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Prevention of Type II Diabetes

Louis Pasteur once said, "When meditating over a disease, I never think of finding a remedy for it, but, instead, a means of preventing it"

Diabetes Mellitus has been around for a very long time. There are volumes of literature written on the treatment of Diabetes Mellitus over the past decades or so. But a question often asked is, "Is Diabetes preventable?" And if so, how can it be prevented?

There are both genetic and environmental contributions to the development of Type II Diabetes Mellitus. Several gene mutations have been recently identified which lead to specific subtypes of Type II Diabetes. However, the nature of the genetic factors which predispose to Type II Diabetes in the majority of patients is still largely unknown.

In the majority of Type II diabetes patients, insulin resistance is the primary pathophysiologic abnormality. Besides genetic causes of insulin resistance, there have been studies indicating that environmental factors also influence insulin sensitivity. This will prove to be an interesting point, because epidemiological studies have also suggested that environmental or lifestyle factors play a role in the development of Type II Diabetes. The hypothesis, therefore, is that of an interplay between the genetic component and the environmental component, leading to insulin resistance.

Three main environmental risk factors are said to influence insulin sensitivity, and thereby contributing to the increased incidence of Type II Diabetes. These three factors are :

- (a) Obesity - both the degree and duration,
- (b) High fat diet - this translates into higher calories. Also, insulin resistance may result from elevated levels of circulating free fatty acids.
- (c) Sedentary lifestyle - this refers to low physical activity.

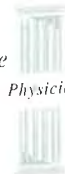
The presence of these three environmental risk factors is clearly seen in societies which have become more developed, more urbanized, more modern, and reflected in the increase in the number of diabetics. Some have even referred to this phenomenon as the "epidemic" of Type II Diabetes.

Where, then, do we go from this knowledge of the role of environmental factors acting in concert with unknown genetic predisposing factors? This ultimately leads us to the role of Primary Prevention of Diabetes. In fact, this becomes for us a critical role, both socially and economically. No longer do we just look at "curing" Diabetes. Instead, it becomes even more important now for us to be able to detect at-risk groups, and implement interventional strategies by modifying the "environmental" factors of obesity, high fat diet and a lack of physical activity.

Given the mortality and morbidity of Diabetes, and the accompanying social and economic costs, it becomes logical to think of prevention of Diabetes as the goal of all physicians. Indeed it must be the goal of the twenty first century.

Dr Paul Goh Soo Chye

Section Editor



President's Column

Family Medicine Research

Those of us that have followed the history of the College would agree that we have finally achieved the recognition of Family Medicine as a distinct discipline.

One of the four criteria of a discipline is the presence of ongoing research. The other three criteria are: a body of knowledge, an assessment system and peer recognition. To achieve continued viability in the discipline of Family Medicine we need to be able to describe our work, define those areas of research with hitherto unanswered questions, and try to provide answers through Family Medicine/General Practice research.

The research blue print

What is Family Medicine/General Practice research and how do we go about it? Much has been written about the subject. Perhaps the ideas of James Mckenzie deserve a re-visit. As long ago as 1920, he identified three steps in research:

- To describe the common symptoms and problems encountered in general practice
- To detail each case and to follow it up to study the impact of the disease and prescribed treatment
- To teach research methods to doctors to enable them to do research

Herein lies the strategic plan of primary care research. We need to explore the obstacles that lie in our way. As a start, we could make a list of the common problems that we do not know very much about except for the fact that they are common. Many questions come to mind once we take such a line of thought. Take upper respiratory tract infections for example, which account for a quarter to a third of a doctor's work. When is it viral and when is it bacterial? What treatment regimes are cost effective?

Cross-sectional studies are easy to do but they do not tell us much about causative factors nor the

results of treatment or non-treatment. Hence, we need to go beyond such methods of study and consider other methodologies such as case control, cohort studies and intervention studies. This will necessitate the use of particular mechanisms to capture information that can be obtained on the follow-up of the subjects. All these highlight the need for short and effective research methodology courses.

Getting participation

One of the strategies in Family Medicine/General Practice research has been the formation of research networks. There is no doubting the usefulness of such an approach, for such networks from the fundamental basis of a system that supports the doctor carrying out the research. It also provides the doctor with important channels of communication and a platform on which to exchange and share one's experience and expertise.

Where do we go from here?

The College Research Committee has initiated some thinking and work in this area. We look forward to your response to the Committee's invitation to you to join in its activities. Together, we will provide answers to unanswered questions in our discipline of Family Medicine.

Dr Alfred W T Loh

President

College of Family Physicians Singapore



Invited Articles

Hepatitis A Vaccination

Chow W C

Summary

As the herd immunity against hepatitis A decreases in our population, many of our patients are becoming more susceptible to acute hepatitis A infection. This is made worse by the increased mobility of the population who travel to highly endemic areas. While it is usually a self-limiting illness, considerable morbidity could arise in patients above 40 years of age.

Hepatitis A vaccine is highly efficacious. However, bearing in mind the cost involved, target groups should be identified for prophylactic vaccination.

Introduction

It has been reported in many countries that there is a changing prevalence of hepatitis A antibody (anti-HAV IgG) in the population with the improvement of sanitation in the community.^{1,2} This is also the case in Singapore where there was an overall decline in the anti-HAV IgG seroprevalence rate of more than 10% (33% to 21.4%) over a 5 year period between 1987 and 1991.^{3,4} In a survey based on sera collected in 1994 from the southeastern part of Singapore, the seroprevalence of anti-HAV IgG was only 6.5% among youngsters between 15-24 years of age, and barely more than one-third (37.5%) of those in the 25-34 year age group were protected.⁵

While acute hepatitis A is rather benign and may even be subclinical in children, it is associated with various morbidity and possible death from fulminant hepatic failure in adults, especially in those aged above 40 years.

In Singapore, where its people travel extensively due to socioeconomic reasons, the changing trend of its seroprevalence of anti-HAV IgG has two significant implications. Firstly, it means that the working population which is also the most mobile and susceptible population is at the highest risk of contracting hepatitis A infection. Secondly, being older, these infected patients will tend to

have more severe disease, unlike their counterparts in the highly endemic areas. In 1996, there was an increase in incidence of acute viral hepatitis by 19.1%, compared to the previous year. Nearly half (47.8%) of these were due to acute hepatitis A. Forty-three percent of the acute hepatitis A cases were imported, these accounted for more than two thirds of all the imported cases of acute viral hepatitis. The peak incidence of acute hepatitis A was found in the 25-34 year age group and this was the age group that was associated with the highest rate of morbidity.

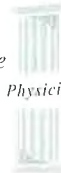
Hence, the recent availability of hepatitis A vaccine has come in timely. Nevertheless, it is not cheap. The target population who should benefit from such prophylaxis should therefore be defined. The pros and cons of hepatitis A vaccination in high risk groups will also be discussed.

Hepatitis A vaccine

Currently, the hepatitis A vaccines available in Singapore are both formaldehyde-inactivated, alum-adsorbed whole virus vaccines. After propagation in a cell culture medium, the viruses are extracted from the lysed cells and purified. These viruses are then inactivated by formaldehyde and adsorbed to an aluminium hydroxide adjuvant. Expressed in different units, there are 50 units and 1440 ELISA units of viral antigens available in 1 ml of Vaqta^R (Merck Sharp & Dohme (I.A) Corp) and Harvix^R (Smithkline Beecham Pharmaceuticals), respectively. Preservatives are found in Harvix^R but not in Vaqta.^R

Both of these preparations are available in a 1 ml single dose vial to be given to the patients intramuscularly. They will induce specific humoral response with production of specific anti-HAV antibodies.

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Invited Articles

Vaccine administration

Adults above the age of 18 or 16 years were recommended to be given a full 1 ml dose of Vagta^R or Havrix^R, respectively, during primary vaccination. A booster dose of the same dosage should be given 6-12 months later to ensure prolonged protection. For children below the recommended adult age, half the adult dosage should be given in the same schedule. No recommendation has been given for very young children who are less than 1 or 2 years old.

All injections should be given intramuscularly. The preferred site of vaccination is the deltoid region which gives the best humoral response, in terms of the anti-HAV IgG geometric mean titre (GMT).

Efficacy and adverse effects of the vaccine

The hepatitis A vaccines are highly immunogenic and efficacious in providing short and long-term protection against clinical acute hepatitis A in both adults and children.⁷⁻¹⁰ Ninety-five percent or more of the vaccinees developed protective levels of anti-HAV IgG antibody one month after the primary vaccination, and all patients would have protective level of hepatitis A antibody six months later. It was estimated that this protective level of antibody will persist for a minimum of at least 20 years.^{11,12}

This efficacy of the vaccine in developing anti-HAV IgG antibodies corresponded to the observation of significantly less incidence of clinical hepatitis A among the vaccinees than those who were not vaccinated.^{9,10,13} Particularly in an outbreak setting, this effect was apparent within four to eight weeks after a single dose vaccination.^{9,10} As for those who developed clinical hepatitis A after vaccination, they tend to have milder disease, with shorter duration of illness and only mild elevation of transaminases.¹³

There were no serious adverse effects associated with hepatitis A vaccination. Most of the adverse reaction were due to local affects at the site of injection which consisted of pain, tenderness, swelling and redness.

At a trial on hepatitis A vaccine (Havrix^R) conducted in Singapore in 1993, similar immunogenicity and reactogenicity data were obtained.¹³

Indications and contraindication for hepatitis A vaccination

Frequent travelers, particularly those who travel to areas of high or intermediate endemicity, should be vaccinated against hepatitis A. For full protection, it should be administered at least four weeks before travel. For travelers who travel to high risk areas within 4 weeks of vaccination, additional passive immunisation with immunoglobulin should be considered for complete protection.

Other groups, such as homosexuals, intravenous or oral drug abusers, haemphiliac patients and persons with multiple sexual partners should receive hepatitis A vaccination too. In addition, persons who have occupational risk of infection and who are at high risk of transmission of infection, and patients who have chronic liver disease should be considered for vaccination. These include medical and nursing personnel, food handlers, and workers at day-care centres. This is to prevent the development of outbreaks of hepatitis A infection in the communities. The rationale for immunising patients who have chronic liver diseases is because of the tendency of more severe liver disease and fulminant hepatic failure in patients who have underlying chronic liver disease and who develop superinfection of acute hepatitis A.¹⁴⁻¹⁶ These include hepatitis B and C carriers.

Studies have been done to show that it is safe to administer hepatitis A vaccine to patients with chronic liver diseases and HIV-1 infection. However, the immunogenic response was inferior to that observed in the healthy subjects.¹⁷⁻¹⁹

The main contraindication to hepatitis A vaccination is history of hypersensitivity reaction to alum, or in the case of Havrix^R usage, to the preservative 2-phenoxyethanol. The safety of hepatitis A vaccine in pregnancy has not been verified. Its administration during pregnancy

Invited Articles

should be determined on a case-to-case basis, weighing the risks against the benefits in each individual situation.

Serologic tests before and after vaccination

While there is no increased risk of adverse reaction in vaccinating someone who is already immune to hepatitis A, we may be increasing health cost by vaccinating many unnecessarily. Based on our local seroprevalence pattern of anti-HAV IgG, it will probably be cost-effective to administer hepatitis A vaccine to any person below 40 years of age without prior anti-HAV IgG testing. Whereas for individuals who are over 40 years of age, prevaccination testing of anti-HAV IgG should probably be done to verify his/her immune status, and to only vaccinate those who are tested negative.

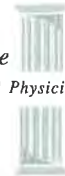
As both the locally available hepatitis A vaccines are highly immunogenic, post-vaccination testing of response to vaccination will not be necessary.

The future

With the availability of such efficacious hepatitis A vaccines, the future development lies in finding one which has less local adverse effects or which is more convenient in its administration. Inactivated hepatitis A vaccine based on virosomes without adsorption to aluminum may provide similar protection with less local adverse effects.²⁰ The development of an oral candidate hepatitis A vaccine,²¹ or a combined A/B vaccine²² will simplify vaccine administration.

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Overview of Endocrine Hypertension

Loh KC

Although endocrine hypertension is uncommon, its diagnosis provides clinicians with a unique treatment opportunity. Unlike essential hypertension, individuals with endocrine hypertension can often attain surgical cure or achieve a dramatic response to appropriate pharmacologic therapy.

The purpose of this overview is to provide the general medical audience with the current perspective in the diagnosis and treatment of these challenging conditions. However, the details and complexities involved are not included as these fall beyond the scope of our discussion. We shall confine our discussion to adrenal mediated hypertension, that of mineralocorticoid hypertension and pheochromocytoma.

Mineralocorticoid Hypertension

Aldosterone is the principal mineralocorticoid hormone produced in the adrenal cortex. Its primary function is to promote sodium retention and potassium loss in the collecting duct through increases in sodium channel activity, apical potassium permeability and the number of Na⁺, K⁺-ATPase. Normally, the major regulators of aldosterone secretion are the renin-angiotensin system and potassium, with corticotropin (ACTH) having only acute stimulatory actions. Mineralocorticoid hypertension is most commonly due to excessive or autonomous aldosterone production from an adrenal adenoma or bilateral adrenal hyperplasia. However, under certain circumstances, deoxycorticosterone (DOC) and cortisol are also important in the pathogenesis of hypertension. The causes of mineralocorticoid hypertension are summarised in Table 1.

