

INTRODUCTION

Dear Friends and Colleagues,

Welcome to the second med bulletin from The Harley Street Clinic Heart and Cancer Centre. Acute stroke (ischaemic or haemorrhagic) remains a significant health burden, accounting for approximately 9% adult annual mortality in Singapore (MOH website). This issue will discuss the benefits of screening for stroke and the management of risks such as hypertension and atrial fibrillation. We also present an article which highlights the critical importance of timely intervention (thrombolysis, thrombus aspiration) to mitigate brain injury and improve outcomes. Anxiety disorders are commonplace in today's society and an article which helps us to distinguish generalised stress from a clinical entity is also presented. The question relating to the nutritional benefits of different food groups, is commonly asked by cancer sufferers and this is addressed in our final article.

With best wishes,

Dr. Reginald Liew, Dr. Rohit Khurana and Dr. Sue Lo

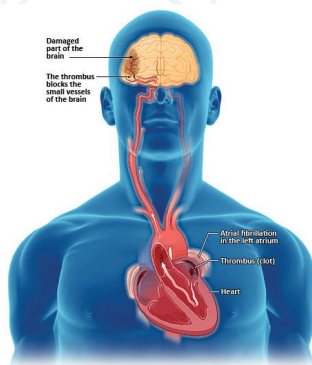


ATRIAL FIBRILLATION AND STROKE- A HIDDEN EPIDEMIC

Atrial fibrillation (AF) has for many years been regarded as a trivial condition, but it is now recognised that this common arrhythmia is an independent contributor to mortality, morbidity and impaired quality of life. An estimated 15% of strokes are a result of untreated AF, but most people don't know what AF is – much less know if they have it. The prevalence of AF increases with age- it is very unusual in people below the age of 30 but affects as many as 1 in 20 (i.e. 5%) of people over the age of 65. **It is estimated that as many as 50,000 people in Singapore have AF with the number in Singapore and worldwide set to double by the year 2050.** These data provide a warning to doctors today of an "AF epidemiological timebomb" waiting to happen, which some have called the "AF epidemic". AF can lead to stroke due to the formation of blood clots in the left atrium during AF when the atria do not fully eject blood- these clots can dislodge and travel to the brain (or other parts of the body) resulting in an ischaemic stroke.

Why is AF on the increase? The answer is multifactorial and due to an ageing population, people living longer with heart diseases (such as hypertension, coronary artery disease and heart failure) and the increasing prevalence of other conditions, such as sleep apnoea, diabetes, obesity and the metabolic syndrome.

What can doctors do in the fight against AF? One of the most important roles of the family physician in managing patients with AF is to help diagnose the condition or have a high index of suspicion in patients with symptoms and risk factors and refer to an appropriate specialist. Many patients, especially older people, are not aware of symptoms and AF may be first picked up by the finding of an irregular heart beat at a routine medical check-up. Nonetheless, these individuals may be at risk of a stroke, **so early detection and treatment can have an enormous impact on the patient's well-being and quality of life.** Patients with AF should have some baseline investigations done, such as a 12-lead ECG, blood tests (including renal and thyroid function), echocardiogram (to assess cardiac function and valve anatomy) and ideally see a specialist when first diagnosed to determine the best course of management.



How can the risk of stroke be reduced in patients with AF? The risk of stroke and thromboembolism can be calculated using the CHA2DS2-VASc or more recent CHA2DS2-VASc score, which are based upon a number of patient characteristics, including age, hypertension, diabetes, history of stroke/TIA, vascular disease and gender.

The higher the total score, the higher the stroke risk- current international guidelines recommend starting oral anticoagulation (with warfarin or a novel anti-coagulant drugs, NOACs) in patients with a CHA2DS2-VASc ≥ 1 . Those at low risk (CHA2DS2-VASc of zero) do not need any anticoagulation. The use of aspirin for stroke prevention in AF is no longer recommended as aspirin confers very little benefit in stroke prevention, whilst exposing the patient to side effects and an increased risk of GI bleed.

The introduction of NOACs, such as dabigatran, in recent years has made an important contribution to how patients with AF are managed. A number of well-conducted international, randomized controlled trials have convincingly shown that NOACs are as good as warfarin (and some are even superior) in lowering the risk of stroke in AF, whilst being associated with a lower risk of brain haemorrhage compared with warfarin. From the patients perspective, NOACs are a lot more convenient to take as they do not require regular INR monitoring and they have very little interactions with dietary intake or other drugs, unlike warfarin.

