squamous intraepithelial lesions (SIL). Therefore, whenever possible, the diagnosis of ASCUS is followed by a qualifier that explains the reason for the diagnostic uncertainty and offers the most likely diagnosis (for example, possibly reactive or suggestive of SIL).

A significant percentage (20-25%) of patients whose smears show ASCUS with atypia are found to have SIL on colposcopy and biopsy. Only a small percentage (<17%) of the SEL are detected on a follow-up pap smear only. It is therefore a management dilemma for the practitioners as whether to follow the report of ASCUS with colposcopy and biopsy or a repeat pap smear. In this presentation, the Bethesda System, the various qualifiers with ASCUS, and the current management options for women with the diagnosis of ASCUS, LSIL, and HSIL will be discussed.

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Domestic Violence

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Domestic violence is the leading cause of injury to women between the ages of 15 and 44 in the United States, more than car accidents, muggings, and rapes combined (Uniform Crime Report, FBI, 1991). Up to 2 million women are beaten by their husbands, ex-husbands, and boyfriends in the United States every year. Up to 4,000 of these women will be battered to death (U.S. Department of Justice, 1994). It is estimated that a woman is beaten every 15 seconds by someone close to her. When alarmingly high figures of physical and sexual abuse of children, and physical abuse of the elderly in the families are added to the above statistics, the enormity and scope of the problem of domestic violence in America becomes evident.

This paper discusses myths about domestic violence and contrasts them with facts. Psychiatric aspects of domestic violence including causes, psychodynamics, and the profile of the perpetrator are described.

Domestic violence may be the single most common etiology of injuries in women presenting to health care systems. Physicians have a responsibility to identify, educate, and appropriately manage and/or refer patients in violent relationships. Offering protection to the battered woman is of utmost importance, yet there are only 1,500 shelters for battered women in the U.S. There are three times that many animal shelters.

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Nonpalpable Breast Lesions: Stereotactic Automated Large Core Biopsies

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Due to increasing use of screening mammography and

a medical malpractice environment that often prompts biopsy of less-suspicious breast lesions, the number of surgical breast biopsy has risen dramatically in recent years. Nationwide, approximately one million women per year undergo surgical breast biopsy nationwide. Only 10-15% of mammographically detected suspicious breast lesions prove to be malignant by open surgical biopsy. Surgical biopsy, however, is expensive, time consuming, potentially disfiguring, and physically and emotionally traumatic for the patient. This procedure frequently requires a preoperative needle localization under mammographic or ultrasound guidance. Fine needle aspiration biopsies of breast lesions has been advocated to reduce the number of unnecessary surgical procedures. There are, however, significant insufficient sampling and false negative rates with this technique. Since 1988, stereotactic core biopsy has been increasingly used for diagnosis of nonpalpable breast lesions. The use of a 14-gauge biopsy needle allows a sufficient volume of tissue for a definite pathologic diagnosis. There are no false positive diagnoses. Core biopsy of the breast lesions also can be performed under ultrasound guidance. Recent comparative studies have shown that core biopsy of the breast is as accurate as surgical biopsy. In addition, core biopsy of the breast has definite advantages over surgical biopsy. The procedure takes less time to perform, there is no incision or scar, no anesthesia is required, and the cost is 25-50% less than surgical biopsy. It is estimated that if percutaneous core biopsy were to replace surgical biopsy for diagnosis of nonpalpable breast lesion, it would save the health care system at least \$1 billion a year.

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Can Exercise-Related Incontinence be Minimized by the Use of an Electric Stimulating Device?

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Introduction: A substantial number of women (30%) suffer from exercise-related incontinence. The percentage of females that cease to exercise because of urinary incontinence has been estimated to range from 20% - 40%.

Aims: To study the impact of nonsurgical management (use of an electric stimulating device) on resumption of exercise and quality of life of women with genuine stress urinary incontinence during exercise.

Materials and Method: Seven patients whose chief complaint was leakage of urine during exercise were treated with an electric stimulating device for active pelvic floor stimulation. All women were evaluated with a medical history, a physical, a neurological exam, uroflowmetry, a urine culture, a standing stress test, a Q-tip test, and a 20-minute pad

test with standard exercise filling the bladder up to 75% of its capacity. All women completed a quality-of-life questionnaire and a urinary diary including leakage episodes before and after treatment of six weeks' duration.