Table 1. Causes of Mineralocorticoid Hypertension

Primary Aldosteronism

Aldosterone producing adenoma (APA) or
Conn's syndrome
Bilateral idiopathic hyperaldosteronism (IHA)
Aldosterone-producing renin-responsive
adenoma (AP-RA)
Primary adrenal hyperplasia (PAH)
Aldosterone-producing carcinomas
Glucocorticoid-remediable aldosteronism (GRA)

Normal or Suppressed Aldosterone levels

Cushing's syndrome
(esp. ectopic ACTH production)
Congenital adrenal hyperplasia
(11-hydroxylase and 17-hydroxylase deficiency
subtypes of CAH)
Syndrome of apparent mineralocorticoid excess
(AME)
Licorice or carbenoxolone ingestion
Liddle syndrome

1. Primary Aldosteronism

This accounts for 1-2% of all patients with hypertension, although some recent cross-sectional studies suggest that its prevalence may be as high as 5-10%. The majority of patients (2/3) harbour an aldosterone-producing adrenal adenoma (APA), classically termed Conn's syndrome. About a third of patients have bilateral idiopathic hyperaldosteronism (IHA). Less frequently encountered conditions include primary adrenal hyperplasia (PAH), aldosterone-producing renin-responsive adenoma (AR-RA), aldosterone-producing carcinomas and glucocorticoid-remediable aldosteronism (GRA).

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Invited Articles

Clinical features

Patients with primary aldosteronism manifest hypertension as a result of increased salt and fluid retention, leading to volume expansion and increased cardiac output. In the chronic state, there is also an increase in total peripheral resistance. This is accompanied by hypokalaemia from renal potassium wasting, and metabolic alkalosis. However, hypokalaemia may not be obvious, particularly in an individual compliant with a low salt diet prescribed for hypertension. The degree of hypertension is usually moderate, but it may be refractory to the usual pharmacologic treatments. There are no specific physical findings, although patients with marked hypokalaemia may complain of polyuria, polydipsia, muscle weakness and cramps.

Diagnosis

The diagnostic evaluation of primary aldosteronism can be divided into three phases :

i) Screening tests

The best screening test is the measurement of a random upright plasma aldosterone concentration (PAC) to plasma renin activity (PRA) ratio under conditions of normal salt intake. It is noteworthy that numerous anti-hypertension medications may interfere with the renin-angiotensin-aldosterone axis on the one hand, whereas it may not be practical to discontinue therapy prior to testing on the other. In clinical practice, it is acceptable to perform the screening test while the patient is on pre-existing anti-hypertensive drugs except for spironolactone; the latter should be discontinued for at least 6 weeks. In primary aldosteronism, one expects to find an elevated PAC from functional autonomy, and a suppressed PRA as a result of negative feedback on the renin-angiotensin system, thus giving rise to an elevated PAC to PRA ratio. A ratio of PAC (in ng/dL) to PRA (in ng/mL/h) greater than 20 is 95% sensitive, but only 75% specific for primary aldosteronism. However, a repeat test after drug withdrawal should be performed if the screening result is negative with concomitant diuretic or angiotensin-converting enzyme inhibitor therapy.

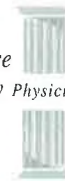
ii) Confirmatory tests

The confirmatory test for hyperaldosteronism requires the demonstration of failure to inhibit aldosterone overproduction under conditions whereby the renin-angiotensin-aldosterone axis should normally be suppressed. This can be accomplished in the outpatient setting by doing a 24 hours urine aldosterone measurement after the subject has adequately received a high salt diet and oral NaCl tablet supplement for 3 days. A concomitant urine sodium determination is helpful to ensure adequacy of salt loading. Urinary aldosterone excretion of greater than 12 ug/24 hours in the setting of adequate salt loading (urine sodium greater than 200mmol/24 hours) is consistent with hyperaldosteronism. Alternatively, this can be performed in the hospital with intravenous saline loading. In either case, one should be wary of aggravated hypertension and/or hypokalaemia during the study, and adequate potassium replacement is necessary.

iii) Subtype differentiation studies

The third phase of the evaluation involves subtype differentiation studies; this is essential in guiding the therapeutic approach as only APA and PAH subtypes are amenable to unilateral adrenalectomy. This requires one or more tests, of which the first is imaging the adrenal with CT using fine cuts. When a solitary unilateral adenoma (> 1cm) and normal contralateral adrenal morphology are found on CT in a patient with biochemically confirmed primary aldosteronism, unilateral adrenalectomy is a reasonable therapeutic option. However, additional testing is required for subtype differentiation if CT imaging shows normal appearing adrenals, minimal unilateral adrenal limb thickening, unilateral microadenoma (<1cm), or bilateral nodules. This is not an uncommonly encountered situation as up to one fifth of patients with APA harbour microadenomas (<1cm) which may not be clearly identifiable on imaging; whereas 10% of normal individuals may have incidental findings of non-functional adrenal nodules (incidentalomas) on imaging study.

Traditionally, the postural stimulation study is employed to differentiate between APA and IHA, as APA is amenable to surgical cure while IHA is



best treated medically. This test was developed in the 1970s and it was based on the finding that circulating aldosterone levels in patients with APA show a diurnal variation (ACTH responsive) and are relatively unaffected by changes in angiotensin II levels, whereas IHA is characterised by increased sensitivity to a small change in angiotensin II that occurs with standing. However, it was subsequently found that some patients with APA were sensitive to angiotensin II (called AP-RA), and that some patients with IHA were responsive to ACTH and showed diurnal variation in aldosterone secretion. At best, the accuracy of the postural stimulation test is about 85%. Many centres have thus discontinued the postural study, as it is unsafe to have surgical decisions solely based on it.

Adrenal venous sampling is currently the gold standard to determine a unilateral source of aldosterone production. This technique was in fact developed in the late 1960s. However, its utility in early years was limited by technical difficulties in cannulating the right adrenal vein. To improve diagnostic accuracy, adrenal venous sampling for aldosterone should be carried out with synacthen infusion, and concomitant cortisol measurements should be obtained. The differentiation between APA and IHA is made by comparing the "cortisol-corrected" aldosterone concentrations in the right and left adrenal veins, and the infrarenal portion of the IVC.

Treatment

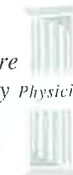
The treatment goal is to prevent morbidity and mortality associated with hypertension and hypokalaemia. The majority of patients (80-90%) with APA, AP-RA, and PAH are potentially curable by unilateral adrenalectomy which can be performed via laparoscopic surgery. However, a proportion of patients may have persistent hypertension following adrenalectomy. This may suggest the co-existence of primary hypertension, as this is often correlated with older age and duration of hypertension. For patients with IHA, only medical treatment is recommended as the

average cure rate is low (<20%) after unilateral or bilateral adrenalectomy. Medical therapy consists of the use of mineralocorticoid receptor antagonist, spironolactone, at 100-360 mg daily. The dose should be carefully titrated according to clinical response and renal function. Due to its anti-androgen effect, long-term use of spironolactone is undesirable in men as it can induce painful gynaecomastia. An alternative potassium sparing agent like amiloride should therefore be used. In addition, IHA patients often require additional anti-hypertensive medication like calcium channel blockers or angiotensin-converting enzyme inhibitor.

Glucocorticoid Remediable Aldosteronism (GRA)

GRA is an extremely uncommon, monogenic (single gene defect) hypertension due to fusion of the aldosterone synthase gene (P450 aldo synthase) in zona glomerulosa with the regulatory gene for cortisol production (P450 c11) in zona fasciculata of the adrenal cortex respectively. GRA appears to cluster in Anglo-Saxon families. It is suspected by the following constellation of factors: severe hypertension of early-onset with a strong family history of hypertension and/or strokes, and biochemical evidence of hyperaldosteronism when assessed. However, there is much phenotypic variation in GRA kindreds, with some having mild hypertension while others having normokalaemia as the rule.

As the chimeric gene is under ACTH regulation, a biochemical hallmark of GRA is the overproduction of 18-oxygenated cortisol compounds which represent hybrid steroids. Currently, an international registry is available which offers direct gene testing and family screening. Traditionally, GRA has been treated by the administration of dexamethasone. As this is associated with cushingoid side effects, alternative therapies include salt restriction, spironolactone, amiloride and other anti-hypertensive agents.



Invited Articles

2. Mineralocorticoid-like Hypertension associated with normal or low Aldosterone levels

In certain circumstances, patients with mineralocorticoid-like hypertension actually have low normal or suppressed plasma aldosterone concentrations. Except for Cushing's syndrome, most of these conditions are relatively uncommon but nevertheless they should be recognised. We shall describe some of these conditions with emphasis on the pathophysiologic mechanisms involved:

Cushing's syndrome (hypercortisolism)

In Cushing's syndrome, particularly from ectopic ACTH secretion, very high plasma levels of deoxycorticosterone (DOC) and cortisol would overwhelm the mineralocorticoid receptor to produce mineralocorticoid hypertension.

Subtypes of congenital adrenal hyperplasia (CAH)

CAH due to deficiency of the enzyme 11 hydroxylase leads to the accumulation of the precursor 11-deoxycorticosterone (11-DOC), whereas 17 hydroxylase deficiency results in excess of 11-DOC and corticosterone. Excessive levels of these precursor steroids are associated with potent mineralocorticoid activity with consequent hypertension and hypokalaemia.

Syndrome of apparent mineralocorticoid excess (AME)

AME is another form of monogenic hypertension due to an autosomal recessive 11 β hydroxysteroid dehydrogenase deficiency. This enzyme normally inactivates cortisol to cortisone at the level of the distal tubule. Its deficiency allows access of cortisol to activate the mineralocorticoid receptors in the kidney. The diagnosis is made by detecting an excess of urinary metabolites of cortisol compared to that of cortisone. Treatment is with spironolactone or amiloride, together with low dose dexamethasone. Unlike cortisol, dexamethasone does not bind to the mineralocorticoid receptor.

Licorice and carbenoxolone ingestion

Both compounds produce an inhibition of the 11 β hydroxysteroid dehydrogenase enzyme, leading to a reversible condition with a very similar pathogenesis as the AME. Common source of licorice include candies and antelope horns used as traditional Chinese remedies.

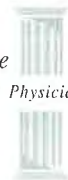
Liddle syndrome

This is actually a non-endocrine cause of mineralocorticoid hypertension. It is caused by mutations of the amiloride-sensitive epithelial sodium channel (ENaC). The mutations result in constitutive activation of the sodium channel without the need for the agonist aldosterone to bind to its receptor. This causes increased sodium absorption in the distal nephron, potassium wasting and hypertension with both suppressed PRA and PAC. The condition responds to amiloride or triamterene, whereas spironolactone is ineffective since no mineralocorticoid is involved.

Conversely, autosomal recessively inherited inactivating mutations of ENaC lead to a rare-life-threatening disease (pseudohypoaldosteronism type 1) characterized by severe neonatal salt wasting, hyperkalaemia, metabolic acidosis, and unresponsiveness to mineralocorticoid hormones.

Catecholamine-mediated Hypertension

Catecholamine secreting tumours can either arise from chromaffin cells of the adrenal medulla (termed pheochromocytomas; 90% cases) or from the sympathetic ganglia (termed functioning paragangliomas or extra-adrenal pheochromocytomas; 10% cases). Pheochromocytoma is a rare but potentially devastating cause of endocrine hypertension, estimated to occur in 0.05% to 0.3% of hypertensive patients. Besides the risk for lethal paroxysm, at least 10% of the tumours are malignant. About 10% of the tumours are familial: the associated conditions include familial pheochromocytoma, multiple endocrine neoplasia type 2 (MEN-2A and 2B), neurofibromatosis type 1 (NF-1) and von Hippel-



Lindau disease. Advances in molecular genetics have uncovered many of the mutations responsible for the familial disorders, such as the germline mutations in the RET proto-oncogene in MEN 2 syndrome. However, genetics of sporadic pheochromocytoma is largely unknown.

Clinical features

Patients harbouring catecholamine-secreting tumours may be either asymptomatic or have protean manifestations. The symptoms are due to the pharmacologic effects of excessive levels of catecholamines or co-secreted peptide hormones.

Table II. Signs and Symptoms of Catecholamine Excess

Paroxysmal nature

- Headache
- Sweating
- Palpitation (forceful heartbeat with or without tachycardia)
- Anxiety or fear of impending doom
- Tremor
- Pallor
- Fatigue or exhaustion
- Nausea and vomiting
- Epigastric or chest pain
- Dyspnoea
- Hypertensive spell
- Visual disturbances

Persistent nature

- Hypertension
- Orthostatic hypotension
- Cold hands and feet
- Peripheral cyanosis
- Weight loss
- Fever
- Increased sweating
- Tremor
- Constipation
- Congestive heart failure
- Hyperglycaemia
- Symptoms related to ectopic hormone production (eg. ACTH, CRH, GHRH, PTHrP, etc)

Table 2 summarises the signs and symptoms associated with catecholamine-secreting tumours. Patients often manifest spells or paroxysms, corresponding to episodic hormonal secretion by the tumour. The spells may be either spontaneous or precipitated by postural change, anxiety, medication, or manoeuvres that increase intra-abdominal pressure. Similarly, the hypertension may be sustained or paroxysmal. Hence, it is imperative that the detection of pheochromocytoma requires a high degree of clinical alertness. In a review of a series by the author, only 89% of the patients with surgically-proven pheochromocytoma had documented hypertension, and only 50% of the patients presented with two or more features of the classical triad of headaches, palpitations and diaphoresis. Pheochromocytoma is also known to cause ectopic hormone syndromes, the commonest being Cushing's syndrome from ectopic ACTH production.

