

In any idyllic rural retreat someone may have set up a sawmill closeby, there may be blasting to re-route a road and giant Boeings may grind away 12,000 metres above where one lives. Soon after occupying my retreat I found myself to be next to a busy Helipad with 15 massive second-hand Russian helicopters—and directly on the runway approach of a busy rural airport, and also close to four farmers' shooting ranges specialising in automatic weapons, in response to our long ongoing state of rural emergency.

The search for silence is seldom well rewarded. I went to live for a year on the Lowveld 10 metres from the fence of the Kruger Park and not 80 metres from where a tar road entered one of the park gates. Unfortunately the Mozambique border was only 3 kms away and I was kept awake most of the night by bursts of heavy machine gun fire and mortar bombs as Frelimo and Renamo argued out their differences. Further away was the noise of heavy army trucks and of elderly Dakotas flying miners to the great city previously known as Lourenco Marques.

Now I live alone in a small one-bedroom cottage, and wake early and listen to the calls of the many birds in this garden—only 54 species recorded—very low for this region. I never listen to the radio and seldom to the TV unless there are special natural history, rugby or other programmes. At 7.30 a.m. I get up and start my day—lock the firearm away, open the various windows and curtains and turn off the security lights and re-check the Civil Protection 27 MHz radio. I switch on the various demand gas appliances. Breakfast is a cup of tea and a biscuit, and then at 8 o'clock the thrice-weekly elderly 'Help' arrives; I unlock all the security doors, and greet her in Swazi and give the briefest household instructions and re-lock all the doors because of the current frequent attacks on domestics during the mornings. I then check that my doubly-front-and-back-chained 'KT' (Toyota Hi-Ace Kombi) has not been stolen in the night—it is the most desired vehicle in Africa. I greet the neighbour's Shangaan gardener courteously in his own language and talk briefly about the extent of my refuse. My study is my bedroom and during the hour or so when the 'Help' is sorting it out, we do not need to utter a single word. Silence obtains until 11 o'clock. Then chaos tends to set in; I take the slightly longer but attractive rural route into our 'Dorp' and park near a Sotho chap with a machine gun who guards a massive chicken depot and kindly watches my car. We have a short greeting's talk, short because my Sotho is limited. In the supermarket, chaos reigns as I am one of the few Zulu-speaking customers and am greeted in succession by virtually all the black till ladies there, especially as they know that I am an Inkatha supporter. Here there is a minimum of 20 minutes of noise—not unpleasant I might add. The next stop is the Post Office where I am a good friend of a number of black pavement vegetable 'ladies', and this riotous bedlam lasts about 60 seconds. I then jump back into the Hi-Ace and drive slowly along a road with an unbelievable 100 km view to a peaceful Country Lodge, run by ex-Rhodesian (not Zimbabwean) friends, for half an hour's pleasant conversation amongst ideally peaceful surroundings—generally accompanied by 2 iced gins. Then home, and no single word spoken from 1 p.m. until 8 a.m. the next morning unless the phone rings.

I have a minimum of 20 hours of part-silence daily excluding quiet evening music which is as good as or better than silence. No matter how small one's budget may be, silence if obtainable is an inexpensive contributive path to contentment. This is not as much silence as in a Trappist monastery, but infinitely pleasurable. It is Virgil's *Ultima Thule*, or as near as one can get to it.

FOURTH EUROPEAN STROKE CONFERENCE, 1995

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At the Fourth European Stroke Conference, held in Bordeaux last June, 283 papers were presented. No striking new development was announced but the conference provided a good general view of the present state of the art and of prospects for improvements in both prevention and treatment of stroke.

Trials for acute stroke therapy

There is increasing interest in the development of drugs for stroke treatment and of the methodology for testing them. Assessment scales are widely used in stroke research and are loved by pharmaceutical companies. However, they only carry a flavour of what is happening to the patient and do not include any assessment of the patient's quality of life. What is important and needed in stroke trials is clearly defined end-points. Due to the heterogeneity of stroke, multi-therapy trials may be more appropriate, for example a combination of thrombolytic agents with neuroprotectors. There is still a lack of co-ordinated effort in stroke research. Centralisation of information with the development of networks of research centres may ensure adequate quality control and the development of new therapies.

Thrombolytic treatment

Results from three thrombolytic trials for acute ischaemic stroke were presented.

The European Co-operative Acute Stroke Study (ECASS) used recombinant tissue plasminogen activator within six hours of the onset of the stroke. Whilst 620 patients were randomised, 104 were later found to be ineligible due to protocol violations. Results analyzed with and without these patients suggest that thrombolysis is safe and effective for selected patients.

The Multicentre Acute Stroke Trial-Europe (MAST-E) randomised patients to either streptokinase or placebo in patients with a middle cerebral artery infarction. The trial was prematurely stopped due to an increased number of deaths and haemorrhagic events in the active treatment group. However, the Barthel score at 6 months was significantly better in the streptokinase group.

The Australian Streptokinase (ASK) trial looked at whether there was a reduction in mortality and morbidity at three months in patients randomised to active or placebo therapy. Again there were more deaths in the streptokinase group compared to placebo. However, for patients treated within three hours there were no concerns for safety or efficacy and the trial is continuing to recruit patients within this limit.

