Stroke prevention: getting to the heart of the matter

About 6 million people in Europe have atrial fibrillation (AF). These individuals have a fivefold greater risk of stroke than the general population, and AF is thought to account for up to one in five ischaemic strokes. Strokes related to AF are generally more severe, cause greater disability, and lead to a worse outcome than non-AF-related strokes. These patients are therefore an important target population for reducing the overall burden of stroke. Yet as highlighted in a report by Action for Stroke Prevention, a group of health experts from across Europe, countless opportunities to prevent stroke are missed. The report, launched in the European Parliament in December, 2009, calls on European Union policy makers and national governments to take action to improve stroke prevention in patients with AF to avert a major public health crisis. Neurologists are crucial to the effective implementation of the report's recommendations.

AF is commonly undetected until a patient has a stroke. The report highlights the need for initiatives to raise awareness of the early signs of AF and for coordinated screening strategies (eg, routine pulse taking followed by electrocardiographic monitoring) in primary care, which is currently not standard practice in many countries. In particular, paroxysmal AF is under-recognised, and many patients do not undergo long-term monitoring of cardiac rhythms. Once identified, patients with AF are a joint concern for cardiologists, who see them before stroke, and neurologists, who see them after stroke. But neurologists should also have a key role in diagnosis because they see many elderly patients who may have previously undetected AF.

Anticoagulant therapy with warfarin reduces the risk of stroke in patients with AF by two-thirds and is highly cost-effective. However, warfarin is commonly underused: only 54–61% of patients with AF who are at high risk of stroke receive anticoagulation therapy. Concerns about the increased risk of intracranial haemorrhages and the need for careful monitoring of treatment are key reasons for the underuse of warfarin. The report identifies the need to educate physicians about available management options, and emphasises the importance of adherence to accepted guidelines: when used according to such guidelines, the benefits of warfarin generally outweigh the potential risks. More consistency in the use of validated risk-stratification tools is needed to reliably identify patients who are at greatest risk of stroke and are therefore most likely to benefit from anticoagulation therapy. Facilities for monitoring warfarin treatment are not available in many countries and effective services need to be developed to ensure equal access to adequate treatment.

A new wave of treatment strategies that may not require special monitoring are in clinical development. Among them are the oral direct thrombin inhibitor dabigatran, oral direct factor Xa inhibitors such as rivaroxaban (funded by Bayer Schering Pharma, the sponsors of the recent report), and indirect factor Xa inhibitors, as well as several non-pharmacological approaches such as left atrial appendage occlusion devices. The most advanced of these strategies is dabigatran. The results of the recent RE-LY trial showed that, compared with dose-adjusted warfarin, dabigatran at a dose of 150 mg twice daily led to a greater reduction in stroke risk and at a dose of 110 mg twice daily resulted in significantly fewer major haemorrhages. Importantly, with both doses, the rate of intracranial haemorrhage was less than one-third of the rate with warfarin.

Several questions about dabigatran remain. First, dabigatran has not been tested in frail elderly patients, so it is not clear whether the results from RE-LY can be generalised to this vulnerable population. By contrast, the results from the BAFTA trial suggested that warfarin is highly effective in this patient group. Second, more research is needed to understand its interactions with other drugs such as P-glycoprotein inhibitors. Third, once approved, the cost of dabigatran is likely to be higher than that of warfarin treatment and dose monitoring, and access to the drug will depend on the pricing. Moreover, the introduction of a new and possibly costly treatment should be weighed against the costs of improvements in diagnostic facilities and use of currently available treatment options.

Because AF falls between clinical specialties—cardiology, neurology, and geriatrics—it does not have the high profile that it deserves. Moreover, there is an imbalance between the burden of disease and the amount of research done; the Action for Stroke Prevention report highlights the need for more research into the causes, prevention, and treatment of AF and stroke prevention in these patients. Neurologists should have an active role in driving developments in clinical practice and in leading research efforts to improve the prospects for the millions of patients with AF. ■ *The Lancet Neurology*

For the **Action for Stroke Prevention report** see http://stopafib.org/downloads/news221.pdf

For the **RE-LY trial** see *N Engl J Med* 2009; **361:** 1139–51

For the **BAFTA trial** see *Lancet* 2007; **370:** 493–503

For more on **anticoagulant therapy in patients with AF** see *Eur Heart J* 2006; **27:** 1954–64; and *Am Heart J* 2007; **153:** 1006–12