Diagnosis

i) Biochemical confirmation

Early diagnosis and appropriate pharmacologic blockade is essential to avert potentially lethal complications that may be precipitated by drugs, intravenous contrast agents, anaesthesia or surgery. The diagnosis usually rests on laboratory demonstration of excess secretion of catecholamines and its metabolites. Over the recent years, this has been greatly facilitated by the increased availability of high-pressure liquid chromatography (HPLC) technique in most laboratories to accurately determine fractionated free catecholamines and/ or metanephrines in the urine or plasma. This has eliminated to a great extent the need for special dietary restrictions and the avoidance of numerous drugs prior to biochemical testing. Except in a situation of crisis, plasma catecholamine determination is less useful than 24-hour urinary measurement, as it only assesses a single time-point. The diagnostic sensitivity of 24-hour urinary fractionated catecholamines or metanephrines is greater than 90% in most centres, and this increases to 95-100% with the inclusion of both measurements. Conversely, measurement of urinary vanillylmandelic acid (VMA) has limited usefulness due to its poor sensitivity and

Invited Articles

specificity. With current methodologies, perturbation studies are not necessary for diagnosis.

ii) Localisation studies

Tumour localization should be performed only after biochemical confirmation of the diagnosis. As the majority of clinically diagnosed adrenal pheochromocytomas are macroadenomas (>1cm), CT or MRI study are generally adequate in localising these lesions. MRI is preferred in localising extra-adrenal tumours and has the advantage of producing a characteristically bright signal with T2 imaging. Conversely, ¹³¹I-MIBG (iodine-131 labelled metaiodobenzylguanidine) scintigraphy may be useful to rule out bilateral tumours or extra-adrenal tumours before planning surgery, particularly in childhood-onset cases or in patients with familial disease. MIBG is a structural analogue of guanethidine, which has structural similarities to norepinephrine, and is selectively taken up by adrenergic neurones and the adrenal medulla. MIBG scintigraphy offers good specificity (95-100% depending on series); however, its use is restricted by a low sensitivity for small lesions, limited accessibility and high cost.

Treatment

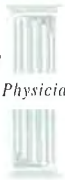
Surgery provides the definitive cure for pheochromocytoma. It is important to note that preoperative preparation with alpha-adrenergic blocking drugs (eg. phenoxybenzamine, prazosin, terazosin) coupled with adequate intravascular volume repletion and careful intraoperative monitoring have substantially decreased the high surgical morbidity noted previously. Beta-adrenergic blocking drugs (eg. atenolol, propranolol) may be added to control tachycardia aggravated by the alpha-adrenergic blockade. However, its use should not precede alpha-adrenergic blockade as this may lead to hypertensive crisis from unopposed alpha-adrenergic mediated peripheral vasoconstriction.

Long-term follow-up of surgically cured patients is necessary to exclude recurrent or malignant disease, which may manifest many years later. Like most endocrine-active tumours, surgical

debulking remains the cornerstone for palliation in patients presenting with recurrent or metastatic disease. Tumour-targeted therapy using ¹³¹I-MIBG with high specific activity has shown some promise in selected patients with soft tissue metastases.

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Original Articles

An Unusual Case of Throat Pain

Tan NC, Tan LKS

Abstract

A diagnosis of Eagle's syndrome need to be considered for patients with persistent throat pain after excluding an underlying oropharyngeal tumour. Eagle's Syndrome occurs when an elongated styloid process causes recurrent throat pain or foreign body sensation or odynophagia. Diagnosis can usually be made on physical examination by digital palpation of the styloid process in the tonsillar fossa, which will exacerbate the pain. Radiological investigation such as skull x-ray confirms the diagnosis. Treatment of Eagle's syndrome is primarily surgical.

Key words: Eagle's syndrome, odynophagia, styloid process

First consultation

Mdm Ang is a 38 years old housewife who is on regular follow up for hypertension at a local polyclinic. During her blood pressure review, she complained of a 'lump' over the left side of her throat which caused odynophagia or pain during deglutition. She even gestured how she had been frequently using her finger to feel for the painful throat lump. She was, however, unsure of the duration of the symptom. Mdm Ang had not been ill and had no dysphagia to solids or liquids. There was no definite history of neck trauma or foreign body ingestion.

Examination of her oropharynx showed erythema over the left tonsillar fossa. No foreign body, enlargement of the tonsils or cervical lymphadenopathy was noted.

In view of the redness of the left tonsillar area which suggested inflammation, the provisional diagnosis was tonsillitis, which is a common cause of odynophagia in the primary care setting. She was treated with a course of Penicillin with the advice to return if her symptom did not abate.

Second consultation

Mdm Ang returned to the polyclinic two months later for her blood pressure check-up, her throat pain continued to disturb her. She had also consulted several doctors during this period of time but to no avail. A repeat physical examination did not reveal any new abnormality. Mdm Ang admitted her fear of a pharyngeal tumour, a differential diagnosis which need to be excluded.

Her persistent symptom appeared definite and an ENT referral was offered. Mdm Ang was initially diffident about accepting the referral. This reluctance could have stemmed from her previous futile consultations. She was eventually convinced of another ENT review.

Unexpected diagnosis

A prompt reply from the ENT surgeon revealed an unusual diagnosis. Mdm Ang's throat symptom arose from an elongated styloid process known as Eagle's syndrome. In retrospect, the diagnosis can usually be made by digital palpation of the styloid process in the tonsillar fossa, which will exacerbate the pain. Skull x-rays with Towner and lateral views showing an elongated styloid process confirmed the diagnosis.

Eagle's syndrome

In 1973, Eagle first proposed the relationship between pharyngeal and cervical pain in two patients and the observation of an elongated styloid process. Eagle also reported a 4% incidence of elongation of the styloid process in the general population, although few have symptoms. There is some controversy over the existence of this syndrome. The radiological findings are classical and demonstrate a calcified elongated styloid process. (see Fig 1)

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Fig.1 Skull X-Ray showing the elongated left styloid process

Several causes for the elongation of the styloid have been proposed including:

- 1) persistence of the cartilaginous attachment to the temporal bone, providing a source of bone growth,
- 2) calcification of the stylohyoid ligament.

The mechanism for the pharyngeal/cervical pain could be due to nerve compression by the styloid process or degenerative and inflammatory changes at the ligamentous portion of the styloid attachment. However, the precise mechanism is not known.

The treatment for this syndrome is to shorten the styloid process, which can be done via intra-oral approach (see photograph) or external approach. The carotid artery is the vital structure to avoid in such a surgical procedure.



Fig.2 Another view of the elongated styloid process from the lateral skull X-Ray

Approach towards making a diagnosis

The initial diagnosis of tonsillitis was made in view of the symptom, physical sign and its relatively high prevalence in the community. Tonsillitis is a common cause of odynophagia which a general practitioner encounters in his practice. Serious differential diagnosis such as foreign body ingestion and obvious oropharyngeal tumour need to be excluded. Masquerades such as unerupted or impacted molar teeth, cranial nerve (trigeminal or glossopharyngeal) neuralgia should be borne in mind. The pitfall in this case is the lack of awareness of an underlying structural etiology. Digital examination of the oropharyngeal site of tenderness would have been the pivotal sign.

Mdm Ang's persistent throat pain led her to consult several doctors. Her help-seeking behaviour provided a hunch that perhaps an organic lesion could be the cause of her symptom.

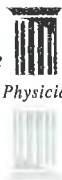
The establishment of a doctor-patient relationship by the second consultation created an avenue to modify her help-seeking behaviour and to manage her continuing problem. A doctor's earnest approach and sincere desire to help a patient overcome her problem is the foundation of a firm doctor-patient relationship. It is such rapport that convinced Mdm Ang to undergo on ENT review. Surgery is being planned for Mdm Ang.

Conclusion

Eagle's syndrome, though not a common occurrence, is probably under diagnosed and should be considered in the differential diagnosis of prolonged odynophagia. The diagnosis may be missed unless a careful history is taken and the tonsillar fossa is palpated. The treatment is primarily surgical shortening of the elongated styloid process.

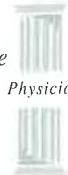
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Assessment of Diabetes Control and Complications in Patients seen in one Government Polyclinic

Kwan Y S, Goh L G, Thai A C

Abstract

Objective: The profile of patients with diabetes seen in one Government Polyclinic, with emphasis on the prevalence and control of risk factors was studied.

Method: This was a consecutive, cross-sectional study over a period of two weeks (28 March to 10 April 1997), of patients with diabetes mellitus seen for follow-up care. The criteria for inclusion were: age 40-70 years, diabetes of at least one year and on pharmacological treatment. Complications were considered only if these were on pharmacological treatment. The targets for control of risk factors are based on the American Diabetes Association's 1997 recommendations.

Results: There were 307 patients. The mean age was 57.5 years. Females made up of 53.4% of the patients. The ethnic distribution was 71.8% Chinese, 13.3% Malay, 13.3% Indian and 1.6% others. The mean age of onset was 49.4 years. The mean duration of diabetes was 8.2 years. All were NIDDM and 43.1% were on sulphonylurea alone and 48% were on both sulphonylurea and metformin. A quarter had BMI > 25. Fifty percent had a HbA1c level of >8%. 51% were treated for hypertension, 17% for ischaemic heart disease and 17% for dyslipidaemia. Twenty percent had macroalbuminuria. One-third of patients with hypertension was not on treatment.

Conclusion: This group of patients showed a high prevalence of risk factors for coronary and renal complications of diabetes. Greater attention to the continuing care of diabetes is indicated.

Introduction

Diabetes affects 12% of Singaporeans aged 30 to 69, and this prevalence has been on the rising trend (ref. 1). Diabetes can give rise to many debilitating complications, with diabetic nephropathy being

one of the leading causes of chronic renal failure in Singapore. The vast majority of diabetic patients who are receiving treatment are managed either at the Ministry of Health's polyclinics or by private general practitioners. Although private general practitioners see 80% of all outpatient attendance, it is estimated that up to 50% of patients with diabetes are seen at the polyclinics. In 1993, diabetes mellitus accounted for 9.3% of all attendances at the Government Polyclinics and 2.1% at the general practitioners' clinics (ref 2). Knowing how well these 50% of patients are cared for would help facilitate further planning with regards to diabetes care in the polyclinics.

Objectives

The main objective of this study was to analyse the profile of patients with diabetes in one government polyclinic. Emphasis was placed on prevalence and the control of risk factors.

Methodology

This was a consecutive, cross-sectional study over a period of two weeks (28 March to 10 April 1997). Case records of patients with diabetes mellitus who were seen for follow-up were collected on the day of consultation and the data collected. An average of 50 to 70 patients with diabetes were seen per day at the polyclinic.

The criteria for inclusion into the study were: age 40 to 70 years, diabetes of at least one year and the patient must be on pharmacological treatment. Patients on dietary control only were excluded to avoid any ambiguity in diagnosis. Some patients, although meeting the inclusion criteria, were new to the polyclinic and were only seen for a couple of visits, without much available data. These were excluded too.

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THE COLLEGE MIRROR

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College and WONCA

Since its inception, the College has been a staunch member of WONCA, the world network of Family Physicians. Various College members have contributed to WONCA by serving the organisation in different capacities, as well as through teaching, through the production of reports and documents, and by making presentations of their latest research at World Conferences, Regional Conferences and at Asia Pacific Workshops and meetings. All this has been in the cause of advancing the practice of Primary Health Care and the development of the discipline of Family Medicine.

As a tribute to the College and its contributors, WONCA has honoured one of the College's Council Members and current Censor-in-Chief, Associate Professor Goh Lee Gan, with the award of the Fellowship of WONCA. This is WONCA's most prestigious award and is made to individuals who have rendered outstanding service to the organisation and contributed to the development of medicine on an international scale. We are deeply honoured. See what Professor Goh has to say about the work of our College in WONCA on page M4.

FROM THE EDITOR'S DESK

WONCA 2004 Goes to America

The College came close to the staging the WONCA 2004 World Conference. Singapore was one of the two possible countries to be chosen for this event. The last time the College hosted a World Conference was the 10th WONCA World Conference in 1983.

The Singapore team presented its bid at the WONCA World Council Meetings on 12 June 1998, but lost to the big giant, America. WONCA 2004 will therefore be held in Orlando, Florida, USA. See the full report on page M5.

Climbing Mount Everest

How does climbing Mount Everest grab you? Read about this in the Singapore Family Physician Journal, under "Reflections".

