Male erectile dysfunction—defined as “the inability to achieve or maintain an erection sufficient for sexual intercourse”—is one of the most common sexual dysfunctions in men. Although erectile dysfunction can be primarily psychogenic in origin, most patients have an organic disorder, commonly with some psychogenic overlay. Some men assume that erectile failure is a natural part of the aging process and tolerate it; for others it is devastating. Withdrawal from sexual intimacy because of fear of failure can damage relationships and have a profound effect on overall wellbeing for the couple.

Since erectile dysfunction often accompanies chronic illnesses, such as diabetes mellitus, heart disease, hypertension, and a variety of neurological diseases, physicians from many medical disciplines will see patients with this disorder.

Methods
The publications comprising this review were selected from a formal search of the full Medline database (using the terms erectile dysfunction, impotence, and penile erection). Articles from the authors’ personal collections are also included.

Prevalence
The Massachusetts male aging study measured several health related variables in 1290 men aged 40 to 70 years. Erectile dysfunction was very common. Fifty two per cent of the men reported some degree of impotence—mild in 17.1%, moderate in 25.2%, and complete in 9.6%. Complete impotence was reported by 5% of men at 40 years of age and 15% at 70 years of age; however, a higher prevalence of complete impotence was seen in men with concomitant illnesses. Erectile dysfunction is more common with advancing age, and since the aged population will increase, its prevalence will continue to rise.

Anatomy
The penis is made up of three corpora—the ventral corpus spongiosum and the two dorsal corpora cavernosa—surrounded by the tunica albuginea. The blood supply is provided by the cavernosal arteries, which are branches of the penile artery. Branches of the cavernosal artery, the helicine arteries, open directly into the cavernous spaces. Blood drains from here into post cavernous venules, which coalesce to form larger veins that pierce the tunica albuginea before joining the deep dorsal vein, or the cavernosal and crural veins.

The penile blood vessels and trabecular smooth muscle have both motor sympathetic and parasympathetic innervation from fibres arising in the thoraco-lumbar and lumbosacral regions. The striated muscles outside the tunica albuginea are innervated by lumbosacral somatic nerves. Sympathetic, parasympathetic, and somatic systems act in a coordinated way. Interruption of any of these pathways, particularly the parasympathetic nerves, may preclude normal erections.

Physiology
In the flaccid state, the smooth muscle cells of the penile arteries and the corpora cavernosa are in a state of tone (contraction). Relaxation of the smooth muscle (arterial and cavernosal) causes increased inflow of blood into the lacunar spaces of the corpora cavernosa (fig 1). The arterial pressure expands the relaxed...
trabecular walls, thus expanding the tunica albuginea with subsequent elongation and compression of the draining venules. This mechanism of veno-occlusion restricts the outflow of blood through these channels. After ejaculation or cessation of the erotic stimuli, the smooth muscle surrounding the arteries and the lacunar spaces contracts. The inflow of blood is reduced and the venous drainage of the corporal spaces is opened, returning the penis to the flaccid state. Erection of the penis is thus a haemodynamic event under the control of the autonomic nervous system. Coordination of the neuronal activity from psychogenic stimuli occurs in the hypothalamus while reflexogenic erection involves a polysynaptic coordination in the sacral parasympathetic centres.

Several neurotransmitters are involved in penile erection. A principal neural mediator of penile smooth muscle relaxation, and therefore of erection, is nitric oxide. Nitric oxide accounts for the biological activity of endothelial derived relaxing factor. It is formed from its precursor, L-arginine, by nitric oxide synthase. Nitric oxide activates guanylic cyclase to form intracellular guanosine monophosphate, a potent second messenger molecule for smooth muscle relaxation. The importance of this pathway is shown by the clinical finding that selective inhibitors of phosphodiesterase-5 (which breaks down cyclic guanosine monophosphate) facilitate erection.

Nitric oxide synthase is present in abundance in the pelvic plexus, the cavernous nerves, the dorsal penile nerves, and nerve plexuses in the cavernosal arteries and helicine arteries. A different isoform of nitric oxide synthase located in endothelial cells may be responsible for the relaxation of the corpus cavernosum by nitric oxide in response to haemodynamic shear stress or bradykinin stimulation. Cyclic adenosine monophosphate formation is stimulated by vasoactive intestinal polypeptide and prostanoids (prostaglandin E2, prostaglandin F), which also contribute to penile smooth muscle relaxation.

