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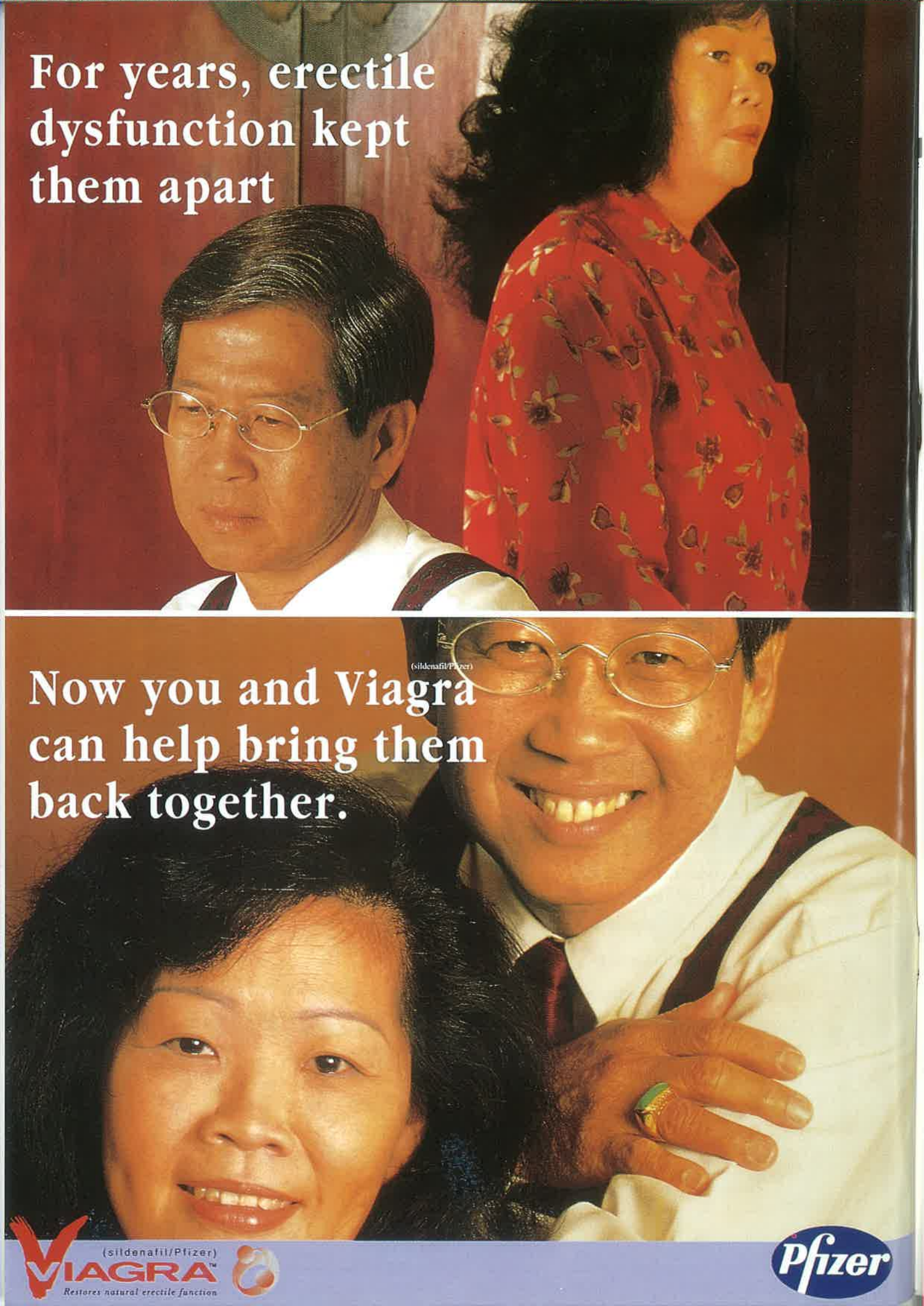
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The Singapore Family Physician

Cardiovascular Health

Tan CB

Coronary artery disease continues to remain the major cause of death in Singapore. There are many risk factors for coronary artery disease, many of which are lifestyle related. The recent National Health Survey published in 1998 had shown changing trends in the prevalence of hypertension, diabetes, obesity and smoking in the Singapore.[1] Some of these findings of the survey are worrying.

The prevalence of hypertension has risen from 22.2% in 1992 to 27.3% in 1998. The population with raised cholesterol level is 25.4% in 1998 as compared to 19.4% in 1992. The mean cholesterol level is now 5.5 mmol/l. The proportion of the population with high LDL has also risen similarly to 26.6% in 1998.

However there are some good news too. The prevalence of diabetes aged 18 to 69 years was 9.0% similar to 8.6% in 1992. The obesity level is 6.0% similar to 5.1% in 1992. The proportion of the population who exercise regularly has rose from 13.6% to 16.8%. The proportion of daily cigarette smokers has fallen from 18.3% in 1992 to 15.0% in 1998.

Family physicians play an important role in promoting healthy lifestyles. A population strategy for primary prevention and to reduce overall cardiovascular risk is possible through dietary measures, smoking cessation and weight management.[2] All patients seen during consultation should be advised on a diet high in fruits and vegetables, high in legumes and whole grains, reduced salt intake, reduced total fat, saturated fat and cholesterol and moderate alcohol consumption. Patients who smoke or are overweight should be advised to stop smoking and reduce weight respectively.

The National Health Survey had also found that 62.1% of the Singapore residents who had diabetes had not been previously diagnosed. Similarly 53% of those with hypertension were undiagnosed previously. That is to say that for every person seen by family physicians for hypertension and diabetes there is another person out in the community with these conditions undiagnosed and untreated.

Family physicians play a pivotal role in screening the community for obesity, hypertension, diabetes and hypercholesterolemia. The rampant use of executive health screening by primary care clinics and hospitals is fashionable but not evidence-based. Family physicians should discard the executive health screening and move towards evidence-based screening. Screening should be targeted at the at-risk population. For cardiovascular health, patients aged 40 years and above should be screened for obesity, hypertension, diabetes and hyperlipidaemia.

As the majority of these conditions are seen primarily at the primary care level, family physicians again play the key role in managing these conditions effectively so as to reduce cardiovascular and cerebro-vascular complications.

The National Health Survey had shown changing trends in the prevalence of these cardiovascular risk factors. In order to improve the overall cardiovascular health of Singaporeans, family physicians must take on the lead role in actively promoting primary prevention through lifestyles modifications, evidence-based screening of at risk population and finally providing quality and effective treatment for these conditions to reduce complications and mortality.

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Dr Tan Chee Beng
Honorary Editor

President's Column

College Going Global

Lim LH

Every organisation from the commercial hub to the academic fraternity has been responding to the Government's call to globalise or at the least regionalise. The College of Family Physicians has, in its own way, contributed to this vision of the Government.

In 1998 our College responded and sent a team of doctors under the leadership of A/Prof Goh Lee Gan to Indonesia to organise a course in Family Medicine. Last year the clinical course for General Practitioners sitting for their Master of Medicine in Family Medicine was conducted in Myanmar. At the same time our clinical teachers and their counterparts from Myanmar held clinical meetings at their various Hospitals. We had also in the past helped Family Physicians to set up their own College in China.

The College has now chalked up another first in Asia when the World Organization of Family Doctors (WONCA) Secretariat will be located in Singapore and Dr Alfred Loh, the College's Immediate Past President, has been appointed WONCA Chief Executive Officer designate. He will assume office in May 2001 when the present CEO retires.

WONCA's presence in Singapore is prestigious. It will serve as a catalyst for international medical organisatibns, academic and other institution to hold their meetings in Singapore to the benefit of our members. However, we should also make our presence felt overseas by not only attending but presenting papers at international medical meetings and also continue to contribute our expertise in Family Medicine to other Third World Developing countries.

A/Professor Lim Lean Huat
President
17th Council (1999-2001)

The Singapore Family Physician

Cardiovascular Risk Factors In Asia

Tan Kok Soon

Summary

In the past 30 years, large declines in coronary heart disease mortality have occurred in the West while developing countries, including most of the countries in Asia, have witnessed an alarming increase in coronary heart disease (CHD) prevalence and mortality. The concept of cardiovascular risk factors was derived from studies based mainly on Caucasian populations. Whether these results are directly and fully applicable to Asian populations have not been clearly defined. There is thus a need for more Asian data on cardiovascular risk factors and their relationship to CHD in the various ethnic groups in Asia.

Singapore has recently published its second National Health Survey (1998) on the prevalence of the major cardiovascular risks factors and their distribution amongst its multi-ethnic population.[3] The difference in CHD prevalence and mortality in the various groups in Singapore can be explained by the variations in the risk factors profile of these groups.

Introduction

From 1993 to 1996, the incidence rate of acute myocardial infarction (AMI) in Singaporeans aged between 20 - 64 years declined from 76 to 72 per 100,000 population.[1] Despite this decline, death from heart and hypertension disease as a group still accounted for 25.2% of all deaths in 1998 and was the second commonest cause of death after cancers. Furthermore, the decline in the incidence rate of AMI was different in the three major ethnic groups in Singapore. It was most evident amongst Indians where the age-standardized incidence rate of AMI fell from 241 to 184 per 100,000 population from 1994 to 1997. In Malays, it fell from 145 to 133 per 100,000 population in the same period while for Chinese, hardly any change in the incidence rate was noted. It was 66.5 in 1994 and 67.3 per 100,000 population in 1997. These figures also demonstrated the marked difference in incidence rate for AMI amongst the different ethnic groups, with Indians having almost a 3 fold higher incidence of AMI compared with Chinese.[1]

From a global perspective, cardiovascular disease accounted for almost 12 million deaths annually. It remains the commonest cause of death worldwide. Apart from the burden of premature death, cardiovascular disease also contributed substantially to the morbidity burden and accounted for 85 million disability-adjusted life years (DALYs) in 1990. The mortality and morbidity burden is likely to increase in the next 20 years and the weight of this burden will be felt mainly in developing countries and Asia.[2]

In USA and many other western countries, a declining trend in mortality for cardiovascular disease has been evident since the 1940's (Fig. 1). This decline in rates has been almost 2.7% per year since the 1970's and coincided with improvements in the management of the major cardiovascular risk factors, more vigorous and effective primary and secondary treatment and prevention.

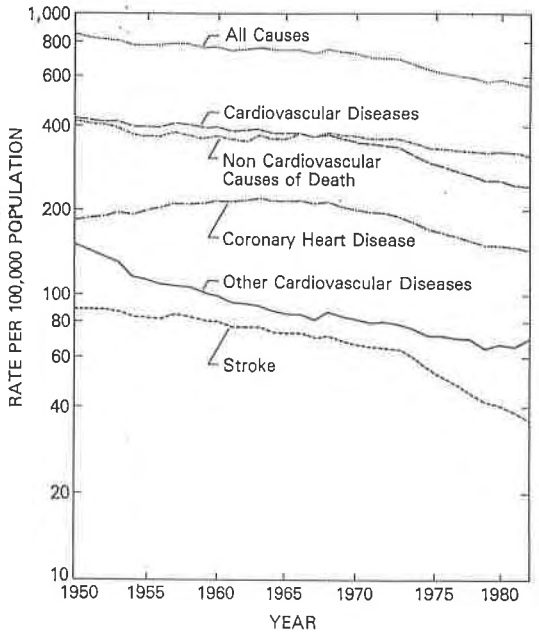

FIGURE 1: Death rates: for all causes of death, for total cardiovascular disease and its subgroups, and for total deaths not caused by cardiovascular disease; United States, 1950

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However, for most developing countries in Asia, the incidence of AMI mortality rate is still on an upward trend. In China and India, AMI mortality rate per 100,000 population is expected to increase by 21% and 18% respectively in men between 1990 and 2000.[3]

With the anticipated global epidemic of cardiovascular disease, which will disproportionately affect developing countries in Asia, an understanding of cardiovascular risk factors and their associated risks in different ethnic and geographical regions will be essential in the control of this epidemic.

Risk Factors for Cardiovascular Disease (CVD)

The concept of cardiovascular disease risk factors was derived primarily from epidemiology studies carried out in western population. Whether the well known association between these risk factors and CVD equally applied to the various ethnic groups in Asia had not been fully determined. Coronary risk factors referred to conditions which have been demonstrated by statistical means to increase the susceptibility of an individual to the development of coronary artery disease.

The major conventional and 'emerging' risk factors for cardiovascular disease are listed in Table 1.

Conventional	Emerging
Smoking	Lipo protein (a) levels
Hyperlipidemia	Hyperhomocystinemia
Hypertension	Coagulation factors
Diabetes Mellitus	Dietary Factors
Obesity	Infection
Lack of Physical Activity	Stress & Occupation
Alcohol Consumption	Abdominal obesity

Table 1. Cardiovascular Risk Factors

Smoking

There is ample evidence to suggest that the link between smoking and the development of coronary artery disease is causal.[4] Risk for AMI from smoking is seen across geographical regions and in different ethnic groups. The risk for the development of AMI in smoker is 2 to 3.8 times that of non-smoker in studies carried out in the UK, Italy, India, China or Japan.

Smoking accounted for 6% of deaths globally in 1990. This is projected to increase to 12.3% by the year 2020. In China alone, it is expected that by 2025, smoking will cause 2 million deaths annually.

Hyperlipidemia

In epidemiological studies based on Caucasians, elevated total and LDL-cholesterol were strong risk factors for coronary heart disease (CHD). In the Seven Countries study, the different rates of coronary heart disease across the countries studied could be explained primarily by the variations in total cholesterol levels.[5] Furthermore, a strong inverse relationship between HDL-cholesterol and risk of CHD was demonstrated.

However, total and LDL-cholesterol levels have not been as strongly associated with the risk of CHD in certain ethnic groups. A hospital-based study in India showed no relationship at all between CHD and any of the lipids parameters.[6] Others have shown that elevated triglycerides and a low HDL-cholesterol level were more consistently associated with CHD in South India. In rural Chinese women, the mean cholesterol level, triglyceride and HDL- cholesterol were 155 mgldl, 75 mgldl and 59 mgldl respectively. Although the mean total cholesterol and LDL-cholesterol were lower and HDL-cholesterol levels were higher than western means, serum cholesterol was still directly related to CHD mortality even at these lower levels in the Chinese.[7]

Hypertension

Hypertension has been shown to be a strong and independent risk factor for CHD.[8] Risks for the development of CHD due to hypertension was continuous and graded. Regional and rural-urban

variation in prevalence was wide across regions. The prevalence of hypertension in rural India was 6%, urban India 17%, Thailand 7.2%, rural Nepal 6%, Italy 30% and USA 23%. However, the odds ratio associated with hypertension and AMI was between 2 to 3 in studies based on South Indians, Chinese, Japanese and Europeans.

Diabetes Mellitus and Impaired Glucose Tolerance

Diabetes mellitus (DM) is a major risk factor for CHD. There were wide regional and ethnic variation in the prevalence of diabetes. The prevalence of frank diabetes was 11% in Japan, 2.4% in China, 8% in Singapore Chinese, 16% in Singapore Indians, 6% in Italy and 6.6% in white Americans. The prevalence of DM was 4 - 5 times higher in South Indians compared to that of Europeans by the age of 55 years.[9]

Although DM and an abnormal glucose tolerance has long been known to be risk factors for CHD, data are now emerging to suggest that even raised glucose levels within the non-diabetic range may be associated with CHD.[6]

Obesity

Data from the Framingham study indicated that obesity was a significant independent risk prediction for CHD, especially among females.[10] Apart from smoking, there was a direct relationship between obesity and all the other major cardiovascular risk factors including blood pressure, hypertriglyceridemia, hyperinsulinemia and an inverse relationship with HDL-cholesterol.

Wide regional variation in the prevalence of obesity was again apparent. The prevalence of obesity in North America was 30%, 17% in Italy, 9.8% in urban China and 2.8% in rural China. The change from a poor to an affluent society is usually accompanied by an increase in obesity. In Singapore, the obesity rate in children increased from 2.3% in 1976 to 16% in 1993.[11] Similar secular changes were noticeable in China.

Apart from total obesity, the distribution of fat too, is a marker of increased risk of CHD. Abdominal obesity, as measured by an increase in waist-to-hip circumference ratio was associated with myocardial infarction, angina pectoris, stroke and death.[12] This association was independent and unrelated to total obesity. Central obesity was also associated with an abnormal glucose-insulin metabolism, hypertension and low HDL cholesterol and raised triglycerides levels. South Asians were more likely to have abdominal obesity compared with Europeans and this may explain partly the higher incidence of diabetes and CHD amongst the former.

Alcohol

The CHD mortality rate in France remained low despite having similar saturated fat consumption, serum cholesterol, blood pressure and smoking rates. This "paradox" has been attributed to the high consumption of alcohol in France. While heavy drinking increases CHD mortaliy, 'moderate' consumption of alcohol was beneficial with an inverse association well established. An average intake of 2 drinks to 6 drinks/day has been shown to reduce risks of CHD compared with non-drinkers. Although this inverse association was seen with moderate intake of alcohol either in the from of beer, wine or liquor, one study suggested that this association could be accounted for on the basis of the intake of red wine only. [13] Benefits of alcohol may be due to its effect on increasing HDL-cholesterol levels, decreasing platelet aggregation and fibrinogen, increasing fibrinolytic activity and in the case of red wine, the possible additional beneficial effect of flavinoids as antioxidant agents. However, caution should be exercised in extrapolating these results to Asian populations. Furthermore, alcohol has complex clinical and metabolic effects and because of its deleterious effect in excess, advising patients to drink alcohol as a preventative measure should be done with extreme care if at all.

Psychosocial Factors

Psychosocial factors which appeared to influence or exacerbate CHD include perceived job stress, role ambiguity, job autonomy, unemployment and retirement. [14] A prospective study of Swedish men showed that self-perceived psychological stress such as a feeling of tension, instability, anxiety, or sleeping difficulties, was associated with an

increased risk of AMI or death. A second type of psychosocial factor related to CHD was the Type A behaviour which is characterised as highly competitive, ambitious, impatient and in constant struggle with their environment. Type A men had 2.2 times the prevalence of CHD compared with type B men, a personality characterised by being more passive and less disturbed by environmental stress.

Physical Inactivity

In 1992, the American Heart Association issued a position statement that there was a relation between physical inactivity and cardiovascular mortality, and that inactivity was a risk factor for the development of CHD. It was estimated that as many as 250,000 deaths per year in the United States were attributable to a lack of regular physical activity. A recent study showed that regular exercise reduced the risk of CHD and that men who walked <0.25 mile/day had a 2 fold greater risk of CHD than those who walked >1.5 mile/day.[15] The risk of CHD was reduced by 15% for every 0.5 mile/day increase in walking distance. This study emphasized the importance of physical activity (regular exercise) rather than physical fitness. Physical fitness per se with no participation in physical activity provided no protection against CHD or all-cause mortality.

Hyperhomocystinemia

Homocysteine is a sulphur-containing amino acid formed after demethylation of the amino acid methionine. Very high levels (>100 umol/L) of homocysteine as seen in individuals with homocystinuria were characterised by premature vascular thrombosis of arteries and veins, by age 30 years. There is now a body of evidence to suggest that even mild to moderate fasting hyperhomocysteinemia (>12 umol/L) is an independent risk factor for atherosclerosis.[16] The attributable risk, after adjustment for other conventional cardiovascular risk factors was 1.4. However, until the results of homocysteine reduction trials for CVD prevention with folate are available, screening and treatment with medications for hyperhomocysteinemia in the general population is not recommended.

Lipoprotein (a)

Lp (a) is a genetically determined plasminogen-like apolipoprotein that is associated with CHD. A study in Hawaiian men of Japanese ancestry demonstrated that there was in increase in risk for MI in those with high levels of serum Lp (a) . The risk was 1.2 to 2.5 fold higher for the highest quartile. Lp (a) levels varied considerably across regions and its levels may be genetically determined. Migration study on South Asians showed that urban South Asians in Britain has similar levels of Lp (a) compared to their siblings in rural India despite differences in their glucose and lipid profiles.

Cardiovascular Risk Factors Profile in Singapore

The second National Health Survey was conducted in 1998 on a random sample of 4,723 Singaporean aged between 18 and 69 years. It set out to measure the prevalence of some of the major conventional risks factors for CHD.[18]

Smoking

The survey showed that 15% of Singaporeans smoked daily, and 78% were non-smoker. This compared favourably with other countries in Asia and the West. In China, 34% of residents smoked, 43% in Japn, 37% in Thailand and 75% in the United States. Smoking was a predominantly male habit in Singapore, with 27% of men and 3% of women smoking. Malay men were more likely to smoke compared to Chinese and Indian men. The overall prevalence of smoking declined between 1992 and 1998 although the proportion of female smokers remained constant.

Hyperlipidemia

Sixty-one percent of residents were found to have high or borderline total cholesterol levels (>5.2 mmol/L). LDL-cholesterol was high or borderline high (>3.3 mmol/L) in 57% while HDL-cholerterol was low (<0.9 mmol/L) in 5.2% of residents. Interestingly, total and LDL-cholesterol levels in Indians, who have the highest prevalence of AMI, were only marginally higher compared with Chinese but substantially lower compared

with Malays. However, HDL-cholesterol in Indians was lower compared with other ethnic groups. This was consistent with findings in South Indians elsewhere that elevated total and LDL-cholesterol were not consistently associated with CHD while low HDL-cholesterol was.

Hypertension

The prevalence of hypertension was 27% in the population surveyed. There was an increase in prevalence from 22% in 1992. The majority (53%) of those noted to be hypertensive were not previously diagnosed and only 30% of patient with hypertension had good BP control. This compared with the NHANES III survey in the US which showed that 32% of hypertensive Americans were unaware that they were hypertensive and 29% had BP controlled below 140/90 mmHg.

Diabetes Mellitus

The crude prevalence of diabetes mellitus was 8.5% in men and 9.6% in females. There was a substantial difference in the prevalence of DM in the 3 main ethnic groups. Indians have a higher prevalence of DM (15.8%) compared with Malays (11.3%) or Chinese (8%). Again, this high prevalence in Indians was consistent with data on South Asians which showed a 4 - 5 fold higher prevalence of DM compared with white Europeans. This may explain in part the higher risks of CHD in this ethnic group.

Impaired glucose tolerance test was found in 15% of the population. However, its prevalence was highest in Malays (20%). Indians and Chinese have similar prevalence of IGT (Ω 14%).

Only 47% of those with diabetes mellitus have good blood sugar control.

Obesity

Obesity is an increasing problem for Singaporeans. With increasing standards of living, the prevalence of obesity has been increasing. The crude prevalence of obestiy was 6.0% in 1998 compared with 5.1% in 1992. Obesity was most common in Malays (16.2%), followed by Indians (12.2%) and Chinese (3.8%). On the other hand, abdominal obesity, as measured by a hip waist ratio of >1.0 in men and >0.85 in women was most prevalent in Indian women (23%).

Physical Activity

In light of the effectiveness of regular physical activity in reducing risks of CHD[15], it was disappointing that the survey showed that 55% of the population was inactive and that only 17% exercised regularly. Running, jogging, swimming, brisk walking, cycling and gym workout were the common forms of activities carried out.

Conclusion

Although much is now known about cardiovascular risks factors, the extrapolation of these data to an Asian population wholesale may not be fully justifiable as the associated risks of the major conventional and emerging risk factors in different ethnic groups and regions in Asia may be different. Hence, further research in this region is required further to assess the relative importance of each risk factor in the development of CHD in the different ethnic groups of Asians. In Singapore, the differnce in prevalence of CHD between the different ethnic groups can probably be explained by the variations in the risk factors profile of the various groups.

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The Singapore Family Physician

Treatment Strategies of Essential Hypertension

Jayaram Lingamanaicker

Introduction

Several prospective clinical trials have shown that good blood pressure control results in significant reduction in cardiovascular mortality and morbidity. Hence, there are clear indications for prompt detection and institution of long-term therapy. Most patients with hypertension do not have any symptoms and hence they go undetected. Cardiovascular disease remains the second leading cause of death in Singapore and imposes an enormous financial burden. The continued high prevalence of hypertension and its related complications of heart failure, renal failure and stroke make this disease a public health concern. These disturbing facts support the need to prevent, detect and treat essential hypertension adequately.

Definition

Hypertension is defined as systolic blood pressure of 140mmHg or diastolic blood pressure of 90 mmHg or greater, or taking anti-hypertensive medication.

It is useful to provide a classification of blood pressure for follow up and treatment of hypertension (Table 1).

Table 1. Classification of Blood Pressure

Category	Systolic (mmHg)		Diastolic (mmHg)
Optimal	<120	and	<80
Normal	<130	and	<85
High-Normal	130-139	or	85 - 89
Hypertension			
Stage 1	140-159	or	90-99
Stage 2	160-179	or	100-109
Stage 3	≥ 180	or	≥ 110

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The positive correlation between blood pressure and cardiovascular disease is continuous, consistent and strong. Though the classification of blood pressure is arbitrary, it aids the physician to make treatment decisions to prevent complications of persistently raised blood pressure. Two or more readings are taken to classify blood pressure, the highest reading, be it systolic or diastolic is taken for the above classification.

Technique of Blood Pressure Measurement

To detect and institute therapy, blood pressure should be properly measured and documented using standardised equipment which is reliable. The following techniques are recommended:

- Patient should be seated with arms bared and supported at heart level. Blood pressure is recorded after five minutes' rest.
- Should refrain from smoking or ingest caffeine thirty minutes before procedure.
- Proper cuff should be used for accurate recording. It should cover at least 80% of the arm circumference. Obese patients require larger sized cuff.
- Appearance of the first sound is taken as Systolic blood pressure and the disappearance of the sound is taken as Diastolic blood pressure.
- Two or more readings separated by at least two minutes, not differing by more than 5 mmHg should be averaged.
- Lying and standing Blood pressure are recorded under special clinical circumstances.

Once the blood pressure is properly measured and documented, the physician should then undertake to follow up the patients as shown (Table 2).

Table 2. Follow up Based on the Initial Blood Pressure

Initial Blood Pressure (mmHg)		
Systolic Blood Pressure	Diastolic Blood Pressure	Follow up recommended
<130	<85	Recheck in 2 yrs
130-139	85-89	Recheck in 1 yr
140-159	90-99	Confirm within 2 mths
160-179	100-109	Evaluate or refer within 1 month
≥180	>110	Evaluate or refer to source of care immediately or within a week

Risk Stratification

In addition to the level of blood pressure, risk factors like age, sex, diabetes mellitus, smoking, dyslipidaemia and target organ damage determines the risk for cardiovascular diseases.

Based on this assessment and level of blood pressure, the patients risk group can be determined as follows.

Risk Group A

This group includes patients with stage 1, 2, 3 hypertension with no risk factors and who do not have any target organ damage or clinical cardiovascular disease. Stage 1 patients are candidates for vigorous lifestyle modification (up to one year) whereas Stage 2 and 3 need pharmacotherapy.

Risk Group B

The majority of the patients belong to this group. These patients are non-diabetics with no clinical cardiovascular disease or target organ damage but have one or more risk factors.

Stage 1 Blood pressure patients need lifestyle modification (up to six months) and Stage 2 and 3 need pharmacological therapy.

Risk Group C

This group consists of diabetic patients and those with clinical cardiovascular disease or target organ damage. All these patients in addition to lifestyle modification need prompt pharmacological therapy.

This simple classification which links directly to treatment goals is useful to the practising physician for identifying risk strata for individual patients and act as guideline for treatment.

Lifestyle Modification

Lifestyle modification has proven to be effective in controlling and potentially preventing hypertension in certain patients and therefore should be strongly encouraged to adopt these measures. However, to attain this goal, systematic team approach may be needed in some instances. The following are the measures to be taken.

- Lose weight.
- Limit alcohol intake to no more than 30 ml Ethanol for men and 15 ml for women (Women absorb more Ethanol than men do), 720 ml beer, and 300 ml wine per day.
- Reduce sodium intake to no more than 100mmol per day (2.4g sodium or 6g sodium chloride).
- Stop smoking and reduce intake of saturated fat for overall cardiovascular health.
- Increase aerobic physical activity (30-45 minutes most days of the week).
- Maintain adequate intake of dietary potassium (90 mmol per day).
- Maintain adequate intake of dietary calcium and magnesium for general health.

Drug Therapy Consideration

Antihypertensive drugs used should ideally have the following characteristics for smooth control and better adherence.

- 24 hour efficacy - once daily dosing

- 50% of the peak effect remaining at the end of 24 hours
- Smooth control throughout the day
- Once daily dosing - compliance is good

Special Considerations

Special considerations in selection of pharmacotherapy include concomitant diseases that may be beneficial or adversely affected by these agents. Quality of life improves and possibly maintained by judicial use of these drugs. Reducing blood pressure with medications has shown to reduce greatly cardiovascular mortality and morbidity. Five large trials comprising 12,483 elderly patients have shown to reduce coronary heart disease by 19%, stroke by 34% and vascular deaths by 23%. These and other data have fortified the importance of prompt and continuing therapy for high blood pressure patients.

Oral Hypertensive Medications Available

The following table (table 3) gives an overview of the currently available hypertensive medication groups.

Table 3. Antihypertensive Medications

Diuretics	Loop Diuretics	Potassium Sparing Agents	Peripheral Agents	Central Alpha-Agonists	Alpha Blockers	Beta-Blockers
Chlorthalidone	Bumetanide	Amiloride	Guanadrel	Clonidine hydorchloride	Doxazosin	Acebutalol
Hydrochlorothiazide	Ethacrinic acid	Spiranolactone	Guanethidine	Guanabenz acetate	Prazosin	Atenolol
Indapamide	Frusemide	Triamterene	Reserpine	Guanfacine hydrochloride	Terazosin	Betaxolol
Metolazone	Torsemide			Methyldopa		Bisoprolol
						Carteolol
						Metoprolol
						Nadolol
						Penbutalol
						Pindolol
						Propranolol
						Timolol

Table 3. (cont'd) Antihypertensive Medications

Combined Alpha and Beta blockers	Vasodilators	Calcium channel blockers - Nondihydropyridines	Calcium channel blockers - Dihydropyridines	ACE inhibitors	Angiotensin II receptor blockers
Carvedilol	Hydralazine	Diltiazem	Amlodipine	Benazepril	Losartan
Labetalol	Minoxidil	Mibefradil	Felodipine	Captopril	Valsartan
		Verapamil	Isradipine	Enalapril	Irbesartan
			Nicardipine	Fosinopril	
			Nifedipine	Lisinopril	
			Nisoldipine	Moexipril	
				Quinapril	
				Ramipril	

Initial Drug Therapy

Once the decision to institute drug therapy is taken and there are no specified indications for the use of any particular medication, a diuretic or a beta-blocker should be chosen. Several randomised trials have shown these agents to reduce mortality and morbidity. There are compelling indications for the use of certain drugs as data have shown to be beneficial (Table 4). In situations where there is no data to support, the choice should be individualised, using the drug that suits the patient best. If the response to the initial drug therapy is unsatisfactory even after reaching the maximum dose, the following should be considered:

1. Add a second agent from another class if the first agent is well tolerated.
2. If there are adverse reactions or no response, another agent from a different class is substituted.

If a diuretic is not used as first line drug, then it is usually indicated as a second agent, as its addition enhances the effect of the first agent. If the second agent controls the blood pressure well, then an attempt to withdraw the first agent may be considered.

Table 4. Considerations For Individualizing Antihypertensive Therapy

Compelling Indication	Drug Therapy
Diabetes Mellitus Type 1 with proteinuria	ACE I
Heart Failure	ACE I, Diuretics
Isolated Systolic Hypertension	Diuretics, Calcium Channel blockers
Myocardial Infarction	ACE I, Beta blockers
May Have Favourable Effects	**Drug Therapy**
Angina	Beta blockers, Calcium Channel blockers
Atrial tachycardia & Fibrillation	Beta blockers, Calcium Channel blockers
Cyclosporine induced Hypertension	Calcium Channel Blocker
Diabetes mellitus type 1 & 2 with proteinuria	ACE I, Calcium Channel blockers
Diabetes Mellitus Type 2	Low-dose Diuretics
Dyslipidaemia	Alpha blockers
Essential Tremor	Beta blockers
Heart Failure	Carvedilol, Lorsartan
Hyperthyroidism	Beta blockers
Migraine	Beta blockers, Calcium Channel blockers
Myocardial Infarction	Diltiazem, Verapamil
Osteoporosis	Thiazides
Preoperative hypertension	Beta blockers
Prostatism	Alpha blockers
Renal insufficiency, caution in renovascular hypertension and creatinine >265 micro mol/L - (3mg/dL)	ACE I

High Risk Patients

High risk patients with stage 3 hypertension, those in group C, or those at high risk of stroke or coronary event need modification of therapy and may require more than one agent after a short interval if not responding to single therapy. (Drug therapy should be started with minimum delay in some patients with Systolic blood pressure of 200 mmHg or greater and diastolic blood pressure of 120 mmHg or greater). Patients with symptomatic target organ damage may require hospitalisation.

Step Down Therapy

After one year of effective control of blood pressure, an effort to decrease the dosage and reduce the number of agents can be considered. The reduction should be made deliberate, slow, and in a progressive manner. Step down therapy is usually successful in patients who are also making lifestyle modifications. After the step down therapy, the patient should be followed up regularly as blood pressure usually rises again, sometimes after months or even years after discontinuation, especially when the patient does not follow lifestyle modifications.

Adherence to Therapy

The major therapeutic challenge is poor adherence to medications, which is unfortunately seen in a large proportion of patients. Attempts to improve adherence should be made and the patients should be educated as to the ill effects of raised blood pressure at every opportunity. Patients have the responsibility to be active and well informed participants in their own care, and to achieve maximum physical and emotional well being. Heath care professionals have the responsibility to educate the patients in all aspects of hypertension.

