COLLEGE OF FAMILY PHYSICIANS SINGAPORE

The SINGAPORE FAMILY PHYSICIAN

INFECTIOUS DISEASES UPDATE

- Tuberculosis
- Chickenpox Vaccine
- Travel Medicine Update
- Antibiotic Use
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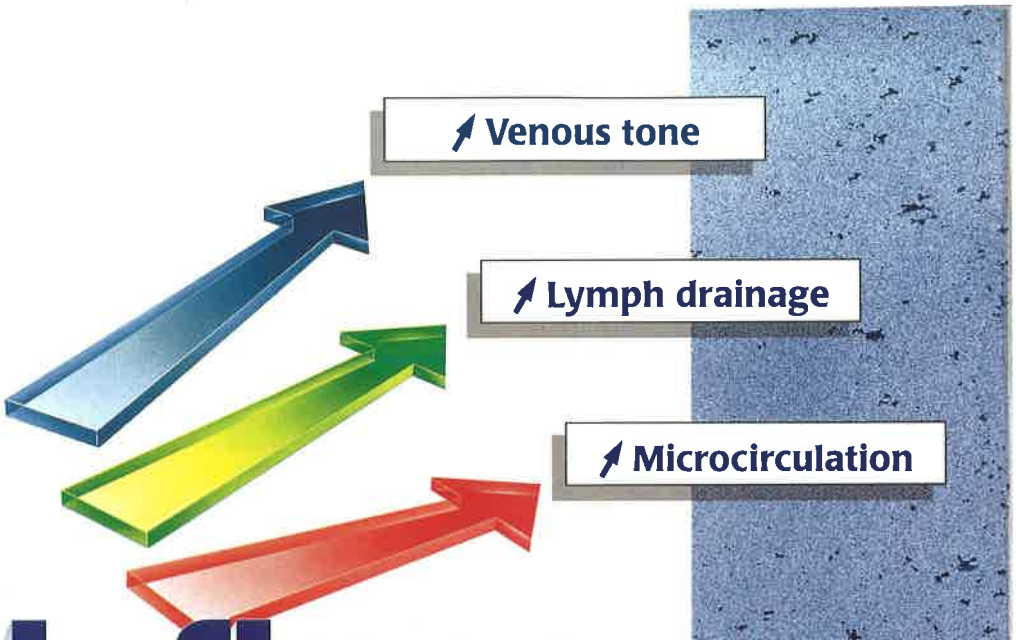

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EDITORIAL

INFECTIOUS DISEASES – A THING OF THE PAST OR A SCORCH OF THE PRESENT?

Infectious diseases such as tuberculosis, malaria and cholera used to be prevalent and were the leading causes of morbidity and mortality in Singapore about 40 to 50 years ago. However with rising standards of living, health, hygiene and an improved diet, these diseases appear to be on the decrease and are increasingly replaced by so-called "diseases of affluence" such as gout, ischaemic heart disease, diabetes and cancer.

Correspondingly, there appears to be a lack of interest in the study and treatment of infectious diseases as compared to the current interest in the early diagnosis and treatment of various types of cancers, newer drug therapy in the management of hypercholesterolemia and other metabolic diseases such as obesity. Herein lies the hidden danger. In recent years there has been a resurgence of tuberculosis worldwide with the increase in the incidence of multi-drug resistant TB and also the emergence of drug-resistant malaria and newer diseases such as AIDS and also hitherto unknown diseases such as melloidosis have been increasingly diagnosed.

In addition, international air travel has exposed us to a wide host of infections which were previously not encountered as more people travel to exotic destinations for holidays such as Nepal and South America, or businessmen heading for nearby countries such as China and Vietnam. It is, therefore, important that general practitioners know the hazards of international travel and the article on Travel Medicine by Dr Chad Meyer is both relevant and timely.

Closer home, the constant influx of migrant workers into Singapore brings with it an increasing incidence of diseases such as TB, malaria and AIDS, of which we have to remain alert and vigilant, not only in awareness but also in early clinical suspicion and diagnosis. In this regard, there is an excellent article, "Update on Tuberculosis" by Dr Jane Yap of Tan Tock Seng Hospital, which is worth reading and taking note of recent developments in TB worldwide.

Other articles featured in this month's journal include one on antibiotic usage by Prof Vernon Oh of the Department of Pharmacology and the latest study on the efficacy of chickenpox vaccine on children and adults conducted by A/Prof Lee Bee Wah of National University Hospital.

We hope that you will enjoy reading these articles and find them useful, informative and helpful in your clinical diagnosis and management.

Dr David H K Lim

UPDATE ON TUBERCULOSIS

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In April 1993, the World Health Organisation declared tuberculosis (TB) a global emergency. It is estimated that one third of the world's population is infected with tuberculosis. Each year there are 8 million new cases and half of them are infectious. Nearly 3 million died from tuberculosis in 1995, surpassing the worst years of the epidemic in the early 1900s, when an estimated 2.1 million people died annually. TB deaths have reached a historic level. TB is now the leading infectious killer of youth and adults. It causes more deaths than other infectious diseases like AIDs and malaria added together. It is responsible for one third of the deaths in HIV-positive persons[1].

Tuberculosis infection has increased for several reasons. Migration and worldwide international travel help to spread the infection. HIV positive patients are more susceptible to the infection. These dual infections form a fatal combination. Poor social economic conditions in developing countries and complacency about the disease in developed countries are other reasons. For example, in many States of America, interest in TB faded into the background because it was declining satisfactorily. Hence funds allocated to the disease were cut back, dedicated TB clinics closed and traditional TB physicians no longer considered important to TB control. It was forgotten that patient compliance was the key to success to TB control and the prevention of multidrug resistance. Hence, TB treatment was relegated to general medical clinics and the comprehensive system of supervised therapy with monitoring of compliance, and progress was dismantled. As a result of this, the incidence of multidrug resistant TB (MDRTB) also rose and this aggravated the TB situation. Short course chemotherapy is ineffective for MDRTB. The success rate of treatment is low and mortality rate is high in MDRTB.

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In Singapore, concerted effort for the control of TB was started in 1957, with the formation of Tuberculosis Control Unit under the Ministry of Health. A year later, TB notification became compulsory by law under the Infectious Diseases Act and the Tuberculosis Registry was started. The incidence rate of TB was diligently brought down from 303 per 100,000 residents in 1960 to 56 per 100,000 in 1987. However, it has remained fluctuating between 50 to 55 per 100,000 since then. Although it is lower than most developing countries it is high compared to developed nations. The incidence of MDRTB is still very low in Singapore. Although the situa-tion in Singapore is not alarming yet, vigilance needs to be continued.

RE-ESTABLISHING CONTROL OF TB

This resurgence of TB calls for a coordinated international effort to prevent and control TB. Sixty-six TB experts met during the winter of 1994, at the American Lung Association Conference on Re-establishing Control of TB. Recommendations were put up for an international effort to control TB[2].

Public health surveillance on TB has to be improved. HIV infection, institutional TB and drug resistant TB will be some of the factors that

will affect the global TB epidemiology. Molecular epidemiology using restriction fragment length polymorphism analysis (RFLP) has been used to identify laboratory cross-contamination, exogenous reinfection with MDR-TB in AIDS patients, and to confirm epidemiologically suspected transmission in a variety of settings, for example hospitals, prisons, congregate living facilities and outpatient clinics. It may be integrated into basic TB Control for monitoring the efficacy of current disease control efforts.

Good public health infrastructure is important. It consists of all the resources that support services basic to an effective control program. It includes appropriate leadership, usually the health department. This leader must have full governmental commitment, funding and legislative support. A cost-effective and proven drug treatment exists, but careless TB treatment practices are triggering bacilli that are resistant to once-effective drugs. MDR-TB develops when anti-TB drugs are not taken on a consistent basis, or are not taken for the entire course. Therefore directly observed treatment, short-course (DOTS) whereby a health care worker watches the patient swallow each dose of the medicine is recommended for all TB cases. This is the only way to ensure that patients take their medications and complete the treatment, rendering them cured. Candidates for DOTS are those with positive smear in their sputum, those who require treatment after prior failure, patients with MDR-TB, the non-compliant, those who fail to improve on treatment, those who abuse substances (drugs, alcohol), and patients with mental, emotional or certain physical impairments that interfere with their ability to self-administer medications.

Treatment outcome is an important measure of the performance of a TB control programme. Drug resistance surveillance is another important assessment. Primary drug resistance reflects the results of a TB programme that was inefficient in the past. It reflects ongoing transmission and the need for improved case-finding and containment. Acquired drug resistance reflects poorly functioning TB control programme at the current time. It indicates the need to improve effectiveness in managing cases and ensuring that patients adhere to and complete therapy. Few studies have assessed the importance of patient and public educational intervention for TB control. However it is felt that education contributes to TB control and is essential for success with DOTS. Specific training to develop TB experts as well as general physician education on TB are recommended.

At present, the only effective measure for TB control is identification and treatment of patients with active disease or dormant infection to interrupt the chain of transmission. However this may not be achieved in developing countries as they may lack the necessary resources. BCG vaccination shows protection against haematogenously disseminated TB in childhood. However protection against TB in adults varies from 0 to 80%. Meta-analysis showed 50% protection[3]. It has been found that BCG induced tuberculin sensitivity does not correlate with vaccine-induced protection. Hence research on for-mulation and development of a universally effective TB vaccine is another important step towards international TB control.

The advent of multidrug resistant strains, particularly in the presence of HIV infection, results in devastating mortality rates. Rifampicin was the last effective drug for TB introduced 30 years ago. There is an urgent need for new effective drugs. The most promising new developments are the fluroquinolones such as ciprofloxacin and ofloxacin. In the study by Mohanty et al[4], 18 patients who received 2 months of daily treatment with streptomycin, isoniazid, pyrazinamide and ciprofloxacin (2SHZC) followed by isoniazid plus ciprofloxacin for 4 months (4HC) showed 95% sputum conversion. However, 16.6% relapsed bacteriologically as compared with the group with 2SHRZ/4HR regimen, 5.9%. Derivatives of rifampicin such as rifabutin and rifapentine also show promise. In particular, Rifapentine may be considered for intermittent polychemotherapy because of its long half life[5]. Rifabutin is active against some rifampicin-resistant strains. *Mycobacterium tuberculosis* produces intracellular beta-lactamase. Hence inhibitors of beta-lactamase or beta-lactamase resistant anti-biotics have potential as new drugs[6].

Besides research on developing new drugs, the genetic structure and physiology of *Myco-*

bacterium tuberculosis should be studied in depth. The entire genome should be mapped. Genes that regulate cell division, cell-wall synthesis, and transition from the vegetative to the dormant state should be defined. Tuberculin skin test lacks sensitivity and specificity. A simple, sensitive and specific test to detect *Mycobacterium tuberculosis* infection is needed. This must be based on additional knowledge regarding protein products of *Mycobacterium tuberculosis* and on the immune responses to these products.

With regard to preventing transmission of infection in hospitals and institutions, very little is known about the mechanism for controlling airborne TB transmission. The absolute and relative values of ultraviolet light, various protective respirators and protective ventilation have to be carefully evaluated. Preventive therapy trials in human for eradicating infection due to MDR-TB should be evaluated further.

DRUG RESISTANT TB

Primary drug resistance occurs in persons who are initially infected with drug-resistant organisms because of exposure to a person with drug-resistant TB. Secondary or acquired drug resistance develops when drug resistant organisms are selected because patients are treated with an inadequate regimen or fail to take a regimen appropriately. Multidrug resistance refers to strains of *Mycobacterium tuberculosis* which are resistant to both isoniazid and rifampicin, with or without resistance to other drugs. It is usually secondary to inadequate therapy. However, if it is not brought under control, it may become primary drug resistance.

Drug resistant TB gives major threats. To the individual, the outcome of treatment is poor and to the community, exposure is longer. The presence of drug-resistant organisms at the start of therapy is associated with 83 times greater risk of treatment failure (11.6% vs 0.15%), and 2 times greater risk of relapse (11% vs 5%)[4]. 73% treatment failure had been reported in MDR-TB[7]. In the study by Globe et al[8], in 171 negative patients treated for MDT-TB between 1976 and 1983 with a median of 4 drugs, the overall response rate was 56% and mortality rate 37% over 51 months. Another study[9] analysed 173 patients with MDR-TB, treated between 1983 and 1993. 52% of these patients were HIV infected. Mortality was much higher in the HIV infected group. 20% were cured as compared to 56.1% in the HIV negative group.

Spontaneous mutation in the bacterial population occurs with a constant but infrequent rate. This is a natural phenomenon which cannot be influenced by man. One in 10^5 organisms for example is resistant to streptomycin. Fortunately the chromosomal loci for resistance to the various drugs are not linked, the risk of double mutation resulting in multidrug resistance is therefore extremely small. Drug resistant TB is more commonly due to selection of resistant mutants secondary to inadequate treatment. Patients with acquired resistant TB may infect contacts. Primary resistant TB may be developed in these contacts. HIV infected individuals who are also infected with *Mycobacterium tuberculosis* are more likely to develop active disease. Diagnosis and treatment in this group may be delayed and hence transmission prolonged.

TB Control programme managers when faced with drug resistance should understand the treatment delivery process (TDP) well[8]. Three processes can be distinguished:

- from diagnosis to prescription (e.g. who treats, any treatment guidelines),
- from prescription to supply (e.g. quality control of drugs)
- from supply to drug intake (e.g. compliance, supervision, fixed combination tablets).

Once the faulty process is identified, they can then carry out the necessary intervention strategy[10].

HIV AND TB

In 1994, there were 5.6 million individuals infected with both HIV and TB. Majority were from Africa and South East Asia. There is no evidence that HIV-infected TB patients develop drug-resistant TB under adequate treatment. However HIV can influence the magnitude of drug resistant TB problem due to increased susceptibility to the disease.

The adverse interactions of TB and HIV are

bidirectional. The alveolar macrophages in the initial non-specific response to *Mycobacterium tuberculosis* are limited. The antigen presenting function of macrophages is also impaired. CD_4 lymphocytes are less responsive to mycobacterial antigen. TB accelerated the course of HIV disease via the production of α-TNF.

TB precedes other AIDS defining illness by up to 2 years in about half of the cases. There is a higher proportion of cases with extra-pulmonary or disseminated disease. Chest X-ray usually shows atypical features of TB when the patient is more immunocompromised. There is also a higher rate of adverse drug reaction. Sputum positivity for acid fast bacilli is the same as that of immunocompetent patients. The response to chemotherapy is also equally good, however recurrence of TB is 3 fold higher. This may be relapse or reinfection[11].

One year of isoniazid chemoprophylaxis had been shown to reduce risk of TB by 71%. The subgroup with positive Mantoux test showed 83% reduction in risk of coming down with the disease[12].

IMMUNOTHERAPY

The concept of immunotherapy was first introduced by Robert Koch in 1890 with repeated injections of old tuberculin. However it could cure as well as kill. With increased knowledge of immunity and failure of chemotherapy, combination of immunotherapy and chemotherapy may be a promising TB treatment.

A suspension of killed strain of Mycobacterium vaccae is given. It increases immune recognition of common mycobacterial antigens and promotes TH1 activity. Hence it enhances protective effect and diminishes tissue necrotic effect. It promises to reduce duration of treatment and may prove valuable in treatment of MDR-TB. One study[12] showed clinical cure in $^{11}/_{41}$ cases of MDR-TB treated for 1-12 years.