Aetiology of erectile dysfunction

Normal erectile function requires the coordination of psychological, hormonal, neurological, vascular, and cavernosal factors. Alteration in any one of these factors is sufficient to cause erectile dysfunction. Not uncommonly, a combination of factors is involved.

Chronic systemic illness

Diabetes mellitus, heart disease, and hypertension are all commonly associated with erectile dysfunction. Results from the Massachusetts male aging study showed that the age adjusted prevalence of complete impotence was 28% in treated diabetic patients, 39% in those with treated heart disease, and 15% in men taking antihypertensive treatment. The prevalence in the whole study population was 9.6%. Complete impotence has also been observed to increase with the severity of depression; almost 90% of severely depressed men report complete impotence. Peripheral vascular disease leading to insufficient arterial blood supply is another common cause. In addition, an association between low plasma concentrations of high density lipoprotein and erectile dysfunction has been found. Other diseases such as peptic ulcer, arthritis, and allergy are also associated with an increased prevalence of erectile dysfunction.

Hormonal factors

The role of testosterone in erectile dysfunction is not clear. Some men continue to achieve erection even after castration. The fall in free serum testosterone and increases in concentrations of sex hormone binding globulin with aging may be associated with loss of libido and reduced frequency of erection, but restoration of normal testosterone concentrations does not usually improve sexual function. Patients with hyperprolactinaemia, frequently associated with low testosterone values, can develop low libido and erectile dysfunction by unknown mechanisms. Testosterone replacement treatment, without correction of concurrent hyperprolactinaemia, does not resolve erectile dysfunction associated with hyperprolactinaemia.

Local conditions

Poor blood supply as a result of congenital malformations or trauma is a less common cause of erectile dysfunction that can affect the young male. Peyronie’s disease is a specific condition of the penis in which the development of fibrous plaques in the tunica albuginea, sometimes extending into the erectile tissue, may cause pain (in the early inflammatory stage) and penile deviation, making coitus impossible. Inability to retain pressurised blood in the corpus cavernosum follows disruption of the veno-occlusive mechanism, which can be caused by Peyronie’s disease, congenital, or the result of trauma or surgery.

Drug induced erectile dysfunction

Around 25% of erectile failure seen in clinic patients is caused by medication. Erectile dysfunction may affect 10-20% of patients taking thiazide diuretics, and to a lesser extent, patients who are using ß blocking drugs. This may be a result of reduced perfusion pressure, as blood pressure falls in response to the medication, or probably a direct (but unknown) effect on smooth muscle. Further support for this mechanism comes from the observation that treatment of hypertension with the a adrenergic receptor blockers is not associated with erectile failure, and possibly even enhances pre-existing poor sexual function, despite lowering arterial blood pressure.
Erectile dysfunction commonly complicates antidepressant treatment with both monoamine oxidase inhibitors and tricyclic antidepressants. Benzodiazepines and selective serotonin reuptake inhibitors have been reported to cause erectile failure, decreased libido, or ejaculatory problems. Cimetidine, digoxin, and metoclopramide cause erectile dysfunction, as do anabolic steroids, either through a direct effect on penile tissues or through suppression of normal androgen production.

Up to 75% of patients in alcohol rehabilitation programmes have erectile dysfunction. In chronic alcohol abusers erectile failure may be the result of a combination of psychogenic and organic factors (for example, neuropathy).

Psychogenic causes
Psychogenic influences are the most likely causes of intermittent erectile failure in young men. Anxiety about “performance” may result in inhibitory sympathetic nervous system activity, and anticipatory anxiety can make the condition self perpetuating. A psychogenic component is often present in older men, secondary to an organic cause. Underlying relationship problems are a common cause of erectile failure and this possibility should be explored in men of all ages.