Summary:

AF is very common in Singapore, an important cause of stroke and appears to be on the rise. Early detection and appropriate treatment of the condition can lower the risk of stroke and improve patients' prognosis and well-being.

By **Dr. Reginald Liew**

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The Singapore Ministry of Health in their Health Facts (Singapore) 2013 States lists cardiovascular disease as the 4th principal cause of death. Each year, about 9000 patients are hospitalized for treatment of stroke. A National Geographic article published in 2006 states internationally, stroke was the third most common cause of death, after cancer and heart disease.

A rational approach to the management of stroke is to identify the etiology related to the main systems disorders of brain, heart, blood vessels, blood and metabolic abnormalities in relation to age and gender of the patient. In the young stroke patient ie below 40 years, attention should be focused on structure and pathophysiology of the heart such as prolapsing mitral valve, septal defects, and paroxysmal rhythm disturbance. The blood should be screened for coagulopathy and vasculitis.

In the older group, apart from the heart, endovascular and intramural blood vessels abnormality take on more importance particularly those related to hyperlipidemia and diabetes mellitus. Obesity, sleep apnea syndrome, excessive alcohol consumption and sequelae of infectious disease should be routinely looked for.

In the management of stroke, time is of the essence. It is now well established early intervention within 4-5 hours should be targeted. Measures include thrombolysis, support of cell function and clot removal. In hemorrhagic stroke, size of clot and location determine crucial timing of decompression and clot removal to facilitate brain recovery.

Current treatment of acute stroke understands good outcome is achievable with precision of diagnosis, early and timely intervention, measures to improve cell recovery in the immediate phase. In the stroke recovery phase, a good program of rehabilitation and prevention reduce the morbidity and mortality of patients. In these respects, public education assumes crucial importance.

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STROKE AND HYPERTENSION

The 2014 AHA guidelines provided guidance on stroke and hypertension management.

Primary Prevention

Blood pressure (BP) lowering is associated with a 30% to 40% stroke risk reduction, within hypertensive, stroke-free individuals, compared to placebo. Most trials however, defined hypertension as systolic BP ≥ 160 mm Hg or diastolic BP ≥ 100 mm Hg (i.e. grade2 /3 hypertension). Initiation of therapy for patients with grade 1 hypertension (systolic BP <140 mm Hg and diastolic BP <90 mm Hg) is of uncertain benefit .The most recent European guidelines assign a class I recommendation to initiating therapy for grade 1 hypertension only in the presence of high-risk features (target-organ disease, cardiovascular disease (CVD) or chronic kidney disease). Therapy for low- or moderate-risk grade 1 hypertension is a class IIa recommendation. More conservative recommendations were advocated for people older than 60 year old, to commence therapy when the systolic BP ≥ 150 mmHg and the diastolic BP ≥ 90 mmHg.

Acute Stroke

More than 70% of patients with an acute stroke have a history of hypertension, nearly half of whom can be expected to have poor BP control at baseline.

Whether high blood pressure reflects a hypertensive response or is consistent with premorbid values, it carries prognostic significance. Marked hypertension magnifies the risk of adverse cardiovascular events, renal injury and encephalopathy. Observational ischemic stroke data indicate that marked hypertension at clinical presentation is associated with up to a 5-fold increase in the rate of clinical deterioration and poor neurologic outcome, particularly when systolic BP > 180 mm Hg.



The benefit of treating hypertension for acute stroke is uncertain, but warranted within the first 24 hours in specific situations (ie, thrombolysis, SBP >220 mm Hg, or DBP >120 mm Hg). However, restarting antihypertensive therapy is reasonable after the first 24 hours for patients who have pre-existing hypertension and who are neurologically stable.

Secondary Prevention

Hypertension control is probably the most important intervention for secondary prevention of ischaemic stroke. A meta-analysis of 10 randomized controlled trials (RCTs) of secondary TIA or stroke prevention confirmed that anti-hypertensive treatment, compared to placebo, resulted in a significant 22% risk reduction over a 2-5 year period. The magnitude of secondary stroke risk reduction was proportional to greater degrees of systolic BP reduction.

Limited data specifically assess the optimal BP target for secondary stroke prevention. However, RCT evidence among high-risk patients with diabetes indicates that there is no benefit in achieving an aggressive systolic BP of <120 versus <140 mm Hg. Observational studies among hypertensive patients with diabetes, coronary artery disease or patients with a recent ischemic stroke, suggest that there may even be harm associated with systolic BP levels <120 mm Hg.

