The more surprising finding is that the excess mortality remains even when suicide and accidental deaths are excluded. The highest increase is among those with organic psychotic conditions, especially any type of dementia, but is raised for all psychiatric diagnoses^{5 20} and paradoxically is greater for those aged under 40.¹¹ Among the psychiatrically ill there have been accounts of sudden death, death with no organic disease, and also of unexpected death from known physical illness.²¹ Most of the excess mortality from natural causes is, however, from common conditions: cardiovascular disease and arteriosclerosis,²² pulmonary infection,²³ and influenza.¹¹ Whether there is an excess of deaths from malignancy is debatable.^{11 22}

Postulated causes for the excess mortality may be divided broadly into biological and psychosocial. Kendler has considered that genetic factors are important in mortality from trauma (suicide and accident) and those with schizophrenia and from diseases (natural causes) among those with neurotic conditions.²⁴ Psychiatric illness and physical conditions resulting in death may be linked in three ways: the mentally ill may have an increased exposure to known causes of disease or death—for example, tobacco, alcohol, and dangerous driving; for a given degree of environmental exposure they may have an increased susceptibility to develop illness (psychosomatic disorder); and mental illness may adversely affect the outcome of a physical disease.²⁵

The excess mortality could be accounted for by several different psychological theories. The cluster theory suggests that illnesses tend to cluster in different bodily and psychological systems in the same individual, that there is a higher concentration of some illnesses in a minority of the population, and that several illnesses tend to occur within a few years of the whole life span.²⁶ The affect of hopelessness may be associated with the early stages of a severe physical illness,²⁷ and many studies have looked at the association between adverse life events and the subsequent onset of serious illness and death.²⁸ The experience of loss has been related to increased mortality,²⁹ and the inability to communicate distressing emotion verbally (alexithymia) may be related to the onset of physical illness.³⁰ Type A behaviour patterns, with competitive striving, aggressiveness, hostility, and continuous working to time limits, have been related to an increased incidence of coronary heart disease.³¹ Very different life stresses may result in a common pathological pattern of illness resulting in death,³² and in certain predicaments the untoward event has had a last straw effect, resulting in premature death.³³ Associations have also been sought between abnormal psychological states and accident proneness.³⁴

With this bewildering array of findings and theories one might concur with Tsuang and Simpson's answer to their self imposed question: "Mortality studies in psychiatry—should they stop or proceed?": "There is a continuing need for mortality studies and increased opportunities for integrating these investigations with other longitudinal studies of psychiatric population."³⁵ The study of mortality is the hardest fact of psychiatric epidemiology and can give useful information on the course of mental disorders and the efficacy of treatment.

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Asymptomatic hyperuricaemia

Defining hyperuricaemia exactly is difficult,¹ but practically it is a urate concentration above 420 $\mu\text{mol/l}$ in men and 360 $\mu\text{mol/l}$ in women. Sometimes hyperuricaemia will be found on routine screening in a person who has never had gout, and as it may be a risk factor for gout, renal disease, and ischaemic heart disease the question arises whether any treatment should be offered.

Prolonged hyperuricaemia certainly carries a risk of gouty arthritis proportionate to its severity and duration. The prevalence of gout is high in populations whose uric acid concentrations are above those found in Europe, and the height of the serum urate concentration correlates with the prevalence of gout. Data from the Framingham study showed that 90% of those with urate concentrations above 540 $\mu\text{mol/l}$ had gout,² but only 10 men had this degree of hyperuricaemia and other studies have not confirmed such a high incidence of gout. For example, Fessel found that only three of 66 men with concentrations above 540 $\mu\text{mol/l}$, in

whom pre-existing gout, cardiovascular and renal disease, and diabetes had been excluded, developed gout after four years.³ 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.⁴ 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%⁵ to 73%,⁶ 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.⁷ 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.⁸ 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.⁴

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.⁹ 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.¹

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.^{10 11}

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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.¹ Once it is excluded, however, they may participate without restriction. Similar advice has been given by the American Committee on Sports Medicine,² 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,³ 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.⁴

Atlantoaxial instability was recognised over 150 years ago,⁵ 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."⁶ 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.⁷⁻¹⁴ Since Spitzer's original observation several cases have been published of atlantoaxial subluxation in Down's syndrome associated with neurological problems,¹⁵⁻³⁰ 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.³¹ Martel studied 70 patients with Down's syndrome "largely selected at random" (but mostly male) and found atlantoaxial instability in 14.³² Semine found an atlanto-odontoid interval greater than 4.5 mm in 10 of 85 children with Down's syndrome;