Evaluation
A goal directed approach has been successfully used by workers such as Lue for the management of patients with erectile dysfunction. The patient’s medical and sexual history should be taken, and details of any concomitant medication, tobacco and alcohol consumption, and the presence of risk factors for erectile dysfunction (for example, vascular or surgical) should be noted. Preservation of nocturnal and early morning erections generally means that there is no organic basis for erectile dysfunction. The quality of erections during sleep can be assessed with portable home devices (such as Rigiscan) that measure changes in penile girth and rigidity, or in a sleep laboratory.

Measurement of blood pressure, palpation of peripheral pulses, and a neurological examination should be undertaken, including the bulbocavernous reflex and anal sphincter tone. The secondary sexual characteristics should be examined for signs of hypogonadism and any local abnormality in the external genitalia should be noted. The penis should be palpated for Peyronie’s plaques and the testes examined for size and consistency. Further investigations are likely to be guided by the clinical findings, but should include measurement of free testosterone and prolactin concentrations.

Vascular evaluation of the penis
A complete diagnostic investigation, and therefore a full vascular assessment, may not be important for most patients, since only a few will be treated surgically. The best minimally invasive method currently available for studying arterial blood supply to the penis is colour duplex Doppler ultrasound, which assesses the integrity of the arterial supply to the penis and provides some useful information on the veno-occlusive mechanism. More precise assessment of this mechanism requires specialised invasive tests—cavernosometry and cavernosography—which are performed if surgery is contemplated.

Treatment options
Psychosexual counselling
Patients who have a sizeable psychogenic component may be helped by psychosexual counselling. Since the recognition that an organic element is present in most patients, this approach is increasingly being used in conjunction with pharmacological treatment.

Hormonal therapy
Testosterone may improve erectile dysfunction in some patients with diagnosed hypogonadism. Testosterone should not be used in eugonadal men with erectile dysfunction as it may enhance prostatic hyperplasia or promote the growth of occult prostate cancer. New transdermal formulations of testosterone and dihydrotestosterone, as well as oral formulations without associated liver toxicity, have been developed. Hyperprolactinaemia is usually managed with bromocryptine or similar drugs. Less commonly, surgery is used to remove tumours secreting prolactin.

Drug treatment
Drugs that are currently available have limited effectiveness. Trazodone, given as a single agent, has been effective in some studies, but not others. Side
Vascular surgery

Arterial reconstructive surgery is sometimes indicated in men with arterial occlusive disease, but careful selection of patients is required. The best results are obtained in young patients with isolated arterial lesions following trauma. Venous surgery, with extensive ligation of the veins that drain the corpora cavernosa, is sometimes used as the last resort before the implantation of a penile prosthesis in young men with veno-occlusive disease. The results are generally poor as only 30% of patients report long term improvement.

Conclusions

Although the ideal treatment for erectile dysfunction has not yet been found, important advances have been made. Greater openness in society has stimulated research and made it easier for patients to seek help. However, doctors are generally reluctant to discuss the topic with their patients. Training in the management of sexual dysfunction needs to improve at both undergraduate and postgraduate level. The public too requires better information about the availability of treatment.

Hypopituitarism may develop secondary to pituitary infarction after coronary artery bypass grafting

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continued over
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Pituitary infarction may present in many different ways ranging from the entirely silent to the florid neuro-ophthalmological features of apoplexy. It may occur in a normal or an adenomatous pituitary and may be precipitated by haemodynamic changes. We present two cases of panhypopituitarism which occurred during coronary artery bypass grafting.

Case 1
A 57 year old man was referred to our endocrine unit because of impotence and reduced libido. Twenty months earlier he had undergone coronary artery bypass grafting. Before surgery he had had normal potency, but erectile dysfunction and reduced libido occurred immediately after. Three months before surgery he had complained of tiredness; his concentration of free thyroxine was 3 pmol/l and thyroid stimulating hormone was 50 mU/l. Primary hypothyroidism was diagnosed. He was treated with thyroxine, which led to clinical improvement and normalisation of thyroid function before surgery.

