BRITISH MEDICAL JOURNAL

LONDON, SATURDAY 2 OCTOBER 1982

Thyrotoxic atrial fibrillation: an underdiagnosed condition?

A finding of atrial fibrillation should always beg the question of its aetiology. Generations of medical students have been taught that the most common causes are rheumatic or ischaemic heart disease and hyperthyroidism, and that in a distinct minority, known as "lone" atrial fibrillators, there is no apparent reason for the arrhythmia. To a large extent recent epidemiological studies from Framingham[1] have confirmed this teaching, identifying rheumatic heart disease and cardiac failure as the cardiovascular disorders which most often lead to atrial fibrillation, with hypertension, coronary heart disease, and stroke being less likely to do so. Most patients with these causes of atrial fibrillation can be identified readily by careful history, clinical examination, chest radiography, electrocardiogram, and echocardiogram—the investigations which should form the basis of assessment of all patients with this arrhythmia.

An important omission in the discussion of the Framingham analysis and the accompanying leading article[2] was the absence of consideration of hyperthyroidism as a factor in their patients with "lone" atrial fibrillation (31% of the total). Atrial fibrillation develops in 10% to 15% of patients with overt hyperthyroidism,[3] and is most common in those aged over 60, reflecting both a reduction in the threshold for atrial fibrillation with age and an increase in the prevalence of coexisting ischaemic and other forms of heart disease. Though the electrophysiological basis for atrial fibrillation is poorly understood,[4] in hyperthyroidism the shortened duration of the action potential probably increases electrical excitability within the atrium and so predisposes to the arrhythmia.[5]

The clinical diagnosis of hyperthyroidism is not always obvious in elderly patients, in whom atrial fibrillation may be the dominant feature in the absence of goitre, classic eye signs, and other manifestations of thyroid hormone excess. The astute physician, however, may find clues such as proximal myopathy, palmar erythema, or failure of digoxin to slow the ventricular rate without the addition of beta-blockers. The interpretation of confirmatory biochemical tests of thyroid function may present difficulties if sole reliance is placed on the widely used measurements of serum total triiodothyronine and thyroxine. Many other illnesses (for example, cardiac failure or pneumonia) and many drugs (including beta-blockers, anticonvulsants, and antirheumatic agents) may produce a fall in total thyroid hormone concentrations. The extent of this reduction may be sufficient to bring these concentrations in patients with mild hyperthyroidism within normal limits. In these circumstances the concentrations of the free hormones, which are metabolically active, should mirror thyroid state more accurately than the total hormone concentrations. Though free hormone assays are becoming widely available, the various commercial kits produce disparate results in patients with non-thyroidal illness.[6] An added complication is that even increases in thyroid hormone concentrations within the normal range may be sufficient to trigger the onset of atrial fibrillation in susceptible people.[7] Fortunately, in the absence of hypopituitarism a lack of response of serum thyroid-stimulating hormone after the intravenous administration of 200 μg thyrotrophin-releasing hormone (the thyrotrophin-releasing hormone test) is an indication of hyperthyroidism irrespective of the concentrations of serum total thyroid hormones. A normal response excludes such a diagnosis. Hyperthyroidism should not, therefore, be dismissed as a cause of otherwise unexplained atrial fibrillation without recourse to the thyrotrophin-releasing hormone test, which takes only 20 minutes and is ideally suited to the outpatient clinic. Furthermore, the relative frequency of hyperthyroidism should be borne in mind: this is a common condition, affecting about 1% of the population,[8] and may therefore coexist with ischaemic and rheumatic heart disease.

Why is it important not to overlook a diagnosis of thyrotoxic atrial fibrillation? Firstly, this is one of the few chronic forms of the arrhythmia which is potentially reversible, and effective antithyroid treatment may be expected to produce spontaneous reversion to sinus rhythm in 60% of patients.[9] Direct-current cardioversion is successful in about half the remainder. Secondly, the risk of systemic embolism is not insignificant[10]: it is probably as great as in rheumatic mitral stenosis. Indeed, most of the deaths among the lone atrial fibrillator group in the Framingham study were from cerebrovascular events.[1] Patients with thyrotoxic atrial fibrillation should be treated with anticoagulants until stable sinus rhythm has been documented for at least six months—or indefinitely if the arrhythmia persists.

Thyrotoxic atrial fibrillation is almost certainly underdiagnosed—either because it is not considered or because appropriate thyroid function tests are not performed. When a thyrotrophin-releasing hormone test was added to the measurement of serum total triiodothyronine and thyroxine one in eight of the patients attending a cardiology clinic with apparently lone atrial fibrillation had hyperthyroidism.[11] Similar proportions of patients with potentially reversible

atrial fibrillation may well be found among other groups labelled as lone fibrillators.

