progress in Sheffield only one third of insulin treated diabetics wished to attempt continuous subcutaneous insulin infusion, and one third of these abandoned it within a few weeks.^{19,21} Moreover, it may be hazardous. Episodes of keto-acidosis occur more frequently in those treated by continuous subcutaneous insulin infusion than in those having conventional treatment, even when patients have been properly supervised.^{8,19,21} The reason is uncertain. Perhaps the subcutaneous reserve is too small to meet increased demands at times of infection or other stresses, however slight.

The introduction of continuous subcutaneous insulin infusion is an important advance. Who should be offered this treatment? The most cautious recommendation would be that the technique is still under evaluation and should be used only in trial conditions. There is no clear indication for continuous subcutaneous insulin infusion in the management of diabetic complications, except perhaps in some cases of painful neuropathy; this aspect of treatment with continuous subcutaneous insulin infusion has still to be examined properly by long term trials.¹⁷ Continuous subcutaneous insulin infusion has a limited place in planned pregnancies, when even the most conscientious patient may have difficulty with her diabetic control, but during pregnancy continuous subcutaneous insulin infusion generally offers no advantage over conventional treatment,²⁰ and babies may still be very large.^{19,21} It is clearly unsuitable for those with "brittle" diabetes, who are usually emotionally unstable and for whom continuous subcutaneous insulin infusion offers no advantage. There remains a group of patients who prefer continuous subcutaneous insulin infusion as the treatment of choice and who benefit in ways already described. They must be well motivated, reliable, able to monitor their own blood glucose concentrations regularly, and have access to expert advice day and night.

P J WATKINS

Consultant Physician,
Diabetic Department,
King's College Hospital,
London SE5 9RS

- Pickup JC, Keen H, Parsons JA, Alberti KGMM. Continuous subcutaneous insulin infusion: an approach to achieving normoglycaemia. *Br Med J* 1978;i:204-7.
- Pickup JC. Pumps in practice: practical aspects of continuous subcutaneous insulin infusion (CSII). *Diabetic Medicine* 1984;1:27-32.
- Home PD, Marshall S. Problems and safety of continuous subcutaneous insulin infusion. *Diabetic Medicine* 1984;1:41-4.
- Home PD, Capaldo B, Burrin JM, Worth R, Alberti KGMM. A crossover comparison of continuous subcutaneous insulin infusion (CSII) against multiple injections in insulin-dependent diabetic subjects. Improved control with CSII. *Diabetes Care* 1982;5:466-71.
- Pickup JC, Home PD, Bilous RW, Alberti KGMM, Keen H. Management of severely brittle diabetes by continuous subcutaneous and intramuscular insulin infusion: evidence for a defect in subcutaneous insulin absorption. *Br Med J* 1981;282:347-50.
- Green SA. Pump therapy in children. *Diabetic Medicine* 1984;1:44-7.
- Buysschaert M, Marchand E, Ketelslegers JM, Lambert AE. Comparison of plasma glucose and plasma-free insulin during CSII and intensified conventional insulin therapy. *Diabetes Care* 1983;6:1-5.
- Mecklenburg RS, Benson JW, Becker NM, et al. Clinical use of the insulin infusion pump in 100 patients with type 1 diabetes. *N Engl J Med* 1982;307:513-8.
- Chasson JL, Ducros F, Poliquin-Hamet M, Lopez D, Lecavalier L, Hamet P. Continuous subcutaneous insulin infusion (Mill Hill infuser) versus multiple injections (Medi-Jector) in the treatment of insulin dependent diabetes mellitus and the effect of metabolic control on microangiopathy. *Diabetes Care* 1984;7:331-7.
- Reeves ML, Seigler DE, Ryan EA, Skyler JS. Glycemic control in insulin dependent diabetes mellitus: comparison of out-patient intensified conventional therapy with continuous subcutaneous insulin infusion. *Am J Med* 1982;72:673-80.
- Kroc Collaborative Study. Blood glucose control and the evolution of diabetic retinopathy and albuminuria. *N Engl J Med* 1984;311:365-71.
- Lauritzen T, Frost-Larsen K, Larsen HW, Deckert T, Steno Study Group. Effect of 1 year of near normal blood glucose levels on retinopathy in insulin-dependent diabetics. *Lancet* 1983;ii:200-3.
- Dahl-Jorgensen K, Hansen KF, Sineland E, Brinckmann-Hansen O, Aagaens O, Aker Diabetes Group. Long-term strict control in type I (insulin-dependent) diabetes mellitus: effect on late diabetic complications [Abstract]. *Diabetologia* 1983;25:149.
- Lauritzen T, Frost-Larsen K, Larsen HW, Deckert T, Keiding N, Nielsen G. Continuous subcutaneous insulin infusion. Long term strict control in type I (insulin-dependent) diabetes mellitus: effect on late diabetic complications. *Lancet* 1983;ii:1445-6.
- Atherton A, Hill DW, Keen H, Young S, Edwards EJ. The effect of acute hyperglycaemia on the retinal circulation. *Diabetologia* 1980;18:233-7.
- Pietri A, Ehle AL, Raskin P. Changes in nerve conduction velocity after six weeks of glucoregulation with portable infusion pumps. *Diabetes* 1980;29:668-71.

