

commoner than generally supposed. With the multiplication of these agents, no doubt further cases will emerge. From the practical point of view particular care must be exercised in using these preparations, especially in patients with pre-existing oesophageal obstruction, and, in general, tablets should be swallowed with water or dissolved first. We hope that increased awareness of the possibility of oesophageal injury will lead to greater care in the use of these drugs and to the formulation of safer preparations.

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Requests for reprints to Mr H R Matthews.

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# Sudden death during ambulatory monitoring

A LAHIRI, V BALASUBRAMANIAN, E B RAFTERY

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## Summary

**Three patients with ischaemic heart disease died suddenly while being monitored with an ambulatory tape recorder. Two had terminal ventricular fibrillation initiated by paired bidirectional ventricular ectopic beats against a background of scattered ectopic activity; both had had ventricular tachycardia during routine treadmill exercise testing in the week before death. The third patient developed bizarre ventricular complexes followed by asystole.**

**Sudden death may be due to ventricular fibrillation initiated by paired ventricular ectopic beats with changing morphology, or asystole following bizarre ventricular complexes. Exercise testing may have an important predictive value.**

## Introduction

The electrocardiographic antecedents of sudden death outside hospital and the changes taking place during this event are not clearly understood because death seldom occurs during ambulatory monitoring. In 1978 three patients, out of 346 assessed for ischaemic heart disease, died suddenly while being monitored with an ambulatory tape recorder. All three were on long-term treatment for arrhythmias and two had had exercise tests in the two weeks before death. We report the findings in these three cases in the hope that they will help to elucidate possible predictors of sudden death.

Department of Cardiology, Northwick Park Hospital and Clinical Research Centre, Harrow, Middx HA1 3UJ

A LAHIRI, MB, BS, research fellow  
V BALASUBRAMANIAN, MD, FACC, honorary senior registrar  
E B RAFTERY, MD, FRCP, consultant physician

## Case reports

**Case 1**—A 59-year-old television executive came under our care in 1974 for angina. An exercise electrocardiogram showed a 4 mm down-sloping ST depression in lead V5 and a 2 mm depression in leads V4 and V6. He was treated with propranolol, 80 mg thrice daily, and glyceryl trinitrate. His exercise tolerance improved and he was reviewed regularly in the outpatient clinic. Routine investigations revealed no biochemical risk factors. He was not obese and did not smoke. Three years after the first episode he was admitted into the coronary care unit with an acute inferior myocardial infarction. He had a very stormy stay, with primary ventricular fibrillation and multiple multifocal ventricular ectopic beats, which responded to an intravenous lignocaine infusion. He was discharged taking propranolol, 80 mg thrice daily; frusemide, 80 mg a day; and potassium supplements. In the course of 11 months his angina gradually increased and he complained of palpitations. A graded treadmill exercise test (fig 1) showed significant ST segment depression during exercise; it was stopped when he developed ventricular tachycardia at a rate of 250 beats/min. He rapidly returned to sinus rhythm. The total ventricular ectopic count in the exercise period was 18, and a short run of supra-ventricular tachycardia also occurred. Another notable feature was considerable tachycardia during minor grades of exercise despite

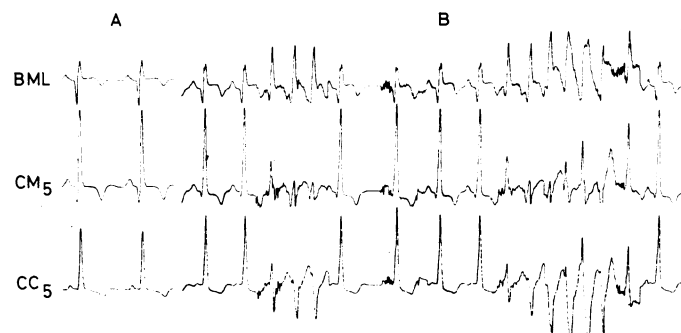


FIG 1—Case 1: ECGs before exercise (A) and during exercise (B), the latter showing ST-segment depression in CM<sub>5</sub> and CC<sub>5</sub> and runs of ventricular tachycardia (CASE, Marquette Electronics). BML—bipolar monitoring lead; CM<sub>5</sub> and CC<sub>5</sub>—bipolar leads.

beta-blockade. A week later an ambulatory recording was started with a Medilog Mark 1 tape recorder. On the third day of recording he was brought to the hospital in a collapsed state with ventricular fibrillation, which did not respond to DC defibrillation and vigorous resuscitation. The tape recording, consisting of three 24-hour periods, was carefully analysed. The first 24 hours showed sporadic ectopic activity with long-cycle beats ( $R-R^1/QT > 1$ ). On the second day occasional paired ectopics and multifocal ectopics occurred. The ectopic activity was identical on the third day except for the period just before death (fig 2). There was a short period of ventricular bigeminy followed by a pair of bidirectional ectopics. This was followed by a short-cycle ectopic ( $R-R^1/QT = 0.98$ ), which triggered a bout of ventricular tachycardia, ventricular flutter, and fibrillation. The rhythm alternated between ventricular flutter and fibrillation for 21 minutes, after which asystole supervened. Necropsy was not carried out.