Coronary artery bypass grafting was performed after investigation of exertional chest pain which occurred after myocardial infarction. It was an uncomplicated procedure; the left internal mammary artery was grafted to the left anterior descending artery and the saphenous vein was grafted to the obtuse marginal artery. Recovery immediately after surgery was uneventful and the patient was discharged on the ninth day after surgery despite plasma concentrations of sodium having fallen from a normal preoperative value to 125 mmol/l (normal range 135 to 144 mmol/l). He was readmitted 1 week later with nausea, weakness, a mild fever of 37.5°C, and severe hyponatraemia (plasma sodium concentration 114 mmol/l) (table 1). Urea and potassium concentrations were normal. The results of a full blood count were normal and blood cultures were negative.
The hyponatraemia was thought to be dilutional and attributed to inappropriate secretion of antidiuretic hormone, although no tests were done to confirm this. The fever gradually resolved without intervention. After 3 days during which fluid intake was restricted, the patient's sodium concentrations rose to 120 mmol/l and he was discharged. He did not complain of headache or any other neurological symptoms.

The patient was referred for endocrine evaluation. The patient had hypogonadotrophic hypogonadism; normal thyroid function (he was taking 150 μg thyroxine daily); undetectable concentrations of prolactin; a low concentration of insulin-like growth factor 1, which resulted in reduced urinary excretion of 17-hydroxycorticosteroid (results not shown). There was no evidence of diabetes insipidus. The results of dynamic endocrine assessment are shown in table 2. Magnetic resonance imaging of the pituitary confirmed the suspicion of pituitary infarction (fig 1). The patient was treated with hydrocortisone and testosterone and continued taking thyroxine. His condition improved and libido and potency returned to normal.

### Case 2

A 61 year old man was referred with an 18 month history of increasing malaise and debility and of reduced libido, potency, and frequency of needing to shave. Five vessel coronary artery bypass grafting had been performed 18 months earlier for extensive coronary artery disease. Venous grafts were inserted to the first diagonal branch of the left anterior descending artery, the first and second obtuse marginal arteries, and the patent ductus arteriosus. A left internal mammary artery was inserted to the left anterior descending artery. The procedure and postoperative course were uneventful, but at discharge on the tenth day after surgery the plasma concentration of sodium was 117 mmol/l (table 1).

Ten days after discharge the patient was readmitted as an emergency with general malaise, anorexia, and fever. His temperature was 39°C, his blood pressure was 90/50 mm Hg, and there was dullness to percussion at the right base of chest. He was hyponatraemic with a sodium concentration of 122 mmol/l; urea and potassium concentrations were normal, as were the results of a full blood count. A small right pleural effusion attributed to the previous surgery was seen in a chest x-ray; 300 ml of bloodstained aspirate were obtained from the effusion. The patient was treated for suspected pneumonia with broad spectrum antibiotics and intravenous normal saline. He made a gradual recovery, although his fever was slow to resolve. Cultures of the aspirate and of blood were sterile. Titres of mycoplasma, legionella, and viruses did not rise. The plasma concentration of sodium rose slowly but did not reach normal values. By the time of discharge 11 days later his plasma sodium concentration was 130 mmol/l. He did not complain of headache and did not describe any neurological abnormalities.

The results of the routine investigations performed after referral for endocrine evaluation are shown in table 1. These suggest hypogonadotrophic hypogonadism; the low concentrations of insulin-like growth factor 1 suggest growth hormone deficiency with secondary hypothyroidism. Concentrations of prolactin were undetectable and plasma sodium concentration was low. Together with the other supporting data, the subnormal cortisol response to tetracosactrin confirms the diagnosis of hypothalamic-pituitary-adrenal deficiency occurring secondary to pituitary dysfunction (table 2). There was no evidence of diabetes insipidus. Magnetic resonance imaging of the pituitary confirmed the diagnosis of pituitary infarction (fig 2). Replacement treatment with hydrocortisone, thyroxine, and testosterone led to full recovery with restoration of normal sodium concentrations, potency, libido, and drive.

