

whom pre-existing gout, cardiovascular and renal disease, and diabetes had been excluded, developed gout after four years.<sup>3</sup> Recent data in healthy men from Boston show an annual incidence of gouty arthritis of 0.1% for urate concentrations below 420  $\mu\text{mol/l}$ , 0.5% for those of 420-534  $\mu\text{mol/l}$ , and 4.9% for those of 540  $\mu\text{mol/l}$  or more.<sup>4</sup> The risk of developing gout thus seems to be low, and in any case gouty arthritis can be treated.

Acute uric acid nephropathy, in which massive deposits of uric acid crystals form within the renal tubule and pelvis, follows excessive nucleoprotein degradation, which occurs most commonly after chemotherapy for malignant disease. It is easily prevented by allopurinol. Estimations of the frequency of stone formation among patients with gout range from 4%<sup>5</sup> to 73%,<sup>6</sup> and stones may be associated with hyperuricaemia without gout. Interstitial deposition of sodium urate may impair renal function, but abnormalities of tubular or glomerular function may themselves lead to hyperuricaemia—and working out the sequence of events in an individual patient is often difficult. The risks do not, however, seem to be great. A recent American survey of many people with hyperuricaemia and normouricaemic controls followed over years showed that azotaemia attributable to hyperuricaemia is generally mild and no more common than azotaemia in normouricaemic people.<sup>7</sup> The risk was thought to be of no clinical importance (at least until serum concentrations of urate were very high), and the risks of urolithiasis also seemed small. Another investigation in which glomerular and tubular function was measured in many patients also showed that hyperuricaemia (or uncomplicated gout alone) does not in itself cause renal insufficiency.<sup>8</sup> When renal insufficiency is seen in patients with gout it tends to be related to hypertension, ischaemic heart disease, or pre-existent renal insufficiency. Similarly, the Boston study found no evidence of renal deterioration attributable to hyperuricaemia.<sup>4</sup>

The results of numerous studies have yielded conflicting results on the relation of asymptomatic hyperuricaemia to cardiovascular disease. Although hyperuricaemia may be related to heart disease if the patient is obese, hypertensive, and taking medication, hyperuricaemia has not been shown to be an independent risk factor.<sup>9</sup> The evidence thus invites a conservative approach to the man or woman with asymptomatic hyperuricaemia. A full clinical assessment is necessary, as for a patient with gout, with particular reference to dietary and drug (diuretic) history and cardiac and renal function. Overproduction of uric acid (indicating the possibility of a specific purine enzyme abnormality with its genetic implications and the increased risk of uric acid stone formation) should be detected by a 24 hour urinary urate estimation with the patient on a low purine diet.<sup>1</sup>

Very rarely will the doctor have to prescribe urate lowering drugs. Mild hyperuricaemia may safely be left untreated, but opinions differ about high concentrations—say, above 540  $\mu\text{mol/l}$ . This degree of sustained hyperuricaemia is rare without some readily apparent underlying cause, but many would hold that such people, particularly if hyperuricosuric, should be treated with allopurinol. The drug does, however, have side effects, and in recent reports of deaths from allopurinol toxicity the drug has been prescribed in many cases for trivial and inadequate reasons.<sup>10 11</sup>

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## Atlantoaxial instability in Down's syndrome

Patients with Down's syndrome may injure their cervical cords through atlantoaxial subluxation, and the sponsors of the special olympics in the United States have stopped them participating in high risk sporting activities until the presence of atlantoaxial instability has been excluded.<sup>1</sup> Once it is excluded, however, they may participate without restriction. Similar advice has been given by the American Committee on Sports Medicine,<sup>2</sup> and similar guidelines have been approved in Britain by the Royal Society for Mentally Handicapped Children and Adults (Mencap).

Advice from the Department of Health and Social Security,<sup>3</sup> which has been endorsed by the British Orthopaedic Association (L Klernerman, personal communication), suggests that there is no justification for routine screening of all patients with Down's syndrome for atlantoaxial instability but only for those likely to engage in vigorous sporting activities, such as trampolining, diving, or violent contact sports. Those found to have normal radiographs of the cervical spine should not be restricted in their activities. Those found to have atlantoaxial instability but no abnormal neurological signs should be encouraged to continue with previous activities—except more vigorous high risk sports. Alvarez, in contrast, believes that all patients with Down's syndrome should be screened both radiologically and neurologically at least annually.<sup>4</sup>

Atlantoaxial instability was recognised over 150 years ago,<sup>5</sup> but its association with Down's syndrome became apparent only in the 1960s. Spitzer found that nine of 29 patients with Down's syndrome showed "forward displacement of the atlanto-occipital joint and an abnormally thin and small shape of the atlas vertebra."<sup>6</sup> Many other skeletal abnormalities are to be found in Down's syndrome, including abnormalities of the odontoid process and laxity of the transverse ligament of the atlas.<sup>7-14</sup> Since Spitzer's original observation several cases have been published of atlantoaxial subluxation in Down's syndrome associated with neurological problems,<sup>15-30</sup> and sometimes spinal cord damage appears to have occurred either spontaneously or after minor trauma.

