THE SINGAPORE FAMILY PHYSICIAN

College of Family Physicians Singapore

Vol. 25 No. 1 /Jan – Mar 1999

MITA(P) No 191/03/98

The College Mirror

COLLEGE OF FAMILY PHYSICIANS SINGAPORE
16th COUNCIL (1997-1999)

President	:	Dr Alfred Loh Wee Tiong
Vice President	:	Dr Lim Lean Huat
Censor-in-Chief	:	A/Prof Goh Lee Gan
Honorary Secretary	:	Dr Richard Ng Mong Hoo
Honorary Treasurer	:	Dr Arthur Tan Chin Lock
Council Members	:	Dr Soh Cheow Beng
		Dr David Lim Hock Kuang
		Dr Lee Kheng Hock
		Dr Tan Chee Beng
		Dr Tan See Leng
		Dr Kwan Yew Seng
Honorary Editor	:	Dr Lau Hong Choon

BOARD OF CENSOR

Censor-in-Chief	:	A/Prof Goh Lee Gan
Censors	:	Dr James Chang Ming Yu
		Dr Lau Hong Choon
		Dr Lim Kim Leong
		Dr Lim Lean Huat

CONTINUING MEDICAL EDUCATION COMMITTEE

Chairman	:	Dr Richard Ng Mong Hoo
Ex-Officio	:	A/Prof Goh Lee Gan
Secretary	:	Dr Tan Chee Beng
Members	:	Dr Lau Hong Choon
		Dr David Lim Hock Kuang
Librarian	:	Dr Gerard Low Mun Heng

UNDERGRADUATE TEACHING COMMITTEE

Chairman	:	Dr David Lim Hock Kuang
Ex-Officio	:	Dr Lim Lean Huat
Members	:	Dr Lawerence Ng Chee Lian
		Dr Hong Ching Ye

PRACTICE MANAGEMENT COMMITTEE

Chairman	:	Dr Tan See Leng
Members	:	Dr Philip Koh
		Dr Wong Chiang Yin

FINANCE COMMITTEE

Chairman	:	Dr Arthur Tan Chin Lock
Ex-Officio	:	Dr Alfred W T Loh
Secretary	:	Dr Richard Ng Mong Hoo

RESEARCH COMMITTEE

Chairman	:	Dr Lee Kheng Hock
Ex-Officio	:	A/Prof Goh Lee Gan
Secretary	:	Dr Loh Kok Chi
Members	:	Dr Choo Kay Wee
		Dr S C Emmanuel
		Dr Angeline Chua Poh Gek
		Dr Antony Tam Wai Yan
		Dr Lawrence Ng Chee Lian

PUBLICATIONS COMMITTEE

Chairman & Honorary Editor	:	Dr Lau Hong Choon
Administrative Editor	:	Ms Yvonne Chung
Section Editors	:	A/Prof Goh Lee Gan
		Dr Arthur Tan Chin Hock
		Dr Lawrence Ng Chee Lian
		Dr Paul Goh Soo Chye
		Dr Helen Leong Soh Sum
		Dr Tan Chee Beng
		Dr Tan Ngiap Chuan
		Dr Shirley Goh Choon Kee
		Dr Siaw Tung Yeng
		Dr David Cheong
		Dr Tok Sock Cheng
		Dr Jonathan Phang Siung King
College Mirror Editor	:	Ms Yvonne Chung
Editorial Assistant	:	Ms Katy Chan

SECRETARIAT

Administrative Manager	:	Ms Yvonne Chung
Administrative Assistant	:	Ms Katy Chan

The Singapore Family Physician

Graves' Disease

The specialisation and subspecialisation in medicine, and the rapid advances in medical science and therapeutics have render many illnesses which were once considered untreatable in the past, potentially curable. This has made the practice of Family Medicine become more complex and challenging over the years.

Family physicians are seeing more patients with complex medical problems increasingly at the ambulatory care level. Family physicians have the challenging task of managing these patients by providing early diagnosis, early treatment and referral, managing disease complications and finally managing terminal stages of the illness.

Family physicians also need to coordinate care for these patients by working closely together with hospital specialists in the management of these complex medical problems as patients move from primary care to secondary care and vice versa.

Graves' disease is one such condition that is both managed at the primary care and secondary care levels. Family physicians need to be aware of the different clinical presentations of Graves' disease. It can pose a diagnostic challenge especially in the elderly.

The management of Graves' disease is equally challenging. There are a number of treatment options ranging from drug therapy, surgery to radio-iodine therapy. Family physicians should be familiar with these treatment modalities, their advantages and limitations so that they can help patients make informed decisions on their treatment options.

Thyrotoxic relapses pose a management dilemma for doctors and patients often require other treatment modalities to control the illness. In the continuing care of these patients family physicians need to be monitor the disease progression, look out for disease complications as well as treatment complications. Many patients eventually develop hypothyroidism and require life long thyroid hormone replacement. These patients continue to see their family physicians for replacement therapy and long term monitoring.

Family physicians play a pivotal role in the management of chronic diseases. They are in the ideal setting to provide continuing care, health education and counselling for their patients.

With the rapid development of therapeutics and medical technology, many diseases are increasingly being managed at the primary care level. There is a need for family physicians to continually keep themselves updated with medical literature and therapeutic advances in these areas. In this way, family physicians can manage patients with chronic diseases more effectively at the primary care level, hence reducing complications, morbidity and mortality.

Dr Tan Chee Beng
Section Editor

The Singapore Family Physician

The Benefits of College Membership

Dear Members

Greetings again from your President

With the Annual General Meeting of the College just around the corner (23 May 99), the task of encouraging members to attend the AGM has again surfaced. As this AGM involves the election of a new Council and Office Bearers, it is important that a quorum be present to vote. To achieve this objective, members must feel that they have a role to play and have a stake in the College, i.e. they must be able to identify with the College and its objectives.

During the past years, I have received feedback from members that they do not perceive any special advantage being a member. The benefits spelled out in the Constitution of the College do not seem to have an impact on the members. This has caused considerable concern to the Council.

At recent Council Meetings, the issue of benefits for College members was thoroughly discussed. After much deliberation, it was felt that some of the benefits that used to be given on an ad-hoc basis from time-to-time, in addition to those stated in the Constitution, should be spelled out clearly and made known to all members. These are listed below for your perusal. It is hoped that these benefits would help to endear more members to the College and make membership more meaningful for all. The Council hopes that it would also inspire some members to come forward and serve in the various sub-committees and training courses held by the College.

To **improve** the benefits enjoyed by members, the Council has agreed that:

- There will be ***substantial differences*** in course fees/registrations fees payable by College Members and non-members for CME events
- College members will be given information in advance on future courses, lectures and seminars, over non-members
- Priority registration will be given to College members for CME courses, lecture and seminars over non-members
- College Members can attend any two sessions of each Module of the Family Medicine Teaching Programme (a modular course consisting of 8 sessions) FREE OF CHARGE (please contact College staff in advance)
- Automatic registration for the SMC-CME Programme at no additional cost
- Complimentary copy of the quarterly Singapore Family Physician Journal and College Mirror
- Complimentary CME Calendar of events
- Use of College Library facilities for reference purposes

In my message in the inaugural issue of the 'new look' ***Singapore Family Physician*** Journal incorporating the ***College Mirror*** newsletter (Vol23, No3 1997), I stated that the College of Family Physicians Singapore should reflect the inspirations of its members. The College does, after all, exist to serve its members.

With good wishes.

Dr Alfred W T Loh
President
College of Family Physicians Singapore

The Singapore Family Physician

Thyrotoxic Graves' Disease: Diagnosis and Treatment

Loh K C

Introduction

Graves' disease is the most common cause of hyperthyroidism. It consists of one or more of the following features: 1) thyrotoxicosis, 2) goitre, 3) ophthalmopathy and 4) pretibial myxedema. A strong familial predisposition is noted: about 15% of patients with Graves' disease have a close relative with the same disorder, and 50% of relatives of patients with Graves' disease have detectable circulating thyroid auto-antibodies. Recent evidence suggests that the thyrotropin receptor (TSHR) is the primary autoantigen responsible for this condition. Graves' disease may occur at any age, with a peak incidence in the 20-to-40 year age group. Females are affected about five times more commonly than males.

Pathogenesis

Graves' disease is an autoimmune disease that develops as a result of a complex interaction between genetic susceptibility and likely environmental factors. Currently, there are extensive studies on the role of thyroid antibodies, T-cells and cytokines in the pathogenesis of Graves' disease and it is not intended to review this complex topic here.

In patients with autoimmune thyroid disease, the intrathyroidal lymphocytic infiltrate may be the initial abnormality and this can be correlated with the titre of circulation thyroid antibodies. With this background in susceptible individuals, thyroid-specific T lymphocytes are further activated either extra-thyroidally, perhaps via stress-related mechanisms, or as a result of a direct infectious assault on the thyroid cells which changes their antigen presenting status. Extrathyroidal activation may also result from crossover specificality between a thyroid antigen and an infectious agent. Once activated, the thyroid-specific T-cells induce B-cell proliferation and secretion of TSHR antibodies. Hyperthyroidism ensues if the repertoire of thyroid autoantibodies secreted are predominantly stimulating in nature, so called thyroid stimulating immunoglobulins or TSI.

Clinical Features

The common signs and symptoms of thyrotoxic Graves' disease are listed in Table 1. The thyroid gland in Graves' disease is usually diffusely enlarged because of follicular hyperplasia and hypertrophy induced by the circulating TSI. One of the earliest metabolic derangements observed in thyrotoxic patients is extensive weight loss

Table 1. Common Clinical Manifestations of Thyrotoxicosis.

Symptoms
heat intolerance
increased perspiration
tremor
palpitation
exertional dyspnoea
hyperactivity
nervousness
weakness
appetite change (usually increase)
weight loss (usually decrease)
diarrhoea
irritability
insomnia
menstrual disturbances (usually reduced flow)
General Signs
goitre (usually diffuse for Graves' disease)
hyperactivity
tachycardia or atrial arrhythmia
systolic hypertension and increase pulse pressure
warm, moist, smooth skin
stare and eyelid retraction
tremor of extremities
hyperreflexia
proximal myopathy
Autoimmune Signs for Graves' disease
infiltrative ophthalmopathy
thyroid acropachy
localised myxoedema

Dr Loh Keh Chuan,
FACP, FACE, FAMS
Consultant, Endocrine Unit
Department of
General Medicine
Tan Tock Seng Hospital
Moulmein Road
Singapore 308433
E-mail:
keh_chuan_loh@notes.ttsh.gov.sg

despite normal or increased caloric intake. This reflects both depletion of body adipose stores and loss of muscle mass. There is also altered carbohydrate metabolism, and patients with pre-existing diabetes are always aggravated by thyrotoxicosis.

The cardiovascular manifestations constitute some of the most profound symptoms and signs of thyrotoxicosis. The majority of patients have palpitations, which refer to both a rapid heart rate as well as the sensation of forceful cardiac contraction. Resting tachycardia occurs in up to 90% of patients, and atrial fibrillation is noted in 10-15% of thyrotoxic subjects. Other common cardiovascular symptoms include exercise intolerance and dyspnoea on exertion. In older patients, cardiac manifestations may predominate with absent of other classic thyrotoxic symptoms, possibly due to relative paucity of adrenergic activity. Patients with thyrocardiac disease may develop congestive cardiac failure, however this is uncommon in the absence of atrial fibrillation.

The skin of thyrotoxic patients is usually warm, erythematous and moist, as a result of increased dermal blood flow. Other cutaneous changes associated with thyrotoxicosis include eczematous dermatitis, pruritis, urticaria, diffuse hair loss, alopecia areata, and abnormalities in nail growth. The classic gastrointestinal manifestations of thyrotoxicosis are rapid intestinal transit and increased frequency of loose stools.

Almost all patients with thyrotoxicosis have some reduction in muscle power. This is most prominent in large proximal limb muscles, and usually it is associated with easy fatiguability. Patients commonly present with weakness of the legs on climbing stairs. Common neuropsychiatric manifestations in thyrotoxicosis include nervousness, irritability, and tremulousness. Some older patients may present with severe depression and a visible absent of clinical features of hypermetabolism, so called "apathetic thyrotoxicosis".

In our Asian population (especially amongst the Chinese and Japanese), up to 4-8% of thyrotoxic males may present with acute attacks of generalised paralysis, so called thyrotoxic periodic paralysis. The paralysis typically occurs in the waking hours following bed rest after a heavy carbohydrate meal the preceding evening. This is believed to result from an intracellular flux of potassium due to increased Na-K-ATPase pump activity. Restoration of euthyroidism effectively prevents episodes of weakness of paralysis, but symptoms can occur with recurrence of thyrotoxicosis.

Autoimmune manifestations of Graves' disease include infiltrative ophthalmopathy, pretibial; myxoedema, and thyroid acropachy. Graves' ophthalmopathy is the most common extrathyroidal autoimmune manifestation of Graves' disease, however clinically significant ophthalmopathy remains an uncommon finding amongst our Asian patients. The natural history characteristically consists of an initial progressive phase over 3-6 months, a lengthy plateau phase, followed eventually by gradual spontaneous improvement in most patients. During the progressive phase, vision-threatening complications such as optic neuropathy or corneal ulceration may develop that demand urgent therapy. Pretibial myxoedema is almost always associated with Graves' ophthalmopathy and the process commonly involves the pretibial region, although it can affect other areas as well. This is characterised by localised skin thickening due to glycosaminoglycan accumulation in the dermis and subcutaneous tissues. Thyroid acropathy is the least common manifestation of autoimmune thyroid disease, and it almost always occurs in association with ophthalmopathy and dermopathy. Typically, this presents as soft tissue swelling of the hands and feet, usually in association with clubbing go the fingers and toes.