LABORATORY DIAGNOSIS

The only rapid laboratory diagnostic method used widely is microscopy. It is however not specific as MOTT can give positive acid fast bacilli. Its sensitivity is improved by the use of fluorescent stains. Rapid culture method is best provided by the Bactec System. Detection period is reduced to 1-2 weeks. Nucleic acid amplification is an alternative to increasing number of organisms by culture, This method directly increases the amount of nucleic acid target by in vitro enzymatic means. Polymerase chain reaction is most widely used. Drug susceptibility testing can be speeded up by molecular method for example, detection of genetic mutation, or using luciferase reporter gene to assay drug action. No single immunoassay has yet emerged as a routine laboratory test. Elisa competition assay with monoclonal antibody TB72 which binds to 38KDa antigen, an immunodominant antigen of *Mycobacterium tuberculosis*, holds some promise. However, we hope that serology may play a role in diagnosing smear negative TB, extrapulmonary TB, differentiating MOTT in smear positive cases, monitoring compliance, defining contacts who would benefit from chemoprophylaxis and lastly in assessing efficacy of new vaccines.

CONCLUSION

It is hoped that the resurgence of tuberculosis in the late 1980s and reaching global emergency in 1993 has made everyone realise that the control of the disease has failed. Coordinated international efforts at controlling this ancient disease should be stepped up before it returns to the pre-chemotherapy era.

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THE ROLE OF CHICKENPOX VACCINE IN HEALTHY CHILDREN AND ADULTS

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SUMMARY

The Oka strain live attenuated varicella vaccine (Merck Sharp and Dohme) was licensed by the Food and Drug Administration in 1995, for use in individuals 12 months of age or older who have not had varicella. Vaccination against chickenpox is most efficacious in childhood. The recommended schedule of immunisation is one dose for children between 12 months to 13 years, and 2 doses 4 to 8 weeks apart for those 13 years or older. The risk of zoster after immunisation is expected to decrease as the attenuated virus is likely to result in fewer latent infections compared to that of natural infection. As with other live vaccines, the main concern of widespread immunisation is that of waning immunity, and booster doses may be required. In the tropics, like Singapore, the peak incidence of chickenpox occurs in adolescence and young adulthood and is associated with low herd immunity to chickenpox in the young adult. Although chickenpox is a benign disease in children, in adults it is associated with more severe disease, thus making a case for the need of universal immunisation of populations in the tropics.

Keywords: *varicella, chickenpox, vaccine, children, adult*

INTRODUCTION

In 1995, the Oka strain live attenuated chickenpox vaccine (Merck Sharp and Dohme) was licenced by the Food and Drug Administration (USA) for immunisation of non-immune healthy adults and children above the age of 12 months[1,2]. Prior to this, the vaccine had already been available in several countries, including Singapore, but confined only to use in the immunocompromised. In addition, a few countries, including Japan, Korea and a number of European countries, had licenced it for use in healthy subjects. However, its recent licensure in the United States has acted as an endorsement for its use in healthy individuals, and several countries, including Hong Kong and Philippines, have followed suit. It is now available for use in Singapore. With this in mind, this article aims to discuss the role of the chickenpox vaccine in healthy children and adults.

THE NEED FOR VACCINATION – EPIDEMIOLOGICAL PERSPECTIVES

Chickenpox is transmitted from person-to-person through direct contact with skin lesions and by airborne respiratory droplet. It is one of the most contagious diseases, and resembles other childhood infections like whooping cough and measles. Within households, 80% to 90% of exposed susceptible contacts will develop

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chickenpox[1,3]. In the United States, as in other temperate regions, varicella is typically an illness of children under the age of 10 years[4,5]. However, in Singapore, like other tropical countries, the peak incidence of chickenpox occurs in adolescence and young adults[6], and is also associated with low herd immunity in our young adult population[7]. The reason for these epidemiological differences between these climatic regions is still uncertain, but there has been speculation that the higher environmental temperatures of the tropics hampers virus transmission, thus postponing varicella to an older population[7].

Chickenpox is usually benign in children, but is more severe in adults, with a tenfold higher likelihood of hospitalisation or death than for healthy children[5]. The most common serious complication in adults is varicella pneumonia. In Singapore, cases of fatal chickenpox in immunocompetent patients have been reported[8]. In addition to its medical complications, chickenpox has economic and social costs. Work absenteeism from chickenpox contributes substantially to the cost of the disease. Cost-benefit studies in the United States have shown that the universal immunisation is cost effective[9,10]. These factors support the need for the prevention of chickenpox in our community.

THE CHICKENPOX VACCINE

At present, the only available chickenpox vaccine is the live attenuated Oka strain of varicella-zoster virus. After numerous failed attempts at developing an attenuated virus strain, the wild virus obtained from a healthy Japanese boy, Oka, with natural chickenpox, was successfully attenuated by many passages in the laboratory in the 1970s[11]. From this attenuated Oka strain, a vaccine was developed and licenced for use in Japan in 1987 (Oka/Biken) and Korea in 1988 (Oka/Biken)[12]. Over 2 million doses of this vaccine have been given[1]. Its development outside Japan and Korea was made possible by the availability of master seed lots of this attenuated strain to pharmaceutical industries of the United States and Europe. The Oka strain vaccine is currently being marketed by Biken (Japan), Merck Sharp & Dohme (USA), and SmithKline Beecham Biologicals (Belgium).

RECOMMENDATIONS FOR USE

The American Academy of Pediatrics (1995) recommendations for use of the chickenpox vaccine in healthy subjects[1] are summarised in Table 1. The vaccine is given by subcutaneous injection. The recommended dose of the vaccine,

Table 1: Summary of Recommendations for the Use of Live attenuated Chickenpox Vaccine[1]

1. Age 12 months to the 13th birthday: One dose of varicella vaccine for universal immunization for all healthy children who lack a reliable history of chickenpox. Varicella vaccine may be given simultaneously with measles-mumps-rubella (MMR) vaccine, but separate syringes and injection sites must be used. If not given simultaneously, the interval between administration of chickenpox vaccine and MMR should be at least 1 month.
2. Healthy adolescents and young adults *Two doses of vaccine 4 to 8 weeks apart* Longer intervals between doses do not necessitate a third dose, but may leave the individual unprotected for the intervening months.
3. Contraindications and cautions *Pregnancy and Lactation* Varicella vaccine should not be administered to pregnant women, because the possible effects on fetal development are unknown. When postpubertal females are immunized, pregnancy should be avoided for 1 month after immunization. It is not known if vaccine-acquired VZV is secreted in human milk or if it would infect the infant. *Allergy to Neomycin* Varicella vaccine should not be administered to individuals who have had anaphylactoid reaction to neomycin, because trace amounts of neomycin are included in the vaccine. *Salicylates* It is unknown whether Reyes syndrome results form the administration of salicylates after vaccination for varicella in children. The vaccine manufacturer recommends that salicylates should not be administered for 6 weeks after varicella vaccine has been given.

0.5 ml, should contain a vaccine dose of not less than 1500 plaque-forming units. This vaccine also contains trace amounts of neomycin.

The preparation available in the United States, the Oka/Merck (Merck Sharp and Dohme, USA) vaccine, however, requires storage at a temperature of minus 15°C or lower. This storage requirement may hamper its widespread use in clinics which do not have such freezer facilities. It is a lyophilised preparation and once reconstituted, it has to be used within 30 minutes, as the vaccine virus diminishes rapidly, rendering it ineffective[1].

A reformulation of the Oka strain vaccine, Oka/SmithKline Beecham, which is marketed by SmithKline Beecham Biologicals, is more heat stable and can be stored at 2°C to 8°C, with a shelf life of up to 2 years[13]. This vaccine is available in Belgium, Germany and Sweden and, recently launched in the Philippines and Singapore.

Efficacy

The Oka strain vaccine is highly immunogenic, particularly in children. Cell-mediated immunity induced in adults is significantly lower than that in children[14]. Cell-mediated immunity is important for the long term efficacy of live attenuated viral vaccines[14]. Seroconversion rates of more than 90% have been reported after a single dose in children[12,13,15,16]. It is less immunogenic in adolescents and adults, and therefore, the requirement of 2 primary doses to achieve similar seroconversion rates as in children[17,18]. Seroconversion, however, does not always protect from breakthrough disease[15]. In children, the reported rates of protective efficacy against chicken pox varied from less than 70% to more than 96%, depending on the vaccine dose[15,19]. Generally, vaccine doses with higher plaque-forming units (PFU) had better protective efficacy[15]. It is however, heartening to note that "breakthrough" chickenpox is generally milder than the natural disease in children[12,20,21,22]. and adults[17,23]. In adults, however, the protective efficacy is lower, with two reports of protective efficacy of about 50%[17] and 70%[23] respectively.

Adverse Reactions

The vaccine is generally well tolerated. The most common side effects are pain, fever, chickenpox-like rash at the site of injection within 2 days of vaccination or, less commonly, a generalised chickenpox-like rash 1 to 3 weeks post-immunisation[15]. Our experience with the adverse effects of SmithKline Beecham Biological/Oka reformulated vaccine were similar with mild injection site erythema or swelling (24%), fever (19%), vesicular rash (3%)[13].

Long Term Concerns

There have been some concerns raised with regard to the effect of universal chickenpox immunisation. These have centred around concern over the length of protective immunity conferred by the vaccine, and vaccine-related latent infection, resulting ultimately in herpes zoster.

It is still uncertain whether children immunized with chickenpox vaccine would develop lifelong immunity[24]. There have been arguments that if protective efficacy declines with time, widespread immunisation may create a population of adults at risk of serious illness, resulting in the conversion of a relatively benign childhood illness into an adult illness with increased morbidity. There has been encouraging evidence from long term follow-up studies of persistence of antibody after 6 years[19], 10 years[25], and 20 years[26] post-immunisation. On the other hand, the subclinical boostering effect from contact with 'wild' chickenpox may diminish when most people are immunised and 'wild' varicella becomes rare. In this regard, a monitoring system has been set-up in the United States to determine the need and timing of booster immunisations[15].

The second concern is whether the chickenpox vaccine can cause latent infection resulting in zoster. The evidence so far has also been encouraging. In USA, the incidence of zoster was not increased in healthy immunised children[23]. In a study on leukaemic children, the evidence of herpes zoster was lower in vaccinees compared to those who had natural chickenpox[27,28]. In another study, only 1 of 302 vaccinated adults developed zoster[29].

In conclusion, there is a need to prevent chickenpox in our community. The only vaccine

currently available is the live attenuated Oka strain varicella vaccine. It is highly immunogenic and well tolerated. Although the vaccine virus may cause latent infection, there is evidence that the incidence of vaccine-related herpes zoster is lower compared to that caused by the wild virus. The question of the need and timing of booster immunisations to ensure long term protective immunity will, however, have to be addressed.

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MANAGEMENT OF HERPES ZOSTER OPHTHALMICUS – AN APPROACH FOR THE FAMILY PHYSICIAN

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Summary

Herpes zoster ophthalmicus (HZO) is an infection caused by the varicella-zoster virus in the ophthalmic division of the trigeminal nerve. This is a result of either reactivation of the latent virus or repeat exposure to the virus itself. Besides causing postherpetic neuralgia, HZO can cause sight-threatening complications. Any of the ocular structures can be afflicted with consequent ophthalmic sequelae. Early diagnosis and timely treatment of HZO can reduce the incidence and severity of complications associated with this disease process.

Keywords: *Acyclovir, ophthalmic complications, postherpetic neuralgia, varicella-zoster virus.*

INTRODUCTION

Herpes zoster of the ophthalmic division of the trigeminal nerve (herpes zoster ophthalmicus, HZO) is a medical condition that usually presents initially to the family physician. With a good knowledge of the natural history of the disease, the family physician can effectively help the patient understand the disease process and its complications.

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NATURAL HISTORY OF HERPES ZOSTER

Herpes zoster is caused by the varicella-zoster virus. The patient's first contact with the virus results in clinical or subclinical chickenpox. Subsequently the virus remains latent in sensory ganglia such as the trigeminal (gasserian) ganglion and dorsal root ganglia.

The latent virus reactivates when the patient's immunity declines as a result of age or disease. The virus then passes along the sensory nerve and causes vesiculopustular eruptions on the dermatome supplied by the nerve. A rarer second mode of occurrence is when the patient is re-exposed to the virus itself. Individuals who have not suffered from chickenpox are at risk of acquiring chickenpox if they are exposed to patients with herpes zoster.

Herpes zoster is two to three times more com-

mon in patients over 60 years of age compared to the general population. Immunocompromised individuals have an incidence ten times that of immunocompetent individuals. These include patients with lymphoma and acquired immune deficiency syndrome as well as those under treatment with radiotherapy or immunosuppressives.

DISTRIBUTION OF HZO

Ten percent of herpes zoster affects the ophthalmic division of the trigeminal nerve. The most frequently affected branch of the ophthalmic division of the trigeminal nerve is the supraorbital branch.

Figure 1: Herpes Zoster Ophthalmicus with Bilateral Periorbital Oedema

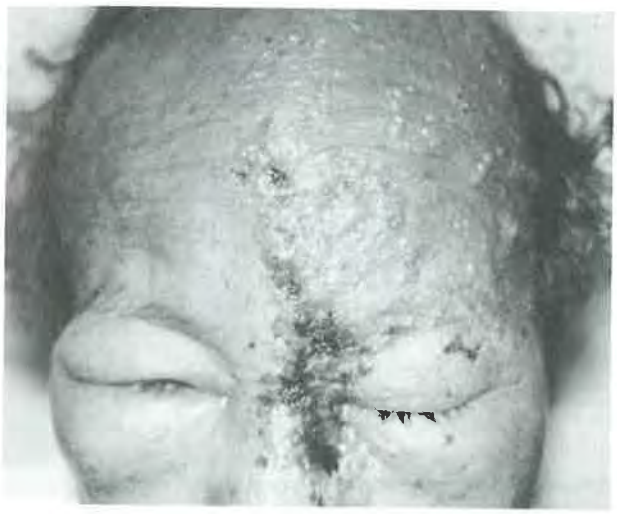
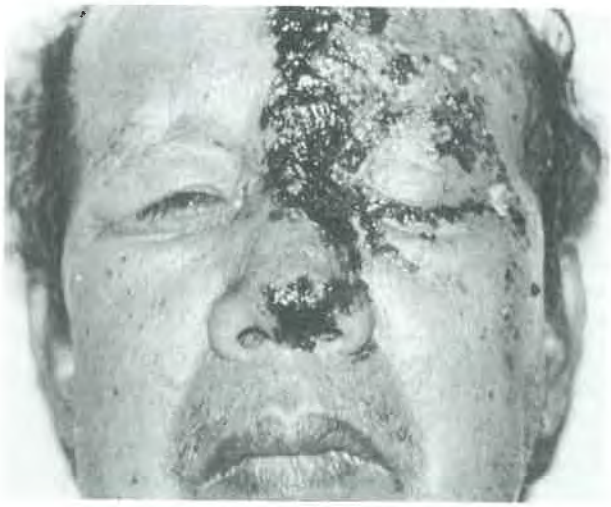


Figure 2: Crusting Ulcers in Herpes Zoster Ophthalmicus



The most serious ocular affliction results from involvement of the nasociliary branch. This branch supplies the eye and the side of the tip of the nose. Cutaneous vesicles and pustules at the side of the tip of the nose (Hutchinson's sign) therefore indicates a greater likelihood that the eye may also be affected. However, even if the nose is not affected, ocular involvement may still occur.

