

# Sporadic myalgic encephalomyelitis in a rural practice

B. D. KEIGHLEY, MB, MRCP

General Practitioner, Balfour, Stirlingshire

E. J. BELL, PH.D, MRC.PATH.

Top Grade Virologist, Regional Virus Laboratory, Ruchill Hospital, Glasgow

**SUMMARY.** Twenty patients presenting with chronic ill-defined illnesses in a rural practice were investigated virologically. The only positive finding was the detection of elevated Coxsackie B titres in 16 of these patients. Three had experienced mainly cardiovascular symptoms; the remaining 13 are thought to have suffered from myalgic encephalomyelitis. This is a distressing and often prolonged illness, the cause of which is as yet unknown but is suspected of having a viral aetiology.

## Introduction

**M**YALGIC encephalomyelitis (ME) has often been reported in epidemic form, the most notable being that among hospital personnel at the Royal Free Hospital in London in 1955.<sup>1</sup> The illness may also occur in sporadic form,<sup>2</sup> but such reports are scant since the symptomatology is so complex that individual cases may be overlooked. The possible causes of this bizarre illness were listed in a review article,<sup>3</sup> which also pointed out that it is now untenable to dismiss myalgic encephalomyelitis as a purely hysterical manifestation. However, this opinion is still held among many hospital clinicians.

Behan<sup>4</sup> stated that despite extensive virological studies no single virus has been implicated as the causative agent of myalgic encephalomyelitis. However, he suggested as a possible cause for the disease an immunological abnormality following a viral infection.

In 1980 an outbreak of myalgic encephalomyelitis was seen in a rural practice in Ayrshire. Preliminary results<sup>5</sup> suggested that the Coxsackie B group of viruses might be implicated since the only positive laboratory findings were elevated Coxsackie B neutralizing antibody titres in a significant number of the patients. This prompted one of us (B.D.K.) to investigate patients in this rural practice whose protracted and atypical illnesses appeared similar to those seen in Ayrshire. A group of 20 patients was found, most of whom had defied adequate

diagnosis in other terms; 16 of these patients were found to have significantly elevated neutralizing antibody titres to the Coxsackie B group of viruses.

## Patients and methods

Between February 1981 and May 1982 serum samples from a total of 20 patients were submitted for virological tests, in particular the estimation of neutralizing antibodies to group B1-6 Coxsackieviruses.

The criteria for selection of patients were necessarily loose. Patients whose illness had proved difficult to diagnose either in the practice or at specialty outpatient departments formed the core of the study. These were patients who, on the basis of a subjective assessment by the doctor, had unexplained chronic illnesses involving more than one body system and who in other circumstances might have been labelled as having a functional condition. Indeed, many of the patients included in the study had been dismissed back to the practice by hospital clinicians with the implication that there was no organic basis for their problems.

As the study progressed, and a pattern to the mixture and complexity of the symptoms developed, more patients either presenting *de novo* or who had previously presented with a diagnostic problem were brought into the study. Several of these patients were referred to Dr P. O. Behan, consultant neurologist in Glasgow; all but one had the diagnosis of myalgic encephalomyelitis confirmed.

It was felt that the total impact of this organism on one small practice of 2,500 patients should be shown, and so those patients who presented with symptoms often associated with Coxsackie infection—that is, cardiovascular illness—were also included in the study.

## Results

Twenty patients were selected for virological studies, 17 of whom had suspected myalgic encephalomyelitis (see Table 1). As reported previously,<sup>4</sup> women were more commonly affected than men (11 females, six males). Their ages ranged from 27 to 65 years with clustering in the third decade. Unlike Fegan and Bell's<sup>5</sup> findings, no children were affected and no more than one member of a family group was involved. There was no evidence of an epidemic in this widely scattered practice.

Virological studies revealed that 13 (76 per cent) of the 17 patients with suspected myalgic encephalomyeli-

tis had elevated Coxsackie B neutralizing titres (Table 2). Of the 11 female patients, eight (73 per cent) had titres  $\geq 512$  and one (9 per cent) a titre of 256. The corresponding figures for the six male patients were three (50 per cent)  $\geq 512$  and one (17 per cent) of 256, respectively. The remaining four patients, not listed in Table 2, all had titres of 128 for one or more of the Coxsackie B viruses, a level not normally regarded as significant.<sup>6</sup>

These patients experienced a variety of symptoms and in Table 2 they have been grouped into body systems. However, this does not imply that the patient suffered from all the symptoms in the group. The group of symptoms common to nearly all was the non-specific one of malaise, tiredness and exhaustion on physical or mental effort. The other predominant symptoms were those related to psychological health, and nearly all

patients suffered from either anxiety or depression, but usually a combination of both.

