

PROFESSOR DR HJ HAMIDON HJ BASRI

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BSc(Med), MD(UKM), MMed(UKM), AM(Mal)

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INTRODUCTION

Stroke is defined as "a clinical syndrome characterized by rapidly developing clinical symptoms and/signs of focal and at times global loss of cerebral function lasting more than 24 hours with no apparent cause other than that of vascular origin". This means a sudden neurological deficit (face or limb weakness, speech difficulties, etc) due to either ruptured or blocked arteries. When one develops a stroke, one will change. This can manifest as physical, emotional, mental, intellectual, and even behavioural changes. The change will not only affect the person, but also the people around such as family members and friends. Somebody needs to take charge and devote his/her life to looking after the stroke patient. The problem does not stop there. The whole complex family equilibrium will be disrupted. This new person will need 24-hour care, sometimes without ever needing to sleep. Some may be able to talk, but with much sarcasm and hate. Unthinkable hurtful words may also be said which was previously impossible to be uttered by this once caring and loving person. The deep pain caused by this new person may divide even the most cohesive family structures. To add salt to the wound, somebody will need to feed him with expensive nutritional food and change his pampers, urine tube, feeding tube, special stockings and much more, on a regular basis. This can be really costly and create financial constraints for the family. Furthermore, who can withstand doing this job 24 hours a day, 7 days a week? Yet, this new person will show no regard or appreciation for the sacrifices made by the family, yelling and saying many other hurtful words. We have heard of many maids running away from their employers due to this reason. Eventually, one of the children will have to stop work and take care of their parent full time. However, this is not a 3-month, or a 1-year job. This full time job will be arduously long; and last for years until he/she passes on. One day the child may

give up and pass the responsibility of care-giving to another child. This will go on until ultimately nobody wants to take care of the parent anymore. In their subconscious mind, this new person is no longer the loving parent he/she once was, but a grumpy, difficult and troublesome person that nobody wants to be with. A truly sad ending. No parent deserves this. In Malaysia, it is not yet a culture to send parents to a nursing home. To do this is equivalent to failure. The children will try to avoid this at all cost. Thus, the problem will stay within the family until the patient dies. With poor care, he/she will eventually die early due to complications. To a lot of affected families and care-givers, death is the only ultimate solution to this nagging problem which is indeed a sad affair.

This scenario quite commonly happens with patients suffering severe stroke. In reality, most stroke patients develop mild strokes. However, this is actually a warning sign that future strokes are just around the corner. It is obvious that if the warning signs are not heeded, the above story-line will repeat itself.

More than 15 years ago, when a stroke patient with severe neurological deficits presented at the hospital, the doctors would counsel the relatives on the grave prognosis. In other words, tell them that there is no hope. Today, with advancements in medicine, stroke patients are no longer considered a lost cause. If they get treatment early enough, the disability can be minimized. The risk of a second more disabling stroke can be reduced and better care is available to reduce complications. For those who suffer major neurological deficits, it will not be the end of the road. It would just be the beginning of a long and an arduous rehabilitation for both patient and care-giver.

THE BURDEN OF STROKE

Every year, 15 million people suffer from a stroke. Of these, 5 million will die and another 5 million will suffer permanent disability. 87% of stroke deaths are in low and middle-income countries. It is estimated that in the year 2030, strokes will occur in epidemic proportions especially in developing countries like Malaysia. It is projected that the number of deaths will rise to 6.5 million in 2015 and to 7.8 million in 2030. The reason is due to increasing age, changing life-styles and increase in risk factors. The incidence of stroke is 1:2000. In Malaysia, there are about 300 to 1000 stroke admissions per year, based on hospital-based studies. It is between the second to third leading causes of death in the country depending on the year studied. Stroke is also a major cause of disability in adults. This has a major impact on the country as it causes a usually productive person in his/her prime to suddenly become disabled. The suddenness of the onset of stroke is what makes it so devastating. It is distressing to see a person become so disabled and dependent suddenly, in just a few seconds. Their bright and happy days suddenly become a thing of the past. Due to the anticipated phenomenal cost of treating stroke patients in developing countries by the year 2030, World Health Organization (WHO) has set a target of a 2% reduction per year. This can be achieved through better control of risk factors, and improved case management and treatment. The experience of developed countries show that sustained interventions can achieve at least 4% annual reduction in stroke mortality. However, in order to achieve this, efforts must be made within our own country. There are a lot of changes to be instituted and misconceptions to be corrected.

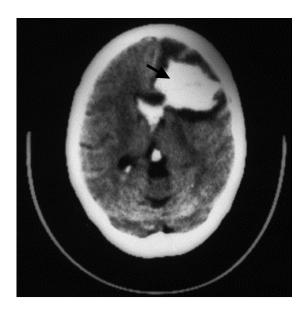
"Verily, never will God change the condition of the people until they change it themselves" Al-Raad: 11

A young newly-wed lady accountant in her thirties was shopping with her husband in a big shopping mall in Kuala Lumpur. Suddenly she could not move her right arm and leg and fell down (right hemiplegia). She tried to call to her husband but unfortunately she could not utter a single word (aphasia). She was rushed to the hospital and there she was told that she had suffered a major stroke involving her left middle cerebral artery territory (MCA). The first few days were very difficult and she cried all day long. She could not swallow on her own and was totally dependent on her husband. Her world had suddenly crumbled in just a few seconds. She kept on asking what she had done wrong, or if she could have possibly done something earlier which might have been prevented the stroke. Unfortunately, of course, it was already too late.

STROKE SUBTYPES IN MALAYSIA: IS THERE A DIFFERENCE?

There are two major types of stroke. The commonest is the ischaemic stroke which comprises about 75% of occurences, and the haemorrhagic stroke which accounts for about 25% of the cases. Comparison of Asian and Caucasian data (Hamidon BB 2005) showed that occurrence of haemorrhagic strokes are less prevalent among the Caucasian population. The percentage of haemorrhagic strokes among Caucasians is only between 10-15%. There has been no prevalent study carried out in Malaysia and the data are mainly hospital based. As haemorrhagic strokes are usually more severe, the proportion of such victims turning up at hospitals is naturally higher compared to those suffering from other forms of stroke. Hence this information must be treated with caution. The in-hospital prevalence of ischaemic stroke is definitely underreported compared to haemorrhagic stroke. This is especially true in developing countries where public education on stroke is poor

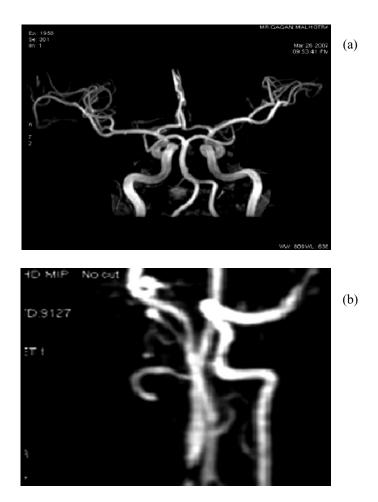
and healthcare is difficult to reach. A minor transient weakness of the limbs occurring for just 2-3 minutes is likely to be ignored. This will usually be blamed on tiredness, not enough sleep, fever or many other causes. Unless the person is well educated on stroke symptoms, he will probably not present himself at the hospital.