SIGNS AND SYMPTOMS OF HZO

Initially, patients may have prodromal symptoms of headache, malaise, cutaneous hyperesthesia, fever and chills. This is followed a few days later by flushing and dermal hyperaemia. Finally there is a single crop of rash on the forehead, scalp and upper eyelid. This is usually associated with periorbital edema. In severe cases, the periorbital edema may spread to the contralateral eye (Fig 1). The rash is initially maculopapular. It then becomes vesiculopustular and finally forms crusting ulcers (Fig 2).

In the early phase of the disease, patients often experience severe neuralgic pain. After the cutaneous lesions have healed, patients may experience postherpetic neuralgia which can be prolonged and severe.

Ophthalmic involvement in HZO is best summarised in Table 1. The cutaneous lesions of HZO scar up and heal within 21 days whereas ophthalmic involvement can persist for weeks to months. Central nervous system complications of HZO include encephalitis and hemiplegia but these are rare.

It is therefore important for the family physician to elicit symptoms of redness, ocular pain, decreased vision and double vision to exclude possible ophthalmic involvement. Clinical examination of the patient should include visual acuity test, pupillary reflexes, extraocular movement examination and inspection of the eyelids, conjunctiva, cornea, anterior chamber and ocular fundus.

TREATMENT

a) Treatment of ocular complications

In the event of any ocular involvement, it is best to involve an ophthalmologist in the joint management of the patient as these complications may be sight-threatening. Depending on the type of ocular involvement, treatment may include the use of antibiotic, corticosteroid, and cycloplegic eyedrops and antiglaucoma medication.

b) Treatment of cutaneous lesions

The aim of treatment is rapid healing of the skin without formation of massive crusts which results in scarring of nerves and postherpetic neuralgia.

Treatment includes moist compresses, topical antibiotics (to prevent secondary bacterial infection) and oral acyclovir in a dosage of 600 to 800 mg 5 times a day for 7 to 10 days. This should be initiated within the first 3 to 5 days after cutaneous eruption to be effective. Oral acyclovir hastens the resolution of cutaneous lesions and reduces the incidence and severity of ocular involvement. However, acyclovir seems to have no effect on postherpetic neuralgia.

Systemic corticosteroids have been advocated in the hope of reducing postherpetic neuralgia. However, this is not well-proven. The possibility that systemic corticosteroids may cause disseminated herpes zoster should be borne in mind.

CONCLUSION

The early diagnosis and timely treatment of HZO by family physicians can reduce the incidence and severity of sight-threatening complications in this disease process.

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Table 1: Ophthalmic Involvement in HZO

Structure	Involvement	Corresponding Symptoms
(1) Lids	periorbital edema	swollen lids
	vesicles and pustules	rash
	ptosis	droopy lid
(2) Conjunctiva	hyperaemia	red eye
(3) Cornea	keratitis ulceration thinning perforation	painful eye poor vision
(4) Anterior Chamber	iridocyclitis secondary glaucoma	painful eye poor vision
(5) Others	episcleritis scleritis	red painful eye
	extraocular muscle palsy	double vision
	chorioretinitis optic neuritis	poor vision

TRAVEL MEDICINE GUIDELINES FOR FAMILY PRACTITIONERS

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INTRODUCTION

Singapore's central location in Southeast Asia, its proximity to South Asia, and the readily available air, sea, and overland links within the region, facilitate holiday and commercial travel. Residents of Singapore are fortunate to live in an environment in which the common classical tropical diseases have been eliminated. However with only brief travel from Singapore, travellers accustomed to a pristine environment can place themselves at risk of many travel-related illnesses. Studies have shown that travellers commonly obtain travel medicine from friends, professional contacts, and travel agents. Travel agents, in particular, are cited as being poor sources of accurate information; considering that they are in the business of promoting travel, some may even downplay the hazards of particular travel destinations.

FAMILY PHYSICIANS AND TRAVEL HEALTH

Family physicians, in contrast, are the ideal providers of travel medicine. The family physician is primarily responsible for immunizations and other preventive health care. Review of the immunization record at the time of travel also serves as a useful survey of the regular recommended vaccinations (diphtheria, tetanus, measles, polio, and hepatitis B), and the need for primary or booster vaccinations. In addition, the family physician has the best understanding of an individual patient's medical conditions, including chronic diseases (diabetes, hypertension, cardiac and pulmonary disorders, drug allergies, etc) and how these conditions may be affected by specific travel. Finally, a family physician can efficiently provide travel medicine advice for an entire family; the alternative would be for each family member to obtain consultations from separate specialists (gynaecologist, paediatrician, internist). Such fracturing of health care is not only inefficient, but may contribute to poor medical preparation for travel. A pre-travel consultation is ideally made six to eight weeks before departure. Many patients do not know how to seek travel medicine advice, and those that request information often do so in a tangential manner – after being seen for another medical condition. We recommend that all family physicians display notices in their waiting areas and treatment rooms, clearly stating that travel medicine advice is available through the clinic, and should be sought prior to travel. Most clinics can maintain travel guidelines for the common travel destinations: China. India, Indonesia, Malaysia and Thailand. In addition, each clinic should have resources available for current information; this may include public health journals, national epidemiological reports, and on-line internet resources. Additionally, resources such as the Singapore CDC's Traveller's Health and Vaccination Clinic may be phoned for selected information. One excellent use of resources is to identify a bright, energetic, and enthusiastic nurse on the clinical staff, and encourage her/him, in conjunction with a physician member of

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the health care team, to develop travel medicine advisory skills, and a travel medicine program for the clinic.

SOURCES OF INFORMATION ON TRAVEL HEALTH

Travel medicine personnel must make a commitment to "stay current" with changes in information. Alternatively (as a minimum standard), if the clinic cannot provide travel medicine advice, it should maintain a list of medical facilities in Singapore where current travel medicine information is available. Patients could then be referred for appropriate pre-travel medical preparations. The Communicable Disease Centre's (CDC) Traveller's Health and Vaccination Clinic is one such resource. Appointments and information may be obtained by calling 359-5958, fax 256-4436.

Some useful literature resources include:

1) *Health Information for International Travel* (updated each year), published by the USA CDC, and available from: Superintendent of Documents, US Government Printing Office, WashDC 20402; tel: 1-202-783-3327.
2) *International Travel and Health, Vaccination Requirements and Health Advice*, 1996, published by the World Health Organization, and available from Select Books, Tanglin Shopping Centre #03-15, Singapore; tel: 732-1515, fax: 733-0855.
3) *Travel Medicine, The Medical Clinics of North America,* vol 76: 1261-535, 1992.

The CDC in Atlanta, USA also maintains an international "Traveller's hotline" with telephone recordings of country specific information 1-404-332-4559. The Singapore CDC's Traveller's Health and Vaccination Clinic 359-5958, (fax 256-4436) provides similar information.

The following internet sources (Table 1) provide useful international travel information; they have the advantage of timely periodic updates, and patients familiar with the internet may be given a list of these addresses for their personal use.

Because patients frequently misunderstand or do not remember the details of information provided during clinic visits, written notes for the traveller will increase the usefulness of the consultation. Additional concerns include the need for overseas health insurance and medevac

Table 1: Internet Sites on International Travel Information

Canada, Health Information Network	http://hpbl.hwe.ca:8300/
France, Le Réseau Sentinelles	http://www.b3e.jussieu.fr/sentiweb
United Kingdom Com. Disease Surveillance Centre	http://www.open.gov.uk./cdschome.htm
United States, M.M.W.R. (Morbidity Mortality Weekly Report)	http://www.cdc.gov/epo/mmwr/mmwr/html http://www.cdc.gov/cgi-bin/mmwrsearch.pl http://www.cdc.gov/travel/travel.html#georec http://www.cdc.gov/travel/seasia/htm
World Health Organization	http://www.who.ch/ http://www.iss.it/yellow/
WHO, Weekly Epimemiological Record	http://www.who.ch/wer/issues.ht
International Society of Travel Medicine	http://www.istm.org/
Travel health online:	http://www.tripprep.com/index.html

insurance (medevac air transportation may cost S$20 – 40,000 or more). Local medevac insurance companies include SOS and AEA.

COMMON MEDICAL PROBLEMS ASSOCIATED WITH TRAVEL

The more commonly encountered medical problems associated with travel include: auto-vehicle injuries, diarrhoeal diseases, acute respiratory infections, and a list of infectious diseases including Japanese encephalitis (JE), rabies, tetanus, measles, varicella, malaria, and enteric fever.

Motor-Vehicle Accidents

In most studies accidents accounted for 25% of travel-related deaths. Emergency transportation and A&E centres in the region do not provide the services available in Singapore. Travellers should be advised to avoid using motorbikes, and to wear seat belts whenever they are available, avoid intoxicating substances and stimulants while driving, restrict to daylight hours whenever possible, ride only in well maintained vehicles with competent drivers, avoid speeding, and always drive defensively.

Travellers' Diarrhoea

The majority of enteric pathogens associated with travellers' diarrhoea are not destroyed by temperature ranging from 0° to 65°C. As a result ice made from contaminated water can serve as a vehicle for infection. Foods heated to 65°C or greater ("too hot to touch") generally are safe; however, re-warming usually does not achieve this temperature throughout the food. In areas lacking potable tap water, beverages are best taken without ice, and foods should be consumed as soon as possible after their preparation. Although alcohol in drinks will not destroy enteric pathogens, the carbonation process does; hence, carbonated soft drinks and beer are usually safe. When purchasing bottled water, the traveller should observe that the bottle has not been previously opened (to insure against contaminated tap water being dispensed from a "bottled water container." Staphylococcus growing in non-refrigerated milk, cream, or similar dairy products can produce a heat-stable toxin which survives very high temperatures; milk used in coffee or tea may contain these toxins which cause a gastroenteritis characterized by nausea and frequent vomiting. Since the gastric barrier in the stomach is a first line of defence, individuals with peptic disease on histamine type-2 blockers, or the even more powerful proton pump inhibitors, appear to be more susceptible to shigella, typhoid and non-typhi salmonellas, cholera and giardia.

Diarrhoea can be clinically separated into three therapeutic categories: 1) acute invasive, 2) acute non-invasive, and 3) chronic. Our working definition of chronic diarrhoea is persistence beyond two weeks; in the evaluation we consider parasitic causes (*G. lamblia, E. histolytica, Isospora belli*, and *Cryptosporidium*), as well as metabolic and environmental: hyperthyroidism, food allergies, excessive coffee intake, inflammatory bowel disease, etc. Travellers' diarrhoea usually presents as either acute invasive or non-invasive disease. Treatment is based on differentiating these two groups of diarrhoea.

Invasive diarrhoea (dysentery) is commonly caused by one of the following organisms: enteroinvasive *E. coli* (EIEC), enterohemorrhagic *E. coli* (EHEC - belongs to sero group 0157:H7, which produces a shiga-like toxin and is responsible for the hemolytic uremic syndrome), *Shigella, Salmonella, Campylobacter*, and *E. histolytica*. These organisms are characterized by large bowel infection. Clinically there is a small volume of diarrhoea with blood and mucus; associated fever and abdominal cramps are common. Since small volumes of fluid are lost, re-hydration is not the primary therapeutic concern. Appropriate antibiotics need to be administered – in the past trimethoprim-sulfa was sufficient, but due to bacterial resistance (particularly *Campylobacter, Shigella,* and *E. coli*), ciprofloxacin (500 mg twice a day for 3-5 days) has become a widely preferred treatment. If the patient is not toxic, and if close follow-up is possible, trimethoprim-sulfa (160/800 mg twice a day for 3-5 days) may be a rational approach. Anti-motility drugs (lomotil and imodium) permit more extensive tissue damage, and should not be used for invasive diarrhoea. We tell the patient, "if you have fever, or blood or mucus in the stool, do not take Lomotil or Imodium."

Non-invasive diarrhoea is frequently caused by

one of the following organisms: enterotoxigenic *E. coli* (ETEC), Norwalk virus, and rotavirus. These organisms secrete enterotoxins which inhibit normal absorption of fluids in the small intestine; the result is a "leaky membrane" with both water and electrolyte losses. Prompt treatment of the resulting dehydration and electrolyte depletion is important. Juices and clear liquids may supplement glucose or cereal based ORS; however, juices do not contain sufficient electrolyte mixes and are not appropriate treatment for moderate to severe diarrhoeal dehydration. Rehydration salts (available as ORS sachets) dissolved in potable water are the essential treatment. Starch-based rehydration solutions may be even more effective than glucose-based ORS; starch in the form of "cereal-based rehydration" (rice, potato mash, or corn mash soups) is an effective and safe form of treatment. Antimotility drugs may help, but should be taken sparingly, Bismuth subsalicylate (Pepto bismall) will bind the enterotoxin; if available through local pharmacies this agent may be beneficial. Bismuth subsalicylate should not be used by persons taking anticoagulants or hypoglycemics, or by persons hypersensitive to aspirin. Kaolin and pectin preparations are not felt to be effective.

In general we routinely do not recommend prophylactic antibiotics. However, their use may be appropriate for patients with medical conditions which might decompensate with travellers' diarrhoea (diabetes, cardiac disease, decreased gastric acidity, immune compromised conditions). Prophylactic regimes include: trimethoprim-sulfa 160/800 mg twice a day, norfloxacin 200-400 mg once per day, or ciprofloxacin 500 mg once per day. An alternative strategy (where bismuth subsalicylate is available) is two tablets four time a day during travel (maximum 3 weeks), combined with empirical antibacterial treatment if travellers' diarrhoea occurs.

IMMUNIZATIONS

When considering immunizations for travellers, one approach is to immunize against all potential pathogens regardless of exposure risk. This subjects the patient to an increased risk of vaccine adverse reactions, and considerably increases costs. We recommend that a risk assessment be made, and that recommendations be based upon potential exposure risk. Attenuated "live virus" vaccines should also be avoided during pregnancy, during lactation, and in persons with altered immune states (HIV associated immunodeficiency, and persons receiving chemotherapy, corticosteriod therapy, or radiation therapy; the live virus vaccines include: measles, mumps, rubella, and yellow fever. It is helpful to have an immunization "flow sheet" in the patient's medical record; this permits a quick review of vaccines previously received and those still required.

One of the dilemmas of providing travel medicine is the uncertainty about what to recommend for a particular location. It is unrealistic to expect family practitioners, or even tropical medicine or infectious disease specialists, to know detailed public health data for each country (including sub-regions: states, provinces, islands). However, each clinic providing travel medicine advice must have sources of reliable, and up-to-date public health and travel medicine information. Tables 2 and 3 provide outlines for the Asian region.