Causes of Inadequate Response to Therapy

Hypertension should be considered resistant if blood pressure cannot be reduced below 140/90 mmHg when the patient is on adequate and appropriate triple drug therapy. For older patients, resistance is defined as failure of an adequate triple therapy to reduce systolic pressure to below 160 mmHg. The following should be considered:

- Pseudoresistance - "White coat resistance" and inappropriate cuff size
- Non-adherence to therapy
- Volume overload - most common cause
- Drug related causes - Wrong type, too low dose, inappropriate combinations, rapid inactivation and drug actions and interactions
- Associated conditions - Smoking, increasing obesity, insulin resistance, Ethanol intake, Anxiety-induced hyperventilation or panic attacks etc

Antihypertensive Drug therapy in Pregnancy

The Working group on High Blood Pressure in Pregnancy allows continuation of drug therapy in women with long-standing hypertension (except for ACE inhibitors and angiotensin II receptor blocker-produce foetal abnormalities). The following drugs are recommended for treatment of hypertension if the diastolic blood pressure is 100mmHg (lower when there is target organ damage) or greater than 105 mm Hg.

Central alpha-agonist	-	*Methydopa*
Beta-blockers	-	*Atenolol, Metoprolol and Labetolol*
Calcium channel blockers	-	*Nifedipine, Amlodipine, Diltiazem etc. Potential synergism with magnesium sulphate, precipitous fall of blood pressure*
Diuretics	-	*Not recommended in preeclampsia. Prescribed before gestation or for salt sensitive patients*
Vasodilators	-	*Hydralazine is the drug of choice*

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Conclusion

The significance of blood pressure reduction is beyond question and it has been shown to reduce the cardiovascular mortality and morbidity dramatically. It is a sad fact that even in the USA, only one third of the hypertensive population is under proper control and several European countries are far worse off. It is prudent for us in Asia to detect and treat this common condition promptly. The continued high prevalence of high blood pressure and its related complications like stroke, coronary heart disease and renal failure make this condition a public health problem of great dimension. These disturbing facts support the need for urgent professional education and to translate the results into improved health.

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Hypertension - Causes And Complications

Tan Ru San

Introduction

Hypertension is a common medical condition, and is a major risk factor for the development of cerebrovascular and coronary heart disease, congestive cardiac failure and renal dysfunction. The general practitioner needs to keep abreast of the latest practice guidelines, so that he or she can optimally investigate and manage the hypertensive patient.

In this article, we shall review the causes and complications of hypertension, and will end with a discussion on an approach to the evaluation of the hypertensive patient.

Hypertension - Definition

The blood pressure of individuals in a population conform to a normal bell-shaped distribution. The level of blood pressure is, in turn, continuously related to the risk of target organ damage. Hypertension is best understood as the arbitrary limit above which the epidemiological evidence of benefit of intervention outweighs the risk of inaction.

The 1997 Sixth Joint National Committee (JNC VI) and the 1999 World Health Organization-International Society of Hypertension (WHO-ISH) define hypertension as a systolic blood pressure (SBP) ≥ 140mmHg and/or a diastolic blood pressure (DBP) ≥ 90mmHg. The classification of blood pressure levels in adults (men and women) is detailed in Table I.

Table I. Classification of Blood Pressure

Category	Systolic (mmHg)		Diastolic (mmHg)
Optimal	<120	and	<80
Normal	<130	and	<85
High-Normal	130-139	or	85 - 89
Hypertension			
Stage I	140-159	or	90-99
Stage II	160-179	or	100-109
Stage III	≥ 180	or	≥ 110

When systolic and diastolic pressure fall into different categories, the higher category shall be used.

Pertinent elements of these new practice guidelines include:

1. Incorporation of cardiovascular risk assessment as an integral component. The optimal target blood pressure is a function of the overall cardiovascular risk status. High-risk individuals should have lower target blood pressure levels. For instance, a hypertensive diabetic adult should ideally attain a blood pressure ≤ 130/85mmHg on treatment.

2. Recognition of the importance of SBP control. Contrary to past teaching, we now know that the level of SBP is a better predictor of clinical events than the DBP.

3. No age distinction. Elderly hypertensives derive equal, if not more, benefit from stringent blood pressure control. The therapeutic goal in older patients is the same as in younger patients, i.e. < 140/90mmHg (with an interim goal of SBP < 160mmHg in difficult cases).

These guidelines are based on the average of blood pressure readings taken at ≥ 2 visits after the initial screening. The significance of accurate blood pressure measurement cannot be overstated. To minimize inter-observer variability, the proper procedure must be adhered to. With the patient comfortably seated and bare arm supported, blood pressure is taken using calibrated equipment with appropriately sized cuff (the cuff bladder should encircle and cover two-thirds the length of the arm). Ensure that prior to measurement, there is at least 5 minutes' rest, and no smoking or caffeine ingestion for at least 30 minutes. Both SBP and DBP are recorded, and the average of ≥ 2 reading documented.

Some patients only have hypertension in their physicians' presence: white-coat hypertension. Home self-measurement and ambulatory blood pressure monitoring are 2 techniques that may be helpful in this situation. They consistently produce

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lower readings than clinic readings: readings ≥135/85mmHg are considered high. While useful, these methods have never been validated by large-scale clinical trials. Hence, they should serve as adjuncts to, but never supplant, clinic blood pressure measurement.

Hypertension - Causes

Most patients have primary (also called essential or idiopathic) hypertension. The exact pathophysiology is poorly understood. Multiple factors are implicated, including excess sodium intake and decreased excretion, overactive sympathetic and reninangiotensin-aldosterone systems, endothelial dysfunction, genetic factors, etc. These lead to increased cardiac output and/or peripheral resistance. As blood pressure is the product of cardiac output and peripheral resistance, hypertension results.

A minority (<10%) of hypertensive patients has recognizable secondary etiology (see Table II). These are important because some of these causes may potentially be curable by operation or are amenable to specific pharmacological intervention. Among the secondary causes of hypertension, chronic renal parenchymal disorder is most prevalent, followed by renovascular disease. Endocrine conditions occur in less than 1%, the most common probably being primary aldosteronism. Drug-induced causes must not be forgotten: patients on steroid therapy or women on oral contraceptives may be susceptible to iatrogenic hypertension.

When should we screen for secondary hypertension? Secondary hypertension should always be considered when elevated blood pressure is found in the young patient. Conversely, hypertension occurring for the first time after the age of 50 years is suggestive of atherosclerotic real artery stenosis. Certain disgnoses are associated with characteristic symptoms or signs. Severe hypertension, hypertension unresponsive to drug therapy, or the presence of hypertensive target organ damage should alert the physician to look out for secondary causes. (See Table III.)

Some of the commoner causes of secondary hypertension will be reviewed below.

Table II. Causes of hypertension

Primary (essential, idiopathic)

Secondary

Renal diseases

Renal parenchymal disease
acute glomerulonephritis, chronic nephritis, polycystic kidney disease, hydronephrosis, diabetic nephropathy

Renovascular disease
renal artery stenosis (atherosclerotic, fibromuscular dysplasia)
intrarenal vasculitis
renin-producing tumors

Endocrinopathies

Adrenal hypersecretion
cortical (Cushing's syndrome, primary aldosteronism)
medullary (pheochromocytoma)

Acromegaly

Hypothyroidism & Hyperthyroidism

Exogenous hormones
estrogens, glucocorticoids, mineralocorticoids

Coarctation of aorta

Pregnancy-related hypertension

Miscellaneous (neurological disorders, acute stress)

Renal Disease

Renal parenchymal disease

Renal parenchymal disease resulting from acute glomerulonephritis, chronic nephritis, diabetic nephropathy, can cause hypertension. In end-stage renal disease, blood pressure control is impossible without concomitant renal replacement therapy such as dialysis.

Renovascular disease

About two-thirds of cases of renal artery stenosis are attributable due to atherosclerosis, the remainder is due to fibromuscular dysplasia. The former usually presents after 50 years of age (frequently with concomitant coronary, cerebral or peripheral vessel disease), whereas the latter presents before age 20. The hypertension is typically severe and refractory to drug therapy. An abdominal renal bruit (classically systolic and diastolic) may be audible. The diagnosis can be confirmed by post-captopril (administration of captopril diminishes ipsilateral renal blood flow) isotopic renography, renal artery duplex sonography or renal angiogram.

Endocrinopathies

Although rare, endocrine causes of hypertension such as primary aldosteronism and pheochromocytoma are important because surgery extirpation of the culprit endocrine tumor may bring about complete cure.

Primary aldosteronism

Primary aldosteronism may be due to solitary adenoma (Conn's disease) or bilateral adrenal hyperplasia. In a hypertensive patient who is not on diuretic treatment, a serum potassium level <3.2mmol/l (unprovoked hypokalemia) or excessive urinary excretion of potassium >30mmol/day should prompt further investigations to rule out primary aldosteronism. Plasma aldosterone/renin ratio will be high. The etiology of hyperaldosteronism (adrenal adenoma versus hyperplasia) may be differentiated using further specialized investigations, such as postural tests, abdominal imaging and adrenal venous sampling.

Pheochromocytoma

Pheochromocytoma presents as persistent or paroxysmal hypertension, with sudden spells of headache, sweating, palpitations, nervousness and pallor. Orthostatic hypotension is common. The cause is a catecholamine-secreting tumor growing in the adrenal medulla. 10% of tumors occur bilaterally; and 10% may be malignant. The 24-hour urine vanillylmandelic assay has low sensitivity and specificity. 24-hour urine metanephrine assay would be a superior screening test, as it is less likely to be affected by diet. In borderline cases, plasma levels of catecholamines may be tested.

In the workup of patients with suspected pheochromocytoma, it is crucial to clinch the biochemical diagnosis before proceeding to perform imaging studies of the adrenal glands. The adrenal gland may contain a benign cyst or functionally inconsequential tumor (incidentoloma) which may deceive the inexperienced doctor into performing an unnecessary operation.

Hypertensive Complications - Target Organ Damage

Hypertension causes damage in multiple organs, especially the heart, brain and kidneys. (See Table IV.) Hypertension can exert its deleterious effect on these organs in two ways.

Firstly, elevated systemic blood pressure per se imposes a strain on the various tissues. In the heart, the cardiac muscles undergo gradual hypertrophy to compensate for the increased afterload. In the kidneys, nephrosclerosis occur. Occasionally, an acute rise in blood pressure can have catastrophic consequences. For instance, severe hypertension can lead to acute pulmonary edema, aortic dissection, hemorrhagic stroke and hypertensive encephalopathy. The latter is classically encountered in malignant hypertension where severe hypertension induces cerebral edema.

Secondly, hypertension accelerates atherosclerosis. In the presence of other risk factors like diabetes, hyperlipidemia and smoking, this effect is amplified. Coronary artery involvement gives rise to coronary ischemia, manifesting as angina pectoris or acute coronary syndromes. Cerebrovascular atherosclerosis leads to ischemic strokes or transient ischemic attacks.

Frequently, we will see a combination of hypertensive and atherosclerotic complications in the same patient. For instance, heart failure in a

hypertensive patient may be attributable to both left ventricular hypertrophy as well as coronary artery disease. The ventricular hypertrophy can conceivably exacerbate coronary ischemia by increasing myocardial oxygen demand.

Renal parenchymal disease and hypertension are inextricably linked. Renal pathology leads to glomerulosclerosis and progressive loss of nephrons, resulting in hypertension. In turn, hypertension elevates intraglomerular pressure, further injuring more nephrons. A vicious circle thus ensues, with escalating blood pressure and renal damage. Aging and other factors, such as the presence of diabetes, contribute to this process.

Aggressive blood pressure lowering may arrest renal deterioration, and is thus crucial to the management of secondary hypertension due to renal disease. Blood pressure should be controlled to <130/85mmHg. If proteinuria exceeds 1g/day, the recommended target blood pressure is <125/75mmHg.

Evaluation of The Hypertensive Patient

The aims of evaluation are:

1. To rule out reversible etiology, i.e. exclude secondary hypertension;

2. To assess for target organ damage and cardiovascular disease;

3. To identify other risk factors or disorders that may guide treatment.

The first step in the complete evaluation is a comprehensive medical history and physical examination. When taking a history, the duration of hypertension, past cardiovascular disease, family history, lifestyle habits and current and previous medications (do not forget to ask for a history of oral contraceptive use in female patients) should be elicited. In particular, look out for symptoms that may suggest the cause of hypertension (see table III). When measuring blood pressure, take the average of ≥2 readings, and confirm an elevated blood pressure in the contralateral arm if necessary. Measure the height, weight, and waist circumference. Be sure to perform thorough cardiac, peripheral vascular, abdominal, neurological and fundoscopic examination if you are seeing the patient for the first time. Assess for target organ damage (i.e. clinical evidence of left ventricular hypertrophy, stroke, and retinopathy) as well as seek out signs that may implicate particular etiology (e.g. radiofemoral delay, renal bruit, cushingnoid appearance, etc.)

Table III. Indications to screen for secondary hypertension.

Onset <20 years or >50 years
Blood pressure >180/110 mmHg
Refractory hypertension despite maximal therapy
Target organ damage *fundoscopic hypertensive changes ≥grade 2* *serum creatinine >1.5mg/dl* *cardiomegaly (chest X-ray) or left ventricular hypertrophy (electrocardiogram)*
Features indicative of secondary causes *Labile blood pressure, paroxysmal palpitations, sweating (pheochromocytoma)* *abdominal bruit (renal artery stenosis)* *radiofemoral delay (coarctation of the aorta)* *unprovoked hypokalemia (primary aldosteronism)*

Screening investigations include full blood count, serum chemistry (potassium, sodium, creatinine, and fasting glucose), lipid profile (total cholesterol, HDL cholesterol and triglycerides), urinalysis and electrocardiogram. These tests facilitate quick assessment of target organ damage (e.g. left ventricular hypertrophy on electrocardiogram, elevated creatinine in renal involvement) and help to identify other factors (e.g. diabetes, hyperlipidemia) that will place the patient at increased coronary risk. Optional screening tests include creatinine clearance, 24-hour urinary protein, renal ultrasonography (for thorough renal assessment), echocardiography (to quantify ventricular hypertrophy), glycosylated hemoglobin (to assess long-term diabetic control).

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Table IV. Target Organ Damage in Hypertension

Heart	
	Coronary artery disease
	Left ventricular hypertrophy
Brain	
	Hypertensive encephalopathy
	Cerebral vascular accident
Kidneys	
	Proteinuria
	Overt azotemia

Depending on the outcome of initial screening, specialized tests can be ordered if secondary hypertension is suspected (see above).

At the end of the evaluation, we must be able to stratify the patient into high or low risk categories. The high-risk category will include patients with preexisting clinical cardiovascular disease (e.g. coronary artery disease, peripheral vascular disease, stroke) or evidence of target organ damage (e.g. nephropathy, retinopathy). Major risk factors include male sex (or the postmenopausal state in women), positive family history (family history of cardiovascular disease, men <55 yr, women <65yr), smoking, dyslipidemia and diabetes.

Conclusion

Hypertension is a common disease. It is important to understand the causes and complications of hypertension. To manage the patient well, we must evaluate his or her risk status by first performing a comprehensive clinical workup, followed by screening tests. The following must be conscientiously sought: major risk factors, and presence of target organ damage or clinical cardiovascular disease. The high-risk patient should be treated aggressively. In particular, diabetic patients as well as patients with renal impairment should have lower target levels of blood pressure while on treatment.

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Management of Heart Failure

Tan Kok Soon

Summary

The management of heart failure has changed dramatically over the last two decades. Genuine benefits in improving mortality and morbidity with drug therapy have been demonstrated by a number of landmark studies. The efficacy of angiotensin converting enzyme inhibitors, betablockers, diuretics, digoxin, spironolactone, angiotensin II receptor blockers and hydrallazine/ nitrates in improving symptoms, reducing need for repeat hospitalisation and/or mortality has been shown. Despite these successful trials, prognosis of chronic heart failure in the community has changed little in the last 20 years. Physicians should be more aggressive in instituting effective therapy in their patients with heart failure resulting from left ventricular systolic dysfunction.

Introduction

The management of heart failure has changed dramatically in the last two decades with the publication of several major trials in patients with chronic heart failure. However, despite the success of treatments in these clinical trials, there is little evidence that the prognosis of chronic heart failure in the community has improved.[1]

This may be due to the fact that patient selection in these studies may not be representative of the general population and that doctors are failing to institute effective therapy in their patients in the light of these studies.

Heart failure is a relatively common condition. The National Health and Nutrition Examination Survey in the US gave a prevalence rate of heart failure of 20 per 1000 population[2], while the annual incidence of heart failure is 2 per 1000 population in those aged 45 - 54 years and increasing to 40 per 1000 population in men aged 85 - 94 years.[3]

The disability and ill health effects of chronic heart failure means that patients need frequent medical attention. The impairment of quality of life caused by heart failure is worse compared with other chronic diseases such as chronic lung disease, arthritis, diabetes mellitus, angina pectoris or hypertension.[4] Apart from exacting a personal cost to sufferers in terms of disability and ill health, heart failure is also a major economic burden on healthcare systems. The direct cost of chronic heart failure in developed countries is estimated to be 1 - 2% of total healthcare expenditure.[5] In the UK, this represents 10% of total expenditure on cardiovascular disease while in the US, expenditure on heart failure equals that on hypertension.

Definition & Diagnosis

The classic definition of heart failure as "the pathophysiological state in which an abnormality of cardiac function is responsible for failure of the heart to pump blood at a rate commensurate with the requirements of the metabolising tissues", while contributing to the understanding of chronic heart failure, is of limited clinical use as few patients are evaluated in these terms in practice. Hence the definition such as that used by the European Society of Cardiology is clinically more useful. (Fig. 1)

Subjective	Symptoms of heart failure
Objective	Evidence of important cardiac dysfunction
Retrospective	Response to appropriate therapy for heart failure

Figure 1. Definition of Heart Failure based on ESC Guidelines

The cardinal symptoms of chronic heart failure are breathlessness (esp. on exertion), fatigue and ankle swelling. Other symptoms, such as the presence of a productive cough or wheezing may be useful to making a differential diagnosis. The signs of heart failure include peripheral oedema, a raised jugular venous pressure, displaced apex beat, a third heart sound, gallop rhythm and

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pulmonary crepitations. However, a clinical diagnosis made from symptoms and signs alone are often insensitive, particularly in patients with mild heart failure. Hence, clinical suspicion of heart failure often requires confirmation by more objective tests such as an ECG, CXR, pulmonary function test, echocardiography, nuclear cardiology and cardiac catheterisation. Once a diagnosis of heart failure is established, symptoms may be used to classify the severity of heart failure, such as the use of the New York Heart Association classification and to monitor response to therapy. In most patients, investigations to determine the etiology of the heart disease is warranted. However, this should be done selectively and only if the elucidation of the etiology of the heart failure is essential in ensuring optimal management for the individual patient.

Therapeutic Goals

The goals of treatment in heart failure is to:

a) Maintain or improve the quality of life by improving symptoms, avoiding side effects; retarding the progressive deterioration in cardiac function and preventing serious adverse events such as acute myocardial infarction or stroke.

b) To prolong life.

General Management

General advice regarding diet, smoking, rest, exercise and patient education are often given to patients although such recommendations are based mainly on opinions and often the extrapolation of data from its clinical context.

Dietary Advice

Patients are generally advised to avoid excessive salt intake. Although this intuitively appears reasonable, there is no evidence that extreme salt restriction in heart failure is effective or that it improves symptoms on its own or in patients treated with diuretics. Furthermore, extreme salt restriction may exacerbate diuretic induced hyponatremia.

Patients are advised to reduce weight if obese and to avoid excessive fluid intake as this may exacerbate heart failure or hyponatremia in patients with severe hear failure.

The intake of alcohol and cholesterol and saturated fat should be in moderation and limited unless alcohol-related heart disease is suspected, in which case, alcohol should be excluded. However, little data exist to support the use of lipid-lowering therapy for patients with heart failure.

Smoking

Smoking should be strongly discouraged as it increases the risk of reinfarction in those with coronary artery disease, reduces oxygen carrying capacity of blood and increases sympathetic nerve activity.

Bed Rest

Exercise training is associated with improving patient's well-being and an increase in exercise capacity. However, the ideal duration, frequency and intensity of exercise training are unknown.

Patient Education

Patient education has been shown to improve well-being. Education and counselling should be encouraged.

Drug Treatment

As chronic heart failure due to left ventricular systolic dysfunction contributes to the majority of patients with heart failure, the recommendations below are primarily for this group of patients.

Angiotensin Converting Enzyme Inhibitor (ACE Inhibitor)

All patients with heart failure due to left ventricular dysfunction should receive an ACE inhibitor unless contra-indicated.[6] ACE inhibitors are also indicated in patients with LV systolic dysfunction without clinical evidence of heart failure.

The only absolute contra-indications to the use of ACE inhibitors are pregnancy and a history of allergy to ACE inhibitors. Relative contra-indications are renal dysfunction, renal artery stenosis and hypotension. ACE inhibitors should be started at a low dose and the dose increased gradually to the maximum tolerable dose. Patients with a systolic BP < 90 mmHg, taking high doses of diuretics (eg >80 mg frusemide), over 75 years old, and raised creatinine levels should have ACEI started under specialist advice. The plasma concentrations of creatinine and potassium should be known beforehand and these repeated one week after starting an ACE inhibitor.

A persistent, irritating dry cough and giddiness are the most common symptomatic side effects of ACEI. The development of an ACEI related cough may neccessitate the withdrawal of the drug. Occasionally, withdrawal of the ACEI until the cough settles and the reintroduction of the same drug at a low dose or another ACE inhibitor may be attempted. Angiotensin II antagonists do not cause a cough and may be substituted (see below).

Diuretics

Diuretics should be used in patients with pulmonary oedema or peripheral oedema.[7] In those without evidence of fluid retention, a trial of monotherapy with an ACE inhibitor should be tried. Loop and thiazide diuretics are both effective in the treatment of heart failure. However, thiazides may not be effective in those with renal dysfunction. A combination of loop and thiazide diuretics is sometimes used to provide a powerful diuresis in patients with resistent peripheral oedema.

The use of potassium-sparing diuretics other than spironolactone should be used with caution when in combination with ACE inhibitors. Apart from spironolactone, little evidence exists to show that the use of diuretics improve long term mortality in patients with heart failure.

Spironolactone

A recent study has shown that the addition of spironolactone, 25 mg om to patients with left ventricular systolic dysfunction and in severe heart failure, who are being treated with an ACE inhibitor; a loop diuretic and in most cases, digoxin, substantially reduces the risks of mortality by 30%.[8] Furthermore, symptomatic improvement and a reduction in the frequency of re-hospitalisation were demonstrated in patients given spironolactone. The only significant side effects reported were gynecomastia or breast pain in men. The incidence of serious hyperkalemia was minimal. Nevertheless, careful monitoring of serum potassium level in patients receiving combination therapy should be carried out.

Digoxin

Digoxin has no important effect on overall mortality in the treatment of heart failure although it can reduce the need for repeat hospitalisation due to decompensation of heart failure.[9] Is should be used, however, in patients with heart failure and atrial fibrillation when symptoms persist despite treatment with combination therapy.

The optimal dose of digoxin required in Asians has not been fully established but doses of between 0.125 and 0.325 mg are required in Caucasians to achieve a serum level of digoxin that is in the therapeutic range. Routine monitoring of plasma levels of digoxin is not required but may be useful in patients with renal dysfunction or in patients whose symptoms may be due to excessive digoxin.

Hydrallazine, Nitrates and other Vasodilators

The major heart failure trial, the Veterans Administration Heart Failure Trial (V-HeFT-I) was the first to show that survival could be improved with drug treatment.[10] However, the dosage required (hydrallazine 100 mg tds and nitrates 40 mg qds) resulted in a high incidence of side effects such as headache, and a correspondingly poor patient compliance record. However, their combined use is indicated in patients intolerant of ACE inhibitors, though, this role may be replaced by the use of angiotensin II receptor antagonists (see below). Unfortunately, except for amlodipine, which although failing to improve survival, at least has no adverse effects on patients with severe heart failure, subsequent

trials with other vasodilators such as the other calcium antagonists, flosequinan and epoprosternol have all yielded disappointing results with worsening survival when used in the treatment of hear failure.

Betablockers

Although ß blockers have been used to treat heart failure patients in Scandinavia for more than two decades, it is only recently that compelling evidence has emerged that ß blockers such as carvedilol, metoprolol and bisoprolol improve mortality, symptoms, left ventricular functions and reduce the need for re-hospitalisation in patients with mild to moderate heart failure or in those with stable NYHA Class IV patients.[11] However, about 5% of patients will not tolerate its use due to hypotension or worsening heart failure. Hence, therapy should be initiated under a specialist's guidance and only in stable patients. Starting dosage should be low (carvedilol 3.125 mg bd, bisoprolol 2.5 mg od or metoprolol 6.25 mg tds) and dose titration carried out at two weekly intervals or a slower rate to a target dose of 25 mg bd of carvedilol, 5 mg of bisoprolol or 50 mg bd or tds of metoprolol.

Calcium Antagonists

Calcium antagonists should be avoided in patients with heart failure. However, in heart failure patients requiring additional therapy for control of angina or hypertension, amlopidine can be used safely.[12]

Aspirin and Warfarin

In heart failure patients, even in those where ischemic heart disease is the cause, routine use of aspirin or warfarin is not necessary unless there is a specific indication such as atrial fibrillation on-going ischemia or the presence of a left ventricular thrombus.[13] No long term benefit has been demonstrated with aspirin therapy in post infarction patients in heart failure and there is even concern that aspirin may be harmful and may negate the benefit of an ACE inhibitor on mortality and morbidity.

Angiotensin Receptor Blockers (ARB)

A number of studies are currently underway with angiotensin blockers of the AT_1 receptor with agents such as losartan, candesartan, valsartan and irbesartan that will establish the role of ARB's in the treatment of heart failure. In the ELITE I heart failure study, a survival benefit was observed in symptomatic patients treated with losartan compared with captopril.[14] Preliminary results from ELITE II suggested that in patients intolerant of captopril, losartan can be safely substituted. However, there is insufficient data yet to make any firm recommendation about the role of ARB's in the treatment of heart failure. A summary of the specific recommendation for patients with chronic heart failure due to LV systolic dysfunction is shown in Table 1.

Agent	For Symptoms	For Prognosis
ACE Inhibitors	Yes	Yes
Beta blockers (Carvedilol, Metoprolol, Bisoprolol)	Yes	Yes
Diuretics	Yes	No
Spironolactone	Yes	Yes
Digoxin	Yes (if A. Fib present or severe failure)	No
Nitrate/ Hydrullazine Combo	Yes (if ACEI intolerant)	Yes (if ACEI intolerant)
Amlopidine	Yes (if concommitant angina/ hypertension)	Possibly (Non ischemic cardiomyopathy)

Table 1: Chronic Heart Failure due to Left Ventricular Systolic Dysfunction

Patients with End-Stage Heart Failure

Patients with heart failure refractory to medical therapy who are candidates for surgical intervention should be referred for specialist assessment. Revascularisation may be an option in those whose LV dysfunction is due to hibernating myocardium. Heart transplant remains an option for suitable surgical candidates with a failing heart. Cardiomyoplasty and "remodelling" of the left ventricle (Batista procedure) remain experimental procedures.

Prognosis

The 12 month mortality rate for patients with asymptomatic (NYHA Class I) heart failure is 0-10%, rising to 10-20% in NYHA Class II, 30-50% in NYHA Class III and 30-70% in NYHA Class IV heart failure. Hence, the survival of patients with severe heart failure is very poor, often with a mortality equal to or more than that of the majority of cancers.

Recent clinical trials suggest that improving the outcome of patients with heart failure is possible and the medical community should be more aggressive in implementing effective treatment for these patients who otherwise face an appalling outlook with progression of their disease.

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The Singapore Family Physician

Cardiovascular Syncope - Diagnosis, Investigation & Treatment

Teo Wee Siong

ABSTRACT

Syncope may be a benign condition and yet in some patients, represent a marker for a life-threatening condition. Thus it is important to diagnose the correct underlying cause of syncope. Most of the patients are admitted to the general medical wards and are often still referred to the neurologist for initial assessment. Cardiac causes of syncope are however very important as the prognosis may be more guarded especially in those with significant underlying heart disease.

The commonest cause of syncope, especially in the younger patients with no underlying structural heart disease, are the neurally mediated syncope. In the older patients, syncope due to bradyarrhythmias such as sick sinus syndrome and atrioventricular block are important. Tachyarrhythmias due to supraventricular tachycardia, ventricular tachycardia and even ventricular fibrillation or Torsade de pointes are less common causes of syncope. Orthostatic hypotension, especially drug induced, should never be forgotten. Obstructive cardiovascular causes of syncope are rare but correctable and hence should be investigated for. These include aortic stenosis, hypertrophic obstructive cardiomyopathy, pulmonary embolism, pulmonary stenosis, atrial myxoma, and mitral stenosis. Noncardiac causes especially neurological causes must be investigated when clinically indicated.

The clinical evaluation includes a thorough clinical history and physical examination. Important investigations include a 12 lead ECG and continuous ECG monitoring with telemetry or ambulatory Holter monitoring or transtelephonic monitoring. The upright tilt test has become a useful tool in patients suspected of having vasovagal syncope. In patients who have underlying significant heart disease, signal average ECGs and/or an electrophysiological study may sometimes be indicated. The echocardiogram is useful to exclude obstructive causes of syncope or other structural heart disease while the coronary angiogram may be useful in some patients to investigate for coronary artery disease.

The treatment depends on the exact diagnosis for the cause of the syncope. This is especially in the elderly, who may have several medical problems, each of which could possibly account for the syncope. In general, patients with neurally mediated syncope need only reassurance and avoidance of stimuli that provokes it. Rarely patients with a more malignant form of vasovagal syncope require drug treatment or even a pacemaker. Patients with obstructive lesions may require surgery. In patients with bradyarrhythmias, a pacemaker may be necessary while tachyarrhythmias can be treated with drugs, ablation, surgery or devices.

Introduction

Syncope is derived from the Greek word "synkope" meaning a cessation or a pause, literally a pause in one's conscious state. It has been defined as "transient loss of consciousness, characterized by unresponsiveness and loss of postural tone with spontaneous recovery not requiring specific resuscitation intervention". [1] Syncope has to be differentiated from the other causes of sudden loss of consciousness such as seizures and transient sleep.

Syncope is an important cause for hospital admission but its true prevalence in Singapore is not known. Most patients are admitted to the general medical wards and are often still referred to the neurologist for initial assessment. In the USA, syncope is responsible for 3% of emergency department visits and 1% of hospital admissions.[2,3]

Cardiovascular syncope is probably more common than previously believed. A clear and thorough history is needed so as to suggest the appropriate investigations. Syncope may often be a benign condition and yet in some patients represent a marker for a life threatening condition.

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Cardiac causes of syncope are very important as the prognosis may be more guarded especially in those with significant underlying heart disease. There is a fine line between syncope and sudden death as syncope without spontaneous recovery results in death of the patient! Hence it is important to recognize the correct underlying cause of syncope and decide on the appropriate treatment. This paper reviews the approach to syncope especially cardiovascular syncope and provides a guide for further investigations and management.

Etiology Of Syncope And Cardiovascular Causes Of Syncope

Table 1. Etiology of Syncope

1. Cardiovascular

Neurally Mediated syncope
- Vasovagal syncope
- Carotid sinus hypersensitivity
- Situational syncope – micturition, cough, deglutition, defecation
- Exercise associated variant

Cardiac syncope
- Tachyarrhythmias
  - Paroxysmal Supraventricular tachycardia
  - Atrial fibrillation
  - Ventricular tachycardia
  - Torsades de pointes – acquired, congenital
  - Polymorphic ventricular tachycardia
  - Ventricular fibrillation
- Bradyarrhythmias
  - Heart blocks
  - Sick sinus syndrome
- Obstructive cardiovascular disease causing syncope:
  - Left ventricular outflow obstruction eg. Aortic stenosis, Hypertrophic obstructive cardiomyopathy
  - Right ventricular or pulmonary outflow obstruction eg. Pulmonary embolism, Pulmonary hypertension
  - Left ventricular inflow obstruction eg. Left atrial myxoma, Mitral stenosis
- Other cardiovascular causes: Acute Myocardial infarction, Dissecting aneurysm

Orthostatic hypotension
- Idiopathic
- Secondary causes – Diabetes, Neurological, Volume depletion, Drugs

2. Non cardiovascular

Neurologic
- Epilepsy
- Cerebrovascular

Metabolic
- Hypoglycemia,
- Hypoxia
- Hypocalcemia
- Hyperventilation (hypocapnia)
- Ethanol

3. Psychogenic

Panic attacks

Hysteria

4. Unknown

The etiology of syncope is shown in Table 1. In the majority of isolated syncopal episodes, neurally mediated vasovagal syncope is the commonest.[4] Other neurally mediated syncope include the carotid sinus syncope and situational syncopes related to micturition, defeacation, deglutition and coughing. In the younger patients, neurally mediated syncope is probably the most common cause. In the elderly patients, especially those with underlying heart disease, vasovagal syncope is less common and it is important to exclude cardiovascular causes of syncope such as orthostatic hypotension, cardiac arrhythmias especially bradyarrhythmias due to atrioventricular block or sick sinus syndrome, obstructive valvular disease such as calcified aortic stenosis and hypersensitive carotid sinus syndrome.

Cardiac causes of syncope are very important as the prognosis may be more guarded especially in those with significant underlying heart disease. Tachyarrhythmias such as supraventricular tachycardia, ventricular tachycardia and even ventricular fibrillation or Torsade de pointes may be causes of syncope. Obstructive cardiovascular causes of syncope are rare but correctable and hence should be investigated for especially when clinically suggestive. These include aortic stenosis, hypertrophic obstructive cardiomyopathy, massive pulmonary embolism, pulmonary stenosis, atrial myxoma, and mitral stenosis. The most common cause for this group is aortic stenosis. Hypotension resulting from orthostatic hypotension especially drug induced is common in the elderly and should not be forgotten. Primary orthostatic hypotension is a much less common disorder.

