resistant to most of the commonly used antituberculosis drugs. In M kansasii infections, however, treatment with three drugs is often effective, in the in-vitro drug resistance being of no prognostic importance. Amikacin, doxycycline, or cotrimoxazole may possibly be of benefit in M marinum infections.

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Prolactinoma: a question of rational treatment

The introduction of assays for human prolactin1 and the use of drugs such as bromocriptine for treating hyperprolactinaemia2 have had a major impact on the diagnosis and initial management of prolactin-secreting tumours. Many problems, however, remain. How common are prolactinomas? What is known of their pathophysiology? What tests can be used to distinguish reliably between prolactinomas and other causes of hyperprolactinaemia? What is the clinical course of the condition? Which patients require treatment? What type of treatment should be given? Only when these questions can be answered satisfactorily shall we be able to formulate a rational policy for long-term management.

Prolactin is principally under inhibitory control by dopamine secreted by the hypothalamus,3 so that in theory either a deficiency of dopamine or decreased sensitivity to it on the part of the pituitary lactotrophs could lead to the development of a prolactinoma. Studies on the function of normal anterior pituitary tissue surrounding tumours suggest that there is decreased hypothalamic secretion of dopamine,4 implying a reduced response of the tumour lactotrophs to dopamine as compared with that of the normal prolactin-secreting cells.6

The hyperprolactinaemia that results then stimulates the release of dopamine.7 Prolactinomas seem to then develop as a primary pituitary disorder and not secondary to hypothalamic disease, so that selective surgical removal of the tumour, preserving anterior pituitary function (microadenomectomy),8 may restore normal hypothalamic control.9 10

Early studies11 suggested that most women with prolactinomas would present in early reproductive life with amenorrhoea and infertility. In fact, any type of menstrual abnormality may be associated with hyperprolactinaemia, including dysfunctional uterine bleeding, regular anovulatory cycles, or cycles deficient in luteal-phase progesterone.12 The incidence of galactorrhoea is variable (30-80%)13 14 depending to a large extent on the care taken by the clinician to examine the breasts and the meaning placed on traces of fluid expressed. Impairment of the visual fields due to an expanding tumour is fortunately rare (occurring in 7% of cases).15 In contrast, men present later (mean 39 years) with impotence (90%) and obesity (48%).16 17 Galactorrhoea is unusual, but many patients have evidence of suprasellar expansion, often reflecting the delay in diagnosis of a prolactinoma as the cause of impotence. In both sexes the clinical and biochemical features of hypogonadism may be reversed by treatment which lowers serum concentrations of prolactin—provided that secretion of pituitary gonadotrophins is adequate.14 15

Hyperprolactinaemia is not always attributable to a prolactinoma: other possibilities include pregnancy, prolactin-stimulating drugs, renal failure, and hypothyroidism.18 19 When the serum concentration of prolactin is consistently high (mean of three samples above 2000 mU/L) a confident diagnosis of a prolactin-secreting macroadenoma can be made if the pituitary fossa is obviously enlarged on plain skull radiographs. (An empty fossa syndrome must be excluded later.) Testing the visual fields and computed tomography are useful in defining the extent of the tumour, but the suprasellar region may be assessed more accurately by positive contrast (metrizamide) cisternography.20 Carotid angiography may be needed before surgery to ensure that the pituitary fossa is not occupied by an aneurysm.21 The effect of the tumour on the function of the rest of the pituitary should be assessed.

Macroadenomas that extend above the sella to affect the optic pathways have usually been decompressed by the transfrontal route with postoperative external irradiation to prevent recurrence19 and treatment with bromocriptine should hyperprolactinaemia persist. More recently treatment with bromocriptine has been shown to shrink pituitary tumours.20 22 and such treatment may therefore be an alternative to neuro-surgery—even in patients with visual impairment—provided that special care is taken in monitoring response to treatment. Macroadenomas without any substantial suprasellar extension do not require transfrontal surgery but are usually too large to be "cured" by transsphenoidal microsurgery.23 24 Bromocriptine is the treatment of choice to lower prolactin concentrations and to restore fertility. While there is no evidence that bromocriptine is teratogenic,25 26 patients are usually advised to discontinue treatment as soon as pregnancy is confirmed. Such patients have a real risk (35%) of expansion of the tumour during pregnancy.27 The risk can be kept to a minimum if the tumour is treated with external pituitary irradiation26 or yttrium-90 implantation.28 Alternatively, an expectant policy may be justifiable,29 with monthly assessment of the visual fields and the serum concentrations of prolactin. Concentrations raised above the expected range for the stage of pregnancy16 or symptoms suggesting enlargement of the tumour are immediate indications for treatment with bromo-
criptine. The prolactin response to oestrogen provocation may be a guide to the risk of expansion of the tumour in pregnancy. Women with macroadenomas who do not intend to have children may be treated with radiotherapy to inhibit growth of the tumour. Radiotherapy may also reduce serum concentrations of prolactin, and so avoid indefinite and expensive treatment with bromocriptine.

The diagnosis of a microprolactinoma is more difficult. The pituitary fossa is not obviously enlarged, and the differential diagnosis rests between prolactinoma, hypothalamic disease, and "functional" hyperprolactinaemia. Subtle abnormalities in the contour of the sella turcica may indicate the presence of a microadenoma, but recent evidence suggests that these abnormalities should be interpreted with caution. Greater reliance should be placed on the serum concentration of prolactin; when this is over 2000 mU/L a microprolactinoma is the likely diagnosis, but the possibility can also be entertained at lower concentrations on the basis of an inhibited response to dynamic testing. Release tests may accurately identify a microprolactinoma, and these are essential before transphenoidal microsurgery—but we are no nearer understanding the pathophysiology of hyperprolactinaemia in patients with normal response. Might these patients also harbour microadenomas? Autonomous secretion by small microprolactinomas may have too small an effect to produce inhibition of the normal lactotrophs via the feedback loop. Nevertheless, whatever the response to dynamic tests, all these patients can be treated with bromocriptine to restore fertility and relieve symptoms. The risk of expansion of a microprolactinoma during pregnancy is small (6%), but monthly follow-up throughout pregnancy is still advisable, with testing of the visual fields and assessment of serum concentrations of prolactin. The commitment of treatment with bromocriptine is presumably indefinite (and expensive), and a case may be made for withholding treatment if the patient is asymptomatic and has finished her reproductive life. Long-term follow-up of the results of transphenoidal microsurgery are now becoming available. Two-thirds of patients achieved a cure for up to eight years after operation. A rational plan of management cannot be made, however, until we learn more of the clinical course of this disorder.

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