[9] Dash H, Johnson RA, Dinsmore RE, Francis CK, Harthorne JW. Cardiomyopathic syndrome due to coronary artery disease. II: Increased prevalence in patients with diabetes mellitus: a matched pair analysis. *Br Heart J* 1977;**39**:740-7.

[10] Rubler S, Dlugash J, Yuceoglu YZ, Kumral T, Branwood AW, Grishman. A. New type of cardiomyopathy associated with diabetic glomerulosclerosis. *Am J Cardiol* 1972;**30**:595-602.

[11] Hamby RI, Zoneraich S, Sherman L. Diabetic cardiomyopathy. *JAMA* 1974;**229**:1749-54.

[12] Pearce MB, Bulloch RT, Kizziar JC. Myocardial small vessel disease in patients with diabetes mellitus. *Circulation* 1973;**48**, suppl IV:6.

[13] Regan TJ, Lyons MM, Ahmed SS, *et al.* Evidence for cardiomyopathy in familial diabetes mellitus. *J Clin Invest* 1977;**60**:885-99.

[14] Ledet T. Diabetic cardiopathy. Quantitative histological studies of the heart amongst young juvenile diabetics. *Acta Pathol Microbiol Scand (A)* 1976;**84**:421-8.

[15] Fischer VW, Barner HB, Leskiw ML. Capillary basal laminar thickness in diabetic human myocardium. *Diabetes* 1979;**28**:713-9.

[16] Factor SM, Okun EM, Minase T. Capillary microaneurysms in human diabetic heart. *N Engl J Med* 1980;**302**:384-8.

[17] Rynkiewicz A, Semetkowska-Jurkiewicz E, Wyrzykowski B. Systolic and diastolic time intervals in young diabetics. *Br Heart J* 1980;**44**:280-3.

[18] Ahmed SS, Jaferi GA, Narang RM, Regan TJ. Preclinical abnormality of left ventricular function in diabetes mellitus. *Am Heart J* 1975;**89**:153-8.

[19] Shapiro LM, Leatherdale BA, Coyne ME, Fletcher RF, Mackinnon J. Prospective study of heart disease in untreated maturity onset diabetics. *Br Heart J* 1980;**44**:342-8.

[20] Seneviratne BIB. Diabetic cardiomyopathy: the preclinical phase. *Br Med J* 1977;i:1444-6.

[21] Sanderson JE, Brown DJ, Rivellese A, Kohner E. Diabetic cardiomyopathy? An echocardiographic study of young diabetics. *Br Med J* 1978;i:404-7.

[22] Shapiro LM, Leatherdale BA, Mackinnon J, Fletcher RF. Left ventricular function in diabetes mellitus. II: Relation between clinical features and left ventricular function. *Br Heart J* 1981;**45**:129-32.

[23] Shapiro LM, Howat AP, Calter MM. Left ventricular function in diabetes mellitus. I: Methodology, and prevalence and spectrum of abnormalities. *Br Heart J* 1981;**45**:122-8.

[24] Fuller JH, Keen H, Jarrett RJ, *et al.* Haemostatic variables associated with diabetes and its complications. *Br Med J* 1979;ii:964-6.

[25] Barnes AJ, Locke P, Scudder PR, Dormandy TL, Dormandy JA, Slack J. Is hyperviscosity a treatable component of diabetic microcirculatory disease? *Lancet* 1977;ii:789-91.

[26] McMillan DE, Utterback NG, La Puma J. Reduced erythrocyte deformability in diabetes. *Diabetes* 1978;**27**:895-901.

[27] Tchobroutsky G. Relation of diabetic control to development of microvascular complications. *Diabetologia* 1978;**15**:143-52.

[28] Knowler WC, Bennett PH, Ballentine EJ. Increased incidence of diabetic retinopathy with elevated blood pressure. *N Engl J Med* 1980;**302**:645-50.

[29] Paetkau ME, Boyd TAS, Winship B, Grace M. Cigarette smoking and diabetic retinopathy. *Diabetes* 1977;**26**:46-9.

[30] Pickup JC, Keen H, Viberti GC, *et al.* Continuous subcutaneous insulin infusion in the treatment of diabetes mellitus. *Diabetes Care* 1980;**3**:290-300.

Motor neuron(e) disease

Even allowing for loss of the "e" in translation across the ocean, the apparently simple concept of Motor Neurone Disease is far from universally accepted within the constellation of motor neurone diseases.

We may without trepidation let "motor neurone diseases" refer to all disorders characterised primarily by progressive weakness attributed to lesions of the anterior horn cell, whether or not any other parts of the neuraxis are affected. The major groupings included in this definition are the heredofamilial spinal muscular atrophies, with their own subtypes both eponymal and numerical, and motor neurone disease; lead or mercury intoxication contributes small numbers.