Six of the patients reported symptoms related to the vestibular system and this effect has not previously been allied to Coxsackievirus infection.

### Case reports

Three illustrative case histories of patients with clinically confirmed ME are presented.

#### Case 1 (Female aged 48 years, housewife)

Past history of referral to ENT consultant in 1972 because of true vertigo. The consultant thought there was some evidence of vestibular disorder.

The patient presented in May 1976 with an attack of true vertigo associated with a period of family stress. She was referred to a consultant neurologist who thought her symptoms were a stress response and not due to a labyrinthine disorder.

In November 1976 she was referred to a consultant psychiatrist. In September 1977 she was referred to a second ENT consultant, and a further report was made by the neurologist. No organic cause for the illness was found by either consultant, but the patient continued to have a chronic and severely debilitating emotional illness of agitated depression.

In March 1978 the psychiatrist said he still felt that there was an organic component to the illness, but that he could not define it. In the meantime the patient was started on a mono-amine oxidase inhibitor and there was some improvement.

**Table 1.** Twenty patients with atypical chronic illness.

Diagnosis	Number of patients	Number of patients with raised Coxsackie B titre	
		$\geq 512$	256
Suspected ME	17	11	2
Other illness	3	2	1

**Table 2.** Details of patients with raised Coxsackie B neutralizing antibody titres.

Case number	Age (years)	Sex	Onset of ME	Symptoms*	Illness		Highest Coxsackie B titre recorded
					Duration (months)	Resolved	
1	48	F	May 1976	ADE	72	No	>1024 (B4)
2	39	F	Mar 1977	ABCEFG	62	No	1024 (B3)
3	56	M	Sep 1977	ABEG	56	No	>1024 (B4)
4	41	F	Sep 1978	ABE	44	No	256 (B1)
5	39	F	Mar 1979	ABCEG	38	No	512 (B4)
6	35	M	Sep 1979	ABDE	25	Oct 1981	512 (B4)
7	31	F	Oct 1979	ABDEG	31	No	>1024 (B4)
8	43	F	Nov 1979	ABE	30	No	512 (B3)
9	27	F	Jan 1980	ACDEF	29	No	1024 (B1)
							>1024 (B4)
10	47	F	Jun 1980	ACEF	23	No	512 (B4)
11	39	M	Jul 1981	ABCDEFH	10	No	512 (B4)
12	65	M	Oct 1981	ACE	Died Jan 1982	No	256 (B4)
13	52	F	Nov 1981	AEG	6	No	>1024 (B4)
14	70	F	Mar 1982	ADG	2	No	512 (B4)
15	39	M	Mar 1982	B	1½	Apr 1982	512 (B4)
16	55	M	Apr 1982	AB	2	No	256 (B3)

Cases 1, 2, 4, 8, 11, 13: diagnosis of myalgic encephalomyelitis confirmed by consultant neurologist.

\*Key to groups of symptoms

A = General symptoms: malaise, tiredness, exhaustion on physical or mental effort.

B = Cardiovascular: chest pain, palpitations, tachycardia.

C = Musculoskeletal: polyarthralgia, muscle pains, back pain.

D = Vestibular: true vertigo, dizziness, tinnitus.

E = Psychological: anxiety, depression or both.

F = Gastrointestinal: nausea, diarrhoea, abdominal cramps, epigastric pain.

G = Central nervous system: headaches, paraesthesiae.

H = Genitourinary: dysuria, urethral discharge.

In November 1979 her symptoms continued unabated; a referral was made to a consultant physician in case hypoglycaemia was causing her symptoms. No abnormality of carbohydrate metabolism was found.

In June 1981 elevated Cocksackie B2, 4 titres were found and she was referred to Dr Behan, who confirmed the diagnosis of myalgic encephalomyelitis.

This patient is the worst affected in the group and after six years continues to suffer from acute anxiety, exhaustion and prostration after physical or mental effort, constant tiredness, depression with fits of crying, dizziness and faintness. She has recently been referred to a second psychiatrist.

*Case 11 (Male aged 39 years, joiner)*

Past history of unexplained illness in 1974 consisting of dysuria and mucoid penile discharge, left-sided anterior chest pain and painful swelling of both knees. Extensive investigation by consultant physician and consultant rheumatologist produced no satisfactory explanation for his symptoms, which settled spontaneously after 20 months.

