

Correspondence

Letters to the Editor should not exceed 500 words.

Lumps in the Breast

SIR,—Your brief leading article on "Lumps in the Breast" (2 July, p. 1), though containing much sound advice, cannot be completely endorsed. The assumption that diffuse lumps are probably benign and that discrete lumps are probably malignant is much too broad a generalization. A proper perspective is essential. It is traditional to equate cancer with a lump: "No lump, no cancer," and "The lump is the cancer." This is outmoded by the conception that early cancer is microscopic and that a cancerous lump is a late cancer. It is never possible to say that any breast does not contain a cancer until that breast has been serially sectioned and every field examined, which is not only an absurd but also an impractical proposal.

We are left with a spectrum of possibilities. At one end is the obvious, typical contracted cancer where there can be no doubt of the diagnosis on clinical grounds, because there is nothing else like it. Near to it is the picture of a localized firm mass deforming the breast and attached to skin. Here the probability of cancer is great, but not certain, for there are conditions such as duct ectasia, fat necrosis, and chronic abscess which are like it. At the other end of the spectrum are lumps in the developed breasts of teenage girls. Here the probability of cancer is extremely small, though a few cases have been reported. Such a lump is likely to be hyperplastic mastitis or fibroadenoma, and examination will settle the diagnosis in 99.9% of cases.

Between these clear limits lie numerous categories of breast disease where the probability of cancer is less certain on purely clinical grounds. One of them is the numerically large group in which a solitary lump has the physical signs suggesting fluctuation. Aspiration transforms the possibilities simply and dramatically, and is a most valuable procedure. If there is no residual mass the probability of cancer is reduced to that of any woman of the same age group who has no palpable lump. The probability is not abolished, nor even reduced to that of the teenager with a breast lump.

The group which corresponds to your third "finding"—"the typical rubbery, nodular thickening of so-called chronic mastitis"—has the same probability of cancer being present as the woman whose solitary cyst has just been aspirated. It is not satisfactory to reassure the patient that the condition "will not become malignant" and to "report again only if a discrete lump is ever found." The probability of breast cancer can be better assessed if the patient is told "I do not think it is a cancer, but I want to see you again after your next period and re-examine you. There may be a change

in the findings which will enable me to give you greater reassurance." A diagnosis of chronic mastitis at one examination will often be borne out by re-examination, because the condition is subsiding, but in many cases the initial diagnosis is wrong and cancer is found to be present by submitting all the lumps, in both breasts if necessary, to histological examination.

Eczema of an inverted nipple is another example of uncertain probability which can be made more certain by intermediate procedures such as biopsy, smear technique, or brief but efficient local treatment. In cases of discharge from the nipple the probability of cancer is not high unless there is a co-existing lump.

Enough has been said to make it clear that the most important breast disease, cancer, cannot be confined within the category of a lump in the breast. Nevertheless, the finding of a lump in the breast is going to remain for a long time the most important way of finding and treating breast cancer. I am troubled by the fact that the average size of lump discovered by women in this country is about 1½ in. (3.2 cm.). In many of these cases, perhaps 50% or more, metastasis has already taken place. Nobody knows how small breast carcinoma has to be before the metastasis rate drops significantly but it is reasonable to suppose there is a critical size, perhaps different for different types of cancer. Dr. Haagensen has written about American women who discover lumps 4 mm. in diameter in their own breasts.¹ Is it too much to hope that a majority of British women could be trained to find similarly sized lumps by routinely palpating their own breasts? I feel they might do much better than any corps of examiners, however careful and experienced.—I am, etc.,

Birmingham.

FAUSET WELSH.

REFERENCE

- ¹ Haagensen, C. D., *Diseases of the Breast*, 1956. Saunders, Philadelphia.