Hepatitis A

Serological surveys of Hepatitis A virus immunity (HAV IgG prevalence) were conducted in Singapore in 1975, 1984-5, and 1993[1]. The data shows a dramatic decrease in HAV immunity coincident with improved public health standards. The 1993 survey showed 97.5% of children and young adults (age less than 25 years) and 69% of those 25-34 to be non-immune for hepatitis A. Today most acute hepatitis A is associated with travel outside Singapore. Effective vaccination (Havrix, Smith-Kline Beecham) is now available using either two doses of 1440 Elisa unit (EU) vaccine, or three doses of 720 EU vaccine. Pediatric (6 months to 17 years) formulations (Havrix Jr) are available as three doses of 360 EU, or two doses of 720 EU vaccine. This vaccine is highly effective in preventing hepatitis A, provides protective immunity for at least ten years, and should be made available for travellers.

Hepatitis B

Universal Hepatitis B vaccination for all newborns was implemented in Singapore in September, 1987. Epidemiological data show that

teenagers and young adults are more at risk for acute hepatitis B infections[2,3]. Because most current teenagers and young adults did not receive perinatal Hepatitis B immunizations, vaccinations of this group is a good preventive health measure. Review of immunizations at the time of travel affords an opportunity to identify these individuals and to offer them vaccination (three doses of a recombinant vaccine over six months). Travellers might also be at increased hepatitis B risk as a result of sexual behaviour, or receipt of blood products if being treated abroad for trauma and shock.

Japanese Encephalitis (JE)

Japanese encephalitis is a viral disease transmitted by a species of *Culex* mosquitoes which inhabit rice paddy. Travellers who limit activities to urban centres, or rural areas outside of rice cultivation, are at low risk for JE and generally do not require vaccination. Travellers to JE endemic areas where rice cultivation and pig farming are practised should receive a primary series of three JE vaccinations (Biken labs, Osaka) over a one-month interval. Boosters are recommended every three years.

Rabies

Rabies remains a significant problem in South Asia, as well as most areas of Southeast Asia (Singapore, Malaysia, and Vietnam excepted). 98% of human rabies results from exposure to dogs. Individuals who anticipate potential exposures to street dogs (runners, and travellers to rural areas, for example) are at increased risk for rabies exposure, and should receive rabies pre-exposure vaccinations. Pre-exposure rabies consists of three intramuscular injections administered over 28 days. If bitten by a potentially rabid animal, two additional doses of

Table 2: Vaccine Guidelines

Country	Hepatitis A	Hepatitis B	Japanese enceph.	Meningo coccal	Rabies	Typhoid
Bangladesh	R	R	IR	N	IR	R
China	R	R	IR	N	IR	R
Hong Kong	R	R	N	N	N	R
India	R	R	IR	R: NORTH	IR	R
Indonesia	R	R	IR	N	IR	R
Japan	N	R	N	N	N	N
Cambodia	R	R	IR	N	IR	R
Korea	R	R	N	N	IR	R
Laos	R	R	IR	N	IR	R
Myanmar	R	R	IR	N	IR	R
Nepal	R	R	IR	R	IR	R
Pakistan	R	R	N	R	IR	R
Philippines	R	R	IR	N	IR	R
Sri Lanka	R	R	IR	N	IR	R
Taiwan	R	R	IR	N	N	R
Thailand	R	R	IR	N	IR	R
Vietnam	R	R	IR	N	IR	R

R for Recommended, IR for Individualize recommendation, N for Not required

the vaccine need to be administered (ideally on the day of exposure and three days later) to assure high levels of protective antibody. A number of unfortunate incidents have demonstrated that pre-exposure vaccine may not prevent rabies if the two post-exposure doses are not given. This needs to be clearly emphasized to patients.

The exact need and timing for pre-exposure doses is controversial. Although some package inserts still recommend pre-exposure boosters every three years, leading authorities have suggested that immune memory is sufficient for ten years or more after the primary three injections. One additional problem is that up to 5% of individuals receiving pre-exposure boosters will have a delayed hypersensivity response, often requiring administration of oral steroids.

Individuals who have not received a pre-exposure course of rabies vaccine, may be effectively immunized after a rabid animal bite. This is accomplished with five injections of

Table 3: Malaria Risk And Prophylaxis

Country	Areas of risk	Chloroquine resistance	Prophylaxis
Blangladesh	All, except Dhaka	widespread	mefloquine
China	Rural only, except no risk in northern provinces bordering Mongolia, and in western provinces of Heilungkiang, Kirin, Ningsia Hui Tibet, Tsinghai NOTE: Cities and popular rural sites on usual tourist routes are generally not at risk	Confirmed in sountern China, Hainan Island and provinces bodering Myanmar, Laos and Vietnam	chloroquine mefloquine in areas of chloroq. resistance
Hong Kong	NONE		
India	All, including cities of Delhi, Bombay	confirmed	mefloquine
Indonesia	Rural only, except high risk in areas of Irian Jaya No risk in cities of Java and Sumatra, and no risk for main resort areas of Java and Bali	confirmed	mefloquine
Japan	NONE		
Cambodia	All areas except no risk in Phnom Penh	confirmed	mefloquine
Korea	NONE		
Laos	All areas except no risk in Vientiane	confirmed	mefloquine
Malaysia	limited to rural areas of Peninsular Malaysia and Sarawak	confirmed	mefloquine
Myanmar	Rural areas only: Yangon and Mandalay no risk	confirmed	mefloquine
Nepal	Rural in Terai district (south) and hills below 1200 m No risk in Kathmandu	confirmed	mefloquine
Pakistan	In all areas below 2,000 m	confirmed	mefloquine
Philippines	Rural only, except no risk in provinces of Bohol, Catanduanes, Cebu, Leyte	confirmed Basilian, Luzon, Mindanao, Mindoro, Palawan, Sulu	chloroquine mefloquine in areas of chloroq. resistance
Sri Lanka	All areas, except no risk in Colombo	confirmed	mefloquine
Taiwan	NONE		
Thailand	Rural areas	confirmed	doxycycline
Vietnam	Rural only; no risk Red and Mekong Delta	confirmed	confirmed

(source: *Health Information for International Travel*, CDC, USA)

rabies vaccine over 30 days combined with rabies immune globulin (RIG) which is administered on the first day (simultaneous with the first rabies vaccine dose). One limitation of the post-exposure vaccination schedule is the scarcity of RIG. If available it is usually only stocked in speciality centres in large urban centres, and is very expensive (the average adult dose of RIG generally costs S$600-800 from the manufacturer. Since 10-14 days are required for the development of post-vaccine protective immunity, RIG provides passive immunity during this interval. If pre-exposure vaccination has not been received, and RIG is not immediately available, rabies virus may become established in the wound. If rabies subsequently enters nerve tissue, rabies encephalitis is inevitable. Wounds to areas of the body which have high concentrations of nerves (the face and hands) are higher risk. Vigorous cleansing and irrigation of the wound serve to reduce the viral load and form a mainstay of initial treatment.

Meningococcal Vaccine

Meningococcal vaccine is recommended for travellers to areas where meningococcal disease is epidemic. This includes Nepal, northern India, and the "meningitis belt" of sub-Saharan Africa. The vaccine is also required by Saudi Arabia for Haj pilgrims to Mecca. A single dose of the vaccine is effective in children older than two years, and adults; boosters are recommended every three years.

Typhoid Vaccine

The emergence of multi-drug resistant S. typhi has increased the need for typhoid prevention, and vaccination is recommended for travellers to South and Southeast Asia. Two effective vaccines are available. One is an oral vaccine containing live attenuated *Salmonella typhi* bacteria (Ty21A). It is administered as three capsules taken every other day. Because the attenuated bacteria is heat-sensitive, the capsules need to be kept refrigerated if patients carry them to their homes for administration. Antibacterials, and anti-malarias (mefloquine and doxycycline) may kill the Ty 21A bacteria; these medications must be avoided during the 4-5 days associated with oral vaccination. Because younger children have difficulty swallowing the capsule, this vaccine is not recommended for children less than six years. An improved injectable typhoid vaccine (Typhim Vi) has recently become available. It has the advantage of being more immunogenic than the previous injectable vaccine, and does not produce the significant local and systemic toxicity which was common with the earlier vaccine. Although the injectable vaccine is recommended for younger children, both vaccines are effective in adults. Boosters are required every three years.

Yellow Fever

Yellow fever does not exist in Asia. Endemic areas are restricted to parts of South America and Africa. This is a live virus vaccine, and should not be administered to a pregnant woman, or to persons with altered immune function. Vaccinations are provided at registered centres, and boosters are required every 10 years.

ROUTINE IMMUNIZATIONS

Routine immunizations are vaccinations that everyone should keep up to date regardless of travel status. These include diphtheria, tetanus, polio and measles. If primary immunizations during childhood were incomplete, part or all of a primary series should be administered. Pertusis vaccine is not administered to older children and adults.

Tetanus and Diphtheria

To avoid adverse reactions, the tetanus-diphtheria combination used for adult immunizations (Td) contains a reduced amount of diphtheria toxin relative to the childhood vaccine (DT or DPT). Boosters should be given every ten years. For travellers going to remote destinations (where Td would not be readily available if required at the time of injury), a booster may be prudent at five years.

Polio

Individuals who received four or five doses of polio vaccine during childhood should receive one adult booster dose of either oral polio vaccine (OPV), or enhanced injectable polio vaccine (eIPV). Since eIPV is a killed virus vaccine, it is the recommended vaccine for primary immunizations in adults who have not previously been adequately immunized. The eIPV vaccine is also recommended for pregnant women, and persons with altered immune status.

Measles, Mumps, Rubella

A single dose of MMR is recommended for children at 15 months, with boosters of either monovalent measles vaccine or repeat MMR at either 4-6 years or at early adolescence[4].

Varicella

As varicella vaccine becomes available in Singapore, it would appear reasonable to offer this vaccine to any adolescent or adult who does not have a history of previous chickenpox. Serologic studies of national guard recruits have demonstrated low levels of immunity to varicella virus. Considering the increased incidence of complicated infections in adults, this should become another vaccine offered at the time of routine office visits or at the time of travel medicine consultations.

MALARIA

While malaria remains endemic in many rural areas of Southeast Asia, it is rarely a problem in urban centres. The reason for this is not primarily a result of sanitation or public health measures. Anopheline mosquitoes in Southeast Asia require clear water for breeding sites. Urban areas have decreased fresh water through reductions in foliage, and through contamination of surface waters. In South Asia *An. stephensi*, a formerly rural mosquito, has "adapted" to the urban environment. The mosquito uses roof-top water storage containers for its breeding sites (oviproduction and larval development). As a result, urban malaria exists in Bangladesh, India and Pakistan.

Of the four species of human malaria, *Plasmodium falciparum* accounts for more than 95% of deaths. We consider falciparum malaria a medical emergency. Anyone returning from a malarious area with fever, regardless of the chemoprophylaxis measures used, should be thoroughly evaluated for malaria. Too commonly, travel histories are not obtained from patients with fever, and patients often do not volunteer this information unless specifically asked about recent travel. Failure to make an early diagnosis permits falciparum malaria to progress with resultant severe complications including pulmonary and renal failure, malarial coma, and death. Initial examination should include thick and thin smears for malaria (rapid diagnosis using QBC buffy coat microscopy or histadine-rich antibody reagent strips are alternative diagnostic tools with sensitive comparable to thick and thin smear microscopy). If lab results are negative for malaria and fever persists, additional studies should be obtained in 12 hours. If the returning traveller is toxic and no other source of fever has been found, it is rational to begin empirical treatment for falciparum malaria while continuing to obtain diagnostic studies every 12 hours. Positive microscopic (thin smear) diagnosis permits confirmation of the malaria species. *P. falciparum* resistance to quinine and mefloquine in some areas of Thailand, Myanmar, and Kampuchea may complicate treatment. When treating falciparum malaria it is recommended that if available assistance be obtained from someone who has had experience with this disease. *P. vivax* and *P. ovale* generally are sensitive to chloroquine; both have capability for relapsing malaria and effective treatment should include a "radical cure" of the hypnozoite with primaquine. Warrell, Molyneux, and Beales[5], and White[6] provide two excellent references for malaria treatment.

Malaria Prophylaxis

Prevention of malaria entails measures to avoid mosquito contact (applying insect repellents, wearing long sleeves and pants in evening and night-time, sleeping in well-screened rooms and/or under bednets / mosquito nets. The use of a chemoprophylaxis is supplemental. With the development of widespread chloroquine-resistant falciparum malaria in the late 1980's, mefloquine and doxycycline became, and remain, the primary agents for chemoprophylaxis. In certain areas of northern Thailand, Myanmar, and Kampuchea mefloquine is no longer effective. Regimens include mefloqione 250 mg salt (adult) or 5/kg salt (child), once each week; or doxycycline taken as 100 mg each day (adult) or 2 mg/kg (for the child 9 or older, max 100 mg). Prophylaxis should begin two weeks before departing and continue for four weeks after returning from the malarious area.

Mefloquine rarely causes serious side effects (less than 1%) when taken in prophylactic doses. However, hallucinations and psychotic reactions are anecdotally reported, and the drug should not be recommended to individuals with a history of neuropsychiatric problems including seizures,

depression, and major psychosis. It should also not be given to persons receiving beta blockers (hypertension, arrythmias, CAD, migraine).

The major side effects from doxycycline are gastro-intestinal (including reflux esophagitis), and photosensitivity. Persons taking doxycycline should avoid sun exposure as much as possible, and/or use sun screens.

Patients frequently fail to complete 4 weeks of malaria chemoprophylaxis after leaving the malarious area. It is important to remember that medications used for chemoprophylaxis (mefloquine, doxycycline, chloroquine) do not prevent malaria infection. They prevent the erythrocytic phase of malaria infection from occurring, and hence clinical malaria. The pre-erythrocytic phase (liver cell infection) occurs despite these medications. In falciparum malaria, the (pre-erythrocytic) hepatic phase lasts for up to four weeks. If chemoprophylaxis is stopped after the third week (or earlier), infection will spread unchecked from the hepatocytes to red blood cells, and full blown falciparum malaria will result.

Pregnancy presents unique problems for malaria prevention and treatment. Pregnancy is associated with an increased incidence of severe and complicated malaria, and chemoprophylaxis regimens are limited to mefloquine (preferably not given during the first trimester, although a teratogenic syndrome has not been noted). Unless travel cannot be postponed, it is best for a pregnant woman to avoid travel to malarious areas.

SEXUALLY TRANSMITTED DISEASES (STD'S)

Persons need to be reminded that the HIV epidemic has arrived in South and Southeast Asia. By the year 2000 Asia will exceed the number of HIV cases in Africa. The HIV epidemic is well established in India and Thailand, and serologic studies of prostitutes throughout the region have shown high HIV sero positive rates. Other serious STD's include hepatitis B and C viruses. Travellers should be advised of the high risk of sexual contact with prostitutes. If avoidance is not practised, condoms should always be used. Patients should also be advised that condoms have a low failure rate for preventing pregnancy and STD's (i.e. they are not risk-free).

SUMMARY OF TRAVEL GUIDELINES

In summary, the following guidelines are recommended for South, Southeast and East Asia (modified from CDC on-line information, http://www.cdc.gov/travel/).