Picture 1 Haemorrhagic stroke: occurs when the arteries rupture. The blood (arrow) accumulates in the brain parenchyma. This type of stroke is more common in Asians as compared to Caucasians

Data from other Asian countries (Japan, Korea, China, Singapore and Thailand) showed that the prevalence of intracranial artery stenosis is about 50%. Our local data showed almost similar results (48%) in patients with ischaemic stroke. The Caucasian data only recorded up to 15% cases of intracranial stenosis. Lacunar infarcts (small infarcts less than 15mm) and silent cerebral infarcts have also been shown to be more prevalent in the local and regional Asian

data. However, these studies differ in methodology and were mainly hospital-based. Thus, the results of the comparison must be treated with caution.



Picture 2 Intracranial artery stenosis (a) is more common among Asians than in Caucasians (b)

A local study comparing the Malaysian population and the Australian population (majority being Caucasians) showed similar results (Ng WK 1998). It also showed that more cardio-embolic strokes recorded in the Caucasian data. This is due to the higher mean age of onset of the stroke. With increasing age, the risk of developing atrial fibrillation and cardio-embolic stroke is higher. The mean age of the Malaysian population was 61 years compared to 71 years in the Caucasian group. This can only mean that our arteries age earlier and thus we are at risk of developing stroke earlier. This strengthens the importance of initiating primary prevention measures early

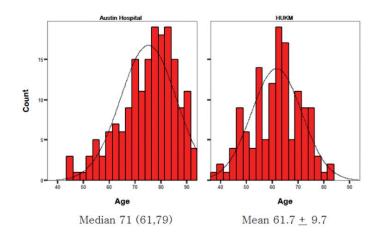


Figure 1 Stroke onset is earlier by 10 years among the Malaysian population compared to the Australian population (mainly Caucasian)

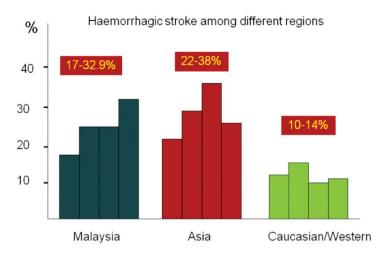


Figure 2 There is more cases of haemorrhagic stroke among the Asian population

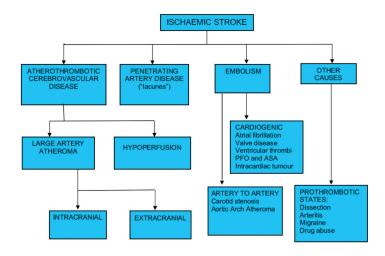


Figure 3 Stroke pathophysiology algorithm

PREVENTING A STROKE: START EARLY

When we are young, the world is ours for the taking. It feels like we are capable of doing anything and our bodies seem invincible. However, everything in this mortal world has its life span, even our bodies. When a stroke occurs, this means that the arteries have aged. This happens after years of development of plaque in the vessels. The plaque slowly thickens and hardens the arteries. The arteries then become increasingly narrower until a critical point when there is lack of oxygenized blood to the brain, causing ischaemia. If there is rupture of the plaque, the lumen will be totally occluded causing a stroke.

As the process is slow, trying to prevent a stroke must start early. To know how to prevent a first stroke (primary prevention), we must understand the risk factors associated with developing this condition. There are five major risk factors, namely age, diabetes mellitus, hypertension, smoking and hypercholesterolaemia. Basically, these risk factors are responsible for narrowing of the arteries. High circulating cholesterol, sugar and substances associated with smoking aid in the deposition of plaque and hence narrowing of the arteries. When narrowing is seen all along the arteries, this means that the arteries have aged and hence the occurrence of a stroke will be just a matter of time. The question then is when a stroke will occur.

Diabetes mellitus occurs when our body (mainly the pancreas) is no longer able to maintain blood sugar levels within the normal limits. As a result excess sugar in the blood will circulate throughout the body and at the same time reach vital organs. In simple words, the excess sugar literally poisons the body. This includes the arteries. Excess sugar in the blood will enhance cholesterol deposition into the endothelium of the arteries and further narrow the blood vessels.

Every 1mmol/l increase in blood sugar will increase stroke risk by 21%.

There is a log linear relationship between increasing blood pressure and stroke risk. Lowering the blood pressure (10-12 mmHg systolic and 5-6 mmHg diastolic) will also reduce stroke risk by 38%. This makes high blood pressure a strong risk factor in stroke occurence. Years of increased pressure on the complex system of arteries will inevitably cause damage in the form of ruptured plaque, weakened vessels (microaneurysms) and even ruptured arteries, if the pressure is too high, causing haemorrhagic stroke.

It is never too late to stop smoking. This message should be a reminder to all smokers. Cigarette smoking increases the risk of stroke by 50%. However, the risk normalizes 2-4 years after cessation of smoking. Smoking is an act of poisoning your own body. Unlike diabetes mellitus, this is intentional.

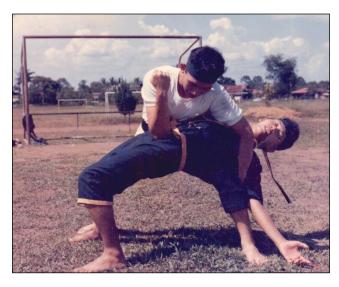
There is only a weak relationship between high cholesterol levels and risk of stroke. However, reducing cholesterol levels (total cholesterol 1.2mmol/l and LDL 1.0 mmol/l) will reduce risk of stroke by 22% in patients with underlying vascular diseases. This is achieved after maintaining low levels of cholesterol for years with anti-cholesterol agents (mainly statins). It is therefore prudent to start taking stroke prevention measures at an early age. When atherosclerosis (hardening of arteries) is advanced, it may be too late.

Secondary prevention using pharmacologic agents involve antiplatelets and anti-coagulants, depending on whether the stroke is thrombotic or embolic. Aspirin has been proven to reduce stroke risk by 23%. The evidence from the International stroke trials (IST) and Chinese acute stroke trials (CAST) resulted in efforts to find a more potent anti-platelet agent. The CAPRIE trial showed that clopidogrel is superior to aspirin by 8.7% it terms of stroke risk

reduction. The benefit over aspirin is certainly very small despite the overall cost of clopidogrel. Combination therapy using clopidogrel and aspirin showed no additional benefits as compared to use of either aspirin or clopidogrel alone (The CHARISMA and MATCH trial). There were also more haemorrhagic complications in the combination group. Combination of aspirin and persantin has shown promise of increased stroke reduction compared to aspirin alone (ESPS II, ESPRIT trial) but with more than one third of the patients withdrawing due to headaches. This combination is not available in Malaysia. About 15 years after aspirin was proven to be beneficial, only clopidogrel has shown small superiority in potency.