Important non-cardiac causes include neurological causes due to epilepsy, cerebrovascular and metabolic causes such as hypoglycemia and hypoxia. It is however probably less common than previously estimated. Occasionally patients with recurrent undiagnosed syncope may have various psychiatric illnesses from anxiety disorder and panic disorder. They are generally younger, have multiple episodes, have a lower prevalence of heart disease and may have other nonspecific complaints associated with syncope such as headache, fatigue, dizziness and palpitations. [5] However about 30-50% of patients with syncope will be found to have no identifiable etiology and further extensive evaluation is needed. [6]

Clinical Differentiation Between Cardiac And Non-Cardiac Causes Of Syncope

Classical features suggesting neurally mediated syncope

Neurally mediated syncope are often associated with painful or an emotionally upsetting experience and/or preceded by prodromal symptoms such as nausea, diaphoresis, or hearing loss and signs such as marked pallor. Loss of consciousness is usually brief and recovery rapid.

Classical features suggesting cardiac syncope

Typically cardiac tachyarrhythmias, transient AV block or asystole causing syncope have a sudden loss of consciousness with virtually no warning, though the patient will at times feel that he is about to faint just before he loses consciousness. Witnesses will describe that the patient appears collapsed, lying motionless, pale and when examined, pulseless. Within a minute or two however, consciousness returns and there may be flushing noted. Incontinence and tonic clonic movements may occasionally be noted especially if prolonged. A history of rapid heartbeat prior to syncope may suggest a rapid tachycardia as the cause, but patients with rapid tachycardia may have syncope without any awareness of a racing heart. Unlike epilepsy, recovery is rapid and confusion unusual. Unlike neurological causes, focal neurological deficits are not noted.

Differentiation between Cardiac syncope and Epilepsy

There is a complex relationship between the heart and epilepsy. Cardiac arrhythmias may provoke epileptic seizures and have been misdiagnosed as having had epilepsy. Linzer et al described patients who despite normal or nonspecific electroencephalographic findings, were treated or offered treatment with long-term anticonvulsant agents and were subsequently, diagnosed to have an arrhythmic or neurally mediated syncope. [7] This is because patients with neurally mediated syncope or asystole may have seizures like activity and hence be misdiagnosed to have epilepsy. [8] On the other hand, epileptic seizures may alter autonomic functions and provoke severe cardiac arrhythmias. This is especially the case with complex focal seizures (of temporal lobe origin) and grand mal seizures, resulting in tachycardia, ictal bradycardia syndrome or asystole. [9]

Table 2. Diganostic features of seizure & syncope

	Seizure	Syncope
Prodrome	++	+++
Clonic tonic motion	+++	++
Incontinence	++	++
Tongue biting	++	+
Postictal phase	+++	+/-

Seizures are often preceded by an aura, may be accompanied by convulsive activity and loss of bowel or urinary continence are typically followed by a confusional state. Diagnostic features distinguishing seizure from syncope is shown in table 2. The most useful distinguishing feature between seizure and syncope is the absence of a postictal state. The presence of a post ictal state by itself does not allow differentiation between seizure and syncope as transient confusion (rarely persisting for > 30 seconds) may follow an episode of prolonged attack of cardiac syncope. However the clear absence of a postictal phase, almost always exclude a seizure as an explanation for the syncope episode. Clonic tonic movements have also been considered diagnostic of epilepsy. However it may also occur in cardiac syncope and hence may not be diagnostic.

Differentiation between cerebrovascular neurologic abnormality and cardiac syncope

The presence of a primary cerebrovascular neurologic abnormality is sometimes suggested by the history, particularly when syncope is associated with focal seizures, headaches, visual or auditory disturbances. Brainstem ischemia due to verterbrobasilar transient ischemic attacks, basilar artery migraines and subclavian steal syndrome may lead to drop attacks or syncope but loss of consciousness is generally associated with other neurologic symptoms eg vertigo, dysarthria, diplopia, ataxia and other signs referable to the brainstem. In the absence of at least some focal neurologic findings, a vertebrobasilar etiology for syncope is probably doubtful.

Differentiation between cardiac syncope and metabolic disorders

Hypoglycemia tends not to produce an abrupt and transient loss of consciousness which helps to distinguish this condition from syncope.

Clinical Evaluation And Further Investigations

The clinical evaluation requires a thorough clinical history and physical examination. A careful history is perhaps the single most productive part of the diagnostic work-up. Important points in the history to be elucidated are listed in Table 3. A thorough physical examination is needed and is shown in Table 4. Carotid sinus massage should however be done only with ECG monitoring and after checking for carotid artery bruit. Patients with carotid sinus syncope will show prolonged aystole (Figure 1).

Table 3. History taking for patient with syncope

Did patient truly lose consciousness?
Any warning symptoms (prodrome)
nausea & diaphoresis - vasovagal syncope
palpitations
Rapidity (sudden or gradual onset) with which LOC occurs, Duration of LOC, speed of recovery
How fast recovery of mental function?
Does the pt have a memory of the event?
Can a situational relationship be established?
Rise abruptly
Post micturition
Defecate
Postprandial
Cough
Swallow
Intense pain
Sight of blood
Related to neck pressure eg shaving of neck, wearing tight collar
History of preceding palpitations
Relationship to exercise or exertion
Was the syncope witnessed or unwitnessed?
Any seizure activity?
Urinary incontinence
Tongue biting
Post syncope confusion
Neurological abnormalities
Associated injuries
Recent use of drugs esp vasodilators
Single or recurrent episodes
Family history of syncope or sudden death
History of underlying heart disease eg previous myocardial infarction

Table 4. Physical examination for the syncope patient
General condition - pallor
Pulse Regularity – for detection of arrhythmias Difference in pulse pressure between arms- subclavian steal, Aortic dissection
Blood pressure in both arms
Orthostatic changes in blood pressure (immediately, every 2 minutes and up to 10 minutes)
Carotid arteries for carotid bruit, subclavian bruit
Auscultate for cardiac murmurs
Neurological examination
Carotid massage

In view of the multiple etiology of syncope, the history is extremely vital to decide on the most appropriate initial tests. The type of investigations chosen initially also depends on the severity of the presentation, associated injuries, age and presence of underlying heart disease. In young patients who present with a first episode of syncope with no significant injuries and a history suggestive of vasovagal syncope or a situational syncope, no further evaluation beyond a careful history, physical examination and 12 lead ECG is needed. However even single syncopal episodes when associated with physical injury or occurring in individuals with high risk occupation or vocations (eg pilots, commercial divers, window cleaners) or accompanying certain high profile activities (eg athletes) may warrant further assessment. [10] Similarly patients with syncope and underlying heart disease are best admitted and evaluated in the hospital for ECG monitoring and considered for exercise stress testing, tilt table testing or an electrophysiological study if needed.

Figure 1

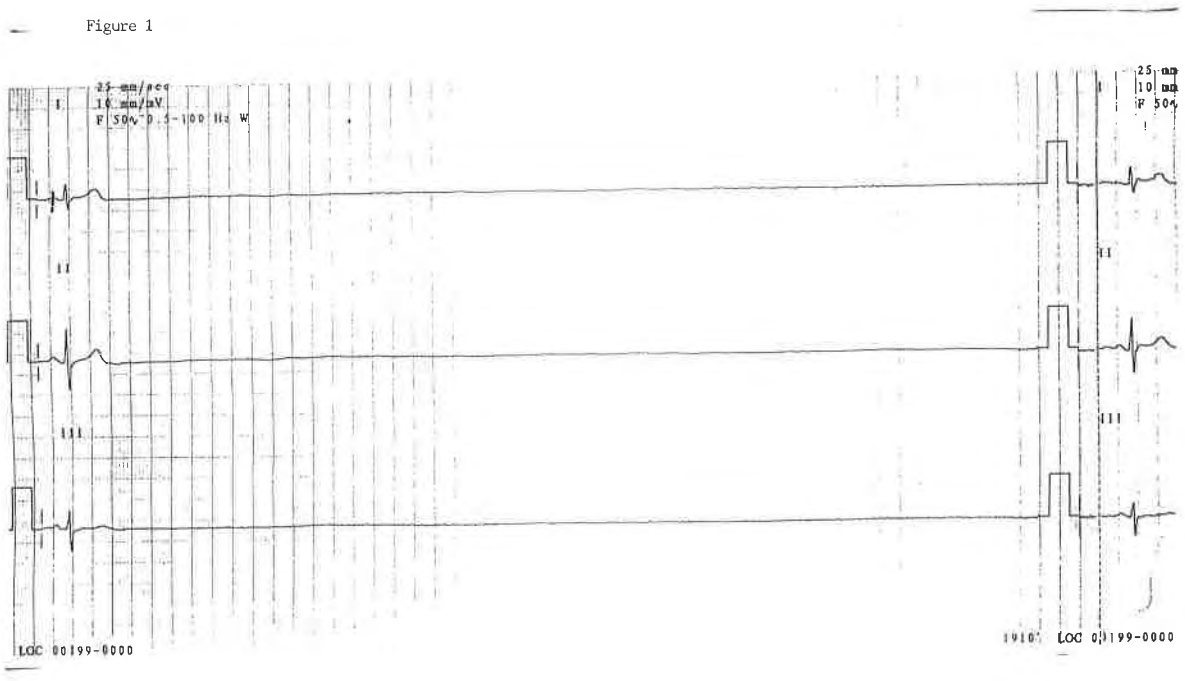

Figure 1: Carotid sinus syncope with asystole of 10 seconds elicited during carotid sinus massage

Table 5. Investigations for cardiac syncope
Ambulatory (Holter) ECG
Exercise stress test
Transtelephonic ECG monitoring - event and loop recorders
Tilt table testing
Signal average ECG
Echocardiogram
Electrophysiological study
Coronary angiogram
Insertable loop recorder

Further investigations of the syncopal patient may be needed and is shown in table 5. Important investigations include a 12 lead ECG and continuous ECG monitoring with telemetry or ambulatory Holter monitoring or transtelephonic monitoring. Routine blood tests are usually non-diagnostic but are commonly performed. These include blood sugar and electrolytes especially potassium, magnesium and calcium. When neurological cause of syncope is suspected, referral to a neurologist is necessary. However routine neurologic testing, including electroencephalography, computed tomography, and carotid and transcranial Doppler ultrasonography, should be reserved for patients who have neurologic signs or symptoms or carotid bruits. [11]

Only about 2% to 11% of patients with syncope have an abnormal 12 lead ECG or rhythm strip with severe abnormalities that are diagnostic of syncope. [5] Thus the presence of a normal ECG does not exclude a cardiac cause of syncope. Resting ECG abnormalities that may be detectable include conduction abnormalities such as bundle branch blocks with or without bifascicular block, arrhythmias, or previous myocardial infarction. Occassionally the ECG may show the long QT syndrome associated with Torsades de pointes, the Brugada syndrome (Figure 2) associated with ventricular fibrillation [12, 13] or preexcitation pattern due to the Wolff-Parkinson-White syndrome, (Figure 3) which is well known to be associated with supraventricular tachycardia or rapid preexcited atrial fibrillation.

A 24-hour Holter monitor is recommended when symptoms suggest arrhythmic syncope and in patients who have syncope of unexplained cause, heart disease, or an abnormal electrocardiogram. Ventricular tachycardia (Figure 4) and the sick sinus syndrome (Figure 5) can sometimes be detected. The diagnostic yield is however low because the arrhythmias may be transient and not present during the 24 hours of monitoring. [14] Also if no arrhythmias are found and no symptoms occur during monitoring, arrhythmic syncope is not necessarily excluded. Hence repeated Holters may be necessary especially if the index of suspicion for an arrhythmia is high.

In patients with significant symptoms occurring on an infrequent basis, the transtelephonic event recorders can be extremely helpful. These devices record an ECG rhythm when an event button is pushed. This can then be transmitted over the telephone. Memory loop devices continuously record the ECG, and when activated, records the ECG rhythm for a period of up to 5 minutes before and after the activation (Figure 6).

The signal-averaged electrocardiography which detects low amplitude late potentials on the surface ECG, may be useful in selecting patients for electrophysiological studies, especially when coronary disease is present and ventricular tachycardia is suspected. In patients who have a history of syncope related to exertion, an exercise test is useful but should be preceded by an echocardiography. [11] Abnormalities that may be detectable on the exercise stress test include presence of severe ischemic heart disease, exercise related supraventricular or ventricular tachycardia, heart block, abnormal chronotropic response suggesting sick sinus syndrome, or the exercise variant neurally mediated syncope.

Figure 2

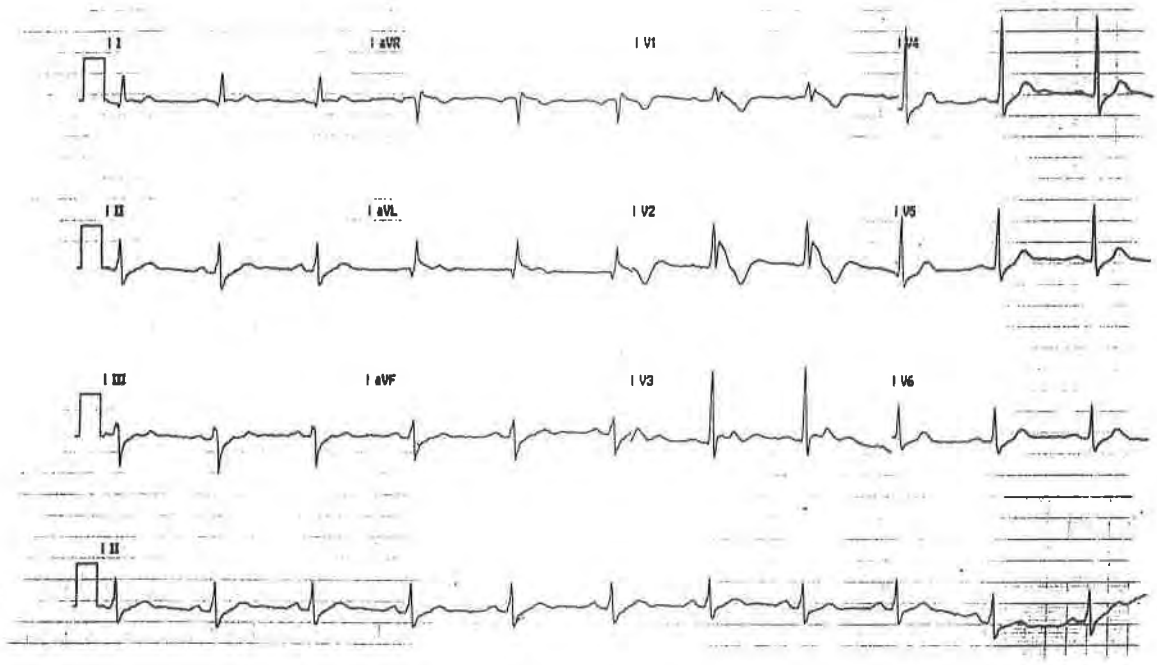

Figure 2: 12 lead ECG showing the Brugada syndrome with right bundle branch block and ST segment elevation in V1-2

Figure 3

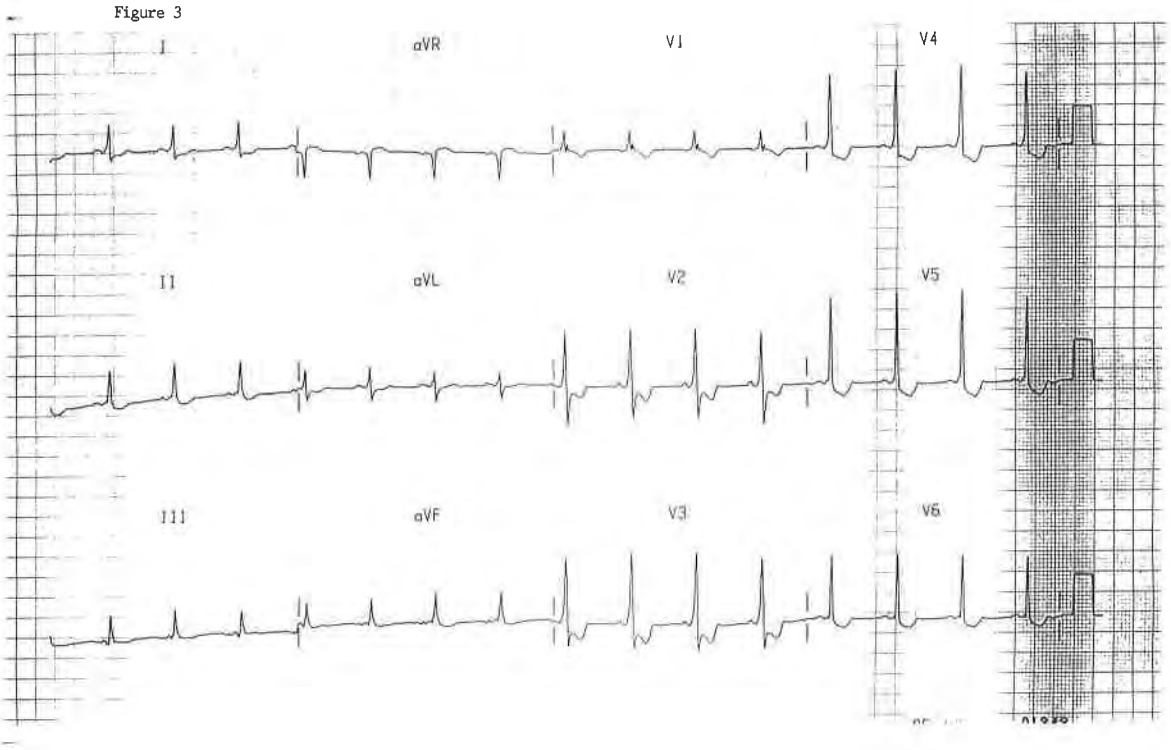

Figure 3: 12 lead ECG showing preexcitation pattern consistent with the Wolff-Parkinson-White syndrome

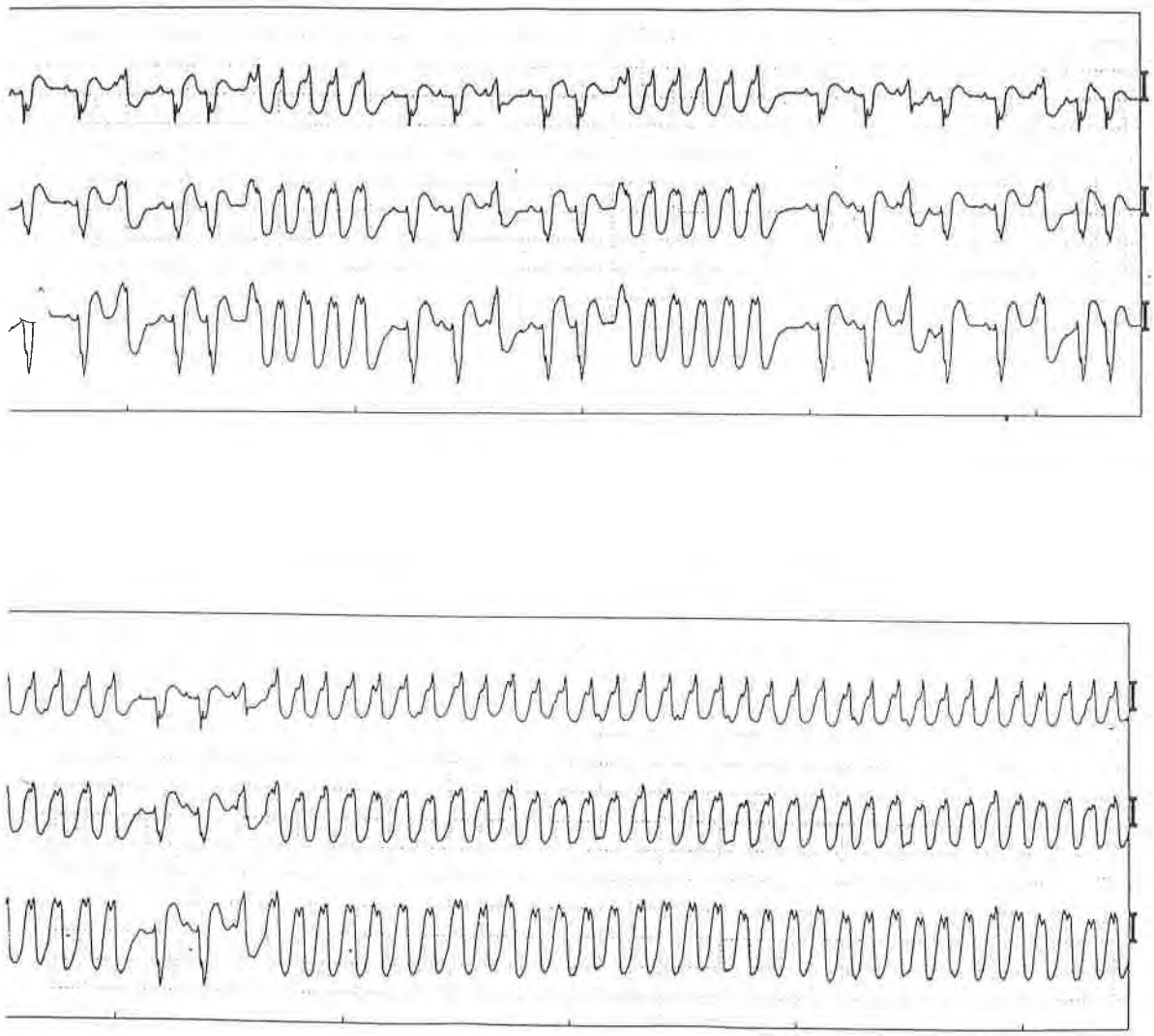

Figure 4: Holter ECG recording showing rapid ventricular tachycardia that resulted in syncope in a patient with history of extensive anterior myocardial infarction

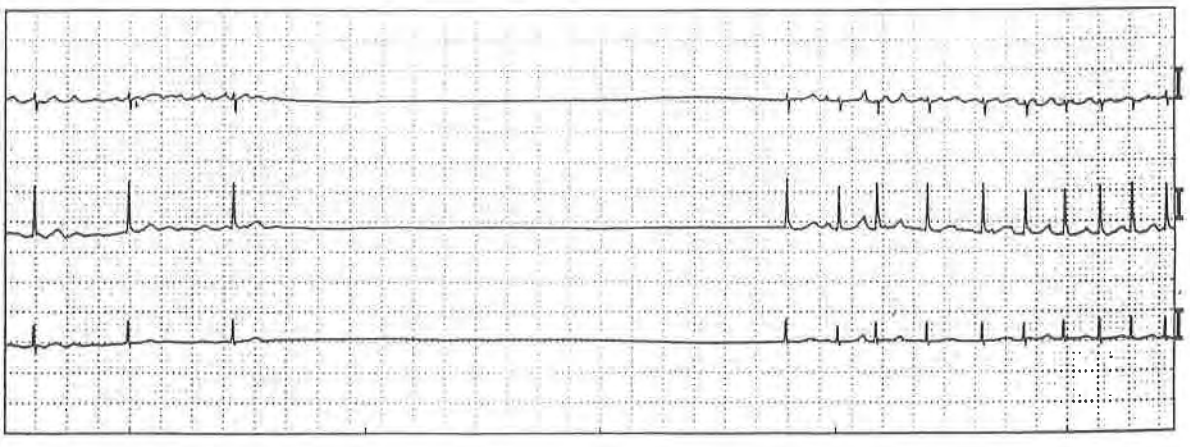

Figure 5: Holter ECG recording showing sick sinus syndrome. On termination of atrial fibrillation, there is a 4.2 seconds pause

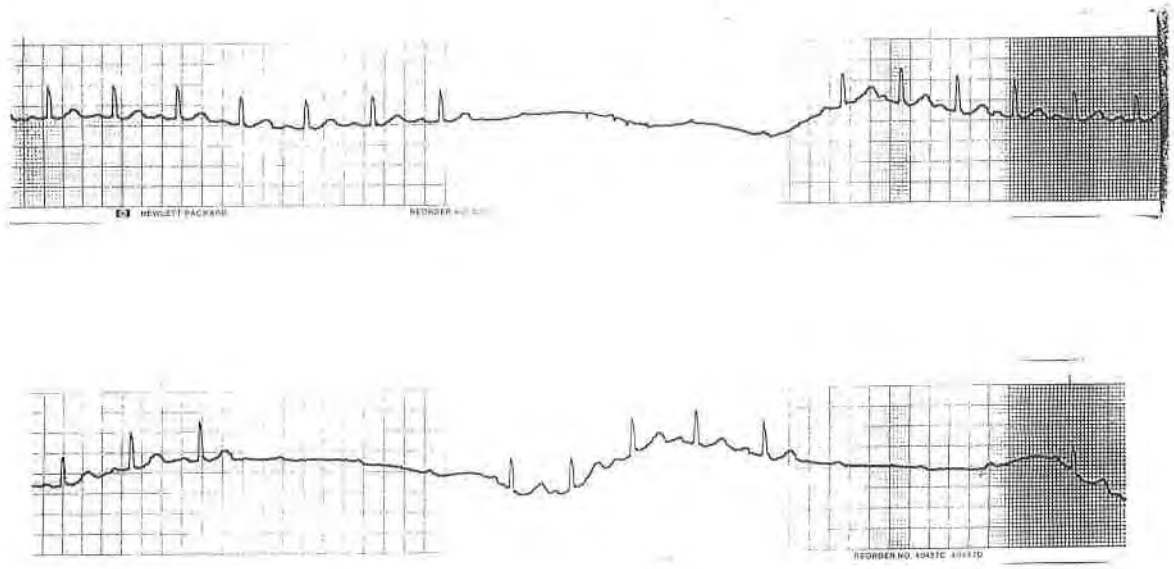

Figure 6: Transtelephonic ECG monitoring showing intermittent ventricular standstill resulting in syncope

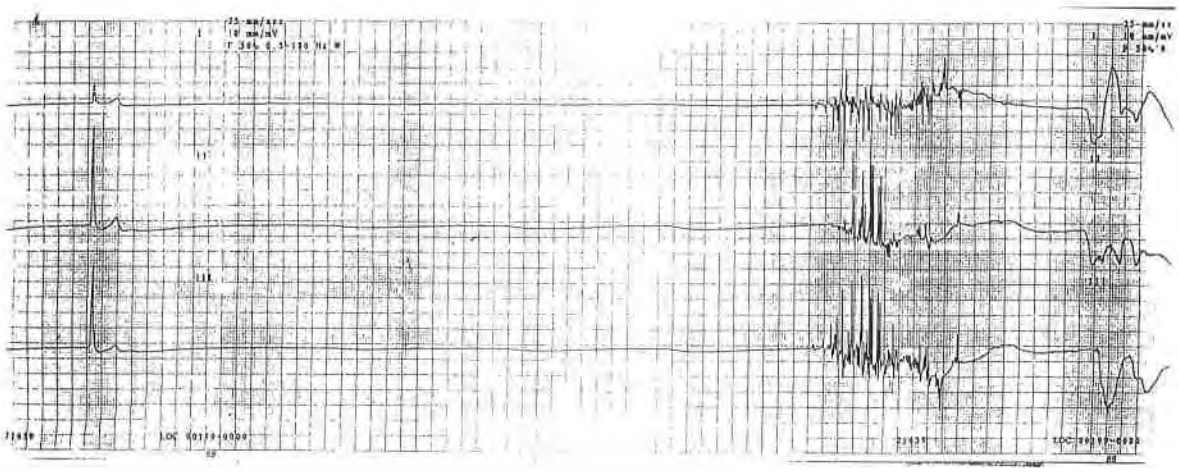

Figure 7: Head upright tilt test showing prolonged asystole resulting in syncope

In recent years the upright tilt test has become a very useful tool in patients with recurrent syncope suspected of having vasovagal syncope and should be the initial test especially in patients with a normal ECG and no underlying heart disease. Rarely, patients may have a more malignant form of vasovagal syncope with prolonged asystole during head upright tilt testing as shown in Figure 7.

Intracardiac electrophysiologic studies are most useful only in patients who have organic heart disease and otherwise unexplained syncope. Clearly abnormal results such as sustained ventricular tachycardia (especially when easily induced), sinus node recovery time ≥ 3 seconds, Infra-Hisian block with atrial pacing, prolong HV interval of ≥ 100 msec or supraventricular tachycardia associated with hypotension may account for the cause of syncope.

The echocardiogram and coronary angiogram may be useful in some patients to investigate for the underlying heart disease. The echocardiogram is especially useful to look for obstructive causes of cardiac syncope. Despite the use of a wide range of investigative tools, a diagnosis may however not be obtained in up to 41% of patients.[15] Even after referral for head-up tilt testing and electrophysiological testing, 26% of patients may remain undiagnosed.[16] In such patients with a negative electrophysiological study and tilt table, the implantable "loop recorder" was found to be useful for making the diagnosis when episodes are too infrequent for standard ambulatory monitoring.[17,18]

Management

The treatment depends on the correct diagnosis for the syncope. This is especially in the elderly who may have several medical problems, each of which could possibly account for the syncope. Management and exclusion of volume depletion, hypoglycemia, anemia, electrolyte abnormality, or drug toxicity is standard.

In general patients with neurally mediated syncope need only reassurance and avoidance of stimuli that provokes it, except in patients with a malignant form of vasovagal syncope who rarely may need pacemakers. Adequate hydration and salt intake is encouraged. In some patients, beta blockers, disopyramide or midodrine (a new alpha agonist) may be tried. Carotid sinus syncope patients however generally require a permanent pacemaker. Patients with obstructive cardiac lesions such as critical aortic stenosis usually require surgery. In patients with syncope due to bradyarrhythmias such as complete heart block or sick sinus syndrome, a pacemaker is definitely needed while tachyarrhythmias can be treated with drugs, ablation, surgery or devices. Implantable defibrillators are often needed for ventricular tachyarrhythmias which are hemodynamically unstable and associated with syncope, as the risk of sudden death is often still too high after drug therapy including amiodarone.[19] Patients with suspected neurological causes of syncope require evaluation by the neurologist and patients with suspected psychiatric causes need referral to a psychiatrist.

Conclusion

Syncope is an extremely common and important condition in medical practice that requires very careful evaluation. It can represent a perfectly benign condition with spontaneous resolution as often occur in vasovagal syncope or may be a precursor for sudden cardiac death if the syncope had been related to transient asystole or ventricular tachyarrhythmias. The correct diagnosis and treatment is vital.

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Hyperlipidaemia Management Strategy

Vanessa Au Shu Chuan

Introduction

During the past decade, various randomised studies have taken centre stage in hyperlipidaemia management. In addition, the National Cholesterol Education Program (NCEP) guidelines were produced to aid clinicians in determining when and how aggressively hyperlipidaemia should be treated.

Cholesterol and triglycerides are carried in the blood bound to lipoproteins. The clinical importance of hyerlipoproteinemia derives chiefly from the role of lipoproteins in atherogenesis, and the greatly increased risk of acute pancreatitis associated with severe hypertriglyceridaemia. Various epidemiological studies and randomised controlled studies have suggested a 2 - 3% decrease in coronary heart disease (CHD) risk for each 1 mg/dl increase in the HDL, after correction for other CHD risk factors. The studies were: Framingham Heart Study, Prospective Cardiovascular Munster study, Lipid Research Clinics Coronary Primary Prevention, Multiple Risk Factor Intervention Trial, Helsinki Heart Study, Scandinavian Simvastatin Survival Study, Cholesterol And Recurrent Events trial, Post Coronary Artery Bypass Graft. These studies argue for early intervention in hyperlipidaemia.

National Cholesterol Education Program (NCEP) guidelines

The management of hyperlipidaemia is made easier by having the NCEP guidelines (see table 1) at hand (perhaps in one's pocket book or pasted on top of the worktable). These guidelines were formulated to guide physicians in the management of hyperlipidaemia, lipids being one of the many cardiovascular risk factors of a patient. The NCEP guidelines use LDL cholesterol in its recommendations. In a patient with hyperlipidaemia, the level to which the LDL-cholesterol has to be lowered depends on whether it is for primary intervention or for secondary intervention for cardiovascular disease.

Table I: National cholesterol eduction programme: adult treatment guideline (1993)

Risk Factors*	Diet	Diet & drug	Goal
<2 risk factors, no AVD	>160 mg/dL	>190 mg/dL	<160 mg/dL
>/=2 risk factors, no AVD (primary)	>130	>160	<130
AVD (secondary prevention)	>100	>130	<100

*negative risk factors for CAD. HDL >=60 mg/dL (>=1.6 mmol/l) (substract one risk factor). AVD atherosclerotic vascular disease.

Coronary Heart Disease - Risk Factors

Hyperlipidaemia is but one of the several risk factors for atherosclerosis, and, by extension, myocardial infarction and cerebrovascular disease. The treatment of hyperlipidaemia is therefore one of the ways to decrease the risk of atherosclerosis/ coronary heart disease.

The risk factors for atherosclerosis are:

- age and gender (men more than 45 years of age, and post menopausal female or female more than 55 years of age)
- a positive family history (myocardial infarction in a male member of the family occurring at less than 55 years old, and in a female member of the family at less than 65 years old)
- a history of premature atherosclerosis
- smoking
- diabetes
- hypertension
- low HDL-cholesterol (less than 35 mg/dL).

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Hence when faced with a patient with hyperlipidaemia, the decision to intervene depends on the number of risk factors and whether or not the patient has evidence of coronary heart disease.