■ Yvonne Chung

News from the college

Visit of 2nd Permanent Secretary (Health)

The College had the honour of a visit by Mr Moses Lee, 2nd Permanent Secretary (Health), on 20 May 1998. He was accompanied by Dr Lam Sian Lian, Deputy Director of Medical Services (Public Health), and Mr Willie Tan, Deputy Secretary.

It was an opportunity for the Council Members and staff of the College to be better acquainted with Mr Lee and his team. The Council had useful and informative discussions on the role of the College in the discipline of Family medicine, in particular, in the training of doctors and the provision and accreditation of Continuing Medical Education (CME).



Mr Moses Lee (right) with members of the council

Mr Lee commended the College in its work and what it has contributed and achieved in helping to promote the standards of practice in Family Medicine and the profile of the Family Physician/GP. The College has in the

immediate future, plans to organise hands-on skills training for our members.

College AGM

The 26th AGM was held on Sunday 11 May 1998 at 3.00pm. This was a non-voting AGM. Many issues concerning the future direction of the College were discussed. The President reiterated the importance of encouraging members, particularly, the younger ones, to participate in College activities and build upon the foundations laid by previous Councils. Only with the presence of 'new young blood' can the College continue to strive forward.



The next AGM is in May 1999 and this will be a voting AGM. The

College looks forward to having more younger members in the next Council.

■ YC

■ YC

Report

DUBLIN WONCA '98

The 15th WONCA World Conference was held in Dublin, Ireland, from 14 June to 18 June 1998. This triennial event brings together family doctors from all over the world. Five members from the College represented Singapore.

The theme "People and their Family Doctors: Partners in Care" was chosen to highlight the central place that Family Medicine occupies in the healthcare system as well as the special relationship that exists between the Family Physicians/GPs with their patients. The venue of the conference was the Royal Dublin Society, a place usually used for horse shows and exhibitions of livestock, but cleverly converted into a conference centre with one large plenary hall and 26 seminar rooms.

This year's conference saw the highest number of registrants in the history of WONCA. More than 4000 doctors registered for the conference. At the opening ceremony, the President of Ireland, Mary McAleese said in her speech "the prime motive driving family medicine is the impulse of love, the impulse which says we must care". The attendants were also treated to an entertaining Irish cultural show.

The scientific programme consisted of two plenary lectures in the mornings, followed by simultaneous sessions. After lunch was another plenary lecture which, again, was followed by simultaneous sessions. These sessions comprised symposia, workshops and free-standing papers. All the delegates were assured of an interesting and informative work schedule. Our very own

A/Prof Goh Lee Gan was invited to be a Plenary Speaker. He presented his Plenary Lecture on "Patient-centered care revisited - paradigm, research and education".

Despite a busy schedule, the delegates had time to visit the many beautiful sights in Dublin and experience the unique Irish culture, not to mention the famous Guinness brew.



Members from Singapore

At the end of the three and a half days of conference, the delegates had thoroughly enjoyed themselves, gained and shared much knowledge, made many new friends and strengthened old ties. These ties will be renewed when we meet in Durban, South Africa, for WONCA 2001. At the closing ceremony the conference ended on a perfect note with none other than the song "When Irish eyes are smiling..."

Dr Kwan Yew Seng

An interview with A/Prof Goh Lee Gan

College Mirror: Prof, we understand that there are only a handful of people who are recipients of the WONCA Fellowship award. Can you tell us more about this?

A/Prof Goh: The WONCA Fellowship is an award given every three years by the WONCA World Council. Up until the World Council met in June (1998) there were only nine members. Now there are twelve. The other two recipients this year are Dr Douglas Garvie from the UK, a past Chairman of Council of WONCA, and Dr Don Rae from Canada, a past President of WONCA.

College Mirror: What are your contributions to WONCA?

A/Prof Goh: My contribution to the world stage has been largely in the Asia-Pacific region. Together with Dr Zorayda Leopando of the Philippines and the country organisers, we have carried on the idea of educational workshops for Family Medicine teachers that was proposed by the Working Party on Medical Education in the Asia Pacific Region in 1990 at the Bali Conference. Dr Lindsey Knight was the Chairman of the Working Party. We had a successful workshop in Manila in 1993 on *Core Curriculum in Family Medicine*. Spurred by that success, we have worked with Dr George Pereira and his team in Macau to run the workshop on Clinical Teaching in 1995, with Dr Thuriappah and his team in Malaysia to run the workshop on Family Medicine Research in Kuala Lumpur in 1996, and a workshop on *Curriculum Planning and Assessment* in Seoul in 1997. There will be a workshop on *Quality Assessment* in Taipei in March 1999.

I was also a member of the WONCA Task Force to China in 1992-93. This team consisted of four members. The other three other members were Dr Martine Granek-Catarivas, Dr Giora Almagor (both from Israel) and Dr Tang-Tat Chau (from Taiwan). This China Task Force was convened upon the invitation of the Department of Medical Education of the Ministry of Public Health, China. It was tasked to study the health delivery systems in primary care and medical education facilities in the country, and to make recommendations to a curriculum framework for the future training of doctors in China. The report was subsequently published and is entitled: *Medical Education and the Development of General Practice/Family Medicine in China*. The recommendations have since been implemented to much positive effect.

I must quickly add that a large part of my contribution is made possible by the goodwill and help from many, many colleagues in the Asia Pacific Region. I would therefore like to thank them, too many to mention by names specifically, but they know who I am referring to.

College Mirror: Thank you Prof, for giving us an insight into your work upon the world stage.

A/Prof Goh: Thank you for inviting me for the interview.

BID TO HOST WONCA 2004

The last time the college played host to a WONCA World Conference was in 1983. The college felt that the time was ripe for Singapore to host the conference in the year 2004, making it 21 years since the last time the conference was held here. Family Medicine, both locally and around the world, has advanced tremendously in the past two decades. Having a world conference for family doctors in Singapore will expose the local family doctors to experiences from colleagues around the world. Furthermore, it would bring the world's attention to Singapore.



*Members of the Bidding Team: (L to R)
Dr Wong Chiang Yin, Dr Kwan Yew Seng,
Ms Yvonne Chung, Dr Tan See Leng*

The 15th World Conference this year was held in Dublin, Ireland. It is during this conference that countries, which want to host the conference in the year 2004, will present their bids to be hosts. The bidding is usually held during the WONCA executive meetings held just before the conference. In Ireland, the meetings were held in Killarney, a picturesque countryside town situated by a lake. Singapore was vying with USA for the bid, clearly a case of "David vs Goliath". The committee comprised members of the college council who were



*Ms Yvonne Chung who presented
the bid*

young and had fire in their guts, not afraid of losing but always giving everything they had.

During the bidding, both countries gave a presentation on their convention facilities, tourist attractions, and the proposed scientific program for the conference. Sadly the vote went to USA. Although we lost the bid, the committee felt that what really matters is that we had gained much experience, and made many friends from other

colleges, friends who said they said support us if we made a bid for the conference in the year 2007. Despite losing the bid, our Organising Committee led by Dr Tan See Leng, deserves our heartiest congratulations for putting up the bid.

After 2004, the next WONCA World Conference will be in 2007. Come and join us and be part of the Singapore team to bid again at the Durban Meeting in 2001!



Dr Alfred Loh (2nd Left) with members of the WONCA World Council

Dr Kwan Yew Seng

WELCOME TO NEW MEMBERS

A warm welcome to the following doctors who were accepted as Associate Members in the months April to June 98.

- ◆ Dr **Chong** Chun Hon
- ◆ Dr Colin **Ngeow**
- ◆ Dr Don **Lau** Vi Hok

- ◆ Dr Kim Alana **Hayes**
- ◆ Dr **Tng** Wei Chiang
- ◆ Dr **Soh** Soon Beng

CME

In its continuing effort to promote relevant CME for Family Physicians/GPs, the College has worked successfully with many organisations.

April 1998

6th Workshop and Seminar on Male and Female Sexual Dysfunction

The College nominally sponsored the **6th Workshop and Seminar on Male and Female Sexual Dysfunction**, organised by the Department of Obstetrics and Gynaecology, National University Hospital, on 18-19 April 1998. This 2-day seminar was covered up-to-date issues and included overseas experts giving their views on the Indonesia and Taiwan experience with injection therapy and partner acceptance.

May 98

2nd HIV Seminar for Family Physicians

The College jointly organised the **2nd HIV Seminar for Family Physicians** with the Department of Infectious Diseases, Tan Tock Seng Hospital, on 31 May 1998. Dr Richard Ng, Chairman of the College's CME Committee, chaired the session which discussed issues relevant to general practice, ranging from diagnosing HIV in the clinic to medico-legal and ethical issues.

June 98

Clinical Ophthalmology Course for the Family Physician

The College also worked with the Department of Ophthalmology, Tan Tock Seng Hospital, and nominally sponsored the **Clinical Ophthalmology Course for the Family Physician** on 7 June 98. In addition to lectures on the management of various eye conditions such as dry eye, blepharitis, conjunctivitis and contact lens wear complications, participants were also given demonstrations of useful ophthalmic procedures as well as hands-on experience in ophthalmic examinations. Dr Lim Lean Huat, Vice-President of the College co-chaired the event.

■ YC

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FAMILY MEDICINE TEACHING PROGRAMME

MODULE 4 – 27 MARCH 1999 TO 5 JUNE 1999

SMC-CME Accreditation: 2 CME Points Per Session

Venue: Lecture Theatre, COMB, Level 1

Time : 2.30 pm – 5.00 pm

PSYCHIATRIC DISORDERS IN GENERAL PRACTICE

Overview, Neuroses, Personality Disorders

| Date | Topic | Speaker (s) | Chairman |
|----------------------------------|--|--|--------------------|
| Session I 27 Mar 99 | Overview, Neuroses, Personality Disorders | Dr Ong Thiew Chai | Dr Bina Kurup |
| Session II 3 Apr 99 | Overview of Community Psychiatry, Chronic Schizophrenia, Psychogeriatrics | Dr Leslie Lim | Dr Kevin Koh |
| Session IV 10 Apr 99 | Practice Management Computer Use In The Clinic | Dr Cheong Pak Yean | A/Prof Goh Lee Gan |
| Session III 17 Apr 99 | Psychiatric Emergencies Alcoholism | Dr Tay Liam Kai | A/Prof Goh Lee Gan |
| Session V 8 May 99 | The Elderly Patient Ageing, Fitness & Assessment | Dr Philip Choo Dr Tan Chee Beng | Dr Tan Chee Beng |
| Session VI 15 May 99 | The Elderly Patient Stroke & Rehabilitation | Dr Suresh Sahadevan Dr Noor Hakim S/N Harbans Kaur | Dr Noor Hakim |
| Session VII 22 May 99 | The Elderly Patient The Frail Elderly | Dr Jonathan Phang Dr Lee Kng Swan | Dr Kevin Koh |
| Session VIII 5 June 99 | The Elderly Patient Prescribing In The Elderly | Dr Ding Yew Yoong | Dr Tan Chee Beng |

1999 JULY INTAKE
Family Medicine Training Programme
PRIVATE PRACTITIONERS STREAM
Announcement from Graduate School of
Medical Studies, NUS

The Family Medicine Training Programme (FMTP) is a structured 2 year part-time 'supervised' Private Practitioners Stream (PPS) Course. It offers an opportunity for private General Practitioners who wish to enhance their skills and knowledge in the whole area of Family Medicine without disrupting their professional practice. The course consists of weekly tutorials, monthly workshops, short hospital attachment, FMTP Modular Courses and a short Family Medicine refresher course conducted by Visiting Lectures. Private GPs who wish to seek admission into the M. Med. (Family Medicine) Examination must undergo this supervised training.

Those interested in finding out more details about the PPS training programme, such as admission requirements and programme structure may wish to purchase the PPS guidebook (S\$5) and the M. Med (Family Medicine) Training Guide (S\$5) available at the school.

| | | |
|-------------------|-------------------|---|
| Application Fee: | *\$20.60 | (non-refundable) |
| Registration Fee: | *\$51.50 | (non-refundable once application is accepted) |
| Course Fee: | *\$3400.00 | (excludes FMTP Modular Courses) |

*** Please note that all fees are subject to change without notice.**

Cheques or bank drafts should be made in Singapore Dollars payable to the 'National University of Singapore'.

CLOSING DATE: FRIDAY, 30 APRIL 1999

For application forms for the course, kindly contact the Graduate School of Medical Studies Tel: 874 6576

Update on Ultrasound Course

The Committee on Ultrasonography has reviewed the course syllabus which will be finalised by year end. The Committee is also in the process of working out the practical attachments. The syllabus covers principles on ultrasonography, antenatal problems and gynaecological problems detectable by ultrasound.

College Gifts and Accessories

KENZ Stereophonette Stethoscopes

Open up to a whole new world of KENZ stereophonette auscultation.

These KENZ stereophonette stethoscopes were first launched in Singapore at the College's 6th Scientific Conference and are now available at a discounted price of \$150.

The discrete two-channel design-it's left and right ear tubes are independently connected to right and left semi-circular microphones in the chest piece - allows the stethoscope to differentiate between the right and left auscultatory sounds. This is something not achieved by traditional monoaural stethoscopes.



