Some long-term sequelae of Coxsackie B virus infection

COXSACKIE VIRUSES are small RNA-containing particles (picornaviruses). They belong to the complex group of enteroviruses which inhabit the human intestine and can cause a wide spectrum of disease. Besides the three serotypes of poliomyelitis virus, the enterovirus group comprises no less than 23 Coxsackie viruses in group A, six in group B, and 31 echoviruses, as well as the more recently classified enterovirus types 68–71. Coxsackie is a small town on the Hudson River in New York State where, nearly 40 years ago, the then new virus was demonstrated in the faeces of two children with poliomyelitis-like disease. Echoviruses, originally not associated with any known human disease, are named after the initial letters of enteric cytopathogenic human orphan virus.

Coxsackie viruses and echoviruses affect many systems but predominantly the central nervous system and muscles. Certain viruses are associated with particular syndromes: aseptic meningitis is associated with Coxsackie A9, B2–5 and echoviruses 4, 6, 9, 11, 16 and 30; muscle weakness with Coxsackie A7 and A9; cerebellar ataxia with Coxsackie A9 and echoviruses 4, 6 and 9; herpangina with several Coxsackie A viruses; enanthems and exanthems with many Coxsackie A (but not B) viruses and several echoviruses. Coxsackie A16 may cause hand, foot and mouth disease. Myocarditis, pericarditis, epidemic myalgia, orchitis and generalized disease of the newborn are the preserve of Coxsackie B viruses types 2–5. Coxsackie B viruses also cause intercostal myalgia, pleurodynia or Bornholm disease, which is named after the Baltic island on which occurred one of the earliest recognized outbreaks.

Proof of enteroviral infection requires the demonstration of virus from throat washings or from cerebrospinal fluid early in a meningitic illness, or from faeces over a longer period, together with a fourfold rise in antibody titre to show that infection has actually taken place rather than that the patient is perhaps one of many in the community asymptomatically harbouring the virus during an outbreak.

The *Journal* recently reported[1,2] from Scottish general practices two series of patients with that 'difficult to diagnose' symptom complex of benign myalgic encephalomyelitis (BME) or epidemic neuromyasthenia (EN) in association with higher Coxsackie B virus antibody titres than would have been expected in the general population. Calder and Warnock[3] now report that 38 of 81 patients with symptoms suggesting BME in their Dunbartonshire practice also had high Coxsackie B virus antibody titres.

Characteristic clinical features of BME are headache, myalgia, lymphadenopathy, mild fever, and various neurological symptoms including cranial nerve palsies and transient paraesthesiae.[4] A relatively constant complaint is extreme exhaustion brought on by slight physical effort and often associated with emotional lability and failure to concentrate. Three outcomes of BME are described: complete recovery; recovery only after initial relapses; and finally, permanent incapacity.[5]

The aetiology of BME remains unknown although a viral origin has often been suggested. The high but mainly static antibody titres to Coxsackie B viruses described in the three recent papers[1-3] hint, but do not prove, that BME may be causally related to Coxsackie B infection. In parallel, Bell and her colleagues[6] showed that patients, mostly with chest pains, admitted to a general medical ward had raised Coxsackie B virus antibody titres at $\geq 1:256$—nearly five times more often than was found in the general population. The authors recognized, however, the need for a more rapid and specific diagnostic test.

Controversy continues as to whether the term BME should be preferred to EN. As more than 50 per cent of patients have no myalgia and as the adjective 'benign' poorly describes an illness which, although not fatal, can cause serious handicap, loss of employment and altered life style, Ramsay[7] prefers the term EN. By contrast, McEvedy and colleagues,[8] after reviewing 15 recorded outbreaks including the Royal Free disease of 1955, concluded that the illness has no organic basis and is due either to mass hysteria on the part of the patients or an altered medical perception of the community. May and colleagues[9] also rejected the conclusion of the 1978 international symposium,[7] that the illness is a specific disease entity probably with a viral but not a psychogenic aetiology. They questioned the wisdom of vigorously researching future outbreaks "since the investigation itself may increase the severity of the symptoms and signs".[9]

Although some epidemics of BME have involved districts or all-male institutions, most took place in residential institutions with a wholly or largely female

population. The three reports from general practices[1-3] are therefore highly relevant being much less likely to reflect mass hysteria than studies from female residential institutions in the grip of an outbreak. Calder and Warnock[3] point out that their practice look after the families of naval personnel but not the servicemen themselves, some of whom will presumably reside together. Despite the warnings of May and colleagues,[9] further studies of BME would therefore seem desirable. General practitioners may have an advantage in being able to view the illness more objectively.

The proportion of any practice population with high Coxsackie B virus antibody titres must relate to the last epidemic. In their study Bell and her colleagues[6] sampled their normal controls between 1973 and 1978 and their hospital patients between 1979 and 1980 but argue that as the last epidemic of Coxsackie B virus infection was in 1965 their results are unlikely to be biased. Future studies by general practitioners would be enhanced by a control sample taken contemporaneously from the same population because of the well recognized and numerically considerable proportion of subclinical infections that occur in all enteroviral outbreaks. Unless sera can be stored deep frozen pending later examination, it might be prudent to await the general availability of specific immunoglobulin M (IgM) testing[10] that may decisively confirm or refute the present hypothesis that BME may be causally related to enteroviral infection or more specifically to infection with one of the Coxsackie B viruses.

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Prescribing—a suitable case for treatment

OF THE many activities undertaken by doctors in general practice, prescribing has for long attracted considerable attention. Although about one third of consultations in general practice do not lead to a prescription, nevertheless two thirds do.

Prescribing decisions by general practitioners are causing concern on two quite separate fronts. On the one hand, the profession, patients and government are concerned about the quality of prescribing, its safety, its relevance and its effectiveness, while on the other, government is increasingly concerned that the cost of general practitioner prescribing dwarfs the cost of hospital prescribing. The prescription costs of the average British general practitioner now exceed the cost of the doctor's own income and all his expenses combined.

Given these twin pressures of quality and cost, it is natural that studies of general practitioner prescribing will continue to be of interest. One of the new developments is the possibility of employing computerized techniques both to analyse data from such studies and to provide information to the doctors who write the prescriptions. It has now become possible to link computer technology with modern ideas in continuing education where the importance of participation and feedback are increasingly accepted. These are not new ideas; evidence to the Tricker Report by the Royal College of General Practitioners[1] emphasized the importance of computerizing the Prescription Pricing Authority so that in the future individual practitioners would be provided with a quick and professional analysis of the consequences of their prescribing decisions.

In *Prescribing—a suitable case for treatment,*[2] Dr Conrad Harris and his colleagues from the Department of General Practice at St Mary's Hospital Medical School, London, applied these ideas to a group of general practitioners in London. First, they analysed the prescriptions and compared them with a control group, but also—and this is the central point of this study—they offered educational programmes to the experimental group of practitioners and, working with the Prescription Pricing Authority, offered them information about their prescribing decisions.

In fact, the experimental group reduced their level of prescribing substantially more than the controls, and furthermore, the reduction in prescribing was selective. The cost per thousand patients rose for all groups but was considerably less for the experimental group whose costs were calculated as £136.00 per doctor at November