Laboratory evaluation

In most patients, the clinical symptoms and signs will accurately identify the diagnosis of thyrotoxicosis. In addition, if the patient has a diffuse goitre and ophthalmopathy, the cause is Graves' disease. Nevertheless, there can be considerable variability in terms of the clinical presentation and disease severity amongst patients. In patients suspected clinically of having thyrotoxicosis, serum thyroid stimulating hormone (TSH) and free thyroxine (T4)

concentrations should be measured. The diagnosis is confirmed by finding a low serum TSH value (often suppressed below the functional sensitivity limits of the new generation TSH assays) and a high serum free T4 value. If the serum TSH is low and the serum free T4 value is normal, the patient could have triiodothyronine (T3)-associated or subclinical hyperthyroidism, the two entities are distinguished by measuring serum T3 concentration. If the serum TSH value is normal or high and the serum free T4 value is high, then the patient should be evaluated for TSH-induced thyrotoxicosis, such as TSH secreting pituitary adenoma.

Assays for antibodies directed against the TSHR in Graves' disease can either measure that ability of the patient's serum to compete for binding of TSH to its receptor (called thyrotropin-binding inhibitory immunoglobulins or TBII) or the ability of the patient's serum to simulation induced by patient's serum (termed thyroid stimulating immunoglobulins or TSI). However, the clinical utility for these assays is currently limited.

Thyrotoxicosis caused by inflammatory processes (eg. subacute thyroiditis, postpartum thyroiditis) has a transient and self-linking course due to the release of preformed hormones consequent to thyroid follicular disruption. In suspected cases, radioactive iodine uptake (RAIU) study should be performed to differentiate them from Graves' disease. Thyroidal RAIU is absent or low in patients with destructive thyroiditis and high in patients with hyperfunctioning Graves' disease. The causes of hyperthyroidism are listed in Table 2.

Table 2. Causes of Thyrotoxicosis.

Primary Hyperthyroidism
- Graves' disease
- Toxic nodular goitre
- Toxic adenoma
- Excessive iodine ingestion (eg. amiodarone-induced)*
- Gestational thyrotoxicosis (patients with severe hyperemesis gravidarum)
- TSH-secreting pituitary adenoma (rare)
- Activating mutations of TSH receptor (very rare)
- Selective pituitary resistance to thyroid hormone (very rare)

Destructive Thyroiditis
- Subacute thyroiditis (de Quervain's)
- Silent thyroiditis
- Postpartum thyroiditis

Non-thyroidal Disease
- Thyrotoxicosis factitia
- Metastatic thyroid cancer (rare)
- Struma ovarii (very rare)

*Amiodarone is an iodine-rich compound which can produce thyrotoxicosis either by increased glandular hormone synthesis (primary hyperthyroidism) or destructive thyroiditis.

Definitive Therapy

The treatment of Graves' disease is directed toward lowering the circulating thyroid hormone concentrations to re-establish a eumetabolic state. All three currently available modalities of treatment for Graves' hyperthyroidism, viz. the use of antithyroid drugs, radioactive iodine, or surgery - are equally effective in this regard. It is often a matter of debate as to which is the best therapeutic option, and opinions vary according to country and continent. The final choice often depends on a number of factors, not the least of which are the physician's experience and the patient's preferences. Ideally, the patient should be informed of the indications and implications of all forms of therapy, including risks, benefits, and side effects, and should participate in the decision-making process.

1. Antithyroid Drugs

Treatment with antithyroid drugs is a viable first-line option in patients with new-onset Graves' hyperthyroidism. However, the recognition of a high probability of relapse after discontinuation of antithyroid drug therapy has dampened enthusiasm for its use in some countries like the United States. Antithyroid drug is the treatment of choice for hyperthyroidism in pregnancy, and it is commonly used for treating childhood Graves' disease. When used as a primary mode of treatment for thyrotoxicosis, it is hoped that a remission of Graves' disease will eventually occur. Antithyroid drug is also used to lower thyroid

hormone levels prior to ablative therapy with radioactive iodine or surgery.

Antithyroid drugs are thionamide derivatives and they fall into two basic classes: the thiouracils (propylthiouracil or PTU) and imidazoles (carbimazole thiamazole or methimazole). Carbimazole is rapidly metabolised to its active compound thiamazole or methimazole, hence the two drugs can be considered similar. Both PTU and carbimazole are extremely effective in controlling thyrotoxicosis by inhibiting specific steps in thyroid hormone biosynthesis. To some extent, the choice between the drugs resides on personal preference. However, some notable differences do exist between these two classes of thionamides, which in turn may dictate their choice in the individual patient.

Carbimazole is the preferred antithyroid drug because of the better patient compliance with its single daily dosing. It has a longer duration of action because of its relatively long serum as well as intrathyroidal half-life. Other advantages of carbimazole include a more rapid restitution of euthyroid state, and a lower incidence of agranulocytosis when used in lower doses. However, PTU is the preferred drug in pregnancy, lactation and thyroid storm. This is because PTU has greater serum protein-binding and lower lipid solubility, and hence it is associated with lower placental transfer as well as lesser secretion in breast milk. PTU also has the ability to inhibit T4 to T3 conversion, which is advantageous in patients with severe thyrotoxicosis. A comparison of selected pharmacologic features of the antithyroid drugs is shown in Table 3.

Table 3. Pharmacology of Thionamides.

	Propylthiouracil	Carbimazole or Methimazole
Relative therapeutic potency	1	10-50 x
Oral absorption	complete	complete
Serum protein binding	75%	negligible
Serum half-life	1-2 h	4-6 h
Duration of action	8-12 h	24 h
Transplacental passage	very low	low
Levels in breast milk	very low	low

The usual starting dose of PTU is 100-150 mg three times daily, and the dose for carbimazole being 20-30 mg daily. Besides non-compliance, virtually all patients can be controlled on antithyroid drugs if sufficiently high doses are used. The mean time to achieving euthyroidism is usually 6-12 weeks; factors that determine the speed of recovery include disease activity, the initial degree of hyperthyroidism, and the intrathyroidal hormone stores. When used as a primary mode of treatment, antithyroid drug is usually given for a period of 12-24 months. In the dose-titration regime, the dose of antithyroid drug is titrated individually according to clinical response and thyroid function results. The ability to decrease the dose with continuing treatment probably reflects waning of disease activity, possibly due to a decline in TSI production.

Antithyroid drugs are generally safe and fewer than 5% of patients experience adverse reactions (Table 4). Most of the side effects are mild and fall into allergic category, such as fever, rash, urticaria, pruritis, and arthralgia. The more serious, but fortunately rarer, side effects include agranulocytosis, aplastic anaemia, toxic hepatitis, cholestatic jaundice, vasculitis, and a lupus-like syndrome. Agranulocytosis is the most feared problem and all patients prescribed with

Table 4. Adverse Reactions associated with Thionamides.

Minor (1-5%)
- fever
- rash
- urticaria
- pruritis
- arthralgia
- transient leukopenia

Major (0.3-0.5%)
- agranulocytosis
- aplastic anaemia
- toxic anaemia
- toxic hepatitis
- cholestatic jaundice
- lupus-like syndrome
- vasculitis
- insulin-autoimmune syndrome

thionamides should be cautioned to stop the drug immediately and get their white cells counts checked if they develop high fever, severe sore throat, or other signs of infection. In the case of minor drug-related side effects, one antithyroid drug may be substituted for the other, with the awareness of the possibility of a 10% crossover reaction. However, the occurrence of agranulocytosis should preclude the use of any thionamide formulations.

Role of Block-Replace Regime

In 1991, Hashizume and co-workers reported a novel "block-and-replace" regime for Graves hyperthyroidism in which thyroxine was continued alone after the combination therapy was stopped resulted in a negligible relapse rate of 1.7%. Such a finding has the potential to revolutionise the management of Graves' disease but unfortunately subsequent studies from Japan as well as Europe and North America failed to confirm any benefit from using various block-replace methods. Therefore, such regimes are no longer widely used because of the need for concomitant thyroxine administration and the risk of increased serious side effects associated with higher thionamide doses. Furthermore, the continual administration of thyroxine after stopping antithyroid drug may delay the diagnosis of recurrence (as serum TSH levels may remain suppressed with thyroxine therapy) as well as causing exacerbation of thyrotoxicosis in the event of recurrence.

However, the block-and replace regime may have a practical value in situations whereby a more stable control of the thyroid status is important, as in patients with significant ophthalmopathy in an attempt to avoid hypothyroidism (as hypothyroidism may exacerbate ophthalmopathy). Other indications for its use include patients with "brittle hyperthyroidism" in whom thyroid function fluctuates from one extreme to the other at successive clinic visits, and patients who could not attend regular clinic visits for appropriate dose titration.

Dr Loh Keh Chuan
FACP, FACE, FAMS
Consultant, Endocrine Unit
Department of General Medicine
Tan Tock Seng Hospital
Moulmein Road
Singapore 308433
E-mail:
keh_chuan_loh@notes.ttsh.gov.sg

Remission and Antithyroid Drug Therapy

Remission rates in patients with Graves' disease after a course of medical therapy have been reported to vary from 14% to 80%. Despite the difficulty to predict which patients are most likely to have remission, certain factors like a small goitre and mild biochemical thyrotoxicosis at the beginning of therapy are associated with improved odds of long-term remission. Features during therapy that are favourable predictors of remission include a decrease in goitre size, the ability to control the thyrotoxicosis with small doses of drug, and normalisation of serum T4 to T3 ratio. In general, longer courses of therapy are associated with improved remission rates after the drug is stopped. Serum TSI concentrations normally decrease during antithyroid drug therapy; the failure of its disappearance during treatment signifies almost certain relapse after drug discontinuation. Although the presence of persistent TSI activity has prognostic value, its absence is not useful as a prognostic indicator as there is still a 20-50% chance of relapse in individuals without TSI activity. Table 5 provides a summary of factors affecting remission in Graves' hyperthyroidism.

Table 5. Factors affecting Remission in Graves' Disease.

Factor	Probability of Remission
Disease severity:	
Large goitre	decrease
Severe TFT derangement	decrease
Persistently elevated TSI	decrease
Other patient-related factors:	
Prior relapse	decrease
Pregnancy	increase
Post partum period	decrease
High dietary iodine intake	decrease
Therapy-related factors:	
Longer duration of therapy	probably increase
Higher drug dose	probably no effect
Block-replace regime	probably no effect

TFT: thyroid function test
TSI: thyroid stimulating immunoglobulin

The Singapore Family Physician

2. Radioactive Iodine

Radioactive iodine (RAI) is commonly used as the first-line treatment of Graves' disease in the United States, whereas this usually constitutes the second-line option in other parts of the world. In contrast to antithyroid drugs, both RAI and surgery represent the ablative form of treatment for thyrotoxicosis. Following RAI therapy, most patients experience symptomatic improvement by 4-6 weeks, with complete reversal of hyperthyroidism by 2-3 months. The primary drawback of RAI therapy is the high incidence of subsequent hypothyroidism, which may occur in up to 80% of patients. Treated patients therefore require long-term monitoring and thyroxine replacement when appropriate.

RAI is contraindicated during pregnancy because of possible teratogenic effects if administered within the first trimester, and fetal hypothyroidism if given after 10 weeks. Women are also advised to postpone pregnancy after RAI treatment, the usual waiting period being 4-6 months. RAI should be deferred in women who are breastfeeding, because the radioisotope is secreted in the breast milk. RAI therapy may also cause exacerbation of eye disease in patients with clinically significant ophthalmopathy. However, this untoward outcome can be prevented by concomitant administration of systemic glucocorticoids. Cigarette smoking should be discouraged as it has a deleterious effect on the course of ophthalmopathy.

3. Thyroid Surgery

Described in 1900, subtotal thyroidectomy was the first available therapeutic option for Graves' hyperthyroidism, and it antedates the use of thionamides and RAI, both of which were not introduced until the 1940s. However, surgery has progressively become a less desirable alternative and there is little reason to consider surgery except in special circumstances. These include patients with a coincidental thyroid nodule in which malignancy is suspected, patients requiring ablative treatment but having extreme aversion to RAI, and the extremely rare pregnant patients who are intolerant of antithyroid drugs. Besides the expense related to surgery, other drawbacks include the risk of anaesthesia and possible complications of surgery to the neck structures, the two most feared complications being hoarseness of voice (due to recurrent laryngeal nerve paralysis) and permanent hypoparathyroidism. There is also the possibility of recurrence if inadequate amounts of thyroid tissues are removed. Like RAI therapy, long-term follow-up is necessary to rule out hypothyroidism in surgically treated patients.

Adjuvant Therapy

1. β-Adrenergic Blockers

The adjunctive use of β-adrenergic antagnoists has significantly improved the management of symptomatic patients by alleviating the hyperadrenergic manifestations of thyrotoxicosis such as tremor, palpitation, anxiety, and heat intolerance. Other manifestations of increased β–adrenergic responses, such as lid lag, lid retraction, widened palpebral fissures and hyperreflexia are also ameliorated by β-adrenergic blockade. Treated patients also have a small, though unlikely clinically significant, decrement in serum T3 levels because of the inhibitory effect on T4 deiodination by β-adrenergic blockers.

Although propranolol is the β-adrenergic blocker originally used for throtoxicosis, newer agents (eg. atenolol or metoprolol) that are long-acting and more cardioselective are now commonly used. The usual starting dose of propranolol is in the range of 80-160 mg per day in 2-4 doses; similar effects are produced by 50-100 mg per day of atenolol or metoprolol. The drug is gradually withdrawn as serum thyroid hormone levels return to normal. β-adrenergic blockade is contraindicated in patients with a clear history of asthma, and it should be cautiously used in patients with rate-related heart failure.

2. Iodinated Contrast Agents

Iodide-containing oral cholecystographic agents (eg. ipodate sodium or iopanoic acid) have been shown to inhibit thyroid hormone synthesis and release as well as the peripheral conversion of T4 to T3. Ipodate sodium is given in a usual dose of

1 g daily; this results in rapid restoration of euthyroidism because of its potent inhibition of T4 deiodination. However, it has limited value in long-term therapy because of the ultimate escape of thyroid hormone synthesis from the effect of iodide. Another drawback is that the thyroid gland becomes saturated with iodide, rendering it resistant to subsequent therapy with either RAI or thionamides. Therefore, antithyroid drugs should be given before ipodate or other iodide-containing substances (even if only 1-2 hours) to prevent new hormone stores from incorporating iodide.