SALE

Kenz stereophonette stethoscope

UP

S\$285 each

NOW

S\$150 each

College Briefcases

UP

S\$25 each

NOW

S\$20 each

College briefcases

College Conference briefcases are available at a discounted price of only S\$20 each (similar ones are retailing at S\$40 but without the embossed College logo of course).



College Silk Ties and Scarves

The College ties are all made of 100% pure silk and come in 3 colours: claret red, dark green and navy blue at only S\$25 each.

The 100% silk scarves are beautifully designed with multi-coloured orchids, the national flower of Singapore, at only S\$30 each.

You are most welcome to come to the College and have a look at any of the above items. They make idea gifts to yourselves or friends and colleagues.



Announcements

New Book Announcement

| Title | Author/Editor |
|--|---|
| The Potential for Health | Kenneth C Calman |
| History Taking, Examination, and Record Keeping in Emergency Medicine | H R Guly |
| Research Methods and Audit in General Practice | David Armstrong & John Grace |
| Professional Development in General Practice | David Pendleton & John Hasler |
| A Textbook of Family Medicine | Ian R McWhinney |
| Professional Education for General Practice | Peter Havelock John Hasler Richard Flew Donald McIntyre Theo Schofield John Toby |
| Critical Appraisal of Epidemiological Studies and Clinical Trials | Mark Elwood |
| Medicine and the Internet | Bruce C McKenzie |

1999 TAIPEI WONCA

Asia Pacific Regional Conference
March 6-10, 1999, Taipei, Taiwan

Health for All by the Year 2000 : Family Medicine-Meeting Old Challenges

General Innovation Service (GIS)

1999 WONCA Asia Pacific Regional Conference Secretariat

6F, 400, Sec. 1, Kee Lung Rd., Taipei, Taiwan 110.

Tel: +886-2-2722-1227

Fax: +886-2-2723-4187

E-mail: pcogis@ms14.hinet.net

WONCA ASIA PACIFIC REGIONAL CONFERENCE 2000

General Practice in the New Millennium

The Future for Primary Health Care

20-24 June 2000

Christchurch, New Zealand

For further information, please contact:

Conference Innovators Ltd

P O Box 1370

Christchurch

New Zealand

Tel: +64 3 379 0390

Fax: +64 379 0460

Email: WONCA@conference.co.nz

INVITATION

We invite your comments, suggestions or anything of interest that you would like to share with other members and Family Physicians. Please send your articles by fax at 222 0204 or by email at rccfps@pacific.net.sg

Or simply mail it to:

The Editor
The College Mirror
College of Family Physicians Singapore
College of Medicine Building
16 College Road #01-02
Singapore 169854

WE WELCOME YOUR CONTRIBUTIONS!

Original Articles

The targets for the control of risk factors were based on the American Diabetes Association's 1997 recommendations (ref 3). Investigation results, blood pressure and body mass index recordings were taken only if they were done within one year from the time of data collection. For complications of hypertension and dyslipidaemia, only those who were on pharmacological therapy were included in the study.

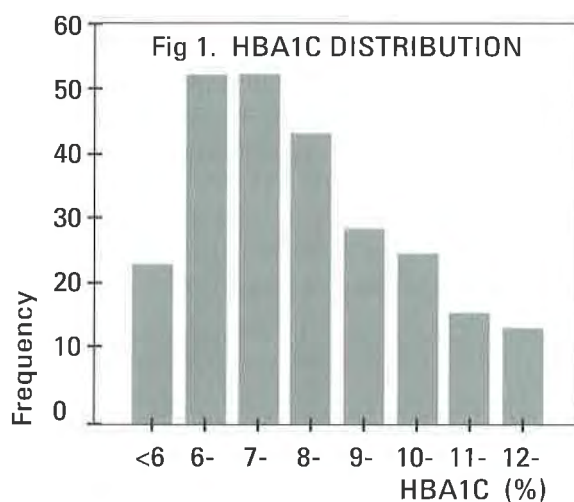
Data entry was made using DBASE IV and data analysis was made using SPSS Windows version 7.

Results

The total number of patients collected was 307. The mean age was 57.5 years, with a range of 40 to 70 years. Males comprised 46.6%. The ethnic distribution was 71.8% Chinese, 13.3% Malay and a significant over representation of Indians at 13.3%. (The national percentage of Indians was 7.1%).

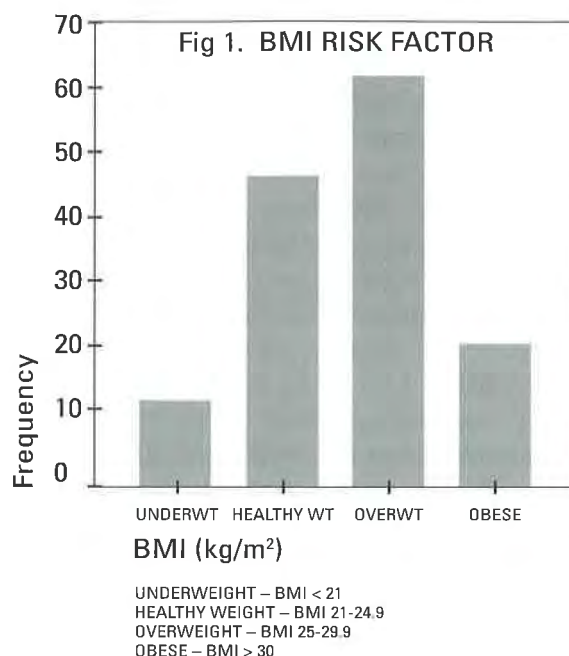
The mean age of onset was 49.4 years, with a range of 32 to 68 years. The mean duration of disease was 8.2 years. All were non-insulin dependent diabetes mellitus and 43% were on sulphonylurea alone, 7 % were on metformin alone, and 48% were on both sulphonylurea and metformin.

Glycosylated haemoglobin values were available for 81.8% of the patients. Almost 50% was found to have unsatisfactory control as evidenced by a HbA1c of more than 8% (Figure 1). Twelve



patients (4%) had blood sugar levels of more than 17 mmol/L. All of them were on oral hypoglycaemics only.

A body mass index measurement was available in only 45.3% of patients. 26.4% did not have good weight control, namely they had a body mass index of more than 25 (Figure 2).



The three complications taken into consideration were hypertension, ischaemic heart disease and dyslipidaemia. 51.1% (157) of the patients surveyed had hypertension, 17.3% (53) had ischaemic heart disease and 16.9% (52) had dyslipidaemia.

Of the 157 patients who were on treatment for hypertension, 71.6% had a systolic blood pressure of ≥ 130 mmHg, while 55.5% had a diastolic pressure of > 85 mmHg.

Among the patients who were not on treatment for hypertension, 37.6% had a systolic pressure of ≥ 130 mmHg, and 23.4% had a diastolic pressure of ≥ 85 mmHg.

Serum lipid values were available in 228 (75%) of patients and it showed that 25% had raised low-density lipoprotein cholesterol (> 3.35 mmol/L) and triglycerides (≥ 2.3 mmol/L). Decreased

Original Articles

high-density lipoprotein cholesterol ($<0.9\text{mmol/L}$), a risk factor for coronary heart disease, was found in 7.8% of the patients.

Of those who were on treatment for dyslipidaemia, 18.6% had LDL cholesterol levels of $\geq 3.35\text{mmol/L}$, 51.1% had triglyceride levels of $\geq 2.3\text{mmol/L}$ and 19.1% had low HDL cholesterol levels.

Among those who were not on treatment for dyslipidaemia, 41.6% had raised LDL cholesterol, 30.7% had raised triglycerides and 8.6% had low HDL cholesterol.

Two thirds of the patients had their urine tested with dipstix for protein. Of these, 20.8% had macro-albuminuria.

Discussion

This study shows that 39% of NIDDM patients aged 40-70 years did not have adequate blood sugar control. There was a high prevalence of risk factors for coronary and renal complications of diabetes.

The fact that a significant number did not have data like glycosylated haemoglobin or serum lipids available indicates the need to pay greater attention to the continuing care of diabetes in our polyclinics. This should not just involve doctors but also nurse educators and dietitians as they play a very important role in the care of patients with diabetes.

The importance of regular screening of risk factors cannot be over-emphasised. There is a need for doctors to be more vigilant and to treat such risk factors more aggressively if we aim to reduce the rate of complications like nephropathy. If such long-term complications can be delayed or avoided, it will greatly reduce the cost of caring for our diabetic population.

The small percentage of patients on such insulin could be explained by the reluctance of patients to be on insulin injections or failure of the doctors to start insulin therapy. There were 12 patients who had blood sugar levels of more than

17mmol/L but who were not on insulin. Perhaps their treatment should be reviewed.

More than one-third of the patients with hypertension was not treated. This indicates the need to review the situation and the need for pharmacological treatment to be considered. It is important that even borderline blood pressure receives attention. Non-pharmacological treatment should be initiated for those with mild elevations of blood pressure. The same applies for dyslipidaemia.

71% of patients who were on treatment for hypertension did not have well-controlled systolic blood pressure, while 55% did not have well-controlled diastolic blood pressure. Similarly, 19% of patients who were on treatment for dyslipidaemia did not have properly controlled LDL cholesterol levels, while fifty-one percent did not have well-controlled triglyceride levels. Their treatment may need to be reviewed.

Conclusion

This study is useful in highlighting the state of control of patients with NIDDM seen in the Government Polyclinic. There was a high prevalence of risk factors for coronary artery disease, i.e. hypertension and dyslipidaemia. The treatment of these risk factors needs to be reviewed, with a view of being more aggressive to achieve better control. Renal involvement as evidenced by macro-albuminuria was present in a fifth of the patients. Greater attention to continuing care is needed.

Acknowledgements

Many thanks to the doctors at Hougang Polyclinic for their help in collecting the data, and to Ms Alice Chew for her clerical assistance.

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HIV Infection and your practice

Leo YS

Summary

AIDS was first described in the year 1981 and HIV, the causative agent was isolated in 1983. Since then, the illness caused by HIV continues to amaze physicians. In recent years, a tremendous amount of knowledge has been accumulated to further understand the pathogenesis of the infection, improve management and outcome of the disease. This review article aims to provide a broad overview of the disease and the rapid advancement of treatment related to this illness.

Key Words: Anti-retroviral Therapy, HIV, Laboratory Markers, Natural Course, Opportunistic Infections, Pregnancy.

Introduction

A new disease entity known as Acquired Immune Deficiency Syndrome (AIDS) was first described in 1981 in North America. The syndrome was recognised when a group of previously healthy young homosexual individuals became ill with pathogens of low virulence. The clinical evidence suggested that they suffered from a severely depressed immune function of late onset of which the aetiology was uncertain. In 1983, the Human Immune Deficiency Virus (HIV) was isolated as the primary etiologic agent causing AIDS. Since then, a tremendous amount of knowledge on HIV infection has been accumulated to broaden our understanding of the immunopathogenic mechanisms responsible for diseases suffered as a result of profound immune deficiency. In recent years, a major breakthrough on HIV medicine include i) the use of protease inhibitors containing combination treatment regimens that are capable of significant suppression on viral replication that correlates with favourable survival outcome and ii) the use of plasma viral load assessment for disease prognosis and monitoring therapeutic response to HIV treatment.

Natural course of disease progression in adults

i) Clinical manifestation

The main target of destruction for HIV disease is the immune system. The manifestation of diseases associated with HIV infection is very much dependant on the degree of destruction of the immune function. The clinical events occur as a result of impaired immune function which follow a reasonably predictable chronological order. It starts with an intense period of viral replication immediately following the acquisition of the virus which may last for two to four weeks before the onset of an immune response and clinical illness. This acute viral illness from seroconversion or known as primary HIV infection generally lasts from one to two weeks and occurs in 53% to 93% of cases (1). Most of the clinical manifestations from seroconversion illness are self-limited and resolves at the time that antibodies to the virus become detectable in the patient's serum. Thereafter, most patients will enter a stage of asymptomatic infection lasting for months to years (2,3).

After seroconversion, the entire course of HIV infection can be broadly subdivided into three phases (Fig.1). The early phase of infection with CD4 count above 500cells/ul, the intermediate phase when CD4 count falls between 200 to 500cells/ul and the advance phase with CD4 less than 200cells/ul(3).

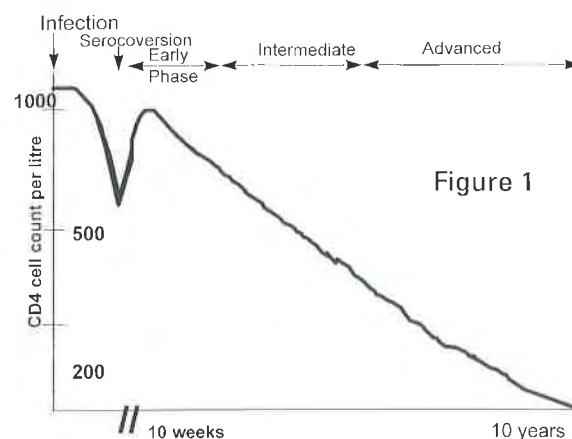


Figure 1

Management Tips

During the early phase of HIV infection, several auto-immune disorders may occur as a result of polyclonal activation of the immune system. These immune syndromes may serve as clinical clues to early HIV diagnosis. The auto-immune conditions that are described with strong association with HIV include idiopathic thrombocytopenia purpura (ITP), Guillain-Barre syndrome, mononeuritis multiplex, Sjogren syndrome, polymyositis and others (3).