This further strengthens the theory that to prevent stroke, we must start early. Primary prevention should be emphasized rather than secondary (preventing a second stroke) prevention. When a stroke has occurred, most arteries are already diseased and narrowed and so, despite the use of multiple expensive medication, reduction of stroke risk is still small.

Promoting a healthy lifestyle is important and this must start early. When a person is active, exercising regularly, eating healthily, and stays away from smoking and alcohol, the risk of developing stroke and heart disease in the future will be reduced significantly. This should be a culture within the Malaysian family. Rather than going out to eat, they should be going out to exercise. With physical activity becoming a deep-rooted daily routine, our future generations will definitely become a healthier community. To age gracefully live healthily.



Picture 3 Outdoor activities such as Silat should be promoted for healthier living and it may help prevent vascular events in the future.

STROKE RECOGNITION: FAST

Act fast if you develop a stroke. The more you wait, the more neurons will die (millions in minutes). This is because blood supply to the affected brain is totally blocked. There are now medications (thrombolytic therapy) to recanalize the occlusion. The best result is when the patient is brought for thrombolysis within 90 minutes after onset of stroke. In such instances with thrombolysis, a severe deficit may be changed to minimal or no deficit (NINDS trial). Since time is of the essence for the brain, the public needs to know how to recognize early symptoms of a stroke. FAST does mean fast. "F" for facial muscle weakness, "A" for arm weakness, and "S" for speech difficulty. Any of these three means "T" for time to go to the hospital as soon as possible and so the saying "Time is brain".

The problem in Malaysia and many parts of the developing world is lack of knowledge of stroke symptoms. More than half of stroke patients and their immediate relatives do not realise that they are having a stroke. Some even equate a stroke to a heart attack. Stroke is a brain attack. Failure to recognize stroke has caused significant pre-hospital delays. Those who know that they are having a stroke think that it is only temporary and that they can overcome it. Some wait for their children to return home from work to take them to the hospital and some are even taken to traditional healers. All this can be attributed to poor knowledge of stroke, its natural history and treatment options. If these patients realise that the stroke symptoms are preliminaries to a bigger, more devastating stroke and rushing to the hospital early may help to reverse their symptoms, they will definitely rush to the hospital. Unfortunately this does not happen often and many patients turn up late to the hospital. Some even come weeks after the onset and complications have already occurred (Zamri M, Hamidon BB 2008).

Table 1 Common features of stroke: signs are what the doctors assess and symptoms are what the patients perceive.

Common Signs of Stroke	Equivalent Symptoms
Contralateral hemiparesis/ plegia	Weakness on one side of the limbs i.e. Left or right upper and lower limb weakness
Facial paralysis	Weakness of the facial muscles on one side. Face is asymmetric
Dysphagia	Inability to swallow food/fluids. Usually the patient will choke during swallowing

Gaze paralysis/diplopia	Inability to move the eyes to one side. There may also be double vision
Visual field defects e.g. hemianopia	Inability to see one side of the visual field usually on both eyes
Cognitive deficits	Memory loss
Confusion/coma	Drowsy and unaware of surroundings/coma

IN-HOSPITAL DELIVERY SYSTEM: ARE WE READY?

It will be a tragedy if stroke patients arrive early at the hospital but the hospital system is not ready to accept them. Without an efficient system, a targetted early thrombolysis will not be achieved. An ideal system will be where when a potential patient is identified by the paramedics and the acute stroke team is alerted early, even before the patient arrives. With these immediate response measures, potential patients can be actual candidates for thrombolysis. The process begins from the emergency room triage: doctor see the patient, complete the brain imaging and a decision is made within 30 minutes. The medical staff involved need to understand that delay for these patients means that they may be disabled for life. So, every second counts.

An example of a good in-hospital system to treat stroke is the acute stroke emergency calls (AST). When a patient is identified as having a stroke and onset is at the early stages(either through the paramedics or house calls), then an alert system is activated. This alert system will page/sms the stroke specialist/physician, stroke nurse, ER doctors, radiologist, radiographer and the neurology/medical doctor on call. With the patient identified as a possible candidate for thrombolysis, the hospital staff will be ready to accept

the patient and reduce delays in managing him/her. This system has been shown to reduce in-hospital delays and improve the outcome for stroke patients (Hamidon BB 2007).

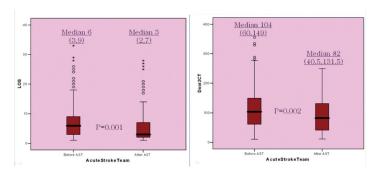


Figure 4 The formation of the acute stroke team has significantly reduced delay from door to brain CT and the length of hospital stay

MANDATORY BRAIN IMAGING

Brain imaging can be done using a computerized tomography (CT) or magnetic resonance imaging (MRI) system. Except in certain selected patients, brain CT is usually enough to make a diagnosis of the type of stroke. The previously developed clinical scoring system has failed to differentiate ischaemic and haemorrhagic stroke.

According to the current clinical practice guidelines, it is mandatory for all stroke patients to have brain imaging done. To treat a stroke patient without knowing the type of stroke is disastrous. When a haemorrhagic stroke patient is given anti-platelets, the bleeding will increase further and there will be a grave prognosis with a high mortality rate. However, it is probably impossible to equip all hospitals with brain imaging facilities. To solve this problem, many countries has adopted a centralised system where stroke patients are channelled directly to a hospital with CT or MRI scan facilities, especially those which offer thrombolytic service.

The channelling goes through a common emergency medical call system which advises the ambulance where to go. This idea has been implemented in the Klang valley through a project called KRISIS or Kuala Lumpur Regional Stroke Intervention Strategy.

Regional Approach

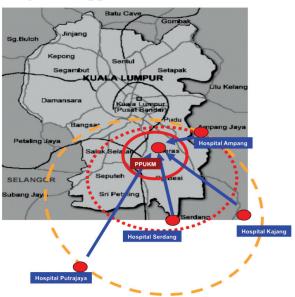
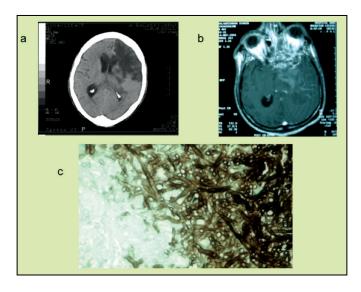


Figure 5 The KRISIS approach: channelling the patient to where best hyperacute stroke therapy is available

The difficulties in getting early brain imaging for stroke patients has been a major stumbling block in managing these patients despite the availability of the service. This is an issue in many parts of Malaysia. The treating physician must coordinate the stroke services with the emergency and radiology departments. The stroke clinical practice guidelines (CPG) will be able to guide them to standard stroke treatment protocol agreeable to all parties. This also includes early brain imaging.