J COLIN FORFAR
Lecturer in medicine
ANTHONY D TOFT
Senior lecturer in medicine

Royal Infirmary,
Edinburgh EH3 9YW

1 Kannel WB, Abbott RD, Savage DD, McNamara PM. Epidemiologic features of chronic atrial fibrillation. The Framingham Study. *N Engl J Med* 1982;**306**:1018-22.
2 Selzer A. Atrial fibrillation revisited. *N Engl J Med* 1982;**306**:1044-5.
3 Sandler G, Wilson GM. The nature and prognosis of heart disease in thyrotoxicosis. A review of 150 patients treated with ^{131}I. *Q J Med* 1959; **28**:347-69.
4 Abildskov JA, Millar K, Burgess MJ. Atrial fibrillation. *Am J Cardiol* 1971; **28**:263-7.
5 Freedberg AS, Papp JG, Williams EMV. The effect of altered thyroid state on atrial intracellular potentials. *J Physiol (Lond)* 1970;**207**:357-69.
6 Kaptein EM, Macintyre SS, Weiner JM, Spencer CA, Nicoloff JT. Free thyroxine estimates in nonthyroidal illness: comparison of eight methods. *J Clin Endocrinol Metab* 1981;**52**:1073-7.
7 Forfar JC, Feek CM, Miller HC, Toft AD. Atrial fibrillation and isolated suppression of the pituitary-thyroid axis: response to specific anti-thyroid therapy. *International Journal of Cardiology* 1981;**1**:43-8.
8 Tunbridge WMG, Evered DC, Hall R, *et al.* The spectrum of thyroid disease in a community: the Whickham Survey. *Clin Endocrinol* 1977;**7**: 481-93.
9 Nakazawa HK, Sakurai K, Momotani N, Hamada N, Ito K. Timing of cardioversion application in thyrotoxic atrial fibrillation. *Circulation* 1980;**62**, part II: 296. (Abstract.)
10 Staffurth JS, Gibberd MC, Fui SNT. Arterial embolism in thyrotoxicosis with atrial fibrillation. *Br Med J* 1977;ii:688-90.
11 Forfar JC, Miller HC, Toft AD. Occult thyrotoxicosis: a correctable cause of "idiopathic" atrial fibrillation. *Am J Cardiol* 1979;**44**:9-12.

Routine immunisation in adults

Immunisation policies are generally aimed at vaccination in childhood. Traditionally, immunisation in adult life has only been for travel abroad, certain types of occupational exposure to infection, and contacts of particular infections. More recently, however, the problems of rubella and influenza have focused attention on routine immunisation of adults. Since most of the immunisation programmes for common childhood infections were not introduced until the second world war, theoretically many middle-aged men and women in Britain are still susceptible to these infections. Should they be advised to seek immunisation?

Firstly, we need to remember that before routine immunisation was introduced most people gained a natural immunity to these infections. Whether we need to immunise adults depends on whether this immunity has waned and on the state of each infection in Britain today. With diphtheria, whooping cough, and measles the answer is a fairly straightforward no. Diphtheria is almost never seen in Britain now, and routine adult immunisation need not be considered, even though 35% of people of all ages—and 44% of those over 35—are still, theoretically, susceptible.[1] Similarly, immunisation against whooping cough is unnecessary in adults as less than 1% of notified cases of whooping cough occur in those over 35. Moreover, the severity of whooping cough decreases with age.[2] The number of people reaching middle age who have not had measles is small—less than 0·5% of notified measles occurs in patients aged over 25.[3] The notification rates for measles in adults do not appear to have increased since the immunisation campaign began in 1968.[3] Unless the number or rate (as opposed to the proportion) of cases of measles in adults rises substantially adults do not need to be immunised.

The question of tetanus immunisation of adults is less easy to answer. Tetanus is not a communicable disease in the sense that it can spread from person to person or that man acts as a reservoir of infection, so that to all intents and purposes only those immunised are protected; herd immunity cannot be relied on to protect the non-immune. Though many men would have been immunised during the second world war, many adults, mostly women, are susceptible to the infection (and about one child in five is still not being immunised). The 20 notifications of tetanus each year seriously underestimate the incidence, and the true figure is probably over 100 cases.[4] Most are in adults, especially middle-aged to elderly women, and tetanus is a serious disease, with an estimated case fatality rate of 10%.[4] For these reasons, immunisation with tetanus vaccine (which is safe and effective) should perhaps be encouraged in adults who are not immune, though routine immunisation would be impracticable and probably not cost effective. The initial course of three injections should be followed by a booster dose about every 10 years,[5] but there is no need to start a fresh course when an earlier series of injections has lapsed. Paradoxically, whereas many adults are unimmunised, others are possibly over-immunised.

With rubella vaccine the problem is complex. Routine vaccination of adults is clearly not required, because our strategy is designed to ensure the immunity of women during their childbearing years rather than to reduce the overall incidence of infection in Britain. Nevertheless, an unacceptably large number of women of childbearing age are still susceptible, and 2220 pregnant women with proved infections were reported to the Communicable Disease Surveillance Centre in the epidemics of 1978 and 1979. Clearly we need to identify and vaccinate more of those women who slipped through the vaccination net at school, and those susceptible who are too old to have been offered routine vaccination at school. But, as with all selective vaccination strategies, achieving a high uptake in the target group is difficult.

The problem of routine adult vaccination becomes even more complex with polio vaccine because of the small but measurable risk of paralysis after giving the live attenuated vaccine. For every 5 million doses administered, one case of paralysis will occur in a recipient and two in contacts.[6 7] About 2½ million doses are used in England and Wales each year, so that we should expect one or two cases of vaccine-induced paralytic poliomyelitis a year. Because of the risk of paralysis in contacts the current recommendation in Britain[8] is for parents to be offered vaccine at the same time as their children. Both parents must be immunised together, because if only one of them receives live vaccine the other presumably runs the risk of paralysis from the spouse as well as the child. In practice, most families have at least one working parent so that the recommendation is probably implemented only rarely—but the difference between the risk of one in 2·5 million doses for contacts and one in 5 million for recipients is a negligible improvement, especially if the risk of vaccine-associated poliomyelitis (like the natural disease) rises with age. Inactivated polio vaccines are said to be safer, but immunity takes somewhat longer to develop, and they cannot be recommended for vaccination of contacts, with either the vaccine or the wild virus.