NCEP guidelines

In a patient without coronary heart disease, lowering the cholesterol constitutes primary prevention. The NCEP guidelines recommend that people with fewer than 2 cardiovascular risk factors should have their LDL-cholesterol lowered to 160 mg/dl, whereas those with 2 or more risk factors ought to have their LDL-cholesterol lowered to 130 mg/dl.

In a patient with a history of coronary heart disease, lowering the cholesterol is part of secondary prevention. The NCEP guidelines recommend that the LDL-cholesterol be lowered to 100 mg/dl.

It must be stressed that diabetes mellitus is counted by the NCEP as 2 risk factors. The reason is that atherosclerotic events occur earlier in diabetics and, are more severe and more likely to be fatal.

In many laboratories, LDL cholesterol is estimated by the Friedewald equation:

[units in mg/dl] **LDL = TC - HDL - TG/5**
[units in mmol/L] **LDL = TC - HDL - TG/2.2**

TC = total cholesterol, HDL = HDL-cholesterol, TG = triglycerides. TG/5 gives an estimation of the VLDL provided TG < 400 mg/dl (< 4.5 mmol/l).

As TG levels are associated with meals and are raised especially after a fatty meal, a fasting blood specimen is required when the formula is used. Where it is possible to measure the LDL directly, a fasting blood specimen is not needed.

As mentioned, the NCEP guidelines use LDL-cholesterol for its recommendations. This contrasts with lipid management guidelines found in the European literature. In the European literature, treatment guidelines are based on both cholesterol and triglycerides. The American literature and the European literature are not in agreement as to whether an elevated triglyceride level is by itself a risk factor for CAD.

General approach to a patient with dyslipidaemia

Hyperlipidaemia is classified into primary or secondary hyperlipidaemias. It is further classified according to the type of lipid (cholesterol or triglyceride) that is raised (see figure 1).

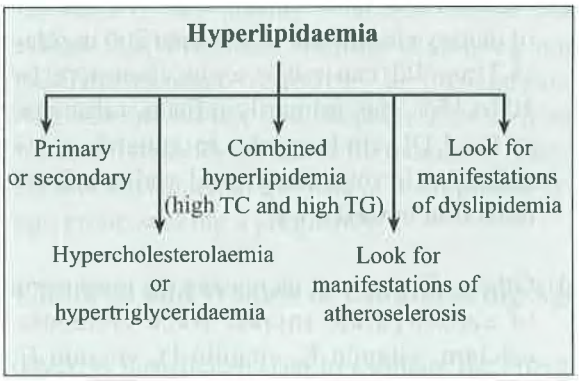

Figure 1 Common causes and presentations of hyperlipidaemia: general clinical tips

Primary dyslipidaemias are inherited. The common causes of secondary dyslipidaemia are diabetes mellitus, nephrotic syndrome, chronic renal failure, hypothyroidism and steroid therapy. If the dyslipidaemia persists despite correction of the underlying condition, then one would treat as for a primary dyslipidaemia.

In the evaluation of a patient with dyslipidaemia, one should look for the manifestations of atherosclerosis (peripheral pulses and vascular bruits) and the manifestations of dyslipidaemia (corneal arcus, xanthelesmas, xanthomas, and hepatomegaly).

Non-Pharmacological Approach

Non-pharmacological measures that help lower cholesterol are essential in both primary and secondary prevention of coronary heart disease. In primary prevention, attempts to lower cholesterol should always begin with non-pharmacological measures. For all patients who

are on lipid lowering drugs, non-pharmacological means must be emphasised as being crucial in lowering the lipid levels.

Ways to lower cholesterol are:

a) Restriction of calorie intake. Endogenous cholesterol production is greatly stimulated by caloric intake in excess of the requirements for physical activities and basal metabolism.

b) Restriction of fat intake per se.

c) Reduction of cholesterol intake. Restriction of dietary cholesterol to less than 200 mg/day (5.2 mmol/d) can reduce serum cholesterol by 10 to 15%; this primarily reflects a decrease in the LDL-cholesterol. In general, a 1% reduction in total cholesterol yields a 2-3% reduction in CHD risk.

d) Others. The role of increasing the proportion of carbohydrate intake, trace elements, calcium, vitamin E, vitamin D, vitamin C, pyridoxine and magnesium is controversial. Alcohol ingestion causes secondary hypertriglyceridaemia due to overproduction of endogenous cholesterol (VLDL); chronic alcohol intake may also be associated with hypercholesterolaemia due to increase in cholesterol synthesis and decrease in the conversion to bile acids. In recent years, several reports have suggested that low level consumption of alcohol may be associated with improved cardiovascular health. An increased HDL-cholesterol may be contributing to this benefit; however, the increase in the HDL-cholesterol does not hold true for everybody. It has also been pointed that these studies have not been vigorously conducted to account for confounding factors such as diet and physical activity. Furthermore, the detrimental effects of alcohol on health are well known. For these reasons, alcohol consumption as a means to correct dyslipidaemia should not be carelessly promoted.

Statins (competitive HMG CoA reductase inhibitors)

In general, statins are used for hypercholesterolaemia and fibrates are used for hypertriglyceridaemia.

Hydroxymethylglutaryl Co A reductase is the rate-limiting step in cholesterol synthesis. Statins are competitive inhibitors of HMG CoA reductase. The inhibition of cholesterol synthesis causes an increase in the expression of LDL-receptors on hepatocyte membrane and therefore enhances the clearance of LDL-cholesterol from the circulation.

This category of drugs is most effective for the treatment of hypercholesterolaemia; their effects are amplified significantly when used in combination with either nicotinic acid or with a resin. Common but transient side effects include nausea, change in the bowel function, flatulence, abdominal pain, headaches and insomnia, fatigues and rashes. Myopathy occurs in < 5% of patients and can cause a marked increase in the creatinine kinase; severe myopathy can lead to rhabdomyolysis. The incidence of myopathy is increased when the statins are used in combination with fibrates, Cyclosporin A, erythromycin or nicotinic acid. Myopathy is rapidly reversible upon stopping the drug. Patients on statins should be advised to report muscle pains. Moderate, often intermittent, elevations of aminotransferases can occur; transaminases must be measured regularly when the patients are on statins, especially if the patient has underlying hepatic dysfunction, including alcohol abuse. Statins should be discontinued when the transaminases exceed three times the upper limit of normal. Last but not least, drug interactions with digoxin and warfarin have been reported.

Fibrates

Fibrates (e.g. Gemfibrozil, Fenofibrate, Benzafibrate and Ciprofibrate) are prescribed for hypertriglyceridaemia. Fibrates are associated with myositis (reflected by elevations in the creatinine kinase) and this is more common in those with renal impairment. Fibrates can cause an elevation in transaminases and regular

monitoring of transaminase levels is advised. Other common side effects include gastrointestinal disturbances as flatulence, change in bowel habits and abdominal pain. Some fibrates potentiate gallstone formation. Fibrates also interact with warfarin and potentiate the action of warfarin.

Bile Acid Sequestrants/ Resins

Bile acid sequestrants are not recommended as first-line drugs by the American Diabetic Association Consensus Panel. While it primarily lowers total and LDL-cholesterol, it has little effect on HDL-cholesterol. It increases VLDL-triglycerides particularly if the levels are already >250 mg/dl (2.8 mmol/l). Small doses may be used as adjuvant therapy in patients with elevated VLDL-triglycerides and elevated LDL-cholesterol, especially if a fibrate is the primary drug therapy. Resins must be used with care in diabetic patients with gastrointestinal autonomic neuropathy because they may produce constipation or faecal impaction. They have no adverse effects on glucose control. Resins can also cause malabsorption of certain drugs, e.g., thyroxine, digitalis glycosides, warfarin, thiazides and beta-blockers. To ensure that these drugs are absorbed, they should be taken 1 hour before the intake of the resin.

Nicotinic Acid

Nicotinic acid substantially lowers total cholesterol, LDL-cholesterol and triglycerides; it increases HDL-cholesterol. In short, 'it does everything good'. It is, however, not recommended as the first-line drug in hyperlipidaemia management in a diabetic patient because it increases insulin resistance and fasting and post-prandial hyperglycaemia and hyperinsulinemia. Nicotinic acid can also cause hepatic dysfunction and should be avoided in those with hepatic parenchymal disease.

Probucol

This is an antioxidant, and can lower, to a moderate degree, serum cholesterol by approximately 10%. Probucol lowers LDL cholesterol; it can however also lower HDL cholesterol by 20-25%. The lowering of HDL cholesterol is a theoretical disadvantage of using Probucol. There is little influence of Probucol on serum triglycerides. Probucol can cause a prolongation of the QTc interval particularly in individuals with myocardial damage or in those who have arrhythmias. An ECG should be recorded before starting Probucol. Other side effects of Probucol include diarrhoea and gastrointestinal reaction as dyspepsia. Angioedema is a rare complication. Probucol can remain in the body fat stores for 6 months, hence, should be avoided in a female of the reproductive age group seeking a pregnancy.

Children and Women of Childbearing Age

There is insufficient data to evaluate the effects of the lipid-lowering drugs on the foetus. Therefore, women of childbearing age should be cautioned and should be given the drugs only if pregnancy is being actively avoided.

In patients with hypertriglyceridaemia, oral contraceptives containing estrogens should preferably not be used.

Conclusion

Hyperlipidaemia is a common problem seen in general medical clinics. It may be primary hyperlipidaemia, where drugs are the mainstay of management. More commonly, however, the hyperlipidaemia is secondary to another disease entity, or to dietary indiscretion; in this circumstance, it would be prudent for the patient to be on non-pharmacological measures first to control the hyperlipidaemia, and to treat the secondary causes of hyperlipidaemia. One should consider starting drugs if the non-pharmacological measures or the treatment of the other medical conditions fail to bring the cholesterol/ triglycerides down to prescribed targets. Hyperlipidaemia, diabetes mellitus, hypertension,

obesity and smoking commonly exist together and increase the CAD risk of the patient; these risk factors must be dealt with as a whole. Generally, statins (HMG CoA reductase inhibitors) are prescribed for hypercholesterolaemia and fibrates for hypertriglyceridaemia. When using statins, fibrates, and nicotinic acid in the pharmacological management of hyperlipidaemia, we must be aware of possible hepatic dysfunction. Myositis can occur in those on statins or fibrates. Significant drug interactions can also occur in patients who are on statins or fibrates.

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Heart Disease In The Elderly

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Introduction

Older persons, those over 65 years of age, are increasing in both absolute numbers and as proportion of the population in Singapore. In 1980, 4.9% of the population was aged ≥ 65 years. This will increase to 18.4% in the year 2030. Heart disease is the most common cause of morbidity and mortality in the elderly. In the Western population, the prevalence of symptomatic coronary artery disease in population aged >65 years is 20%, and it accounts for 80-85% of all cardiac deaths in this age group. Other causes are congestive heart failure, hypertensive heart disease and valvular heart disease. In Singapore, heart disease is the second most common cause of death as a whole but it creeps up as top cause in patients over 60 years of age.

There are three cardiovascular changes related to aging, namely;

1) normal age-associated changes in cardiac anatomy

2) normal age-associated changes in cardiovascular physiology and

3) normal age-associated changes in pharmacokinetics and pharmacodynamics in the elderly (tables 1, 2, 3).

These changes, together but at different rates with age-related changes in the kidneys, brain or musculoskeletal system, may alter the presentation, complicate the diagnosis or treatment of heart disease in the elderly. Common cardiovascular problems in older persons include coronary artery disease, congestive heart failure, hypertension, atrial fibrillation or other cardiac dysrrhythmia[1].

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Table 1. Normal age-related changes in cardiac anatomy

Myocardium	
	Increased heart weight, left ventricular mass, LV wall thickness.
	Fibrosis, collagen accumulation
Chambers	
	LV cavity size decreased, long axis shortens
	Rightward shift and dilatation of the aorta
	Senile septum
Valves	
	Calcific and fatty degeneration of valve leaflets and annuli
Coronary arteries	
	Dilatation, tortuosity, and arteriosclerosis
Conduction system	
	Fibrosis and loss of specialized cells and fibers
	Loss of pacemaker cells in sinoatrial node
	Fibrosis of atrioventricular node and left anterior fascicle

Table 2. Normal age-related changes in cardiovascular physiology

Decreased aortic elasticity; aortic impedance increases
Decreased myocardial relaxation; diastolic dysfunction develops
Peak exercise heart rate declines
Peak exercise ejection fraction maintained by a larger diastolic volume
Systolic blood pressure increases
Valvular regurgitation (mild) develops
PR, QRS, QT prolongs; left axis deviation develops
Diminished reactivity to chemo- and baroreceptor Decreased sensitivity to ß-agonists
Altered pharmacokinetics / pharmacodynamics

Table 3. Age-related pharmacological changes in the elderly
Pharmacokinetics (bioavailability)
Reduced gastric emptying time, gastrointestinal motility and splanchinic blood flow
Decreased mucosal absorptive surface
Less lean body mass and decreased blood volume
Reduced cellular enzyme activity (primarily affects oxidation)
Reduced glomerular filtration rate and tubular secretion
Reduced albumin levels in poor nutrition elderly
Pharmacodynamics (altered sensitivity to drugs)
Reduced B-1 adrenergic responsiveness
Reduced baroreceptor response

Coronary Artery Disease

The hypothesis that conventional risk factors are not important in the elderly, because age itself is such as powerful risk factor, is no longer widely accepted. Better data are now available with regards to smoking, hypertension and lipids. In the Coronary Artery Surgical Study Registry's subgroup involving patients older than 55 years, a statistically significant reduction in the risk of myocardial infarction or death occurred in patients with advanced coronary artery disease if they quit smoking. Smoking cessation will likely benefit patients at risk in all age groups.

Elevated blood pressure, either systolic or diastolic or both, remains as an important modifiable risk factor. The Framingham study demonstrated that patients 65 to 94 years with systolic pressure ≥180 mmHg had a three to fourfold increased risk of coronary artery disease compared with those with systolic blood pressure <120 mmHg. A diastolic blood pressure >105 mmHg carried two to threefold higher risk than those with diastolic blood pressure <75 mmHg. There appeared to be a J-shaped risk curve in this older age population. It is postulated that the lower diastolic perfusion pressure may be proischemia. But this interpretation is confounded by possible comorbidity, resulting in lower blood pressure and increased morbidity and mortality. Nonetheless, recent trials in the treatment of hypertension in the elderly have been shown to reduce morbidity and mortality, as well as in the reduction of cognitive impairment in the elderly.

Many, although not all, studies have shown that elevated plasma cholesterol to be a risk factor in coronary artery disease, including the very old. However there may be some diminution in the relative risk as the elderly age. Nevertheless, because the absolute risk for coronary event over a short period is higher in older persons, the attributable risk to elevated plasma cholesterol increases with age. Subgroup analyses of recent statin trials support lipid lowering in the elderly. In the Scandinavian Simvastatin Survival Study, 518 hypercholesterolemic patients who were ≥ 65 years old at enrollment had similar lipid lowering effect and relative risk reduction as those of younger patients.

An important age relationship in coronary artery disease is the striking gender differential. The event rate is 1:5 in favour of females at age 35, but women experience steadily increasing frequency of events, so that by age 70, the ratio is almost 1:1.

Stable coronary artery disease - clinical presentation of myocardial ischemia may be atypical. Symptoms such as dyspnea or giddiness are common in the elderly. On the other hand, comorbidity may produce complaints that mimic coronary artery disease. Lack of vigorous physical activity in the elderly produces little chest pain even in the presence of severe coronary artery disease. Associated other cardiac pathology, inability to perform adequate exercise due to pulmonary or orthopaedic conditions and age-associated changes in baseline ECG complicate the diagnosis and performance of diagnostic tests. Moreover, the presence of common comorbid conditions such as renal insufficiency or diffuse atherosclerosis makes coronary angiography or percutaneous coronary angioplasty more hazardous in older patients. The short-term and long-term angiographic and clinical follow-up in elderly patients aged ≥ 75 years who underwent

coronary artery stenting had significant higher rates of procedural complications and worse six month outcomes than the younger cohort. Overall survival in the elderly population at twelve months post-coronary artery stenting was 91%, but with a low event-free rate of 54% [2].

Acute myocardial infarction - the diagnosis of acute myocardial infarction is more difficult in the elderly. As in stable coronary artery disease, dyspnea is a more common complaint than the typical infarctional chest pain. Other presentation of acute myocardial infarction includes heart failure, arrhythmia, acute confusion, stroke or even silent infarction. A large proportion of elderly patients with myocardial infarction has ST segment depression (rather than elevation) and lower cardiac enzyme elevation.

The in-hospital mortality and subsequent mortality, reinfarction and complications are all increased in the elderly. There is an increase in the risk of intracranial hemorrhage in the very elderly whenever thrombolytic therapy is used. However data from large trials suggested that advanced age alone, in the absence of other contraindication, should be seen as an indication for thrombolytic therapy, not a contraindication. There is a tendency for primary angioplasty to produce less cerebral hemorrhage, thus possibly a better survival benefit. Older patients who were aged ≥ 75 years and had cardiogenic shock appeared to have a less favourable outcome if emergency revascularization strategy was adopted rather than the strategy of an initial medical stabilization and delayed revascularization as clinically determined [3].

Congestive Heart Failure

Heart failure is one of the most common diagnoses for admission to acute care hospital in the elderly. The syndrome may be due to myocardial dysfunction of systolic or diastolic origin, ischemia, hypertension, valvular heart disease, cardiac arrhythmia or rarely restrictive pathology. Age-associated changes in the cardiovascular system contribute to its development and complicate its diagnosis and treatment.

Many older patients presenting with signs and symptoms of heart failure have normal or only slightly reduced systolic function. This is particularly important in older age group because up to 40% of those over 60 years old with heart failure have predominantly diastolic abnormality.

The distinction between systolic or diastolic heart failure cannot be made confidently by history, physical examination or chest X-ray. The distinction is best made with Doppler echocardigraphy. Studies with angiotensin converting enzyme inhibitors indicate improved survival and decreased morbidity in older, as well as in younger patients with systolic dysfunction. Diuretics are useful to relieve congestion symptom. Digitalis improves clinical outcomes though not necessary survival rate. The therapeutic / toxic window for digitalis is narrower in the older age group because of a decreased inotropic effect without a corresponding decrease in arrhythmogenic potential. Because of age-associated changes in renal function and pharmacokinetics and pharmacodynamics, the maintenance dose of digitalis should be decreased in the elderly. Drug-drug interaction is also common.

Patients with predominantly diastolic heart failure are often seen in those with hypertension or coronary artery disease. There is a delay in early filling and elevated end diastolic pressure in the left ventricle. Although short-term diuretic therapy improves the steep pressure-volume chamber relationship, it is necessary to maintain adequate preload that is needed to fill the stiff diastolic left ventricle. Hence, excessive use of diuretics after the relief of pulmonary congestion should be avoided. Regression of left ventricular mass and improved diastolic function is also important and can be achieved by using angiotensin converting enzyme inhibitor or calcium channel blocker. Beta-blocker is indicated to control ischemia and to prevent excessive ventricular rate in predominantly diastolic heart failure [4].

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Hypertension

Systolic hypertension or an elevated pulse pressure, rather than diastolic hypertension, is a better predictor of coronary artery disease, heart failure, stroke, renal failure and all cause mortality. Secondary hypertension such as atherosclerotic renovascular hypertension or primary aldoeteronism should be considered in those hypertensive first presented after age 60 years. Older persons are more likely to exhibit pseudohypertension, white coat hypertension or postural hypotension.

Pseudohypertension is due to increased stiffening of the brachial artery that is not easily compressed by the blood pressure cuff, resulting in an erroneously high blood pressure reading. This can be detected by a positive Osler's manoeuvre. White coat hypertension is a condition whereby a person's blood pressure is consistently elevated in the physician's office or clinic, but normal at other times. Self-measurement of blood pressure using a reliable blood pressure measurement set or ambulatory blood pressure monitoring will help to distinguish this condition and true hypertension. Postural or orthostatic hypotension is said to be present when there is a fall of ≥20 mmHg in systolic or ≥10 mmHg diastolic blood pressure on changing from a supine to an upright position. Rarely atherosclerotic disease of the subclavian artery may produce pseudohypotension in the elderly.

Trials of hypertensive patients older than age 60 years old have shown that drug therapy reduces stroke, coronary artery disease heart failure, mortality, and recently, impaired cognitive function. The goal of treatment in older persons should be the same as that of younger patients to blood pressure below 140/90 mmHg, although an interim goal of systolic pressure below 160 mmHg may be necessary in those with marked systolic hypertension. Thiazide diuretics or beta-blocker in combination with diuretics are recommended in older patients if all things are being equal and there is no compelling indication to use other antihypertensives. Nitrendipine has been shown to be useful in isolated systolic hypertension in the elderly [5,6]. Major outcome trials so far have either excluded or recruited too few patients who were over the age of 80 years old.

The benefit-risk comparison from active treatment will be assessed in a large Hypertension in the Very Elderly Trial [7].

Cardiac Arrhythmia

Cardiac arrhythmia are common in the elderly due to:

a) age-associated changes in cardiac conduction system,

b) increasing prevalence of hypertension, heart failure and coronary artery disease and

c) proarrhythmic effect of the commonly used cardiac medications.

Supraventricular and ventricular ectopics are commonly seen in subjects over 60 years old. Although these are usually asymptomatic in healthy individuals, they may produce hemodynamic deterioration or compromise cerebral blood flow if the arrhythmia is frequent and in the presence of underlying heart disease.

Atrial fibrillation is common in the elderly. The prevalence is 10% in persons over 70 and increase to 15% by mid-80, and is responsible for considerable morbidity and mortality, especially stroke and congestive heart failure. Patients at highest risk of stroke are those over age 75 years old, impaired ventricular function, history of thromboembolism, presence of hypertension and diabetes, and dilated left atrial size on echocardiography. The goals in treatment of atrial fibrillation are to prevent thromboembolic complication and arrhythmia-related symptoms such as heart failure. Warfarin decreased the annual stroke rate from an average of 4.5% to 1.4%. The annual rate for major bleeding was 1.3% in the warfarin group versus 1.0% in the control group. Hemmorhage was associated with age, excessive anticoagulation, and poorly controlled hypertension. Nevertheless, the benefit of anticoagulation still outweighs the risk in elderly patients. The target INR should be kept

below 3.0. Control of rapid ventricular rate with medications such as digoxin, calcium channel blocker or beta-blocker is equally important. The decision to convert atrial fibrillation to sinus rhythm in the elderly is complex and problematic.

Conclusion

Cardiovascular care and expenditure provided to the elderly patients will increase because of the growing number of older persons. Physicians should familiarize themselves with the age-associated changes in the cardiovascular system, and the altered manifestations of heart disease in the elderly, in order to understand, to diagnose and to treat them correctly and optimally. Patients and the relatives can then be given better information and more realistic expectation. Although aggressive medical or surgical approaches may be considered for selected individuals, many elderly patients with multiple comorbidity may require an integrated approach among the cardiologists, geriatricians, cardiothoracic surgeons, physiotherapists and home nursing care providers.

The quality of life, rather than the quantity, may be a more important consideration in the overall management of many elderly patients with heart disease.

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Sexual Activity And Heart Disease

Chee Tek Siong

Introduction

In our medical schools, sexual behavior and dysfunction was traditionally taught during lectures in Psychiatry. The advancement in medicine and the introduction of various modalities in the management of erectile dysfunction has inadvertently resulted in the proliferation of 'experts' in sexuality. The gynecologists, the endocrinologists, the urologists and the dermatologists have all entered the arena. The cardiologists and the geriatric physicians are now starting to give advice to patients on sexual problems.

Cardiovascular effects of sexual intercourse

Cardiovascular effects of sexual activity in normal and in patients with coronary artery disease had long been studied, usually under the experimental or clinical settings. Cardiac and metabolic expenditures during coitus vary from patients to patients, types of sexual activity and conditions under which sexual intercourse took place. In a laboratory setting, healthy males with their usual partners achieved an average peak heart rate of 110 bpm with female-on-top position and an average heart rate of 127 bpm with man-on-top coitus. The metabolic equivalents (METs) were 2.5 and 3.3 METs respectively during orgasm. Occasionally the maximal heart rate could reach 185 bpm or 5.4 METs at orgasm.

Smaller study with electrocardiographic monitoring during intercourse in patients with coronary artery disease revealed increased ventricular ectopic activities. One third of the patients with previous myocardial infarctions developed electrocardiographic criteria for ischemia during intercourse, although majority of the ischemia was silent. Compared with exercise stress tests, all patients with ischemia during coitus also demonstrated ischemia at exercise stress tests [1,2]. As there is a significant individual variation of cardiovascular responses among patients, to simply equate a level of cardiac metabolic expenditure during sexual intercourse to an activity such as 'climbing 2 flights of stairs' may underestimate the level of cardiovascular response. The hemodynamic changes associated with sexual intercourse may be far greater with an unfamiliar than with a familiar partner, in an unfamiliar than familiar setting or environment, and after a heavy meal and consumption of alcohol.

Sexual activity and myocardial infarction

It was estimated that sexual activity was a likely contributor to the onset of myocardial infarction in only 0.9% of the cases. The relative risk of triggering onset of myocardial infarction among patients with a history of angina (RR 2.1) or prior infarct (RR 2.9) was not significantly greater than that observed in those without prior cardiac disease (RR 2.5). Although the average relative risk in the 2 hours after sexual activity was 2.5, its absolute risk was extremely low. Data from the Framingham Heart Study indicate that the baseline risk that a 50-year-old, nonsmoking, nondiabetic man will experience an myocardial infarction is approximately one chance in a million per hour. The absolute risk of myocardial infarction, by engaging in sexual activity, would increase his hourly risk to two in a million, and only for a two-hour period. The baseline yearly risk of reinfarction or death for an individual with a prior infarct is approximately 10%. For individuals in the 10% annual risk group, sexual activity would transiently double the risk from 10 in a million per hour to 20 in a million per hour. Moreover, regular exercise appeared to lower, and possibly eliminate the small and transient risk of myocardial infarction associated with sexual activity [3]. By explaining this data on the absolute risk, it should be possible to decrease sexual dysfunction currently caused by unrealistic fears of resumption of sexual activity in patients with stable angina or following myocardial infarction.

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Heart disease and sexual activity

Significant and serious cardiac conditions may be aggravated by sexual intercourse. Significant aortic stenosis, Eisenmenger syndrome or severe pulmonary hypertension of various causes, uncontrolled and severe hypertension, unstable angina or decompensated heart and malignant arrhythmia will all require careful evaluation and treatment by the specialists prior to engagement in sexual activity. Individuals with less severe valvular heart lesions, stable angina, controlled heart failure, uncomplicated congenital heart diseases, post coronary artery bypass surgery can resume sexual activity when they are emotionally and physically ready. If the patients can achieve greater than 5 or 6 METS on an exercise stress test without demonstrating myocardial ischemia, or undue dyspnea or discomfort, the risk during coitus with a familiar partner, in familiar settings, without the added stress of a heavy meal or alcohol ingestion, is probably low and acceptable.

Sexual activity, Sildenafil and coronary artery disease

A large proportion of patients with cardiac events, particularly those after myocardial infarction, does not return to normal sexual activity. Many factors, including normal age-related changes in sexual response, medication-induced sexual dysfunction, vascular changes associated with risk factors (e.g. diabetes, hyperlipidemia, and smoking), emotional insecurity or depression may influence sexual function in these patients.

Recently, the availability of an orally effective drug (Sildenafil) for the treatment of erectile dysfunction has caused some concern. Patients with occult or clinical coronary artery disease, compensated heart failure but with low normal plasma volume or blood pressure, and in hypertensive patients on multi-drug regimen are potentially high-risk groups. Sildenafil is absolutely contraindicated in patients concurrently taking any form of nitrates, as this drug interaction may result in a precipitous fall in blood pressure. Physician should exclude the use of Sildenafil within the 24-hour period before giving nitrate in patients presenting with possible angina or infarction to the clinic and emergency department. After 24 hours, the administration of nitrate may be considered. It is essential to have the ability to support the patient with fluid resuscitation, alpha-adrenergic agonist and to put the patient in a Trendelenburg position, and even intra-aortic balloon counterpulsation if nitrate and Sildenafil have been inadvertently given. A small number of men had died after ingesting Sildenafil. The US Food and Drug Administration and the manufacturer are aware of the deaths but believe the drug continues to be safe for patients. But some pharmacoepidemiologists remain skeptical. One such critic is Professor John Urquhart who argues that the percentage of men dying after taking Silfenafil is much greater than the percentage of deaths of men who took local preparation of alprostadils. He cited that there were 1.5 to 4.5 deaths per 1 million for local alprostadils, while the deaths per 1 million prescriptions for Sildenafil was 49 [4]. The unanswered question remains: are some men who take Sildenafil dying because of the underlying disease or because of the drug? Case report on acute myocardial infarction following Sildenafil intake in a nitrate-free patient has been published[5]. Recently, it was shown that there was no adverse hemodynamic effects of oral sildenafil in men with coronary artery disease who were scheduled to undergo percutaneous coronary revascularization[6].

Although majority of the patients may be given Sildenafil safely by the frontline general practitioners, patients in the moderate or high-risk groups should be referred for cardiac assessment before prescribing Sildenafil or any other erectile dysfunction treatment. In doubtful cases, graded exercise testings or equivalents will be important and informative. Management of erectile dysfunction in patients with cardiovascular disease will always be secondary to stabilizing their cardiovascular status and optimizing drug therapy for cardiovascular symptoms.

Conclusion

Recent advances in the management of coronary artery disease and other cardiac conditions have dramatically improved and even altered the prognosis of the patients. However, despite these favorable prospects, physicians and patients are

too often burdened by the misconception that sexual activity is dangerous and should be avoided. Studies on the cardiovascular effects of sexual intercourse in patients with heart disease have demonstrated that sexual activity requires a similar level of exertion as a number of other natural daily activities with metabolic equivalents of approximately 3 to 5 METs. Although there is an increase in the probability of acute myocardial infarction when one engages in sexual intercourse, the absolute risk is small, even in those with coronary artery disease or prior infarction. This small excess in risk can be reduced or eliminated with regular exercise. The introduction of Sildenafil has resulted in many patients with high coronary risk profiles or various heart diseases to resume sexual activity. Despite its relatively infrequent cardiac deaths associated with the use of the drug, the physicians have been advised that " treatment for impotence generally should not be used in persons for whom sexual activity is inadvisable because of their underlying cardiovascular status."

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The Singapore Family Physician

Malaria Update

Oon Chong Teik

Introduction

Malaria is the most important parasitic disease of man. It is a protozoan infection of the red blood cells transmitted by the bite of a female anopheline mosquito. The world "malaria' comes from Italy and means bad air. As in the old days the disease was thought to be from the marshes.[1]

Charles Laveran (1880) discovered the parasites in the red blood cells, but it was not till 1897 that Ronald Ross identified the anopheles mosquito as the vector of human malaria. Both Laveran and Ross received the Nobel Prizes for their discovery.

Until the 19th Century, malaria was found in Northern and Southern Europe, North America and Russia. It has since been eradicated in these areas, but there has been a resurgence in the tropics, accompanied by increased resistance in the anopheline vector and to antimalarials in the parasite.

About 300 - 500 million people have malaria and 1.5 to 2.7 millions die yearly. It threatens 2400 millions people or 40% of the world population. The major impact of the disease is in sub-Saharan, Africa where 90% of worldwide cases are reported: Asia and the Americas have 5 - 20 million cases per year with 80% occurring in Asia.[2] In 1998, 405 cases were reported in Singapore with 5 deaths. All the cases were contracted abroad.[3]

Malaria is a disease caused by four species of the protozoan parasites of the genus Plasmodium. P. falciparum, P. vivax, P. ovale and P. malariae. The benign malarias P. vivax, P. ovale and P. malariae do not cause death unless from a ruptured spleen or the patient has other intercurrent illnesses. Most deaths and severe illnesses are due to P. Falciparum. P. ovale and P. malariae are found mainly in Africa.

The epidemiology of malaria transmission and severity of the disease vary from region to region and even from person to person in a village. Some of these are due to a particular species of the parasite, the degree of compliance with a drug regime, local patterns of drug resistance and an individual's immunity,

Malaria vector and disease transmission

There are 400 species, about 80 can transmit malaria and each has its own behaviour pattern eg. tree top breeding (fringe malaria) and difficult to eradicate with insecticides. The best is Anopheles gambiae, it is hardy, bites frequently, silent in flight, long lived and occurs in high density (flight range is 4 kms and in general within 2 km of breeding site). Breeding coincides with the rainy season and increased humidity favours survival. Most anopheles mosquitoes bite indoors at night but some are outdoor feeders. Malaria transmission does not occur below 16°C or above 33°C and at altitudes > 2000 metres as sporogony in mosquito cannot take place.

Climate change increases the risk of airport malaria which occurs when people are infected by mosquitoes that arrive by aircraft. Six cases of malaria were described in and around the main airport in Paris during the hot summer of 1994.[4] Recently another three cases of malaria all within a few kilometres of Luxembourg International airport were reported. Again the cases occurred in hot weather and all aircraft arriving from infected countries are being sprayed.

Malaria can also be transmitted by blood transfusion, transplantation or from needle sharing among drug addicts.

Malaria mosquitoes are attracted to fatty acids released by human skin and attracted less to cattle odour octenol. Cattle mosquitoes are not attracted to human odours. Researchers hope to isolate scent that could bait mosquitoes eg. Limburger cheese. This may explain why mosquitoes prefer to dine on the smellier parts of our body!

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Development of the malaria plasmodium in the mosquito after a blood meal (sporogony) takes 8 - 35 days depending on temperature during another feed. Mature sporozoites are injected reaching the liver (pre-erythrocytic stage) in 45 minutes. On average, parasites of malaria are detected in the blood after the liver stage on microscopy about the 11th day.