Without brain imaging (at least a brain CT), other stroke mimickers may also be missed.

A diabetic man presented with sudden onset of hemiparesis similar to a stroke symptom. Urgent brain CT (followed by MRI) showed a small infarct with mass extending from the sinuses. Biopsy revealed a type of fungus which can invade the brain arteries causing a stroke. The diagnosis was angio-invasive aspergillosis mimicking a stroke (Norlinah MI, Hamidon BB 2007).



Picture 4 Brain CT showing features mimicking an ischaemic stroke (a). MRI showed a mass extension from the sinuses (b). Biopsy showed growth of the fungus Aspergillus (c)

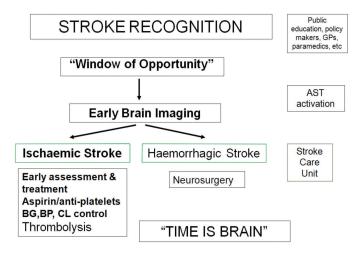


Figure 4 An algorithm on the management of acute ischaemic stroke

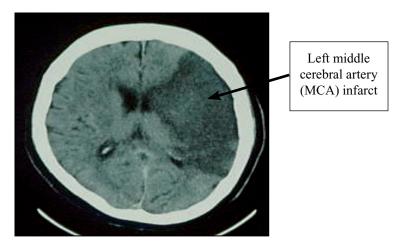
HYPERACUTE TREATMENT: SAVING YEARS OF GOOD QUALITY LIFE

"Time is brain" and "urgency is key". The EXPRESS trial has shown that usual stroke therapy (i.e. Anti-platelets aspirin or clopidogrel, anti-hypertensive agents, anti-diabetic agents, statins, etc) given within 24 hours reduces stroke recurrence by 80% in 3 months. This achievement is due to significant reductions in blood pressure, blood glucose and cholesterol levels in affected patients. Success in preventing a second stroke is imperative. This is because recurring strokes will cause more neurological deficits. The problem with our stroke patients is that they believe that strokes only happen once. They should always be reminded that they are at higher risk of developing a second more disabling stroke within 2 weeks after the first stroke.

There were many sceptics when thrombolysis for stroke was introduced in the 1990s. This was because of high incidence of

bleeding complications after the thrombolysis agent was given. The landmark NINDS trial showed an overall bleeding complication of 6.7%. However, recently, with more careful selection of patients, bleeding complications have reduced and if it occurs, does not affect mortality. The SITS-MOST European post-marketing study has shown this effect. The trial also proved that the benefit and bleeding complications are similar with the randomized control trials. In offering thrombolysis service, good selection of cases is key to successful recanalization, improvement in functional outcome and reduction in bleeding complications. Parameters such as stroke clinical severity scoring (NIHSS), CT criteria (ASPECT), time after stroke onset (best within 90 minutes but can be extended up to 3 - 4.5 hours), site of occlusion and other co-morbidities must be analysed before thrombolysis is performed to achieve an optimum result.

A patient with severe stroke - unable to talk (aphasia), unable to move his right upper and lower limbs (hemiplegia), unable to see on his right visual field (homonymous hemianopia), unable to look right (gaze palsy) and neglecting the right side (hemineglect) - can suddenly reverse back to normal with this treatment. The improvements can be really dramatic. To treating doctors, this will be a very satisfying accomplishment. However, it can easily become a disaster (bleeding complications) if the selection of patient is wrong.



Picture 5 A huge stroke (ischaemic type) on the left side of the brain: this may be avoided if the patient comes early and thrombolysis given.

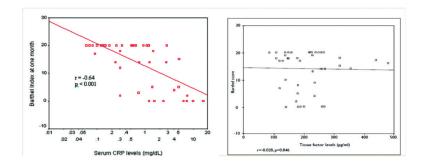


Figure 7 Stroke functional disability is associated with high tissue factor and c-reactive protein (CRP) levels (Hamidon BB 2004, Halim AG 2006).

STROKE AFTERMATH: THE NEW BEGINNING

A physician in his 50s had been leading a healthy lifestyle. He played badminton three times a week, had no major vascular risk factors and enjoyed good income in a private hospital. He developed a major left hemispheric stroke due to an unknown cause. After that event, he was a totally different person. He was not able to tend to his daily needs. His wife suffered too as she needed to be with him all the time - changing diapers, feeding him milk (specific for improved nutrition), dressing and cleaning him (bathing, brushing teeth, etc) - on a regular basis. He also cried frequently when his needs were not fulfilled. This brought back memories of the days when she (the wife) had to take care of their small baby. In fact, he was truly like a small baby. After the event, he needed to re-learn all the deficits that had occurred, similar to a developing child. He had to learn to walk, to balance against gravity, to understand and express himself (speech and cognition), to interact and to control his emotions. The family and carer too needed to persevere. This needs a lot of patience, energy, time, financial and emotional support from the family. The good doctor is fortunate that he had all that. He almost lost his tenacity for life if not for the support of his wife and family. After 2 years, he is now able to be independent in his activities of daily living and enjoy his remaining life. Despite not being able to practice anymore, he is happy with a good quality of life after a stroke.

There is actually life after a stroke. It is a new beginning. However, the path leading to the destination will not be easy. There are many trials and tribulations waiting in the form of post-stroke complications.

THE INEVITABLE COMPLICATIONS: DAMAGE CONTROL

Almost all patients who experience a major disabling stroke will develop complications. The list of complications is extensive. It includes medical (pneumonia, urinary tract infection, deep vein thrombosis, gastrointestinal bleeding, pulmonary embolism, sleep disordered breathing, bed sores, frozen shoulder, falls, etc.) and neurological (recurrent stroke, haemorrhagic transformation, extension of infarct, acute hydrocephalus, uncal herniation, seizures, vascular dementia, depression, behavioural changes, etc) complications.

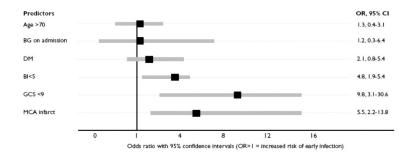


Figure 8 Early infection after a stroke is independently predicted by poor functional disability, poor Glasgow coma score (GCS) and large hemispheric strokes.