Here I shall use motor neurone disease as a generic entity. Its components are, firstly, amyotrophic lateral sclerosis for the combination of lesions of the anterior horn cells and pyramidal tract; secondly, progressive myelopathic (spinal) muscular atrophy when lesions are limited to the anterior horn below the foramen magnum; and, thirdly, progressive bulbar palsy for anterior horn affections of the brain stem. A patient with both progressive bulbar palsy and progressive myelopathic muscular atrophy would arbitrarily be classified as progressive bulbar palsy. And it is in this context that most European workers have, at least until recently, used motor neurone disease. Nevertheless, in the colonies in particular there are still some rebels who prefer amyotrophic lateral sclerosis as the generic term regardless of the sign of Babinski. But further to confound the question there is one European centre which seems to employ motor neurone disease as precisely equivalent to Charcot's disease of upper and lower motor neurone.

Appeal to the International Statistical Classification of Diseases, Injuries, and Causes of Death helps not at all. The new (9th) revision, in use since 1979, puts motor neurone disease and all its subtypes into one fourth-digit code under a three-digit rubric for "Anterior horn cell disease." Earlier editions were more discriminating and more variable. Nevertheless, even accepting motor neurone disease=amyotrophic lateral sclerosis+progressive bulbar palsy+progressive myelopathic muscular atrophy does not solve our problems. There is "lytico," né "Guamanian amyotrophic lateral sclerosis," or "the Marianas Islands form of amyotrophic lateral sclerosis," or "the Western Pacific form of amyotrophic lateral sclerosis." First described for Chamorro natives of the island of Guam, the entity clinically and—initially—pathologically appeared identical with sporadic motor neurone disease. It is known to affect natives of Rota and Saipan (thus "Marianas"), and there are also foci of the identical disease within the Kii peninsula of south-eastern Honshu, Japan—plus another focus, without pathological proof, in certain villages of West New Guinea (thus "Western Pacific"). In these areas its occurrence is 20 to 50 times as common as is sporadic motor neurone disease. But more than frequency distinguishes this disorder. In the same places, and even in the same patients, there is another highly prevalent illness called the Parkinson-dementia complex, with a unique pathological character later discovered to be present even in those with only the amyotrophic lateral sclerosis syndrome.[1–3] Most recently there may be emerging a "Madras amyotrophic lateral sclerosis," a sporadic disorder which adds sensorineural deafness to the clinical constellation of slowly progressive motor neurone disease.[4] And large clinic series in the Occident may include perhaps 10% or fewer in whom motor neurone disease is inherited as an autosomal dominant trait.[5]

Nevertheless, the great bulk of the patients we see with motor neurone disease are of unknown origin and implacable progression, unaltered by treatment. Epidemiologically,[6] this "true" motor neurone disease seems to be distributed uniformly about the world. Death rates within and among countries are for the most part between one and 1·5 per 100 000 population a year. Almost all deaths are now attributed to amyotrophic lateral sclerosis. There is consistent male excess at 1·5 to 1. In the United States there is also white:non-white differences of about 1·6:1. The age-specific rates rise from almost nil near age 50 to a sharp maximum at age 70. This configuration holds for all lands and both sexes and colours.

Average annual incidence rates for motor neurone disease or amyotrophic lateral sclerosis are also mostly about one to 1·5 per 100 000 population; point prevalence rates range from one to seven per 100 000, but the more complete studies suggest a prevalence of some five per 100 000. Age specific incidence

rates mirror the mortality rates, with a male excess and a sharp peak at age 65, with but one exception. In Rochester, Minnesota, the rate for those age 75+ is apparently higher than that for age 65-74.[7] The prevalence rates by age are also similar to our other indices: male excess and a pronounced maximum at age 65.[6] If amyotrophic lateral sclerosis has an incidence of 1·2 to 1·5 and a prevalence of four to six, then the calculated average duration is about three to four years—which is what is customarily taught.

Aside from age and sex, uniformly accepted risk factors for amyotrophic lateral sclerosis have not been defined. Race is uncertain; the deficit for blacks in United States mortality data has not been assessed in the appropriate morbidity surveys. Rates in the Orient are in accord with those in the Occident. No consistent variations have been reported in HLA patterns. Several case-control studies have been carried out in a search for risk factors. Space precludes their review in any detail. A recent work[8] suggesting a relation with heavy metals based on prior occupation has methodological flaws and seems unconfirmed in other works. Perhaps the most complete retrospective case-control survey is that of Kondo and Tsubaki.[9] They found a significant excess of mechanical injury in the five years before onset for both males and females. In a "prospective" comparison of data recorded in United States military records for patients later dying of amyotrophic lateral sclerosis and matched controls drawn from the military during the second world war there was found to be an excess of operations and injuries before service among the patients with amyotrophic lateral sclerosis. Admissions to hospital during service were in excess among patients with amyotrophic lateral sclerosis only for trauma and in particular for fractures—especially of the limbs.[10] Data from other retrospective series also show a trend to an excess of trauma, even though not usually of statistical significance.