In P. vivax and P. ovale infection, some of the hepatic hypnozoites develop slowly to reach maturity in a few weeks or months, causing relapses which is the characteristic of these two species.

If treated inappropriately, P. falciparum can be present for a maximum duration of two years, P. vivax four years, P. ovale four years and P. malariae forty years.

Symptoms of Malaria

1. Flu-like illness
2. Fever - P. malariae if untreated has a 72 hour cycle (Quartan malaria). The other malarias termed tertian have 48 hour cycles, but P. falciparum commonly spikes daily as it often has two broods in the circulation out of phase. These characteristic fever charts are seldom seen today as malaria is treated early.
3. Chills
4. Headache
5. Muscle Ache
6. Fatigue
7. Nausea
8. Vomiting
9. Diarrhoea

These symptoms can occur up to one year after return from travel. In endemic areas due to repeated infection, a patient may be asymptomatic.

Severe and Complicated Malaria[5]

This only occurs with P. falciparum because of its tendency to cause sequestration. Sequestration is characteristic of P. falciparum infections. The infected red cells sticks to the venules of vital organs eg. brain, placenta, kidney etc. Uninfected red blood cells also become stiff and unable to pass through. This leads to microcirculatory obstruction, reduces oxygenation, causing lactic acidosis, leading to still births and coma. In very severe or fatal cases of cerebral malaria, because of heavy sequestration in the brain and vascular beds, parasites may not be found in the peripheral blood. Coma in cerebral malaria is caused by sequestration and not by increased intracranial pressure or cerebral oedema as the brain scan or magnetic resonance only shows mild swelling due to increased blood flow.

In clinical practice, anyone with any degree of impaired consciousness or cerebral dysfunction should be treated with urgency as in cerebral malaria.

Any patient with >2% parasitaemia carries increased risk of a fatal outcome. But 10% or more is critical. Other factors are Hb 5gm. Urine output <400cc in 24 hours, Serum creatinine >3mg; pulmonary oedema, hypoglycaemia <40mg, BP <50mm Hg in children 1-5 years, <70mm Hg in adults. Repeated convulsions, acidaemia PH <7.25 or plasma bicarbonate<15 mmol/litre. Bilirubin >3mg. Hyperpyrexia and macroscopic haemoglobinuria.

Immune suppression occurs in severe malaria resulting in septicaemias due to gram negative organisms, salmonella, melioidosis etc. Meningitis is not uncommon as well as respiratory tract infection from a wide range of organisms.

Diagnosis of Malaria

1. Blood film (Giemsa stain) is the traditional test.
   Thin film - to diagnose species of infecting malaria parasite and for parasite counting.
   Thick film - if parasites are scanty, they can be seen.

2. **Parasight F and I.C.T. test**[6]
   Both are rapid stick tests with a monoclonal antibody against P. falciparum histidine - rich protein 2. This specific histidine - rich protein is found on the surface of infected red cells. (Both tests are rapid and accurate with sensitivity and specificity of about 95%).

   A rapid stick test similar to the above that can detect both P. falciparum infection and other plasmodium infections is expected to be available soon.

   Blood samples from some of the Egyptian Pharoah's tombs have shown malaria was not an uncommon cause of death in those days.

The Acridine Orange (AO) Test[7]

A rapid test using acridine orange stain. All malaria parasites emit fluorescence on microscopy using a halogen lamp and light filters.

It takes only minutes compared to conventional microscopy and can detect parasitaemia more than 0.02% (1000 parasites/ul blood)

Polymerase Chain Reaction (P.C.R)

This is a new method which is capable of detecting a single copy of a specific target nucleic acid sequence which can be magnified about a million fold over previous techniques to improve the diagnosis of pathogen and malarial disease. Using this method it is possible to detect that a variant form of P. ovale had arisen, and also a hybrid of P. malaria with P. vivax which is under investigation.

Kawamoto hypothesized the presence of the African species P. ovale and P. malariae (now in S.E.Asia) were due to African troops (Ghanian and Nigerian) being in South Myanmar during World War II.[7]

Using the PCR method on the Thai – Myanmar border in Rawang, Japanese and Thai researchers here have found in a survey of 83 patients, 11 patients, were infected with all the 4 species of malarial parasites.[8]

Drugs in Malaria

Chloroquine is still very good for the asexual forms of P. vivax, P. ovale and P.malariae, but resistance to P. vivax. is present in some parts of Indonesia, Papua New Guinea and Myanmar.

Long term treatment and accumulation of up to 100 gms can cause irreversible retinopathy (>5 years prophylaxis.) P. falciparum resistance is widespread worldwide. Side effects are nausea, vomiting, skin rash, myopathy, neuropsychiatric symptoms etc.

Sulfadoxine / Pyrimethamine (Fansidar)

Fansidar resistance P. falciparum is widespread in S.E.Asia. In Thailand P. falciparum is totally resistant to Fansidar. In some areas of Africa P. falciparum is still sensitive to the drug. It can cause skin rash, hepatitis, bone marrow depression and gastro-intestinal symptoms.

Quinine was introduced in the 17th century and is still very effective. It is the drug of choice for severe chloroquine resistant falciparum malaria, but there is decreased sensitivity and in some cases total resistance along the Thai Myanmar and Thai Cambodia borders. Its side effects are tinnitus, vertigo, nausea, vomiting, phlebitis, hypoglycaemia and can cause cardiovascular collapse.

Mefloquine was introduced in 1980. It is used for treatment and chemoprophylaxis. Problems are side effects which occur more during treatment than in prophylaxis. It has a long half life (15 -33 days) and side effects affect fairer skin people more than those with darker skin. They are giddiness, psychosis, anxiety state, hallucinations, bradycardia and arrhythmias. It can be used up to 3 years as prophylaxis in non-immune persons[9] and is also safe in all trimesters of pregnancy. Total resistance has occurred on the Thai-Myanmar and Thai-Cambodia borders. It is not recommended in patients with epilepsy, psychiatric disorders and cardiac conduction abnormalities.

Halofantrine

Halofantrine acts against asexual forms of multiple drug resistant falciparum malaria. Declining efficacy is due to wide individual variation in drug absorption which relies on heavy food and fat intake. Bioavailability is increased with fatty foods. Main concern of this drug is prolongation of the QT interval. It is dose dependent. Sudden deaths have occurred with this drug. An improved formulation Lumefantrine is being assessed.

Artemisinin (Qinghaosu)

A herbal medicine known in China for 2000 years for treating fevers and "rediscovered" in 1971. The drug is extracted from the leaf of the Chinese weed (Artemisia annua) or sweet wormwood. It is also used as flavouring in vermouth. Artemisinin is the most active of the antimalarials, acts rapidly, shortens coma, fever and unrelated to existing antimalarials. It acts rapidly against the malarial trophozoite, rings and gametes.

In humans no obvious toxicity has been detected in the doses used, but high doses in animals can cause haemopoietic, cardiac and nervous system toxicity.

Other derivatives of artemisinin are artesunate, artemeter and arteether. These are available in parenteral forms, tablets and suppositories. Artemesinin if used as a monotherapy has a high rate of recrudescence. It is best to combine it with another drug with a longer half life eg. Mefloquine.

Malarone (Atovaquone and proguanil hydrochloride)

Atovaquone is a broad spectrum antiparasitic drug used for treatment of opportunistic infection eg. toxoplasmosis, pneumocystis carinii pneumonia in the acquired immunodeficiency syndrome. In combination with proguanil, it has excellent results in multiresistant P. falciparum infection.

Treatment of P. Falciparum

P. falciparum has developed resistance to most antimalarials in use especially in Thailand, but the parasite is still sensitive if drugs are given in combination. Common combinations are Quinine-Tetracycline, Artesunate-Mefloquine. In the Thai Myanmar border, there is resistance to all the known antimalarials. Newer combinations being used are Artemeter-Lumefantrin, Atovaquone-Proguanil. Other drugs being tested are dihydroartemisinin, pyronaridine, INR 238605, arteether and etaquine.

Malaria Drug Resistance

Resistance to antimalarials is thought to arise from several point mutations of the malaria parasite gene, giving the mutants a survival advantage in the presence of antimalarial drugs. This is particularly so with the lethal variety P. falciparum. The characteristic of a drug that makes it vulnerable to development of resistance is a long half life, a shallow concentration effect and with one or two base pair mutation that confirm a reduction in susceptibility to antimalarials. Development of resistance can be delayed or prevented by drug combination. The artemisinin derivative is the most potent and reduces the parasite biomass by about 10,000 fold per asexual life cycle to a level when host defences or another drug can clear the infection.[10]

Types of resistance in Malaria[11]

RI Disappearance of parasites on blood film with clinical recovery.
Recrudescence weeks later (within 28 days of last treatment dose)

RII Reduction in parasitaemia
(>75% fall in 48 hours) parasitaemia does not clear within 7 days.

RIII No response to treatment (at 48 hours)
Parasitaemia does not fall by > 75%.

Preventing Mosquito Bites[12]

No prophylactic drug is totally effective against malaria. In area where transmission is low, the risk of adverse reaction from prophylaxis may exceed the risk of infection.

1. Wear long sleeved shirts, long pants and a cap if possible.

2. Apply insect repellent Deet to exposed skin. (N.N diethylmetatoluamide)

3. Do not swallow or get into the eyes or rub on open wounds.

4. Use concentration of 30 -35%. It can last for 4 hours, but concentrations among repellents can be up to 95%. A review of Deet toxicity, topical application, only 2 cases of systemic toxicity in adults and 13 cases of toxic encephalopathy in children were reported despite 40 years of extensive use.

5. Spray living areas and sleeping areas with an insecticide to kill mosquitoes.

6. Use a mosquito permethrin impregnated bed-net and spray permethrin on clothes.

7. Sleep in air-conditioned room.

Using all these preventive measures reduces the risk of malaria to about half compared to travellers taking no precautions.

Malarial Prophylaxis

It must be emphasized when prescribing antimalarial prophylaxis, no antimalarial drug is completely effective, and should a fever develop it could still be malaria, and can occur as early as 6 days. Prophylaxis prevent multiplication of parasite in circulating red cells. Once infection emerges from hepatic incubation the drug blocks clinical illness. Start 1 -2 weeks prior to departure, so unexpected effects can be detected and therapeutic concentration is present on arrival. Continue for four weeks after leaving malaria endemic area. Travellers who sustain many bites or are long time residents of malaria areas may harbour occult malaria. The hypnozoite stage can mature from hepatocytes, weeks, months or years after leaving the area.

All drugs available today for malaria prophylaxis have adverse side effects. Due to the seriousness of malaria, it is best to tolerate the temporary side effects, if not another drug is prescribed so they do not remain without protection for the rest of the journey. The decision travellers often take with regard to antimalarial drugs is often based on folklore hearsay rather than sound advice. This ineffective treatment included

(1) homeopathy

(2) using electronic buzzers

(3) alcohol

(4) ingestion of garlic etc.

Advice should be given by well informed professionals who are familiar with the guidelines of malaria prophylaxis, rather than acquaintances or media who may not give a balanced public health message; keeping to a recommended prophylactic regime is better than non-compliance or irregular prophylaxis, and should malaria be contracted the severity may be attenuated.

Mefloquine is the most likely prophylactic drug prescribed (except on the Thai-Myanmar-Cambodia border where there is P. falciparum resistance and doxycycline is used), as there is no other drug as effective at present. After careful assessment of the risk in chloroquine sensitive areas, chloroquine alone or chloroquine and proguanil can be given. The later combination is more effective in Africa rather than in Asia, but has more side effects. Comparing the incidence of serious side effects (life threatening, severe disability resulting in admission), between the administration of chloroquine and proguanil or mefloquine is 1:13,000 and 1:10,000 respectively. Trivial side effects were similar for both regimes, but there was an excess of gastrointestinal side effects with chloroquine and proguanil.[13]

Use of prophylaxis for inhabitants of malarious areas is controversial, but is generally agreed pregnant women should take antimalarial prophylaxis. Pregnant women should avoid travel in pregnancy, especially in the second and third trimesters as they are prone to severe malaria, often complicated by pulmonary oedema, hypoglycaemia, prematue labour and foetal death due to placental insufficiency. Pregnant women living in multiresistant areas should have blood films done weekly. In pregnancy, mefloquine, chloroquine, pyrimethamine, proguanil and quinine are safe and sulphonamides are safe until term (there may be risk of kernicterus in the newborn.)[14, 15]

In severe malaria the most resistant P. falciparum is on the eastern and western borders of Thailand. The efficacy of quinine declining has led to the use of artemesinin derivatives in pregnant Karen women. Artemesinin is safe in the 2nd and 3rd trimester, but a small series followed up there showed it may be safe even in the 1st trimester.[16] Recently there is a report of resistance to artesunate in 2 cases.[17]

Standby Treatment For Malaria
(depends on locations)

The following drugs are for travellers not taking prophylaxis who suspect they have contracted malaria, in chloroquine resistant areas.

a) Mefloquine

b) Sulfadoxine-pyrimethamine (Fansidar) or plus Mefloquine.

c) Quinine

d) Artesunate

e) Malarone (atovaquone and proguanil)

The should seek medical evaluation after taking standby treatment as such treatment is only a temporary measure.

G-6PD-Deficiency

Primaquine is used to eradicate latent malaria (P. vivax and P. ovale) incubating in the liver. Primaquine-resistant strains however, have been reported from Iran Jaya, Papua New Guinea and Ecuador.[18] In patients with G-6-PD deficiency primaquine can cause haemolysis.

Haemolysis is usually related to severity of deficiency and quantity of primaquine given. The severity of haemolysis varies in different races when G-6-PD deficiency is mild as in the African races, a standard course of primaquine can be given. In the Mediterranean and some Asian variants, haemolysis can be severe.

Primaquine should not be given to patients with a history of previous haemolysis or haemolysis with quinine. Care should be taken if primaquine is given to patients with G-6-PD deficiency of 10% or less on quantitative analysis. Haemoglobin and urine for haemoglobinuria should be monitored, but mild G-6-PD deficiencies should be treated to eradicate the infection together with regular monitoring. (N.J. White Personal Communication). Tefenoquine a 5 – phenoxyprimaquine is a new drug undergoing trial which should improve the radical treatment of P. vivax infections.[19]

Malarial Vaccines

Development has been long and arduous with many pit-falls, research has concentrated on the different stages of the life cycle of the parasite. The problems encountered are polymorphism of malaria antigens, parasite induced immunosuppression. At the present time these vaccines will not give complete or lasting protection, but may be to attenuate infection and prevent death. Further research is needed.

Conclusion

There has been a resurgence of malaria in many countries in S.E.Asia, parts of Africa and South America due to climatic changes, economic and political upheaval resulting in decreased health spending, poverty and migration of people from

social disruption. With improved techniques eg. the acridine orange staining method and polymerase chain reaction, it has been shown that all the species causing human malaria are now present in S.E.Asia.

Hybridization has been detected among species especially P. malarie and P. vivax and is now under study.

The Thai-Myanmar and Thai-Cambodia border areas continue to be monitoring zones for drug assessment in the changing patterns of multi drug resistance to P. falciparum. In some of these places, resistance has occurred to all the known drugs in use. Increasing insecticide resistance is also a threat.

The artimisinin compounds is now established as the most potent and active of the antimalarial drugs with very low side effects. Combination treatment for P. falciparum infection should always be used to prevent development of resistance. Mortality in malaria is reduced by early detection and treatment.

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The Singapore Family Physician

Travel Vaccinations: an insight on some difficult vaccine decisions

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Introduction

The average traveller today is educated, well informed of potential health risks and more aware of the need for prevention and prophylaxis against travel related infections. Much of this awareness is promoted by the multitude of web-sites on travel medicine and the ease of information retrieval on the Internet. It is increasingly more demanding on the travel medicine practitioner to keep abreast of new information, new vaccine development and emerging infectious diseases all over the world. Fortunately, there are very useful publications, web-sites and information sources that help us discharge the demands of this job.

The area of travel vaccinations has always been a "grey area" for many family physicians. The aim of this article is to look at some of the more difficult vaccine decisions and their indications in travellers. The price of prevention is not cheap and many travel vaccinations are not as cost-effective as childhood vaccines used in National Immunisation Programmes.

In general, travel vaccines may be broadly classified into 3 main categories : (what we call the 3 "R"s)

1. ***Routine*** : These are vaccines we have received in childhood (e.g. oral polio vaccine, tetanus toxoid, mumps, measles, rubella vaccine, diphtheria vaccine, etc). Routine boosters are recommended for normal maintenance of health e.g. a tetanus booster is recommended every 10 years even if one is not travelling.

2. ***Required :*** The only required vaccine as regulated under the International Health Regulation (World Health Organisation) is yellow fever vaccine. An international certificate of vaccination against yellow fever issued by a WHO designated vaccination centre is required for entry or re-entry if a traveller had been in a yellow fever endemic region.

3. ***Recommended :*** Travel vaccines not in the above 2 categories are broadly classified into this category. These vaccines are recommended based on relative risks of the traveller acquiring the infection during travel e.g. typhoid, Japanese encephalitis, rabies, etc. These vaccines are not required for movement across borders but would be recommended if the traveller has a significant risk of being exposed to these infections based on their pattern of travel, life-style practices, season of travel or duration of travel.

Since the first 2 categories are quite clear-cut, it is the last category of vaccines that we will be discussing in this article. For the purpose of discussion, I have chosen 4 vaccines and will highlight their indications in the context of travel. These are rabies vaccine, Japanese encephalitis vaccine, meningococcal vaccine and last but not least, I will discuss the controversy of varicella vaccine - is it a travel vaccine ?

Rabies vaccine

Rabies is an acute fatal viral encephalomyelitis. It is endemic in most parts of the world including many developed countries. The disease is difficult to control and eradicate because it exists in extensive animal reservoirs including dogs, bats, racoons, skunks, foxes, wolves, coyotes, and has been reported in bears, cats, tigers, cattle, etc. Although canine rabies is prevalent in many developing countries, the epidemiology of the disease in animals varies from region to region. As the vaccine is relatively expensive, it is not recommended in routine vaccination of all travellers to rabies endemic regions. It was estimated that routine use of rabies vaccine for all US travellers to Thailand, where rabies is endemic, would cost US$50 million per rabies

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death averted. This is clearly not cost-effective and hence, rabies vaccination will need to be guided by indications. For international travellers, recommendations are based on local incidence of rabies in the destination country, the availability of anti-rabies biologics, the duration of travel (if > 4 weeks, the longer the duration of exposure, the higher the risks) and the intended activities (e.g. outdoor activities and contact with animals). Indications are therefore based on risks and not on destination alone.

The current indications for rabies immunisation are :

1. Continuous exposure to high concentrations of virus : These include rabies virus research laboratory workers and production workers in rabies biologics.

2. Frequent exposure usually episodic but sometimes exposure may be unrecognised : These include rabies diagnostic laboratory workers, spelunkers (cave explorers - bats exposure), veterinarians, vet students and staff, animal control workers and animal handlers, wildlife park workers in rabies epizootic areas.

3. Infrequent exposure (usually episodic) : This category may include travellers to areas where rabies is enzootic and immediate access to medical care including vaccines may be limited.

4. Rare exposure : This includes the population at large. No pre-exposure immunisation is necessary but medical evaluation of animal bites is necessary to assess the need for post-exposure immunisation.

5. Pre-exposure immunisation may be indicated where there is a possibility of an unrecognised exposure (e.g. in young children who are unable to report an exposure) or when post-exposure treatment may be delayed or unavailable. In some developing countries, locally available vaccines may carry a high risk of adverse reactions.

In general, however, all travellers to rabies endemic region should be educated about rabies risks and the need for medical evaluation in all cases of animal bites regardless of their rabies vaccination status. It must be emphasised that pre-exposure rabies immunisation does not eliminate the necessity for post-exposure treatment in case of a bite. For immunised persons, you will need 2 boosters as well as wound management, possibly a tetanus booster and antibiotics. For the unimmunised, you may require rabies immunoglobulin as well as a series of 5 rabies immunisation shots.

For more information on the epidemiology of rabies, you may refer to the web-site at WHO or RABNET.

Japanese encephalitis vaccine

Japanese encephalitis (JE) is an acute viral encephalitis that is caused by a mosquito-borne arbovirus. The disease is endemic in many parts of rural Asia including China, Japan, Korea, Indochina, Nepal, Indian subcontinent, Oceania and Southeast Asia. The case fatality is about 30% and neurologic sequelae are reported in about 50% of survivors.

Transmission is seasonal and vary with the rainy season (mosquito breeding season) or irrigation practices. The risk to short term travellers (< 4 weeks) who confine their travel to urban centres is generally very low. A knowledge of JE endemic areas and the season of transmission is crucial to the vaccination decision making process. (See reference). The vaccine can be associated with mild local and systemic side effects in up to 20% of vaccinees and serious allergic reactions in 0.6% of vaccinees. Serious adverse reactions have been reported up to one week after vaccination and vaccinees should be warned of delayed reactions. Persons with multiple allergies and a past history of urticaria appear to be at a higher risk for serious allergic reactions to the vaccine and the risks - benefits of the vaccination should be weighed carefully.

The decision for vaccination should take into account the endemicity of the disease, the duration of travel, season of transmission as well as the

activity of the traveller. In general, travellers with extensive outdoor activities (hiking, camping, biking), staying in rural areas during transmission season are at high risk even if the trip is brief but the risk is higher if the duration of exposure increases. Long term travellers (> 30 days) to endemic areas or relocating families may consider vaccination because of the duration of exposure. JE vaccination is part of the Childhood Immunisation Programme in certain countries e.g. China, Taiwan, Thailand, etc.

Meningococcal vaccine

Meningococcal disease is an acute bacterial infection characterised by sudden onset of fever, headache, nausea and vomiting and frequently with a petechial rash or macules on the lower limbs. It is associated with high mortality if not diagnosed or treated early.

Meningococcal vaccination is required for all pilgrims going on Haj or Umrah to Mecca, Saudi Arabia but it is not a requirement for entry into any other countries.

Serogroup A is responsible for most of the epidemics but serogroup C and B have also been implicated. There are 2 polysaccharide vaccines available : the first one is a bivalent (against serogroups A & C) and the other is a tetravalent vaccine (against serogroups ACYW-135). There is no commercially available vaccines against serogroup B. Polysaccharide vaccines are safe and immunogenic in adults but they are not recommended for children under the age of 2 years as the antibody response is suboptimal. A new conjugate meningococcal vaccine is being developed for use in children and will appear on the market in the near future.

The current indications for meningococcal vaccination are as follow :

1. Travellers to the sub-Saharan meningitis belt extending from Mali eastwards to Ethiopia. Epidemics of serogroup A and C meningococcal disease occur frequently during the hot dry season from December through June.

2. Pilgrims going to Mecca, Saudi Arabia for the performance of Haj or Umrah

3. Travellers to any area experiencing an outbreak of meningococcal infection should be vaccinated - travel advisories will be issued in such circumstances.

4. College students residing in dormitories or institutions that have experienced sporadic outbreaks of meningococcal disease are also advised to have vaccination.

5. Individuals who have complement deficiencies or who had splenectomies are also at risk for meningococcal disease and should be vaccinated.

6. There is also a place for post-exposure prophylaxis with antibiotics in conjunction with the use of vaccination.

Varicella vaccine - is it a travel vaccine ?

Varicella infection or chickenpox is a mild self limited viral disease of childhood and sometimes of adults. In many developed countries, the majority of children have antibodies to varicella and are immune. However, in many rural communities and developing countries, many young adults are not immune to the disease and chickenpox is a disease of adults. There is also a low level of herd immunity in these communities. Therefore, if the traveller is non-immune to varicella and if the trip is a long one, the risk of contracting chickenpox is a real one. This is particularly so if the traveller has close contact with the local community.

The other downside of getting chickenpox during travel is that you lose precious travelling time and may need to be isolated from your other travelling mates. In the worst case scenario, you may be admitted to a local hospital with sub-optimal conditions and subjected to nosocomial risks and medical mis-management. You may also be at risk for complications of chickenpox like encephalitis and pneumonitis requiring air evacuation to a tertiary medical centre or back home which may set you back substantially in terms of costs unless you have medical evacuation insurance coverage.

Hence, it may be prudent to determine the varicella immunity status before you embark on long term travel and get vaccinated if you are non-immune. It will save you much hassle in terms of trip disruption and costs of acute medical care in the event of an infection.

Conclusion

These so-called difficult vaccine decisions are actually made less difficult if one tries to understand the epidemiology of these diseases and their transmission patterns. All vaccine decisions must be based on risks and not on destinations because no two travellers are at the same risks even if they are going to the same country. We need to understand the traveller's pattern of travel, season of travel, activities, duration of travel, level of contact with the local population and last but not least, his or her medical background. As in all good medical practice, taking a detailed history is the basis for all sound clinical decisions.

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The Singapore Family Physician

Prevention of Malaria in Travellers

Wong Sin Yew

Introduction

Malaria remains the leading cause of death from an infectious disease amongst travellers. This is a very tragic fact as malaria deaths are in most cases preventable. Malaria prevention can be divided into two main components :

1. Chemoprophylaxis

2. Personal Protective Measures

It must be emphasised that a third component involving patient education, in particular symptom education (of the disease) is incorporated into chemoprophylaxis and personal protective measures.

Travel medicine practitioners should be familiar with the signs and symptoms of the disease, the epidemiology of malaria, geographic pattern of the disease, commonly used anti-malarial prophylactic agents and their side effects, in order to advise travellers appropriately. The two most commonly used sets of evidence-based guidelines for recommendation of chemoprophylaxis are :

1. World Health Organisation (WHO) guidelines, contained in the book "International Health & Travel" which is updated annually and

2. Centres for Disease Control (CDC, Atlanta) guidelines published in the book "Health Information for International Travel" printed every 2 - 3 years.

(These publications contain country specific recommendations for malaria chemoprophylaxis as well as detailed description of regions within the country. The information is updated regularly.)

In this article, we will discuss the goals of prevention, the commonly used drugs and their side effects and some common errors in management of malaria prevention.

Who should receive prophylaxis ?

Malaria chemoprophylaxis should not be given routinely to all travellers to the tropics. Many of these drugs are expensive and have associated unpleasant side effects and therefore should not be prescribed without good indications. Unjudicious use of malaria chemoprophylaxis can also be dangerous to certain populations of travellers e.g. pregnant travellers, those with epilepsy, psychiatric disorders, G6PD deficiency, cardiac problems, etc.

In general, malaria risks are minimal in major cities, urban centres and tourist resorts with the possible exception of India where there is significant urban transmission of disease. Malaria prophylaxis should not be recommended for travel to most large urban centres in Southeast Asia, for instance. There is no risk of transmission at an altitude of 2,000m above sea level. However, malaria transmission can also be very focal and restricted to certain locales, hence it is impossible to predict accurately at all times the risks of malaria. We all tend to err on the side of safety in situations where there are no data to assist us.

Pre-Travel Malaria Advice : What are the goals ?

The primary goal is to identify the high risk traveller and recommend prophylaxis to him/her with the appropriate anti-malarial agent. This would involve a detailed history taking of the pattern of travel, the intended activity, the living conditions, the season of travel and the duration. (rainy season = mosquito breeding season but dry season has been associated with mosquito-borne diseases because of water storage and irrigation practices).

The second goal would be to identify drug intolerance and adverse effects from chemoprophylactic agents. For this, the traveller will need to consult his doctor ahead of time before his intended trip. In general, travellers are

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advised to visit their doctor 4 - 6 weeks before departure to allow them to complete their vaccinations and for adequate protective antibodies to develop. This lead time will also allow travellers to try out anti-malarial agents for side effects and to switch to an alternative in case of an adverse reaction. Anti-malarial prophylaxis has to be commenced at least 1 week before entering the malarious zone to allow time for achieving adequate drug levels as well as to identify drug intolerance.

The pre-travel malaria advice should also include patient education on personal protective measures against mosquito and insect bites as well as symptom education on malaria. The importance of early diagnosis and treatment cannot be overemphasised because much of the mortality from malaria is due to delayed diagnosis and delayed treatment or sometimes, failure to diagnose.

In exceptional circumstances, the doctor may also prescribe stand-by treatment for the traveller in case of breakthrough infection while on chemoprophylaxis or if the patient is not on chemoprophylaxis, for other reasons.

Common Errors

Some of the common errors encountered in pre-travel malaria advice include :

1. Inappropriate chemoprophylaxis recommendation
2. Failure to obtain an accurate travel history
3. Failure to report drug intolerance leading to non-compliance
4. Failure to address the importance of personal protective measures
5. Omission of symptom education of malaria

The traveller must also understand that there is no anti-malarial chemoprophylactic agent that will give complete protection against malaria and that full compliance with their chemoprophylaxis regimen together with the practice of PPM (see below) will afford a high degree of protection against malaria.

Personal Protective Measures (PPM)

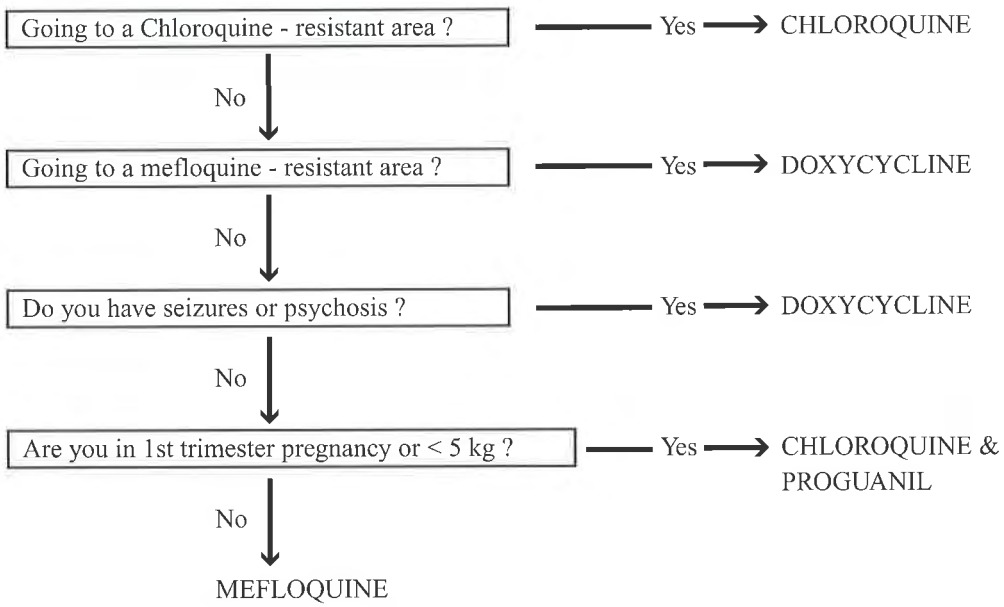
In general, any traveller who is recommended chemoprophylaxis against malaria or who is at risk for insect/mosquito-borne diseases should be instructed on PPM to minimise their exposure to bites.

In general, PPM would include the following :

1. Avoid being outdoors between the hours from dusk to dawn as this is the feeding times of malaria causing Anopheles mosquitoes.
2. Use an insect repellent containing N,N-diethyl-3-methylbenzamide (DEET) on exposed skin while outdoors
3. Wear long sleeved shirts and long pants to prevent bites
4. Use permethrin to treat bed-nets and clothings if going to heavily infested areas.
5. Burn pyrethrum containing mosquito coils
6. Sleep in air-con rooms with windows shut
7. Use fine wire-net window screens

Decision Tree in Malaria Prophylaxis

The following algorithm will summarise steps in arriving at the choice of an anti-malarial agent for chemoprophylaxis :



NB : To use this algorithm, you will need to know the map of malaria zones. There are 2 areas with Mefloquine-resistant malaria viz; Thai-Myanmar border and Thai-Kampuchea border where Doxycycline would be the agent of choice for chemoprophylaxis.

Some Commonly Used Chemoprophylactic Agents

According to the WHO guidelines, the 4 most frequently used malaria chemoprophylactic regimens are :

1. Chloroquine
2. Chloroquine / Proguanil in combination
3. Mefloquine
4. Doxycycline

Chloroquine

Chloroquine is still the anti-malarial of choice in chloroquine-sensitive areas e.g. North Africa, Carribean, Central America, temperate South America and parts of the Middle East. The dose is 500mg salt (300 mg base) once a week starting one week before travel, weekly while in malarious area and for 4 weeks after returning. The main side effects are gastrointestinal upset, dizziness, blurred vision and itching. It should be used with caution in patients with a history of epilepsy, psoriasis or cardiac problems. Long term usage of chloroquine will require ophthalmologic screening for retinopathy.

Chloroquine / Proguanil

Proguanil is not used alone for prophylaxis of malaria because of the rapid development of resistance. The combination of weekly Chloroquine with daily proguanil has been shown to be effective in the prophylaxis of malaria in Africa but this combination is inferior to mefloquine or doxycycline. However, it is safe for use in both pregnant travellers and children. The dose of proguanil is 200 mg daily combined with chloroquine 500 mg (salt) weekly, starting one week before travel, weekly (daily for

proguanil)while in the malarious area and for 4 weeks after returning. The main side effects are due to the chloroquine component and are as described above. A newer formulation containing a lower dose of chloroquine (100 mg)combined with the usual dose of proguanil (200 mg) in one tablet and taken daily is available in some overseas countries. This newer daily formulation has been reported to be more effective than once weekly chloroquine + daily proguanil.

Mefloquine

This is the anti-malarial of choice in chloroquine-resistant areas. The dose is 250 mg once a week starting one week before departure, weekly while in malarious area and for 4 weeks after returning. The main side effects are gastrointestinal upsets, dizziness, nightmares, disturbance of concentration, neuropsychologic and neuropsychiatric effects (one study reported incidence of 1 : 13,000). It should be used with caution in the first trimester of pregnancy, cardiac arrthymias, beta blockers, calcium channel blockers and contraindicated in those with epilepsy and psychiatric disorders.

