SIR,—I should like to make a few comments on the report by Mr. D. Dow and Mr. R. H. Whitaker about prostatic contribution to normal acid phosphatase (21 November, p. 470).

Fifty men who had undergone transvesical prostatectomy had their acid phosphatase determined before and after operation. In all benign hyperplasia was substantiated by histological examination. Acid phosphatase was determined according to Kind and King¹ as modified by Hansen.² Our "normal" population comprised 128 men and 128 women, drawn from the W.H.O. blood-pressure-investigation project in Bergen (see Table). No difference in acid phosphatase content in serum could be found in patients before and after removal of the prostate, neither could any significant difference in acid phosphatase content be found between men and women. The contribution to serum acid phosphatase from the normal (or the hyperplastic) prostate is clearly insignificant.

It is more difficult to discuss the problem of acid phosphatase and prostatic cancer. To ascribe raised phosphatase levels to metastases is hardly justified.³ On the other hand, normal acid phosphatase levels in carcinoma are no proof against metastases.⁴ In our experience, the finding of a raised serum acid phosphatase, and especially of the tartrate-labile fraction (upper limit of normal 1.5 u/l.) is highly suspicious of carcinoma or infarction of the prostate, and the possibility can be excluded only by thorough histological examination.

Determination of serum acid phosphatase might be of value during surgical intervention on a carcinomatous gland. In hyperphosphataemic patients, if the carcinoma is confined to the gland, a successful surgical removal is followed by an immediate fall to normal level (see Fig.). In most patients given oestrogens the

wholly done by an automated method⁶ with the sensitivity preserved. Though the value of L-tartrate is questioned,⁷ I feel this merits a place because, firstly, haemolysed sera could not be analysed without its use, and, secondly, because tartrate is a highly specific competitive inhibitor of prostatic acid phosphatase.

In conclusion, I believe determination of serum acid phosphatase deserves its place in urological practice. Its value and limitation should however, be remembered: normal levels are of no value; raised levels, especially of the tartrate-labile fraction, are highly suspicious of carcinoma (or infarction) of the prostate. Finally, careful sampling, with due regard to any drugs the patient is taking, the lability of the enzyme, substrate specificity, urological intervention, and status of the haematopoietic tissue is mandatory.⁸—I am, etc.,

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Hypertension during Chlorimipramine Therapy

SIR,—During a clinical preliminary investigation of chlorimipramine (a new tricyclic antidepressant) involving 26 patients with depression three cases of hypertension developed in initially normotensive patients.¹

A 54-year-old woman who five years earlier had been treated with guanethidine and hydro-flumethiazide for hypertension was treated with chlorimipramine with rapid increase in dosage to 100 mg. Blood pressure was initially 150/100. Chlorimipramine had to be withdrawn because of rise in blood pressure to 180/115 and 190/125, increasing to 180/140 and 200/120. Ten days after withdrawal of the drug blood pressure returned to normal.

A 63-year-old man in poor condition because of arteriosclerosis and diabetes mellitus was treated daily with 50 mg chlorimipramine. The highest blood pressure before treatment was 160/100. After 16 days the blood pressure, which throughout the treatment had been in the region of 160/80, was found on three consecutive days to have risen to 185/100, 205/100, and 220/110. Chlorimipramine was withdrawn and the blood pressure fell to normal.

Chlorimipramine was given to a 58-year-old woman whose initial blood pressure was 150/105. The dosage was increased to 100 mg daily. After five days the blood pressure in the supine position was 220/150, while in the upright position after five minutes it was 190/140. After

withdrawal of chlorimipramine the blood pressure fell to its original level in the course of four days.

Animal experiments with chlorimipramine² have demonstrated that the drug potentiates the effect of the catecholamines noradrenaline and adrenaline. That tricyclic antidepressant drugs potentiate in man also, the blood pressure raising effect of noradrenaline and adrenaline has been investigated quantitatively by Svedmyr.³

The three patients in our department who developed hypertension had not received adrenaline, noradrenaline, or monoamine-oxidase inhibitors. They had been given chlorimipramine only and after withdrawal of the drug the blood pressure returned to normal without any specific therapy. This strengthens the impression that chlorimipramine was the causative factor. It should be noticed that the three patients were elderly, the youngest was 54 years of age, and that their blood pressure before treatment was at the upper limit of normal.

It was not investigated whether the food contained indirectly acting catecholamines such as tyramine, but it seems unlikely that the mechanism causing the rise in blood pressure is the same as with monoamine-oxidase inhibitors, since in animal experiments it has been shown that chlorimipramine inhibits the indirectly acting catecholamines.² A blockade of the amine uptake in noradrenaline neurones resulting in an increasing extracellular concentration of noradrenaline³ could be the cause. As Carlsson⁴ has shown this is not very probable, as chlorimipramine and imipramine are the weakest of the tricyclic antidepressants to block the amine uptake. Thus no pathophysiological explanation of the rise in blood pressure can yet be given. —I am, etc.,

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Female Medical Practice

SIR,—It was interesting to read in *One Hundred Years Ago* (2 January, p. 37) of the announcement of Miss Elizabeth Garrett's marriage and its compatibility with female medical practice.

Interesting in that 100 years later marriage and female medical practice as the career structure is arranged at present are far from completely compatible. Most women doctors find themselves dropping out or filtered off into general practice or peripheral subjects such as family planning, and it is only the exceptions who combine a family with a career in the mainstream of medicine. This is surely not just from a lack of will on their part, but unfortunately reflects the extent to which the medical profession has advanced in the last 100 years.—I am, etc.,

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Acid phosphatase levels in a 76-year-old man with carcinoma of the prostate without metastases or local extension outside the capsule who had transvesical prostatectomy.

acid phosphatase is found to be within normal limits, regardless of the progress of the disease.³

Mr. Dow and Mr. Whitaker find that estimating the acid phosphatase is too time-consuming, and, performed as described, I agree. However, the determination can be simplified,^{2,5} or

Ages and Acid Phosphatase Levels

Group	No	Average age (Range)	Total S.A.P. (u/l.)	Tartrate labile S.A.P. (u/l.)
			Mean $\pm$ S.D. of mean	
Healthy women	128	44 (27-73)	2.5 $\pm$ 0.18 (1.3-4.6)	0.6 $\pm$ 0.05 (0.0-1.6)
Healthy men	128	50 (28-72)	2.9 $\pm$ 0.21 (0.9-4.9)	0.8 $\pm$ 0.08 (0.0-1.8)
Men with benign prostatic hyperplasia				
Preoperatively	50	70 (54-87)	2.8 $\pm$ 0.19 (1.5-4.4)	0.6 $\pm$ 0.05 (0.2-1.5)
Postoperatively	50	70 (54-87)	2.6 $\pm$ 0.16 (1.4-4.4)	0.7 $\pm$ 0.06 (0.1-1.5)