Some conditions exist for which short-term iodide therapy can be useful. Patients with life-threatening thyrotoxicosis or thyroid storm will benefit from the use of iodide to effect rapid control of their disease. The combination of iodides and β-adrenergic receptor blockers are effective for disease stabilisation and prevention of worsening thyrotoxicosis in patients with uncontrolled hyperthyroidism who require emergency nonthyroid surgery. Patients who develop a severe allergic reaction to antithyroid drugs can be similarly controlled whilst preparing for definitive thyroid surgery.

3. Anticoagulation

Atrial fibrillation occurs in about 10-15% of hyperthyroid patients, with older patients being more commonly affected. In view of the possible risk of systemic embolisation, anticoagulation therapy should be considered, particularly in patients with organic heart disease or congestive heart failure.

Suggested Reading

1. Singer PA, Cooper DS, Levy EG, et al. Treatment guidelines for patients with hyperthyroidism and hypothyroidism. JAMA 1995; 273:808-12.

(Note: treatment guidelines drawn by the American Thyroid Association; provides the management of Graves' hyperthyroidism the American way.)

2. Vanderpump MPJ, Ahlquist JAO, Franklyn JA, et al. Consensus statement for good practice and audit measures in the management of hypothyroidism and hyperthyroidism. BMJ 1996; 313:539-44.

(Note: consensus statement provided by the British working group consisting of the Royal College of Physicians of London and the Society for Endocrinology, UK.)

3. Cooper DS. Antithyroid drugs for the treatment of hyperthyroidism caused by Graves' disease. Endocrinol Clin North Am 1998; 27:225-47.

4. Wartofsky L, Glinoer D, Solomon B, et al. Differences and similarities in the diagnosis and treatment of Graves' disease in Europe, Japan and the United States. Thyroid 1991; 1:129-35.

(Note: survey conducted on physician members of the American, European and Japanese Thyroid Associations respectively to examine their treatment preferences for Graves' hyperthyroidism)

5. Young ET, Steel NR, Taylor JJ, et al. Prediction of remission after antithyroid drug treatment in Graves' disease. Q J Med 1988; 66:175-89.

6. Okamura K, Ikenoue H, Shiroozu A, et al. Reevaluation of the effects of methylmercaptoimidazole and propylthiouracil in patents with Graves' hyperthyroidism. J Clin Endocrinol Metab 1987; 65:719-23.

7. Hashizume K, Ichiwara K, Sakuri A, et al. Administration of thyroxine in treated Graves' disease. Effects on the level of antibodies to thyroid stimulating hormone receptors and on the risk of recurrence of hyperthyroidism. N Engl J Med 1991; 324:947-53.

(Note: A randomised controlled study demonstrating a negligible relapse rate using the novel "block-and-replace" regime in Japanese patients with Graves' hyperthyroidism. Findings considered peculiar because of the failure to replicate the results in other major studies, as cited in references 8-10)

8. Melver B, Rae P, Beckett G, et al. Lack of effect of thyroxine in patients with Graves' hyperthyroidism who are treated with an antithyroid drug. N Engl J Med 1996; 334:220-4.

9. Tamai H, Hayaki I, Kawai K, et al. Lack of effect of thyroxine administration on elevated thyroid stimulating hormone receptor antibody levels in treated Graves' disease patients. J Clin Endocrinol Metab 1995; 80:148-4.

10. Rittmaster RS, Abbott EC, Douglas R, et al. Effect of methimazole, with or without thyroxine, on remission rates in Graves' disease. J Clin Endocrinol Metab 1998; 83:814-8.

11. Bartalena L, Marcocci C, Bogazzi F, et al. Relation between therapy for hyperthyroidism and the course of Graves' ophthalmopathy. N Engl J Med 1998; 338:73-8.

(Note: a prospective study to evaluate the progression of ophthalmopathy in patients with Graves' hyperthyroidism randomly assigned to receive treatment with radioiodine, radioiodine and prednisone, or antithyroid drug)

The Singapore Family Physician

Stroke

N Venketasubramanian

Summary

Stroke is a major cause of death and disability in Singapore. From the history, clinical examination and appropriate investigations, the risk factors, clinical syndrome, and stroke subtype and mechanism are derived. Drugs to safely and effectively reperfuse or neuroprotect ischemic brain tissue are under investigation. Specific treatment is available to reduce stroke recurrence. Good general management of the patient is essential. Stroke patients are best managed in a stroke unit. Rehabilitation should be started early. Stroke prevention and stroke support should be actively pursued. The general practitioner is in a key position to play a major role in the acute and long-term management of the patient with stroke.

Keywords

stroke, cerebrovascular disease, risk factors, subtypes, investigations, treatment, prevention

Introduction

Stroke is Singapore's third leading cause of disability. The crude death rate for stroke has been between 50 to 60/100 000 since 1970, accounting for 10 to 12% of all deaths. In parallel with the ageing population, the number of patients dying in or discharged from Singapore hospitals for stroke has been rising, exceeding 8000 in 1996; the number is likely to cross 10 000 by the year 2000. As up to 25% of acute stroke patients first see the general practitioner(GP) before coming to hospital, and most will return to their GP for follow-up after discharge from hospital, the GP plays a key role in the early and subsequent care of the patient with stroke.

Terminology

Stroke is said to have occurred when there are "rapidly developing clinical signs of focal (at times global) disturbance of cerebral function lasting more that 24 hours, or leading to death, with no apparent cause other than that of a vascular origin". The term "transient ischemic attack" (TIA) is used when the signs resolve completely within 24 hours. Most true TIAs resolve within minutes. The term "reversible ischemic neurologic deficit"(RIND) is no longer used.

Risk Factors

The common stroke risk factors are listed in Table 1. While there is no clear racial predilection for stroke in Singapore, the mortality rate form stroke is highest among the Malays. From the Tan Tock Seng Hospital Stroke Data Bank(TTSHSDB), the mean age of stroke patients was 65.4yr, with 54.5% males. The proportion of stroke patients with a history of hypertension was 67.8%, smoking 22.3%, diabetes mellitus 39.7%, hyperlipidemia 6.3%, heart disease 24.5%, previous stroke or TIA 22.3%.

Non-modifiable Risk Factors	Older age Male sex ?Race
Modifiable Risk Factors	Hypertension Smoking Diabetes Mellitus Hyperlipidemia Atrial fibrillation, heart disease Prior stroke or TIA Severe carotid stenosis

Table 1. Stroke Risk Factors

Clinical presentation

The common clinical presentation of stroke are listed in Table 2. The symptoms may occur suddenly, or may be noticed only after awakening from sleep. About 20% of strokes get worse during the hours or days following the onset.

Weakness of one side
Numbness of one side
Slurred of incoherent speech
Loss of vision in one or both eyes
Diplopia
Vertigo in association with other symptoms
Sudden very severe headache
Drowsiness or loss of consciousness

Table 2. Common Clinical Presentations of Stroke

Dr N Venketasubramanian, MBBS, MMed (Int Med), FAMS (Neurology)
Consultant Neurologist
Director Stroke Program, Tan Tock Seng Hospital
Clinical Coordinator (Stroke), National Neuroscience Institute
Singapore

Type and place of practice: clinical neurology in a restructured government teaching hospital

Address for correspondence:
Dr N Venketasubramanian, Consultant Neurologist
Department of Neurology
Tan Tock Seng Hospital
Moulmein Road
Singapore 308433
Tel: 256 6011
Fax: 253 2884
Email: ramani_nv@notes.ttsh.gov.sg

The lacunar syndrome is a distinct clinical entity that is easily recognised. The more common manifestations include "pure motor stroke" (weakness of face, upper and lower limb of one side), "pure sensory stroke" (numbness of the face, upper and lower limb of one side), "sensorimotor stroke" (weakness and numbness of the face, upper and lower limb of one side), and "ataxic hemiparesis" (unilateral limb ataxia out of proportion to the mild weakness). There are no cortical signs (aphasia, neglect, anopia, apraxia, drowsiness) or brainstem signs (lower motor cranial nerve palsies). It is usually due to a small deep infarct from occlusion of a small artery (small vessel disease). The prognosis is generally good in terms of recovery and stroke recurrence.

Stroke mechanisms

Strokes are either ischemic or hemorrhagic. The various stroke mechanisms and subtypes are listed in Table 3. From the TTSHSDB, 26% of strokes are hemorrhagic and 74% ischemic. Approximately 1.8% were due to subarachnoid hemorrhage(SAH), 24.2% hypertensive hemorrhage, 39.0% small vessel occlusion, the remainder large artery occlusion from various causes. It is important to differentiate among the different stroke subtypes and mechanisms as treatment and prognosis are different. The important differential diagnoses of stroke are listed in Table 4.

Ischemic Stroke	Small vessel disease Intracranial atherosclerosis Artery-to-artery embolism, eg from carotid stenosis Hemodymanic effects of extracranial disease Cardioembolism Hypercoagulable state Others
Hemorrhagic Stroke	Aneurysmal subarachnoid hemorrhage Ruptured arteriovenous malformation Hypertensive hemorrhage Bleeding tendency Others

Table 3. Stroke Mechanisms and Subtypes

Brain tumour – primary, metastatic
Abcess
Subdural hematoma
Metabolic disturbance – hypo/hyperglycemia, hypo/hypernatremia
Post-ictial state
Multiple sclerosis
Complicated migraine
Others

Table 4. Important Differential Diagnoses of Stroke

Acute management

The acute management begins as early as in the GP's clinic, and continues in hospital. The usual acute measures are listed in Table 5. A capillary sugar must be done to exclude hypoglycemia. Excessive lowering of high blood pressure in the acute phase of stroke may be detrimental. Patients with hyperglycemia or hyperpyrexia have a poorer outcome. Intravenous dextrose infusions are avoided.

Avoid excessive lowering of blood pressure
Control hyperglycemia
Treat hyperpyrexia
Administer oxygen if hypoxic
Avoid feeding if unable to take and retain safely

Table 5. Acute General Management of Stroke

Stroke Unit

A stroke unit refers to a geographical co-location of stroke patients, or a mobile multidisciplinary team of health professionals interested and knowledgeable in the care of the stroke patient. Stroke units have been shown to reduce stroke mortality, morbidity, length of stay, cost of hospital care and the need for institutionalisation. Team members may comprise doctors, nurses, therapists, dieticians, medical social workers and nurse educators. The family should be involved as soon as possible in the care of the patient. The team works together to optimise patient care, rehabilitation goals and discharge planning.

Investigations

Investigations are required to confirm the diagnosis, exclude differential diagnoses, differentiate ischemic from hemorrhagic stroke,

detect risk factors, determine the mechanism of the stroke, and detect complications. The investigations usually performed are listed in Table 6.

General Investigations	Brain scan – CT or MRI Full blood count Electrolytes, sugar Chest X-ray Electrocardiogram
Ischemic Stroke	Lipid profile Ultrasonography – extracranial, transcranial Procoagulant sceen in younger patients KIV CT or MR angiography KIV catheter angiography
Hemorrhagic Stroke	Coagulation profile KIV catheter angiography

Table 6. Investigations for Suspected Stroke

Acute Intervention

A number of clinical trials have shown the benefits or lack thereof of, a number of therapeutic interventions:

1. *Thrombolytics.* Intravenous recombinant tissue plasminogen activator (rTPA), when administered within 3 hours of stroke onset, has been shown to increase the number of patients with no or minimal disability without a significant increase in midterm mortality. There is however a 10-fold increase in potentially fatal intracranial hemorrhage. The issues of which thrombolytic agent, dose, route of administration, time window and patient selection are still unresolved.

2. *Neuroprotectants.* Previous trials of neuroprotectants either failed to show efficacy or had unacceptable side effects. Nimodipine has been shown to be beneficial in SAH. Trials are in progress to discover a neuroprotectant that is both safe and effective. If found, it may even be administered by the GP before sending the patient to hospital.

3. *Early use of antiplatelets, anticoagulants.* The large International Stroke Trial and Chinese Acute Stroke Trial have shown the benefits of early administration of aspirin for ischemic stroke, in terms of reducing recurrence as well as improving outcome. Subcutaneous fraxiparine, when given early after stroke, was found in a Hong Kong study to improve outcome at 6 months. However, a repeat of this study in an international population failed to show the same benefit.

4. *Surgery.* Early clipping of ruptured aneurysms of patients with SAH has reduced the risk of recurrent hemorrhage, and improved outcome. Evacuation of intracerebral hematomas has not been shown to be of value. Decompression craniectomy reduces mortality in patients with massive hemispheric infarction, but does not reduce morbidity. Evacuation of cerebellar hematomas and posterior fossa decompression of cerebellar infarcts are clearly of benefit. Extraventricular drainage may be required for acute hydrocephalus. Angioplasty and intra-arterial instillation of vasodilators have been successfully performed for post-SAH vasospasm.

Reducing stroke recurrence

The risk of a recurrent stroke after the first stroke is 5 to 15% per year, depending on the mechanism. A number of interventions are useful, and may be employed in the setting of a clinical algorithm (Figure 1).

1. *Anticoagulants.* Anticoagulants have been shown to reduce the risk of recurrent stroke in those with atrial fibrillation. The recommended target INR is 2 to 3. Anticoagulants are widely used for stroke in evolution, crescendo TIAs and basilar artery thrombosis. Heparin, low molecular weight heparins and heparinoids reduce deep venous thrombosis and pulmonary embolism. Patients who are frail, unwilling to take medication reliably or return for regular follow-up are not suitable candidates for long term anticoagulation.