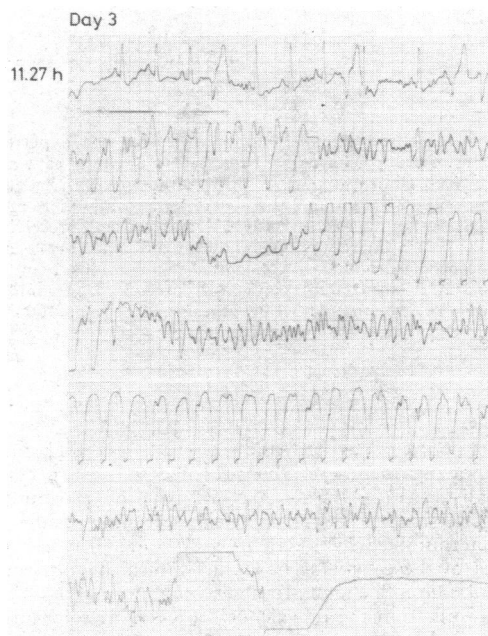


FIG 2—Case 1: Continuous ambulatory ECG showing onset of ventricular flutter and fibrillation followed by asystole (Mark 1, Oxford Instruments).

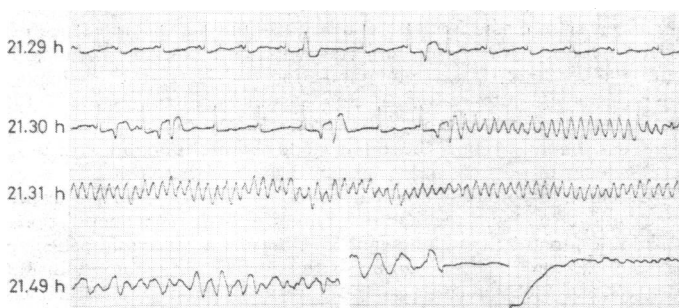


FIG 3—Case 2: Ambulatory ECG showing a short-cycle ventricular ectopic beat precipitating ventricular flutter degenerating into ventricular fibrillation and asystole (Mark 1, Oxford Instruments).

*Case 2*—A 56-year-old woman came under our care when she was admitted with an inferior myocardial infarction and acute pulmonary oedema in October 1978. She made a good recovery and was discharged from the hospital taking digoxin, 0.25 mg a day, and frusemide, 40 mg a day, with potassium supplements. During follow-up she complained of angina on exertion. Digoxin was withdrawn since there was no clinical heart failure, and she was treated with propranolol, 80 mg thrice daily, and isosorbide dinitrate, 10 mg thrice daily. An exercise test showed multiple multifocal ectopics with a run of three ventricular ectopics (total of 69 ectopics), and the test was stopped. Three days later continuous ambulatory monitoring was started. On

the first day of recording she suddenly collapsed at home and was brought to the hospital, where she was pronounced dead on arrival. The tape recording over the first 14 hours showed occasional long-cycle ventricular ectopics ( $R-R^1/QT > 1$ ). There was a pair of paired multifocal unidirectional short-cycle ectopics just before death ( $R-R^1/QT = 0.9$  and  $0.8$ ). The terminal arrhythmia was ventricular flutter degenerating into ventricular fibrillation for 12 minutes and then asystole (fig 3). There was no intervening ventricular tachycardia.

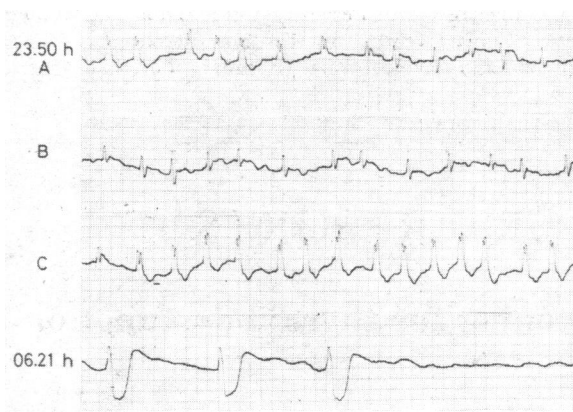


FIG 4—Case 3: Ambulatory ECG showing atrial fibrillation with bundle-branch block pattern and finally bizarre, slow ventricular complexes (30 beats/min) leading to asystole (Mark 1, Oxford Instruments).