Travellers should:

1) pay attention to the quality of their drinking water and food,
2) receive Hepatitis A vaccine (except for travel restricted to Japan),
3) consider booster doses of tetanus (Td) and polio (OPV/eIPV) vaccines,
4) Depending on the locations to be visited, planned activities, and health of the traveller, the following vaccines should be considered: Hepatitis B, Japanese Encephalitis, Typhoid, and Rabies (pre-exposure).
5) Consider varicella vaccination.
6) Finally, the normal "childhood" vaccines should be up-to-date: Measles, Mumps, Rubella (MMR Vaccine); Diphtheria, Tetanus, Pertussis (DTP Vaccine) [<7 years of age], and Polio vaccine.
7) For malaria prevention, follow precautions to prevent mosquito bites, and take weekly mefloquine for South Asia; weekly mefloquine or daily doxycycline for Southeast Asia; and chloroquine or mefloquine for East Asia (China only).
8) Exercise caution when travelling by motor vehicles.

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USE AND MISUSE OF ANTIBACTERIAL ANTIBIOTICS

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Summary

Antibacterial antibiotics can produce satisfying results for the family physician. However, anti-drug resistance in many important pathogens curbs the clinical effectiveness of available drugs. Widespread use of antibacterials in the community and in the hospitals has shifted anti-drug resistance patterns among bacteria. Pathogenic bacteria pass into patients, the ward or clinic, and from care givers. Making new drugs can only briefly overcome multiple-drug resistance, which arises through natural selection. All doctors must control multi-drug resistant bacteria through informed and self- restrained prescribing, and appropriate hand washing between patients.

Keywords: *Antibacterial drugs, natural selection, resistance, enzymes, nosocomial infection, host response*

INTRODUCTION

Originally 'antibiotics' meant microbial products which, at low concentrations, killed or prevented the multiplication of other micro-organisms. Ethanol would be an antibiotic except that it kills microbes only at high concentrations. 'Antibiotics' now also includes synthetic and semi-synthetic compounds made by modifying a natural molecule. Indeed, among prescribers the word signifies 'any useful antimicrobial substance", which in practice is usually an *antibacterial antibiotic*.

Usually doctors prescribe antiviral and anti-fungal antibiotics in an established manner to ordinary patients, mostly for local or surface infections, e.g. herpes simplex infection, herpes zoster or chickenpox, or infections by fungi and yeasts respectively. Systemic antiviral and anti-fungal drug use in immune-deficient patients is highly specialised and prolonged.

Anti bacterial drugs ('antibacterials') have a great potential for good and bad effects in the community because of high usage and cost. I will therefore address only salient problems facing doctors dealing with patients who may need **antibacterial drug** treatment. For optimum prescribing, doctors should refer to guides such as the British National Formulary[1], and produce their own updated guides according to prevailing local bacteria and their sensitivity to available drugs.

WHAT ARE THE BIG PROBLEMS?

For 100 years since sulphanilamide started the chemistry revolution, antibacterials have significantly decreased death and damage. On average, antibacterials add perhaps 10-12 years to the

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average life expectancy, while subtracting about 30 minutes due to adverse reactions[2]. In our market driven world, antibacterials make huge profits for transnational pharmaceutical companies, which influence many nations' economies. Suffice to say that many caring doctors believe we should restrain adding to the vicious cycle of 'new drug (profit), useless drug, newer drug (more profit), useless drug ....'

WHY DO WE HAVE ANTIDRUG AND MULTIDRUG RESISTANCE?

Bacteria are among the oldest (about 3500 million years) and most successful life forms. They owe their biological success to evolution through natural selection. The environment has continually chosen the fittest bacteria. Specific bacteria adapt to the pressure of new antibacterial drugs, mainly by making 'mutant' variants of drug-degrading enzymes. These mutants are promiscuously passed between bacteria via plasmid DNA. Antibiotics given to livestock and pets all select resistant clones of *Esch. coli* and *Staphylococcus aureus*. Unknowing or uncaring clinicians feed this mechanism through antbacterial misuse in patients.

One important example is *Clostridium difficile*, which mainly affects the elderly. It produces either symptomless carriage in the colorectum, diarrhoea or colitis, including pseudomembranous colitis. The colitis is serious, hard to treat, and costly over an average 3 weeks in hospital. *C. difficile* is the commonest cause of hospital-acquired diarrhoea. The community incidence of infection is unknown, because in Singapore most laboratories do not detect *C. difficile* or its toxin in stool specimens from family practice. Surveys elsewhere show an overall increase in *C. difficile* infection, ahead of *Salmonella*. There are three major reasons for the increase.

Firstly, *C. difficile* clones which cause disease come from (a) other patients, (b) directly from the surroundings – the bacterium produces spores which survive drying for months and survive the usual disinfectants, requiring detergents, and (c) from the hands of carers in and out of hospital[3]. Secondly, in some communities gut colonisation by *C. difficile* has risen by 60% in 10 years, probably due to indiscriminate prescribing of antibacterials by doctors in hospitals and the community[4]. Many antibacterials damage the protective anaerobic gut flora, thereby allowing bacteria like *C. difficile* and *Esch. coli*[5,6] to flourish, and sometimes to cause disease.

ARE SOME DRUGS MORE RISKY?

Low-risk drugs are less prone to upset the delicate balance of gut flora[3]. These are (1) the aminoglycosides, e.g. gentamicin, and amikacin, (2) trimethoprim, useful in urinary tract infection, (3) the 4-quinolones, e.g. ciprofloxacin, nalidixic acid; (4) the macrolides, which are narrower in antibacterial action, e.g. erythromycin; and (5) ureidopenicillins, e.g. carbenicillin, azlocillin, piperacillin – all parenterally administered[7]. High-risk drugs include the cephalosporins, for which there is evidence that in many countries the use of 2nd-generation (e.g. cephazolin, cephalexin) and 3rd-generation drugs (e.g. cefuroxime, ceftriaxone, cefotaxime) has jumped six- to seven-fold in 15 years[8].

HOW TO CONTROL *C. DIFFICILE* INFECTION?

Hand washing greatly decreases hospital-type diarrhoea. Secondly, it may also be effective to recommend the low-risk drugs, where appropriate, over the high-risk ones, targeting those community homes or hospital wards with a high rate of *C. difficile* infection. Finally, tranfers of patients from one unit or ward to another, and from one hospital to another, spreads the very pathogenic *C. difficile* clones. Doctors should therefore discourage unnecessary transfers.

Like that of methicillin-resistant *Staphylococcus aureus* (MRSA), the *C. difficile* story is a paradigm for the control of difficult bacteria. Over the past 15 years some outbreaks caused high mortality[3]. We do not know if excessive antibacterial use selects more virulent bacteria for circulation, but this is likely. There is experimental and clinical evidence that less antibiotic use generally decreases the drug-resistant bacteria. Overuse of oral vancomycin for *C. difficile* promotes resistant enterococci, so we should restrict vancomycin to confirmed colitis, and alternatively give metronidazole. All doctors should therefore avoid behaviours which promote dangerous multipile-drug resistant bacteria.

IN-HOSPITAL PRESCRIBING POLICY

The Pharmacy & Therapeutic Committee of the National University Hospital runs a staged antibiotic scheme, whereby only registrars can prescribe second- or third-line antibacterials in the first 24 hours, after which the team must justify continuation on a special form. We continually remind doctors to restrict their antibacterial prescribing to clinically reversible infections. The Microbiology Department enforces infection-control, and updates doctors about patterns of antibacterial drug resistance. We screen the entry of subnourished elderly patients into intensive care units, where they are unlikely to survive hospital-acquired septicaemia. Yet prescribing standards can improve further, because we lack clear criteria under ever-changing conditions.

HOW ELSE CAN WE CURB ANTIBIOTIC RESISTANCE?

A recent strategy is to give antibacterial vaccines to high-risk patients to decrease infection, decrease antibacterial use, and thus to prolong antibiotic effectiveness. Examples are the *Haemophilus influenzae type b* vaccine, and the less effective pneumococcus vaccine. This is an expensive strategy.

USING ANTIBACTERIAL DRUGS IN THE COMMUNITY

Prescribers should consider factors relating to both the host, the pathogen, and the intended antibacterial. For the patient, you should think about:- (a) the severity of illness; (b) patient's age, because the young and the elderly require dosage reduction, and the very old patient is especially prone to adverse drug reactions[9]; (c) if a woman, whether she is pregnant, breast-feeding, or taking an oral contraceptive; (d) resistance to infection (immune system status); (e) history of allergy or atopy.

For the drug, consider (i) are the liver or kidneys impaired?, (ii) can the patient take the drug by mouth?, and (iii) are there important interactions with the current medication?

We need methods to identify bacteria accurately within a few hours. So far this has only been practicable for a few bacteria, e.g. the Mycobacteria. You should note that the bacterium's sensitivity to antibiotics is important, but should not accept it slavishly (see below). Do update yourself with information on the prevalent organisms and the antibacterial sensitivity. Current knowledge is vital to empirical antibiotics selection before sensitivity is known.

Questions to Ask before Starting Therapy

Always test these precepts before starting treatment:- (1) Am I treating a viral or other non-bacterial infections with an antibacterial drug? In a patient with influenza-like illness without systemic upset the likelihood of non-bacterial infection is 95-97%. (2) With sicker patients, have I taken careful samples of body fluids or tissue for culture and sensitivity testing?

Blindly prescribing an antibacterial in patients with unexplained fever causes serious diagnostic difficulty. Empirical treatment for severe infection or septicaemia is best given in hospital. An exception to the latter:- when you suspect bacterial meningitis and entry to hospital will take hours, you should give an i.v. or i.m. dose of cefuroxime or ceftriaxone, then admit the patient to hospital stat.

The site, the type and severity of infection determine drug dosage, the duration of therapy, and the route of administration.

Deciding on the Right Dose and Duration

'Standard' dosing in serious infections may cause treatment failure or death of the patient. Less severe infections usually respond to an antibacterial given every 8 hours. In severe infections you should give most antibiotics every 6 hours, or more often. Twelve-hourly administration suffices for some drugs with prolonged plasma half-times, e.g. trimethoprim. With aminoglycosides like gentamicin, you must increase dose intervals beyond 8 hours in renal dysfunction, sometimes to 24-48 hours.

The adage runs, "Give just enough drug for just long enough." The type of infection and clinical response decide how long to treat for. A single dose of a well-chosen antibacterial may cure simple urinary-tract infections. Unduly long courses are wasteful and may increase adverse reactions. Immunocompetent patients rarely need longer than 3-5 days' treatment.

Immunodeficient patients need longer courses, or may need combined antibiotics. Do not forget diabetics, chronic alcohol abusers, patients with chronic renal or liver dysfunction, patients taking long-term corticosteroids and other immunosuppressants, and subnourished persons with a body mass index under about 17 kg/m^2.

Clinical Wisdom

The doctor should always decide wisely, and tailor the guidelines to individual infections. Uncomplicated urine and respiratory infections often respond to first-line drugs even when the *in vitro* sensitivity report implies 'resistance'. Minor infections mostly respond clinically within 48-60 hours. Be expert with a few antibacterials than inept with many untested ones! Sicker patients require in-hospital treatment. As patients initiate more and more litigation, falling prey to drug salespeople is a weak defence in any court of medicine or law. To have 'tried several expensive drugs in turn or together' is an increasingly weak defence.

PERSISTENT DIFFICULTIES

Actual prescribing falls short of the established practice. Many doctors feel that they have to 'play safe' and prescribe antibacterials to patients who probably have viral infections. Many patients demand antibacterial treatment for the same reason. The pharmacist mediates, but cannot modify prescriptions. In Singapore the linkage between drug prescribing and income further complicates the problem. We need to know the incidence of antibiotic-related disease, and how and why family physicians prescribe antibiotics. Without such information it is hard to devise useful guidelines. The solution is community-based research.

Patients and doctors alike must accept that in the long run everyone loses out to the drug companies, and to the bacteria. Some patients will suffer harm, and others will die because of multidrug resistance. All of us are potential victims.

EVOLUTION ACTS IN SOCIETY AS IN NATURE

Both traditional extrinsic pathogens and commensal bacteria evolve continually to resist antibacterials. Attempts to restore the gut flora by giving cultures of *Lactobacillus spp*, have met with little success. Making new drugs can only briefly overcome multiple-drug resistance, which arises through natural selection. Moreover, a drug company may spend US$600-800 million over 10-12 years bringing one antibacterial to the market. As prescribers are better informed the profit from new antibiotics falls; many companies now avoid making antibiotics. The answer is not in economics, but in society expecting higher professional standards.

CONCLUSIONS

By altering the microbial balance inside and outside our bodies, antibiotic prescribers have diverted and accelerated the natural selection of powerful survivors among important pathogenic bacteria. Attempts to restore the microbial balance in the gut using 'beneficent' bacteria show little success. Doctors should not treat viral infections with antibacterial drugs. Before giving an antibacterial to sick patients, you should first take careful samples for culture and sensitivity testing. The best overall strategy for keeping the usefulness of antibacterial drugs is to write fewer antibiotics prescriptions, and wash your hands more often between examining patients.

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COMMUNITY ACQUIRED URINATRY TRACT INFECTION

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Summary

Urine culture can be used to identify the pathogens present in community acquired urinary tract infection in Singapore. A non-randomized survey on 500 positive urine culture results in Singapore showed that the three main pathogens found are *E. coli* (75%), Klebsiella (11.8%) and Proteus (8.6%). Antimicrobial susceptibility testing showed that quinolones, nitrofurantoin, cefuroxime and amoxycillin/clauvinic are effective in treating urinary tract infection. Nalidixic acid is found to be the most cost effective antibiotic among them.

Keywords: *urinary tract infections, urine culture, community acquired UTI*

INTRODUCTION

Bacterial resistance is one of the common causes of treatment failure for patients with urinary tract infection. This problem is compounded by the widespread use and misuse of antimicrobials.

The purpose of the study is to find out pathogens present in urinary tract infection in the community setting and their sensitivities to different common antibiotics.

MATERIALS AND METHODS

500 consecutive positive urine culture results done in 1996 were selected. The cultures were done for ambulatory patients by a private laboratory.

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Positive results refer to cultures with more than 100,000 bacteria count. The pathogens were tested against an array of antimicrobials using the disc diffusion method. The results were reported as sensitive, moderately sensitive or resistant.

The pathogens were tested against a standard set of antimicrobials as defined by the laboratory.

LIMITATIONS OF THE STUDY

The source of the urine culture was not standardized. Hence we do not know whether the data was from the patients with primary infections or recurrent infections or whether pre-treatment or post-treatment was given. The age and sex of the patients were not available.

RESULTS

The most common organism grown was *E. coli* followed by Klebsiella, Proteus and other less common organisms as shown in Table 1.

Anti microbial sensitivity test performed showed that the quinolones, nitrofurantoin, amoxycillin/clauvinic and cefuroxime are superior to

cotrimoxazole and ampicillin in urinary tract infection as shown in table 2.

DISCUSSION

The antimicrobials that were used for sensitivity testing include:

a) Inhibitors of cell wall synthesis (beta lactams) e.g. ampicillin, amoxycillin/clauvinic, cefuroxime.

   Beta lactams act on the growing bacterial cell by inhibiting the cross-linking of peptidoglycan strands. Without the cross linkage, the cell wall is weakened and defective. Major limitations are the widespread distribution of beta lactamase enzymes among clinically important bacteria. Beta lactamases break open the beta lactam ring of the antibiotic rendering it inactive.