2. *Antiplatelets.* The long term use of antiplatelets has been shown to reduce the recurrence of stroke, myocardial infarction and vascular death. While aspirin is the most widely used

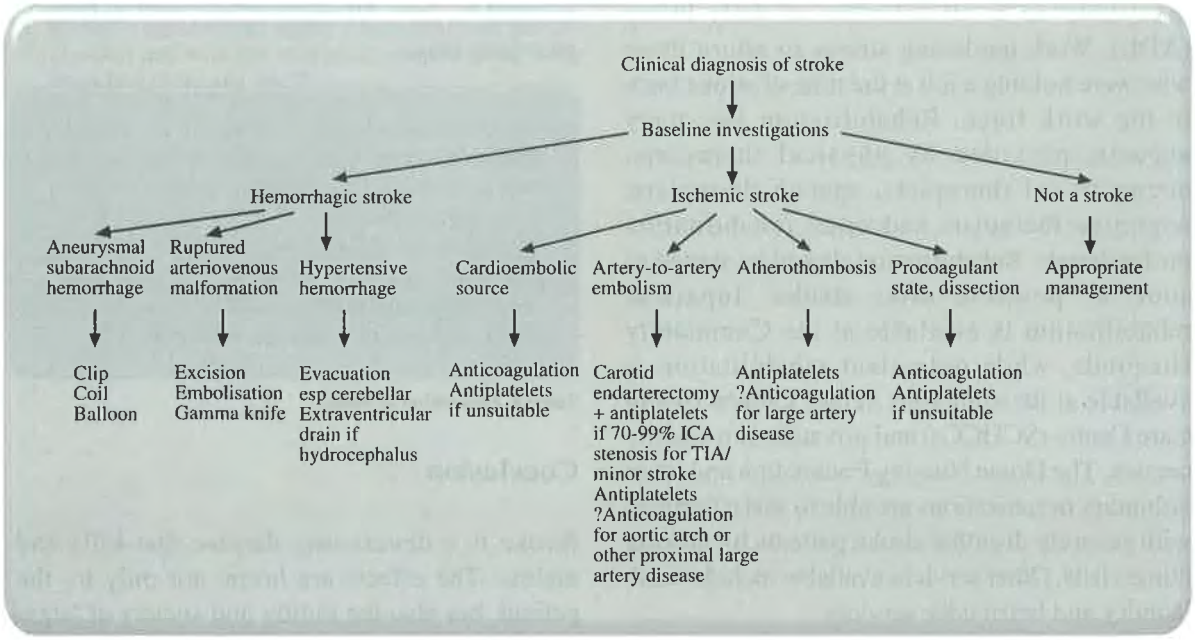


Figure 1. Treatment algorithm for stroke

drug, other effective agents include ticlopidine, clopidogrel and the combination of aspirin and dipyridamole. The optimal dose of aspirin is uncertain; higher doses carry an increased risk of hemorrhage.

3. *Carotid endarterectomy.* Carotid endarterectomy for severe symptomatic stenosis in patients with TIA or minor stroke significantly reduces the risk of another event. Angioplasty and stenting are still under investigation.

4. *Surgery/Interventional Neuroradiology.* Aneurysms may be clipped, or have coils inserted, or be trapped between balloons. Arteriovenous malformations(AVMs) may be excised surgically; some may be embolised by "glue", either as a curative or pre-operative measure. Small deep AVMs may be obliterated by gamma-knife irradiation.

General Management

While the results of investigations and treatment are awaited, the general management of the patient should not be forgotten (Table 7). This holistic approach involves attention to the many other aspects of the illness that, if neglected, will adversely affect the outcome.

Adequate fluid and nutrition
Avoid aspiration pneumonia; avoid oral feeding if unable to take safely
Institute bladder and bowel care
Regular turning to reduce the risk of pressure sores
Adequate skin care and hygiene
Consider deep venous thrombosis prophylaxis
Monitor for complications

Table 7. General Management of Stroke

Care givers of stroke patients, especially of patients who are severely disabled, would need care giver training to equip them with the required skills to adequately care for the patient at home. The many aspects include feeding, bathing, turning, skin care and hygiene.

Recovery and Rehabilitation

Post-stroke recovery is a natural process. Studies have shown that 10 to 30% of stroke patients recover fully, about one third recover partially, and one third do not recover at all; about 10 to 20% die from the stroke. Most of the recovery occurs in the first 3 to 6 months, though recovery may occur for up to 2 years or more.

Rehabilitation is a cornerstone in stroke management. Rehabilitation aims to return the patient to as functional a state as possible, with

independence in all activities of daily living (ADL). Work hardening strives to return those who were holding a job at the time of stroke back to the work force. Rehabilitation has many aspects, provided by physical therapists, occupational therapists, speech therapists, cognitive therapists and other rehabilitation professionals. Rehabilitation should be started as soon as possible after stroke. Inpatient rehabilitation is available at the Community Hospitals, while outpatient rehabilitation is available at the numerous Senior Citizen Health Care Centre (SCHCCs) and privately-run therapy centres. The Home Nursing Foundation and other voluntary organisations are able to assist families with severely disabled stroke patients by making home visits. Other services available include meal, laundry and befriender services.

Stroke Support

The effects of stroke are felt not only by the stroke patient but also the family and loved ones. The involvement of stroke support groups would provide much-needed psychological support, so that patients and families do not feel alone with their problems. Stroke support groups have been established in many of our hospitals. The Singapore National Stroke Association, established in 1996, is a national-level support group that conducts many activities, including stroke support, social activities and public education programs.

Stroke Prevention

"Prevention is better that cure", goes the old saying. This applies particularly to stroke, where the disease kills or disables. Whilst little can be done about the ageing process or gender, there are many measures that are effective in reducing stroke risk (Table 8). The preventive role of hormonal replacement therapy in postmenopausal women is still under study. Red wine and other alcohol, taken in moderation, may be protective. Carotid endarterectomy for severe asymptomatic carotid stenosis may be beneficial if performed by a skilled surgeon. There is no role for aspirin prophylaxis in the well person without stroke risk factors. While the risk of stroke may never be reduced to zero, all these efforts will definitely go a long way.

Control hypertension
Stop smoking
Treat diabetes mellitus, hyperlipidemia
Treat atrial fibrillation
Continue medications for prior stroke, TIA
?hormonal replacement therapy
?moderate alcohol intake
?surgery for asymptomatic carotid stenosis

Table 8. Prevention of Stroke

Conclusion

Stroke is a devastating disease that kills and maims. The effects are borne not only by the patient, but also the family and society at large. The General Practitioner plays a vital role in the chain of activities, ranging from prevention, acute care, post-discharge follow-up and support for the patient and family with stroke. The General Practitioner, who often is the health professional closest to and mostly highly regarded by the family and patient, is in a unique position to do more for this disease than any other person in the health care field.

Further Reading

1. Venketasubramanian N. Stroke in Singapore – An Overview. Singapore Med J 1999;40:48-52

2. Venketasubramanian N. Stroke management in the Decade of the Brain. Singapore Med J 1998;39:2-3

3. Furlan AJ, Kanoti G. When is thrombolysis justified in patients with acute ischemic stroke? Stroke 1997;28:214-8

4. Wahlgren NG. Pharmacological treatment of acute stroke. Cerebrovasc Dis 1997;7(Suppl 3):24-30

5. Antiplatelet Trialists Collaboration. Collaborative overview of randomised trials of antiplatelet therapy – I: Prevention of death, myocardial infarction and stroke by prolonged antiplatelet therapy in various groups of patients. Br Med J 1994;308: 81-106

6. Dyken ML. Antiplatelet agents and stroke prevention. Semin Neurol 1998;18:441-50

7. Sherman DG. Heparin and heparinoids in stroke. Neurology 1998;51(Suppl 3):S56-8

8. EAFT (European Atrial Fibrillation Trial) Study Group. Secondary prevention in non-rheumatic atrial fibrillation after transient ischemic attack or minor stroke. Lancet 1993;342:1255-62

9. Atrial Fibrillation Investigators. Risk factors for stroke and efficacy of antithrombotic therapy in atrial fibrillation: analysis of pooled data from five randomised controlled trials. Arch Intern Med 1994;154:1149-57

10. Goldsten LB, Hasselblad V, Matcher DB, McCrory DC. Comparison and meta-analysis of randomised trials of endarterectomy for symptomatic carotid artery stenosis. Neurology 1995;45:1965-70

11. Stroke Unit Trialists Collaboration. Collaborative systematic review of the randomised trials of organised inpatient(stroke unit) care after stroke. Br Med J 1997;314:1151-9

The Singapore Family Physician

New Treatment Modalities in Stroke

N Venketasubramanian

Stroke has been Singapore's third leading cause of death and accounts for a rising number of hospital admissions. Clinical trails performed in the last decade have found promising new stroke therapies that may favourably impact on death and disability and improve recovery.

1. Thrombolytics. By lysing thrombi or emboli occluding cerebral arteries, thrombolytics aim to achieve early recanalisation and reperfusion of ischemic tissue. The large North American study has shown that the fibrinolytic drug recombinant tissue plasminogen activator (rTPA) given intravenously within 3 hours of stroke onset increases the proportion of non- or minimally disable stroke patients by 30% without significantly increasing mid-term mortality. There is, however a 10–fold increased risk of potentially fatal cerebral haemorrhage. The two European Cooperative Acute Stroke Studies (ECASS I & II) with rTPA have failed to show the same benefit. It appears that the therapeutic time window is probably less than 3 hours, and definitely less than 6; however, the window for the posterior circulation may be up to 24 hours. The optimal time window, drug, route of administration, type of stroke that benefits most is still unknown. Fibrinogenolytic agents such as ancrod derived from the snake venom are still under study. It is unlikely that thrombolytics will be administered by GPs in their clinics as patients with hemorrhagic stroke may accidentally be given this drug.

2. Neuroprotectants. Lack of adequate perfusion results in an ischemic cascade, with the release of excitatory amino acids, superoxides, free radicals, lipolysis and inflammatory agents, to name a few. Neuroprotectants hope to block this cascade at one or more points. Nimodipine has been found to effective in reducing the detrimental effects of vasospasm after subarachnoid hemorrhage. At this time, no other neuroprotectant that has been proven to be effective in stroke. The drugs that have undergone trials so far have either been ineffective or had unacceptable side effects. Many trials are still in progress. The therapeutic time window is probably less than six hours. If found to be effective and safe, neuroprotectants may be administered by the GP to the acute stroke patient in the clinic, while awaiting the arrival of the ambulance.

3. Anticoagulants. Anticoagulants have been found to be effective in reducing the risk of recurrent stroke in those with atrial fibrillation. Despite the lack of evidence, anticoagulants are widely used for stroke-in-evolution/progression, basilar artery thrombosis and crescendo transient ischemic attacks (TIAs). Heparin, heparinoids and low molecular weight heparins reduce the risk of deep venous thrombosis and pulmonary embolism in stoke patients. Nadroparin was found in a Hong Kong study to reduce the proportion of disabled stroke patients when started within 48 hours of stroke onset. A repeat of this study in a more international group of patients failed to show benefit.

4. Surgery. In cerebellar infarcts or hemorrhage with brainstem compression, posterior fossa decompression craniectomy or hematoma evacuation reduces mortality with little resultant morbidity. However, for massive supratentorial infarction with midline shift decompression craniectomy, while reducing mortality from 70-90% to 50%, still leaves survivors severely disabled. This procedure may best be reserved for younger patients with non-dominant lobe infarction and good surgical risk. Evacuation of intracerebral hematomas has not been proven to be useful. Extraventricular drainage is performed for those with acute hydrocephalus. Extracranial-intracranial bypass is of value in those with moya-moya disease.

5. Stroke Units. Stroke units refer to a geographical co-location of stroke patients, or a mobile multidisciplinary team of healthcare professionals interested and trained in the care of stroke patients. Stroke units reduce death,

Dr N Venketasubramanian,
MBBS, MMed (Int Med),
FAMS (Neurology)
Consultant Neurologist
Director Stroke Program,
Tan Tock Seng Hospital
Clinical Coordinator
(Stroke),
National Neuroscience
Institute
Singapore

disability, length of stay and cost of care, as well as the need for institutionalisation of stroke patients. The team may comprise doctor, nurses, therapists, medical social workers, dieticians, and nurse educators.

6. Others. Antiplatelets, oral anticoagulants, carotid endarterectomy, carotid angioplasty/ stenting, aneurysm clipping/coiling/trapping and arteriovenous malformation (AVM) surgery/ embolisation/gamma knife are discussed in accompanying papers.

Clinical trials will provide newer and better modalities of treatment for our patients. It is likely that a cocktail of therapies will be used to maximise the benefits and reduce the risks.

Review Article

The Singapore Family Physician

Central Nervous System Involvement in Systemic Lupus Erythematosus

Julian Thumboo, Boey Mee Leng

Introduction

Systemic lupus erythematosus (SLE or lupus) is an inflammatory multi-system disease of unknown aetiology and diverse clinical manifestations. It is characterised by autoantibodies against components of the cell nucleus, immune complex mediated tissue damage, and a variable course and prognosis (1). Lupus in Singapore is somewhat similar to that seen in other countries (2). Central Nervous System (CNS) involvement in lupus has consistently been associated with increased mortality in SLE patients (3), highlighting the importance of diagnosing and treating this potentially disabling complication of SLE. This review provides a brief overview of CNS lupus and outlines an approach to the SLE patient with neuropsychiatric symptoms.

Classification and Pathogenesis

CNS lupus may be broadly classified on the basis of clinical manifestations as either diffuse or focal (Table 1) (4). The pathogenesis of CNS lupus is likely to be multi-factorial, and includes the possible mechanisms summarised in Table 2 (4, 5). Focal manifestations are typically persistent, irreversible and associated with abnormal neuroimaging while diffuse manifestations are typically transient, reversible and associated with normal neuroimaging. It has, therefore, been postulated that focal manifestations are due to vascular occlusion while diffuse manifestations are due to autoantibody or cytokine mediated neuronal dysfunction (4). Anti-neuronal and ribosomal-P antibodies are found in up to 90% of patients with diffuse CNS lupus and in 10 to 30% of unselected lupus patients (8), and may play a role in pathogenesis and aid diagnosis of this condition, though this is controversial (6). Anti-cardiolipin antibodies are found more commonly in SLE patients with CNS manifestations, particularly those with focal CNS lupus, and may also play a role in pathogenesis (7).

