Fig. 2—Bromocriptine inhibition of hG.H. and prolaction secretion by somatotrophic adenoma in culture.

due to the prolonged exposure (6 days). hG.H. secretion from another somatotrophic adenoma (data not shown) was inhibited 76-8±2.4% within 24 h by bromocriptine, remained inhibited for 2 days, and subsequently increased in three of four cultures in 24 h when bromocriptine was withdrawn. This change just failed to achieve statistical significance. Further reduction in exposure-time and dosage should allow recovery to be demonstrated.

Despite the marked effects of bromocriptine on tumour hormone secretion, two of four somatotropic adenomas cultured under identical conditions were unaffected (thereby excluding possibilities of general toxicity). These two tumours came from patients with the highest serum-hG.H. of those examined (75 and 1937 mI.u./l). Although we have not yet examined correlations between in-vivo and in-vitro responders, this variability confirms previous reports of bromocriptine effects in acromegaly, suggesting the defect to be within the tumour itself.

The culture techniques described will allow examination of the biochemical nature of these variable responses as well as the cellular mechanisms by which bromocriptine directly suppresses hormone secretion by human mammotrophic and somatotropic tumours.

K. M. thanks the N.I.A.M.D.D., U.S.A., for prolactin assay reagents, University of London Central Research Fund and Humane Research Trust for finance, the neurosurgeons who supplied tumour material, and Sandoz for the bromocriptine.

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M. C. WILKINSON

TUBERCULOSIS IN CERVICAL GLANDS

SIR,—In a Hunterian lecture I showed that the low frequency of tuberculous adenitis associated with skeletal tuberculosis in adults is matched by a similar low frequency associated with pulmonary tuberculosis in adults—namely, 3%. Mr Rocker (July 2, p. 48) reports that cervical-gland biopsy in a pregnant woman aged 32 revealed tuberculosis and that this created a problem because the administration of rifampicin might have a teratogenic effect; the pregnancy was terminated.

I suggest that neither rifampicin nor termination were needed. The presence of tuberculosis in cervical glands need not have been clinically dangerous. The mechanism of immune surveillance could well have safeguarded the woman, especially during pregnancy because estrogens are greatly increased during pregnancy and are known to have a stimulant effect on the macrophages of the mononuclear phagocytic system.

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M. C. WILKINSON

SENSITIVE ASSAY FOR BIOLOGICALLY ACTIVE FRAGMENT OF HUMAN PARATHYROID HORMONE

SIR.—Ideally a radioimmunoassay should measure biologically active molecules. Parathyroid hormone (P.T.H.) in the circulation consists of intact hormone and smaller fragments. The predominant molecules are the mid and C-terminal fragments, which are not biologically active. We have developed a radioimmunoassay specific for the N-terminal portion of human parathyroid hormone (hP.T.H.), which is both sensitive and homologous.

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Although radioimmunoassays for hP.T.H. have been in use for more than a decade, measurement of the N-terminal portion has been unsatisfactory. Attempts to develop homologous assays for the human N-terminal fragment have been frustrated by the difficulty in generating antibodies sensitive enough to measure the small amounts in plasma and by controversy over the amino acid sequence of the native fragment. Two structures, differing by only three amino acids, have been proposed, and conflicting data have been obtained in immunological studies. Moreover, sensitive heterologous or homologous assays for the N-terminal portion of hP.T.H. result in significant overlap between the values in normal and hyperparathyroid sera. Our radioimmunoassay discriminates well between euparathyroid and hyperparathyroid states. We use a 1–34 fragment synthesised following the sequence of Niall et al. (1–34 hP.T.H. N) and antibodies raised against this fragment in the goat. In this immunochromosomal system (anti 1–34 antibodies, labelled and unlabelled 1–34 peptide) hP.T.H. extracted from normal plasma by affinity chromatography, or from para-

The same samples from normal and hyperparathyroid patients were simultaneously assayed using a C-terminal heterologous assay for hP.T.H., labelled and unlabelled pure bovine parathyroid hormone, and antibodies raised in the guinea pig against this molecule. Fig. 2 shows that our assay discriminates well between hyperparathyroid and euparathyroid states. There is some overlap (8%) between normal and abnormal plasmas; a similar degree of overlap has been reported for C-terminal assays. Good discrimination can be obtained when the N-terminal assay is used, though the overlap (14%) is slightly bigger than with the C-terminal assay.

The values detected by the N and C assays were positively correlated (r=0.65; p<0.001). This high correlation could be due to the detection by both assays of the circulating intact molecule or, more probably, to the estimation of amino and carboxy terminal fragments resulting from cleavage of the intact molecule or its fragments.

Our results differ from those done by other workers using heterologous or homologous assays for the N-terminal fragment of hP.T.H. where there was an important overlap between values in controls and disease states. This suggests that the N-terminal fragment in peripheral blood is heterogeneous and that the overlap seen with assays specific for this fragment may depend on the metabolites of this fragment that are detected. Our results with antibodies raised against the Niall sequence substantiate those of Segre and Potts for heterologous radioimmunoassays reacting with the N-terminal fragment (Niall). The low cross-reaction of bovine P.T.H. in our radioimmunoassay implies that our antibodies are directed towards regions in which the primary aminoacid sequence is different or that they are sensitive to conformational changes imposed on the molecule due to these differences in primary structure. The antibody used showed a good cross-reaction with the 1–34 sequence synthesised in our laboratory according to the sequence proposed by Brewer et al. so our results do not conflict with the results using antibodies raised against hP.T.H. which showed immunological similarity between the 1–84 hP.T.H. and the 1–34 human peptide (Brewer sequence). The antibody used is probably directed to antigenic determinants shared by the two proposed sequences.

Radioimmunoassays based on the Niall sequence against the N-terminal fragment of hP.T.H. are useful in the detection of hyperparathyroidism. The simultaneously estimation of N and C circulating fragments will be of a considerable value for a better understanding and diagnosis of primary or secondary hyperparathyroidism and for the study of the heterogeneity of the biologically active fragment of hP.T.H. and its metabolic fate. Overlap between normal and hyperparathyroid values is slight.