cross boundary flow funding for regional specialties would remove from the regional health authority the control over the volume of work that it has at present. Therefore, a proposal that is managerially sound and operates in the private sector and in health services overseas is politically unacceptable in Britain.

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Treating Paget's disease

SIR,—Dr D A Heath's article on the treatment of Paget's disease shows a worrying degree of complacency over this chronic condition (25 April, p 1048). The argument that most patients with this disease do not need to be treated is an old and cherished one, but we believe that Dr Heath has overstated it.

As we have gained experience with the use of intravenous aminohydroxypropylidene diphosphonate in the form of CGP 23339 (not yet commercially available),¹ which is clearly much safer and more effective than oral etidronate, our threshold for treatment has fallen progressively. We have now treated over 100 patients, and a striking feature is that many with rather vague bone pain have general ill health and malaise, which also shows sustained improvement after effective treatment. It seems possible that improved and fairly short treatment regimens with aminohydroxypropylidene diphosphonate will cure the disease without running the major risk of osteomalacia and bone fracture, which are seen with etidronate; the evidence so far is that the drug is extremely safe in both the short and the long term. If this is borne out by further experience the threshold for treatment will fall even lower. Treatment will become routine on diagnosis of Paget's disease, especially in younger patients, who obviously have a long time ahead for the disease to progress. With regard to many of the complications, it is obvious that cure will be the best means of prevention. Leaving it to the drug companies to set the pace for developing and applying new treatments for Paget's disease is in our opinion to shirk our responsibilities.

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1 Cantrill JA, Buckler HM, Anderson DC. Low dose intravenous 3-amino-1-hydroxypropylidene -1,1- bisphosphonate (APD) for the treatment of Paget's disease. *Ann Rheum Dis* 1986;45: 1012-8.

AUTHOR'S REPLY.—Professor Anderson's work on his first 20 cases treated with intravenous aminohydroxypropylidene diphosphonate was known to me when I wrote my review because he was good enough to let me have a preprint of his paper. The essence of his argument is that treatment with aminohydroxypropylidene diphosphonate is safer than oral etidronate and more effective and improves general ill health and malaise. He also seems to be suggesting that treatment may cure the disease.

In my review I discussed the safety of etidronate, and, when used at low doses, it does not seem to carry a risk of clinical osteomalacia or increased fracture rate. Aminohydroxypropylidene diphosphonate is undoubtedly more effective than etidronate in controlling the biochemical markers of the disease, but it remains to be shown that this carries any advantage over mere relief of pain. Informed judgment on the claim to improve ill health is impossible in the absence of proper randomised

controlled comparisons. Placebo responses are recorded in as many as 40% of patients with Paget's disease.

The results in the first 20 patients treated were submitted for publication in June 1986. Presumably the additional 80 patients have therefore been treated in the past 12 months. It seems unwise to talk in terms of cure with such limited follow up.

Whatever Professor Anderson and Mr Cantrill may say, despite the fact that for over eight years favourable reports of aminohydroxypropylidene diphosphonate have appeared, the drug is not available for general prescribing. Possible reasons for this were given in my review. The drug may be obtained on a named patient basis, but the widespread use of the drug in this way would be wrong as it would be bypassing the mechanism for regulating the use of new drugs. Named patient use should be reserved for patients who cannot be managed with existing treatment.

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Bone mineral density in Addison's disease

SIR,—Dr J P Devogelaer and colleagues claim to have produced evidence for an effect of adrenal androgens on bone mass (28 March, p 798). This is a subject that exercised the Leeds group for some time. Our description of reduced adrenal sex hormone concentrations in subjects with early or accelerated postmenopausal osteoporosis and the decline in these hormones in women at about age 60 led us to resurrect the idea of the adrenopause and propose that the postmenopausal woman with accelerated osteoporosis had undergone an early adrenopause.^{1,2} The idea of the adrenopause and that adrenal androgens are important in bone metabolism was, I believe, originally suggested by Albright and Reifenstein in 1948.³ As androgens serve as precursors for oestrogens, however, it has never been clear whether their effect, if any, is direct or indirect through oestrogen production.

The report by Dr Devogelaer and coworkers does not seem to resolve this issue. The rate of calcium loss and the postmenopausal oestrone concentration are known to be related,^{4,6} and the reduced oestrone concentration may therefore account for the lower bone mass in the postmenopausal patients with Addison's disease. The oestrone concentrations reported in their study seem, if anything, rather high.⁷

The preservation of bone in the men does not necessarily mean that the androgens are responsible. Men have an oestrogen concentration above that of postmenopausal women, and it has been suggested that this may contribute to the preservation of bone in aging men.⁴ Dr Devogelaer and colleagues do not report the hormone concentrations in the men with Addison's disease, but it is unlikely that the oestradiol concentrations would be much affected.

If we are looking for an effect of androgens, independent of any action through conversion to oestrogens, then we should look at androgen deficient, oestrogen replete subjects. The ideal model would be postmenopausal patients with Addison's disease receiving oestrogen replacement. The group in the paper by Dr Devogelaer and coworkers who come closest to this are the premenopausal women, who are oestrogen replete but have lost between a half and two thirds of their androstenedione and testosterone and practically all of their dehydroepiandrosterone. These patients, however, have not lost bone.

The relative balance between sex steroids and glucocorticosteroids may be important. Premeno-

pausal women seem to be fairly well protected against the effects of glucocorticoid treatment.⁸ It may well be that high glucocorticosteroid concentrations may be counteracted by high oestrogen concentrations. On the other hand, physiological replacement doses of glucocorticoids might do harm in the presence of extreme sex hormone deprivation—as in postmenopausal patients with Addison's disease.

The precise physiological role of the adrenal sex hormones in older life seems unclear. Why they should be secreted in response to adrenocorticotrophic hormone is also unclear, but it would make an attractive hypothesis to propose that androgen secretion, occurring hand in hand with the physiological secretion of glucocorticoids, protects some parts of the body, such as bone, from the catabolic effects of glucocorticoids. If so, however, whether the effect is direct or through the secondary oestrogen production remains unresolved.

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HIV testing and differential diagnosis

SIR,—Among the excellent points made in the ABC of AIDS, one recommendation sets my teeth on edge. This is the unqualified insistence that the diagnosis should be discussed with the patient before testing for human immunodeficiency virus (HIV).

In some contexts this is clearly excellent advice: in voluntary screening programmes, in genitourinary medicine clinics, when the patient is known to be in a high risk group, and when the patient expresses concern about the possibility. However, we can expect increasingly to see the condition presenting in general practice and in clinics of general and respiratory medicine, neurology, gastroenterology, and dermatology. The proportion of heterosexuals affected is likely to increase and patients may not be aware of exposure to the virus. Previously unsuspected groups may prove to be at risk. In any such individual patient HIV infection may be only one possibility, perhaps a remote one, in a long list of differential diagnoses, but it needs to be excluded or confirmed in the patient's interest and in the wider interest of following the progress of the epidemic.

Many of us would be deterred from ordering HIV antibody testing if we felt that standard practice entailed facing the patient with the possibility of AIDS in such circumstances. After all, we do not discuss the implications of leukaemia before ordering a white cell count or of bronchial carcinoma when ordering a chest radiograph. Even after receiving a positive or suspicious result we are likely to seek confirmation, either by repeating the