   Clauvinic acid has no antibacterial activity per se. It acts as a beta lactamase inhibitor and prevents the amoxycillin from being destroyed by the beta lactamase in the amoxycillin/clauvinic combination.

   Cefuroxime is a beta lactam antibiotic.

Table 1: Urine Culture Results

PATHOGENS	NUMBER	PERCENTAGE
E coli	375	75.0 %
Klebsiella	59	11.8 %
Proteus	43	8.6 %
Coagulase Negative Staphylococcus	11	2.2 %
Pseudomonas	6	1.2 %
Citrobacter	4	0.8 %
Providencia	2	0.4%

Table 2: Antibiotic Sensitivity

ANTIBIOTICS	SENSITIVE No. (%)	MODERATELY SENSITIVE No. (%)	RESISTANT No. (%)
Ampicillin	355 (71. 0%)	10 (2.0 %)	135 (27.0 %)
Amoxycillin / Clauvinic	479 (95.8 %)	11 (2.2 %)	10 (2.0 %)
Cefuroxime	488 (97.6 %)	4 (0.8 %)	8 (1.6 %)
Co-trimoxazole	372 (74.4 %)	25 (5.0 %)	103 (20.6 %)
Ciprofloxacin	500 (100.0 %)	0	0
* Nalidixic acid	468 (95.7 %)	15 (3.1 %)	6 (1.2 %)
* Nitrofurantoin	236 (48.3 %)	244 (49.9 %)	9 (1.8%)
* Norfloxacin	489 (100.0%)	0	0
* Pipemidic acid	483 (98.8 %)	0	0

* Antibiotic sensitivity tests were not performed on the 11 urine specimens which grew coagulase negative staphylococcus.

However its beta lactam ring is relatively resistant to inactivation by the beta lactamases.

b) Drugs acting on nucleic acid synthesis e.g. co-trimoxazole, nalidixic acid, norfloxacin, ciprofloxacin, pipemidic acid, nitrofurantoin

Co-trimoxazole, which is a combination of sulphonamide and trimethoprim, acts on different points of the same pathway in the synthesis of purines.

Nalidixic acid, ciprofloxacin, norfloxacin, pipemidic acid inhibit DNA replication by acting on the bacterial DNA-grase.

Nitrofurantoin act by producing fracture in the bacterial DNA.

Table 2 shows that the quinolones, nitrofurantoin, amoxycillin/clauvinic and cefuroxime are effective in treating urinary tract infections. The chances of encountering resistant strains is 2% or less. If ampicillin is used, there is 27% chance of encountering resistant strains and 20% chance of encountering resistant strains if co-trimoxazole is used.

Table 3 shows that ampicillin and co-trimoxazole resistance is common in *E. coli*, Klebsiella and Proteus infections.

The use of amoxycillin/clauvinic, cefuroxime or the newer quinolones which are many times more expensive, does not show any added advantage over nalidixic acid in treating the three main pathogens of urinary tract infection. Ciprofloxacin, the most active of the newer quinolones, has a greater spectrum of activity than nalidixic acid. It is effective against Pseudomonas and Coagulase negative Staphylicoccus in addition to E. coli, Klebsiella and Proteus.

Nitrofurantoin is effective in killing the three main urinary pathogens. However it requires a higher antibiotic concentration in the sensitivity testing as compare to nalidixic acid.

This study is based on in vitro testing of the pathogens. The result may be different in actual patients due to several reasons:

a) The concentrations of the antimicrobial in the urine may be different for different antimicrobials.

b) The antimicrobial may be inactivated by other organisms in the patient's commensual flora.

CONCLUSION

The most cost effective antibiotic would be nalidixic acid. It is relatively cheap and has a good spectrum of activity against the common urinary pathogens.

Table 3: Sensitivity Pattern for Individual Urinary Pathogens

Pathogens	Ampcillin	Amox/Clau	Cefuroxime	Co-trimoxazole	Ciprofloxacin	Nalidixic	Nitrofurantoin	Norfloxacin	Pipemidic
E. coli	71%(S) 19%(R)	100%(S)	100%(S)	83.3%(S) 6.7%(MS) 10.0%(R)	100%(S)	100%(S)	47%(S) 53%(MS)	100%(S)	100%(S)
Proteus	53%(S) 47%(R)	81%(S) 19%(MS)	81%(S) 19%(R)	28.0%(S) 72.0% (R)	100%(S)	72%(S) 28%(MS)	53%(S) 47%(S)	100%(S)	100%(S)
Klebsiella	42%(S) 5%(MS) 53%(R)	97%(S) 3%(MS)	100%(S)	58.0%(S) 42.0%(R)	100%(S)	95%(S) 5%(MS)	58%(S) 42%(MS)	100%(S)	100%(S)
C. Neg. Staph	36%(S) 64%(MS)	100%(S)	36%(S) 64%(MS)	100.0%(S)	100%(S)	Not tested	Not tested	Not tested	Not tested
Pseudomonas	100%(R)	100%(R)	100%(S)	100.0%(R)	100%(S)	100%(R)	100%(R)	100%(S)	100%(R)

(S) Sensitive (MS) Moderately Sensitive (R) Resistance

Ciprofloxacin is the most efficacious antibiotic. It is able to act against all the urinary pathogens that were cultured in this study.

Acknowledgements

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ISOTRETINOIN: THE ACNE WONDER DRUG

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INTRODUCTION

Isotretinoin is a vitamin A analogue that has been found useful in the treatment of several skin disorders involving keratinization, particularly acne vulgaris. This paper will examine its role in the treatment of acne.

WHY TREAT

Acne is a disorder of keratinization which can lead to significant facial and psychological scarring which afflicts many healthy individuals at the prime of their lives when self and public image is important for personal, career and relationship development. It is left largely untreated for those who find it unacceptable enough to brave the task of seeking help from a doctor who may not be so sympathetic to a "mild cosmetic" disease.

ROLE OF ISOTRETINOIN

The mainstay of treatment is still topical keratolytic drugs and antibiotics either oral or topical depending on the preference of the patient and the experience of the physician. However, there are cases of acne which are non-responsive to antibiotic therapy of sufficiently long duration or who have severe nodulocystic or scarring acne. This is where isotretinoin comes into play.

However, isotretinoin is teratogenic and causes many nuisance, though non-life threatening, side-effects such as dry mouth, dry eyes and cracked lips. Hence, its use in the treatment of acne is curtailed. It has recently been used by dermatologists around the world for less severe forms of acne which are non-responsive to conventional therapy.

Isotretinoin is able to offer prolonged long term benefit even after the regime has been stopped, in contrast to oral antibiotics in which the condition tends to relapse once the patient has been taken off the drug. Isotretinoin provides an 80% reduction in sebum excretion, comedogenesis, and infundibular and surface *Propionibacterium acnes* within 4 to 8 weeks of the start of treatment. In addition, isotretinoin has direct effects on inflammatory processes such as reducing chemotaxis. The ability to produce these modulating effects contrasts with other conventional therapies that only influence one or two of the major etiogical factors.

CLINICAL GUIDELINES:

Whom to treat?

The usual indication for the use of isotretinoin is severe acne, e.g. nodulocystic acne. Other indications may include:

1. Moderate acne unresponsive to otherwise adequate conventional therapies
2. Some unusual variants:
   - acne conglobata
   - gram-negative folliculitis
   - acne fulminans
   - pyoderma faciale
3. Other reasons, e.g.
   - inadequate response to antibiotics and the presence of scarring
   - partial response
   - severe acne

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- severe acne associated with scarring
- partial response in patients who are significantly depressed about their acne

For how long?

The duration of therapy is usually for 4 to 6 months per course depending on the area of involvement. Truncal acne usually requires higher dosages e.g. 1 mg/kg/day as compared to facial acne which would respond to doses of 0.5 mg/kg/day. The total accumulative dose should be greater than 120 mg/kg body weight.

What to do in the case of a female patient?

All female patients on isotretinoin should be on oral contraceptives if they are sexually active. They should be made to sign a consent for termination of pregnancy if a pregnancy inadvertently occurs. All male patients should sign a consent form stating that they understand the teratogenicity of the drug, and that they undertake not to let persons other than themselves possess and ingest this drug.

Can it be repeated?

There is a tendency to relapse if the dose accumulated is lower than that mentioned above. Relapse rates are around 31% at 9 years. Repeat course can be prescribed and response is predictable and safe. Some patients may require 3 to 5 courses, but these are the exception rather than the rule.

CONCLUSION

In conclusion, isotretinoin is a wonder drug in therapy of difficult acne with scarring and psychosocial morbidity. The place it occupies in the armamentarium of dermatological therapeutics is unique and time tested. However, because of its toxicity and teratogenicity, it is recommended that the drug be started and monitored by a physician with interest in the long-term therapy of acne, e.g. dermatologist. It should not be used if the patient is not committed to take contraceptive precautions or if the doctor is not confident.

ANALYSIS OF STUDENT HEALTH PROBLEMS AT AN UNIVERSITY HEALTH CENTRE

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Summary

The health problems encountered at the Health Services of Hong Kong Polytechnic University encompass most of the common illnesses in the community, Although very few presented with chronic illnesses, there was a significant proportion of students with illness suggestive of psychosomatic origin. Also many students presented with complaint which had specific underlying diseases. The University Health Services being so accessible and affordable to students, has the potential to provide services other than simple curative treatment. It can also provide data for research exploring the health seeking behaviour and the 'hidden agenda' for medical consultation of young adults which will be useful for health needs assessment. Health promotion especially on self-coping mechanisms and mental health can be the future challenge for University Health Services.

Keywords: *psychosomatisation, health seeking behaviour, hidden agenda, health promotion, health need.*

INTRODUCTION

The Health Services Section at Hong Kong Polytechnic University (now known as University Health Services) provides basic primary care to all full-time students free of charge (including basic medications), and some of the staff and dependants through reimbursement from insurance. Students have always been regarded as healthy and do not require very much medical attention. This may not be entirely true. The morbidity survey done by Epidemiology Committee of Hong Kong College of General Practitioners in 1985 - 1986[1] showed more than 20% of the patients were from the under 10 age group which was the largest group followed by 20-29 age group (about 20%), then the 30-39 age group (15%). In a survey of General Practice in Shatin new town in Hong Kong[2], 27% of patients were young adults (age 20 - 39). Over 40% of the consultations were from the young adult group (age 20-44) in the 1944 morbidity survey[3]. This group of people may not suffer from serious diseases but are not without illnesses. Therefore, it is important not only to treat their illness, also to understand their health seeking behaviour and provide them the right concepts for health promotion and disease prevention. It is also important to maintain this group of people in good health (physical, psychological and social) as they are the backbone of the society.

Understanding of the distribution of highly

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prevalent health problems in the young adult group is essential for health policy formulation. For this age group, data on morbidity is more meaningful and useful than mortality. For the students, this may be the only time that Health Services are so accessible and affordable that morbidity data can be obtained more readily. Therefore morbidity surveys at the Health Services Section of tertiary institutions can provide useful data for further epidemiological studies of the common health problems in this age group.

OBJECTIVES

- To analyse the health problems of the students encountered at the University Health Service.
- To compare the morbidity pattern of the Student Health Service with other morbidity surveys done previously.
- To provide some background information for planning of future direction of Health Services for students.

METHODS

All students attending one of the physicians at the Health Services Section from 27.1.94 to 9.2.94 were included in the study population. Patients' age, sex, diagnosis or presenting symptoms were all recorded according to ICPC coding (International Classification of Primary Care)[4]. Subsequent follow up for the same problem was not included. The names of the students were not recorded so confidentiality was maintained.

The overall morbidity pattern by system was listed. The health problems encountered during that period were also listed. The morbidity pattern by system was compared with the Hong Kong whole territory morbidity surveys done in 1980, 1981-1982, 1985-86 and 1994[1,3,5,6].

RESULTS

The total number of consultations during the study period was 361 (repeat visits for the same health problems were excluded). More consultations were from female students, 193 consultations constituting 53.5% of all the consultations compared with 168 consultations (47.5%) by male students (the difference in proportion is 0.06 with 95% confidence intervals of -0.01, 0.13 and P value of 0.11).

Table 1 shows the age and sex distribution of the students in the University. The table shows a higher proportion of male students in all age groups and overall and it is statistically significant. It also shows that for male students, the proportion seems to be an increasing trend with age but the reverse is observed for female students, again it is statistically significant. Figure 1 shows the age distribution of the

Table 1: Age and Sex Distribution of HK Poly U Students 1993/94

Sex	Age *Number (%)*						
	19 or below	20	21	22	23	24 or above	Total
Male	2296 (50.1)	1740 (61.7)	932 (69.9)	371 (70.3)	174 (69.9)	255 (51.2)	5768 (51.2)
Female	2287 (49.9)	1080 (38.3)	401 (30.1)	157 (29.7)	75 (30.1)	243 (48.8)	4243 (42.4)
Total	4583 (45.8)	2820 (28.2)	1333 (13.3)	528 (5.3)	249 (2.5)	498 (5)	10011 (100)

Chi Square Value	*DF*	*P value*
266.27	*5*	*$< 10^{-5}$*
82.59 (Mantel-Haenszel test for linear asocciation)	*1*	*$< 10^{-5}$*

patients along with the overall student population. About 50% of the patients are in the age group of 21-21 and for the overall student population, over 50% are age 19 or below.

Figure 2 shows the distribution of consultations by major disease groups. Respiratory problems were the most common (54.3%), followed by both skin and digestive problems, (both 12.9%). Neurological and sense organs problems ranked third when combined together (Total 10.4%, eye problems 4.5%, neurological problems 3.1%, ear problems 2.8%) and the fourth was musculoskeletal 2%), followed by psychological problems (1.6%) in the fifth place. Blood problems and endocrine problems occupied sixth place (0.9%) followed by urological problems (0.4%). Unclassified problems were 2.2%. On average students had 1.6 problems per consultation. Over one third of the students consulted with health problems related to two disease groups.