Tishner and Martel undertook a radiological examination of 18 patients with Down's syndrome and found an atlanto-odontoid interval greater than 5 mm in four.<sup>31</sup> Martel studied 70 patients with Down's syndrome "largely selected at random" (but mostly male) and found atlantoaxial instability in 14.<sup>32</sup> Semine found an atlanto-odontoid interval greater than 4.5 mm in 10 of 85 children with Down's syndrome;

after 12 months only one had developed neurological signs.<sup>33</sup> Pueschel screened 236 patients with Down's syndrome radiologically and found the atlanto-odontoid interval equal to or greater than 5 mm in 17%; in 2.6% of his patients (seven cases), only one of whom was over 18, atlantoaxial instability was associated with abnormal neurological signs (18% of those in whom atlantoaxial instability had been shown radiologically).<sup>34</sup> Six of his seven patients with neurological abnormalities had no history of trauma. The male to female ratio of those patients affected by atlantoaxial instability was 1:2.3. Pueschel found that if the atlanto-odontoid interval was 4.5-6.0 mm the patients remained free of neurological signs, but if the distance exceeded 7.00 mm all patients had neurological signs. Pueschel believes that the intrinsic defect is one of connective tissue since atlantoaxial instability was correlated with hyperextensibility of other joints, such as fingers and elbows.<sup>33</sup> <sup>36</sup>

The prevalence of atlantoaxial instability in patients with Down's syndrome thus seems to be between 12% and 22%, with a higher prevalence among girls and women. Atlantoaxial instability is associated with (and probably causes) damage to the cervical cord in some 2-3% of all patients with Down's syndrome who survive infancy. Most patients in whom cord damage has been recognised have undergone surgical procedures to stabilise the cervical spine, and the results have been generally good.<sup>21</sup> <sup>34</sup> The fact that most cases of neurological damage seem to have occurred spontaneously or after trivial trauma is, however, worrying as avoiding strenuous sporting activity alone may thus not be enough to protect the cervical cord.

Atlantoaxial instability in Down's syndrome fulfils many of the criteria for introducing screening<sup>37</sup>: the association of atlantoaxial instability with cord damage is common and often disastrous; the condition is treatable and easily diagnosed using acceptable and readily available methods; and there is a latent period before cord damage occurs. What is missing is an agreed policy on screening and treatment. The screening of all patients with Down's syndrome for atlantoaxial instability seems to be logical. Down's syndrome is common, and half of all the patients who survive infancy now live until 60.<sup>38-40</sup> It is imperative to ensure their quality of life, but the workload and resource implications of so doing are enormous.

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## Measles and the government

Some time soon children in Britain will be offered a triple vaccine against measles, mumps, and rubella at the age of 15 months. An announcement has been expected for several months, and on 7 April Baroness Trumpington, Parliamentary Secretary for Health, in a curious choice of venue, told Princess Diana and others present at a lunch organised by the National Rubella Council that "we shall take every step to introduce this vaccine generally as soon as practicable."<sup>1</sup>

The *BMJ* has for years been calling for a more effective campaign of measles vaccination,<sup>2</sup> and we have also published evidence on the safety and efficacy of the measles/mumps/rubella vaccine as used in Sweden and elsewhere.<sup>3</sup> Introduction of the new triple vaccine could and should give community physicians, health educators, family doctors, health visitors, and others an opportunity to revitalise the measles campaign and raise the uptake above the present disappointing 60%. The World Health Organisation's target—elimination of measles from Europe by 1995—depends on a 95% uptake of measles vaccination by 1990, so there is not a lot of time.<sup>4</sup>

The lack of any date in the government's announcement is disappointing. It does, however, encourage us to urge the Department of Health to do the job properly this time round. Firstly, mumps and rubella should be made notifiable in order to provide background data. Secondly, once a launch