

likely to fall. More seriously, medical schools are already short of bright working-class entrants (2.5% have parents in social classes IV or V, which constitute about 30% of the population<sup>1</sup>), and this financial squeeze can only act as a further disincentive.

Good arguments can be produced for rethinking the whole system of student grants,<sup>2</sup> but until that comes about the Government should think again about cutting them. We would urge it also to recognise that in equity clinical medical students should receive the same rate for their extra weeks as all students receive for the basic terms.

<sup>1</sup> Royal Commission on Medical Education. *Report*. London: HMSO, 1968. (Cmd 3569.)

<sup>2</sup> Anonymous. What universities should aim at. *Nature* 1982;295:541.

## Mitral valve prolapse and a Marfanoid habitus

Prolapse of the mitral valve may result from a variety of abnormalities of the valvular mechanism and the myocardium. The defect is common, affecting around one person in 20 of the general population,<sup>1-3</sup> and it may produce no symptoms at all or those of disturbed cardiac function.

The course and prognosis in any affected individual seem likely to be directly related to the underlying disorder, so that to facilitate prognosis and management specific syndromes need to be sought within the large heterogeneous group of disorders where mitral valve prolapse is known to occur.

One common factor linking some categories of patients is an underlying connective tissue disease: mitral valve prolapse is a frequent complication of the Marfan syndrome<sup>4</sup> and is occasionally encountered in osteogenesis imperfecta<sup>5</sup> and the Ehlers-Danlos syndrome.<sup>6</sup> Equally, people with mitral valve prolapse sometimes have additional non-specific musculo-skeletal stigmata such as articular hypermobility (R Grahame, personal communication 1982), altered bodily proportions,<sup>7</sup> and thoracic asymmetry.<sup>8</sup> These anomalies may show that the cardiac abnormality in these patients is one facet of an ill-defined generalised disorder of connective tissue.

This association is well known to dysmorphologists and clinical geneticists, but the lack of specificity of the extracardiac manifestations usually foils any attempt to delineate a syndrome. In a recent article in the *American Journal of Medicine*, however, Schutte and his colleagues in Texas have reported that they had identified a dominantly inherited syndrome of mitral valve prolapse in people with distinctive anthropometric characteristics.<sup>9</sup> Their patients had narrow anteroposterior chest diameters and longer arm spans than controls. Unfortunately, the altered habitus was present only in women, and the value of measuring bodily proportions as a diagnostic discriminant in sporadic patients with mitral valve prolapse is therefore limited.

From the genetic standpoint, Schutte *et al*<sup>9</sup> claimed that their findings in first degree relatives in three families were indicative of autosomal dominant inheritance of the syndrome. The lack of pedigree data for formal analysis, however, and the fact that the habitus was not present in men make it difficult to accept their proposals unreservedly. Moreover, in two further instances the results of family studies were negative. Notwithstanding these reservations, however, the diagnostic appraisal of possible heart abnormalities of potentially affected close relatives of individuals with the syndrome seems to be warranted.

The question inevitably arises whether these patients have the Marfan syndrome. The full-blown syndrome, with disproportion of the length of the limbs, arachnodactyly, and dislocated ocular lenses is unmistakable. Nevertheless, atypical or partial examples abound, and as there are no absolute diagnostic criteria diagnostic certainty is often impossible. Schutte *et al*<sup>9</sup> were at pains, however, to exclude individuals with the stigmata of the Marfan syndrome from their series, so this red herring can probably be discounted.

In view of the complexity of the collagen molecule, and on the basis of precedents for extreme degrees of heterogeneity in other conditions, there seem likely to be numerous undelineated disorders of connective tissue where mitral valve prolapse is a syndromic component. Indeed, Schutte *et al*<sup>9</sup> may have already recognised one such entity. These disorders are, however, "soft syndromes," and in the absence of any biochemical marker firm delineation is well-nigh impossible.

As with many problems in medical genetics, resolution of this diagnostic dilemma may ultimately be achieved through recombinant DNA technology.

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<sup>1</sup> Procacci PM, Savran SV, Schreiter SL, Bryson AL. Prevalence of clinical mitral-valve prolapse in 1169 young women. *N Engl J Med* 1976;294:1086-8.

<sup>2</sup> Markiewicz W, Stoner J, London E, Hunt SA, Popp RL. Mitral valve prolapse in one hundred presumably healthy young females. *Circulation* 1976;53:464-73.

<sup>3</sup> Davies MJ, Moore BP, Braimbridge MV. The floppy mitral valve. Study of incidence, pathology, and complications in surgical, necropsy, and forensic material. *Br Heart J* 1978;40:468-81.

<sup>4</sup> Brown OR, DeMots H, Kloster FE, Roberts A, Menashe VD, Beals RK. Aortic root dilatation and mitral valve prolapse in Marfan's syndrome: an echocardiographic study. *Circulation* 1975;52:651-7.

<sup>5</sup> Wood SJ, Thomas J, Braimbridge MV. Mitral valve disease and open heart surgery in osteogenesis imperfecta tarda. *Br Heart J* 1973;35:103-6.

<sup>6</sup> Brandt KD, Sumner RD, Ryan TJ, Cohen AS. Herniation of mitral leaflets in the Ehlers-Danlos syndrome. *Am J Cardiol* 1975;36:524-8.

<sup>7</sup> Salomon J, Shah P, Heinle RA. Thoracic skeletal abnormalities in idiopathic mitral valve prolapse. *Am J Cardiol* 1975;36:31-6.

<sup>8</sup> Udoshi MB, Shah A, Fisher VJ, Dolgin M. Incidence of mitral valve prolapse in subjects with thoracic skeletal abnormalities—a prospective study. *Am Heart J* 1979;97:303-11.

<sup>9</sup> Schutte JE, Gaffney FA, Blend L, Blomqvist CG. Distinctive anthropometric characteristics of women with mitral valve prolapse. *Am J Med* 1981;71:533-8.

## Immunotherapy reassessed

For 20 years now research workers have been looking into the immunotherapy of cancer but clinicians still do not know whether it is useful for their patients.

The concept of a simple treatment that might "mop up" the last remaining cancer cell after initial treatment with surgery or radiotherapy is attractive. Medawar's work in the 1950s on tissue recognition and the rejection of foreign cells and proteins started a hunt for tumour-specific antigens.<sup>1</sup> A series of experiments<sup>2-4</sup> in specially inbred strains of mice showed that tumour-specific transplantation antigens did indeed exist in tumours induced in these mice by chemicals. The combination of this evidence with studies showing that immunotherapy (usually with BCG<sup>5</sup>) worked in experimental tumours in animals raised great hopes for the immunotherapy of human cancer. Sadly, these hopes were largely disappointed as over-enthusiastic clinicians began to use "immunotherapy" in a