The optimal drug regimen to achieve the recommended level of reductions is uncertain because direct comparisons between regimens are limited. The available data indicate that **diuretics or the combination of diuretics and an angiotensin-converting enzyme inhibitor is useful.**

Lifestyle modifications, which include salt restriction; weight loss; the consumption of a diet rich in fruits, vegetables, and low-fat dairy products; regular aerobic physical activity; and limited alcohol consumption are mentioned for all clinical settings of stroke management.

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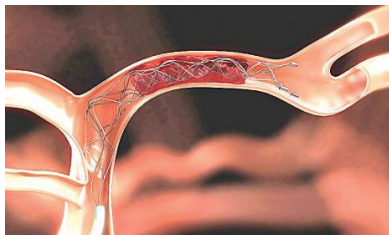
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STROKE! THE TREATABLE KILLER

Even in Singapore ischemic stroke is the fourth leading cause of death, with 10-12% of all deaths attributed to stroke. Due to our diet, life style and genetics the likelihood of intracranial atherosclerosis is prevalent from a much younger age in Asians compared to those in the west. When you combine the incidence of undiagnosed hypertension, this equates to the fact that one in every six Singaporeans will have a stroke in their life time.

Stroke tends to be more prevalent in the elderly. Our population is ageing at a greater rate than any of our neighbouring countries. Thus the likelihood, as a primary physician, you will encounter a stroke patient is very high. Until the end of the 1990's, there were very few options available for treatment of stroke.

This changed with the advent of intravenous tissue plasminogen activator (IV TPA) which could be administered up to three and a half hours after the onset of the symptoms. This method of treatment had remained the gold standard for many years, and in Singapore was the only option until a few years ago. Unfortunately IV TPA was not the panacea that people imagined it to be. It had a very short time frame of administration and there were an extensive list of contraindications including hypertension. The real concern however was that in large vessel occlusions, that were likely to cause the most debilitating strokes or death, the rate of recannulation was less than 8%.



Thus trials were done with intra arterial thrombolysis (IA TPA). This extended the therapeutic window to six hours; however it had a higher incidence of intracranial haemorrhage. It is well known and recognised that the Asian populations are at a much

greater risk of intracranial haemorrhage than those in the west, thus this method was never widely adopted.

In the last few years a new type of device called a stent retriever has come onto the market. This is a device introduced through the groin, navigated via the arteries into the intracranial circulation. The device is then used to ensnare the clot and withdraw it from the cerebral circulation. The procedure can take as little as 7 minutes from the time of puncture of the groin to completion of clot removal. This method of treatment is instantaneously effective, with most patients able to move their hemiparetic side almost immediately, following the retrieval of the clot.

The main advantage however is that the treatment can be offered up to eight hours following the onset of symptoms for anterior circulation strokes and 24 hours for posterior circulation strokes, which can be more devastating. Recent trials such as Multicentre Randomised CLinical trial of Endovascular treatment for acute ischemic stroke in the Netherlands (MR CLEAN) and others have shown the efficacy of this treatment method. It is a method that is only practiced by a handful of operators due to the degree of training required.

In any event it should be remembered that time is brain in stroke. 1.9million neurons are lost per minute that the brain is ischemic. This equates to a loss of 3.5 years per hour taken to administer effective treatment. It is imperative to educate your patients to recognise the symptoms of stroke and to seek effective treatment quickly.

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HELP! I'M FEELING ANXIOUS

We live in a fast paced society, where many of us feel that our lives seem to revolve around juggling demands from work, studies, relationships, and even social activities. It feels like everyone and everything wants a piece of us. So of course it's natural to feel stressed out and anxious from time to time. In fact, a bit of stress is a good thing, because it keeps us on our toes, and motivates us to get things done. It's also a natural built-in warning device that alerts us of dangers around us.

Anxiety symptoms can be psychological or physical, but usually a combination of both. Psychological symptoms include feelings of worry, insomnia, difficulty concentrating, and irritability. Physical symptoms include tremors, palpitations, breathlessness, appetite loss, headaches and gastrointestinal discomfort.

But when does anxiety become a problem? It becomes a problem when the symptoms are out of proportion to the danger present, or when it persists longer than it should. If the symptoms are bad enough to interfere with daily functioning, then it may be serious enough to be an anxiety disorder. For example, if you feel unable to deal with work issues, have trouble eating, cannot sleep well and find yourself worrying most of the time – that might mean you have an anxiety disorder.