The most common complication is pneumonia followed by urinary tract infection (UTI). The reason for the high occurrence of pneumonia is due to dysphagia. Many patients lose control of their normal swallowing mechanism (dysphagia) after a stroke. This deficit is commonly missed by the treating doctor if not assessed properly (Nabil I, Hamidon BB 2005). During normal swallowing, the trachea is closed to prevent food particles from entering the lungs. When this mechanism fails, the food particles

will accumulate, attract bacteria and eventually cause lung infection (pneumonia). All stroke patients with neurological deficits need to be tested with a bedside water swallow test. If dysphagia is present, the patient must be referred to the speech and language pathologist (who deals with swallowing problems) to be properly assessed and managed. Pneumonia has been proven to be a major cause of death among stroke patients (Maujad A, Hamidon BB 2008).



Picture 6 The water swallow test and video fluoroscopy examination is important in stroke patients' assessment to prevent aspiration pneumonia

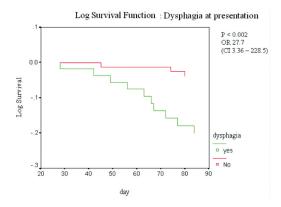


Figure 9 Post-stroke dysphagia is associated with higher mortality depicted in this Kaplan-Meier survival analysis

In cases of severe disabling stroke, the risk of dysphagia is high. If the dysphagia is expected to persist, the use of the percutaneous endoscopic gastrostomy (PEG) tube has been proven to improve the nutritional outcome. The albumin level, haemoglobin level and arm circumference of users of the tube showed significant difference compared to those without the PEG tube (Hamidon BB 2006)



Picture 7 PEG tube use has been proven to improve nutrition outcome of stroke patients

A stroke patient was discharged from the hospital fully dependent on his care-giver. He had post-stroke dysphagia. He was fed with special milk via a feeding tube through his nose (Ryle's tube). The family was worried that he was not getting enough nutrition. In addition, the patient always scolded the family members for not allowing him to eat normally. "How can you do this to me after all the sacrifices I have made for you when I was strong and healthy? Please let me eat. Please give me some food". He also cried and shouted uncontrollably. In the end, the family relented and started feeding him through the mouth. Two weeks later, he developed high grade fever and died due to pneumonia.

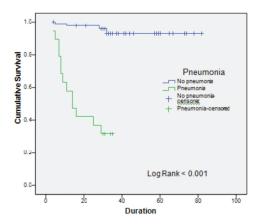


Figure 10 Survival analysis showing an extremely high mortality in patients who developed post-stroke pneumonia. Noradina AT, Hamidon BB 2010

This true story is an example of miscommunication between the treating doctor and the carer. If the family and care-giver are given due explanation on the importance of avoiding oral feeding, this tragedy would not have happened. A combined multidisciplinary stroke team is important to prevent this from happening. The

team would comprise treating doctors, nurses, a pharmacist, physiotherapist, occupational therapist, speech language pathologist and social worker. The patients' problems are discussed on a weekly basis together with the would-be carers. This multidisciplinary combined approach has led to the development of stroke units.



Picture 8 This patient developed a large hemispheric stroke causing him to be totally dependent and bed-ridden. Going to the hospital for follow-ups is a major problem

Another common complication in stroke patients is upper gastrointestinal bleeding. This is especially in the elderly age group (Hamidon BB 2006). Stroke patients are at risk of developing stress ulcers. They are also on anti-platelet agents that can cause bleeding from these ulcers. Sometimes the bleeding is slow but continuous. As a result, these patients may not complain. The care-givers looking after them should be on the alert if stool colour is black and tarry (melaena). This is a sign of upper gastro-intestinal bleeding and the patient should be sent to the hospital as soon as possible. Failure to do this will cause the patient to bleed to death.

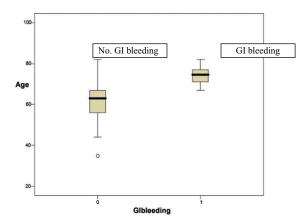
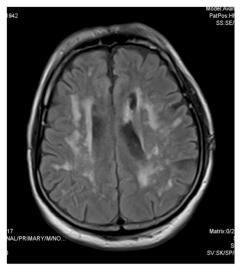


Figure 11 Box plots showing older age post-stroke patients are at higher risk to develop upper gastrointestinal bleeding.

In some patients, after the stroke, he/she will be a totally different person. The behaviour changes and emotions are labile. They can sometimes cry or laugh without any reason. They can easily get angry and shout at people. They have no control of their emotions. A lot of care-givers give up because of this problem. On one hand, this is not the patient's fault (the stroke has damaged the control for emotions at the fronto-temporal region). On the other hand, it is not easy to be around these patients. Spouses or children who persevere in caring for their loved ones should also be looked after by other family members. If not, it will definitely not last long. The common occurrence of leucoaraiosis and silent cerebral infarct in stroke patients has been shown to exacerbate these behavioural changes (Hamidon BB, Thein SS 2007).



Picture 9 Silent infarcts and leucoaraiosis occurring together may be asymptomatic

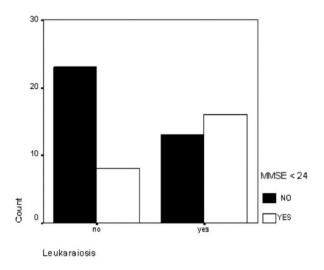
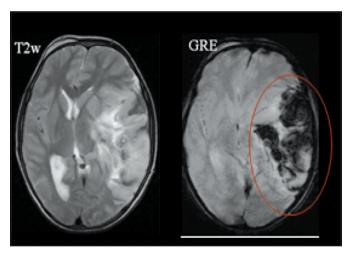


Figure 12 Stoke patients with leucoaraiosis have poorer memory in the mini mental state examination (MMSE)

Haemorrhagic transformation is another post-stroke complication that significantly affects mortality. This is especially true in large hemispheric ischaemic stroke as the new vessels formed an area of "luxury perfusion" around the ischaemic penumbra. This area can easily bleed and cause further damage to the brain. The peak incidence is between 4-7 days after the stroke onset. The haemorrhagic transformation can best be detected by gradient echo contrast MRI imaging. (Azlin A, Hamidon BB 2009).



Picture 10 Gradient echo contrast MRI imaging showing haemorrhagic transformation which is not easily seen in the T2 MRI-weighted imaging

STROKE UNIT: AN IGNORED GEM

Stroke units have been developed since the 1970s. There is clear evidence that stroke units are beneficial to stroke patients. A metanalysis showed that stroke units are able to reduce death and dependency by 25%. Stroke units also reduce length of stay and

the need for institutionalization. Ideally, all stroke patients should be treated and monitored in a stroke unit. The benefit to the patients is independent of age, gender, stroke severity and co-morbidities.