He presented again in July 1981 with renewed symptoms of chest pain, joint pains, tiredness and physical exhaustion. New symptoms developed of nausea, weight loss of 8 kg and fresh haemoptysis. Over the next few months he also developed painful, hot swelling of both knees and tinnitus of the right ear.

He was referred initially to a consultant physician who undertook extensive investigation over many weeks, but found no abnormality.

He was referred to Dr Behan in January 1982, who confirmed the possibility of myalgic encephalomyelitis. In November 1981 he showed elevated Cocksackie B4 titre of 512.

*Case 13 (Female aged 52 years, insurance saleswoman)*

Past history of referral in 1966 for shoulder girdle pain radiating to arms. No abnormality detected. In 1971 she was referred for investigation of vasovagal attacks and headaches; a consultant physician thought her symptoms were menopausal.

The patient presented in November 1981 with an influenza-like illness associated with paraesthesiae of arms and legs, agitation and depression, and frank suicidal thoughts. Her emotional lability, a continuing feeling of tiredness and physical exhaustion have continued in an intermittent fashion. In February 1982 she was referred to Dr Behan, who confirmed the diagnosis of myalgic encephalomyelitis.

In November 1981 she showed elevated Cocksackie B4 titre of  $\geq 1024$ . She has since taken early retirement.

Patients in cases 14, 15 and 16 were included in this study since they exhibited a pattern of illness often associated with Cocksackie B infection. All three showed significantly elevated titres.

## Discussion

Interpretation of the high static Cocksackie B antibody titres seen in our patients is, in the absence of virus isolation, extremely difficult. However, studies by various research workers have indicated that the higher the titre observed the greater is the probability of recent infection. Approximately 1,000 normal adults in the west of Scotland have been tested for the presence of these antibodies. Titres  $\geq 512$  were detected in only 4 per cent and titres of 256 in 10 per cent.<sup>7</sup> In our series the corresponding figures were 65 per cent and 12 per

cent respectively, the former representing a significant difference from the normal adult population.

While it is difficult to draw firm conclusions from such information, it is clear that virological examination on the basis of chronic, atypical symptoms has produced many more positive results than could reasonably be expected from a random sample.

Recent work in Israel<sup>8</sup> has shown that a prolonged atypical illness may follow persistent Epstein Barr virus infection. Like Behan<sup>4</sup> they suggest that the illness may be associated with an abnormal immunological response, and immunologists are already looking at such a theory with more than one possible causative agent in mind.

The group described here are patients who have had miserable illnesses. Most have lost many weeks of employment or the enjoyment of their family, marriages have been threatened, most have had one or more specialist referrals with disappointing results, two have taken premature retirement and one has died from myocardial infarction.

Certainly, if these results are valid, and the figure of incidence in this practice comprising 2,500 patients can be extrapolated to the general population, there is a large number of ill and unhappy patients in the community and it is suspected that many of them are to be found among returning attenders at medical and psychiatric clinics.

## References

1. Anonymous. An outbreak of encephalomyelitis in the Royal Free Hospital Group, London, in 1955. *Br Med J* 1957; 2: 895-904.
2. Ramsay AM, O'Sullivan E. Encephalomyelitis simulating poliomyelitis. *Lancet* 1956; 1: 761-764.
3. Anonymous. Epidemic myalgic encephalomyelitis. (Leading article) *Br Med J* 1978; 1: 1436-1437.
4. Behan PO. Epidemic myalgic encephalomyelitis. *Practitioner* 1980; 224: 805-807.
5. Fegan KG, Bell EJ. Myalgic encephalomyelitis in a rural practice in Ayrshire. *Communicable Diseases (Scotland) Weekly Report* 1981; No 32.
6. Grist NR, Bell EJ. A six-year study of Cocksackie B infections in heart disease. *J Hyg (Camb)* 1974; 73: 165-172.
7. Bell EJ, Irvine KG, Gardiner AJS, *et al.* Cocksackie B infection in a general medical unit. *Scot Med J* 1983; (in press).
8. Tobi M, Ravid Z, Feldman-Weiss V, *et al.* Prolonged atypical illness associated with serological evidence of persistent Epstein-Barr virus infection. *Lancet* 1982; 1: 61-63.

## Acknowledgements

We wish to thank Dr P. O. Behan, Reader and Consultant in Neurology, Department of Neurological Sciences, Southern General Hospital, Glasgow, for examining some of the patients, and for his advice; also Dr G. E. D. Urquhart, Regional Virus Laboratory, Ruchill Hospital, Glasgow, for performing CF studies on our patients.

## Address for correspondence

Dr Eleanor J. Bell, Regional Virus Laboratory, Ruchill Hospital, Glasgow G20 9NB.