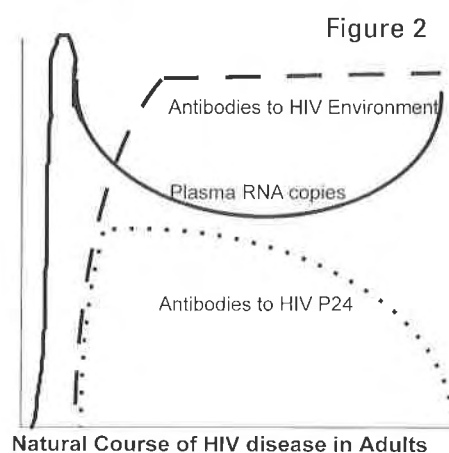
The intermediate phase of HIV infection is characterised by increasing immune deficiency leading to less serious infections, particularly involving the skin and mucosal surfaces. Commonly seen conditions include seborrhoeic dermatitis, warts, tinea, molluscum contagiosum, bacterial folliculitis, oral hairy leukoplakia and gingivitis. Oral candidiasis usually appears late in this phase and are indicative of a high risk of progression to AIDS. Other commonly encountered infections include the reactivation of herpes zoster and herpes simplex viruses. The occurrence of chronic sinusitis is also reportedly more common in HIV patients (3).

Advanced immune depletion with CD4 less than 200 cells/ul usually heralds a high risk of developing an AIDS defining opportunistic infection or malignancy. *Pneumocystis carinii* pneumonia is still by far the most common initial AIDS defining opportunistic infection followed by tuberculosis in the local setting (4). As the immune function continues to deteriorate, patients are at risk of acquiring infections from pathogens of low virulence or reactivation of latent infection. Other common opportunistic infections at the advanced phase of HIV infection include cerebral toxoplasmosis, cytomegalovirus retinitis, cryptococcal meningitis, chronic diarrhoeal disease and *Mycobacterium avium* complex infection (4).

ii) Laboratory markers

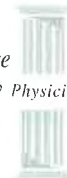
The window period denotes the period after the acquisition of the virus to the time where the infection can be detected by the currently available laboratory techniques which include the detection of viral antigens or antibodies. After seroconversion, the screening methods used

locally to detect the presence of antibodies include enzyme linked immunoassay (EIA) and particle agglutination (PA). Those screened positive need to be confirmed by the Western Blot method. Occasionally, antigen detection methods such as P24 antigen and PCR may be used when early detection of HIV infection is desirable for preventive measures or to guide decisions on the use of anti-retroviral treatment for early HIV infection.



It is well documented that CD4 counts, as markers to assess the level of immunity, may dip significantly during the acute seroconversion period. Thereafter, the CD4 level will bounce back but usually not to the original level and it will then slowly decline over the years (Fig 1). The high level of virus replication during seroconversion period is reflected by the presence of the P24 antigen, high viral load and culturable virus in the blood. After seroconversion, the level of viral antigen falls and remains at a steady level for years till the disease progresses. The level of viral antigen surges rapidly to extremely high levels as the disease progresses and patients become symptomatic (Fig1)(2).

A relatively new technique known as viral load is available locally using RT-PCR to quantitatively assess the amount of viral RNA material present in the plasma. The speed of CD4 decline and disease progression are directly related to the level of viral load at the steady state. The higher the viral load at the steady state the faster the disease



Management Tips

progression. Viral load of 10,000 copies/ml or more is associated with disease progression and is an indicator to initiate anti-retroviral therapy. In the clinical setting, the development of this new molecular technique allows clinicians to prognosticate disease progression and to monitor response to anti-retroviral treatment (5,6).

Medical management of HIV infection

A holistic approach to the management of HIV is essential for a satisfactory outcome. The discussion below is mainly focused on medical management which can be broadly classified into 3 areas:

i) Treating HIV using anti-retroviral agents

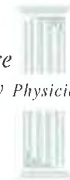
Zidovudine (AZT/ZDY) was the first anti-retroviral agent developed for HIV treatment. It received wide publicity in the mid 80s with trial results suggesting favourable clinical outcomes in the symptomatic and AIDS patients. However, subsequent trials using AZT monotherapy failed to produce the highly expected survival outcome in HIV patients at their intermediate phase of infection. Following that, the pessimism surrounding anti-retroviral drugs retarded the speed of development on anti-retroviral treatment until the mid 90s when results of 2 large trials (ACTG175 and Delta) (7,8) were available to

prove the value of combination treatment using two nucleoside analogues in patients at their intermediate phase of HIV infection. With additional information gained from development of viral load assessment and further understanding of pathogenesis of HIV infection, it is now clear that the approach to successful treatment lies in the initiation of potent combination anti-retroviral agents before any significant destruction on the immune system sets in (6). In most instances, these regimens should include protease inhibitors together with two nucleoside analogues aiming at maximum viral suppression. Maximal suppression of viral replication is essential to minimise the risk of the emergence of resistance which will ultimately lead to treatment failure (6). From the understanding of the pathogenesis of the disease, it seems that the life span of a patient may be prolonged to as long as the regimens are able to suppress viral replication and in turn halt the disease progression.

The rapid development of therapeutic agents against HIV can be easily appreciated that within a short span of 15 years after the discovery of HIV, there were more than 10 anti-retroviral agents approved by FDA for the treatment of HIV infection. Table 1 summarises the anti-retroviral agents available locally.

Table 1 Anti-retroviral agents available in Singapore

| Nucleoside analogues Reverse transcriptase Inhibitors | Non Nucleoside analogues Reverse Transcriptase Inhibitors | Protease inhibitors |
|---|---|---------------------|
| Zidovudine (AZT/ZVD) | Nevirapine | Saquinavir |
| Lamivudine (3TC) | | Indinavir |
| Didanosine (ddI) | | Ritonavir |
| Zalcitabine (ddC) | | Nelfinavir |
| Stavudine (d4T) | | |



Management Tips

ii) Treating illness arising as a result of HIV infection

These may include management of auto-immune disorders, skin and mucosal diseases, opportunistic infections and malignancies. Treatment of each of these conditions varies and is not possible for discussion in this article.

iii) Prophylaxis against common opportunistic infections

The current recommendation by CDCP, Atlanta, clearly spell out the need to prophylax against a few common and preventable opportunistic infections in HIV infected persons. Primary prophylaxis is to prevent the occurrence of the disease. Primary prophylaxis against *Pneumocystis carinii* is recommended when CD4 drops below 200 cells/ul, or occurrence of oral candidiasis (9). Recommendation on primary prophylaxis against other infections include pneumovaccine for invasive pneumococcal infection, toxoplasmosis, disseminated *Mycobacterium avium* complex, and *Mycobacterium tuberculosis*. For most opportunistic infections, secondary prophylaxis is required to prevent the recurrence or relapse of the infections that were previously treated (9).

Update and discussion on special issues

i) HIV in pregnancy

In 1994, the results of ACTG 076 trial clearly indicated that medical intervention with AZT can reduce the risk of vertical transmission of HIV. To date, AZT remains the only agent with proven clinical efficacy in reducing the risk of vertical transmission. Data on the ability of additional agents in further reducing the risk of transmission are being awaited.

However, with the advancement in the use of anti-retroviral treatment, the current evidence in managing HIV in pregnancy is that pregnancy per se should not preclude the use of optimal therapeutic regimens. Therefore, anti-retroviral use in HIV infected women during pregnancy needs to take into account two separate but related issues: 1) anti-retroviral treatment of the women's HIV infection and 2) anti-retroviral chemoprophylaxis to reduce risk of perinatal HIV transmission (10).

In the local situation, although the total number of Singapore female residents detected with HIV infection remained small, the number has increased significantly over the past few years. The first case of perinatal HIV transmission was documented in 1990, since then there were no cases till 1997 when an additional 4 cases were reported (11). For all of these unfortunate children, the diagnosis was missed during pregnancy. They were diagnosed either because they themselves or their parents had become symptomatic with HIV disease. This highlights the point about stressing the importance of routine screening of HIV test for all pregnant females

ii) Useful clues to diagnose HIV infection in the GP's Clinics

The challenge in managing HIV infection is the ability to diagnose the disease early for medical intervention to achieve a better outcome. Acute onset fever, with or without night sweats is a consistent sign of primary HIV infection. Myalgia, lethargy and malaise are frequent, often severe and may persist for several months. Respiratory symptoms are uncommon although some have a dry cough. Clearly, these general features are common to many infections unless other classical features of primary HIV infection are evident that may prompt the request for an HIV serology test. Other features of primary HIV infection to look out for are mucocutaneous ulceration and the transient erythematous, non-pruritic, maculopapular rash (1).

Mucocutaneous manifestations mentioned above are commonly seen in the intermediate phase HIV infection and these may allow physicians with a high index of suspicion to offer HIV testing (3). Seborrhoeic dermatitis, a dermatosis associated with HIV infection, commonly manifesting as an erythematous scaling eruption in the naso-labial folds, medial malar areas and glabella area with scaling of the scalp, beard and eyebrows. Kaposi's sarcoma, an AIDS defining malignancy commonly seen in homosexual men can present as multiple palpable, firm, violaceous nodules involving any cutaneous surface including the oral cavity.

Management Tips

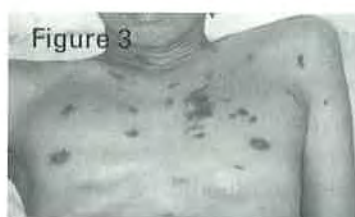


Figure 3

Multiple Kaposi's sarcoma lesions seen on the anterior chest wall.

Close examination of the oral cavity may reveal clues to suspect HIV infection. Oral lesions commonly seen in HIV patients include candidiasis, oral hairy leukoplakia, Kaposi's sarcoma, small recurrent aphthous ulcers, gingivitis, etc. As oral candidiasis is rarely seen in a young, healthy person, it can serve as a predictive marker for HIV infection. Hairy leukoplakia is white thickening of the oral mucosa, often with vertical folds or corrugations that are primarily found on the side of the tongue. Its presence is pathognomonic of HIV infection (3).



Figure 4

Oral leukoplakia at the side of the tongue and thrush covering the tongue.

Pneumocystis carinii pneumonia and tuberculosis are the two most common AIDS presenting conditions in Singapore (4). Hypoxemia is the hallmark of PCP and the typical clinical presentation is progressive dyspnoea, dry cough and fever. Examination of the lungs may be unremarkable but at this stage, it is very likely that the patient will exhibit other signs to suggest HIV infection. These include seborrhoeic dermatitis, oral candidiasis and hairy leukoplakia. Extra-pulmonary tuberculosis is frequently seen in HIV infected patients. In previously healthy young adults with extensive tuberculosis involvement may prompt the clinician to look for other clues and to assess risks behaviour for HIV infection. Blood for HIV testing should be offered in the appropriate setting.

Conclusion

In Singapore, the annual total number of newly detected HIV cases continue to increase significantly. It is not surprising for a practising physician to encounter one or more HIV patients during their course of work. Basic understanding of the disease manifestations are essential for early recognition and diagnosis of the illness to enable therapeutic intervention as early as possible. This is a challenge for primary health care providers.

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Blood Pressure Control and Diabetic Nephropathy

Tavintharan S, Chew LS

Diabetic nephropathy is a major cause of premature death in diabetics, mainly from renal failure or cardiovascular disease. Mogensen in 1984 recognized microalbuminuria as an important clinical predictor of proteinuria and cardiovascular mortality⁽¹⁾. The precise interrelation between hyperglycemia, hypertension and hyperlipidemia in the progression of nephropathy in diabetes is unclear at the moment, but much work is being done to see how treating each of these three injurious agents will affect the progression of diabetic nephropathy.

Diabetic nephropathy occurs in about a third of patients with insulin-dependent diabetes mellitus (IDDM) and the risk in non-insulin dependent diabetes mellitus (NIDDM) ranges from 25 to 50% depending on the ethnicity of the population studied. Diabetic nephropathy is defined as the appearance of clinical albuminuria (albumin excretion rate > 300 mg/24 hours) in a diabetic individual, in the absence of urinary tract infection, other renal disease and heart failure. This is often associated with rising blood pressure. Diabetic nephropathy is a multi-stage condition that takes years to become clinically evident. At the onset, there is usually glomerular hyperfiltration, increased renal blood flow and hypertrophy of the kidney. Most of these changes can be reversed at an early stage and hence screening for microalbuminuria is indeed an essential and rewarding exercise.

Management of a patient with diabetic nephropathy should be aimed at the early stage of incipient disease, that is, at the microalbuminuric stage. The following approach is necessary:

- Smokers should be advised to quit the habit as it well known to be associated with microalbuminuria and its deterioration.
- existing urinary tract infections should be promptly treated, and nephrotoxic drugs avoided.