Unfortunately, despite the overwhelming evidence of the benefits seen over more than 30 years, many countries in the world still do not have a stroke unit. Even in Malaysia, most hospitals do not have a stroke unit. This is despite the fact that a stroke care unit (SCU) is cheaper and easier to set up and maintain compared to a cardiac care unit (CCU). Even in district hospitals, the discrepancy is obvious where CCU is priority. In most hospitals in Malaysia, the medical personnel needed to form a stroke unit are available. However, the concept of regular meetings, dedicated personnel and coordination amongst disciplines is difficult to be accepted in our country. Many medical staff members are already multi-tasking and overworked. There are too many meetings and stroke treatment is not always a priority. This practice has to change as the impact of stroke is usually under-estimated. The effectiveness of a stroke unit does not necessarily depend on the presence of a neurologist. Any physician or medical doctor who has interest in managing stroke patients is equally effective in leading the stroke team.

Stroke treatment usually combines acute stroke care with rehabilitation. The benefit is earlier intensive acute treatment, prevention of complications and early rehabilitation measures. Communication among treating disciplines and towards care-givers is also an important aspect in the functioning of a stroke unit. Every hospital should set up their own stroke unit in accordance with available resources to better manage stroke patients. We should recognise the importance of a stroke unit and not miss the opportunity to benefit from its formation. It has been an ignored gem for too long(30 years).



Picture 11 A stroke team combines many disciplines. A picture of the first stroke team in Malaysia in Hospital UKM

STROKE IN MALAYSIA: WHERE ARE WE?

There are only a few neurologists in the country sub-specializing in stroke. Most of these neurologists are based in the Klang valley. For years, stroke management has been sub-standard. In remote areas, there is no access to a hospital with brain imaging facilities. Even the hospitals that have brain MRI or CT facilities do the scans late (days after admission). There were also cases of patients being discharged without any imaging done and instead being given appointment dates. Without the scans, treatment cannot be instituted as treatment for haemorrhagic and ischaemic stroke is totally opposite. There is an old teaching where stroke patients are assumed to be ischaemic (the majority of cases) and aspirin is given 5-7 days after the onset without a brain scan being carried out. This assumption is dangerous because if this treatment happens to be given to the haemorrhagic group, bleeding will expand and worsen the stroke. Usually the prognosis in these cases is poor. Doctors

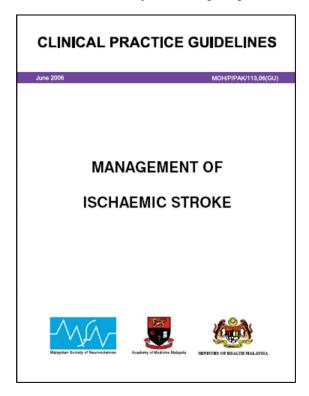
in Malaysia must not take this risk as one quarter of their patients will either worsen or die.

The Malaysian Society of Neurosciences formed the Malaysian Stroke Council in 2003 to discuss and plan stroke programs for the community. In 2006, the Malaysian stroke clinical practice guidelines (CPG) were developed. The booklet was distributed all over Malaysia to help guide doctors to better manage stroke patients. An internet-based national stroke registry has also been developed and is actively collecting data to find out more about this disease. Educating the public and medical personnel via nation-wide road shows, on the urgency to treat stroke fast, is also on-going. This includes the use of phrases like "FAST", "Brain attack" and "Time is brain". The selective use of thrombolysis has also been emphasized. Local doctors were identified to champion the formation of stroke units. A standard blueprint proposal is available to help in the application for a stroke unit. Key performance indicators (KPIs) have also been identified to help stroke units manage their patients according to best current evidence. Thus far, hospitals such as those in Kota Kinabalu (Queen Elizabeth Hospital), Alor Star (Hospital Sultanah Bahiyah), Seberang Jaya, and Penang have successfully set up their own stroke teams. The Malaysian stroke council hopes to further expand the formation of stroke units in other parts of Malaysia.

The National Stroke Association of Malaysia (NASAM) is another organisation that was formed to look after stroke patients' well-being. They have a few branches in Malaysia and is involved in group therapy and rehabilitation. Their formation was initiated by stroke patients themselves and is fast gaining recognition.

CONCLUSION

Stroke is a devastating disease. Not only is the patient affected, but also the whole family structure. It is important that stroke prevention starts early before it occurs. After a first stroke, a myriad of complications can happen. Treatment depends on how early the patient arrives at the healthcare facility. In Malaysia, the hospital system needs to be improved to accept such patients to allow early treatment such as thrombolysis. The use of anti-platelets, antihypertensive, anti-diabetic and anti-cholesterol agents must also be instituted early if need is indicated. Screening for dysphagia is important to prevent aspiration pneumonia, the most common cause of in-hospital mortality. Rehabilitation should be done in a coordinated and multi-disciplinary fashion. . The stroke team formation helps to facilitate coordination between many disciplines to communicate with each other. Proper advice to patient and caregivers can also be combined together during the weekly meetings. After a stroke, patients and care-givers should not feel hopeless and helpless. With immediate action and proper rehabilitation, there is still hope for a new beginning".



Picture 12 The front page of the Malaysian stroke clinical practice guidelines (CPG)

REFERENCES

Antithrombotic Trialists' Collaboration. BMJ 2002. 324: 71-86.

Adams HP, Zoppo D.G, Alberts MJ, et al. 2007. Guidelines for the early management of adults with ischaemic stroke. *Stroke*. **38**:1655-1711.

A.W. Jahangir, H.J. Tan, M.I. Norlinah, W.Y. Nafisah, S Ramesh, B.B. Hamidon, A.A. Raymond. 2007. Intramuscular injection of botulinum toxin for the treatment of wrist and finger spasticity after stroke. *Med J Malaysia*. **62**:319-322.