Clinical Manifestations

CNS lupus occurs in 25 to 75% of SLE patients (8) and may present with diffuse or focal manifestations (Table 1). CNS lupus should be considered in the differential diagnosis of a patient with neuropsychiatric symptoms, especially female patients between 20 to 50 years old. Failure to do so may result in delays in diagnosis & treatment, as CNS lupus may be the initial presentation of SLE. In Singapore, CNS lupus (defined as in the ARA criteria (9) as seizures or psychosis attributed to SLE) was found in 4% of SLE patients at diagnosis, and 12% and 14% of such patients after 5 and 10 years of disease respectively (2). At diagnosis, Malays had a higher risk of CNS and renal involvement than the Chinese. The focal manifestations of CNS lupus generally do not manifest with psychiatric symptoms and are not discussed further in this review.

Organic brain syndrome is a fairly common acute presentation of CNS lupus, and is a diagnosis of exclusion after secondary causes (Table 2) have been excluded. Psychosis occurs in 5-15% of patients with CNS involvement, and is associated with the presence of anti-ribosomal P antibodies (6, 8). Mood and anxiety syndromes may represent a manifestation of lupus or a reaction to lupus or psychosocial factors. A case control study of 30 consecutive lupus patients and 29 age matched controls with rheumatoid arthritis (RA) in Singapore found that lupus patients had more anxiety disorders, depression or psychoses than RA patients (16 vs 6, $p < 0.05$. Odds Ratio = 4.38) (10). Cognitive impairment in SLE is often subtle and is detectable only on formal psychological testing. It has been found in up to 66% of SLE patients, may resolve spontaneously (11) and may be more common in patients with active disease or past CNS lupus, suggesting that these manifestations may be autoantibody medicated and/ or due to damage from a past episode of CNS lupus.

Julian Thumboo, M.B.B.S. (S'pore), M. Med. (Internal Medicine), M.R.C.P. (U.K.)
Senior Registrar
Department of Rheumatology and Immunology
Tan Tock Seng Hospital

Boey Mee Leng, M.B.B.S. (S'pore), M. Med. (Internal Medicine), F.R.C.P. (Edinburgh), F.A.M.S., M.D.
Senior Consultant Rheumatologist and Physician
Mount Elizabeth Medical Centre

Address for Correspondence:
Dr Julian Thumboo,
Department of Rheumatology and Immunology,
Tan Tock Seng Hospital,
Moulmein Road,
Singapore 308433
Tel: 65-3577822
Email:
Julian_Thumboo@notes.ttsh.gov.sg

Name and Address of Institution from which work originated:
Department of Rheumatology and Immunology
Tan Tock Seng Hospital
Moulmein Road
Singapore 308433

Key Words: Lupus, systemic erythematosus; Central nervous system; Review

Differential Diagnosis and Clinical Approach

Diffuse CNS lupus is a diagnosis of exclusion. A diagnosis of CNS lupus is made if evaluation does not show another cause for the patient's symptoms, and is further supported by the presence of active SLE in other organ systems. The clinical approach to a SLE patient with neuropsychiatric symptoms is therefore to rule out secondary causes that may mimic CNS lupus (summarised in Table 2), and to assess lupus activity in other organ systems.

Infection (CNS or systemic) can mimic both CNS lupus and/ or a SLE flare (8), is potentially fatal and is the most important condition to exclude in a SLE patient presenting with acute neuropsychiatric symptoms. Steroid psychosis is another possible cause of neuropsychiatric symptoms in SLE patients, affecting 1.3% of subjects with a prednisolone dose of <40 mg/day and 4.6% of subjects with a dose between 41-80 mg/day (12). It is not related to the duration of corticosteroid therapy or a past history of psychiatric illness, and improves dramatically in < 3 days with a 50% reduction in prednisolone dose. Tricyclic anti-depressants may worsen steroid psychosis and should be avoided if this is suspected. If CNS lupus is suspected in a patient already on treatment with anti-psychotic drugs, care must be exercised in interpreting the results of tests for autoantibodies in such a patient as anti-psychotic drugs per se are associated with the presence of anti-nuclear, anti-cardiolipin and other autoantibodies (13).

The extent and speed of the diagnostic workup is dependant on the severity and progression of symptoms. A detailed history and physical examination to exclude the conditions listed in table 2 is mandatory. If mild depression or anxiety are present, a basic laboratory screen consisting of a full blood count, electrolyte determination and thyroid function tests may be ordered. If cognitive dysfunction is suspected, formal psychological assessment is needed to quantify cognitive dysfunction and assess therapeutic response. If psychosis or organic brain syndrome are present, an urgent septic workup (including a lumbar puncture) and neuroimaging should be performed. Cerebrospinal fluid is usually normal in CNS lupus but pleocytosis (6 - 34%), a low glucose (3-8%) and raised protein levels (22-50%) may be found. Neuroimaging is useful to exclude other CNS pathologies that may mimic diffuse CNS lupus, but does not aid in the diagnosis of diffuse CNS lupus as there are no specific findings for diffuse CNS lupus on either CT or MRI scans. High intensity white matter lesions on MRI are not specific for SLE, and may be present with current or previous CNS lupus, age, or risk factors for atherosclerosis (4). Other tests generally used in this context are the C-reactive protein level (raised in infection, normal in active SLE), anti-double stranded DNA levels (raised in active SLE), serum complement determination (low in active SLE), and a peripheral blood film (for fragmented cells of thrombotic thrombocytopaenic purpura). Tests to exclude secondary causes of neuropsychiatric symptoms should be ordered as clinically indicated. Electroencephalograms (EEG) are abnormal in 54-85% of patients with CNS lupus and in up to 48% of SLE patients without CNS lupus, and are therefore not useful in the diagnosis of CNS lupus. Quantitative EEG techniques may be able to differentiate CNS lupus from normal controls, but cannot distinguish between primary and secondary causes of neuropsychiatric symptoms in SLE patients (8). Data from a prospective study of 52 SLE patients with neuropsychiatric manifestations suggest that diffuse CNS lupus can be confidently diagnosed (sensitivity 100%, specificity 86%, positive predictive value 95%) in a SLE patient if CSF IgG index/oligoclonal bands, CSF antineuronal antibodies or serum anti-ribosomal P antibodies are present (14). Unfortunately the latter two assays are generally not available in clinical practice.

Treatment and Outcome

Therapy for a patient with major neuropsychiatric symptoms should not be delayed pending results of investigations. If the diagnosis is unclear and the patient is ill, treatment for both CNS lupus and likely secondary causes (especially infection) should be instituted. As there are no controlled trials to guide the treatment of these patients, therapy for is CNS lupus is based on case series

and anaecdotal reports. Mild depression and anxiety often respond to antidepressants and psychological support and generally do not need an increase in corticosteroid or immunosuppressive therapy. Subjects with acute psychosis or an organic brain syndrome require treatment with anti-psychotics (to control neuropsychiatric symptoms) and high dose corticosteroids equivalent to 1mg/kg/day of prednisolone (to control the underlying autoimmune processes), and generally respond to treatment over days to weeks. Progressive deterioration of conscious level in this setting suggests severe CNS involvement or a superimposed secondary cause. If secondary causes are excluded, treatment with pulse methylprednisolone and intravenous cyclophosphamide is of benefit in these patients (15). Most patients with diffuse CNS lupus recover with time, with only a minority displaying residual neuropsychiatric symptoms. The presence of psychosis or organic brain syndrome has been associated with decreased survival (3). In summary, CNS lupus is a relatively common complication of SLE which is diagnosed when other causes of neuropsychiatric symptoms are excluded. Therapy includes neuroleptics, corticosteroids and at times cytotoxic drugs.

Table 1. Classification of CNS Lupus

Diffuse Manifestations (35-60%)
Organic brain syndrome
Altered consciousness
Dementia
Psychosis
Organic mood/ anxiety syndromes
Cognitive impairment
Focal manifestations (10 – 35%)
Cranial neuropathies
Cerebrovascular accidents
Transverse myelitis (1%)
Movement disorders (4%)
Seizures (15 – 35%)
Grand mal, focal, temporal lobe, petit mal
Other Manifestations
Headaches
Aseptic meningitis
Pseudotumour cerebri
Normal pressure hydrocehpalus

Table 2. Possible Pathogenic Mechanisms in SLE Patients with Neuropsychiatric symptoms

Primary
Anti-neuronal & other autoantibodies
Vascular occlusion (bland vasculopathy):
Leucoagglutination
Anti-phospholipid antibody related thrombosis
Cardiac/ other emboli
Vasculitis (rare)
Cytokine effects
Secondary (to exclude before diagnosing CNS Lupus)
Infections: CNS or systemic (e.g. encephalitis, septicaemia)
Metabolic: electrolyte inbalances, uraemia, hypoxia
Endocrine: hypoadrenalism, thyroid storm
Drugs: corticosteroids, anti-malarials, non-steroidal anti-inflammatory drugs, alcohol
Accelerated/ malignant hypertension
Intra-cerebral event (e.g. subdural hematoma, subarachnoid haemorrhage)
Thrombotic thrombocytopaenic purpura
Reactive depression

References

1. Pisetsky DS. Systemic lupus erythematosus. In: Schumacher HR, Klippel JH, Kupman WJ eds. Primer on the rheumatic diseases. Atlanta, Arthritis foundation, 1993; 100-105

2. Thumboo J, Fong KY, Chng HH, Koh ET, Chia HP, Leong KH et al. The Effects of Ethnicity on Disease Patterns in 472 Orientals with Systemic Lupus Erythematosus. J Rheumatol 1998; 25:1299-304

3. Gladman DD. Prognosis of systemic lupus erythematosus and the factors that affect it. Curr Opin Rheumatol 1991; 2:694-702

4. West SG. Lupus and the central nervous system. Curr Opin Rheumatol 1996; 8:408-14

5. Bruyn GAW. Controversies in lupus: nervous system involvement. Ann Rheum Dis 1995; 54: 159-67

6. Teh LS, Isenberg DA. Antiribosomal P protein antibodies in systemic lupus erythematosus: a reappraisal. Arthritis Rheum 1994; 37:307-15

7. Toubi E, Khamashta MA, Panarra A, Hughes GRV. Association of antiphospholipid antibodies with central nervous system disease in systemic lupus erythematosus. Am J Med 1995; 99: 397- 401

8. Kovacs JA, Urowitz BM, Gladman DD. Dilemmas in neuropsychiatric lupus. Rheum Dis Clinics North Am. 1993; 19: 795 - 814

9. Tan EM, Cohen AS, Fries JF et al: The 1982 revised criteria for the classification of SLE. Arthritis Rheum 1982; 25:1271-7

10. Lim LC, Lee TE, Boey ML. Psychiatric manifestation of systemic lupus erythematosus in Singapore. A cross-cultural comparison. Br J Psychiatry 1991; 159:520-3

11. Hanly JG, Fisk JD, Sherwood G, Eastwood B. Clinical course of cognitive dysfunction in systemic lupus erythematosus J Rheumatol 1994; 21:1825-31

12. Shapiro H. Psychopathology in the lupus patient. In: Wallace DJ and Hahn BH ed. Dubois' Lupus erythematosus. Philadelphia; Lea and Febiger. 1995: 390-1

13. Cansos RT, Oliveria RM, Nixon RA. Neuroleptic associated autoantibodies: a prevalence study. Biol Psychiatry. 1990; 27:863-70

14. West SG, Emlen W, Wener MH, Kotzin BL. Neuropsychiatric lupus erythematosus: a 10 year prospective study on the value of diagnostic tests. Am J Med 1995; 90: 153-163

15. Neuwelt CM, Lacks S, Kaye BR, Ellman JB, Borenstein DG. Role of intravenous cyclophosphamide in the treatment of severe neuropsychiatric systemic lupus erythematosus. Am J Med.1995; 98: 32-41

The Singapore Family Physician

United Kingdom Prospective Diabetes study (UKPDS)

Summary and conclusions of the various subanalysis of the study

1) Intensive blood glucose control with sulphonylureas or insulin compared with conventional treatment and risk of complications in patients with type 2 diabetes (UKPDS 33 : The Lancet Vol 352 Sept 12, 1998 Pg 837 to 852)

   There were 1573 patients in the sulphonylurea group and 1156 patients in the insulin group versus 1138 patients in the conventionally diet controlled group. It was also an issue of concern that whether or not chronic sulphonylurea and insulin usage was associated with adverse outcomes in the long run.

   Over a period of 10 yrs, it was shown that intensive blood-glucose control decreases the risk of microvascular complications (by 25%, p=0.0099) but NOT macrovascular diseases. But neither did the insulin nor the sulphonylurea groups had an adverse cardiovascular outcome on the patients. All intensive treatment increased the risk of hypoglycemia.

2) Effect of intensive blood-glucose control with metformin on complications in overweight patients with type 2 diabetes (UKPDS 34 : The Lancet Vol 352, Sept 12, 1998, Pg 854 to 865)

   The trial period was slightly more than 10 years. Of the overweight patients, 342 patients were in the metformin group and 542 patients were in the sulphonylurea group and there were 409 patients in the insulin group as well as 411 patients in the diet controlled group.

   It was found that the intensive glucose control of overweight patients with metformin decreases the diabetic endpoints compared to the insulin, suphonylurea and diet controlled groups. Therefore, for obese diabetics, metformin remains the first drug of choice for these patients.

3) Efficacy of atenolol and captopril in reducing risk of macrovascular and microvascular complications in type 2 diabetes (UKPDS 39 : BMJ Vol 317, Sept 12 1998, Pg 713 to 720)

   There were 2 group of patients of which one was treated with atenolol (358 patients) and the other with captopril (400 patients).

   Over a median follow up of 8.4 yrs, it was found that the progression of macrovascular and microvascular complications were reduced similarly in both groups. The atenolol group had 9% of its patients developing microalbuminuria and the captopril group had 5% developing this problem. Deterioration of the retinopathy was 31% in the captopril group and 37% in the atenolol group.

   Both drugs were equally effective in reducing the macrovascular and microvascular complications. Captorpril was not proven to be reno-protective.