There are different types of Anxiety Disorders:

- 1. Adjustment disorders** – where the symptoms are directly related to a stressful event (such as changing jobs, a relationship break-up, or even enlisting for National Service)
- 2. Generalised Anxiety Disorder** – where there is no specific stressful event, but symptoms of anxiety are experienced constantly on most days
- 3. Phobias** – where anxiety symptoms are triggered but certain feared objects and situations (such as insects, blood or public speaking)
- 4. Panic Disorder** – characterised by intermittent episodes of intense anxiety (called panic attacks) while feeling relatively normal in between
- 5. Obsessive Compulsive Disorder** – characterised by repetitive actions or thoughts (such as cleaning repeatedly) which the person finds intrusive and stressful
- 6. Posttraumatic Stress Disorder** – where the symptoms of anxiety are caused by a traumatic, life or limb-threatening event (such as a car crash or being a victim of assault)



Doctors believe that anxiety is caused by chemical imbalances in the brain. A relative deficiency of the neurotransmitter serotonin is thought to be the main cause, but no one knows exactly how this causes anxiety. We do know that some people are more prone to anxiety, and anxiety disorders often runs in families. It can be triggered by stressful events in some cases, while in others it seems to arise for no particular reason. In the United States, up to 18% of the adult population may suffer from an anxiety disorder.

In our local population, many people with anxiety disorders may not seek treatment because they either do not realise that it is a clinical disorder, or are embarrassed to see a doctor about it.

However, all anxiety disorders are treatable conditions. Milder cases can benefit from counselling, relaxation techniques, or certain forms of psychotherapy such as Cognitive Behavioural Therapy and Mindfulness Based Stress Reduction techniques. If symptoms are more severe, tranquilizers or a short course of antidepressants are prescribed. Many people are afraid of side-effects or being addicted to medications, but in truth the risk of such adverse effects is low.

If you know someone who has an anxiety disorder, offer a listening ear and encourage him or her to seek help. Avoid harmful coping methods such as excessive drinking or smoking, which can do more harm than good. Sometimes just talking about their fears and problems goes a long way in helping the person feel better.

By **Dr Adrian Wang**

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NUTRITION AND CANCER

"Doctor, can I eat chicken?", "Doctor, what food should I avoid to prevent cancer?", "Doctor, I haven't been drinking milk or eating soy product as it is bad for breast cancer." I am sure most if not all of us have had similar queries from our patients with regards to what is regarded as 'good food' and what is regarded as 'bad food' for cancers. Although the role of diet in heart disease or diabetes is fairly clear, it is not as clear for cancer. Many foods and nutrients have long been studied for cancer prevention, but finding a specific link between a food and cancer is difficult. This is because food contains many components, including macronutrients, micronutrients (vitamins and minerals), and non-nutrients (phytonutrients from plants, such as beta carotene), that may contribute to cancer prevention. The other factor is the facts that most people eat and drink a variety of foods, this create interactions that are challenging to study. Preparation of food also contributes to the variation, for example, chicken that is cooked by deep frying or steaming could influence the overall health effect.

Here is what is known about selected foods and macronutrients and their connection to cancer:

- Fruits and vegetables. Fruits and vegetables probably protect against several cancers, including mouth, pharynx (part of throat), larynx (voice box), esophagus, stomach. The current recommendation is to consume 5 portions of fruits and vegetables a day.
- Dietary fiber. Fibers are linked to a reduced risk of cancer, particularly colorectal cancer. Current recommendation is for women age 50 and younger consume 25 grams (g) and

men 50 and younger consumer 38 g of fiber each day. For people older than 50, women should consume 21 g and men consume 30 g of fiber each day. This is equivalent to the fiber found in one serving of high fiber breakfast cereal (6 g to 10 g), 5 servings vegetables and fruit (15 g to 21 g), one serving whole grain bread (2 g to 3 g) and ½ cup beans (8 g to 10 g).

- Protein. Meat, fish, shellfish, cheese, and eggs are the major sources of animal protein in most diets. Of those, red meat and processed meat are often studied as risk factors for cancer. Most of the studies suggest that people who eat more red meat have higher risk for developing colorectal cancer than those who eat less red meat, but avoiding processed meats is even more important. Eating processed meat, such as hot dogs, bacon, and salami, increases the chances of colorectal cancer. The study found people can eat up to 18 oz of red meat a week without raising cancer risk. Selecting lean cuts is important (such as flank steak or extra lean ground beef). Research on processed meat shows cancer risk starts to increase with any portion.

- Dairy foods. Dairy foods are a varied food group and are usually a good source of calcium. Multiple studies of dairy foods and cancer have shown conflicting results. Study found that milk probably protects against colorectal cancer, and bladder cancer. There is no concrete evidence to suggest any link between breast cancer and dairies.

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