Results: The age of women ranged from 32-66 years, with a mean of 49.3 and average parity was 2. Pretreatment leakage ranged from 32.4-98.4 gm, and posttreatment from 15-16.0 gm. Average improvement of 62 gm per subject was noted, with a range of 31.9 to 91.5 cc. Comparing the pre- and posttreatment urinary leakage, if the leakage is higher, the difference between pre- and posttreatment values was increased, with an almost linear correlation. Five out of seven patients confirmed improvement in exercise level or resumption of exercise after completion of treatment.

Conclusions: Prospective analysis of the patients having urinary incontinence during exercise treated with an electric stimulating device revealed significant improvement in the amount of urinary leakage. Five out of seven patients who stopped exercising due to stress urinary incontinence restarted exercise. Two out of seven patients kept the device for continued use.

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Prevention of Coronary Artery Disease in Women

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Coronary artery disease is difficult to diagnose in women because of high false positive and false negative stress test results. Therefore, fewer women are sent for therapeutic treatment such as cardiac catheterization. Coronary artery disease is reaching epidemic proportions in women. With increased longevity, more women are living many years in menopause. Coronary artery disease is the leading cause of death among women. Risk of coronary heart disease was highest among smokers who started before age 15. On stopping smoking, one third of the excess risk of coronary heart disease was eliminated within 2 years. Thereafter, the excess risk returned to the level of those who never smoked during the interval of 10-14 years following the cessation. Women who stop smoking will experience an immediate benefit and a further longer-term decline in excess risk of coronary heart disease to the level of those who never smoked. Risk factors for coronary disease in young women included hypertension, hypercholesterolemia, diabetes mellitus, familial coronary disease, and smoking. Long-term prognosis is excellent for those without advanced diabetes mellitus and renal failure. Risk factor modification is important in preventing coronary artery disease. Risk factors for coronary artery disease in women are similar to those of men. Despite the risk to women from heart disease, nearly all randomized, controlled studies on risk factors, treatment,

and outcomes of cardiovascular disease have exclusively involved men, and extrapolation of those findings to women has resulted in several misinterpretations. More recent studies that controlled for different age and risk factors in women found that women have tended to be referred for angiography, coronary artery bypass graft surgery, and angioplasty significantly less often than men. Female patients with coronary artery disease have an increased risk for myocardial infarction in the postmenopausal period because the protective effects of estrogen no longer exist. Common risk factors are hypertension (49%) and diabetes mellitus (34%) of the infarction cases. Although there are no clinical trials involving women, three female cohort studies of aspirin and prevention of myocardial infarction have been published with conflicting results. Although a general recommendation for asymptomatic women to take aspirin to prevent myocardial infarction is not currently indicated, the best available data suggest a beneficial effect, particularly in women at high risk of coronary artery disease. The clinician should therefore consider aspirin use in each patient individually. Postmenopausal women should consider hormonal replacement, after appropriate counseling that would cover the benefits and risks of this therapy. The exact mechanism of estrogen is still under investigation, however, it has shown to reduce the LDL and increase the HDL levels in patients who take estrogen. The normal regimen involves the use of 0.625 mg of conjugated estrogen or its equivalent synthetic estrogen. Unopposed estrogen can lead to endometrial hyperplasia and eventually to uterine adenocarcinoma, thus concomitant use of progesterone is mandatory in patients who have not had a hysterectomy. Recent data suggest that use of estrogen replacement in menopausal women reduces the incidence of coronary artery disease by 25-50%. There are many other proven benefits of hormone replacement therapy, including the prevention of osteoporosis and urogenital atrophy. Decisions about when it is too late to start estrogen, or when it is time to stop will need to be made on a case-by-case basis. For menopausal women, it is important to determine a personal profile of unmodifiable (family history, age, and race) and modifiable risk factors. The goal for every woman must be to control coronary risk factors such as smoking, hyperlipidemia, diabetes, sedentary lifestyle, weight control, stress, and the use of hormone replacement therapy, which have been proven to be amenable to modification strategies. Prevention programs can safely recommend nonpharmacologic intervention, such as better diet, more exercise, and not smoking.