Table 2 shows the detailed breakdown of the diseases or problems for the students. URI was the most common problem (37.8%), follow-ed by allergic rhinitis (7.6%). The third was contact

Figure 1: Age Distribution of Patient and HK Poly U Student Population

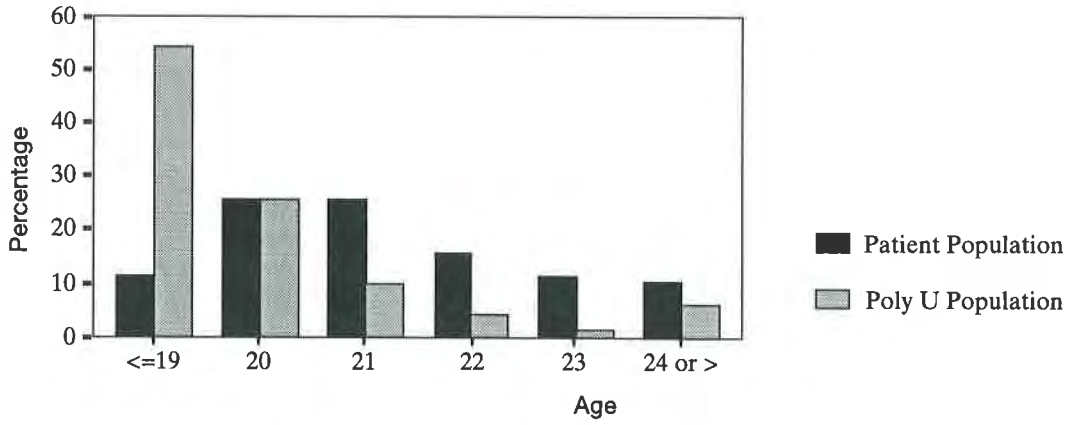
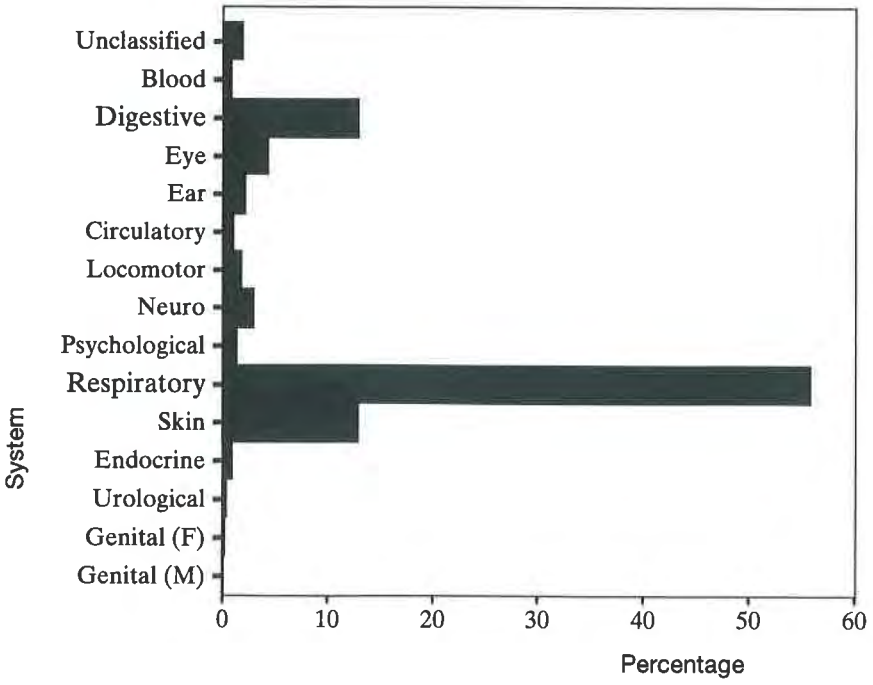


Figure 2: Disease Distribution by System



dermatitis (4%), fourth was flatus/gas pain (3.3%), fifth was acne and acute bronchitis (2.2%), seventh was nausea and vomiting (2.1%), eighth was asthma (1.7%), ninth was vertiginous syndrome (1.7%) and tenth was dermatophytosis. This long list included over 50 health problems which are common in the community.

DISCUSSION

The sex difference in consultations with higher proportion of females attending is not an unexpected finding. The morbidity in women seems to be higher than in men[7]. Although the majority of the students were in the age group below 19, most of the consultations were from age group 20-21. It was not unexpected as those age 19 or below are usually in their first year of University, and they may not be fully aware of the service available. When the students have been in the University for some time, they may have developed a closer relationship with the

Table 2: Reasons for Consultations

Student			Student		
R74	URI (simple cough and cold)	37.8%	F03	Discharge from eye	0.4%
R97	Allergic rhinitis	7.6%	F05	Other problem with vision	0.4%
S88	Contact dermatitis	4.0%	H81	Ear wax	0.4%
D08	Flatus/gas pain	3.3%	'H81'	Ear wax requiring syringing	0.4%
S96	Acne	2.2%	L78	Sprain of knee	0.4%
R78	Acute bronchitis	2.2%	R27	Fear of other respir. disease	0.4%
D09 &Q10	Nausea & Vomiting	2.1%	R21	Sympt/complaint of throat	0.2%
R96	Asthma	1.7%	R02	Shortness of breath	0.2%
H82	Vertiginous Syndrome	1.7%	R01	Pain attributed to respiratory system	0.2%
S74	Dermatopyhtosis	1.4%	S16	Bruise/contusion of skin	0.2%
D02	Stomach Pain	1.4%	S14	Scald	0.2%
D11	Diarrhoea	1.4%	S10	Boil/carbuncle/cellulitis	0.2%
P01	Anxiety	1.4%	S23	Baldness	0.2%
D20	Sympt/complt, mouth, tongue lip	1.2%	S03	Warts	0.2%
R76	Acute Tonsillitis	1.2%	S29	Other Symp/Complt Skin	0.2%
R08	Post nasal drip	1.2%	K73	Congenital Abnormalities of heart/circ. system	0.2%
N1	Vertigo/dizziness	1.2%			
F13	Abnormal sensation of eye	0.9%	K04	Palpitation, awareness of heart beat	0.2%
F72	Blepharitis/stye/Chalazion	0.9%			
T82	Obesity	0.9%	K25	Fear of hypertension	0.2%
N02	Tension headache	0.9%	D06	Other localised abdominal pain	0.2%
N01	Headache (exclude migraine, sinus problem)	0.9%	D21	Swallowing problems	0.2%
			D93	Irritable bowel syndrome	0.2%
D01	Generalised abd pain	0.7%	F15	Abnormal appearance of eye	0.2%
D85	Duodenal Ulcer	0.7%	F16	Symptoms of eyelid	0.2%
B70	Lymphadenitis	0.7%	F82	Detached retina	0.2%
A03	Fever	0.7%	Y99	Other male genital tract include breast	0.2%
R24	Haemoptysis	0.7%			
R73	Voice symptoms	0.7%	X14	Vaginal discharge	0.2%
K96	Haemorrhoids	0.5%	N88	Epilepsy	0.2%
K71	Allergic conjunctivitis	0.5%	L04	Chest symptoms	0.2%
F73	Other infection of eye	0.5%	L81	Other injury	0.2%
S06	Local erythema	0.5%	L93	Tennis Elbow	0.2%
L07	Jaw problem	0.5%	B02	Enlarged Lymph gland	0.2%
R06	Epitaxis	0.5%	H03	Tinnitius	0.2%
L03	Low back pain w/o radiation	0.2%	H02	Hearing complaint (exclude HR4-86)	0.2%
L19	Other symptoms, multiple/ unspecified muscle pain	0.2%	A06	Fainting	0.2%
			A09	Sweating problem	0.2%
S17	Abrasion	0.4%	A12	Allergic reaction	0.2%
S71	Herpes Simplex	0.4%	A82	Late effect of trauma	0.2%
K85	Elevated BP w/o hypertension	0.4%	A91	Investigation of abnormal results	0.2%
F70	Infectious conjunctivitis	0.4%	P06	Insomnia	0.2%

physicians so they would consult more frequently. Therefore, despite a low proportion of students at age 22 or above, they still constitute a large proportion of consultations. Detailed analysis of sex or health problems specific for each age group would be difficult for this study with the small sample size.

Our survey population was in the young age group so we did not encounter many chronic illnesses such as circulatory and endocrine problems compared with other morbidity surveys done in Hong Kong[1-3,5-6]. Table 3 shows the comparison of our surveys with four other morbidity surveys done in Hong Kong over the last fifteen years[1,3,5,6]. Over 50% of patients in our survey consulted for respiratory problems which was higher than many morbidity surveys done locally and aboard. 10.4% consulted with pro-blems of nervous system including eyes and E.N.T. which was much higher than other studies (Table 3). Only 1.6% consulted with psycholo-gical problems which was lower than other studies done previously (the 1994 Hong Kong Morbidity Survey also revealed a low proportion of patients, 1.8% with psychological problems[3]). This is rather unexpected in this age group and also in a developed country like Hong Kong. In a recent article in Asian Medical News, it was estimated that 5 to 20% of general practice consultations were due to depressive illness[8]. There were no cases recorded as depression in this study. It might be due to the short study period. Most probably, psychological problems have been underdiagnosed. Chinese patients tend to somatise their psychological problems. Doctors may not be well-equipped or unable to spend more time exploring underlying psychological problems. Students may not feel free to disclose their emotional problems in that particular setting.

If we analyse the list of health problems excluding URI, then the majority of consultations were related to symptoms without specific underlying diseases. This brings up two important issues. Firstly, somatisation of illness is very common in this age group as ticket for admission. Secondly, the students' health knowledge is inadequate so they have to consult whenever they feel some alteration of their bodily symptoms.

If anxiety (1.4%) is combined with other symptoms that can be psychosomatic in origin such as dizziness (1.2%), headache (0.9%), tension headache (0.9%), fear of respiratory disease (0.4%), non-specific muscle pain (0.2%), palpitation (0.2%), swallowing problems (0.2%),

Table 3: Moridity Patterns of 1980, 1981-2, 1985-6, 1994 compared with the Survey of Student Health Services of HK Poly U *(Rankings are in brackets)*

SYSTEM	1980 (%)	1981-2 (%)	1985-6 (%)	1994 (%)	HK Poly U (%)
Respiratory	46 (1)	49 (1)	48 (1)	47.1 (1)	54.3 (1)
Digestive	13 (2)	9 (2)	13 (2)	10.4 (2)	12.9 (2)
Skin	6 (3)	5 (3)	6 (3)	7.5 (4)	12.9 (2)
Neurological & Sense Organ	3 (7)	2 (9)	5 (5)	5.4 (6)	10.4 (4)
Locomotor	5 (4)	4 (5)	6 (3)	6.4 (5)	2.0 (6)
Psychological	2 (10)	3 (8)	3 (8)	1.8 (10)	1.6 (7)
Circulatory	5 (4)	5 (3)	4 (6)	8.8 (3)	1.4 (8)
Blood	1 (11)	0 (11)	0 (11)	0.4 (11)	0.9 (9)
Endocrine	3 (7)	2 (9)	1 (10)	4.4 (7)	0.9 (9)
Genito-urinary	5 (4)	4 (5)	3 (8)	3.2 (9)	0.8 (11)
General A	3 (7)	4 (5)	4 (6)	3.4 (8)	2.2 (5)

shortness of breath (0.2%), non-specific complaint of skin (0.2%), fear of hypertension (0.2%), irritable bowel syndrome (0.2%), chest symptoms (0.2%), sweating problems (0.2%), insomnia (0.2%); the proportion of this group of patients becomes 7%. This comprises quite a significant proportion of patients seeking primary care in the campus clinic. It has been mentioned in a recent article that approximately 11% of the adult population can be expected to meet criteria for an anxiety disorder at some time during their lifetime[9]. Psychological problems and stress related illness usually present in less classical manner so under-diagnosis and under-reporting can be very common[10,11].

The Health Services Section runs separate health education programmes for prevention and health promotion so not many consultations are for preventive procedures or medical examination. On average, more than one health problem was encountered in one consultation, as the campus clinic provides primary, comprehensive, whole person and continuing care to the problems. For the students, they usually spend two to four years at the University and it may be the only chance to have such close contact with the doctors, so easily accessible and affordable. This provides a golden opportunity to understand their health seeking behaviour and any 'hidden agenda' which is important for health care planners for this age group, and professionals involved in student affairs. In Hong Kong, 70% of primary care is provided in the private sector according to a recent survey[12]. Students may not consult doctors so readily if they are required to pay the full cost, and their health data may not be easily available.

This study has its limitations. It was done within a short period based on consultation of one doctor. It will be ideal to have the data for the whole year from all the doctors so more detailed analysis of health problems can be done at different times of the year, and comparison between different groups of students can be done. The comparison with other studies can only be regarded as reference. Those studies were done some time ago and the pattern of health problems may have changed. Based on the results of this study, one can plan a larger scale study perhaps involving other institutions. It will be of particular importance in exploring those students with illnesses that are psychosomatic in origin.

CONCLUSION

The Health Services at tertiary institutions can provide other services apart from just curative primary care. It can be the ideal place for health education and disease prevention with emphasis of positive health. Students can then become more aware of positive health and enhance their self coping mechanism. This will alter their health seeking behaviour. The health service can also provide basic data for research, looking into the epidemiology and health seeking behaviour of University students, and collaborate with other paramedical departments on health promotion of young adults in the community. The proportion of students with psychosomatic illness was not low so the true prevalence of psychological problems should not be low in this age group. If psychological illnesses can be detected at an early stage, morbidity can be minimised and students can attain quality of life. Screening for psychological problems especially depression may become an important future challenge of University Health Services as very few cases presented in the classical manner.

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TEST YOUR EYE-Q (NO. 1)

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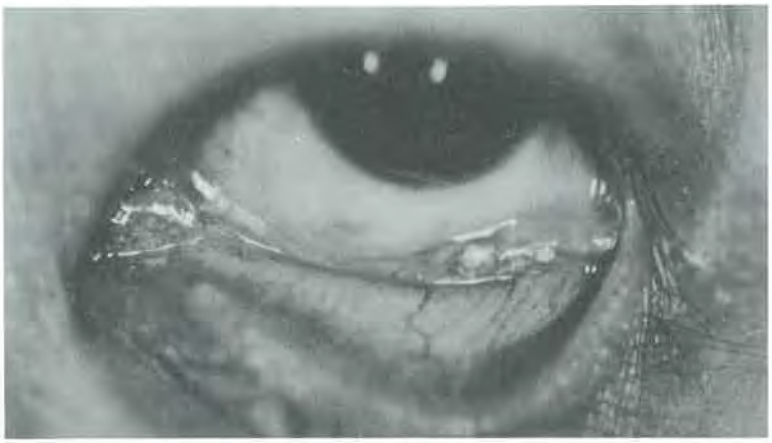
FOREIGN BODY SENSATION IN THE EYE

A 53 year old woman complained of a foreign body sensation and discomfort in her left eye for a duration of one month. She had no history of foreign body entering her eye or previous history of ocular trauma.

Fig. 1 shows the inferior conjunctival fornix of her left eye. Schirmer's test was normal.



1. What does Fig. 1 show?
2. What is the histopathology of these lesions?
3. What is the cause of the patient's symptoms?
4. What is the treatment for the patient?
5. Is it necessary to treat similar lesions in the asymptomatic fellow eye?

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For answers to Eye-Q, please turn to page 227

ANSWERS TO 'TEST YOUR EYE-Q (NO. 1)

(1) Fig 1 shows several small yellowish white deposits in the inferior conjunctival fornix. They are called conjunctival concretions and are commonly found in the elderly and in patients with chronic conjuctival inflammatory conditions.

(2) They are epithelial inclusion cysts filled with epithelial and keratin debris. Secondary calcification occurs occasionally, in which case the lesions are sometimes referred to as conjunctival lithiasis.

(3) The symptoms are caused by a concretion eroding through the overlying epithelium in this patient. Conjunctional concretions are otherwise usually asymptomatic.

(4) The extruding concretion can be removed with a needle point under anaesthesia. Those that are not eroding through the overlying eipithelium may be left alone. A topical antibiotic may be prescribed for a week following the procedure.

(5) No.