Doxycycline

Doxycycline is the anti-malarial of choice for chemoprophylaxis in regions where there is a high incidence of mefloquine resistance viz; the Thai-Myanmar and the Thai-Kampuchea border areas. It is the alternative to weekly mefloquine if the traveller is unable to take mefloquine for whatever reason but is slightly less efficacious than mefloquine in Africa and tropical South America. The usual dose is 100 mg daily, starting 1 week before travel, daily while in the malarious area and for 4 weeks after returning. The main side effects are gastrointestinal upset and photosensitivity. It is contraindicated in children less than 8 years old and in pregnancy and breastfeeding. The traveller should be instructed to use sunscreen with it, not to take it with milk and about the risk of vaginal thrush with prolonged usage because it is an antibiotic.

Conclusion

The key to giving good pre-travel malaria advice lies in knowing your malaria facts well, including malaria regions, commonly used anti-malarial agents and their side effects and answering your travellers' frequently asked questions on malaria prevention. Invaluable to the travel medicine practitioner would be evidence based guidelines like the WHO or CDC guidelines on malaria chemoprophylaxis recommendations.

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The Singapore Family Physician

Screening for Colorectal Cancer

Kum Cheng Kiong

Introduction

Colorectal cancer is the third most common malignant neoplasm worldwide. In Singapore, incidence has been increasing steadily over the last decade. It is now the most common cancer in Singapore if the incidence of both sexes is taken together. In males, the incidence of about 37 per 100,000 is second only to lung cancer. In females, the incidence of about 29 per 100,000 is second to breast cancer. The aetiology of colorectal cancer is a complex interaction between inherited susceptibility and environmental or lifestyle factors. Although, in many countries, the incidence of colorectal cancer correlates positively to the national consumption of meat and fat, and negatively with vegetables, it is unlikely that dietary modifications alone will be effective as a primary prevention tool. There are just too many other factors involved. Even in vegetarians who do not consume meat, the reduction in colorectal cancer mortality is only modest. Thus, screening (secondary prevention by detecting asymptomatic patients in the early stages) is the next best way to reduce mortality.

Widespread screening for colorectal cancer is justifiable as:

1. it is a common cancer with rising incidence
2. detection at an early stage can improve prognosis
3. suitable screening tests easily available

Why should we be screening?

The majority of patients present late. The 5-year case fatality rate is 50%. Screening would detect cancers at the earlier stage. The benefits of earlier diagnosis include:

1) the possibility of avoiding major surgery
2) the likelihood of preserving the sphincters and thus quality of life
3) the possibility of using the laparoscopic approach with its attendant benefits of earlier recovery.
4) improvement of survival rate from the current average of 50% at 5 years to 80% in rectal cancers and 90% in colonic cancers found in the early stages. Colorectal cancers screening trials in US and Europe have effectively reduce the mortality by 15 to 33%. (Table 1)

Table 1. Randomised trials of faecal occult blood test

	Compliance	Duke's stage Screened group	A /B Controls	Decrease in mortality in screened group
Denmark[1]	67%	81%	46%	18%
Sweden[2]	65%	68%	36%	-
US[3,4]	90%	59%	53%	33%
UK[5]	10%	71%	44%	15%

Who to screen?

There are several distinct categories of patients who are at a high risk of having colorectal cancer and they should have already been on a screening program by the hospitals. They include patients with:

1) Familial adenomatous polyposis (<1%)
2) Hereditary non-polyposis colorectal cancer (4-6%)
3) Patients with a past history colon cancer or adenomas
4) Patients with long standing ulcerative colitis or Crohn's disease.

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There is another category of patients with an increased risk compared to the average population. These patients may be missed out in a hospital-based screening program. Here is where family physicians can play an important role in identifying, educating and performing clinic-based screening. These patients include those with:

1) a first degree relative with colorectal cancer, especially if the relative was diagnosed before the age of 50 years (Table 2)

2) a history of ovarian, endometrial or breast cancer.

Table 2. Lifetime Risks of Colorectal Cancer

Population Risk	1 in 50
One 1st degree relative	1 in 17
One 1st degree relative less than 50 years	1 in 10
Two 1st degree relatives	1 in 6
Three 1st degree relatives	1 in 2

In addition, the family physician would be the most cost effective person to screen the average population with no known risk factors. This is an important group of patients as 75% of colorectal cancers are sporadic cases- where the patients are the first in the family to be diagnosed.

How to screen?

There are several screening strategies. The most practical screening method for family physicians would be the faecal occult blood test (FOBT). There are many commercial test kits available, e.g., Haemoccult, Haematest, Haemaplus, etc. They are mostly based on the principle of oxidation of a phenolic compound by haemoglobin to a quinolone compound that is manifested by a change in colour. This is an inexpensive, rapid and simple test that is available in almost all the laboratories locally. There are some kits that allow the patients to test on their own at home (just like pregnancy kits), but these are not sold locally.

False positive results (2 to 5%) may occur in the presence of upper gastrointestinal bleeding, bleeding from haemorrhoids, ingestion of non-steroidal anti-inflammatory drugs (NSAID), and ingestion of meat or uncooked vegetables that may contain compounds that catalyze the change in colour. In order to improve on the specificity of the test, the patient should be advised to avoid meat, fish and uncooked vegetables for 3 days prior to the test. They should also be advised to stop any NSAID or aspirin for the same period. To decrease the false negative rate, send 2 specimens of faeces from 3 consecutive stools. (Table 3)

Table 3. Screening for colorectal cancer

Ask for change in bowel habits, bleeding per rectum, abdominal pain

Avoid meat, fish and uncooked vegetables for 3 days prior to the test.

Stop any NSAID or aspirin for the same period.

Collect 2 specimens of faeces from 3 consecutive stools.
Send to laboratory

If positive, refer for further evaluation by specialist

If negative, repeat one year later

When to screen?

Patients with a family history
Annual faecal occult blood test from the age of 40.

Patients with no known risk factor
Annual faecal occult blood test from the age of 50. (Most cases are diagnosed after 50 years old).

What results to expect?

About 5% of patients that you screened will test positive for occult blood in their stool. These patients should be referred for a colonoscopy or a double contrast barium enema. Colonoscopy is preferred as it can detect small polyps and allow biopsy of suspicious lesions. However, it is more expensive.

A full colonoscopy is recommended instead of just a sigmoidoscopy. Although a majority of cancers occurs in the rectum and left side of the colon, a significant proportion of about 25% are located in the right and transverse colon. For patients with positive FOBT who undergo colonoscopy, 5 to 10% will have colorectal cancer. Another 20 to 30% will have a polyp. The rest have other minor pathologies.

Is it cost effective?

In an analysis by health management organisations in the US, in terms of dollars per life year gain, screening for colorectal cancer is much more cost effective than breast cancer screening, cervical cancer screening and heart transplantation.

Future developments

With greater public awareness of colon cancer, response to screening is expected to rise. Less invasive methods of screening such as CT-colonoscopy and MR-colonoscopy is being developed that will also increase the public's willingness to come forward. Genetic testing is also being refined and standardized. It would allow us to select family members who are at higher risks for more intensive screening.

CONCLUSION

Majority of colorectal cancer are diagnosed in the advanced stages. In the absence of an effective prevention strategy, screening would be the most cost-effective way of reducing mortality. High risk patients are being monitored by the hospitals. The majority of patients with colorectal cancers are sporadic cases with no known risk. These average risk patients and patients with moderately increased risks are currently not being screened. General Practitioners would be in the best position to screen these patients with inexpensive faecal occult blood tests annually. It has already been established that screening alone can reduce mortality from colorectal cancer.

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The Singapore Family Physician

Abdominal Pain In Relation to Colorectal Diseases

Ballan Kannan

Introduction

"The Abdomen has been described as a magic box. You will never know until it is opened".

Abdominal pain tends to be poorly localized unless the parietal peritoneum is involved. The causes of abdominal pain are very wide and may cover an entire textbook of surgery. Even in relation to colorectal disease, they are still wide, as we know every disease can lead to abdominal pain at some point of the disease.

Type

In simple term it can be divided into acute or chronic types. The division is based on duration of pain.

Causes

The causes of abdominal pain can be divided as shown in Table 1.

Table 1

Causes		
a) Acute	(i) Inflammation	- Infective causes - Inflammatory bowel disease - Abscess
	(ii) Obstruction	- Tumours - Adhesions - Hernias - Others: Volvulus Intussusceptions Strictures
	(iii) Perforation	- Acute Diverticulitis - Tumours - Foreign body - Iatrogenic
	(iv) Ischaemia	- Acute Vascular Insufficiency Arterial Venous
b) Chronic	(i) Organic causes	- Diverticular disease - Tumour - Others
	(ii) Functional causes	- Irritable Bowel Syndrome

The pain of acute infective cause is usually sudden onset, colicky and generalized with associated bowel hyperactivity symptoms like diarrhoea. Inflammatory bowel disease also presents with poorly localised abdominal pain but may be associated with bloody diarrhoea. When the pain is diffuse and associated with distension, vomiting and absolute constipation, there is no doubt of the diagnosis of acute intestinal obstruction. Similar features but chronic, intermittent in nature may be due to partial bowel obstruction.

If there is perforation of the bowel from whatever the underlying cause the clinical signs become more apparent and the patient needs urgent treatment. The perforation can be localized (sealed or walled off) or becomes generalized. There will be associated clinical parameters of sepsis like fever, raised white cells counts to general deterioration in conscious level.

Acute abdominal pain due to vascular insufficiency is always a tricky diagnosis because of lack of clinical signs. One should have a high index of suspicion especially when dealing with elderly patient with acute onset of poorly localized abdominal pain with or without per rectal bleeding. They may have predisposing factors like Atrial fibrillation on anticoagulants.

As far as chronic abdominal pain, one should rule out first any underlying organic cause. The pain due to colorectal neoplasm is typically described as non-specific, dull and poorly localized. Chronic diverticular disease can lead to abdominal pain due to spasm of the hypertrophied colonic smooth muscle.

Once an organic cause is ruled out, the diagnosis of irritable bowel syndrome is a diagnosis of exclusion and the treatment is symptomatic.

Referral

All abdominal pains associated with peritonitis either localized or generalized or intestinal

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obstruction need immediate referral to the nearest hospital.

Chronic abdominal pain with features of underlying organic pathology also needs urgent referral.

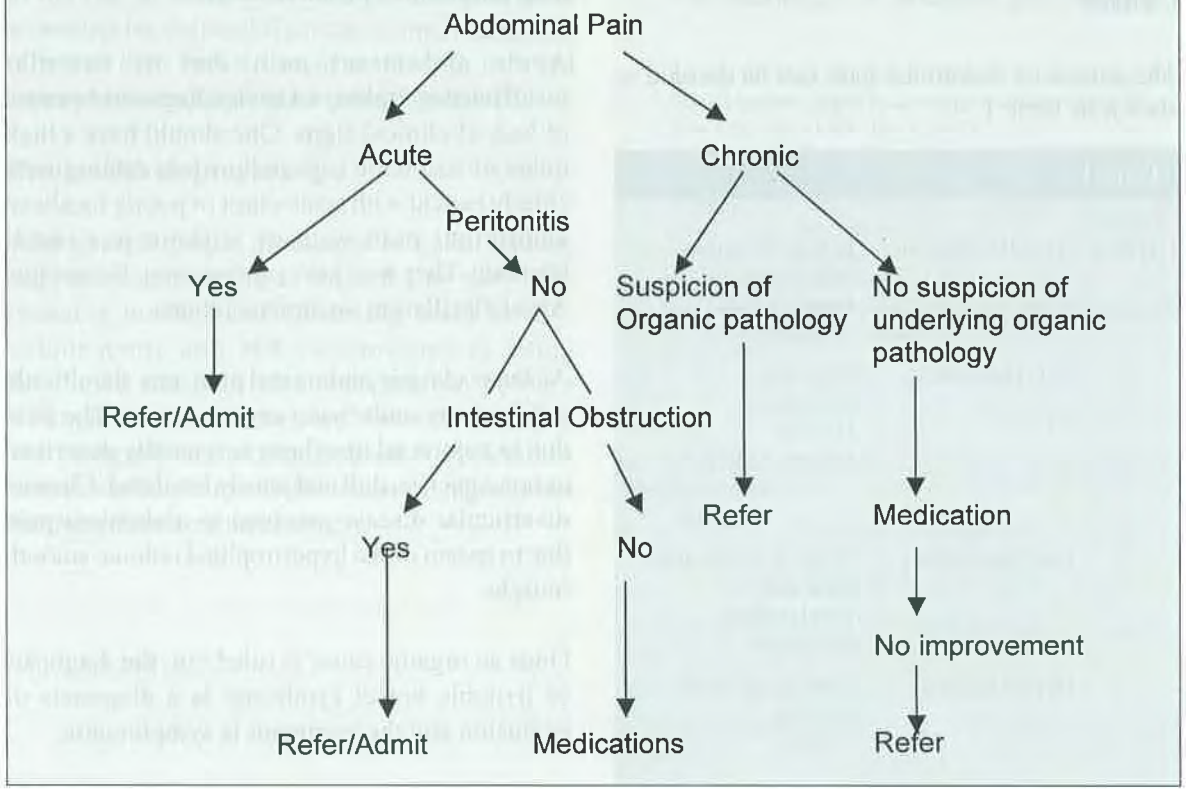
Finally, any abdominal pain which does not resolve with simple symptomatic medications will also need a referral to higher specialized institution.

Investigations

Besides the baseline investigations, abdominal pain suspected to be of colonic origin can be investigated in the clinic with the use of proctoscopy or flexible sigmoidoscopy. Even a full colonoscopy can be done as an outpatient procedure in the endoscopy room with or without sedation.

If acute diverticulitis is suspected, contrast radiography is the procedure of choice using gastrografin and not barium enema as it can lead to intense chemical peritonitis. CT scanning is also useful not only for the diagnosis as well as staging of the disease, it can also be used as a therapeutic procedure to drain intraabdominal abscess. A simple algorithm management of abdominal pain in relation to colorectal diseases is shown in Table II.

Table II: Algorithm



The Singapore Family Physician

Per Rectal Bleeding: When to Refer

SR Brown

Introduction

Bleeding per rectum can be from a variety of sites other than the rectum and even from outside the colon. The plethora of causes presents a diagnostic challenge to the family physician. On one hand the majority of cases are due to a benign cause (usually anal canal type bleeding from haemorrhoids). On the other hand rectal bleeding can be a symptom of a colorectal carcinoma, requiring urgent hospital investigation and treatment. A detailed history and abdominal examination (to include a per rectal exam) may elicit the cause of the bleeding. However, there should be a low threshold for hospital referral when patients present with certain symptoms or symptoms persist despite conservative management. The following article describes causes of per rectal bleeding as well as their symptoms and details when to refer for in hospital treatment.

Causes of Per Rectal Bleeding

When talking about causes of rectal bleeding it is useful to consider three subgroups. This acts not only as an aide-memoir, but also allows distinction of benign causes (usually anal canal type bleeding) from more sinister causes (usually colorectal bleeding). Table 1 gives these subgroups and the various causes. Each of these is considered in turn.

Table 1 Causes of rectal bleeding

Anorectal	Haemorrhoids Anal fissure Solitary Rectal Ulcer Syndrome
Colorectal	Neoplasia Diverticular disease Proctitis/colitis -Radiation -Crohn's/Ulcerative Colitis -Ischaemic -Infective (Campylobacter, E.Coli, TB)
	Angiodysplasia Endometriosis (Cyclical bleeding)
Others	Upper Gastro-intestinal - Oesophageal (varices) - Stomach/duodenum (peptic ulcer/erosions - Pancreas (carcinoma/ pseudocyst eroding into artery) - Small bowel (Meckel's, Tumours, Radiation, Crohn's) Haematological (Thrombocytopenia, Coagulopathies, Leukaemia) Drugs (Anticoagulants, NSAIDs, Steroids, Potassium tablets) Vasculitides (PAN, SLE, Henloch-Schöenlein Purpura)

Anal canal type bleeding

Haemorrhoids

Haemorrhoids are common. It is said one is not a Singaporean unless he or she has piles. Although many present with symptoms, the same anal cushions are found in normal individuals. Exactly what causes symptoms is not known, although constipation and abnormal bowel habit are often blamed.

Haemorrhoid is Greek for 'blood flow' suggesting the commonest form of presentation. Blood is classically bright red as the vascular cushions are arterovenous and bleeding is therefore arterial. Patients usually describe blood dripping from the anal canal, particularly after defaecation. However, this is not always the case and bleeding can occur before or even during defaecation, classically coating the outside of the motion and not mixed within it.

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A per rectal exam may be helpful when the haemorrhoids prolapse. Internal or first degree haemorrhoids cannot be detected by digital examination alone but can be diagnosed and even treated using a proctoscope to view the anal canal. It should be remembered that, as haemorrhoids are so common, they may occur with a lesion higher in the colon, which may be the true cause of the bleeding. Haemorrhoidal treatment alone should therefore be carried out with caution.

Anal fissure

An anal fissure is a tear in the lining of the anal canal. The cause is unknown but the tear is often posterior or occasionally anterior where the blood supply is poorest, suggesting an ischaemic component. The main symptom is pain, often out of proportion to the clinical findings. Patients may complain of bleeding classically smearing the toilet paper on wiping. The tear is often seen on gently parting the buttocks. Digital examination is usually not possible due to anal spasm and pain.

Solitary rectal ulcer syndrome

As the name suggests, this is not actually an anal cause of per rectal bleeding. Patients typically have an anterior mucosal prolapse into the anal canal giving the sensitive of incomplete evacuation. Persistent straining results in traumatisation of the prolapse apex and the resultant bleeding presents as if it were from the anal canal.

Colorectal bleeding

The group includes all bleeding from the colorectal mucosa. It is probably the most important group to diagnose as it contains the neoplastic causes.

Neoplasia

Colorectal cancer is one of the commonest causes of cancer related death with over 570,000 new cases diagnosed worldwide each year. Fortunately most cancers develop from pre-existing polyps and this transformation may take years. There is therefore a unique opportunity for curative treatment and, if diagnosed early enough extensive invasive surgery is unnecessary.

Colorectal neoplasia can present with rectal bleeding of many sorts depending on the site of the lesion. Low rectal lesions may imitate anal canal type bleeding. Often these lesions are palpable on digital examination. Higher lesions present with darker bleeding as the blood has been altered and mixed with stool before being passed. Right-sided lesions may not present with overt bleeding at all but the patient may have anaemia due to occult loss. It is useful to palpate the abdomen carefully in such patients as occasionally a mass from a right colon carcinoma will be felt.

Although the type of bleeding is variable, almost all patients will have associated symptoms such as altered bowel habit, abdominal pain or mucus per rectum. Anyone presenting with rectal bleeding of any sort associated with such symptoms should be assumed to have colorectal cancer until proved otherwise and referred for further investigation.

Diverticular disease

Diverticular disease, or out-pouching of the bowel wall may result in bleeding probably due to stercoral trauma to the delicate vessels at the apex or neck of the sac. The characteristic presentation of patients with diverticular bleeding is one of otherwise healthy individuals who get the urge to defaecate and suddenly pass a large amount of bright red or maroon coloured stool. With inflammation of the diverticulae there may be associated abdominal pain. As right-sided diverticulosis is more common in Asians this pain may be right sided, mimicking appendicitis.

Inflammatory colitis

Inflammation of the colon has many aetiologies. Most present all types of bleeding per rectum, alteration in bowel habit, abdominal pain and passage of mucus. Clues to the aetiology may be obtained by the asking about the length of the history, radiation treatment to the cervix, constitutional symptoms such as weight loss, and in the case of ischaemic colitis, a cardiac history and examination.

Angiodysplasia

One of the commonest causes of rectal bleeding is angiodysplasia. It affects older people and occurs due to degeneration of the mucosal vessels, which become dilated and fragile. Lesions tend to be right sided and present with intermittent, occasionally massive bleeding of various types.

Endometriosis

This is a very rare cause of per rectal bleeding occurring in pre-menopausal women and resulting in typically cyclical bleeding and associated with other symptoms of endometriosis.

Other causes

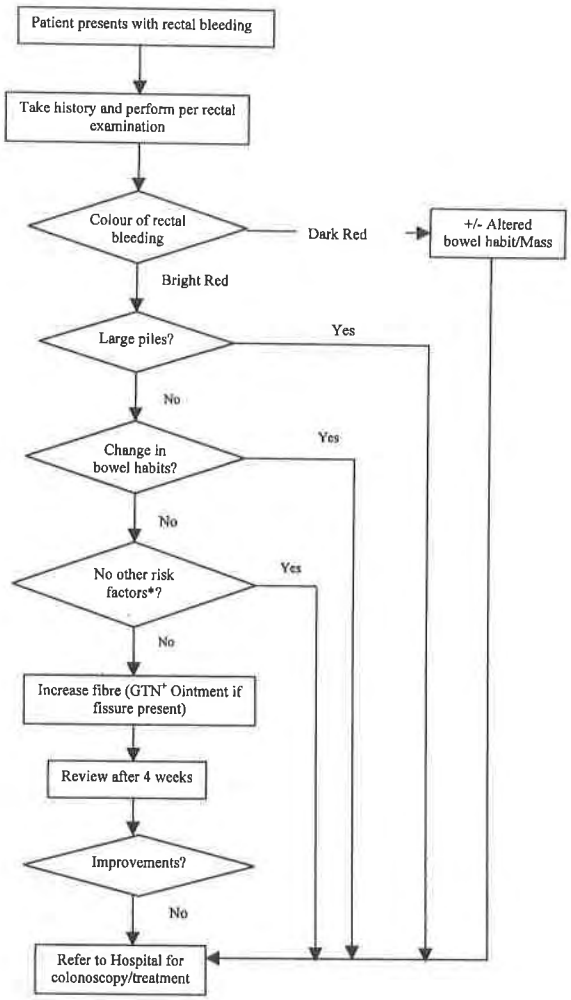
This miscellaneous group of causes includes bleeding from the upper gastrointestinal tract which, if severe enough, may present with fresh rectal bleeding. When the bleeding is slower, the blood presents as melaena. This is essentially tar black and has a characteristic smell. This compares with altered blood which may be more maroon especially when rubbed between gloved fingers, and iron stool which has a greenish hue when rubbed. The patient may be cardiovascularly compromised and requires urgent hospital admission for resuscitation and gastroscopy or operative intervention.

Clotting disorders may cause gastrointestinal bleeding as may certain drugs. These include those affecting the clotting cascade and those causing mucosal inflammation, particularly of the gastric mucosa.

Finally rare causes of rectal bleeding include the vasculitides which may be suspected based on the general medical history of the patient.

When To Refer

Figure 1 gives a suggested protocol for referral. Essentially all patients with rectal bleeding should have a careful history and detailed abdominal examination to include a per rectal digital exam. The type of bleeding and associated symptoms suggesting a colorectal cause warrants urgent hospital referral.



*Risks Factors include patient over 50 years old or a family history of clorectal cancer

+GTN ointment may be introduced in the near future as a medical treatment for acute and chronic anal fissure

Figure 1 Management Flowchart for Rectal Bleeding

Thresholds for referral should be reduced for those above the age of 40 years as well as those with a family history of colorectal cancer. Epidemiological analysis has suggested that patients with one affected close relative are 3 times more likely to develop colorectal cancer compared with the general population. This risk is further increased if there are further affected relatives or if the affected relative is less than 50 years old at diagnosis.

Despite these criteria, there remains a large proportion of patients who are young with no significant family history and who have

symptoms and signs suggestive of benign anal canal type bleeding. This group can be safely treated conservatively without referral to hospital. Suggestions for conservative treatments are given in table 2. Even in this group, if symptoms persist beyond a few weeks, referral for investigation should be considered.

Table 2 Conservative treatment for benign anal canal bleeding

Advice

- Take daily measures to produce soft, easily passed bowel movements such as:
  - Drink plenty of fluid
  - High fibre diet
  - Add bran to food if necessary
  - Regular exercise
- Lose weight
- Do not strain at stool
- Keep the anal area clean
- Use moist toilet paper after defaecation
- Do not sit too long on the toilet

Medical Treatment

- Bulk forming agent (e.g. Fybogel)
- (GTN ointment for anal fissure)

A Novel Treatment For Anal Fissure

As previously mentioned, there is probably an ischaemic component to anal fissure possible resulting in lack of healing. Surgical treatments involve relaxing the internal sphincter which relieves spasm and hence pain of the fissure whilst reducing ischaemia and allowing healing. Recently GTN ointment applied to the anal canal has been shown to relax the internal sphincter and allow healing. This has become established in the West as an alternative to surgery in the treatment of such patients. It is possible with time and further evaluation that this may become an acceptable community treatment in the near future.

Conclusion

Per rectal bleeding may be a result of a variety of aetiologies. A careful history concerning particularly the type of bleeding and any associated symptoms coupled with an abdominal exam and digital rectal exam will often distinguish benign anal canal type bleeding which may be treated conservatively from more sinister causes. Nevertheless there should be a low threshold for referral to hospital if there is any doubt about the site of bleeding, if the patient is above 40 years or has a family history of colorectal cancer or if bleeding from a presumed anal canal cause persists beyond a few weeks.

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The Singapore Family Physician

Symptoms of Diarrhoea In Colorectal Disease

Ho Kok Sun

Introduction

Diarrhoea is a common complaint seen by the family physician. It may also be one of the earlier manifestations of a colorectal cancer. This gives rise to the dilemma of the need for further investigations versus that of practising overly defensive medicine. The purpose of this article is to give an overview of the symptom of diarrhoea in colorectal disease and a general guideline for further investigation and referral.

Definition

Diarrhoea is a loose term that holds different meanings for different patients. Most people describe diarrhoea as watery stools. However, others may take it to mean increased frequency of motion of normal consistency. It may also be taken to mean loose or poorly formed stools. Some patients may mistakenly describe faecal incontinence as diarrhoea. It is important to ask precisely what the symptoms are, as this is suggestive of the underlying cause.

Pathophysiology of Diarrhoea

The gastrointestinal tract is in a continuous state of absorption and secretion of fluid. In normal situation, the oral cavity, stomach and duodenum secrete digestive fluid of up to 5 litres per day. This amount, together with oral fluid intake, passes through the small bowel where some of it is absorbed. About 8 litres of fluid pass into the colon where most of the absorption takes place and only about 200 millilitres is excreted in the faeces.

Diarrhoea may occur as a result of excessive fluid excretion or decreased fluid absorption anywhere within the intestinal tract. This may be due to mucosal inflammation, loss of absorptive surface, bacterial toxins or osmotic contents in the food. Any condition that causes increased gastrointestinal motility may also decrease the time available for fluid reabsorption. In cases of incomplete intestinal obstruction from colonic tumour, the diarrhoea may occur as a result of bacterial putrefaction of faeces.

Causes

There are a large number of possible causes for diarrhoea (Table 1). Most patients usually have diarrhoea lasting a few days from food poisoning or gastroenteritis. Diarrhoea may also be due to recent change in diet with increased milk or milk product intake in patients with lactose intolerance.

Table 1

Causes	Examples
Food intake	lactose intolerance, malabsorption states
Drugs	laxative, magnesium based antacids
Infection	viral, bacterial, protozoa
Inflammation	Crohn's disease, ulcerative colitis
Tumour	colorectal carcinoma
Post-surgery	colectomy, ileal resection, cholecystectomy, gastric surgery
Functional	irritable bowel syndrome

Another common cause is drugs. This includes magnesium-based antacids and antibiotics such as ampicillin or erythromycin.

In patients with previous gastrointestinal tract surgery, diarrhoea can occur as a result of disturbance to the normal fluid absorption and excretion within the lumen. This may be the result of loss of colonic length following a colectomy, loss of ileocaecal valve function, or even following a gastrectomy in which there is loss of regulation of gastric emptying. Patients may also have diarrhoea as a result of blind loop syndrome

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following surgery.

All of the above causes can be easily elicited by taking a detailed history.

Inflammatory bowel disease such as Crohn's disease or ulcerative colitis may also present initially with diarrhoea. This may be associated with blood in the stools. Likewise, colorectal tumours may also present with diarrhoea, either alone or with alternating constipation. In the above causes, there may be associated loss of weight and the course is usually more protracted.

Patients with irritable bowel syndrome may also have predominantly symptoms of diarrhoea. However, this is a diagnosis by exclusion.

Evaluation

History is one of the most important steps in evaluating a patient with diarrhoea. A prolonged history of diarrhoea of more than 2 weeks requires further evaluation if it is not due to recent changes in the diet or drugs. Diarrhoea associated with bleeding, loss of weight, alternating constipating or faecal incontinence is more significant and again requires further evaluation. Any family history of colorectal cancer should also be elicited.

Physical examination is required to assess the severity of the diarrhoea and to help point to the underlying cause. Patients with dehydration from intractable diarrhoea may require hospitalisation for intravenous fluids. Malabsorption states may manifest with clubbing or anaemia. Patients suffering from chronic blood loss from tumour or inflammatory bowel disease may also be anaemic. Palpable abdominal mass may be due to an abscess from Crohn's disease or a large colorectal tumour. Per rectal examination may reveal a rectal tumour. Proctoscopy may show inflamed mucosa in proctitis.

When to Refer

Most causes of diarrhoea are self-limiting and resolve over a few days. For uncomplicated diarrhoea, symptomatic treatment and reassurance is all that is needed. If the diarrhoea occurred as a result of drugs or diet, a change in the drugs and dietary advice should solve the problem.

Patients with severe diarrhoea with dehydration should be referred to hospital accident and emergency for admission and intravenous fluid rehydration.

Patients with diarrhoea associated with bleeding, incontinence and loss of weight should be referred to the specialist clinic early. All other patients can be treated symptomatically initially. However, if the diarrhoea persist after a few weeks of treatment, the patient should also be referred to the specialist clinic.

Hospital Management

Patients with dehydration will be given fluid therapy and optimised before any further investigations are performed.

Basic laboratory investigations include: haemoglobin level to detect occult blood loss, white cell count to rule out infective causes, urea and electrolytes to check for imbalance, thyroid function test if signs are suggestive of hyperthyroidism as a cause of increased gastrointestinal tract motility.

Lower gastrointestinal tract imaging in the form of either a colonoscopy or barium enema would usually be performed to rule out colorectal cancer as the cause of diarrhoea.

Stools for ova and parasites are also useful to rule out infective causes.

Further specific investigations such as stool chemistry and osmolality, small bowel and colonic transit test, rectal compliance test, jejunal aspirate for ova and parasites are only performed if indicated.

Conclusion

Diarrhoea is a very common symptom seen in the general practice. Most causes of diarrhoea are self-limiting and easily treatable. Further investigations should be done if the diarrhoea does not resolve, or is associated with other warning symptoms.

The Singapore Family Physician

Constipation - When to Refer For Further Management?

Cheong Wai Kit

Introduction

Constipation is a common presenting symptom in conditions related to the gastrointestinal tract. We do not know the exact incidence and prevalence rate of the problem, as there is no local or regional epidemiological data on it. What we know is that the Asian population is at least as obsessed with their regular bowel habit as the other races.

Constipation is the end result of multiple etiologies, either directly related to the gastrointestinal tract or indirectly due to various systemic disorders. It is at times very difficult to elucidate the cause of constipation even after a thorough history taking, complete physical examination and basic investigations.

The development of anorectal physiological testing has enabled us to understand better the intricate and complex process of defection. These specialized tests help us to identify the various causes of constipation. We can then be able to categorize the various causes and formulate more effective management plans to tackle the problem. This is important because we would like to operate on the right group of patients to achieve good results and to manage medically the other group of patients whom if operated on will give poor and disastrous results.

Definition of Constipation

The term constipation has different meanings to different people even amongst medical professionals. There is no standard definition available for this symptom. It basically means 'unsatisfactory defecation'. Patients may complain of constipation when they have problems with the frequency of defecation, the consistency of stools or the process of defecation itself. Constipation has been defined as 'having fewer than two bowel movements per week' (Drossman et al., 1982) or 'straining at stool for more than 25 percent of the time and/or two or fewer stools per week' (Drossman et al., 1982) or 'any patient ... who does not pass at least one soft stool daily, without effort, is constipated' (Painter, 1980). That is why in clinical practice it is prudent to find out exactly what the patient is complaining of so that the investigations and treatment can be tailored to the patient.

Etiology

From the initial assessment, we can classify constipation into an acute episode, which is usually less than 2 weeks in duration, and a chronic or recurrent episode. The former is usually self-limiting and more likely due to a benign correctable cause.

The etiology of chronic constipation can be further divided into 2 main categories namely:

1. Definable Constipation
2. Complex Constipation

Definable Constipation

The causes of constipation in this group of patients are usually quite apparent.

Causes of definable constipation:

Habit	repeatedly ignoring the call to stool environmental circumstances
Diet	low fiber diet inadequate fluid
Eating disorders	Bulimia
Medication	antidepressants, codeine, iron supplement, anticholinergics

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Neurological disorders	cerebral tumours, Parkinson's disease, cerebrovascular accident, head injury, spinal tumors, multiple sclerosis, psychiatric disorder.
Endocrine disorders	hypothyroidism hypercalcemia
Metabolic disorders	Diabetes Mellitus uremia hypokalemia

Bowel stricture

Megabowel (colon and/or rectum)

Volvulus

Colorectal tumor

The possible causes of the problem are usually elucidated after thorough history taking, complete physical examination and some basic investigations. A complete examination of the colon and rectum has to be done to rule out structural lesions such as colorectal tumor, colonic stricture, megabowel and volvulus.

Common endocrine and metabolic disorders that can cause constipation such as hypothyroidism, hypercalcemia, diabetes mellitus and uremia can be ruled out using biochemical tests. Neurological disorders originating centrally, at the spinal cord level or pelvic region can cause constipation either directly or indirectly. Constipation is also commonly seen in patients with psychiatric and psychological disorders.