Session 18 (parallel)

Scientific Papers

Friday, August 1, 1997

10:45 a.m. - noon



H-Pylori

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Helicobacter pylori, a mysterious bug, which once was considered to be just a contributor, is now thought to be the causative agent of most peptic ulcer diseases. In fact, most of the ulcers are not thought to be caused by either *H. Pylori* or by nonsteroidal anti-inflammatory drugs. It also is being implicated in gastric cancer and lymphomas, especially MALT lymphomas. Koch's postulate has been fulfilled. Simple diagnostic tests have been developed and different regimens for treatments have been established. It seems that if treated properly, peptic ulcers can be eradicated permanently. That is truly an infectious disease.



Does Meperidine Used with Midazolam Improve Patient Tolerance for Esophagogastroduodenoscopy (EGD)? A Randomized, Double-Blind, Controlled Trial

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American gastroenterologists commonly sedate patients for an esophagogastroduodenoscopy (EGD) using the combination of midazolam and an opioid; whereas only the former is generally used in Europe. We performed a randomized, double-blind, controlled trial to determine whether meperidine, used in addition to midazolam, improved patient tolerance to an EGD as compared to midazolam alone in our patient population.

Method: 120 patients (61 males and 59 females, mean age 48 years) undergoing diagnostic EGD were randomized to receive either 50 mg of meperidine (Group I) or 1 mg of midazolam (Group II). Patients then were given additional midazolam in incremental doses at the discretion of the attending gastroenterologist to induce a state of conscious sedation.

Results: Patients in Group I received a mean dose of 3.8 mg of supplemental midazolam, compared with 4.6 mg for Group II ($p < 0.05$). Patients in Group I showed improved tolerance for EGD compared to Group II in terms of the

need for supplemental doses of narcotics during the procedure (7% vs. 20%; $p < 0.05$), the need for additional medication during intubation of the esophagus (11% vs. 25%; $p = 0.06$), the need for a faculty member to accomplish intubation (7% vs. 20%; $p = 0.051$), physician rating of poor for the overall adequacy of sedation (7% vs. 20%; $p < 0.05$), the presence of retching that interfered with the procedure (21% vs. 39%; $p < 0.05$), and termination of the examination before the entire UGI tract could be inspected (0% vs. 7%; $p = 0.055$). Both groups showed a similar incidence of amnesia (57% vs 63%) and the willingness of patients to undergo another EGD in the future (both 98%).

Conclusion: Meperidine improved the ability of our patient population (an American academic training setting) to undergo an accurate and complete EGD.



Defining the Multiple Modality Approach to the Treatment of Cancer of the Rectum

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Background: Surgical treatment for cancer of the rectum has shown modest improvement over the last several decades with a 5-year survival of 45-50%. Local recurrence of disease continues to be the major cause of failure despite curative resection of tumor. Combined modality, adjunctive therapy with chemotherapy and radiation currently is being utilized in several national programs. This paper highlights our experience with 404 patients with rectal cancer treated in a programmed multimodality approach based on a carefully defined clinical staging of disease at presentation. Our staging was based on the degree of mobility of the tumor and the level of the lesion within the rectum. Tumors that were mobile, early fixed (partial), advanced fixed (total), and frozen pelvis were defined as clinical stages I, II, III, and IV. Tumors above the middle valve of Houston (at 6 cm) were defined as proximal tumors, and those between the anorectal junction and the middle valve were defined as distal cancers. Patients with mobile proximal tumors were treated with surgery and selective postoperative radiation for all high risk Stage B2 and C cancers. All other patients were treated with escalating doses of preoperative radiation (45-70 Gy) \pm chemotherapy. Follow-up in these patients ranges from 3 years to 17 years with a median of 8 years.

Results: Overall 5-year survival of the total group of patients is 74%. Breakdown by pathological stage is 82% for stage A and B1, 67% for stage B2, 74% for stage C1, and 51% for stage C2. Overall local recurrence is 12%; 5% in stage A and B1, 18% for stage B2, 10% for C1, and 17% for C2.

Conclusion: An integrated adjunctive therapy treatment

algorithm based on a clinical staging system results in a significant improvement, in local control and survival of patients, and should be standard practice in management of rectal cancer.



Recent Advances in Invasive Gastroenterology

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The role of endoscopic retrograde cholangiopancreatography (ERCP) in the management of pancreaticobiliary diseases is reviewed with emphasis on the management of postlaparoscopic cholecystectomy complications (like bile leaks, biliary strictures, and retained stones), sphincter of Oddi dysfunction, malignant obstructive jaundice, endoscopic management of pancreatitis, and pseudo-cyst drainage.