- Good glycemic control should be achieved. The Diabetes Treatment and Complications Trial (DCCT) clearly shows the importance of improved blood glucose control and intensified insulin treatment in preventing the worsening of nephropathy and significantly reducing the risk of development of microalbuminuria in those with previously normal albumin excretion rate⁽²⁾. Krolewski, as well as other researchers, have shown that the greatest benefits of good glycemic control occurs when we lower HbA_{1c} to below 8.0%, and this target is well achievable, without subjecting patients to much risk of hypoglycemia⁽³⁾.
- Hyperlipidemia should be treated. It has been hypothesized that HMG CoA reductase inhibitors can help preserve renal function in microalbuminuric hypercholesterolemic type 2 diabetes patients, and this has recently been proven true in a study by Tonolo and coworkers⁽⁴⁾.
- Blood pressure should be controlled to not exceeding 140/90 mmHg.

The Importance of Blood Pressure Control in Diabetics.

Diabetics are at an increased risk of developing hypertension. The choice of antihypertensive therapy is a difficult one as some drugs may affect the risk of cardiovascular events. Calcium antagonists are one of the most commonly used group of antihypertensive drugs, and these also have a role in angina pectoris and certain arrhythmias. However, despite their therapeutic advantages, this group of drugs have now received adverse publicity, especially the short-acting dihydropyridine derivatives, which have been suggested to increase the risk of cardiovascular events⁽⁵⁻⁷⁾. In two separate meta-analysis encompassing 47 trials of short-acting calcium channel blockers, the investigators concluded that short acting nifedipine probably increases the risk

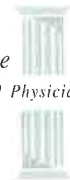
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of reinfarction or death, in a dose-dependent way, whereas the non-dihydropyridine drugs do not increase mortality and may even reduce the risk of reinfarction^(6,8). The prime mechanism of this adverse effect is postulated to be the reflex sympathetic activity associated with the short-acting dihydropyridine group of drugs.

The Appropriate Blood Pressure Control in Diabetes (ABCD) Trial was a trial with a primary objective of comparing the effect of moderate control of blood pressure (target diastolic pressure, 80-89 mmHg) with those of intensive control of blood pressure (target diastolic pressure, 75 mmHg) on the incidence and progression of complications of diabetes⁽⁹⁾. The secondary objective of this trial was to compare the effects of an angiotensin-converting-enzyme (ACE) inhibitor, enalapril with those of a long-acting dihydropyridine, nisoldipine, especially in terms of retardation in progress of diabetic nephropathy. This study was stopped earlier than planned because of the marked difference in the number of myocardial infarcts (25 in the nisoldipine group versus 5 in the enalapril group). The investigators accept that although the difference between the event rates were real, they are unable to conclude whether enalapril is beneficial as an antihypertensive in diabetics or whether calcium channel-blockers are harmful.

The Multicenter Isradipine Diuretic Atherosclerosis Study (MIDAS) showed an increase in cardiovascular events associated with the use of the intermediate-acting calcium channel-blocker isradipine compared with hydrochlorothiazide⁽⁷⁾. This difference was seen largely in patients with impaired glucose tolerance, defined as having a HbA_{1c} of higher than 6.6%, and seen only after three years of the study. The safety and benefit of hydrochlorothiazide will certainly delight health economists as this effective drug is very inexpensive when compared to several other newer antihypertensive drugs. However, we must remember the potential metabolic abnormalities associated with its treatment and be on the lookout for these side effects.

There is increasing evidence on the beneficial role

of ACE inhibitors in normotensive diabetics with microalbuminuria as well as in hypertensive diabetics even in the absence of nephropathy. Studies have shown that with similar blood pressure, ACE inhibitors are better than other conventional therapies and reduce the risk of terminal renal failure⁽¹⁰⁻¹²⁾. ACE inhibitors affect the permeability and size-selective function of the glomerulus and this leads to the decrease in ultrafiltration of macromolecules and proteins⁽¹³⁾. As filtered proteins are toxic to renal tissue, it is hypothesized that the renoprotective action is a result of reduction in protein excretion⁽¹⁴⁾. Whatever the mechanism of action, studies have unequivocally proven the benefit of ACE inhibitors in safely reducing proteinuria as well as reducing the rate of GFR decline more than what would be expected by blood pressure lowering alone.

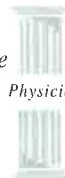
In conclusion, we know that diabetics are prone to premature death, primarily as a consequence of cardiovascular events or nephropathy. Good control of risk factors like hypertension, with minimal side effects, will certainly go a long way in reducing these adverse outcomes. From the current evidence available, ACE inhibitors and low-dose diuretics are favoured as first-line therapy for diabetics with hypertension.

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Tutorials In Family Medicine

Adolescent Suicide

Cai Y

"I can't stop the voices"

Hai Sing is 17 years old and studying in a Junior College. He has been hearing voices for the past 6 months. He hears them scolding him and commenting on his behaviour and action. These experiences increasingly affected his studies and made him very frustrated. In an attempt to stop hearing the voices, he tried to plug his ears with cotton wool. He told his parents of his unsuccessful attempts, "I can't stop the voices!" His parents told me that an uncle has a history of schizophrenia in the past. Hai Sing's symptoms became so distressing that one night, he jumped off the top of his block of flats.

Comment: Hai Sing suffered from schizophrenia and could not tolerate the irritating "voices" in his ears.

"Please don't break up with me!"

Shannu is a 16 years old secondary 4 girl who was admitted to the Singapore General Hospital following the discovery that she had swallowed 60 tablets of Panadol. This happened after Shannu found out that her boyfriend had decided to leave her for another girl.

Shannu had committed a lot of her time and effort to this relationship and had isolated herself from her friends. Her parents strongly objected to her having a boyfriend at such a young age. She neglected her studies and had started to fail in some of her subjects during the preliminary examinations.

Shannu felt extremely insecure as her boyfriend became friendly with another girl. But her possessiveness caused the boyfriend to drift further away. The boy found it increasingly difficult to cope with her unreasonable behaviour. On her birthday, after a bitter quarrel, he insisted on breaking up with her. She tried desperately to save the relationship. She pleaded with him saying, "Please don't break up with me!" But he was unmoved.

Finding no one she could confide in, Shannu decided to end her life by taking an overdose of Panadol at home.

Comment: This is a suicidal attempt in a desperate young girl who has accumulated problems that overwhelmed her. Fortunately she survived the ordeal and is now happily studying in a junior college.

"She is always late!"

Honey is a 15 year old Secondary 3 girl. She had a high IQ and was perfectionist in whatever she did. She was meticulous in her approach to homework and checked her work repeatedly. This became a problem as the examinations approached.

The stress of preparations took its toll on her. Because of this need to be perfect, she was always late in passing up her homework and sometimes could not even finish it. Her teachers called up the mother saying, "She is always late with her work!"

Depression soon set in. In an angry and frustrated state, she decided to slash her wrist one day. She even wrote a short note for her parents and had given away her pet hamster the day before. Luckily, she used a blunt penknife and her mother came home just after she cut her wrist.

She was given counselling to help change her perfectionist attitudes. With understanding from family and teachers, she was soon well enough to return to school.

Comment: Honey was an obsessional and perfectionistic girl who set high standards for herself that lead to frustration followed by depression. The suicide attempt was a culmination of that.

Tutorials In Family Medicine

How many adolescents commit suicide in Singapore?

Studies have shown that 2-4% of adolescents attempt suicide. Based on a local study by Dr Kok LP and colleagues as well as statistics from Registry of Births and Deaths, there were 232 children and adolescents in the age group of 10 to 19 year-olds who committed suicide in the 15 year period between 1980 and 1994. This means that about 16 deaths through suicide are committed by children and adolescents annually.

Suicide in childhood and in the early teenage years is uncommon but it increases sharply in late adolescence and young adulthood. The majority of suicides occur in the age group of 15 to 19 years.

Studies overseas showed that up to 4 times more boys commit suicide than girls. However, in Singapore, there were slightly more adolescent girls dying from suicide in a ratio of 1.25 girls to 1 boy. Taking drugs and alcohol did not figure significantly in our young population.

Adolescent suicide rates in Singapore (per 100,000)

| Age Group | 10-14 | 15-19 |
|-----------|-------|-------|
| 1981-1985 | 0.5 | 5.4 |
| 1986-1990 | 1.2 | 7.1 |
| 1991-1995 | 1.3 | 6.1 |

Source: Registry of Births and Deaths 1981-1995.
National Registration Department, Singapore

Adolescent suicide ages 15 to 19 in 1991

| Country | Rate per 100,000 |
|--------------------------|------------------|
| New Zealand | 15.7 |
| Finland | 15.0 |
| Canada | 13.5 |
| Norway | 13.4 |
| United States of America | 11.1 |
| Australia | 10.5 |
| Singapore | 6.9 |

Source UNICEF Report 1992

What methods did the adolescents use to commit suicide?

Most of the deaths were by jumping from high rise buildings (70.3%) followed by hanging (14%), self poisoning (8.3%) and other methods (7.4%) such as drowning and wrist cutting.

Why do adolescents commit suicide?

All adolescents have emotional or psychological needs which include the needs for love, acceptance, praise and recognition, companionship, sense of achievement and success, responsibility, self esteem and self confidence. Emotional pain arises if these psychological needs are not met. When such pain becomes unbearable and overwhelming with no way out, they may choose the option of ending their lives by suicide.

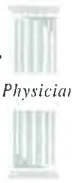
There are usually more than one reason for ending their lives. Suicide is most commonly understood as a desperate act to avoid the pain of living as much as it is an effort to seek death. The suicide attempt, whether successful or not, is a communication of that emotional pain.

Some mental illnesses may also cause an adolescent to become suicidal.

What is the state of mind of adolescents just before the suicidal act?

They experience great ambivalence between wanting to live and wanting to die. As psychological pain increases, their perceptual views narrow and they see no other way out of their problems. They try to escape this intense emotional pain by dying. In the midst of emotional pain, a sense of helplessness, hopelessness and "constricted thinking" results. They then see no other alternative to stop their distress.

But this is a temporary state. If they are given help to reduce their pain of living to a tolerable level, they would choose to live. Many adolescents who have considered suicide have



successfully turned around and continue to lead fruitful and productive lives. Adolescent suicide is thus preventable.

Suicide is a permanent solution to only a temporary problem.

What are the warning signs of adolescent suicide?

- Withdrawn and lonely.
- Sense of hopelessness and helplessness.
- Inability to think clearly, confused or irrational thinking.
- Self destructive thoughts.
- Feelings of worthlessness.
- Tense and agitated.
- Chronic bodily aches and pains.
- Deterioration of personal appearance.
- Failure in school performance.
- Pre-occupation with thoughts of death.
- Increase use of drugs and alcohol.
- Giving away prized possessions.
- Feeling guilt and failure.
- Threatening suicide.
- Previous suicide attempt.
- Hoarding of pills, hiding weapons.
- Describing methods of committing suicide.
- Making a will, writing letters or essays about suicide or death.

What are the risk factors that indicate high suicide risks?

- More than 15 years of age.
- Psychotic disorder.
- Depression.
- Conduct disorder.
- Sexual abuse in childhood.
- Rigid and inflexible temperament.
- Difficulty in school performance.
- Previous suicide attempt.
- Lack of friends and social support.
- Use of alcohol and drugs.
- Disorganised family.

The more the combination of the above factors, the higher is the risk for the adolescent to die by committing suicide.

What are the myths of suicidal adolescents?

- Adolescents who talk about suicide won't do it
- Adolescents who attempt suicide are only trying to get attention. Ignoring a suicidal adolescent is the best thing to do.
- There are no warning signs.
- An adolescent who attempts and fails will never do it again.
- This adolescent is not the type to commit suicide.
- Talking about suicide will cause the adolescent to do it.

None of the above is true. These myths are actually interfering with our ability to reach out and help those who are feeling suicidal.

How can we respond to a suicidal adolescent?

- It is important to ask what is causing the distress.
- Active listening on your part can help to alleviate the distress.
- Avoid making judgmental comments or empty reassurances.
- Give clear message that "I want you to live".
- Do not abandon the person at risk until help is available.
- If you are concerned that the person may in fact carry out the suicidal thoughts, offer your support in obtaining additional help from trusted adults and professionals.

What should you not say or do to a suicidal adolescent?

- Don't promise everything will be well. How are you to know?
- Don't give empty reassurances.
- Avoid oaths of confidentiality. What is the use of keeping a secret if the child is dead?
- Don't suggest methods of suicide.
- Believe what they say about their suicidal thoughts.
- Don't challenge a suicidal person.
- Deflect their emotional blackmails.
- Don't leave them with their friends, sometimes they may decide to die together.

Tutorials In Family Medicine

Further Management

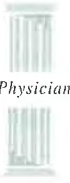
Most adolescents presenting with suicide attempts should be offered out-patient treatment. This takes the form of brief individual therapy and family therapy. Individual therapy aims to improve their capacity to solve problems and handle stress in a more adaptive way. A family approach is often indicated to improve the relationship and communication between the adolescents and the parents so as to enable the parents to understand and support the adolescents in distress. If the suicide risk is high and a major psychiatric disorder is present, the patient should be admitted to a hospital for further treatment.

