The principal problem is that syncope is not a disease entity but merely a symptom with an extensive differential diagnosis, although underlying causes can be broadly divided into cardiac, neurological and psychiatric causes. Consequently, there is no single diagnostic test and in the majority of patients where clinical evaluation and simple non-invasive testing is unhelpful, clinicians are faced with selecting from an ever-expanding array of investigational tools. Many of these may lie outside the clinician’s area of expertise and some may be unpleasant or potentially dangerous. Recording of spontaneous events is difficult in patients with infrequent attacks and diagnosis must be inferred from abnormal laboratory tests. Furthermore, there is no diagnostic gold standard against which to validate the sensitivity of these investigations. Inevitably, this leads to unnecessary and wasteful investigation and an increased risk of a non-diagnosis or worse, a misdiagnosis.

The health care costs associated with blackouts are high due to recurrent hospitalization and investigation. In 1982, in a study of 121 patients with normal clinical evaluation and electrocardiogram undergoing inpatient investigation for blackouts, the cost per new diagnosis was estimated at $23 000[1]. A more recent study of Medicare patients admitted at least once with unexplained blackouts reported that the average annual cost of patients with unexplained syncope was $5165 and estimated that the cost of inpatient assessment in these patients was $800

References

The use of diagnostic tests accounted for a significant proportion of the total health care cost. There is considerable appeal for a simple clinical algorithm to guide the non-specialist in the investigation of patients presenting with blackouts. However, despite the publication of several clinical algorithms none has been widely implemented largely because of their complexity. This reflects the paucity of high quality data regarding the aetiology of blackouts. Most of the data comes from studies in the early 1980s. A variety of settings were reported, including emergency rooms, intensive care units, inpatient services and outpatient clinics without uniform diagnostic criteria. Consequently the populations were extremely heterogeneous and there were wide variations in the frequencies of common diagnoses. Nonetheless, these studies consistently showed that no definite diagnosis could be reached in 38–47% of syncopal patients despite intensive investigation. (An exception was an emergency room study where a diagnostic rate of 87% was achieved; but this study population was highly atypical with almost one third of patients presenting with epileptic seizures. The results can probably be discounted.) These studies were reported before the widespread availability of head-up tilt testing. As vasovagal syncope is the commonest cardiovascular cause of loss of consciousness, one might have expected that diagnostic rates would have improved substantially. However, studies continue to report diagnostic success rates as low as 45–48% in inpatient series.

In the current issue, Ammirati and co-workers report the results of the OESIL 2 study, a prospective multicentre study investigating the effects of implementing a simple diagnostic algorithm in patients presenting to the emergency room with syncope. Patients were initially assessed by clinical history and examination followed by a 12-lead ECG and routine blood tests. If no conclusive diagnosis was reached after the preliminary work-up, patients were separated on the basis of clinical features. Three groups were defined according to the likeliest underlying diagnosis — cardiac syncope, neurally mediated syncope and neuropsychiatric syncope. Each group was subjected to appropriate non-invasive testing. Invasive tests were used only when strictly indicated by abnormal non-invasive testing. There was crossover between groups if a diagnostic limb was completed without a definite diagnosis. Use of the algorithm produced an impressive reduction in the proportion of diagnostic failures, from 54–4% in a preliminary multicentre observational study to 17.5%.

However, although this new algorithm is clearly a step forward, it remains unclear whether it can be widely applied. Most patients were diagnosed only after prolonged inpatient investigation and despite the relative simplicity of the algorithm, patients still faced repeated investigations, particularly if the initial diagnostic hypothesis was incorrect. The population was relatively elderly (mean age 62–5 years) and there are no follow-up data to assess the accuracy of diagnosis or the effectiveness of therapy, although the incidences of common diagnoses were similar to previous studies. Furthermore, the algorithm at present offers little guidance regarding the use of newer monitoring technology, such as external or internal loop recorders. Also, the role of electrophysiological testing is not directly addressed.