Endoscopic ultrasonography (EUS), with the capability of fine needle aspiration, has become a useful tool in diagnosing submucosal lesions and obtaining tissue for histologic diagnosis.

The use of expandable metallic stents for malignant esophageal neoplasms also is reviewed.

Transjugular intrahepatic portosystemic shunt (TIPS) recently has been introduced as a viable option to reduce portal hypertension; its role in the management of variceal bleeding, and intractable ascites is discussed.



Therapeutic Endoscopic Retrograde Cholangiopancreatography (ERCP)

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Therapeutic endoscopic retrograde cholangiopancreatography (ERCP) has simplified the diagnosis of biliary tract and pancreatic disorders. Diagnostic ERCP is utilized by well-trained gastroenterologists in United States. It helps in the diagnosis of common bile duct (CBD) stones, strictures and tumors of CBD, congenital anomalies, and other rare disorders of CBD. It helps to diagnose pancreatic cancer, chronic pancreatitis, and other rare disorders of pancreas. Before the advent of ERCP, these disorders were very difficult to diagnose and treat.

Therapeutic ERCP is an extension of diagnostic ERCP and helpful in treating these diseases that in the past required major and complicated surgery with its associated morbidity and mortality.

We are a group of three gastroenterologists who are engaged in doing therapeutic ERCP in Topeka, Kansas. Last year, we did 150 therapeutic ERCPs out of 300 total diag-

nostic ERCPs. Our data will be presented in detail during the conference.

Briefly, we did an endoscopic papillotomy (EPT), removal of CBD stones with balloons, baskets, and mechanical lithotripsy. We have not used shock wave contact lithotripsy, electrohydraulic lithotripsy (EHL), or extracorporeal shockwave lithotripsy (ESWL) to remove large and complex CBD stones. Data from other centers in United States will be presented. We have placed various kinds of biliary stents across benign and malignant CBD strictures to relieve biliary obstruction. We have not done manometry of Papilla of Vater nor have used nasobiliary drainage catheters. We have helped surgeons before and after laparoscopic cholecystectomy to take out retained CBD stones and stop postoperative cystic duct leak by placing a stent across the area of leak.

The technique of therapeutic ERCP and its complications will be presented during the conference.

Session 19 (parallel)

Scientific Papers

Friday, August 1, 1997

10:45 a.m. - noon



The Role and Responsibility of Physicians During Civilian/ Military Conflict: Islamic Perspective

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Introduction: Statistically armed conflicts have claimed the lives of more than 90 million people in the 20th century. Over the past 20 years, human rights violations have resulted in 44 million refugees and displaced persons, which represents 1/130 inhabitants worldwide. At the present time, 50 countries are engaged in armed conflict. More than 90 million land mines threaten the lives and limbs of ordinary people. Eight percent of war-related deaths in the 1980s were civilians. Rape is used as an instrument of war. In the recent Bosnian conflict, thousands of people lost their lives and approximately one million forced migrations took place. In the Kashmir struggle of 1989, more than 30,000 civilians lost their lives. Physicians and lawyers were the victims of atrocities in both these conflicts.

Islamic Perspective: Man has a common origin, human status, and aim. Other people's interest and right to life, honor, and property are respected as long as the rights of Muslims are intact. Transgression is forbidden. War is justified if the state security is endangered. During destruction of crops, animals, and homes, killing nonfighting women, children, and the aged are forbidden.

Impact: Political killings, forced disappearances, tor-

ture, and rape destroy the bodies and minds of individuals and the well-being of entire communities. Crimes of war and violations of human rights have direct devastating health consequences such as psychological trauma in survivors and their families, victims of torture and rape, refugees and displaced persons, and indirect consequences due to collapse of social infrastructure. Deterioration in supplies of food, water, and effective sanitation frequently trigger massive dislocations of people and widespread disease and starvation. Health services may be overwhelmed by increased health needs under these circumstances. Health professionals are often targets and instruments of state-sponsored human rights violations. The effects of war could be devastating, even for the armed forces participating in war, conflict, or oppression. Some long-term sequelae like the Gulf War syndrome have been recognized recently. Traditional health concerns, which are based on concepts of disease and illness fail to recognize and address the human suffering that is caused by human rights violations and armed conflicts. As physicians, we are well aware of the outcomes of acute medical illness and medicine in the community-setting; however, as a group, we may not be aware of the statistical and social significance of crimes of war. Nuclear and chemical weapons, interpersonal violence, and environmental threats continue to plague the health of the "world community." An understanding of preventative and therapeutic aspects of medical and social care during military or civilian conflicts needs to be developed.