*Case 3*—A 77-year-old man had been treated for ischaemic heart disease and left ventricular failure for three years. A resting electrocardiogram had shown a change from sinus rhythm to atrial fibrillation, and ambulatory recording was started to assess his heart rate. He died suddenly after 14 hours of monitoring. The tape showed atrial fibrillation, sporadic premature beats, and short runs of supraventricular and ventricular tachycardia. The terminal event was slow, bizarre ventricular complexes at 30–40 beats/min ending in asystole (fig 4). No ventricular fibrillation or flutter occurred.

## Discussion

The precise mechanism of sudden death is controversial. The electrocardiographic changes preceding such deaths require careful analysis if rational preventive treatment is to be initiated. Bleifer reported one case where short-cycle ventricular ectopics initiated ventricular tachycardia and fibrillation, followed by death.<sup>1</sup> Hinkle and colleagues reported a similar case.<sup>2</sup> In a case reported by Gradman *et al* the terminal arrhythmic sequence was a couplet with two different morphologies followed by a sinus beat and another ventricular ectopic beat with a coupling interval of about 0.36 seconds initiating rapid ventricular flutter, which degenerated into ventricular fibrillation.<sup>3</sup> Poole and colleagues reported on two patients, one of whom died in primary ventricular fibrillation and the other in asystole.<sup>4</sup> Our three cases are reported in the hope that pooling well-documented cases will improve our understanding of lethal arrhythmias and help to prevent sudden deaths.

The first two patients have some interesting similarities. Both died in ventricular fibrillation initiated by a short-cycle ventricular ectopic beat and preceded by pairs of ectopic beats with different morphologies. Both were being treated with adequate doses of propranolol (as judged by the resting heart rate). The first, case 1, had been taking propranolol for five years, during which he suffered an episode of myocardial infarction complicated by ventricular fibrillation. A year later he died while on treatment. The second, case 2, had no previous history of arrhythmia and even before death did not have increased ectopic activity. A noteworthy feature of both cases was the ventricular tachycardia during exercise testing.

These features suggest that paired ectopics with different morphologies are particularly likely to trigger ventricular

fibrillation, and exercise-induced ventricular tachycardia may be a predictor of such an event. Beta-blockade with propranolol does not seem to protect against this, and specific antiarrhythmic treatment would probably have been more appropriate. We do not yet know, however, which of the several agents available for long-term prophylaxis of ventricular ectopic activity would best inhibit the short-cycle second ectopic beat that would appear to initiate the terminal arrhythmia.

The third patient was similar to the one reported by Pool *et al.*,<sup>4</sup> with slow, bizarre complexes and asystole rather than ventricular fibrillation causing death. Liberthson and colleagues found that 28% of patients have terminal rhythms other than ventricular

fibrillation.<sup>5</sup> Antiarrhythmic treatment is unlikely to be of any value in these cases.

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# SHORT REPORTS

## Screening for thyroid dysfunction in diabetics

The association between diabetes mellitus and primary hypothyroidism is well recognised, although the reported prevalence of hypothyroidism in diabetics varies from 0.2%<sup>1</sup> to 1.7%.<sup>2</sup> Routine biochemical screening of geriatric patients yields a prevalence of hypothyroidism of about 2% and is made more effective by additionally measuring serum thyrotrophin (TSH) concentrations. Thyroid function tests were performed and thyroid antibodies tested for in 255 consecutive diabetic outpatients who were not suspected of having thyroid disorders to determine the prevalence of unrecognised and subclinical hypothyroidism.

### Patients, methods, and results

We recorded the details of the patients in advance from the case notes. Serum thyroxine, triiodothyronine uptake, free thyroxine index (FTI), and TSH were measured in duplicate, by radioimmunoassay, in postprandial venous blood samples. Normal values for our laboratory, determined from 180 healthy volunteers of similar ages, are concentrations of serum thyroxine 75-140 nmol/l (5.8-10.9 µg/100 ml), FTI 70-145, and TSH < 4.5 mU/l.