Existing algorithms are complex and rely on clinical features to triage patients. History and examination remain essential parts of the evaluation of patients with syncope and have been reported to identify the cause in 49–85% of patients. Each patient should, therefore, have an initial work-up comprising a detailed clinical evaluation and resting 12-lead ECG. However, misinterpretation of clinical features is increasingly recognised as an important cause of misdiagnosis of blackouts, particularly in the misdiagnosis of convulsive syncope as epilepsy. It is important that unless the history is absolutely unequivocal, the putative diagnosis should be confirmed by positive laboratory data. The aims of the initial work-up are twofold. Firstly, it should identify patients at high risk of arrhythmic sudden death, requiring urgent investigation. From an analysis of emergency room series, Linzer and co-workers concluded that patients should be admitted to hospital if they had evidence of organic heart disease, chest pain, a history of arrhythmias or were currently taking drugs associated with malignant ventricular arrhythmias. Although ECG abnormalities are common in syncope (up to 50% in one series), clearly diagnostic abnormalities are found in less than 5%.

However, a normal ECG indicates a low risk of sudden death. Secondly, the detailed clinical history should identify patients with a high probability of epilepsy. This would attach maximum significance to classical tonic-clonic seizures, lateralizing neurological signs, prolonged post-attack confusion or difficulty with speech in clear consciousness, history of significant head trauma, or intracranial pathology or chronic neurological deficit. However, the algorithm would not give equal credit to less diagnostic convulsive activity, such as myoclonic jerking, head turning, oral automatisms and visual and auditory hallucinations. These may occur in up to 80% of patients with loss of consciousness due to transient cerebral anoxia. Patients with high quality distinguishing features of epilepsy should be referred for a neurological assessment, including in
most cases, electroencephalography (EEG) and brain imaging. The yield of these tests in other patient groups, particularly in non-convulsive blackouts, is less than 5% and they should not be routinely performed[1,13].

In a comprehensive algorithm, after the initial triage, patients with unexplained blackouts should ideally undergo a uniform investigational protocol. Exceptions could be made for specific clinical features requiring the use of investigations such as exercise treadmill testing, carotid Doppler scanning or coronary angiography, which have a low overall yield and should not be routinely used[1,12]. Conventional diagnostic tools must be reevaluated following the introduction of the insertable loop recorder, with increasing emphasis on the cost-effectiveness as well as the yield of investigations[19]. Head-up tilt testing has the highest yield of all the non-invasive tests[8,12,20] is safe and relatively inexpensive and should be used as a first line investigation. When the tilt test is negative, arrhythmic syncope is the likeliest cardiac cause. Holter monitoring is widely used to investigate syncope. However, because of the episodic nature of attacks in most patients, symptom–ECG correlation is obtained in no more than 2–4%[21,22]. Consequently, although inexpensive, it is probably less cost-effective than the internal loop recorder, where symptom–ECG correlation can be achieved in 88% with long-term use[19]. External loop recorders are non-invasive and may have a lower cost per diagnosis than the internal loop recorder. However, the yield is significantly lower at 35–38%[19,23] largely due to problems with patient compliance. Echocardiography may be useful in evaluating patients with organic heart disease but has little value in patients with structurally normal hearts. There the yield is <5%[19].

Electrophysiology testing has a key role in the investigation of patients with structural heart disease where inducible monomorphic ventricular tachycardia is common and usually clinically significant[5]. However, in the presence of a structurally normal heart and normal ECG, the yield of electrophysiology testing is very low[19,24] and the cost per diagnosis is prohibitive ($73 620 in one recent study[19]). Confining investigation to head-up tilt testing and the internal loop recorder could provide a diagnosis in 90% of patients with unexplained syncope in a minimally invasive and highly cost-effective manner. With improvements in implantable technology, the insertable loop recorder may increasingly be used early in the investigation of blackouts, rather than as a last resort.