4) Tight blood pressure control and risk of macrovascular and microvascular complications in type 2 diabetes (UKPDS 38 : BMJ Vol 317, Sept 12, 1998, Pg 703 to 713).

   The cohort of patients numbered about 1148 who had both diabetes and hypertension and were randomised into 2 groups, one with a tight control (758 patients) of 144/82 mmHg on average and another with less tight control (390 patients) of 154/87 mmHg on average. The follow up was over 8.4 yrs.

   Tight blood pressure control was proven to be of high priority in the management of the diabetic patients in order to reduce the macro and microvascular complications.

Dr Thai Huei Min
MBBS
Family Medicine Trainee
Queenstown Polyclinic

5) Cost effectiveness analysis of improved blood pressure control in hypertensive patients with type 2 diabetes (UKPDS 40 : BMJ Vol 317, Sept 12, 1998, Pg 720 to 726)

The patient cohort consisted of 1148 hypertensive patients with type 2 diabetes and divided into the tight control group (average bp=144/82 mmHg) and the less tight group (bp=154/87). The cost effectiveness ratios were based on use of healthcare resources, time free from diabetes related end points and life years gained. Over 20 hospital based clinics in England, Scotland and Ireland were included.

The tight control of the blood pressure in patients with type 2 diabetes is justified on clinical and economic grounds and with a cost effectiveness ratio that compares favourably with many accepted healthcare programmes.

The Singapore Family Physician

Test Your Eye-Q (No. 7)

A "Growth" in the eye

KG Au Eong , L P K Ang

A 45-year-old male construction worker complained of a slowly enlarging painless "growth" in his left eye for 10 years. He has no visual disturbance.

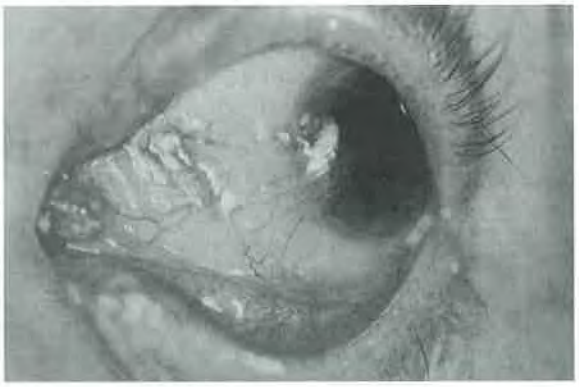


Fig. 1 shows the anterior segment of the eye.

Questions

1. What does Fig. 1 show?
2. What is the histology of the lesion?
3. What are the risk factors for the lesion?
4. What are the indications for removal of the lesion?
5. What is the treatment for this patient?

Answers

1. Fig. 1 shows a wing-shaped fold of conjunctiva and fibrovascular tissue on the nasal aspect of the bulbar conjunctiva with the apex enroaching onto the cornea. It is known as a pterygium.

2. The pathological changes consist of elastoid degeneration of collagen and the appearance of subepithelial fibrovascular tissue. The cornea shoes destruction of Bowman's layer by fibrovascular ingrowth. The epithelium may be normal, thick or thin and may occasionally show dysplasia. The lesion is benign.

3. The main risk factor for pterygium development is actinic (sunlight) exposure. Other risk factors include chronic dry eye, inflammation and exposure to wind and dust.

4. Treatment is indicated when the visual axis is threatened or in cases of extreme irritation. Surgery should not be undertaken casually as the recurrence rate is significant and recurrent pterygia may be worse than primary ones.

5. Treatment of pterygia is by surgical excision. Following excision of the pterygium, the exposed sclera may be covered with a conjunctival graft taken from the superior bulbar conjunctiva (pterygium excision with conjunctival autograft) or be left to heal on its own (bare sclera technique). Other options to reduce the risk of recurrence include the use of beta-radiation and mitomycin C eyedrops post-operatively.

K G Au Eong
* MBBS, M Med (Ophth), FRCS (Edin), FRCS (Glasg)

L P K Ang
** MBBS

*Registrar
**Resident
Department of Ophthalmology
Tan Tock Seng Hospital
Moulmein Road
Singapore 308433

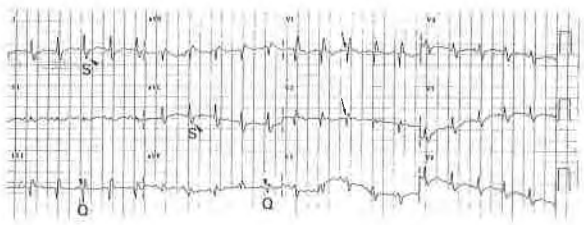
The Singapore Family Physician

Test your ECG knowledge

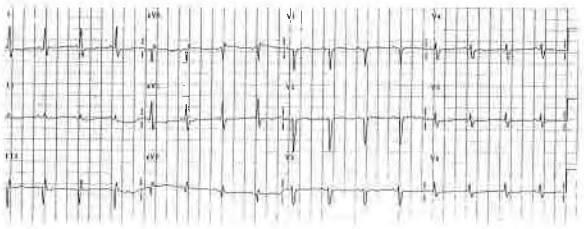
Koo CC

A **68-year old** hypertensive lady complained of sudden breathlessness on her way to the bathroom. She nearly fainted but did not complain of chest pain. She had no recent surgery but smokes cigarettes (Figure 1).

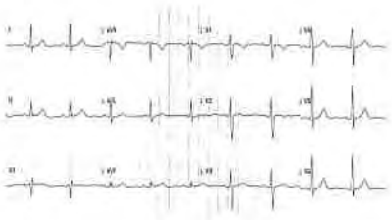
(Figure 1)



(Figure 2)



(Figure 3)



- List the ECG abnormalities
- What are your differential diagnoses?
- What pertinent investigations would you arrange to confirm your diagnosis?
- How would you manage this patient?

Dr Koo Chee Choong
MBBS (Belfast)
FRCP (Edin)
FAMS
6 Napier Road
#02-15
Gleneagles Medical Centre
Singapore 258499

- The underlying rhythm is sinus tachycardia at 130 bpm. These is complete right bundle branch block (RBBB). Note the QR pattern in V1 & V2 (see arrow↓) and slurred S wave in I &VL, V5&V6 (see arrow➘). There is deep Q waves in III & aVF (see arrow➘).

- The differential diagnoses are (1) acute pulmonary embolism, (2) acute left ventricular failure from acute myocardial infarction and (3) acute pneumothorax. Acute left ventricular failure from an acute myocardial infarction is possible as she has coronary risk factors i.e. post-menopausal, hypertension and smokes cigarettes. Moreover, chest pain can be absent in acute myocardial infarction. However, there is no Q wave in lead II and there are no reciprocal ST depression in I & AVL. This makes acute myocardial infarction less likely. Lastly, her normal serial cardiac enzymes and serial ECGs exclude this. Her chest X-ray was normal. This rules out left ventricular failure and acute pneumothorax. Hence, the most likely diagnosis is acute pulmonary embolism.

- The initial diagnosis of acute pulmonary embolism is largely clinical. Pulmonary embolus must be considered in any patient who present with unexplained acute breathlessness. The clinical presentation depends on the "embolic load" to the pulmonary circulation and the cardiopulmonary status. Therefore, the patient can be relatively asymptomatic and only complains of transient breathlessness if the embolus is small. On the other hand, the patient with massive embolus presents with hypotension and haemodynamic collapse! Clinically, she presented with acute breathlessness and near syncope. Her initial blood pressure was low at 90/70mm Hg with resting sinus tachycardia of 130 bpm. Her JVP was not raised and hger lungs were clear. The ECG signs of acute pulmonary embolus are often transient and can even be "normal". These include (1) sinus tachycardia, (2) right bundle branch block, (3) S wave in lead I, Q wave and T wave inversion in III (SI Q3 T3 pattern). The presence of right bundle branch block is suggestive of right ventricular "strain". However, this ECG sign is not specific,

as RBBB is relatively common in the elderly. Furthermore, her T wave was flat in lead III (Figure 1).

- She was treated for acute pulmonary embolus on the basis of her clinical history, signs, ECG and chest X-ray. Her condition improved remarkably fast with intravenous heparin and the right bundle branch block pattern disappeared (Figure 2) within hours of treatment. The lung perfusion (V/Q)scan on the following day confirmed the diagnosis. Unfortunately, this test is not readily available outside office hours! Her coronary angiogram revealed normal coronary arteries. Subsequent investigations ruled out occult malignancies. She was on Warfarin for six months and her condition continues to improve. Her latest ECG (Figure 3) was normal.

Points to remember:

- Acute pulmonary embolus is relatively uncommon but not rare.
- This condition is often not considered especially in ambulant patients without any recent surgery or imobilisation. Always consider pulmonary embolus in any patient with unexplained breathlessness!
- The initial ECG may be "normal" and the chest X-ray may be "normal".
- The ECG abnormalities are often transient and depend on the "embolic load" and cardiopulmonary state of the patient.
- If your clinical suspicion is high, refer the patient to the specialist to confirm the diagnosis.
- Diagnosis is confirmed with the lung-perfusion (V/Q) scan. Ultrafast CT scan is useful to diagnose pulmonary embolus in the main pulmonary artery. Pulmonary angiogram is only considered if the patient requires pulmonary embolectomy.
- If confirmed and treated, the long-term prognosis is good.
- If unrecognised and untreated patients with massive pulmonary embolism carries a high mortality. Repeated pulmonary embolism can lead to pulmonary hypertension with guarded prognosis!
- Most patients respond to intravenous heparin. Some fair better with intravenous thrombolytic agent i.e. streptokinase infusion into the pulmonary artery. Rarely, patients require pulmonary thromboembolectomy. This procedure carries a very high morbidity and mortality.

Figure 1: 69 year old lady presenting with acute breathlessness and near syncope. Note the sinus tachycardia at 130 bpm and complete right bundle branch block pattern. Note the slurred S waves in lead I & aVL. V5&6 (arrow ↘). There is Q waves in III & aVF (arrow ↖) and QR pattern in V1&2 (arrow ↓).

Figure 2: This ECG is recorded twelve hours later after she was on intravenous heparin. Note the QRS complexes are normal without right bundle branch block. However, the Q waves are still present in III & aVF and the poor R wave progression.

Figure 3: This ECG was recorded six months later. Note the R waves have normalized in the chest leads and there are no Q waves in the inferior leads.

The Singapore Family Physician

The Joy of Drawing – The Confessions of a Self Proclaimed Artist

James Chang Ming Yu

Ever since my drawing was displayed on the wall in primary school, I thought I could draw. However, My interest was not nurtured then and I did not draw for years. In medical school the only things I drew were histology slides and I doubted if my drawings were any good. The years flew by, occupied as they were with long hours at the clinic and later by the passion of chasing the small white ball over 18 holes during the weekends. The only times I sketched were when I got bored during meetings and then I would resort to sketching fellow participants so as not to fall asleep. Some of these sketches were not too bad. At least my wife could recognize who the objects of my sketchings were.

Seascape, New Zealand

I married into an artistic family. My father-in-law was a prominent Malaysian artist who had several of his paintings on display in the National Art Galleries of Malaysia and Singapore. I used to watch him with fascination whenever he visited. He would spend his time doing quick sketches around my house. When he stayed longer, he would paint in oils. My mother-in-law was an art teacher in a secondary school. Time came when I decided to learn how to draw. I first tried some adult education courses at the University. The first one turned out to be a sheer waste of time. I spent weeks drawing boxes, side view, end on, face on, any and all views. "Perspective," my teacher said. I ended up with rolls of drawing paper full of charcoal sketches, which I shoved in the drawer. The next course I attended was cartoon drawing. Why I signed up for that course I do not remember. Maybe I thought it would teach me to do caricatures. I did not finish the course. Week after week, the teacher made me copy cartoons, which he drew on the board. He did not say a word during classes and he certainly did not explain why copying his cartoons was vital to my art education. Undaunted, I attended yet another course, this time in oil painting. This one gave me some rudimentary beginnings in oil painting. I learned about canvases, turpentine, both crude and refined, easels, brushes and paints. At last I was beginning to go somewhere. I learned to mix colours on a palette, to prime my canvas before painting and to paint scenes from photographs. I had just visited New Zealand and had come back inspired by all the beautiful scenery I had seen. My interest was whetted when some of my attempts were admired, albeit by kind friends.

Matterhorn, Switzerland

I even joined a group of professional Singapore artists on Sunday afternoons to sketch nude models. One had to

Dr James Chang Ming Yu
MBBS, FCFP, PBM
Family Physician
Chang Clinic
1 Jalan Anak Bukit
#B1-08 to 10,
Bukit Timah Plaza,
Singapore 588996

sketch quickly as the models changed their poses. I felt a sense of great inadequacy compared to these "real" artists, as my sketches invariably seemed to run out of paper when they came to the legs. I ended up with drawings of figures which had long torsos and short legs. My wife was my worse critic. "Why does this lady look like an ape?" she would ask. "Your proportions don't seem right." Anyway, it was an interesting experience while it lasted.

Nowadays, I travel with my sketchbook and my camera. My holidays are mainly quiet ones, spent a few days at a time in golf resorts. These are usually sited in beautiful countryside with scenery that begs to be painted. Sometimes I sketch in pen, sometimes I paint in water colour. More often I take photographs of the scenes I like and convert them to oil paintings when I reach home.

Australian countryside

MacRitchie Reservoir

What has all this new found interest added to my life? Painting is relaxing and fulfilling. It gives me a sense of achievement to start with a blank canvas and to fill it with colour to portray a scene of beauty. I like to paint mountains, especially those with snow. My visit to Switzerland provided me with a couple of paintings of the mountains there, as did my visit to New Zealand. I find oil much more fun and more forgiving than water colour. In oil painting, I can redo parts which I do not like again and again without fear that I will spoil the painting. This I cannot do with water colour. What I paint is what my impression of the scene is. Whether it is realistic or not, I do not quite care. In this area I take a great deal of artistic licence.