Surgery for carotid artery disease

The European Carotid Surgery Trial (ECST) and the North American Symptomatic Carotid Endarterectomy Trial (NASCET), have clearly defined the role of surgical treatment for severe symptomatic carotid artery disease.

The ECST data on morbidity and mortality among those patients undergoing endarterectomy shows that among factors associated with an increased risk of stroke or death were female sex, systolic blood pressure >180 mmHg, peripheral

vascular disease, moderate ipsilateral internal carotid artery stenosis and ipsilateral external carotid artery stenosis. Patients presenting with amaurosis fugax or retinal artery occlusion had a lower risk of stroke than those presenting with a cerebral TIA.

Data from NASCET examined how the prognosis of patients who had severe symptomatic carotid artery disease was affected by occlusion or stenosis of the contralateral carotid artery.

Patients with an occluded contralateral stenosis were more than twice as likely to have an ipsilateral stroke at two years. The perioperative risk of stroke or death was also higher in this cohort of patients. However, the long term outlook for patients who had endarterectomy performed on a recently symptomatic and severely ipsilateral artery was better than for patients treated medically.

The Asymptomatic Carotid Atherosclerosis Study (ACAS) was designed to address the question of whether endarterectomy had a benefit in asymptomatic patients with severe carotid artery stenosis. The participating surgeons from USA and Canada randomised 828 patients to surgery and 834 to medical treatment. Carotid endarterectomy had an absolute reduction of 5.9 per cent in the risk of stroke within five years and a relative risk reduction of 53 per cent. The perioperative complication rates were less than 3 per cent.

The European Asymptomatic Carotid Surgery Trial to identify those sub-groups who would benefit most from carotid endarterectomy is still recruiting patients.

Advances in stroke prevention

Raised plasma concentrations of fibrinogen may be implicated in at least three different atherothrombotic processes, plasma viscosity, the thrombotic process and plaque formation where the fibrinogen/fibrin ratio is important. As numerous environmental and physiological factors influence the fibrinogen level, drugs that reduce it may be of benefit in primary and secondary prevention.

Asymptomatic carotid artery disease is increasingly easy to diagnose and very tempting to operate upon. The ACAS reported a risk of 2 per cent per year for vascular events in these patients. There was a low risk of stroke or death (2.3 per cent) during angiography or surgery and a relative risk reduction of 50 per cent or an absolute risk reduction of 5.9 per cent. Thus operating upon 85 asymptomatic patients with carotid artery stenosis might prevent 1 stroke per year.

At the population level the message is even clearer. In Scotland, if an endarterectomy was carried out on all 40,000 people aged 50–80 years, then instead of 800 individuals only 400 would have a stroke next year. This is a trifling 4 per cent reduction in the 10,000 first ever strokes expected every year in Scotland.

In investigating cardiac disease, transoesophageal echocardiography (TOE) is clearly superior to transthoracic echocardiography (TTE). TOE has identified a strong independent association between atherosclerotic disease of the aortic arch and the risk of ischaemic stroke. In addition with TOE, patients with atrial fibrillation can be stratified as either high or low risk for thromboembolic events. Whilst TOE has changed dramatically our ability to recognise potential cardiac sources of embolism, it does not establish the stroke mechanism and the clinical significance of the presence of indirect cardiac sources, e.g. patent foramen ovale, remains controversial.

People who have suffered a transient ischaemic attack have an increased risk of stroke over the next five years. Several treatments have been shown to reduce this risk. Hypotensive treatment, antiplatelet therapy, anticoagulant therapy for patients with atrial fibrillation and carotid artery surgery and stopping smoking all reduce the risk. Cholesterol-lowering therapy may reduce the risk in patients with hypercholesterolaemia. However despite these impressive reductions in the risk of stroke that can be achieved by these means, from a public health point of view for patients, the possible reduction in absolute number of strokes is less impressive. This is because less than 15 per cent of all stroke patients experience a prior TIA. Therefore the attributable risk of TIA for stroke cannot be more than 15 per cent. Consequently the above strategies which can reduce the total incidence of stroke from 15 per cent to 7 per cent in absolute terms, thus avoiding about 8 per cent of all strokes.

Vascular dementia

Twenty-five per cent of patients aged over 60 years who have cerebrovascular disease have cognitive impairment. The risk of dementia following stroke is nine times that of stroke-free controls. In the USA nearly 500,000 people suffer from stroke with dementia.

It is difficult pathologically to distinguish multi-infarct dementia (MID) from senile dementia of Alzheimer's type, as the two pathologies are often a mixture. However, the two commonest pathologies seen in MID are small vessel disease and watershed infarction.

Radiological studies of dementia have included small numbers of patients and therefore the procedure is of little benefit. Secondly, there is a large variation in definitions and no agreement on number of infarcts needed or volume of tissue loss to help classify patients. Indeed small infarcts may have more clinical sequelae than was first thought; for example, Genu infarcts can lead to cognitive impairment due to damage to thalamo-cortical connections.

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