Potassium in foods**Moderate to high (mmol per usual serving):**

Potatoes (17), pulses (9-22), instant coffee (10), dried fruits (5-24), treacle (9), fresh meat and fish (8-10), All Bran (8), tomatoes (fresh fruit (2-10), beer (3-8), cows' milk (5), oatmeal (5), orange juice (4), nuts (2-6), wines (2-4), vegetables (1-7).

Low (1-3 mmol per usual serving):

Rice, chocolate, human milk, egg, biscuits, bread, cheese, flour, cornflakes.

Very low or absent:

Sugar, jam, honey, butter, margarine, cream, oils, spirits.

Potassium is the major intracellular cation; the more concentrated the cells in a food, the higher the potassium concentration.

The Ministry of Agriculture Fisheries and Food calculated that root vegetables provide a quarter and milk almost another quarter of normal British people's intake, with fruit and other vegetables each providing 10% or less.

Magnesium is distributed in foods somewhat similarly to potassium.

Bran, wholegrain cereals and legumes are the richest sources. Most vegetables contain similar moderate amounts to meat. Green colour (chlorophyll) makes little difference.

Polyunsaturated fatty acids—Healthy couples were changed from a 40% fat diet predominantly saturated to a 23% fat diet, largely polyunsaturated (sodium and potassium roughly constant). Their mean blood pressure fell by 8/5 mm Hg. The polyunsaturated fat probably lowers the blood pressure because of increased synthesis of vasodilatory prostaglandins.

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Lesson of the Week

Muscle contractures associated with glucocorticoid deficiency

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Although Thomas Addison in his original paper in 1855 did not mention muscle contractures as a feature of adrenocortical insufficiency,¹ Gallavan and Steegman in 1937 described two patients with hypopituitarism who were unable to straighten their knees,² and in the same year Anderson and Lyall reported the same phenomenon in a patient with Addison's disease.³ Aubertin and Bergouignan in 1951 observed that contractures may develop spontaneously in adrenocortical insufficiency and were reversed with glucocorticoid replacement therapy.⁴

The following report re-emphasises this clinical entity and describes a further five patients in whom contractures developed insidiously in association with deficiency of glucocorticoids.

Case histories

A 40 year old itinerant Irish labourer (case 1) was referred with painful contractures and flexion deformities of both knees. He had a history of respiratory tuberculosis 10 years before, and in the preceding six months he had been investigated at another hospital for weight loss, lethargy, night

Any patient who develops muscle contractures with flexion deformities, particularly in the legs, in the absence of neurological signs should be screened for glucocorticoid deficiency

sweats, nausea, vomiting, and cough productive of purulent sputum. There had been no evidence to support reactivation of tuberculosis but the serum sodium concentration had been only 129 mmol(mEq)/l and rehydration with intravenous isotonic saline was required. A random plasma cortisol estimation was reported as 868 nmol/l (31.4 µg/100 ml) but a short and more prolonged, five hour Synacthen (tetracosactrin) test disclosed an impaired adrenal response. The serum sodium concentration returned to normal, however, and after treatment of a *Haemophilus influenzae* chest infection he made a prompt recovery.

On readmission he looked wasted and much older than his age. He was withdrawn, apathetic, and of low intelligence. There was vitiligo but no buccal pigmentation or postural hypotension. The hamstrings were taut and knees could not be straightened beyond 30° in the absence of any objective neurological signs. Serum sodium concentration was 127 mmol/l and fell to 113 mmol/l after the introduction of ibuprofen 800 mg twice daily. A request to perform jury service seemed to precipitate a paranoid psychosis, necessitating transfer to a psychiatric unit. At this stage ibuprofen was discontinued and fluid restriction introduced. Serum sodium concentration rose to 136 mmol/l but contractures remained unchanged and seemingly unexplained.

Ten months later, after a gastrointestinal upset, he was admitted under our care with collapse, dehydration, and hypotension. A clinical diagnosis of adrenal insufficiency was made, and after resuscitation with intravenous isotonic saline and hydrocortisone a remarkable improvement ensued. During three months of replacement hydrocortisone therapy aided by

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Clinical details of five patients with muscle contractures associated with glucocorticoid deficiency