Drawing and painting has given me much enjoyment. There are days when the physical activity of golf, my other hobby, has to take a back seat because of the weather or because I just do not feel up to it. As I grow older, I know these days may become more. That's the time when I think my interest in painting will keep me busy. The walls of my clinic and my home are slowly being filled up as I paint. Soon there will be no more space left for display. No matter. The paintings will go on rotation. My patients are already noticing the new paintings on the wall. They come in and tell me that my works of art are improving, or that they like a particular painting of mine. The paintings are becoming conversation pieces. Some of my patients are artists themselves and besides giving me helpful tips, they invite me to their exhibitions and give me copies of their books. I appreciate their interest in my budding enthusiasm for this form of expression and the way they are encouraging me.

I took forward to the day when I can paint with abandonment and allow my imagination to go wild. For the time being I patiently plod on with help from art teachers and fellow amateurs, hoping that my skill as an artist will eventually be honed to a degree that I can be proud of.


CUM SCIENTIA CARITAS

THE
COLLEGE MIRROR

Issue: Jan - Mar 1999
MITA(P) No 191/03/98

On the World Wide Web !

The College has its own website on the world wide web at http://www.cfps.org.sg

Through this link, you will be able to access the latest information about the College and its activities, the latest medical information from around the world and do CME-Online.

Our website is the first in the region that offers on-line CME and this is one of the key features of this website. Doctors in Singapore can participate and gain CME accreditation. It is important that the medical education programme of today and the future maximises the capabilities of the internet system and information technology (IT).

FROM THE EDITOR'S DESK

By getting a combination of our own doctors to provide case-studies, text on current knowledge on medical practice as well as links with other major medical websites, the value of the website in providing up to date and broad range, high quality medical education material is enhanced. It is hoped that the College CME-Online can be a one-stop resource springboard from which to take off to the best internet sites in the world for relevant and practical medical knowledge.

There is also a forum page for you to exchange your ideas, pose questions and give opinions on matters of interest or concern.

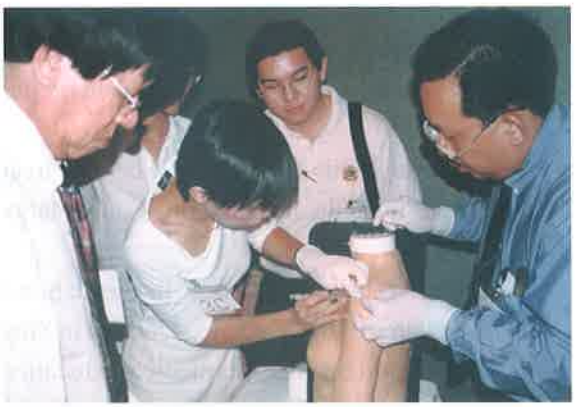
The College is working on a distance learning programme based on the modular Family Medicine Teaching Programme. This is presently at the pilot stage (see article on page M9).

Do serve the net and tell us what you think!

■ Yvonne Chung

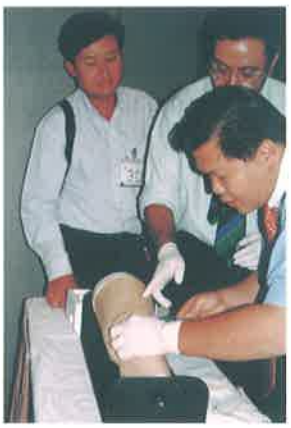
3rd Annual Surgical Update for Family Practice

The 3rd Annual Surgical Update for Family Practice was successfully held on 23-24 January 1999 at Le Meridien Singapore. Taking into account of previous participants' feedback, this year's Surgical Update was expanded to one and a half days instead of the two afternoons as was previously the case. This allowed more time for the Teaching Faculty to present their lectures and facilitate a more interactive programme.



The first day's programme was an Update on Degenerative Disorders in Orthopaedics, and included workshops on injection techniques for common orthopaedic problems. Each group of 10 participants was assigned an instructor and the entire group was rotated through four stations, namely: Hand and wrist, Elbow, Shoulder, and Knee. The small workshops enabled the participants to have more hands-on experience and better instructor-trainee interaction.

The second day's programme was an Update on Upper GIT Diseases and included an interactive session for participants using a hand-held computerised system to express an opinion on certain clinical conditions.



A selective trade exhibition was also held at the venue, supported by Glaxo Wellcome, Johnson and Johnson, and PG Books Pte Ltd.

The College would like to thank the 165 participants who registered for this Surgical Update, the Organising Committee, College Secretariat staff and the Teaching Faculty and Workshop Instructors for their time and for sharing their expertise.

■ Yvonne Chung

1999 WONCA Asia Pacific Regional Conference

Dr Julian Lim (1st left), A/Prof Goh Lee Gan (2nd left), Dr Alfred Loh (2nd right), Dr Kwan Yew Seng (1st right)

The World Organisation of Family Doctors (WONCA) held the Asia Pacific Regional Conference from 6 March to 10 March 1999 in Taipei, Taiwan. The theme was Health for All by the Year 2000. Family Medicine-Meeting Old Challenges.

Singapore was represented by Dr Alfred Loh, A/Prof Goh Lee Gan, Prof K C Lun, Dr Julian Lim and Dr Kwan Yew Seng. The program was packed with interesting plenary lectures, symposia and workshops. There was also a Research Course.

Dr Kwan Yew Seng representing the Ministry of Health, took part in the Open Paper Research contest and won the 2nd prize. The total number of registrants was more than 2000, making this conference a real success.

The social events were unforgettable, including visits to the world-renowned Taiwan National Palace Museum, and a dinner which was also attended by the Mayor of Taipei City.

There was a post-conference workshop workshop on "Quality Assurance in Family Medicine" This workshop enabled an exchange of ideas on Quality Assurance among the delegates from different countries.

We look forward to meeting our friends again in June 2000 in Christchurch, New Zealand.

Dr Kwan Yew Seng

News from the college

Visit by Dr Robert Higgins – President of WONCA

The College had the pleasure a receiving Dr Robert Higgins, President of the World Organisation of Family Doctors (WONCA) on 11 March 1999.

Dr Higgins was accompanied by his wife Barbara, and met with Council Members and staff of the College. Dr Higgins was able to gain first hand knowledge on the work, role and functions of the College as a representative body of Family Physicians in Singapore and as an academic body promoting CME.

Signing the visitor's book – Dr Robert Higgins (left) with Dr Alfred Loh (right)

The Council also explored the possibility of the College becoming host to the WONCA Secretriat in the near future. Dr Higgins explained that the WONCA Secretariat is currently located in Melbourne, Australia. Upon the present Chief Executive Officer's retirement in 2001, WONCA will be "looking for a new home". Being one of the more active colleges in WONCA with a good past track record and as one of the leading colleges in the Asia pacific Region, the College stands in good stead to take on this challenge of hosting a prestigious world body in Singapore. This would undoubtedly bring the world's attention to Singapore and raise the profile of Family Medicine world wide.

Dr Robert Higgins (right) & Mrs Higgins (seated) with members of the College Council

■ Yvonne Chung

College of Family Physicians Singapore

28th ANNUAL GENERAL MEETING

Sunday 23 May 1999

1.30 pm

Lecture Theatrette
College of Medicine Building, Level 1
16 College Road
Singapore 169854

Complimentary lunch will be served from 12.30pm-1.30pm

Elections for the 17th Council will take place at the AGM.

Special Report

Interview with Professor Frede Olesen on 18 March 1999

Professor Frede Olesen visited our College on 18 March 1999. Professor Olesen was the Past President of the Danish College of General Practitioners and WONCA Vice-President of the European region. He is both a practising family physician and a leading academic in Aarhus University, Denmark. Professor Olesen was interviewed by Dr.Lawrence Ng and Dr. Lee Kheng Hock of the College Archive Project team. In the interview held at the College, Professor Olesen spoke about the obstacles that hinder the development of Family Medicine and the importance of primary care in the overall health care system of all countries. An audio recording of the interview is available at the College.

The following are excerpts from the interview.

Going onto the road of academic family medicine

"A couple of years after starting general practice, one of my patients died from cervical cancer. At that time, I come to reflect why we should have deaths from cervical cancer. I began a research project that went on to become a dissertation. I did not know at that time that it would be the case. A dissertation on how to prevent death from cervical cancer by Pap smear screening.....the first big national evaluation of the pap smear programme, world-wide."

In the course of the research, Prof Olesen became interested in teaching and joined the Department of Family Medicine in Aarhus University and eventually became the Head of the Primary Care Research Unit.

".....I enjoy my work (as a GP) and my real profession is a GP although I am in full time research...."

Developing Family Medicine in the early formative years

"In 1969, when I was a medical student, the first Professor of Family Medicine was appointed in Denmark. He complained that he was absolutely alone and absolutely naked....in the way that he had nothing to help him in his work."

"At that time we had one professor, in our country of 5.5 million people and 3,500 general practitioners. Today we have 2 professors in each of the three universities. We already have 2 professors who have retired."

"Back in the mid 1970's, we realised that our universities had a real problem of growing and reaching a critical mass so that research could become self-sustaining. Therefore the College together with the Universities approached the government to arrange for an add-on department for vocational training. We have a part-time boss with 2 to 4 part-time teachers all doing teaching and some research. However, it was difficult to get time to do research. Therefore in the mid 1980's, we still have the same problem of not reaching a critical mass. Therefore, the College

decided we need to develop a primary care research foundation. Again, after a long process of complicated negotiation, we ended up with a foundation that created a research unit."

"Starting from a vocational unit at one end and creating a research unit in the other end, we tried to reach a critical mass of seniors. This was not enough. The important thing is how to develop research in practising doctors."

"The next step came in the overall development of Danish medical education. A new legislation that gives any doctor in the first five years after graduation and before ending up with a specialisation....can get to go out of his training and become a researcher for 1.5 to 3 years to do a PhD. That means that in the Unit that I am head of, we have 8 fully graduated doctors who are on their way to become general practitioners, who stop their career for 2 to 3 years and get fully paid as full-time research workers. They get up to 6 months of formal training and then do their projects and end up with a PhD."

"The last part of the process is how to get research going among practising GPs doing clinical work. This is even more important because out of research comes commitment to quality assurance. We have tried to encourage research by running courses in research.....Doctors are encouraged to start small projects. Out of these small projects, sometimes real big projects come out. If a general practitioner creates a big project, which he usually does during after-office hours, they can apply to the research foundation for support. They can provide for a locum for a quarter or half their working time so that they can finish their work. They can have the locum for one month, three months and even up to three years. "

"That is a very,very ,very, long story, with many steps...Step one was to establish professors in each department and this happened in the sixties. Step two, was to create a critical mass by creating a teaching and research unit. Step three, was to establish full time research opportunities for the young. Step four is to create different foundations where GPs can apply for locums. Step five is to encourage and support GPs who do small, spare-time projects."

"All this happened because of a very action-oriented College which kept very good lines to the Universities. At the same time, they had a good line to the government and to the medical association. At all times, we had some sort of collaboration."

How to set up a family medicine research unit?

"First of all we get collaboration with the University, we were actually, physically at the University. So that was to go into an existing millieu instead of creating one. Next thing we did was to encourage those likely candidates who can head the system. The College gave them scholarships overseas to established centres like England and Netherlands, just to get inspiration....."

Government and General Practice

"Perhaps the most important step is that we kept good lines to the government at all times. If I should be very frank, I have never met a government that is really interested in general practice. (Laughter) But what the government is interested is when everytime we can show that a strong general practice has the potential to make the whole health care service run more smoothly. We have always been very keen to demonstrate to the government that by focusing on general practice, your hospital can run more smoothly. This has always been the foot in the door to the Minister's office. Our greatest success has been that we were able to convince the government. That also means that the government officially states that general practice is the cornerstone in the health care system. This is also reflected in the salary, education...etc.

Building bridges to the Government

" I have followed two strategies.....First, when the College invited foreign speakers, we have always invited government representatives very often to give keynote speeches. By doing so you make them reflect on the issues. We have tried to expose them to international experience. Strategy two is that in our research, we focus on areas

where we can demonstrate a benefit of having a strong general practice." *An example was a research project done in Prof Olesen's research unit. It showed that improving the care of the treatment of diabetes at the primary care level resulted in a 25% decrease in diabetic care workload in a certain hospital without any measurable loss in the quality of care and patient satisfaction.*

Resolving conflicts between organisations responsible for health care

"To my experience there will always be some conflict of interest to some extent. On the other hand we have a lot of areas of common interest. I am quite often invited to speak on management courses and quite often to politicians. I always paint this picture to them. You need to have one room in which you can do our battles because there will always be some battles. This room is created in most countries. But you must also have another room, a room for creating shared care, for creating visions, for creating a more seamless health care system. I always say it is a question of leadership. The battle room will always exist. The room for development depends on the leadership. Leadership in the College, leadership in the medical association, leadership in the government. When I look back and ask where we have successes, it has always been the time where we were able to create this room number two. The other very important thing in this process, is to be self-reflecting. When you point a finger at someone, three fingers are pointing at yourself. This applies to the leaders in all the parties. Reflect on what can I do instead of what the rest ought to do. It is not easy."

Dr Lee Kheng Hock
Dr Lawrence Ng

CME

Launch of the College Website

The College has a new website at http://www.cfps.org.sg

It will be officially launched on **22 May 1999**.

The Website contains

- CME on-line
- Forum page for the exchange of views between members
- College newsletter
- Full text articles of the ***Singapore Family Physician*** journal
- The Sreenivasan Orations - a series of lectures on philosophy & direction of Family Medicine
- College Council and its Committees
- College history and milestones

The easy access of the CME on-line and the College's journal and newsletter will lead to greater international recognition of medical research in Singapore and awareness of the College.

The CME on-line is a self study programme. The syllabus on Family Medicine is preserved as a 8- module programme consisting of 3 sub-modules covering

- Care of specific population groups like child health, adult health, women's health and health of the elderly

- Systematic approach to medical disorders important in the Primary Care setting, ranging from cardiovascular and respiratory disorders to metabolic and nutritional disorders

- Practice management covering topics from medical records to quality assurance

There are also articles for the doctor to read, case studies to challenge his/her diagnostic and management skills, and MCQs.