Adequate fiber and fluids are essential to determine optimal fecal bulk and fecal transit rate through the colon. Repeatedly ignoring the call to stool in instances such as when travelling, when the working environment is inappropriate or when bed bound due to illness can cause constipation. This can result in decreased sensitivity of the rectum to distension and interfere with initiation of the mass emptying reflex. With time, adaptation can occur resulting in a reduced desire to defecate. Taking a drug history from the patient is also important as certain drugs can cause constipation.

Complex Constipation

This group of patients is a bit difficult to deal with, as the causes of constipation are usually not readily apparent. The presentation of this group is usually of a chronic, severe type and alters the patient's lifestyle.

Causes of complex constipation:

Disordered colonic motility	slow transit constipation irritable bowel syndrome
Disordered defecation	
-Structural	Hirschsprung's disease descending perineum syndrome occult rectal prolapse complete rectal prolapse rectocele
-Functional	pelvic floor dysfunction

Here, the causes of constipation are usually functional in origin. It can be divided to problems in the colon or the pelvic outlet. Disordered colonic motility such as slow transit constipation and irritable bowel syndrome (constipation predominant type) can cause problematic constipation.

Disordered defecation can be divided into structural and functional groups. The structural defect in disordered defecation can be due to Hirschsprung's disease, occult and complete rectal prolapse, retocele and descending perineum syndrome. And finally, pelvic floor dysfunction comprises of a group of functional disorders of the pelvic floor, which presents with difficult evacuation of stools.

Clinical Evaluation

A complete history and thorough physical examination including per rectal examination is very important in the assessment of a patient presenting with constipation. Following that, basic laboratory investigations including full blood count, serum urea, electrolyte, creatinine and

glucose levels should be sent for to screen for endocrine and metabolic disorders. Thyroid function tests and the calcium level should be assayed to rule out hypothyroidism and hypercalcemia. A thorough examination of the colon and rectum must be carried out either by colonoscopy or barium enema to rule out any structural lesions.

Any abnormalities in the above tests will direct the clinician to the appropriate line of management. If the initial tests did not show any abnormalities, patients are then treated empirically with a course of high fiber diet, lots of fluid and appropriate laxative treatment. Patients with constipation who are resistant to the initial treatment are then further investigated.

A battery of physiological tests is currently available to assist the clinician in elucidating the cause of the patient's defecation problem. They are divided into 2 main types:

1. Colonic motility test
2. Pelvic floor function tests

Colonic Motility Test

The aim of this test is to measure the rate of transport of intestinal contents through the colon and rectum.

Patients are taken off all laxatives prior to the test. They are then given markers to ingest at the start of the test and an abdominal radiograph encompassing the abdomen and pelvis is then taken about 6 days later to assess the number and the positions of markers retained. In abnormal colonic motility, the markers will be retained in the abdominal colon. If there is pelvic outlet dysfunction, the markers will usually be retained in the pelvis.

This test can also be done using a radionuclide tagged marker instead of the conventional marker (scintigraphic transit time).

The result of this colonic motility test can help to pinpoint the location of the problem to either the colon or the pelvic outlet. If there are upper gastrointestinal symptoms as well, an upper gastrointestinal motility study will need to be carried out to rule out generalized dysmotility disorders.

Pelvic floor function tests

Normal anal continence is a complex process involving integration of somatic and visceral muscles of the anal canal and pelvic floor with intact local, spinal and central nervous systems. These various components of the pelvic floor function can be assessed using different pelvic floor function tests. The basic investigation involves evaluation of resting and squeezing anal pressure, rectal sensation and rectal compliance. Other tests available to complement the anorectal physiological tests are electromyography, perineal descent measurement, endoanal ultrasound, endorectal ultrasound, transit markers study, cinedefecography and ambulatory manometry study.

The anorectal physiological measurements need to be interpreted with the whole clinical picture in mind. There are patients who are totally asymptomatic but have abnormal anorectal physiological measurements and vice versa. Furthermore, there are several different techniques available to measure anorectal physiology. Results obtained may vary.

Management of Constipation

The aim of treatment is to render the patient symptom free and is directed at what the patient perceives as normal satisfactory bowel function.

After the initial evaluation, patients are usually advised to change their diet to include lots of fiber (approximately 30 grams per day) and lots of fluid (at least six to eight glasses of fluid per day). They can also be given supplementary dietary fiber. Besides that, patients are given appropriate laxatives to regulate their bowel habit. These measures will usually cure patients with acute constipation.

Definable Constipation

Management of this group of patients is usually straightforward, as the cause of constipation is

usually quite apparent. Specific pathology elicited is then treated accordingly. Structural abnormalities are treated with surgical intervention. Metabolic and endocrine disorders are controlled using optimal drug regimens. Medications that can cause constipation are substituted with non-constipating alternatives. Occasionally, patients with eating disorders may need to be referred to the dietitian to help plan their dietary intake and to the counselor or psychologist.

Complex Constipation

As the name suggests, the management of this group of patients is usually complex. The majority of these patients have no structural abnormalities and the basic problem is functional in origin. It is important to divide this group of patients into those who require surgical intervention and those for medical treatment. Management must be individualized to each diagnosis. The proposed surgical options for each surgically correctable condition are given below. However opinions differ on the correct management of each problem.

The etiology of irritable bowel syndrome is still not fully understood and this subgroup of patients has no structural or physiological abnormality. Therefore any surgical intervention will have very poor outcome and aggressive medical therapy should be given to alleviate their symptoms. Pelvic floor dysfunction was previously treated surgically. The operations almost always gave poor results. Now we know from all the anorectal physiological tests that pelvic floor dysfunction is a functional disorder and its treatment should be in the form of biofeedback, which is a pelvic floor retraining program. Biofeedback is the retraining of coordinated anorectal and pelvic floor activity, by feeding back biological information to guide the patient. It is a form of behavioral modification therapy to rehabilitate these patients to relearn the reflex process of coordinated defecation. Besides this, dietary modification with the help of a dietitian and also stool bulk formers can be given to optimize the consistency of the stool of facilitate defecation. Finally, help of a psychologist is invaluable in helping these patients to overcome their problem.

So, when to refer patients with constipation for further investigations and management?

Generally, patients with the following presentation should be referred for investigations and management:

1. When constipation is associated with other symptoms which suggest an organic cause

Causes	Management	
Disordered colonic motility	• slow transit constipation	• total colectomy and ileorectostomy
	• irritable bowel syndrome	• medical management
Disordered defecation - structural	• Hirschsprung's disease	• colon-anal anastomosis
	• descending perineum syndrome	• biofeedback
	• occult rectal prolapse	• biofeedback
	• complete rectal prolapse	• anterior resection or perineal sigmoidectomy
	• Rectocele	• repair
Disordered defecation - function	• pelvic floor dysfunction	• biofeedback

2. When constipation does not respond to conservative measures (e.g. high fiber diet, high fluid diet and laxatives)
3. When constipation is chronic, severe and alters patient's lifestyle

Conclusion

When faced with a patient with constipation, a systematic approach should be carried out to identify the cause of the problem. Any patient needing further anorectal physiological tests should be referred to a specialized colorectal surgical unit. Nowadays such units are usually equipped with anorectal physiological testing equipment (available in the Department of Colorectal Surgery, Singapore General Hospital). Following that a rational management plan can be worked out the manage these patients with optimal results.

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The Singapore Family Physician

Diagnosing HIV Infection

Lee Cheng Chuan

Introduction

With the availability of highly active antiretroviral therapy (HAART), many patients with HIV infection / AIDS have been maintained on good health with good quality and productive life. HIV infection is now considered to be a chronic and manageable disease. These potential benefits for the patients challenge doctors to acquire the skills needed to detect unsuspected HIV infection earlier. Diagnosing HIV infection in a patient who is already symtomatic is of paramount importance, as starting antiretroviral therapy early is critical in restoring the immune system and curbing the progression of the disease at this stage. Chemoprophylaxis against some opportunistic infections can also be introduced at the appropriate time if an infected individual is diagnosed earlier and followed-up. Early diagnosis of HIV infection can also benefit the community in that early counselling on safer sexual practices and effective treatment could potentially limit the spread of this infection.

The spectrum of HIV-related disease is wide. While a few conditions are highly specific to HIV infection, many clinical manifestations overlap with disorders common in the general population. The challenge to doctors in both general and specialist practice is to determine when and how to advise patients to consider HIV testing. As HIV largely involves the heterosexual community in Singapore, a lifestyle history becomes less discriminative. Clinical clues that are now clearly defined should assume a greater role. HIV infection should be on the differential diagnosis for symptoms / signs consistent with HIV infection in any patient who has been sexually active in the last 10 years. Clinical events secondary to HIV infection occur in a reasonably predictable chronological order although there is significant difference among patients. The decade between primary infection and the development of an AIDS-defining illness may be punctuated by episodes of symptomatic illness, each offering an opportunity for detection of HIV infection. The clinical spectrum of HIV infection is best presented within 4 broad bands, viz. primary HIV infection, absolute CD4>500 cells/mm^3, CD4 200 -500 cells/mm^3, and CD4<200 cells/mm^3. Each band signifies decreasing immunosuppression and corresponding associated clinical manifestations.

Primary HIV Infection

It is considered that a large majority of primary HIV infection or seroconversion illness in the community is not recognised as being due to HIV infection. More than 50% of patients have this initial syndrome and 95% will seek medical evaluation. Full recovery from primary infection occurs in all but exceptional cases and the infection may remain undiagnosed for many years if this illness is not recognised as due to HIV infection. The primary HIV infection mimics other benign viral infections and was often described as a mononucleosis-like illness viz. fever, pharyngitis and cervical lymphadenopathy. However, this mononucelosis-like illness was seen in only 15% of all patients with primary infection in one study. More often, a combination of signs and symptoms occur during secroconversion (Table 1). Fever, lethargy, malaise, rash, adenopathy and sorethroat are the most common symptoms. Notably, there is absence of rhinitis in this illness. The onset of these symptoms usually occur 1 - 4 weeks after HIV exposure and the median duration of illness is about 20 days (range<1 week - 3 months). The rash during seroconversion is often described as an erythematous maculopapular rash; other rash viz. roseola-like rash, diffuse urticaria and desquamation have been described. The differential diagnosis for HIV seroconversion illness includes Epstien-Barr virus mononculeosis, cytomegalovirus mononucleosis, acute toxoplasmosis, rubella, secondary syphilis, viral hepatitis, primary herpes simplex infection, disseminated gonococcal infection and other viral infections including dengue fever.

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Table 1: Primary HIV infection

Symptoms/Sign (%)	n=12	n=19	n=218
Fever	92	87	72
Lethargy	83		66
Myalgia	92	42	55
Sore Throat	75	48	44
Oral Ulcers		40	30
Rash	50	68	56
Diarrhoea	33	32	23
Headache	58	39	51
Adenopathy	75	55	39

Cooper et at. Lancet 1985 March 9;1:537-40
Kinloch-de Loes et al Clin Infect Dis 1993: 17:59-65
Vanhems et al Clin Infect Dis 1997: 24(5):965-70

Diagnosis of primary HIV infection is difficult and doctors may not feel comfortable suggesting a HIV test for what appears to be a benign viral infection. Nevertheless, a high index of suspicion for this illness is essential. Treatment with antiretrovirals at this stage of infection has been advocated and may represent the best opportunity to tame the virus in the long run. The infection should be suspected when there is a combination of symptoms suggestive of primary HIV infection or when the duration of illness becomes too prolonged to be explained by a benign viral infection. A recent possible exposure to HIV 2 to 4 weeks before the onset of illness should be enquired. It is essential to know that HIV antibody tests viz. the Elisa and Western blot tests may be negative or indeterminate during the illness. A negative antibody test must be repeated about 6 weeks and 3 months later if underlying HIV infection is suspected. An antigen test to detect HIV (PCR) for earlier diagnosis is available but is too expensive and generally not recommended.

CD4>500 cells/mm^3

After primary infection, the immune system recovers and most patients go into a long asymptomatic period. However, high-level active viral replication continues within lymph nodes and plasma CD4 cells during this stage of clinical latency. Persistent generalised lymphadenopathy may be noted by the patient or discovered during routine physical examination 3 - 5 years after initial infection. These enlarged lymph nodes usually disappear before development of an AIDS-defining illness.

This is also the stage where there is polyclonal activation of the immune system. Serum immunoglobulins are raised and a routine liver function test may reveal a raised total protein with a normal albumin fraction. Sporadic autoimmune disorders may be seen at this stage and these include:

- Idiopathic thrombocytopenia (often asymptomatic and detected through routine full blood count)
- Gullian-Barre-like syndrome
- Chronic autoimmune demyelination of peripheral nerves
- Mononeurities multiplex (including cranial nerves e.g. Bell's palsy)
- Polymyositis
- Sjogren's syndrome

HIV test is recommended for any sexually active patient with the above conditions.

Intermediate Phase of CD4 200-500 cells/mm^3

This is the stage where there is moderate immune deficiency. Less severe infections particularly of the skin and mucosal surfaces can be seen during this stage. These infections include:

- Tinea
- Seborrhoeic dermatitis
- Warts

- Molluscum contagiosum
- Bacterial folliculitis
- Gingivitis
- Chronic sinusitis
- Reactivation of herpes zoster and herpes simplex viruses (severe manifestations occur later)

For the above HIV-related disorders common in the general population, decision to suggest HIV test is more difficult. The physician should, in this situation, search for other supporting clinical evidence (e.g. enlarged lymph glands) and significant past medical history e.g. history of sexually acquired diseases, herpes zoster etc. Atypical feature of the presenting condition e.g. multi-dermatomal herpes zoster in young patient also makes underlying HIV infection more probable. A present or past lifestyle that puts an individual at risk for HIV transmission would also be significant here.

Other clinical manifestations occurring at this stage of disease are unexplained oral candidiasis, oral hairy leucoplakia and tuberculosis. The first 2 conditions are more specific but not exclusive to HIV infection and a HIV test should be offered to the patient regardless of lifestyles clues. Tuberculosis may occur at any stage of HIV infection and presentation becomes more atypical with increasing immunosuppression. Extrapulmonary manifestations are also more common with underlying HIV infection. A HIV test should be offered to an individual with tuberculosis.

CD<200 cells/mm^3

A large proportion of patients remain in good health as their CD4 first drops <200 cells/mm^3. This is the stage of advanced immune depletion and there is a high risk of developing an AIDS-defining severe opportunistic infection or malignancy. Patients are at risk of infection with virulent pathogens e.g. severe community acquired pneumonia and septicaemia. Infections with pathogens of low virulence also occur at this stage e.g. pneumoncytis carinii pneumonia (PCP) and disseminated mycobacteria avium complex infection. In severely immunocompromised patients, past infections reactivate to cause more severe illness e.g. cytomegalovirus retinitis and toxoplasma gondii cerebral abscesses. A HIV test is strongly advised for any patient presenting with an AIDS-defining infection.

HIV-related Malignancies and Other AIDS-Defining Conditions

- Kaposi's sarcoma (HHV-8)
- Lymphoma (Burkitt's, immunoblastic, primary in brain)(EBV)
- Invasive cervical carcinoma (HPV)
- AIDS dementia complex (HIV)
- Progressive multifocal leucoencephalopathy (JC virus)
- Wasting disease (HIV)

Many of the AIDS-related malignancies and neurological conditions are in fact, related to opportunistic viral infections e.g. Kaposi's sarcoma is strongly associated with a newly discovered human herpes virus and progressive multifocal leucoencephalopathy is associated with the JC virus. These malignancies are not exclusively due to underlying HIV infection, nevertheless like many conditions described above, they should prompt the doctor to obtain a detailed history and a thorough physical examination for clues to possible HIV infection.

Clinical Presentation of AIDS Patients 1985 - 1998		
Disease category (non-exclusive)	**Number**	**%**
Infection:		
Pneumocystis carinii pneumonia	224	46.3
Cytomegalovirus infection	112	23.1
Unspecified pneumonia	84	17.4
Disseminated tuberculosis	86	17.8
Pulmonary tuberculosis	68	14.0
M. avium intracellulare infection	88	18.2
Other mycobacterial disease	24	5.0
Cerebral Toxoplasmosis	50	10.3
Cryptococcosis	41	8.5
Candidiasis (oesophageal)	40	8.3
Cryptosporidiosis	11	2.3
Isosporiasis	3	0.6
Cancer:		
Kaposi's sarcoma	17	3.5
Lymphoma	35	7.2
Others:		
Encephalopathy	31	6.4
Others	1	0.2

Adapted from Communicable Disease Surveillance Report 1998.

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The Singapore Family Physician

Management of Gallstones Associated with Jaundice*

* Paper presented in part at the Annual Surgical Update, Department of Surgery, National University Hospital on 4/12/99

Ti Thiow Kong

Summary

In Singapore, gallstones are predominantly Western type cholesterol and black pigment stones, jaundice occurring when these stones migrate from gallbladder to bile duct. Less common are primary ductal brown pigment stones associated with Asiatic cholangitis.

Following urgent treatment of sepsis and confirmation of ductal stones by ultrasound, ERCP, MRCP or CT scan, definitive treatment is usually by ERCP extraction of ductal stones followed by laparoscopic cholecystectomy. Alternatively, cholecystectomy and removal of bile duct stones may be by open surgery or entirely by laparoscopy.

For Asiatic cholangitis, biliary-enteric bypass and liver resection reduces recurrent symptoms.

Keywords
- Gallstones
- Cholesterol
- Pigment
- Jaundice
- Cholangitis
- Laparoscopic cholecystectomy
- ERCP

Introduction

This paper reviews the current status in the management of gallstones associated with jaundice.

Materials and Methods

The review is based on a personal clinical and research experience in the management of gallstone disease during the past 20 years at the Singapore General Hospital and the National University Hospital, together with a literature review.

Results

1. Types of gallstones causing jaundice in Singapore

Our study, published in the British Journal of Surgery[1], identified three types of gallstones - cholesterol and black pigment stones similar in composition to stones in the West and brown pigment stones associated with Asiatic cholangitis (Fig.1). We thus confirmed the presence of both Western type and Asiatic type gallstone disease in Singapore. However, with increasing affluence, it appears that as with other parts of East Asia, cholesterol stones are increasing in our population, whereas Asiatic cholangitis has been decreasing in frequency. [2]

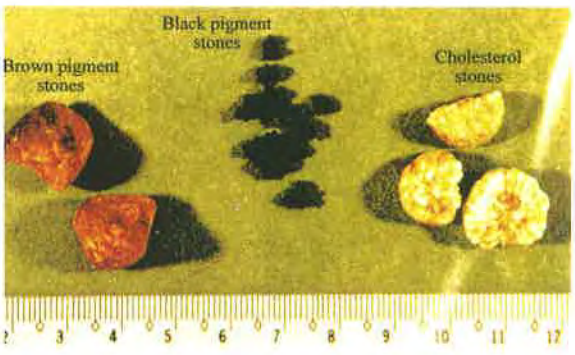

Figure 1. Types of gallstones

In Western type gallstone disease, cholesterol or black pigment stones form in the gallbladder. In 10-20% of patients, these stones migrate through the cystic duct into the common bile duct and cause obstructive jaundice. These secondary ductal stones may pass spontaneously through the ampulla of Vater and jaundice subsides. However, more often then not, obstruction by stones cause not only pain and jaundice but also sepsis. The combination of the 3 clinical features of jaundice, abdominal pain and fever is known as Charcot's triad of cholangitis.

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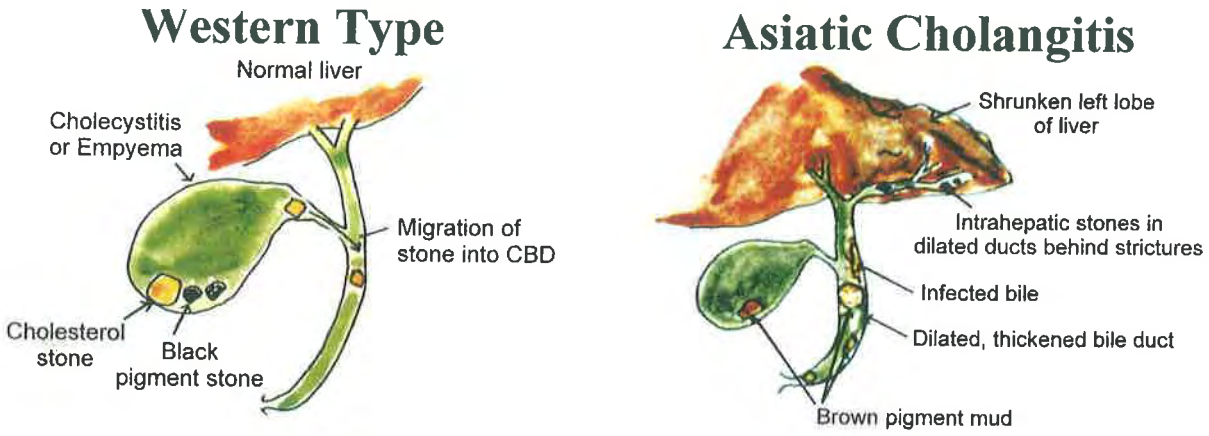
Figure 2. Gallstones and jaundice



Asiatic cholangitis, frequently recurrent and leading to life-threatening septicaemic shock, is associated with primary ductal brown stones which form denovo in the bile ducts, including the intrahepatic ducts and especially in the left lobe of liver (Fig. 2).

2. **Management of jaundiced patient with gallstones**

a) **Urgent treatment of sepsis**

Fever with elevated leucocytosis indicates sepsis and unless treated aggressively, may progress to septicaemic shock and even death. Sepsis in cholangitis is due to intestinal bacteria - predominantly gram-negative organisms e.g. Klebsiella, Proteus Pseudomonas, with gram-positive cocci, Streptococcus faecalis in a subsidiary role. A suitable choice of antibiotics would be Ampicillin / Gentamycin or a third generation Cephalosporin. In severe infections, anaerobes e.g. bacteriodes fragiles are also contributory, and the addition of Metronidazole would be necessary.
Intravenous fluid infusion to replace circulatory volume is an important component of resuscitation of septicaemic shock.

b. **Confirming presence of bile duct stones**

i) **Ultrasound of Hepato-biliary system**

In the ultrasound examination, gallstones in the gallbladder are readily seen to be opacities causing acoustic shadowing (Fig.3). The right panel in Fig.3 shows ductal stones, but more frequently than not, bile duct stones are not visualized by ultrasound. In most cases, the clue to bile duct stones is a dilated bile duct and when this occurs, diagnostic ERCP is performed.

ii) **Diagnostic ERCP**

In most patients with dilated bile ducts, ERCP identifies stones as filling defects in the contrast filled bile ducts (Fig. 4). However, ERCP may show no bile duct stones and this would indicate spontaneous passage of bile duct stones through the ampulla of Vater.

iii) **MRCP**

Reports of refinements in magnetic resonance cholangiography suggest that the image quality is almost as good as ERCP, and has the advantage of being non-invasive. It is likely that this technique will be more frequently employed in the years ahead.

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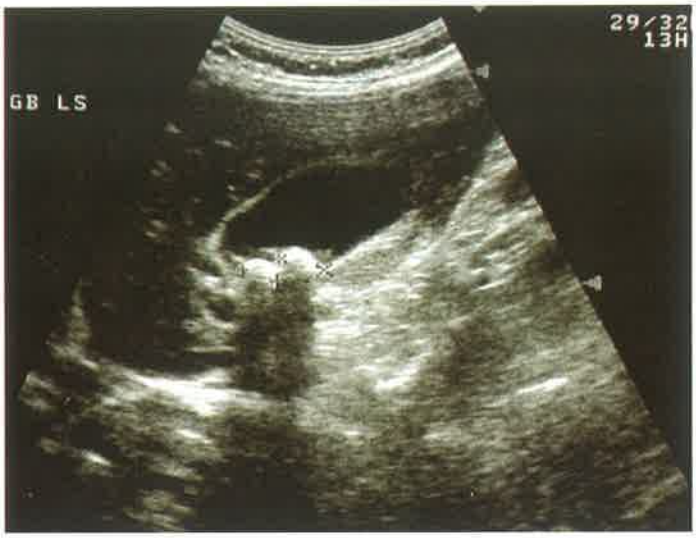
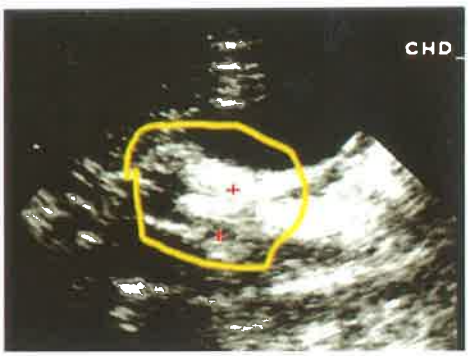
Ultrasound HBS



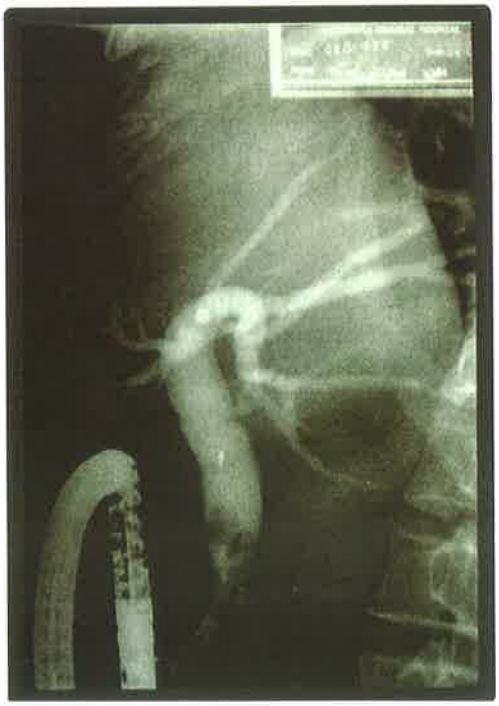
Stones in Gallbladder



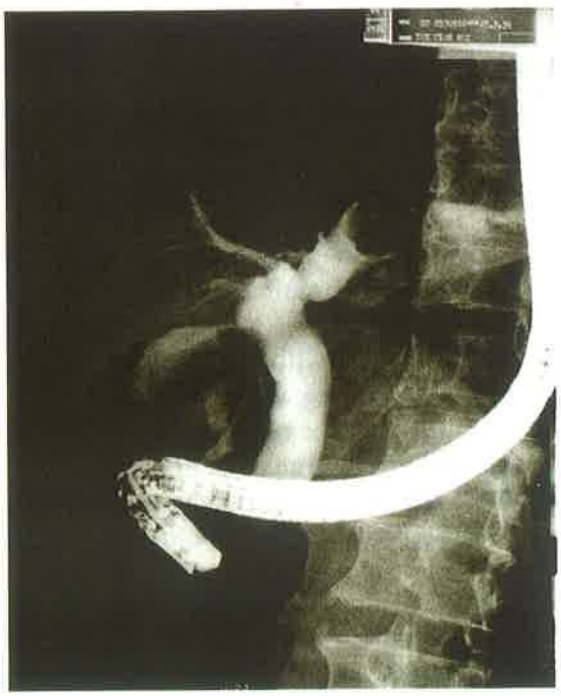
Stone in Bile Duct

Figure 3. Ultrasound in diagnosis of gallstones

ERCP



Stone in Bile Duct



Stone in Hepatic Duct

Figure 4. ERCP in management of gallstones

iv) **CT scan**

Sensitivity of CT scan in detecting bile duct stones can exceed that of ultrasound and is particularly useful when intrahepatic stones need to be distinguished from mitotic disease.

C. **Definitive Treatment**

There are 3 main approaches, depending on the pathology, general fitness of patient and background experience of the managing physician / surgeon.

i) **ERCP extraction of stones followed by laparoscopic cholecystectomy**

This is currently a popular approach. When diagnostic ERCP shows stones in the bile duct, it is usually possible to perform papillotomy ie. widening the ampulla of Vater by cutting it radially, and then extracting the stones with a Dormia basket or dredging it with a Forgathy balloon. Following successful ERCP extraction of bile duct stones, definite treatment is completed by performing laparoscopic cholecystectomy the next day. Cholecystectomy is however, contraindicated in high risk patients with short life expectation.

Although ERCP/ papillotomy is widely done, long term consequence of persistent duodenum-biliary reflux is uncertain. The other 2 alternative approaches to remove bile duct stones avoid damage to the ampulla of Vater.

ii) **Open cholecystectomy and choledochotomy**

This time honoured approach is particularly indicated in patients with large or multiple stones, not amenable to safe ERCP extraction.

iii) **Laparoscopic cholecystectomy and clearance of bile duct stones**

Recent reports suggest that with adequate experience, bile duct stones may be extracted safely during laparoscopic cholecystectomy either through an incision in the common bile duct or through the cystic duct with the help of a choledochoscope. The latter technique is less demanding and will probably be within the skill of most surgeons in the years ahead.

Results of Treatment

Patients with Western type gallstones disease will usually remain well following clearance of bile duct stones and cholecystectomy. Sometimes symptoms may recur from incomplete removal of bile duct stones and this is treated by ERCP extraction or removal of stones by forceps placed through the tract of T-tube previously placed in after choledochotomy. In the medium and long term, stricture of ampulla of vater can occur following papillotomy and cause recurrent cholangitis and this would need correction either by repeat papillotomy or by biliary-enteric bypass.

Management of Asiatic cholangitis

The management of Asiatic cholangitis is more demanding and the results less predictable. This is because stones may not have been completely cleared from the intrahepatic bile ducts or continue to form after initial clearance.

During choledochotomy, syringing is helpful in clearing stones and mud from the dilated bile ducts (Fig.5). Liver segments containing stones in intrahepatic bile ducts may have to be resected. A biliary-enteric bypass reduces the frequency of recurrent symptoms.

Bile duct stones with other pathology

Intrahepatic stones are sometimes associated with intrahepatic cholangiocarcinoma and survival is poor following hepatic resection in these patients.

In contrast, the presence of bile duct stones causing cholangitis could lead to early diagnosis of cancer of ampulla of Vater, as was the present author's experience in 2 patients in whom Whipple's operation resulted in long term survival.

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Asiatic Cholangitis

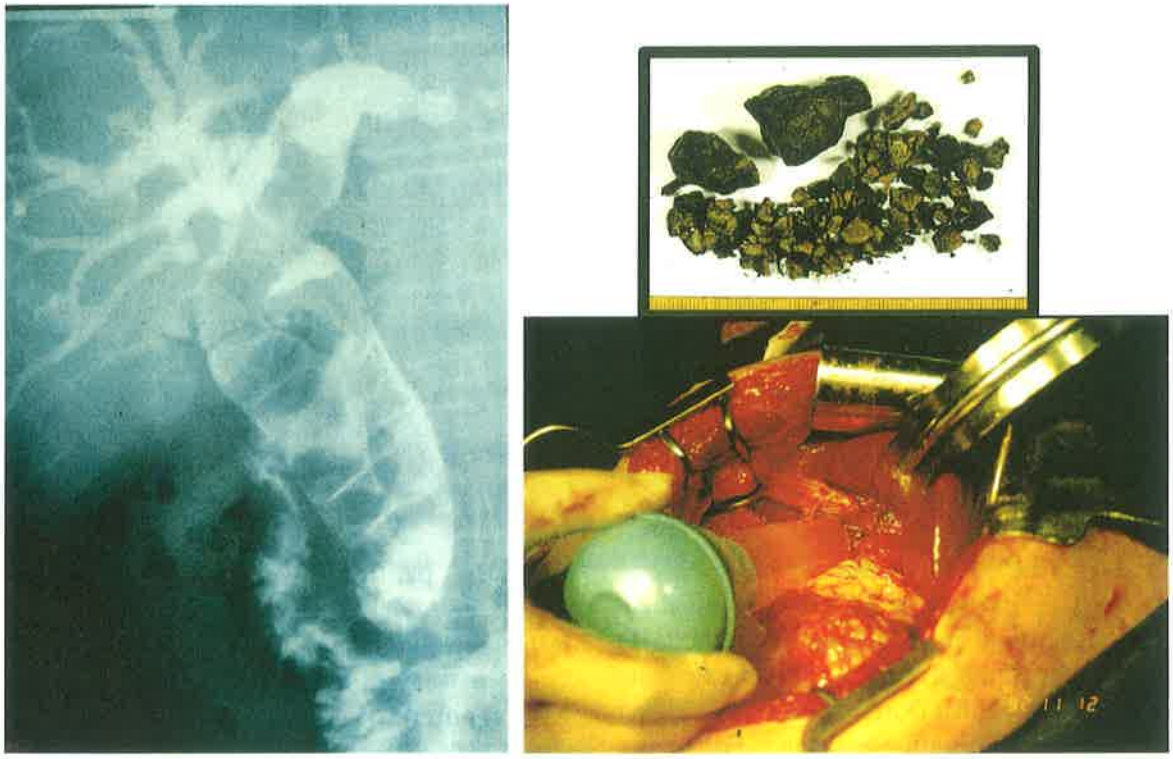

Figure 5. Surgical treatment of Asiatic cholangitis

Intrahepatic and extrahepatic bile duct stones occurred in a young woman with a large choledochal cyst and she has remained well 4 years after resection of choledochal cyst with clearance of stones and hepatico-jejunostomy.

Conclusion

Patients with gallstones and jaundice present with a wide spectrum of pathology. Optimal timing and choice of treatment procedure require good clinical judgement. Treatment options include highly developed skills in endoscopy, laparoscopy and open surgery. The optimal treatment of each patient can only be achieved by a versatile surgeon or a team of doctors fully conversant with the limitations and possibilities of each treatment procedure.

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Battling The Bulge - New Answers?

Nehal Kamdar

Women often gain excess weight after the birth of their first baby or during the menopausal years.