- Boulton AJM, Drury J, Clarke B, Ward JD. Continuous subcutaneous insulin infusion in the management of painful diabetic neuropathy. *Diabetes Care* 1982;5:386-90.
- Viberti GC, Bilous RW, Mackintosh D, Bending JJ, Keen H. Long-term correction of hyperglycaemia and progression of renal failure in insulin-dependent diabetes. *Br Med J* 1983;286:598-602.
- Ward JD. Continuous subcutaneous insulin infusion (CSII): therapeutic options. *Diabetic Medicine* 1984;1:47-50.
- Potter J, Reckless J, Cullen D. Subcutaneous continuous insulin infusion and control of blood glucose concentration in diabetics in third trimester of pregnancy. *Br Med J* 1980;280:1099-101.
- Knight G, Boulton AJM, Drury J, et al. A feasibility study of the use of continuous sub-cutaneous insulin infusion in a diabetic clinic: patients' choice of treatment. *Diabetic Medicine* 1984;1:267-72.

Deaths of athletes

Recent allegations have been made that several Soviet athletes of the 1950s have died young and that their deaths might be attributable to a history of drug abuse, principally of anabolic steroids.¹ Comparisons have been made with a similar cohort of American athletes, the implication being that Soviet athletes take drugs and Americans do not and that as a result the Soviets die prematurely.

Few athletes or coaches are prepared even to discuss drug taking for fear of appearing either to connive at it or worse still to condone it. The subject is taboo. During the Pan American games of 1983, however, a very efficient dope testing team found that no fewer than 19 athletes had "ingested a banned substance" and a further 13 chose to leave for home before their events were run rather than face a dope test. The offending athletes came from Argentina, Canada, Chile, Colombia, Cuba, Nicaragua, Puerto Rico, the United States, and Venezuela. Plainly drugs are used by athletes on both sides of the iron curtain—and everybody knows it.

Fear of the possible side effects does not seem to deter athletes, their desire to win at all costs taking precedence over possible complications in the future. The real deterrent is fear of being caught, since it results in temporary exclusion from competition. This has led increasingly to the use of drugs which are more difficult to detect than synthetic anabolic steroids, such as the naturally occurring hormones testosterone and growth hormone. Distinguishing between exogenous and endogenously produced hormones has proved extremely difficult.

Athletes who take drugs do so because they believe their performance will improve. There is some evidence that this is true of anabolic steroids: large doses aid recovery from exercise, thus permitting heavier training schedules. Weight also increases, giving an advantage to strength athletes such as lifters and throwers.² Improvements in running and jumping ability are also claimed, but the evidence is anecdotal. Testosterone is said to help in the same ways, but there is no evidence whatever that growth hormone improves performance. Belief in the magic powers of hormones is often unshakeable—in much the same way as is the common belief, despite good evidence to the contrary, that taking extra vitamins makes a person more healthy.

Death of top flight athletes during competition is very unusual. Sudden death has, however, been recorded in more ordinary people engaged in sporting activities. Twelve deaths occurred over six years among the joggers of Rhode Island, all but one due to coronary artery disease, seven times the expected mortality in a sedentary population.³ These and similar fatalities in related sports probably result from cardiac arrhythmias, since there are few other causes of sudden death. Indeed, abnormalities of heart rhythm—for example, heart block and frequent ventricular extrasystoles

—are well known to occur in athletes who train hard.⁴ It may be that exercise simply unmasks a pre-existing heart disorder and that those with unrecognised coronary artery disease simply die rather sooner. Perhaps this might account for early death in a handful of athletes. Any suggestion that Russian athletes are more likely to drop dead than their American counterparts remains, however, highly speculative—drugs or no drugs.

MARK HARRIES

Consultant Physician,
Northwick Park Hospital,
Harrow,
Middlesex HA1 3UJ

1 Rich V. Mortality of Soviet athletes. *Nature* 1984;311:402-3.

2 Hervey GR. What are the effects of anabolic steroids? In: Davies B, Thomas G, eds. *Science and sporting performance*. Oxford: Clarendon Press, 1982:120-36.

3 Thompson PD, Funk EJ, Carleton RA, Sturmer WQ. Incidence of death during jogging in Rhode Island from 1975 through 1980. *JAMA* 1982;247:1535-8.