- B.B. Hamidon, A.A. Raymond, M.I. Norlinah, S.B. Jefferelli. 2003. The predictors of early infection after an acute ischaemic stroke. Singapore *Med J.* 44(7): 344-346.
- B.B. Hamidon, A.A. Raymond. 2003. Risk Factors and Complications of acute ischaemic stroke patients at HUKM. *Malaysian Med J.* **58**:307-313.
- B.B. Hamidon, A.A. Raymond. 2003. The impact of diabetes mellitus on in-hospital stroke mortality. *J Postgrad Med.* **49**: 307-310.
- B.B. Hamidon, A.A. Raymond. 2006. The risk factors of gastrointestinal bleeding in acute ischaemic stroke. *Med J Malaysia*. **61**: 288-291.
- B.B. Hamidon, H.M. 2007. Dewey. Impact of acute stroke team emergency calls on in-hospital delays in acute stroke care. *Journal of Clinical Neuroscience*. **14(9)**: 831-4.
- B.B. Hamidon, I. Nabil, A.A. Raymond. 2006. Risk factors and outcome of dysphagia after an acute ischaemic stroke. *Med J Malaysia*. **5**: 541-545.
- B.B. Hamidon, J.P. Joseph, A.A. Raymond. 2007. The predictors of Subclinical cerebral infarcts in ischaemic stroke patients. *Med J Malaysia*. 62:114-116.
- B.B. Hamidon, S.A. Abdullah, Zawawi M.F., Sukumar N., Aminuddin A, A.A. Raymond. 2006. A prospective comparison of percutaneous endoscopic gastrostomy and nasogastric tube feeding in patients with acute dysphagic stroke. *Med J Malaysia*. **61**:59-65.
- B.B. Hamidon, Sapiah S., Hapizah M.N., A.A. Raymond. 2004. The prognostic value of C-reactive protein (CRP) levels in patients with acute ischaemic stroke. *Med J Malaysia*. **59**: 631-637.
- Bamford J, Dennis M, Sandercock P, Dennis M, Burn J, Warlow C. 1990. The frequency, causes, and timing of death within 30 days of a first stroke: the Oxfordshire community project. *J Neurol Neurosurg Psychiatry*. **53**:824-829.
- Baranska G.M., Ryglewicz D., Lechivicz W., Mendel T., Weissbein T. 1993. Risk factors in patients with stroke. *Neurol Neurochir Pol.* 27: 625-632.

- Davenport R.J., Dennis M.S., Wellwood I, Warlow C.P. 1996. Complications after acute stroke. *Stroke.* 27:415-420.
- Davenport R.J., Dennis M.S., Warlow C.P. 1996. Gastrointestinal haemorrhage after acute stroke. *Stroke*. 27:421-424.
- DePippo K.L., Holas M.A. and Reding M.J. 1992. Validation of the 3-oz water swallow test for aspiration following stroke. Arch. *Neurol*. **49**:1259–1261.
- DePippo K.L., Holas M.S. and Reding M.J. 1994. The Burke dysphagia screening test: validation of its use in patients with stroke. Arch. *Phys. Med. Rehabil.* **75**:1284–1286.
- Dobkin B.H. 1987. Neuromedical complications in stroke patients transferred for rehabilitation before and after diagnostic related groups. *J Neurol Rehab.* 1:3-7.
- Dromerick A, Reding M. 1994. Medical and neurological complications during inpatient stroke rehabilitation. *Stroke.* **25**:358-361.
- Ee C.H., Kwan P.E., Tan E.S. 1991. Stroke rehabilitation of elderly patients in Singapore. *Singapore Med J.* 32:55-60
- Gottlieb D., Kipnis M., Sister E. et al. 1996. Validation of the 50 ml drinking test for evaluation of post-stroke dysphagia. Disabil. *Rehabil*. **18**:529–532.
- Hacke W, Kaste M, Bluhmki E, et al. 2008. Thrombolysis with Alteplase 3 to 4.5 hours after acute ischaemic stroke. *N Eng J Med.* **359**:1317-1329
- Haffner S.M., Lehto S. 1998. Mortality from coronary heart disease in subjects with type 2 diabetes and in non-diabetic subjects with and without prior myocardial infarction. *N Engl J Med.* **339**: 229-234.
- Halim A.G., Hamidon B.B., Cheong S.K., Raymond A.A. 2006. The Prognostic Value of Tissue Factor levels in Acute Ischaemic Stroke. *Singapore Med J.* 47(5): 400-403.
- Hamidon B.B., Raymond A.A. 2003. Predictors of in-hospital mortality after an acute ischaemic stroke. *Neurol J Southeast Asia.* **8**: 5-8
- Hamidon B.B. 2006. Percutaneous endoscopic gastrostomy (PEG) outcomes: can patient profiles predict mortality and weaning? Singapore Med J. 47(11): 1013.

- Hatano S. 1976. Experience from a multicentre stroke register: a preliminary report. *Bull World Health Organ.* **54**:541-553.
- Henon H, Durieu I., Pasquier, F., Leys D. 2003. Leukoaraiosis more than dementia is a predictor of stroke recurrence. *Stroke*. **34**: 2935-2940.
- J.P. Joyce, B.B. Hamidon, A. Raymond. 2005. Subclinical infarcts and functional disability in ischaemic stroke patients. *Journal of the Neurological Sciences*. 238:403.
- Johnston K.C., Jiang Y.L., Li M.S., et.al. 1998. Medical and neurological complications of ischaemic stroke: Experience from the RANTTAS trial. *Stroke.* **29**:447-453.
- Jorgensen H.S., Nakayama H., Raaschou H.O., Olsen T.S. 1995. Leukoaraiosis in Stroke Patients: The Copenhagen Stroke Study. *Stroke.* **26**:588-592.
- Jorgensen H.S., Nakayama H., Raaschou H.O., Olsen T.S. 1994. Stroke in patients with diabetes: The Copenhagen Stroke Study. *Stroke*. **25**: 1977-1984.
- Kelly-Hayes M., Robertson J.T., Broderick J.P. et.al. 1998. The American Heart Association Stroke Outcome Classification: Executive Summary. *Circulation.* **97**:2474-2478.
- Kumral E, Ozkaya B, Sagduyu A, Sirin H, Vardali E, Pehlivan M. 1998. The Ege stroke registry: A hospital-based study in the Aegen region. *Cerebrovascular Disease*. 277-288.
- Management of Ischaemic stroke: Clinical practice guidelines. 2006. Ministry of Health, Malaysia.
- Mann G., Graeme J., Cameron D. 1999. Swallowing function after stroke: prognosis and prognostic factors at 6 months. *Stroke*. **30(4)**: 744-748.
- Marina M.B., Sani A., Hamzaini A.H., Hamidon B.B. 2007. Ultrasound guided botulinum toxin A injection: An alternative treatment for drooling. *The Journal of Laryngology and Otology*. **19**: 1-6.
- Martino R., Pron G. and Diamant N. 2000. Screening for oropharyngeal dysphagia in stroke: insufficient evidence for guidelines. *Dysphagia*. **15**:19–30.