Case No	Age (years)	Sex	Glucocorticoid deficiency	Aetiology	Site of contractures	Duration of symptoms (months)	Outcome
1	40	M	Secondary	Isolated deficiency of adrenocorticotrophic hormone	Knees	12	Excellent response after 3 months' replacement therapy
2	28	M	Secondary	Craniopharyngioma excised. Mistaken reduction in replacement dose of cortisone	Knees, hips, shoulders, cervical spine	24	Good response to adequate replacement therapy
3	44	F	Primary	Adrenal tuberculosis	Knees, hips	10	Excellent response after 2 weeks' replacement therapy
4	63	F	Secondary	Hypopituitarism after excision of adenoma + deep x ray therapy. Patient non-compliance with replacement dose of cortisone	Knees	6	Gradual recovery over 6 months
5	55	M	Primary	Adrenal tuberculosis	Knees, right elbow	6	Good response after 4 months' adequate replacement therapy

physiotherapy the contractures disappeared and gait returned to normal. Full bilateral extension of both knees became possible. Further evaluation of his endocrine state showed isolated deficiency of adrenocorticotrophin (a rare disorder recently reviewed by Stackpoole *et al*⁵).

The table summarises this case and gives the clinical details of four others also treated by us.

Discussion

A striking feature of our five cases and those described elsewhere is their remarkable similarity in the insidious onset of contractures and predilection for the legs, the knees being particularly susceptible to flexion deformities. Pain may be severe and the disability so pronounced that walking is impossible. Contractures may be the presenting complaint, as in case 1, and unless there are other manifestations of adrenal or pituitary disease there may be considerable delay in making the correct diagnosis. Other workers have noted that this association has often gone unrecognised or been overlooked. VanderLaan in 1955 described a 75 year old woman with knees and hips fixed in extreme flexion who was thought to have severe arthritis. At necropsy, however, no abnormality of the legs was found but complete pituitary destruction was discovered.⁶ Slater in 1960 described a patient with muscle contractures for several months in whom he found hypopituitarism after embarking on a series of tests of pituitary function to investigate hypoparathyraemia.⁷

The aetiology of the contractures remains a mystery. They are clearly not due to simple disuse as they may develop in fully ambulant patients. There is no clinical, laboratory, or radiographic evidence of joint disease; and, although neurological disease may be suggested by the appearance of the limbs, there are no neurological signs, and neurological investigations—including electromyography, muscle biopsy, myelography, and cerebrospinal fluid analysis—are unhelpful.

Treatment of the glucocorticoid deficiency with cortisone is invariably successful but the longer the delay in diagnosis the longer

it takes for the contractures to resolve. Thorn *et al* in 1942, reporting on a series of 158 patients with Addison's disease at a time when mineralocorticoid treatment as desoxycorticosterone acetate was the sole replacement therapy available, attributed the development of painful and disabling contractures of the thigh muscles in three patients to this drug.⁸ Nevertheless, that these contractures may occur in not only adrenal but pituitary malfunction and with a selective adrenocorticotrophin deficiency (as in our case 1) supports the concept that they must be related to a deficiency of glucocorticoids and not mineralocorticoids.

By describing these five further cases and drawing attention to early publications on the subject we hope further to emphasise this association, which seems to have been forgotten in most modern day textbooks of endocrinology.^{9 10} Any patient who mysteriously develops muscle contractures with flexion deformities, particularly in the legs, in the absence of neurological signs should be screened for possible glucocorticoid deficiency. If the diagnosis is correct an excellent result is usually obtained by the introduction of appropriate glucocorticoid replacement therapy.

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The pH of vegetarians' urine is higher than that of meat eaters. The gut flora differs and transit times are lower in vegetarians. Should prescribing regimens take account of these differences?

There is little direct information on which to base an answer to this question but it is possible to speculate on some of the ways in which vegetarianism might influence the effects of drugs. Increasing urine pH accelerates the elimination of weak acids and delays the elimination of weak bases. Relatively small increases in urine pH may increase the elimination rate of aspirin and this may make it more difficult to achieve anti-inflammatory blood concentrations of aspirin.¹ The blood concentrations of mexiletine and of quinidine are increased in patients with alkaline urine but the clinical importance of this is probably small. Amphetamine abusers are known to prolong the effects of the drug by ingesting baking soda beforehand; similar prolongation would probably occur in vegetarians.

Asian vegetarians metabolise some drugs more slowly than non-vegetarians but this does not appear to be the case for white vegetarians. It may be

due to a low protein intake in the Asian vegetarians rather than to vegetarianism itself.² Fast gastrointestinal transit times have been associated with reduced absorption of poorly soluble drugs.³ Possibly drug availability from slow release preparations could be reduced in vegetarians but there is no information on this. Reduction in bowel flora may affect the bioavailability of some drugs. This is the proposed mechanism for oral contraceptive failure in patients taking oral antibiotics; and there is some evidence that the effect of sulphasalazine may be reduced if bacterial degradation is prevented by antibiotics. There is, however, no evidence that changing the nature of the bowel flora would have a similar effect.—LINDA BEELEY, consultant clinical pharmacologist, Birmingham.

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