CASE STUDY: MR Y B T

E Ng, MBBS (S'pore)

Mr YBT is a 71 year old odd job labourer. He seldom visits a doctor and is not known to have any medical illness other than the usual minor illnesses. He decided to see the doctor this time as he has been experiencing severe chest discomfort on and off over the last one month. He describes it as a central gripping tightness that gave him difficulty in breathing and associated with sweating. He noticed that the pain would come on especially at work when he was carrying heavy loads. The pain gradually disappeared after he had rested for 20 minutes. As a result of this, Mr YBT had to stop working for one month. He also noticed a milder chest discomfort whenever he walked quickly or after he climbed one flight of stairs. He used to be able to manage 5 flights with no problems. He has no history of paroxysmal nocturnal dyspnoea or orthopnoea.

Mr YBT has been smoking 40 to 50 cigarettes a day for the last 50 years. He left China at a young age and is not aware of any family history of any cardiac problems. He has 2 children. His son, who is 41 years old, has recently suffered a haemorrhagic stroke and was found to be hypertensive. The son is currently rehabilitating in Ang Mo Kio Community Hospital. He has a daughter who is 38 years old, not known to have any medical problems, married and staying with her own family. She has been giving him financial help whenever he needed it. Mr YBT stays alone with his elderly wife who is in good health presently.

Physical examination reveals a fit looking 71 year old gentleman. His vital signs are stable: PR 64/min regular and BP 160/90 mmHg. He is not pale and clinically euthyroid. He has nicotine-stained nails, no xanthelesma or thickened tendon Achilles. There is no carotid bruit. Heart sounds are dual and normal. He is not in clinical heart failure.

An ECG was done (Figure 1)

QUESTIONS

1. What is your diagnosis?
2. What other investigations would you do?
3. How would you manage this patient?
4. How would your management differ if the patient was 45 years old?

Medical Officer
Primary Health Division
Ministry of Health

For answers, please turn to page 230

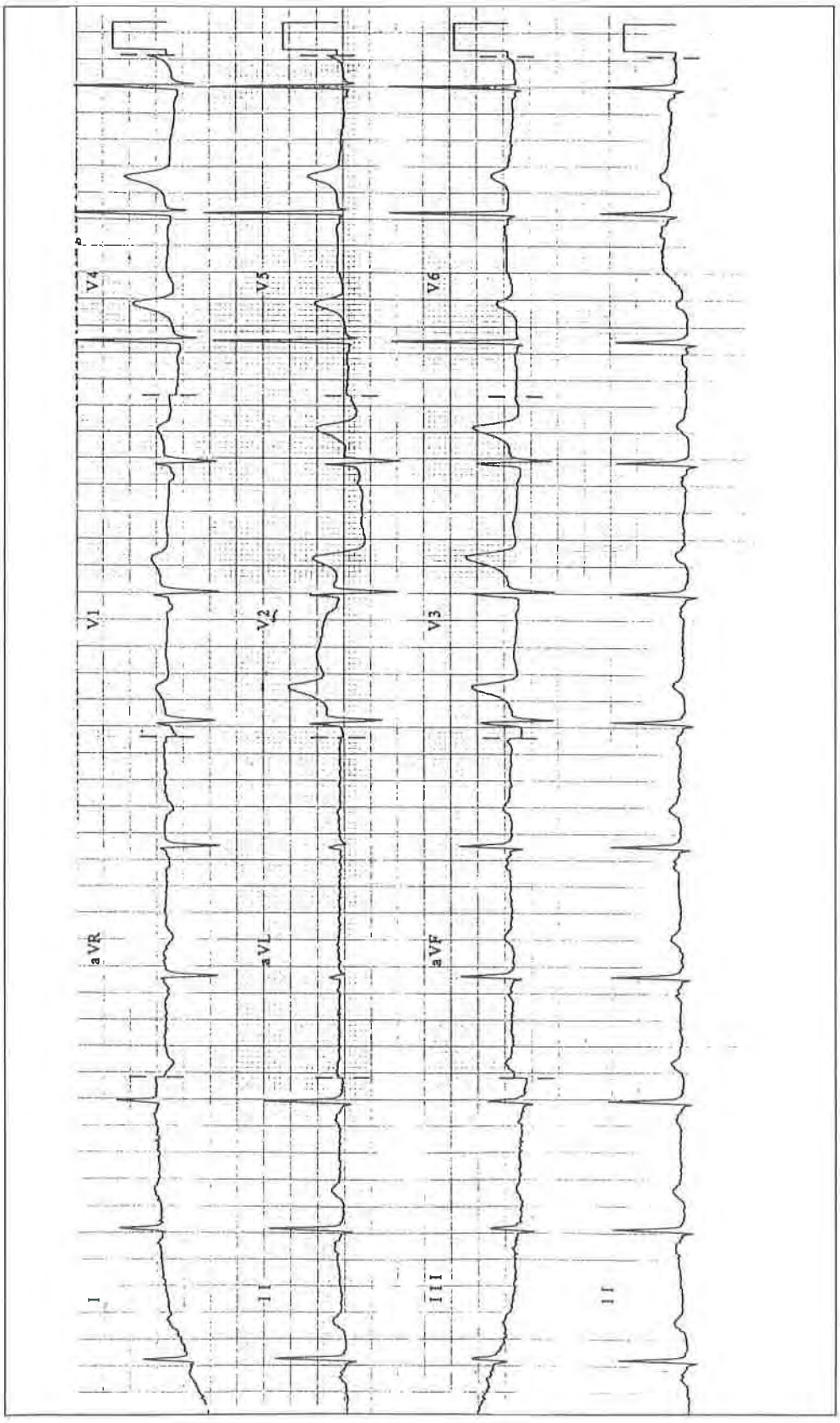

Figure 1: Electrocardiogram of Mr YBT

CASE STUDY
ANSWERS AND DISCUSSION

Q1 What is your diagnosis?

(a) Stable angina pectoris - This is a diagnosis made based mainly on history of the chest pain ie. the nature, precipitating and relieving factors, etc ECG findings are mainly supportive. A normal ECG does not exclude the diagnosis of angina pectoris.

(b) Borderline high blood pressure - A diagnosis of hypertension is not made on a single elevated blood pressure reading. This must be borne in mind and re-evaluated on subsequent visits especially in Mr YBT's case where ECG shows LVH and his son has hypertension and has suffered a haemorrhagic stroke.

Q2. What other investigations would you do (at primary health care level?)

Investigations can be divided into 3 groups:

(a) those assessing risk factors - blood sugar level, fasting lipid level

(b) those assessing precipitating factors - full blood count, thyroid function test. Clinical assessment may suffice but blood test should be done if underlying illness is suspected.

(c) those to assess cardiac status - Chest X-ray to look for cardiomegaly and congestive heart failure.

Q3 How would you manage this patient?

Management of Mr YBT's medical condition would include;

(a) identifying and treating modifiable risk factors,

(b) providing symptomatic relief for pain,

(c) preventing a secondary cardiac event eg. acute myocardial infarction and sudden cardiac health.

On subsequent follow-up visits, Mr YBT's blood pressure readings were 180/90, 190/90 and 160/90. A diagnosis of hypertension was made. His fasting blood sugar lever was 6.3 mmol/l; lipid profile showed total cholesterol of 8.61 mmol/l; HDL chol 1.46 mmol/l; Total chol/HDL ratio 5.90.

(a) Mr YBT has the following modifiable risk factors; smoking, hypertension and hypercholesterolemia.

(i) *Smoking* - This is an established risk factor for coronary heart disease (CAD). However, to normalise a smoker's risk would take at least 10 years or more. Bearing Mr YBT's age in mind, one would have to consider how much benefit he can actually gain from quitting vs his quality of life as he views it if he were to quit. The advice should be offered, but maybe not too strongly insisted upon.

(ii) *Hypertension* - The management of hypertension involves non-pharmacological and pharmacological measures. Low salt diet, regular exercise and maintaining an ideal body weight is again difficult to enforce in an elderly where habits are hard to change. The necessity of treatment and treatment goals should be discussed with him to facilitate compliance. The use of B-blockers or calcium antagonists would benefit Mr YBT for both his hypertension and angina, and there are no contra-indications for their use.

(iii) *Hypercholesterolaemia* – This again involves dietary changes that should be advised and encouraged, but bearing in mind, difficult to achieve. The treatment of hypercholesterolaemia in well elderly has not shown to be of any benefit. But in elderly patients with CAD, the mortality due to cardiac events is significantly reduced by treatment of hypercholesterolaemia. The NCEP guidelines still apply, but the side-effects of the treatment must not outweigh the benefits of treatment.

(b) *Symtomatic Relief of Angina*
This is usually achieved with the use of nitrates like isosorbide dinitrate or sublingual glyceryl trinitrate. As mentioned earlier, B-blockers and calcium antagonists are also effective anti-anginal agents.

(c) *Prevention of Secondary Cardiac Event*
The role of aspirin in the secondary prevention of ischaemic heart disease is well established. The most feared risk of using aspirin in the elderly is probably gastrointestinal bleed. Contraindications should be sought carefully before starting aspirin to minimise risk of bleeding.

Whether a referral to cardiologist is indicated at this stage has to be discussed with Mr YBT and, preferably, also the family. Factors influencing the decision would include his physiological rather than his chronological age, his social circumstances, and also the family support. It is appreciated that Mr YBT is not in the best psychosocial situation at this point in time, with his only son rehabilitating from a haemorrhagic stroke and him having to give up his job due to his health. A trial to optimise medical therapy was given with good response. His angina attacks are much reduced and also less severe. He has almost regained his usual effort tolerance and has resumed work. A less strenuous form of work is advised. Should medical therapy fail, the referral to cardiologist will be reconsidered with referral to the medical social worker for financial assistance if necessary.

The problem with polypharmacy is not only from the side effects from each drug but also from the drug interactions that result. This is especially so in an elderly like Mr YBT where renal and hepatic function may be impaired. Thus a simple drug regime with the least number of drugs would be ideal.

Q4. **How would your management differ if the patient was 45 years old?**

The main difference will lie in the aggressiveness in all aspects. The benefit from quitting smoking cannot be over-emphasised. Referral to Smoking Cessation Clinic may benefit the patient if he encounters any difficulty. Dietary changes must be reinforced to enhance compliance. Referral to a dietician will be useful. A cardiologist referral will be strongly advised from the very first visit, and help from medical social worker sought if necessary.

WORLD HEALTH ORGANIZATION PUBLICATIONS

NEW BOOK ANNOUNCEMENT

Research of the Menopause in the 1990s

Report of a WHO Scientific Group

WHO Technical Report Series, No. 866
1996, vii + 106 pages
Available in English; French and Spanish in preparation
ISBN 92 4 120866 X

This book provides an expert assessment of what is known about the menopause, its immediate and long-term effects on health, and the possibilities for their treatment and prevention. Noting the many methodological problems surrounding research on the menopause, the report makes a special effort to separate those areas where firm conclusions can be reached from those where questions remain and further research is needed. Particular attention is given to the risks and benefits of hormone therapy and to the question of whether research conducted in industrialized countries can be generalized to women living elsewhere. Some 500 references to recent studies are included.

In view of the growing number of postmenopausal women and the significant health problems they face, the report aims to reach conclusions that can help women, clinicians, and policy-makers make the best decisions concerning the management of both immediate symptoms and long-term effects on the cardiovascular and skeletal systems. Equally important is the report's identification of areas requiring further research. Conclusions and recommendations reflect the consensus reached by a group of 25 leading experts.

The report has twelve sections. Methodological problems are addressed in the first, which considers the strengths and weaknesses of various investigative approaches and explain why certain designs are more likely to yield reliable results. Against this background, the next sections review the demography of the menopause and female to male mortality ratios by age and geographic region, and summarize what is known about the endocrinology of the normal menopause, giving particular attention to the relationships between age, level of circulating hormones, and menstrual status. A section on the symptoms of the menopause and their treatment underscores the importance of distinguishing between symptoms that result from loss of ovarian function and symptoms that arise from the ageing process or from the socio-environmental stress of the mid-life years. Subsequent sections provide a brief discussion of the cultural context of the menopause and assess the risks and benefits, for women in the late premenopause, of different contraceptive options.

The most extensive sections attempt to resolve some of the controversy surrounding the use of hormone therapy to reduce the risks of osteoporotic fractures and cardiovascular diseases while also answering the question of whether hormone therapy increases the risk of breast cancer, endometrial cancer, and other gynaecological cancers. Information ranges from advice on calcium and vitamin D supplementation for the prevention of osteoporosis, through the reasons why postmenopausal women are at increased risks for cardiovascular disease, to estimates of the increase in relative risk of breast cancer among women using estrogens alone for different lengths of time.

The report concludes with a balanced discussion of strategies for managing the health consequence of the menopause, emphasizing the need for a clear distinction between short-term therapeutic and long-term preventive goals, since the risks and benefits of the two types of therapy are very different.

REVIEWERS FOR 1996

The Publications Committee would like to thank the following, who have spent invaluable time in reviewing articles for the Singapore Family Physician in the Year 1996:

Dr Chan Nang Fong

A/Prof Goh Lee Gan

Dr Lau Hong Choon

Dr Lee Kheng Hock

Dr Lim Hock Kuang, David

Dr Lim Lean Huat

Dr Tan Chin Lock, Arthur

Dr Tan Tah Chew

Dr Moti Vaswani

Dr Wong Song Ung

GUIDELINES FOR AUTHORS
THE SINGAPORE FAMILY PHYSICIAN

Authors are invited to submit material for publication in the Singapore Family Physician on the understanding that the work is original and that it has not been submitted or published elsewhere.

The following types or articles may be suitable for publication: case reports, original research works, audits of patient care, protocols for patient or practice management and review articles.

PRESENTATION OF THE MANUSCRIPT

The Whole Paper

* Normally the text should not exceed 2000 words and the number of illustrations should not exceed eight.

  Type throughout in upper and lower case, using double spacing, with three centimetre margins all round. Number every page on the upper right hand corner, beginning with the title page as 1.

* Make all necessary corrections before submitting the final typescript.
  Headings and subheadings may be used in the text. Indicate the former by capitals, the latter in upper and lower case underlined.

  Arrange the manuscript in this order: (1) title page, (2) summary, (3) text, (4) references, (5) tables, and (6) illustrations.

* Send three copies of all elements of the article: summary text, references, tables and illustrations. The author should retain a personal copy.

The Title Page

* The title should be short and clear.

* Include on the title page first name, qualifications, present appointments, type and place of practice of each contributor.

* Include name, address and telephone number of the author to whom correspondence should be sent.

* Insert at the bottom: name and address of institution from which the work originated.

The Summary

* The summary should describe why the article was written and give the main argument or findings.

* Limit words as follows: 100 words for major articles; 50 words for case reports.

* Add at end of summary: an alphabet listing of up to 8 keywords which are useful for article indexing and retrieval.

The Text

The text should have the following sequence:

* Introduction: State clearly the purpose of the article.

* Materials and methods: Describe the selection of the subjects clearly. Give references to established methods, including statistical methods; provide references and brief descriptions of methods that have been published but are not well known. Describe new or substantially modified methods, giving reasons for using them and evaluate their limitations. Include numbers of observations and the statistical significance of the findings where appropriate.

  Drugs must be referred to generically; all the usual trade names may be included in parentheses. Dosages should be quoted in metric units.

  Laboratory values should be in SI units with traditional unit in parentheses.

  Do not use patient's names, initials or hospital numbers.

* Results: Present results in logical sequence in the text, tables and illustrations.