### Discussion

In both of these cases it seems that pituitary infarction occurred during coronary artery bypass grafting and this led to hyponatraemia shortly after surgery and

### Table 1 Results of endocrine tests on two patients who developed hyponatraemia after coronary artery bypass grafting

<table>
<thead>
<tr>
<th>Case No</th>
<th>Normal range</th>
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<tbody>
<tr>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Plasma sodium (mmol/l):</td>
<td>132-144</td>
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<tr>
<td>Preoperative</td>
<td>136</td>
</tr>
<tr>
<td>Postoperative</td>
<td>125</td>
</tr>
<tr>
<td>At time of readmission</td>
<td>114</td>
</tr>
<tr>
<td>At time of evaluation by endocrine unit</td>
<td>131</td>
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<tr>
<td>Testosterone (pmol/l):</td>
<td>&lt;0.7</td>
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<tr>
<td>Luteinising hormone (IU/l):</td>
<td>1.3</td>
</tr>
<tr>
<td>Follicle stimulating hormone (IU/l):</td>
<td>&lt;0.6</td>
</tr>
<tr>
<td>Prolactin (mU/l):</td>
<td>&lt;79</td>
</tr>
<tr>
<td>Free thyroxine (pmol/l):</td>
<td>18*</td>
</tr>
<tr>
<td>Thymol (mU/l):</td>
<td>0.99</td>
</tr>
</tbody>
</table>

| Hormone measured* | 4.3 | 5.6 |

*Free thyroxine concentration during treatment with 150 μg thyroxine (see text).
†Age related range.

### Table 2 Results of dynamic endocrine tests on two patients with hyponatraemia after coronary artery bypass grafting

<table>
<thead>
<tr>
<th>Hormone measured*</th>
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<th>2</th>
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<tbody>
<tr>
<td>Luteinising hormone releasing factor test</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hormone measured*</td>
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<td></td>
</tr>
<tr>
<td>0 min</td>
<td>0.6</td>
<td>0.8</td>
</tr>
<tr>
<td>20 min</td>
<td>0.9</td>
<td>0.8</td>
</tr>
<tr>
<td>60 min</td>
<td>1.0</td>
<td>0.8</td>
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<table>
<thead>
<tr>
<th>Cortisol (nmol/l):</th>
<th></th>
<th></th>
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<tbody>
<tr>
<td>0 mins</td>
<td>168</td>
<td>270</td>
</tr>
<tr>
<td>30 mins</td>
<td>275</td>
<td>270</td>
</tr>
</tbody>
</table>

*Luteinising hormone (IU/l) measured for case 1 and follicle stimulating hormone (IU/l) measured for case 2.
†Normal cortisol response is >550 nmol/l at 30 minutes.
The clinical presentation in our two patients shows that silent pituitary infarction may present silently in patients after coronary artery bypass grafting. Although both of our patients developed complete anterior hypopituitarism, partial hypopituitarism may occur in some cases. Increased awareness of this clinical complication of coronary artery bypass grafting should lead to earlier diagnosis and treatment.

Fig 1 Magnetic resonance image of pituitary in case 1. Partially empty sellas of pituitary fossa are visible. Arrow shows residue of pituitary tissue.

Fig 2 Magnetic resonance image of pituitary in case 2 taken both without (top) and with (bottom) contrast. Partially empty sellas of pituitary fossa are visible. Arrows show residue of pituitary tissue.

emphasises the intrinsic vulnerability of the normal pituitary vasculature. Pituitary apoplexy has been described after bypass surgery but, in marked contrast to our two patients, each of the 12 cases reported developed acute neuro-ophthalmological problems within 48 hours of surgery. Surgical decompression was necessary in 11 cases; all of these patients had pituitary adenomas and three had been diagnosed before surgery. The apoplectic presentations were presumed to be secondary to necrosis, haemorrhage, and acute swelling of the pre-existing pituitary tumour.

The clinical presentation in our two patients shows that silent pituitary infarction can also occur during coronary artery bypass grafting in patients without evidence of a pituitary tumour. It is unlikely that hypopituitarism was present before surgery because of the patients' clinical histories and because, in the first case, primary hypothyroidism with raised concentrations of thyroid stimulating hormone had been diagnosed three months before surgery. At necropsy Kovacs and Yao found that 15% of their patients who died within 10 days of bypass surgery had pituitary necrosis. Pituitary infarction probably arises secondary to the major haemodynamic changes which occur during coronary artery bypass grafting with extracorporeal circulation. While hypotension, non-pulsatile flow, and microemboli may contribute to ischaemia, anticoagulant treatment is probably the underlying factor that causes apoplexy and intrapituitary haemorrhage. Additionally, subtle neurological deficits are quite frequently encountered in patients undergoing coronary artery bypass grafting. These two cases show that pituitary infarction may present silently in patients after coronary artery bypass grafting. Although both of our patients developed complete anterior hypopituitarism, partial hypopituitarism may occur in some cases. Increased awareness of this clinical complication of coronary artery bypass grafting should lead to earlier diagnosis and treatment.