Suggested Solution: Educating health professionals about human rights is the first step toward preventing these abuses from occurring. Instruction on ethical standards and the responsibility of the health professionals facing situations involving possible violations of human rights and medical ethics is important. In addition, the most important task is delivered by those who volunteer care to the victims of war in the field. In this connection, Doctors without Borders and Physicians for Human Rights have delivered considerable voluntary medical help to those in need over the past few years, at a risk of personal lives. Physicians can help by being active members of these organizations. In addition, dissemination of important information and facts is an additional responsibility of health care providers and as a group. A lot can be done in this area. Fund-raising for the victims and their families can be adopted by those physicians who cannot contribute in the field. Physicians and health professionals can organize blood drives as the availability of blood products in the field may improve the outcome of victims of armed conflict. Physicians also can contribute in rebuilding the social infrastructure that is destroyed by war or armed conflicts. Improving sanitation, providing immunizations, and rebuilding schools and colleges after the conflict is an important aspect of rehabilitation of the residual society, and health professionals can play an important part.



Commonly Faced Ethical/Legal Issues in the Medical ICU

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Background: Ethical and legal issues pose a constant challenge to the residents and staff in the intensive care unit (ICU). The perception as to how to deal with these various issues varies widely. There is very little medical literature to suggest how these issues are actually dealt with and the various factors that influence the decisions of the health care workers. We evaluated the influence of profession, ethnic background, religious background, belief in God, belief in life after death, and duration as a health care worker upon their decisions in dealing with these issues. We took advantage of the fact that our hospital has a very heterogeneous ethnic and religious population of health care workers.

Methods: Commonly faced issues were collected with the help of the physicians, nurses, and other house staff of the ICU. These were presented in a questionnaire with examples for each ethical/legal dilemma and a yes/no format for answering each question. These were handed out to the physicians, nurses, students, and attorneys. The respondents were further subdivided into various subcategories of religious, ethnic, and professional background.

Results: The following seven issues were dealt with: (1) in the case of a patient who had verbally expressed his wishes and later the health care proxy went against those wishes, 28% of the workers responded that they would go against the patient's wishes unless he or she had documented them. (2) Only 25% of the physicians versus 55% of the nurses thought that noninvasive ventilation should be considered the same as mechanical ventilation. (3) 68% of the physicians and 87% of the nurses felt they would follow a DNR in a terminally ill patient even in the event of a reversible complication. (4) 46% of all respondents felt that they would go against the verbally expressed wishes of the patient if a DNR order was not documented. In this situation, 61% of nurses and 86% of physician assistants were likely to go against the patients wishes vs. 42% of the physicians. (5) 36% of the respondents felt that a "slow code" was justified in a terminally ill comatose patient, 33.5% of physicians as compared to 23% of the nurses. A significantly higher number (56%) of the physicians who did not believe in God justified a "slow code" ($p < 0.05$, $OR = 1.01-8.61$). (6) 57% of all respondents felt that giving morphine to suppress the breathing in a patient being terminally weaned amounted to euthanasia. (7) 41% of the physicians felt that they should be allowed to withdraw life support in a case they thought that it was medically futile to treat a patient in a permanently vegetative state even though the family

wanted to continue treatment indefinitely. Only 29% of the nurses agreed with the statement.

Conclusion: There are no clear guidelines to help the staff in dealing with many important ethical issues faced in the ICU and where they do exist the house staff lacks awareness. Within each professional, religious, or ethnic subcategory the opinion is divided as to how to deal with the ethical/legal issues. No statistically significant differences were noted in comparing the decisions of respondents of various religious, ethnic, cultural, or professional backgrounds. Thus the religious, ethnic, cultural, or professional background of a health care provider has no bearing on his decision making capacity in these situations. Clearly, much more debate, consensus, and education is required in this area.