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Prevention in General Practice

Fowler/Gray/Anderson

2nd edition

Prevention is a relatively **neglected** area in general practice as much emphasis is often placed in the advances in therapeutic medicine. However, there is widespread acknowledgement that avoidance of **disability** and **premature deaths** often depends on prevention. Family Physicians have a pivotal role to play in this as being the doctors of primary contact, are able to exploit the opportunities that family practice provides for influencing the future well-being of significant numbers of people.

The first few chapters of the book deal with the theoretical and **practice management** aspects of health promotion and disease prevention. The latter two-thirds of the book assesses the evidence for the **effectiveness** of prevention in relation to the major causes of disability and premature death, outlines preventive measures and gives practical guidance in carrying them out.

This book was written for family physicians in general albeit a **slant** towards the **UK** practice. It is important to note that while our **UK** counterparts are bound by the National Health Service general practice contract in the implementation of preventive programs, we are not. This is understandably so as issues such as time, commitment, finance, government policies, the direction and goals need to be resolved.

Notwithstanding, this book provides an **excellent** read with its **clear writing** style and authoritative references. Family Physicians will find this book useful in enhancing their knowledge and practice skills in the area of prevention and realise its importance in the total management of the patient.

Ethical Dimensions in the health professions

Ruth Purtilo

2nd edition

The purpose of this book is to introduce the reader to a sound foundation in **basic ethical** theory and emphasise practical approaches in identifying and dealing with common ethical problems. There are five sections in this book and it is highly recommended that the first section is read carefully unless one already has a firm grasp of the ethical concepts. The other four sections deal with the health professional as an individual, a care-giver, a team worker, and his interaction with societal structures.

Dr Purtilo introduces a **five-step** process of ethical decision making and hopes that this will lay a solid

foundation for solving problems. Very interesting too are the many **clinical** situations presented with complex ethical dimensions. She takes the reader through the **dilemmas** thoroughly and poses a series of thought provoking questions leaving the answering and decision-making to the reader.

It must be stressed that very often, there is **no one "right"** answer. Ethical decisions are made solely based on one's understanding of the ethical concepts, and the decision making process is very much moulded by the psychological, social and other practical dimensions of the situation at hand.

*Reviews by***Dr Gerard Low Mun Heng**

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Quiz

Test Your Eye-Q (No.5)

Long-standing poor vision

Au Eong KG, Lee SB

An 82-year-old female inmate of a nursing home complained of decreased vision in her right eye for 15 years. She has no history of trauma to her eye or other significant medical history.



Fig. 1 shows the anterior segment of her right eye.

Questions

1. What does Fig. 1 show?
2. What is the cause of the patient's impaired vision?
3. What is the most likely cause of the patient's condition?
4. What treatment is available for the patient?
5. What are some of the other causes of this condition?

Answers

1. Fig. 1 shows that the crystalline lens in this patient is opaque (cataract) as well as displaced from its usual anatomical position (subluxated). The patient therefore has a dense subluxated cataract.
2. The patient's impaired vision is caused by the dense cataract obscuring the visual axis. Although light rays are able to pass through the pupil above the subluxated cataract, the retinal images formed from these rays are blurred because they are not focused on the retina.

3. The most likely cause of this patient's lens subluxation is hypermaturity of the senile cataract.
4. A cataract extraction and intraocular lens implantation can be performed to improve the patient's vision. In this case, the subluxated cataract can be removed by planned intracapsular cataract extraction or trans pars plana lensectomy. An interior chamber intraocular lens can be implanted after the cataract has been removed at the same surgery. Alternatively, an aphakic spectacle lens can be used to correct the refractive error following the cataract extraction.
5. Lens subluxation may be congenital or acquired. Congenital causes include Marfan's syndrome, Weill-Marchesani syndrome, homocystinuria, hyperlysinaemia, familial ectopia lentis and aniridia. Acquired causes include trauma, chronic cyclitis, syphilis, ciliary body tumour, severe myopia and buphthalmos. Trauma is the most common cause of lens subluxation.

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Quiz

Test your ECG knowledge

Koo CC

A 42 years old female complained of palpitations. She was told that she had an "abnormal" ECG two years ago when she had surgery for acoustic neuroma

(Figure 1)



- ◆ What is the cardiac rhythm?
- ◆ List the ECG abnormalities.
- ◆ How would you further investigate this patient?
- ◆ What are the probable causes for her palpitations?
- ◆ The cardiac rhythm is sinus tachycardia at 120 bpm. Note the P waves before each QRS complexes

(Figure 2)



- ◆ There are several ECG features of *pre-excitation or Wolff-Parkinson-White ECG abnormalities* (lead V3). Firstly the *PR interval is short* i.e. less than 120 milliseconds (less than three small squares). Note how the P wave merges with the QRS complex. Secondly, the *small delta wave* (arrow) at the onset of the QRS complexes. This is the result of early activation of the ventricle by the accessory pathway. Thirdly, the QRS complexes are broadened (more than 120 milliseconds) and the ST segments are *abnormal* with ST Depression and T wave inversion (arrow). The abnormal QRS

complex is the result of early and abnormal ventricular pre-excitation by the accessory pathway (figure 3a). Remember the accessory pathway is an "extra" nerve that connects the atrium to the ventricle.

- ◆ Note the *normal QRS complex* i.e. the fifth QRS complex in lead III (broad arrow). A normal PR interval and QRS complex follow the P wave. This indicates normal conduction via the AV nodal and His-Purkinje system (Figure 3b). Occasionally, patients with accessory pathways have intermittent antegrade conduction via its accessory pathway and at times via the normal AV nodal His-Purkinje system only.
- ◆ On further questioning, the patient has lost a few kilograms in weight, complained of tremorous of extremities and has poor appetite.
- ◆ Her thyroid function is abnormal and is consistent with *thyrotoxicosis*. She was referred to the endocrinologist for further treatment.
- ◆ Remember, *to take a detailed medical history* before referring the patient for further investigations of Wolff-Parkinson-White ECG. Sometimes, the patient can have other causes of palpitations unrelated to the accessory pathway i.e. thyrotoxicosis.
- ◆ Patient with Wolff-Parkinson-White syndrome can have an abnormal ECG relating to early ventricular activation by the accessory pathway. This may be no more than a "cosmetic" effect without any pathological significance. They can lead a perfectly healthy normal life without any troublesome arrhythmias. Furthermore, they do not require anti-arrhythmic drug therapy. On the other hand, the accessory pathway may predispose the patient to re-entrant tachyarrhythmias i.e. *supraventricular tachycardia* (SCV). Less commonly, these patients have *atrial fibrillation*. If the accessory pathways have short refractory period i.e. able to conduct impulses from the atrium fast, the patient is likely to have atrial fibrillation with very fast very ventricular rate and risk of sudden cardiac death!

Quiz

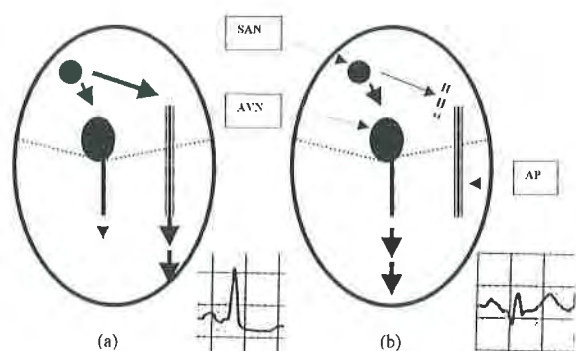
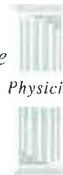


Figure 3

Diagram of sinoatrial impulse conduction via the AVN-His-Purkinje system and the accessory pathway. SAN: sinoatrial node, AVN: atrioventricular node, AP: accessory pathway. Figure 3a: antegrade conduction of the sinus impulse is faster via AP than AVN. Hence, the classical ECG pattern of pre-excitation. Figure 3b: antegrade conduction via the normal AVN system only. Hence, the normal PR interval and QRST complex.



A Point of Digression

The Joy of Bird-Watching

Tan NC

A dash of brilliant blue descending onto the fence caught my attention. It was a handsome collared Kingfisher with its attractive blue plumage. It must have discovered that the fence, shaded by the durian tree behind my consultation room, was an excellent resting spot. The durian tree also had occasional visitors, including the yellow-vented Bulbul and Banded woodpecker. Such sight offer moments of relief from the hustle and bustle of clinic activities. It is comforting to see a variety of birds at the backyard of the clinic in view of the existing housing developments in the vicinity. My clinic colleagues too were amazed and excited at such encounters, though they are more familiar with the crows, mynahs and sparrows.

There are ample opportunities for those who are enthusiastic in meeting our feathered friends in various parts of the island. A good pair of binoculars is a prerequisite to capture a better view of the birds. Joining members of the Singapore Nature Society on their bird-watching excursions will be an excellent orientation to this activity.

Apart from meeting friends of other professions, the 'bird experts' are present to guide the amateurs, who may initially see nothing but leaves and branches! Such weekend excursions allow exploration of various 'ulu' localities in Singapore that you would never dream of visiting. As a bonus, such trips are healthy walking exercises.

My favourite bird spot is the forest adjacent to the Singapore Island Country Club. On one occasion, the reddish brown Rufous woodpecker was seen busy pecking the tree trunk right at the club's carpark. You will be unlucky not to encounter the Greater Racket-tailed Drongo with its unique tail. As the Drongo flies past you, its tail structure gives an impression that two beetles are following its flight. One huge attraction here is a pair of majestic White-bellied sea eagles whose abode is a massive pile of sticks perched on top of a deserted tree.

The Botanical garden is another exciting site with many opportunities to meet the Magpie

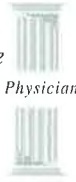
Robins, Orioles, Sunbirds, Pink-necked pigeons, Kingfishers and the squawking Parakeets. Flocks of coastal birds are impressive sights at the Sungei Buloh Nature Park and the Kranji Dam.

Bird-watching is of course not confined to Singapore. Keep your eyes open too if you are taking a vacation abroad. A pair of Hornbills enjoying their berry breakfast next to our chalet on Pangkor Island provided vivid memories of this trip. A Spiderhunter's struggle to devour a moth of similar size at the Kota Tinggi waterfalls was an indelible sight. A boat excursion to see the myriad of waterbirds on an inland lake at the Klu Kut Waterfowl Park near Songkla wrapped up a pleasant vacation in southern Thailand.

Back home, it is heartening to see increasing number of egrets having their breakfast on the grass slope as I pass by the junction of Clementi Avenue 6 and Commonwealth Avenue West on my way to work.

Birdwatching will not only open your eyes to the beauty of the ornithological world but will also nurture your sense of appreciation to the wonders of Mother Nature.

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Reflections

Climbing Mount Everest

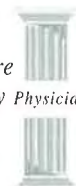
Lee KH

Why do we climb mountains? Because it is there? I do not think so. People do not swim in the cesspit just because it is there. It must be challenging, so challenging that very few have been able to do it. Doing it would then make you better than the rest of the herd. It helps if it is glamorous. Nobody climbs Mount Everest incognito. Not anybody that I have read about in the papers anyway. Other matters like national pride and funding are too crass and mundane for us to dwell upon. May be there is something good in the human spirit that tell us that we should be better than ourselves. I have not seen Mount Everest. I was forced to climb a smaller one in the jungles of Brunei. My motivation was different but it make me respect those who can climb Mount Everest.

Why do family physicians take post graduate examinations? Small minded people would tell you it is for the money. They jump to the conclusion that it is because they want to charge more. Their simple minds tell them that specialist who completed post-graduate examinations are paid more. So these GPs must be up to the same tricks. The reality is that doctors who do such exams loose a lot of money. Patients are not prepared to pay such doctors more and general practice is largely a free market. One doctor estimated that he lost about \$70,000. If he had not spent all that money buying books and paying fees and spend his time earning as a locum and not studying, he would be a richer person. Materially richer that is.

May be it is the love of glamour and the one-upmanship that drives these masochistic people. Wouldn't it be nice if some of these people are motivated to a small extent by the desire to improve themselves? Is it possible that they may actually love the call of medicine and enjoy pursuing knowledge in a science that they are interested in? If there are people who dedicate their lives to study UFOs, is it so difficult to believe that some doctors actually love the profession that they are in and take joy in pursuing knowledge?

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GUIDELINES AND INFORMATION FOR AUTHORS THE SINGAPORE FAMILY PHYSICIAN

Authors are invited to submit articles 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 of articles may be suitable for publication: case reports, original research, audits of patient care, protocols for patient or practice management and review articles.

PRESENTATION ON 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 3 copies of all elements of the article: summary text, references, tables and illustrations. The author should retain a personal copy.
- Their accuracy must be checked before submission.
- All articles are subject to editing.

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 state the purpose of and give the main argument or findings.
- Limit words as follows: 100 words for major articles; 50 words for case reports.
- Add at the 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 patients' names, initials or hospital numbers.

- **Results:** Present results in logical sequence in the text, table and illustrations.
- **Disk & Electronic Production:** If your article is accepted for publication, we may invite you to supply a copy on a 3.5 inch disk, using Microsoft Word software.


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