It would seem to me, then, that trauma—and in particular major trauma to the limbs, is in fact a risk factor for amyotrophic lateral sclerosis. That might indeed explain the relative preponderance of males. What this means in pathogenesis, however, is conjectural; but it seems a lead worth pursuing in this otherwise hopeless disorder.

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[1] Kurland LT, Guamanian ALS: hereditary or acquired? In: Rowland LP, ed. *International conference on human motor neuron diseases*. New York: Raven Press. (In press.)

[2] Yase Y, Matsumoto N, Yoshimasu F, Handa Y. Clinico-epidemiological studies in a new focus of motor neuron disease in Japan. *Neurology India* 1973;suppl **IV**:531-9.

[3] Gajdusek DC. A focus of high incidence amyotrophic lateral sclerosis and parkinsonism and dementia syndromes in a small population of Auyu and Jakai people of southern West New Guinea. In: Tsubaki T, Toyokura Y, eds. *Amyotrophic lateral sclerosis*. Baltimore: University Park Press, 1979:287-305. (Japan Medical Research Foundation, Publ No 8.)

[4] Jagannathan K, Valmikinathan K, Srinivas K, Arjundas G, Ahmed SZ. Special variant of motor neurone disease in Madras. *12th World Congress of Neurology*. Abstracts. Amsterdam: Excerpta Medica, 1981: 336.

[5] Horton WA, Eldridge R, Brody JA. Familial motor neuron disease. Evidence for at least three different types. *Neurology (NY)* 1976;**26**: 460-5.

[6] Kurtzke JF. Epidemiology of amyotrophic lateral sclerosis. In: Rowland LP, ed. *International conference on human motor neuron diseases*. New York: Raven Press. (In press.)

[7] Juergens SM, Kurland LT, Okazaki H, Mulder DW. ALS in Rochester, Minnesota, 1925-1977. *Neurology (NY)* 1980;**30**:463-70.

[8] Pierce-Ruhland R, Patten BM. Repeat study of antecedent events in motor neuron disease. *Ann Clin Res* 1981;**13**:102-7.

[9] Kondo K, Tsubaki T. Case-control studies of motor neuron disease. Association with mechanical injuries. *Arch Neurol* 1981;**38**:220-6.

[10] Kurtzke JF, Beebe GW. Epidemiology of amyotrophic lateral sclerosis. I. A case-control comparison based on ALS deaths. *Neurology (NY)* 1980; **30**:453-62.

Will breast self-examination save lives?

We have no way of predicting at which stage in the clinical course of primary breast cancer it will shed clonogenic cells into the circulation to become the seeds of destruction. Nevertheless, the experimental and clinical data do show that the disease is so heterogeneous that some cancers may be capable of metastasising almost from their inception while others remain locally progressive with little ability for dissemination.[1] Irrespective of these biological variables, chronological factors also determine the prognosis. Even cancers of low metastasising potential may lead to a woman's death if diagnosis and treatment are excessively delayed.

This kind of reasoning has encouraged researchers, clinicians, and government agencies to seek methods of "early" diagnosis which might ultimately lead to a reduction of the deaths from breast cancer, which currently stand at about 12 000 a year in Britain.[2] Two approaches are possible: firstly, to screen an asymptomatic "at-risk" population and, secondly, to educate women to examine themselves and promptly report abnormal findings. Both approaches have attracted professionals and politicians alike, so much so that many have accepted them as articles of faith. Yet these seductively simple approaches should be tested scientifically in the same way as any other clinical hypothesis.

So far as screening is concerned (outside the fee-paying sector), scientific evaluation is being attempted in several countries. In contrast, no publication has shown that educating women to practise breast self-examination has resulted in the detection of an excess of premetastatic breast cancers.

In theory, at least, breast self-examination might be a more fruitful exercise and a less costly endeavour than screening by mammography. The growth patterns of solid tumours can be described by a complex (Gompertzian) function.[3] Screening by mammography might detect cancers at a minimum diameter of, say, 0·25 cm—that is, two doublings before the smallest lump detectable by palpation alone. Breast self-examination might detect all lumps between 1 and 4 cm (that is, the next two doublings), which still remain at an "operable" stage. If the doubling time increases with the size of the primary tumour, as might be expected in the later components of a Gompertzian growth curve, then the time available for dissemination is in theory greater for the period covered by breast self-examination than that for mammographic screening.

In my own breast clinic one-quarter of the women with breast cancer have presented with inoperable tumours over the past two years. So perhaps before we invest huge resources into screening the whole female population to detect cancers less than 1 cm diameter we might turn our attention to persuading women to present themselves with tumours between 1 and 4 cm diameter. The DHSS has already accepted this approach and is currently funding a trial in