*Clinical details and thyroid function in 255 diabetics. (Figures are numbers (%) of patients)*

	Total	Group 1 (clinically hypothyroid)	Group 2 (raised TSH, FTI normal or low)	Group 3 (low FTI, normal or undetectable TSH)	Group 4 (normal FTI, normal or undetectable TSH)
No (%) of patients	255 (100)	7 (3)	77 (30)	25 (10)	146 (57)
Sex:					
Female	157 (62)	6 (86)	73 (95)	9 (36)	69 (47)
Male	98 (38)	1 (14)	4 (5)	16 (64)	77 (53)
Treatment:					
Diet	43 (17)	3 (43)	15 (19)	1 (4)	24 (16)
Tablets	102 (40)	3 (43)	34 (44)	5 (20)	60 (41)
Insulin	110 (43)	1 (14)	28 (36)	19 (76)	62 (42)
Age (years):					
<40	41 (16)	0	6 (8)	9 (36)	26 (18)
40-60	60 (24)	1 (14)	10 (13)	4 (16)	45 (31)
>60	154 (60)	6 (86)	61 (79)	12 (48)	75 (51)
Antibody:					
Present	67 (26)	5 (71)	26 (34)	5 (20)	31 (21)
Absent	188 (74)	2 (29)	51 (66)	20 (80)	115 (79)

TSH = Serum thyrotrophin.  
FTI = Free thyroxine index.

Thyroid antibodies (microsomal and thyroglobulin) were detected by haemagglutination. Patients with a FTI < 60 and TSH concentration ≥ 10 mU/l were recalled, while those with a minor depression of FTI or slightly raised TSH concentrations were reassessed when they reattended the clinic. Statistical analysis was by  $\chi^2$  and Student's *t* tests.

Four distinct groups of patients emerged (table). There was a preponderance ( $P < 0.01$ ) in groups 1 and 2 of women patients and patients over 60 years. Thyroid antibodies were also more common ( $P < 0.05$ ) in

groups 1 and 2 (three patients had been treated for hyperthyroidism). Over a quarter of group 2 have now been reviewed. Many have non-specific symptoms but no clinical hypothyroidism, although 10% had both raised TSH and antibodies. In group 3 there were significantly more men patients ( $P < 0.01$ ), patients under 40 ( $P < 0.05$ ), and patients receiving insulin treatment ( $P < 0.01$ ). There was no significant difference between the mean ( $\pm$  SE of mean) plasma glucose concentration in groups 1 and 2 ( $11.8 \pm 0.7$  mmol/l ( $212 \pm 13$  mg/100 ml)) and in group 3 ( $13.4 \pm 1.5$  mmol/l ( $241 \pm 27$  mg/100 ml)) or group 4 ( $11.5 \pm 0.4$  mmol/l ( $207 \pm 7$  mg/100 ml)). Three patients had been treated for hypothyroidism.

### Comment

The prevalence of hypothyroidism (4%) was higher than that reported<sup>1,2</sup> owing mainly to the presence of unsuspected clinical hypothyroidism (2.7%). This may in part be attributed to the increased effectiveness of biochemical screening using FTI and TSH in determining which patients require detailed thyroid assessment. Most of these patients had mild clinical hypothyroidism and thyroid antibodies. The high prevalence of abnormal thyroid function tests may result from the prevalence (26%) of thyroid antibodies in diabetics, and the influence of poorly controlled diabetes on thyroid hormone concentrations.<sup>3</sup> Thirty per cent of diabetics had raised TSH (group 2) associated with a normal (17%) or low (13%) FTI but no clinical evidence of hypothyroidism. As in group 1, there was a preponderance of women over 60. The presence of thyroid antibodies or a raised TSH (subclinical hypothyroidism) may be associated with an increased risk of developing coronary artery disease, although the pathogenesis remains unclear.<sup>4</sup> There is an annual 2% incidence of overt hypothyroidism in subjects with both raised TSH and antibodies.<sup>5</sup> Thus 10% of our population may develop overt hypothyroidism and require annual thyroid function tests. A low FTI with normal or undetectable TSH (group 3) in young insulin-treated male patients may reflect the influence on thyroid function of insulin insufficiency or possible microvascular disease of the pituitary.

Screening thyroid function in diabetics, particularly elderly women, gives a yield (6%) greater than that found in the geriatric population. In addition to identifying undiagnosed clinically hypothyroid patients, it identifies an "at-risk" group with subclinical hypothyroidism. We feel that such screening is clinically and economically justifiable.

We are grateful to the staff of the diabetic clinic and the department of immunology, Ninewells Hospital and Medical School, for their co-operation.

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Departments of Pharmacology and Therapeutics and Biochemical Medicine, University of Dundee, Ninewells Hospital and Medical School, Dundee DD1 9SY

JOHN FEELY, BSC, MRCP, lecturer

T E ISLES, PHD, senior lecturer