The doctor will be able to start on any module and in any order that suits his/her study plan. This self study plan may be supplemented by face-to-face workshops and clinical skills rounds.

A/Prof Goh Lee Gan
Dr Lee Kheng Hock

ULTRASOUND COURSE

The (long awaited) ultrasound course leading to the award of the Graduate Diploma in Basic Ultrasonography (Obstetrics and Gynaecology), will be launched on Sunday 4 July 1999, with an initial intake of 14 trainees.

This course is jointly organised by the College and the Graduate School of Medical Studies, National University of Singapore. It shall, in the first instance be open to family physicians in Singapore.

The aim is to enable the family physician to be

- proficient in the use of ultrasonography in Obstetrics and Gynaecology
- to use this diagnostic tool appropriately and competently in the primary care setting
  - in the evaluation of a normal pregnancy
  - in the recognition of an abnormal pregnancy.

This will translate to better health care for the population at large; they will enjoy a higher standard of medical care and management at the Family Medicine echelon.

The Ultrasound Committee consists of the following members:

Course Director	Dr Alfred W T Loh
Deputy Course Director	Dr Chew Sing Chai
Faculty Director - NUH	A/Professor Anandakumar
Faculty Director - SGH	Dr Ann Tan
Faculty Director - KKWCH	Dr George S H Yeo
Committee Members	A/Professor Goh Lee Gan
	A/Professor Wong Yee Chee
	Dr Arijit Biswas
	Dr Douglas Ong
	Dr Ong Chiou Li
	Dr Lawrence Ng
	Dr Tan See Leng
Course Administrator	Ms Yvonne Chung
Course Secretary	Ms Angeline Ong

PROGRAMME STRUCTURE

The programme will be structured in modules with a large distance-learning component. There will be an appropriate blend of lectures, hands-on training, log work and formative self assessment programmes. The main teaching faculty will include staff trained in ultrasonography from the National University Hospital, the Singapore General Hopsital and the KK Women's and Children's Hospital. The assessment will be both formative and summative.

Duration of the Course

The course is offered on a part-time basis and must be completed within a maximum period of 24 months.

Course syllabus

The first part of the course is a 2-day weekend lecture session. This session will inlcude an overview of the course and detailed lectures on various aspects of ultrasonography in Obstetrics and Gynaecology.

The lecture syllabus consists of the following 5 modules:

Module 1	Ultrasound basics
Module 2	Obstetrics 1
Module 3	Obstetrics 2
Module 4	Gynaecology
Module 5	Social issues

Between month 2 and month 9 of the course, 2 lectures will be conducted on one day each month. Time shall be allocated for discussion and helping the candidate with any problems that he/she may be facing with the logwork.

Logbook

Participants will be issued with a logbook in which they will be required to log a prescribed series of ultrasound cases and images. They will need to complete the log work before being allowed to sit the examination.

Practical sessions

During the course of the first 36 weeks, participants will be assigned to one of the 3 registered training centres for a 3-hour hands-on session every week. At each session, the particiapnt may perform up to 6 supervised ultrasound scans.

EXAMINATION AND AWARD OF THE DIPLOMA

The participant will be allowed to sit the final examination after he/she has completed 75% of the required 400 scans to the satisfaction of the Ultrasound Committee.

There are 3 parts to the examination:

- 30% Viva (based on logbook)
- 30% Written paper
- 40% Skills assessment

The Diploma will be awarded on passing all sections of the examination and only on completion of all 400 scans within the set time frame of 24 months from the start of the course.

The Graduate Diploma in Basic Ultrasonography (Obstetrics and Gynaecology) will be awarded and issued by the Graduate School of Medical Studies, National University of Singapore.

FEES

The course fee for local participants is S$3,500. This is inclusive of the log book, practical sessions, lectures and examinations.

APPLICATIONS

Applications must be made on the prescribed forms available from the Graduate School of Medical Studies, NUS, or the College of Family Physicians Singapore.

Places will be restricted to 14 eligible applicants on a first come first served basis for the July 1999 intake. All completed application forms together with full payment of the course fee and a non-returnable processing fee must reach the Graduate School of Medical Studies by Monday, 14 June 1999.

ENQUIRIES

For further details and enquiries please contact:

Graduate School of Medical Studies
National University of Singapore
Lower Kent Ridge Road
Singapore 119074

Tel: 874 3301
Fax: 773 1462
Email: pmdgen2@leonis.nus.edu.sg

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

Tel: 223 0606
Fax: 222 0204
Email: rccfps@pacific.net.sg

MINOR SURGERY COURSE

The College will be launching its Minor Surgery Course for Family Physicians in January 2000.

The finer details are still being worked out by the Organising Committee to see how best to fit in a relevant, interesting and practical programme for our busy Family Physicians. We are planning to include live transmissions of surgical procedures followed by practical hands-on sessions. These sessions will cover procedures for

- Lumps and bumps
- Lipomas
- Sabaceous cysts / abcesses
- Incisional lines & sutures
- Ganglions & foreign body excision
- Wedge-resection of in-growing toe nails
- Wound care and wound closure
- Management of jagged wounds-debridement & cleaning
- Intra-articular joint injections / treatment of tendonitis

WELCOME TO NEW MEMBERS

A very warm welcome to the following members who joined the College between July 1998 to March 1999:

Ordinary Members

Dr Lam Marcus
Dr Leong Soh Sum Helen
Dr Lok Ying Fang
Dr Yoong It Siang

Associate Members

Dr Chan Yuan Keun
Dr Chong Chun Hon
Dr Goh Chyen Chye
Dr Hayes Alana Kim
Dr Lau Vi Hok Don
Dr Lee Yu Ming
Dr Lim Hui Ling
Dr Lim Wei Liang Daniel
Dr Loh Weng Keong Victor
Dr Ngeow Colin
Dr Soh Soon Beng
Dr Tan Boon Yeow
Dr Teo Boon See
Dr Tng Wei Chiang
Dr Wang Joon Leong
Dr Wong Liang Fu

Announcements

College of Family Physicians Singapore

7th Scientific Conference & 8th Meditech Exhibition

Family Medicine Facing Demographic Change

28 – 29 August 1999

Venue: College of Medicine Building

&

Four Seasons Hotel

(Sreenivasan Oration & Banquet)

Highlights

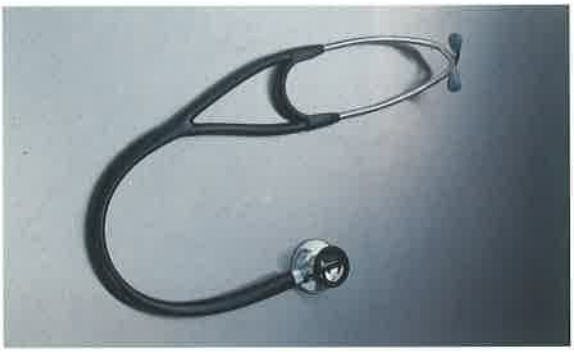
- **Health Screening in the elderly**
  What's effective
  Functional assessment
- **Dementia & Alzhiemers' disease**
  New advances
  Managing dementia
- **Depression in the elderly**
  Recognising & managing depression
- **Osteoporosis & HRT**
  Treatment options
- **Parkinson's disease**
  Early detection
  Getting the best outcomes
  Managing late disease
- **Workshop on male & female sexual dysfunction**
- **Othopaedic medicine for the elderly- the Cyrax method**
- **Office othopaedics**
- **Hands-on othorpaedic workshops**
- **Falls & pitfalls in the elderly**
- **Urinary incontinence**
  Managing the problem
  Continence aids
- **Palliative care**
  Symptom control
  Hospice & dying at home
  Bereavement & counselling
- **Sreenivasan Oration: "Medicine and politics- do they mix?"**
  Dr Tan Cheng Bock

Look out for the discounted rates for College Members and 'early bird' registration details in the flyers coming your way!

College Gifts and Accessories

KENZ Stereophonette Stethoscopes

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



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

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

SALE

Kenz stereophonette stethoscope	UP	S$285 each
	NOW	S$150 each
College Briefcases	UP	S$25 each
	NOW	S$20 each

College briefcases

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

College Silk Ties and Scarves

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

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

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

The Singapore Family Physician

GUIDELINES AND INFORMATION FOR AUTHORS THE SINGAPORE FAMILY PHYSICIAN

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

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

PRESENTATION ON THE MANUSCRIPT

The Whole Paper

- Normally the text should not exceed 2000 words and the number of illustrations should not exceed eight.
- Type throughout in upper and lower case using double spacing, with three centimetre margins all round. Number every page on the upper right hand corner, beginning with the title page as 1.
- Make all necessary corrections before submitting the final typescript. Headings and subheadings may be used in the text. Indicate the former by capitals, the latter in upper and lower case underlined.
- Arrange the manuscript in this order: (1) title page (2) summary (3) text (4) references (5) tables and (6) illustrations.
- Send 3 copies of all elements of the article: summary text, references, tables and illustrations. The author should retain a personal copy.
- Their accuracy must be checked before submission.
- All articles are subject to editing.

The Title Page

- The title should be short and clear.
- Include on the title page first name, qualifications, present appointments, type and place of practice of each contributor.
- Include name, address and telephone number of the author to whom correspondence should be sent.
- Insert at the bottom: name and address of institution from which the work originated.

The Summary

- The summary should state the purpose of and give the main argument or findings.
- Limit words as follows: 100 words for major articles; 50 words for case reports.
- Add at the end of summary an alphabet listing of up to 8 keywords which are useful for article indexing and retrieval.

The Text

The text should have the following sequence:

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

  Drugs must be referred to generically; all the usual trade names may be included in parentheses.

  Dosages should be quoted in metric units.

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

  Do not use patients' names, initials or hospital numbers.
- **Results**: Present results in logical sequence in the text, table and illustrations.
- **Disk & Electronic Production**: If your article is accepted for publication, we may invite you to supply a copy on a 3.5 inch disk, using Microsoft Word software.

Correspondence & Enquiries should be addressed to :

The Honorary Editor
The Singapore Family Physician
College of Family Physicians Singapore
College of Medicine Building
16 College Road #01-02
Singapore 169854
Tel: 223 0606 Fax: 222 0204
Email : rcfps@pacific.net.sg

Circulation

The Singapore Family Physician is published quarterly. It is circulated to all Fellows, Diplomate Members, Ordinary Members and Associate Members of the College of Family Physicians Singapore, and to private and institutional subscribers.

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).

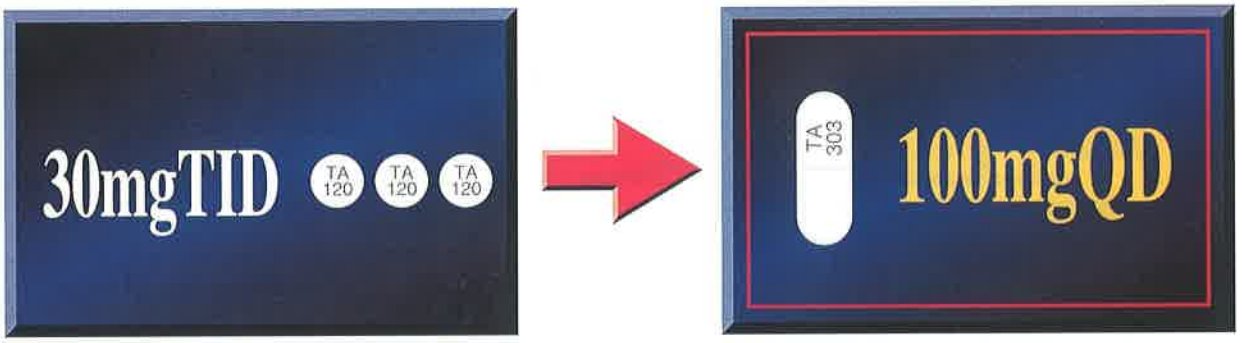
CONVERSION

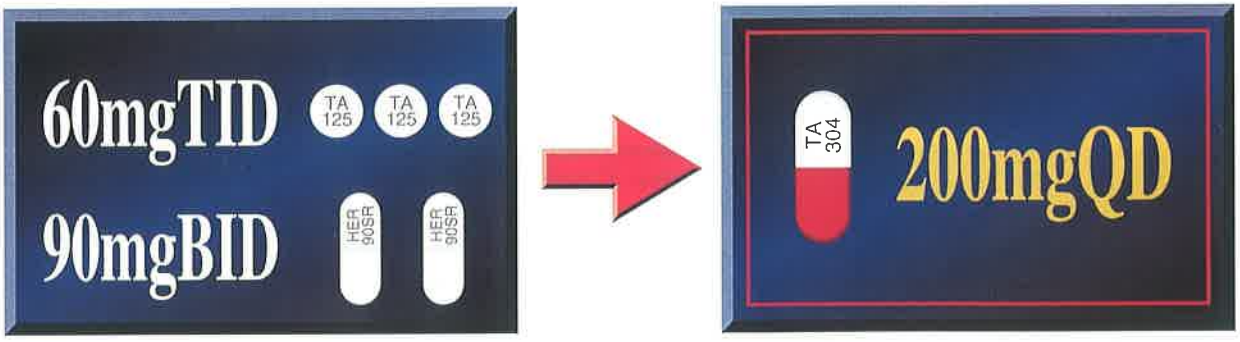
For Angina Pectoris and Hypertension

Sustained Release Ca^{++}-antagonist

HERBESSER® R100 R200

(diltiazem HCl)





24-HOUR CONTROL

Controlled-diffusion delivery system provides continuous plasma levels of diltiazem for the full 24-hour period

Further information is available upon request

PHARMAFORTE SINGAPORE PTE LTD.
6 Tagore Drive, #03-11 Tagore Industrial Building
Singapore 787623
Tel : 452 8488
Fax : 452 7787

TANABE SEIYAKU SINGAPORE PTE LTD.
10 Hoe Chiang Road #14-02 Keppel Towers
Singapore 089315
Tel : 323 0339, 323 0324
Fax : 323 0619