A. M. ZAIDI
A. P. FITZPATRICK
Manchester Heart Centre, Manchester, U.K.

References

Eur Heart J, Vol 21, issue 11, June 2000
The impending global epidemic of cardiovascular diseases

During the past 30 years, large declines in cardiovascular disease death rates have been experienced in several western countries, whereas substantial increases have been experienced in developing countries. These contrasting trends are expected to continue. Over the next three decades, premature morbidity and mortality attributable to cardiovascular disease will almost double globally from 85 million disability adjusted life years in 1990, to 140–160 million DALY in 2020, with about 80% of this burden occurring in developing countries[1]. Other than sub-Saharan Africa, all geographic regions are experiencing a substantial disease burden from ischaemic heart disease (Table 1) and have experienced substantial increases in mortality rates over the last decade (Table 2).

The increases in cardiovascular disease in developing countries are probably a result of at least three contributing factors: first, decreasing mortality from acute infectious diseases and increases in life expectancy result in a higher proportion of individuals reaching middle and old age. Second, lifestyle and socioeconomic changes associated with urbanization in developing nations lead to higher levels of risk factors for cardiovascular disease. Third, special susceptibility of certain populations (e.g. due to specific genes) may lead to a greater impact on clinical events compared to western populations (Fig. 1).

The rates projected in Tables 1 and 2 are based solely upon demographic changes. If the prevalence of various cardiovascular disease risk factors also rise as a consequence of adverse lifestyle changes accompanying industrialization and urbanization, the rates of cardiovascular disease mortality and morbidity could rise even higher than the projected rates. Further, both the degree and the duration of exposure to the cardiovascular disease risk factors would increase as a result of higher risk factor levels coupled with a longer life expectancy. Higher prevalence of both risk factors for cardiovascular disease and disease rates in urban compared to rural communities in India[5,4] and China[5] provide evidence of these trends.

Lifestyle changes observed in countries undergoing transition include changes in diet, physical activity and tobacco use. The globalization of food production and marketing has resulted in greatly increased availability of cheap vegetable oils and fats, and increased consumption of energy-dense foods which may be poor in dietary fibre and several micronutrients[6,7]. Other characteristics of this nutrition transition include a shift from plant to animal protein, and shifts towards refined carbohydrates and sweets, and increased prevalence of obesity. This transition now occurs even in countries and groups with a relatively low level of income, and is further accelerated by urbanization. In South Africa for example, length of time living in an urban

### Table 1  Disability-adjusted life-years lost (in hundreds of thousands) from ischaemic heart disease in 1990 (projected data from the World Bank)[2]

<table>
<thead>
<tr>
<th>Region</th>
<th>Men</th>
<th>Women</th>
</tr>
</thead>
<tbody>
<tr>
<td>EME</td>
<td>56.4</td>
<td>37.2</td>
</tr>
<tr>
<td>FSE</td>
<td>45.2</td>
<td>34.3</td>
</tr>
<tr>
<td>India</td>
<td>49.5</td>
<td>31.9</td>
</tr>
<tr>
<td>China</td>
<td>24.8</td>
<td>17.6</td>
</tr>
<tr>
<td>OAI</td>
<td>35.4</td>
<td>26.7</td>
</tr>
<tr>
<td>SSA</td>
<td>6.7</td>
<td>5.4</td>
</tr>
<tr>
<td>LAC</td>
<td>16.0</td>
<td>11.3</td>
</tr>
<tr>
<td>MEC</td>
<td>15.5</td>
<td>10.6</td>
</tr>
<tr>
<td>Total world</td>
<td>249.6</td>
<td>175.0</td>
</tr>
</tbody>
</table>

EME = European Market Economies; SSA = Sub-Saharan Africa; FSE = Formerly Socialist Economies of Europe; LAC = Latin American Countries; OAI = Other Asia and Islands; MEC = Middle Eastern Crescent.

Note that disability adjusted life years lost from ischaemic heart disease in India are only slightly lower than all the market economies combined.

© 2000 The European Society of Cardiology