- McClatchie G. Survey of the rehabilitation outcomes of stroke. 1980. *Med J Aust.* 1:649-651.
- Moulin T., Tatu L., Crepin-Leblond T., Chavot D., Berges S., Rumbach T. 1997. The Besancon stroke registry: An acute stroke registry of 2500 consecutive patients. *Euro Neurol.* 38:10-20.
- Nabil I., Hamidon B., Rizal A.M., Raymond A.A. 2005. Risk factors and outcome of dysphagia after an acute ischaemic stroke. *Journal of the Neurological Sciences.* 238: 402.
- Neuman H.T. 2000. New magnetic resonance imaging methods for cerebrovascular disease: emerging clinical applications. Ann Neurol. 47: 559-570
- NINDS t-PA Stroke Study Group. Generalised efficacy of t-PA for acute stroke: Subgroup analysis of the NINDS t-PA Stroke Trial. 1997. *Stroke.* **28**: 2119-2125.
- Noradina T., Hamidon B.B., Roslan H., Raymond A.A. 2006. Sleep disordered breathing in patients with recent ischaemic stroke. *Singapore Med J.* 47(5): 1-8.
- Norlinah M.I., Ngow H.A., Hamidon B.B. 2007. Angioinvasive cerebral aspergillosis mimicking an acute ischaemic stroke. *Singapore Med J.* **48(1)**: e1-e4.
- Silver F.L., Norris J.W., Lewis A.J. et.al. 1984. Early mortality following stroke: A prospective review. *Stroke*. **15**:492-496.
- Starkstein S.E., Almeida O.P. 2003. Understanding cognitive impairment and dementia: stroke studies. *Curr Opin Psy.* **16**:615-620.
- Strong K., Mathers C., Bonita R. 2007. Preventing stroke: saving lives around the world. *Lancet Neurology.* **6**:182-187.
- Thein S.S., Hamidon B.B., Teh H.S., Raymond A.A. 2007. Leucoaraiosis as a predictor for mortality and morbidity after an acute ischaemic stroke. *Singapore Med J.* **48**: 396-399.
- Toni D, Lorenzano S, Puca E, Prencipe M. 2006. The SITS-MOST registry. *Neurol Sci.* **27**:260-262

- Van Straten A., Van Der Meulen J.H., Van Den Bos G.A,. Limburg M. 1997. Length of hospital stay and discharge delays in stroke patients. *Stroke.* 28:137-140.
- Vermeer S.E., Hollander M., Van Dijk E.J., Hofman A., Koudstaal P.J., Breteler M.M. 2003. Silent infarcts and white matter lesions increase stroke risk in the general population: Rotterdam Scan study. Stroke. **34**: 1126-1129.
- Vemmos Kn, Bots M.L., Tsibouris P.K., et.al. 1999. Stroke incidence and fatality in southern Greece: The Arcadia stroke registry. *Stroke*. **30**:363-370.
- Wade D.T., Langton Hewer R. 1997. Motor loss and swallowing difficulty after stroke: frequency, recovery and prognosis. *Acta Neurol Scan.* **76**:50-54.



BIOGRAPHY

Professor Dr Hamidon Basri was born on 2nd September, 1969 in Muar, Johor. He received his primary education at the Ismail School, Muar from 1976 to 1982. He was then accepted to study at MRSM Muar from 1982 to 1986. At both primary and secondary schools, he was elected as the head prefect. An active sportsman, he represented his schools in badminton (primary and secondary), football, hockey, volleyball, ping-pong and silat.

Professor Dr Basri furthered his studies at Universiti Kebangsaan Malaysia in 1986 where he received his MD in 1994.

During his university days, Professor Dr Basri was involved in many co-curricular activities. He was the president of the Silat Club and was trained as an instructor of 3 Silat forms. He has performed at various levels in Silat. Being an avid sportsman, he represented the college and won competitions in badminton, squash, football and volleyball. A hidden talent not known to many is his interest in poetry writing where he has won several varsity competitions and performed at poem recitals. Apart from his sports achievements, he has also fared well academically where he has attained the best student title several times.

After graduating in 1994, he was sent to Hospital Kota Bharu to do his housemanship. From 1995 to 1997, he was a medical officer at his hometown, Muar. He joined the Masters in Internal Medicine program at UKM in 1997 and graduated in 2001. Since then, he has trained in Neurology under the guidance of Professor (Dato') Dr Raymond Azman Ali at HUKM (Now known as UKMMC). He did further fellowship and training in Singapore (2003) and Melbourne, Australia (2005) under the guidance of Dr Ramani Venketasubramaniam and the renowned Professor Dr Geoffrey Donnan. respectively.

He was promoted to Associate Professor in 2003 at the age of 33 and the rank of full Professor five years later in 2008, by Universiti Kebangsaan Malaysia. He was the head of the Neurology Unit, UKMMC from 2004 to 2009. In December 2009, he moved to the Faculty of Medicine and Health Sciences, Universiti Putra Malaysia, as Professor of Neurology.

Professor Dr Basri is an ad hoc reviewer of several local and international journals, including Cerebrovascular Diseases, Diabetes and its Complications, Singapore Medical Journal, Medical Journal of Malaysia, Malaysian Journal of Medical Sciences and Medicine and Health. He has also been invited to deliver more than 100 lectures both locally and abroad. His main area of research interest is in stroke and he has published articles in more than 50 publications in local and international journals. He has received more than 10 awards for his research and activities in local and international arenas.

Professor Dr Basri is a life member and now President of the Malaysian Society of Neurosciences (MSN), where he was also the honorary secretary (from 2004-2006) and Vice President (from 2006-2008). He has been the president of the Malaysian Stroke Council since 2008 and played an integral role in the development of the Malaysian stroke clinical practice guidelines. He is also a council member of the Malaysian National Vascular Advisory Board and is the national coordinator for the STROKOP Asian stroke registry.

He is the secretary of the ASEAN stroke chapter of ASNA (ASEAN neurological Association). He was appointed as the international advisor and faculty member of APCAS (Asia-Pacific Congress against stroke) in 2007 and was the lead delegate to several ASEAN regions to promote Stroke treatment in countries like Laos and Thailand.

Professor Dr Hamidon Basri is also active in social humanitarian work. In 2002, he went to Pakistan and Afghanistan under Global Peace Malaysia to help the refugees. He visited Peshawar (Pakistan), Jalalabad and Kabul (Afghanistan) giving aid to the refugees (and local population) in the form of medical services, setting up hospitals, schools and vocational training. During his trip between Jalalabad and Kabul, the ambulance carrying him and 2 other relief workers was ambushed. Luckily he survived the ordeal and continued on. He has witnessed war, extreme cold without electricity, deaths of children and battles being fought for greed. The value for life in a war-torn country is cheap. He even experienced an earthquake measuring 7.1 Richter when he was there. During touchdown at the KL International Airport, he felt blessed to be living in a peaceful country like Malaysia and so was determined to soldier on contributing to the nation and to help maintain the peace that Malaysia is enjoying. Since then, he has been helping in relief work in Kashmir, Acheh and Padang. He is also bent on improving stroke services in Malaysia and the developing world.

"On that account We ordained for the Children of Israel that if any one slew a person- (unless it be for murder or for spreading mischief in the land) it would be as if he slew the whole humanity: and if any one saved a life, it would be as if he saved the whole humanity" Al-Maidah:32



Picture 13 In Kabul, Afghanistan during Qurbani (Aidul-Adha) 2002

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