Commentary: Hypoadrenalism should also be considered in cases of persistent hyponatraemia

P E Belchetz

Coronary artery bypass grafting is being performed with increasing frequency and to great benefit. The number of operations performed in the United Kingdom has risen steadily from 16 000 in 1990 to 22 000 in 1995; mortality fell from 3.7% to 2.7% at the same time (C Munsch, personal communication). A wide range of non-cardiac sequelae are recognised, which include varying degrees of cerebral dysfunction.

The occurrence of pituitary infarction after such surgery can be remarkably silent but may have a seriously debilitating effect, as is clearly described by Davies and Scanlon. Appropriate endocrine replacement treatment is, however, effective. The symptoms which occurred in their two patients are similar to those found in Sheehan's syndrome, especially the long latency before the appearance of clinical features.

The occurrence of pituitary apoplexy after cardiac bypass surgery is well documented and is unlikely to go unnoticed and undiagnosed. The importance of the two cases reported here is the subtle presentation of symptoms of malaise, sexual dysfunction, and persistently high prolactinaemia and splanchnic obesity. I have had similar experiences with a handful of patients—as, I suspect, have other clinicians. Thus what has been described here may be the tip of a sizeable iceberg, the existence of which clinicians should be more aware.

The authors emphasise that the persistent hyponatraemia was an important indicator of the occurrence of pituitary infarction, and they emphasise the likely role of hypoadrenalism as the cause. They dismiss the possibility that the syndrome of inappropriate antidiuretic hormone secretion caused the symptoms; all too often this seems to be the first, and sometimes only, condition thought to cause hyponatraemia. It is important to identify hypoadrenalism when it is the cause of low sodium concentration because treatment with corticosteroids can be life saving, whereas simply restricting fluid intake would be inappropriate. The attribution of hyponatraemia to failure of pituitary adrenocorticotropic hormone secretion may seem puzzling since this hormone primarily affects cortisol secretion rather than aldosterone; however, the reasons are found in the function of glucocorticoid influences on free water clearance in the kidney, rather than the primary influences on sodium metabolism. The osmolar cut off point for the secretion of antidiuretic hormone is reduced in hypocortisolism, so there may be an element of the syndrome of inappropriate antidiuretic hormone secretion in these cases. A further clue to the possibility of hypoadrenalism is the persistent low grade fever seen in both patients; it is, of course, necessary to exclude any infective cause.

These patients were clearly deficient in all six hormones of the anterior pituitary. In cases of partial hypopituitarism in patients with pituitary adenomas there is early loss of secretion of growth hormone and gonadotrophin, although adrenocorticotrophic hormone secretion is preserved, as is thyroid stimulating hormone. Prolactin concentration is unaffected or increased. When hypopituitarism has a vascular aetiology, isolated losses of hormones stimulated by the pituitary-adrenal or pituitary-thyroid axes may occur together with preservation of secretion of gonadotrophin and growth hormone. Additionally, hypoprolactinaemia often occurs. On magnetic resonance imaging or computed tomography, loss of pituitary volume is seen. This is also common in idiopathic hypopituitarism of old age.

The cause of pituitary infarction after coronary artery bypass grafting presumably relates to the cardioplegia, non-pulsatile blood flow, hypotension, and, possibly, embolism or haemorrhage, as discussed by the authors. Acute neuroendocrine changes during cardiopulmonary bypass have been documented. The susceptibility of patients to this complication may be caused by unsuspected pituitary tumours and their vulnerable blood supplies. Hypopituitarism affects mortality from cardiovascular problems. Most pituitary hormone deficiencies are adequately recognised and replaced, with the exception of growth hormone. Growth hormone deficiency is associated with poor cardiac risks factors such as an adverse lipid profile and splanchnic obesity.