4 Ector H, Bourgois J, Verlinden M, et al. Bradycardia, ventricular pauses, syncope and sports. *Lancet* 1984;ii:591-4.

Management of delayed puberty

Most doctors are inadequately briefed to deal with the problems that may arise in the pubertal development of boys and girls. Mismanagement may lead to hypogonadal patients in their late teens being treated too late with large doses of sex steroids in order to bring about the changes of puberty quickly. These patients have suffered from waiting in vain to mature before a diagnosis is made, from then facing the physical changes of adolescence more quickly than they can accommodate emotionally, and from an end result of their sexual development which is often cosmetically unsatisfactory.

The key to the proper management of pubertal delay is early recognition of a problem. Half of all children show the first signs of puberty before their 12th birthdays, and in 97% of normal children signs of puberty, usually breast development in the girl and enlargement of the testes in the boy, have appeared by the 14th birthday.¹ If no such signs have appeared by that age investigation is required. Doctors should be cautious in offering a wait and see approach to such a patient; delayed puberty is a physical sign and not a diagnosis. Once it has started, progress through puberty should be orderly with a succession of physical changes taking place over about three years; arrest at any stage requires explanation as much as does a failure to enter puberty.

Some clinicians believe that delaying the induction of puberty in a hypogonadal patient leads to a final taller stature. In fact, since the extent of the adolescent growth spurt decreases the older a patient becomes what is gained by waiting is lost in the growth spurt; delay will not be beneficial. Indeed, patients with multiple pituitary hormone deficiencies who have received maintenance treatment with growth hormone without sex steroids in their teens end up not only short but disproportionately short, having inadequate growth of the spine.²

Puberty results from pulsatile secretion of gonadotrophin releasing hormone.³ Secretion of this hormone begins in utero, and the hypothalamopituitary gonadal axis in the pre-pubertal child is far from quiescent. Examination by ultrasound shows that ovarian follicles in normal prepubertal girls

wax and wane over long periods, and a girl who has gonadal dysgenesis shows signs of oestrogen deficiency before the conventional age of puberty. Concentrations of gonadotrophin progressively rise as puberty advances, and this may be due to a change in amplitude or frequency of the pulses of gonadotrophin releasing hormone (and experimental evidence shows both of these to be critical in reproductive terms) or to a release of the pituitary gonadotrophes from an inhibiting influence. Whichever of these possibilities turns out to be the case the endocrine and physical changes of puberty may be entirely mimicked by pulsatile administration of gonadotrophin releasing hormone.⁴

In a patient with delayed puberty measuring the serum gonadotrophin concentration may help: a raised concentration indicates gonadal failure, but there are problems in diagnosing the prime cause of pubertal delay due to diminished secretion of gonadotrophin. A response of secretion of gonadotrophin to acute administration of gonadotrophin releasing hormone is not helpful: a satisfactory response may be seen with a deficiency of endogenous gonadotrophin releasing hormone secretion, but a negative response may be reversed by repeated administration of gonadotrophin releasing hormone. A more promising approach is to examine the spontaneous pulsatility of gonadotrophin secretion, but unfortunately this means taking samples at frequent intervals throughout the night. A useful non-invasive assessment of gonadotrophin secretion in girls is available through the interpretation of pelvic ultrasound examination, but a similar welcome short cut is not available for boys.

Treatment should take account of the fact that while the fastest maturing girls and boys take about two years to complete all the physical changes of puberty half will have done so over about three years and most over five years.¹ For replacement purposes, therefore, therapeutic agents should be used in small but gradually increasing amounts over a physiological time scale. This time scale requires an early diagnosis and recognition of a problem.

The pulsatile administration of gonadotrophin releasing hormone, at present a research procedure, seems likely to become the treatment of choice since it is the only one likely to confirm long term reproductive capability in a hypogonadotrophic patient. Until this method of treatment becomes routine most hypogonadal patients will continue to be treated by conventional regimens: human chorionic gonadotrophin or testosterone is used in boys followed by a preparation containing follicle stimulating hormone to induce spermatogenesis. In girls only oestrogens are available, since the long term administration of preparations containing gonadotrophins leads to the formation of large ovarian cysts and dysfunctional uterine bleeding.

If human chorionic gonadotrophin is to be used in a boy it should be given in small amounts—say, 500 units a week in the first instance—and gradually increased as plasma concentrations of testosterone rise. Each incremental step should take not less than six months; proceeding more quickly seriously risks overtaking the emotional development of adolescence. If oral preparations of testosterone are to be used similar considerations apply. Injections of testosterone depot preparations should start at a low dose (say, 100 mg at six weekly intervals) or possibly even less than this to achieve an adult plasma testosterone concentration over two years.

In girls ethinyloestradiol should be introduced in a small dose, probably less than 5 µg daily, for about six months. There should be no question of introducing cyclical oestrogen