The 1998 National Health Survey showed that 21% of the population had a BMI between 25-30 with more men being overweight. (Refer to Table 1) 5% of the population had a BMI 30 or more, with more women being overweight.

Table 1: National Health Survey 1989

BMI	Population	Sex
25-30	21%	23% men 19% women
≥30	5%	6% women 4% women

(Reference Healthscope)

Among the ethnic groups obesity rose markedly in the Malays (11.1% in 1992 to 16.2% in 1998). Among the Indians (11.2% in 1992 to 12.2% in 1998) and Chinese (3.5% in 1992 to 3.8% in 1998), there was a smaller rise.[1]

With the Internet and health magazines etc patients are flooded with information on how to lose weight which often may not be scientifically proven!

So what do people look for when they seek means to lose weight?

The "Zone Diet"

Recent article in the Strait Times reported about the latest fad diet to hit the market, namely the ZONE DIET! Pioneer of this diet is Dr. Atkinson. He advocates having a high protein, low carbohydrate diet and 30 vitamin-mineral supplements to aid weight loss. This diet originated from Hollywood. There were rumours that Madonna and others were energised slim from the Zone diet. Washington celebrities like President Bill Clinton and Vice President Al Gore are also reportedly following the low Carbohydrate diets.

There are even low carbo discussion groups on the Net, and low carbo - recipe exchanges.

CNN recently interviewed a man who lost 64 kg on the Zone diet. His refrigerator was stacked with bacon, steaks, chicken or meat, which he fried or roasted when hungry.

However eating so few carbohydrates will cause the body to go into ketosis in which your body utilizes fat for energy, and possible health risk from this cannot be ruled out.[2]

Appetite Suppressants

Double-blinded randomised trials of longer than 6 months duration show that serotonergic agents like Fluoxetive are not effective in weight loss. Dexfenfluramine and fenfluramine are effective when combined with the diet. However adverse effects include tiredness, diarrhoea and dry mouth. Continued use for more than 3 months is associated with pulmonary hypertension. This risk is estimated at 23-46 cases / million / year. Therefore they have been withdrawn from the market since September 1997.[3]

Surgery

In severe obesity surgery is usually indicated when BMI is more than 40 and all other attempts of weight reduction have failed.

Gastric Bypass and gastric plication are usually done to treat obese patients. However patients often regain the lost weight over time.

Liposuction is a very common cosmetic procedure carried out in the US. It involves the subcutaneous

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infusion of a solution containing a local anaesthetic drug followed by the removal of fat. The operation can be performed under epidural or general anaesthesia depending on the amount of fat to be drained. However this also does not come risk free as Rama B Rao has reported 5 deaths due to Liposuction. Furthermore if the patients are not careful with their diet they will most likely regain lost weight.[4]

Dietary Counselling

This is the corner stone of weight reduction. In a study by Mulrow et al, randomised controlled trials showed that restricting kcal to 1200/day together with a change in lifestyle behaviour resulted in weight loss of approx. 8.5 kg in 20 weeks. Patients were given a meal plan that restricted fats as well as calories. If regular aerobic exercise is done, $^1/_2$ to $^1/_3$rd of weight lost was maintained up to 1 year.[5]

Exercise

For effective weight loss, restriction of calories should be accompanied with an increase in energy expenditure. Men and women who exercise regularly have a lower risk of weight gain over a 10 year period. (William et al 1993) The majority of obese adults were not obese children; this shows that if level of physical activity could be kept up, there would not be weight gain especially in the middle years. Including physical activity in weight loss programs has helped in maintaining weight loss for a longer period of time. (Klem et al 1997) Patients should be advised to be regular initially and then increase the duration of the exercise. [6] Yet 64% of Singaporeans did not participate in any exercise in the National Health Survey 1992. Only 17% engaged in regular exercise in 1998 survey. (National Health Survey 1998 Healthscope)

Discussion: New Developments in Understanding Obesity

Leptin:

Leptin was first discovered in late 1994. It has been portrayed as a cure for obesity. It is a hormone derived from fat cells. Serum levels reflect the amount of energy stored in the adipose tissue. They rise as fat mass increases. Prolonged fasting decreases Leptin levels whereas overfeeding greatly increase them.

Leptin acts by binding to a specific receptor in the hypothalamus to alter neuropeptides that regulate neuroendocrine function and energy intake and expenditure.

The effect of Leptin administration to ob. mice, which were Leptin deficient, led to the high expectation that human obesity could be treated by administration of Leptin. In fact it appears that most obese patients often have increased levels of Leptin indicating that obesity may be linked to Leptin resistant state.

However treatment may have clinical value by making compliance to a low calorie diet easier and in maintaining lost weight. Leptin administration to humans is now know to be safe.[7]

Shaped By Life In The Womb: Research

Article in Newsweek Sept 27th 1999 reviewed recent research questioning the conventional belief that adult illness like obesity, diabetes and breast cancers were a result of unhealthy lifestyle or bad genes. The new research suggests that these conditions may have their roots in the conditions in the womb!

In 1984 Barker saw that neonatal mortality was high in the early 1900 in the regions where deaths from heart disease was high. Generally heart disease is thought to be a disease of affluence! This led him to wonder whether the cause of heart disease should begin in the womb! Barker and his colleagues studied 13,249 men born in Hertfordshire and Sheffield. He found that men who weighed less that 5.5 pounds at birth had a 50% higher risk of dying from heart disease after accounting for socio-economic differences.

Scientist now suggests that during life in the womb, different hormones flow from the mother, and the ability of the placenta to deliver the right nutrients shape the health of the adult. Dr Peter

Nathaneilsz of Connel University explores the fact that if the mother undergoes starvation or undernutrition, the foetus's physiology is reprogrammed, such that the child's metabolism turns everything that she eats into fat. During the Nazi blockade of the Western Netherlands, a famine that lasted from September 1944 to 1945, rations went down to 500 calories per person. Stein and Susser discovered that foetuses, which were exposed to famine early in gestation, had a higher risk for developing adult obesity. This they attributed to the appetite centre in the brain being programmed to overeat.[8]

Orlistat: Xenical

Virtually all-dietary fat is in the form of triglycerides. These are then broken down to monoglycerides and free fatty acids by lipase. If lipase is deficient as in patients with pancreatic there is steatorrhea and weight loss. Aim of Orlistat is to produce a state of steatorrhea and consequently weight loss.

Orlistat reduces the absorption of dietary fat by a maximum of 30%. It causes the fat to be excreted in feces. However it is necessary to follow a low fat diet. Dosage recommended is 120mg t./D.S. However with a higher dosage than this, it does not cause a higher fat loss.

Clinical trials of Orlistat

Randomised placebo controlled studies have demonstrated benefit in long term treatment of obesity.

A multicentre study based in UK recruited 228 patients with a mean wt of 97kgs (BMI 30-43) to examine the benefits of Orlistat over a 12-month period. All the patients were prescribed a low calories diet a deficit of 600 kcal from their requirements. Fat content prescribed was less than 30% for a 4-week period and then continued for 12 months in combination with either Orlistat 12mg or placebo. 139 patients continued the 1-year treatment. The Orlistat group had lost an average of 8.5% of initial weight compared to 5.4% in the placebo group. The treatment group also had reductions in serum cholesterol, LDL: HDL ration.

The treatment of obesity is slow and often frustrating. People are always attracted by false claims of quick weight loss with little effort. However it is necessary to seek professional help in overcoming obesity and weight related problems before it is too late. With the right knowledge and perseverance it is possible to shed those extras and keep them off!

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101 Pitfalls in Obstetrics & Gynaecology for the Unwary

Dr Max Mongelli

Introduction

Office gynecology and often obstetrics is an important aspect of family practice in Singapore. As this field has experienced a rapid increase in medico-legal litigation, it is important to remain vigilant of potential pitfalls.

This article will outline some of the common problems GP's may encounter in their practices. The title is actually an underestimate of the number of pitfalls in women's health if one considers all possible permutations. Hence in this article I can only highlight some of the more common problems. Suggested guidelines are based on UK practice, which are generally applicable to Singapore. Whenever there is any doubt, it is best to discuss individual cases with a specialist in the field.

Confidentiality

As a general rule, confidential information should not be given to relatives, friends, journalists or media without written consent from the patient. For example, information may be disclosed to insurance companies only with written consent.

However, one needs to be aware of a number of exceptions that allow a breach in confidentiality to take place. These include:

- The welfare of someone other than the patient is seriously at risk and the patient will not make a voluntary disclosure. This usually applies to some communicable diseases.
- The doctor has good grounds to believe that a youngster is being abused or exploited.
- Notification of births, deaths, abortions and communicable diseases.
- Request from Courts & Coroners

In some situations **disclosure without consent** may be warranted. This is only justified if the patient's intellectual capacity is limited. This typically applies to youngsters who may be:

- Immature
- Do not have sufficient understanding
- Cannot be persuaded to involve an appropriate person in the consultation
- Disclosure is essential in her best interest.

In these difficult situations the doctor should obtain a second medical opinion and tell the patient in advance that confidentiality will be breached. He or she should also discuss the case with his Medical Defence organisation and / or the Medical Council.

Family Planning

General practitioners are often involved in providing family planning services. Problems may arise when doctors are asked to prescribe contraceptives for the underaged girl. Patient may consent on their own behalf if in the *doctors' opinion:*

- She is mature and sensible, understands risk and benefits
- She is likely to engage in sexual intercourse without contraception
- Her health is likely to suffer without contraception
- Contraception is in the best interest of the girl

Medico-legal claims in relation to family planning usually arise from either adverse effects of

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contraception or failed contraception with unwanted pregnancy. Common causes include:

- Failure to warn patient of the risks related to a particular contraceptive.
  Example: deep venous thrombosis following use of OCP.
- Failure to identify risk factors that contraindicate use of a contraceptive.
  Example: hypertension and OCP.
- Failure to recognise drug interactions.
  Example: antibiotics and OCP.
- Failure to stop the OCP prior to major surgery.
- Failure to recognise perforation following IUCD insertion.
- IUCD insertion performed in the face of active infection.

Post-coital contraception ('morning-after pill') is being used more often as women become better educated about family planning. There are essentially two techniques: high dose OCP's (Yuzpe regime) and IUCD insertion. This method has been studied extensively, and some precautions should be taken before prescribing. Pre-existing pregnancy must be excluded. Contraindications to the IUCD or the OCP also apply. The patient should be counselled regarding differences in efficacy, which is 99% for the IUCD (within 5 days of insertion) but only 75% for the Yuzpe regime.

The Pap Smear

The finding of a cervical cancer after a 'negative' PAP smear can be a disconcerting experience for both the patient and doctor involved. In many cases a false negative test is due to poor technique in obtaining the specimen.

To minimise the risk of a false negative, the following are important points that should be followed when sampling the cervix:

- Do not use lubricant on speculum - use warm normal saline instead.
- Endocervical sampling should be performed in all cases – cytobrush or cotton-tipped swabs can be uses.
- Use two separate slides to minimize air-drying, one for the spatula and one for the cytobrush. These should be clearly labelled, to help localise the abnormal areas.
- Slides should be fixed immediately after transfer to minimise air-drying. Often only mild abnormalities are noted on a smear. Because of the poor reliability of repeat smears, a colposcopy is advisable if these facilities are available.

Pap Smear for Virgins

A common confusion among Singapore GP's is to assume that a 'single' woman is not sexually active. I have seen several instances of women who have never been screened because they were 'single'. As social mores change, one should make direct enquiries about sexual activity before making any assumptions. For Asian women who are truly virgins, there is very little data on the risk of carcinoma of the cervix. The studies published on Western populations are limited and of variable quality. The majority of cervical cancers occur in married women rather than single women, and the vast majority of women in the peak age group of cancer are married.

Epidemiological studies on cervical cancer rates in nuns suggest that this condition is likely to be less common, but rates do not differ markedly from the general population. In fact, there is no substantial evidence that cervical cancers are rare in nuns.

Intractable Vaginal Discharge

A recurrent or irritating vaginal discharge that does not respond to routing antimicrobial therapy is a relatively common problem. In dealing with such cases a detailed history is very important, particularly in distinguishing pruritus vulvae from an irritating discharge originating from the vagina or cervix. A careful inspection of the vulva, vagina

and cervix should be carried out. The following investigations may be required:

- Cervical cytology
- Measurement of vaginal pH with indicator paper
- Wet smear, material for culture
- Colposcopy if appropriate

Four main aetiological groups can be responsible for these symptoms:

1. Cervicitis
2. Recurrent vulvo-vaginal candidiasis
3. Atrophic vaginitis
4. Other

Cervicitis

This is an ectopy of the cervix which has become infected. Colposcopy and biopsy can be very helpful in establishing the diagnosis. Hyperaemic and inflammatory change suggest infection, hence cervical swabs should be taken. Cases that do not respond to antibiotics may benefit from physical destruction of the epithelium by cryotherapy or diathermy.

Recurrent vulvo-vaginal candidiasis (VVC)

As candida is a commensal organism in up to 20% of women, there is a tendency to over-diagnose VVC. It is estimated to affect about 1% of women. It has been associated with defects in immune function and HIV infection. Cases secondary to Candida Glabrata & Tropicalis are more resistant to treatment. Standard treatment consists of clotrimazole 500mg single dose started 1 week before an expected period, followed by a second dose post-menses 2 weeks later. An alternative regime involves the use of systemic anticandidals. Itraconazole 200mg or fluconazole 150mg can be used on day 1 of the menses, for six months.

For Candida Glabrata: itraconazole 200mg daily for a month, + Nystatin 500 iu qds orally and pessaries b.d. for 3-4 months. Liver function tests should be performed periodically as this regime may be hepatotoxic.

Atrophic Vaginitis

This condition is usually found among women who are either postmenopausal, breastfeeding or on medications that cause vaginal atrophy. A distinction should be made between the symptomatic patient with an inflamed atrophic vagina, and the asymptomatic patient with a simple atrophy only. Symptoms include vaginal soreness, dyspareunia, and occasional spotting. Careful inspection will show an inflamed, smooth, atrophic vagina with mural haemorrhages.

Spotting and bleeding are ominous symptoms in post-menopausal women. Although many cases are due to atrophic vaginitis, investigations such as endometrial biopsy or D & C is indicated. Atrophic vaginitis usually responds to topical oestrogen cream for 4-6 weeks.

Other Causes

A variety of less common conditions may give rise to an intractable vaginal discharge. These include:

- Subclinical genital herpes
- Vaginal intraepithelial neoplasia (VIN)
- Lichen sclerosus
- Skin reactions to chemicals such as soaps or deodorants.
- Pinworms, pediculosis

Ectopic Pregnancy

Ectopic pregnancies may occur in 1-2% of all pregnancies, and continue to be significant cause of maternal mortality or near-miss morbidity. Most clinical mistakes are made at the level of diagnosis, and GP's are often the first line of

contact. Up to 70% of cases have atypical presentations - the classical triad of vaginal bleeding, unilateral pelvic pain and a missed period is seen in only a minority of cases. A normal menstrual history does not exclude an ectopic. Ultrasound examination cannot be relied upon to exclude this condition. However, a negative pregnancy test that has been performed by professional staff virtually excludes an ectopic. A special case is that of an heterotopic pregnancy, where both an ectopic and an intrauterine pregnancy coexist. This is a rare condition, generally seen after IVF treatment. Laparoscopic salpingectomy or salpigostomy are both acceptable surgical techniques. In some centres surgery is being replaced by medical treatment such as systemic or local methotrexate injections, in selected cases. The patient must understand that this type of treatment carries a 5-10% failure rate.

Teratogenic Exposure

Given that up to 50% of all pregnancies may be unplanned, it is relatively common for a woman to take medications or have an X-ray in the 1st trimester before she is aware that she is pregnant. Often these patients are very distressed about the possibility of a teratogenic effect, and many request a termination of pregnancy. In order to prevent these occurrences from taking place, the GP should ask four key questions before prescribing to any woman in the reproductive age group:

- Is she using contraception?
- Is she pregnant?
- Is she trying for a pregnancy or at risk of unplanned pregnancy?
- Is it safe to assume she is not pregnant?

Should there be any doubt, a pregnancy test may be required before prescribing potentially teratogenic medications.

Radiological Imaging

Radiation doses from most diagnostic procedures present no substantial risk of causing fetal death, malformation or impaired mental development. Threshold doses for induction of death and gross malformation are well above mean doses of common procedures, except CT scan of the pelvis. Fetal exposure is not considered to justify the greater risk of invasive fetal diagnostic procedures or pregnancy termination. A possible long-term effect is induction of cancer. Current figures suggest that the increase in risk is very small.

Postpartum Thyroiditis

Postpartum thyroid dysfunction occurs in 2-15% of women, with hypothyroidism developing in up to 23% of them after 3-5 years. Thyroid antibodies (TPO Ab, MC Ab) in pregnancy are a predisposing factor. The typical presentation is that of thyrotoxicosis followed by hypothyroidism. Lack of energy and irritability are the most frequent hyperthyroid symptoms, whereas lack of energy, aches and pains, poor memory, dry skin, and cold intolerance are the usual hypothyroid symptoms. At times it may mimic postpartum psychosis or depression. Ultrasonography of the thyroid may show a diffuse or multifocal hypoechogenicity. The duration of the illness is about 6-9 months.

Perinatal Bereavement

Pregnancy losses such as miscarriage or stillbirths are relatively common events that may lead to unresolved grief and adverse psychological effects. They may also follow ectopic pregnancies, or giving up a newborn baby for adoption.

Abnormal grief reactions may present in general practice as:

- loss of self-esteem / inadequacy
- depression / social withdrawal
- sleep disturbances
- feeling fetal movements
- anxiety and fear in next pregnancy

Hence a GP should always enquire about obstetric history in women with these problems. Exacerbation of symptoms may occur around the

The Singapore Family Physician

EDD, on the return of menstruation, or following emotional reactions of other young children.

About 1/5 of families bereaved in the perinatal period may suffer long-term adverse effects.

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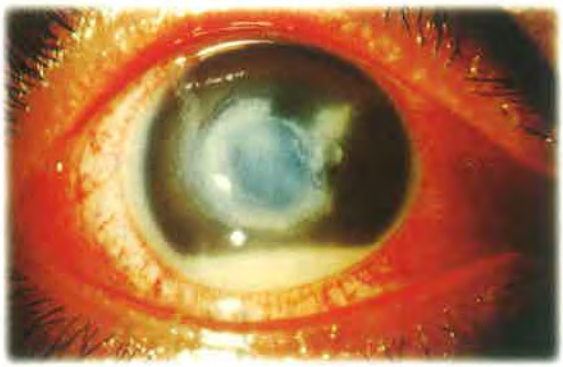
The Singapore Family Physician

Test Your Eye-Q (No. 11)
A Painful Red Eye in a Contact Lens Wearer

Polito A, Au Eong KG***

A 26-year-old male soft contact lens wearer presented with progress redness, pain, photophobia and decreased vision in his right eye for a duration of 3 days. His visual acuity was counting fingers in the right eye. Figure 1 is a photograph of his right eye.



Questions

1. What does figure 1 show?
2. What is the likely diagnosis?
3. What are the risk factors for this condition?
4. What is the initial therapy for this condition?
5. What are the serious sequelae of this condition?

Answers

1. Figure 1 shows a severely inflamed eye with conjunctival infection, a central corneal ulcer with surrounding whitish infiltrates and a layer of inflammatory white cells that have settled in the inferior part of the anterior chamber *(hypopyon)*.

2. The history of contact lens wear, the acute course and the clinical findings are suggestive of an *acute infectious keratitis or corneal ulcer*. The most common organism responsible for this condition is Pseudomonas aeruginosa, a Gram-negative bacterium. Other bacteria responsible for infectious corneal ulcers in contact lens wearers include Gram-positive bacteria (e.g. Staphylococcus aureus) and other Gram-negative bacteria (e.g. Proteus sp.). Acanthamoeba keratitis, a protozoal infection of the cornea, usually has a more chronic course over a period of several weeks.

3. A major risk factor is overnight wear of contact lenses, which is associated with a 5 to 10 fold increase in risk of infection. Other risk factors include poor contact lens hygiene such as the use of non-sterile solution and infrequent or improper cleaning and disinfection regimens. Infectious keratitis can also occur in other clinical settings such as ocular trauma (e.g. corneal foreign body, corneal abrasion) and ocular surface disorders (e.g. exposure keratopathy).

4. Acute infectious keratitis is an ophthalmic emergency and is best managed by an ophthalmologist. Prior to commencement of therapy, corneal scraping should be performed and the specimen sent for Gram-staining and culture and sensitivity to identify the offending organism and target therapy. In addition, the contact lens and its case should also be sent for culture and sensitivity. The patient should never wear the cultured contact lenses again. The initial empirical therapy includes subconjunctival and topical broad-spectrum antibiotics to cover both Gram-positive and Gram-negative bacteria. The antibiotic eyedrops commonly used are fortified gentamicin (15 mg/ml) every hour alternating with fortified cephazolin (50 mg/ml) every hour instilled around the clock (e.g. gentamicin every hour at 1, 2, 3 o'clock, etc and cephazolin every hour at 1:30, 2:30 and 3:30 o'clock, etc). A topical cycloplegic agent (e.g. atropine 1%) is often given to relieve

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ciliary spasm and to dilate the pupil. Hospitalisation is usually necessary unless the patient is able to administer the eyedrops as frequently as every 30 minutes without difficulty. Eye patching should be avoided because it may increase the risk of progression of the infection.

5. An early complication is progressive corneal thinning and perforation leading to endophthalmitis and loss of the eye. Close monitoring of the eye is therefore required until the condition improves. Delayed sequelae include corneal scarring and opacity causing significant visual impairment. A penetrating keratoplasty (corneal transplantation) may be necessary to treat this late complication.

THE COLLEGE MIRROR

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Life-time of Learning Ahead

There is an old Chinese saying that compares learning to rowing a boat upstream. If you are not rowing forward the currents will push you back.

With the recent launch of the GDFM (Graduate Diploma in Family Medicine), the College has provided yet another vehicle for the seekers of knowledge in this upstream journey. Ultimately, we would have a whole array of different types of boats to suit different types of travellers.

For starters, the College will be working to introduce a comprehensive CME programme that would anchor all levels of family physicians and keep them updated and upgraded. Those on this programme will not be swept downstream by the currents of medical and technological advances.

FROM THE EDITOR'S DESK

Those who want to push forward to a higher level can jump on-board the GDFM and row themselves up the creek. This is a user friendly part time diploma course to enable practising family physicians to continue their professional development.

If they enjoy the journey thus far and want to power up their boats even further, they can take up the challenge and go for the Masters in Medicine (Family Medicine) programme.

For the few who wants to head for the pinnacle and drink near the fountain of knowledge, they can go all the way and sign up for the Family Medicine Fellowship Programme (FMFP).

There is another saying that says you can lead a horse to water but you cannot make it drink. There are many reasons why the horse does not want to drink ...may be the horse is not thirsty ...may be the horse is too tired or too hungry to think about water ... or maybe the horse has enough of drinks. Well, the water is available. The challenge is in making the horse drink.

In the world that is changing at a tremendous pace, family physicians need to constantly keep abreast with advances and keep afloat in the ever changing tides and seas.

■ Dr Lee Kheng Hock
Honorary Secretary
College of Family Physicians, Singapore

Launch of the GDFM

The Graduate Diploma of Family Medicine was officially launched on Saturday 1 July 2000 at Lecture Room 2, College of Medicine Building. It was attended by about a hundred doctors and guests. The GDFM marks another milestone for the College. The College was also honoured to have, in attendance our newly appointed Director of Medical Services, Prof Tan Chorh Chuan, CEO National Healthcare Group, Mr Tan Tee How, DDMS (Elderly Care) Dr Ling Sing Lin and other distinguished guests. The launch was marked by a keynote address from Dr Lam Sian Lian, Chairman of the Family Medicine Committee, GSMS. A/Prof Lim Lean Huat, President of the College who gave an introductory address also provided a short historical narrative of the important pioneers of Family Medicine in Singapore. A/Prof Goh Lee Gan gave a history of the professional development and academic milestones of the College. A/Prof Cheong Pak Yean, the GDFM Course Director outlined the training structure and programme of the GDFM.

The beginnings of the GDFM arose form the 28th AGM of the College slightly more than a year ago with a College resolution that an intermediate programme be set up for doctors who were not able to pursue the more demanding and rigorous MMed(FM) examination. The Censors Board was tasked to set up the programme leading to the Diploma in Family Medicine, and to work in collaboration with the Graduate School of Medical Studies. Much planning and discussions led to fruition of the programme.

This first 2-year diploma programme registered 48 doctors, many from the private sector. The aim of the programme is to train doctors in general practice to practise Family Medicine at an enhanced level that cannot be fulfilled by the basic MBBS qualification alone. The intention of the College of Family Physicians, Singapore, is to conduct a diploma programme in Family Medicine that is within reach of most GPs and Family Physicians, including medical officers who do not intend to be specialists. This will bridge the professional education gap in the majority of general practitioners and non-specialist medical officers.

28 tutors were presented with letters of appointment as tutors for the programme. All GDFM trainees will go through all eight modules of the Family Medicine Teaching Programme plus a quarterly tutorial. They are also required to attend a Communication and Counselling Skills Course and a Principles and Practice of Family Medicine Course as well as two elective courses for the duration of the programme. There will also be a Clinical Skills course with attachments to hospitals and clinics to refine clinical skills. The GDFM course will be run annually in order to train as many Family Physicians as possible. I take this opportunity to thank all who have made the launch of the GDFM a success. With their support and assistance, Family Medicine will continue to improve as a discipline and this will augur well for Family Medicine and the health of the nation.

Dr Lau Hong Choon
Censor In Chief

Associate Professor Lim Lean Huat, President of the College, gave the opening address. He remembered the many obstacles and the hard work put into the various training programmes by College members and the supporters.

News From The College

GDFM 2000: Graduate Diploma in Family Medicine - 1 July 2000

Dr. Lam Sian Lian, Deputy Director of Medical Services and Chairperson of the Family Medicine Committee of the Graduate School of Medical Studies, said that well trained family doctors are the keys to better standards of health care for the nation. Better trained family physicians also keep the health care cost down.

48 doctors were accepted for the graduate diploma programme. There was an even mix of private and public sector primary care doctors. 28 doctors were appointed to the teaching faculty of the College to assist in this new teaching programme.

One year after the idea of having graduate diploma in family medicine was mooted in the last Annual General Meeting, the College launched the first course in the Graduate Diploma in Family Medicine. This brings the College closer to its vision of having a trained family doctor for every Singaporean.

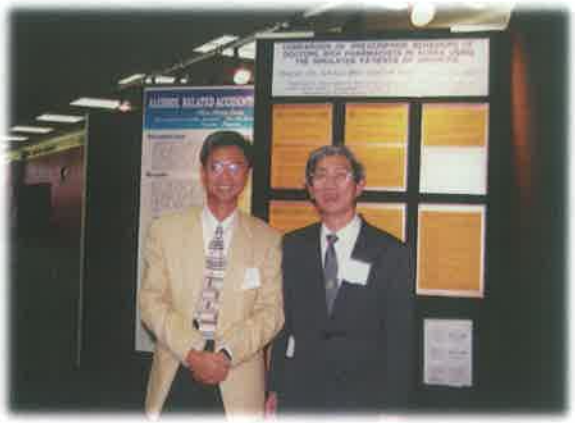
The GDFM is jointly organised by the College and the Graduate School of Medical Studies of the National University of Singapore. The GDFM is designed to be a vocational training course for family doctors and will enable them to practise at an enhanced level. Together with the MCGP/ Masters of Medicine (Family Medicine)and the Fellowship by Assessment, this new course will complete College's comprehensive programme of family medicine training.

A total of 48 doctors were accepted for the first intake. 28 tutors were appointed by the College to its teaching faculty to help run the course. The 2 year course is a distance learning programme that makes it possible for full-time family doctors to participate. The course comprises on-line reading material, workshops, tutorials and clinical skills courses. The first examination of the GDFM will be held in 2002. It is envisaged that the programme will be open to overseas participants in the near future.

Professor Tan Chorh Chuan, Director of Medical Services, Ministry of Health, was the Guest of Honour at the event. He commended the College on its efforts to improve the standard of family medicine in Singapore.

News From The College

General Practice into the New Millenium



WONCA poster exhibits from the Asia Pacific Region

The rising sun peered above the lathery canopy of clouds as the plane flew across the Tasman Sea. Beneath, the stark snow capped peaks of the Southern Alps appeared. Shortly the plane cruised across the green mosaic farmland of the Canterbury Plain to land at Christchurch International Airport. A short taxi ride then brought me to the Christchurch Convention Centre, venue of the WONCA Asia Pacific Regional Conference 2000.

It was not too long ago that a research paper of which I am one of the co-authors, was accepted by Prof Les Toop, chairman of the conference scientific programme, for presentation. Never did I realize that it was going to be such an enriching and mind-stimulating time. The conference programme includes a wide spectrum of talks on multiple facets of Family Medicine, workshops, paper presentation running concomitantly at several venues at the Convention Centre. The delegates were "spoilt" in their choices. The hospitality of the New Zealand hosts was most impeccable, with every effort made to ensure comfort to the delegates and that the programme adhered to the time schedule. They even arranged free physiotherapy to soothe the delegates' aches and pains of the neck and shoulder, not forgetting that they have to carry the 1.3 kg Book of Abstracts around. Truly remarkable!

Each of the speakers of the plenary sessions is well known in his field and had been carefully chosen to support the overall Conference theme of "General Practice into the new Millenium". The highlights include a timely message from New Zealand Governor-General, Sir Michael Hardie Boys that family doctors are of critical importance to the community and the frontline of health care at the opening ceremony.

Dr Patch Adams of the Gesundheit Institute in the USA inspired the delegates with the keynote address on the joy of caring. "We wanted to help people find their own vitality, heir celebration of life. That seemed more essential to them than being cured. People wanted life to have meaning." Dr Adams said he has never prescribed a psychotropic drug like Prozac. "I've never disliked a patient enough to give it to them. Helping a patient to have a happy life requires more creativity than reaching for a prescription pad."

An eye-popping Maori welcome at the Christchurch Convention Centre.

News From The College

Prof John Howie from the University of Edinburgh's Department of General Practice advocated patient "enablement and empowerment" as a better indicator of better quality care than mere satisfaction.

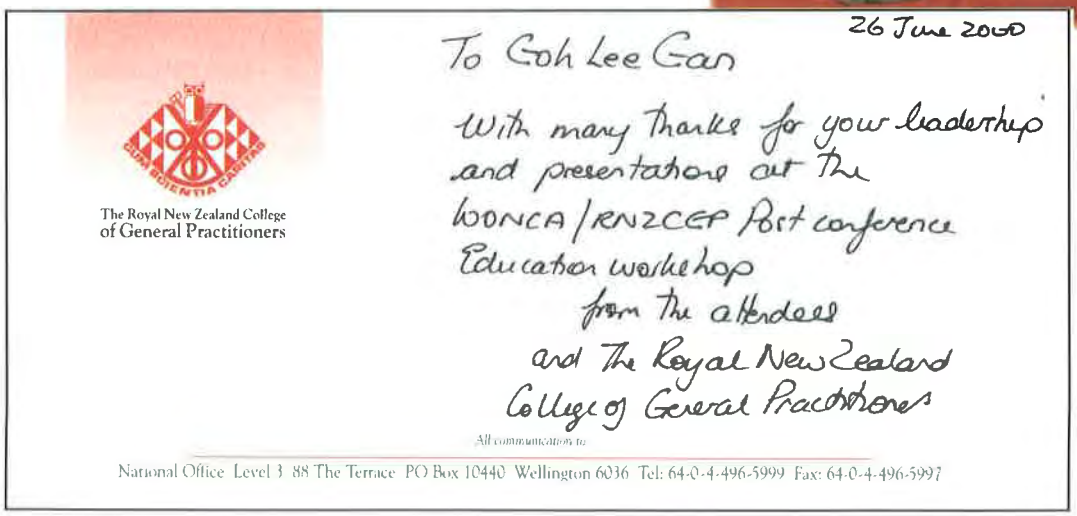
Prof Mike Pringle of the University of Nottingham examined the challenges of Family Medicine, having moved from reactive to proactive care, having taken on chronic diseases management and prevention, is now facing an even more ambitious agenda and their implications for family doctors, their teams and continuous professional development.

RNZCGP orator prof Les Toop of the University of Otago reminded the New Age GP of his multiple responsibilities and involvement in healthcare and unless the latter can adapt to the change to these trying time, he "may suffer the fate of the poor old Moa", an extinct bird in New Zealand.

Prof Jaime Galvez Tan from the University of the Philippines presented a step ladder measurement of the status of Family & Community Healthcare and highlighted the areas of "accessibility", "quality" and "equity". It was enlightening to hear his ideas of innovations of healthcare delivery at community, family and clinic levels. He shared his experience with the set-up of the Family Care Clinic in the Philippines, an innovative method to promote clinic, family and community interaction on the basis of accessibility, quality and equity.

My paper on "relations between morbidity and current treatment modalities of patients who present with acute asthma to polyclinics" went on without a hitch on the first day of the conference, with the benevolent support from Prof Goh Lee Gan. Many ideas sprouted out from the conference, which both of us hope to transplant and propagate back in Singapore. Just as Prof Jaime Tan said in his concluding sentence, "Let's Do It!"

Dr Tan Ngiap Chuan
Registrar
Queenstown Polyclinic



The Royal New Zealand College of General Practitioners

26 June 2000

To Goh Lee Gan

With many thanks for your leadership and presentations at the WONCA/RNZCGP Post conference Education workshop

from the attendees and The Royal New Zealand College of General Practitioners

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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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The journal is also circulated to all relevant government, professional, medical and academic organisations in Singapore, sister Colleges overseas and to the World Organization of National Colleges and Academies of General Practitioners/Family Physicians (WONCA).

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