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Ten-Year Results of Treatment of Advanced Metastatic Cancer with the Multimodality Immunotherapy Program

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Forty five patients with various advanced metastatic cancers were seen at the Institute of Islamic Medicine for Education and Research (IIMER) and its affiliated clinics between 1986 and 1992. Their cancer diagnosis was made between 1985 and 1991. They ranged in age from 1-85 years. All either had received and failed to respond to conventional cancer therapy or were not amenable to a curative conventional cancer therapy before they were started on our multimodality immunotherapy program (MIP). The MIP is an experimental treatment program comprising several alternative nontoxic, mostly unconventional modalities including a nutritional program based predominantly on a vegetarian live food diet, nutritional supplements, fever therapy, ozone and chelation therapy, tumor antigen, exercise, physical therapy, acupuncture, and above all a comprehensive emotional restoration program that includes counseling, biofeedback training, guided imagery, and other visualization techniques. Reviewing the 5- to 10-year results of these patients shows that 13 patients (28.9%) have survived 5-12 years with an average survival of 8.85 years. At the time of this report, three of these 13 patients had died 5, 10, and 12 years after their original cancer diagnosis. Ten patients are still alive. Seven of these 10 patients are doing very well without any evidence of disease, and three have some residual disease 6, 7, and 10 years after their original cancer diagnosis. These results are better than the results of conventional treatment alone for patients with comparable disease conditions.

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Antithrombotic Therapy in the Current Practice and Near Future

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The decision to use antithrombotic therapy involves weighing the risk and benefits of the therapy, whether short-term or long-term, the major risk being of bleeding at a noncompressible site or in a closed cavity, specifically, intracranially and with the risk of thrombosis or embolism if the therapy is withheld. The final decision to anticoagulate is always individualized following the standard guidelines. In the United States, the antithrombotic guidelines are updated every three years with the last update being in 1995. The most important change is to reduce the intensity of oral anticoagulation of international normalized ratio (INR). For most conditions, the recommended range is 2.0 to 3.0. The conditions included are prophylaxis of (high risk surgery) treatment of venous thrombosis, pulmonary embolism, prevention of systematic embolization, tissue heart valves, valvular heart disease, and atrial fibrillation. For mechanical prosthetic valves and prevention of recurrent acute myocardial infarction, a higher PT INR is recommended (2.5-3.5). Because the PT is affected by a number of drugs and food and change in clinical status, it has to be monitored closely. For patients who bleed with therapeutic anticoagulation, a lower level of anticoagulation with addition of antiplatelet therapy is considered. Antiplatelet therapy and platelet active drugs include aspirin, ticlopidine, indobufen, platelet glycoprotein IIb/IIIa inhibitor antibody. The most commonly used is aspirin and has been used in acute myocardial infarction (AMI) primary and secondary prevention of AMI, prior stroke or TIAs, or other high risk thromboembolic conditions including intraoperative and postoperative strokes in carotid artery surgery and atrial fibrillation. Heparin is used specifically during bypass surgery or unstable angina. Other IV agents being currently under trial include heparinoid, danaparoid sodium, and ancrod. Low molecular weight heparins are now available. Thrombolytic agents are used in acute thrombosis in an emergency setting, e.g., AMI pulmonary embolism of hemodynamic significance, etc. Agents that are in use include TPA, streptokinase, antistreplase, and urokinase. N-3 fatty acids, sulfapyrazone, dipyridamolc, and ticlopidine, dermaten sulphate and heparinoids also will be discussed briefly.

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Usefulness of intrathecal Baclofen in spasticity of spinal origin has been well documented in studies. The drug exerts its effect through spinal cord neurons at layer II and III of the dorsal gray matter. The fact that the effect was seen on this test dose within six hours indicates the relief of spasticity in these cases through spinal GABA-B receptors located in these layers of neurons. The Baclofen half life is estimated to be between four and six hours. These factors explain that even in patients with supraspinal spasticity, the relief of spasticity is through spinal mechanism. In the ear-

lier studies, Baclofen doesn't seem to affect the spasticity from alpha motor neurones as determined by the cryotest. The hyperactivity in the fusimotor system responded best by the Baclofen. Improvement in these cases of spasticity of supraspinal origin can be explained by blocking excitatory neuro transmitters, including possible substance P, from nociceptive afferent nerve endings, which tend to produce flexor reflexes when activated, and finally by the disorganization in the spinal neurones.

We report two cases of supraspinal spasticity relieved by intrathecal Baclofen demonstrating intrathecal Baclofen can be considered as an alternative to the various regime available for treatment of spasticity of supraspinal origin. Epileptic seizures can occur with Baclofen therapy. None of our patients hitherto developed seizures, but central nervous system depression, respiratory embarrassment, infection, and blockage of the catheters are some of the complications that should be kept in mind while treating patients with intrathecal Baclofen.

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