SIR,—May I make two comments on your leading article on the management of lumps in the breast (2 July, p. 1)? The first concerns the treatment of cysts. While you admit that aspiration, which "some surgeons advocate" is "a reasonable procedure," one has the impression that you really favour excision. May I voice the opinion, which I share with many other surgeons in all parts of the world, that aspiration is the correct treatment for cysts of the breast. The patient is at once relieved of her lump, and with it also her anxiety and apprehension. Moreover, with the precautions you mention, which with the addition in cases of doubt of cytological examination of the aspirated

fluid will exclude the rare tumour cyst, aspiration is safe. There can be few more completely satisfactory therapeutic procedures in the whole of medicine.

My second criticism concerns your emphasis on the importance of biopsy of doubtful breast lumps without "more than a few days' delay." One thing that the massive surgical attack on cancer during the present century has shown is that, leaving aside incidental mechanical complications such as obstruction, which do not apply in the breast, the important factor in prognosis in cancer in all parts of the body is the inherent biological malignancy of the disease. To continue to spread the impression that prognosis depends on any important degree on treating the disease as an acute emergency is not only propagating an untruth but the resultant psychological and social havoc of such a philosophy is an important cause of the attitude of panic which malignant disease generates. In the case of the breast, a few weeks' observation in doubtful cases is often helpful. Not only does this give the opportunity for fugitive lumps to disappear, but the behaviour of the tumour during this time may occasionally give guidance on the type of treatment indicated.—I am, etc.,

London W.1.

DAVID H. PATEY.

Therapy with Carbenoxolone

SIR,—I have read with interest the paper by Dr. S. D. Mahomed *et al.*, on "Hypokalaemia . . . with Carbenoxolone" (25 June, p. 1581), but I find it difficult to agree with the authors' conclusion that, "as the only other medication was with a barbiturate," carbenoxolone alone should be considered responsible for this effect.

Drugs of this group—that is, derivatives of glycyrrhetic acid—are known to exhibit, in addition to their ulcer-healing activity, a potentiation of the adrenocortical hormones, resulting in mineralo-corticoid-like effects.¹ The clinical picture, which has been observed in only a minority of patients receiving carbenoxolone, is suggestive of raised plasma levels of aldosterone, or cortisol,² and has been attributed to competitive inhibition of the metabolic reactions that deactivate these hormones.³

The administration of barbiturates and other drugs has for some time been known to stimulate the hepatic microsomal enzymes that metabolize drugs and endogenous steroids.⁴ Metabolic reactions which involve hydroxylation are particularly affected, and a barbiturate has been shown to increase the extra-adrenal hydroxylation of cortisol in man.⁵ The biosynthesis of both aldosterone and cortisol requires several hydroxylations of the steroid molecule, and could be subject to stimulation by barbiturates. Moreover, a drug-induced biosynthesis of corticosteroids coupled with the competitive inhibition of their hepatic deactivation by other drugs could interfere with the normal feed-back

mechanisms which control the plasma levels of these hormones.

Although the clinical significance of the effects of barbiturates and other drugs on the biosynthesis of adrenal corticosteroids has yet to be elucidated, and may not even become manifest unless subsequent catabolic processes are simultaneously inhibited, it is hazardous to ignore the potential effects indicated by observations on extra-adrenal tissues. Moreover, it is precarious to attribute to one chemical entity the toxic side-effects which result from the use of a combination of drugs.

Today, the tendency to multiple prescription (polypharmacy) is widespread, but unfortunately the interactions between the different drugs is too often ignored. Not only drugs, but also other chemical substances of the diet and the environment, such as naturally occurring non-nutrients, food and cosmetic additives, pesticides and industrial chemicals, may also affect the metabolism of drugs and endogenous steroid hormones, resulting in changes in their pharmacological and physiological activities. The need for more research into these phenomena is manifestly urgent, for only a true understanding of the mechanisms involved will provide the necessary information to enable a prediction of these drug interactions and thereby the means to avoid their undesirable toxic side-effects.—I am, etc.,

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REFERENCES

- 1 Finney, R. S. H., and Tárnoky, A. L., *J. Pharm. Pharmacol.*, 1960, **12**, 49.
- 2 Hausmann, W., and Tárnoky, A. L., *Brit. J. Pharmacol.*, 1966, **26**, 412.
- 3 Kumagai, A., Yano, S., Otomo, M., and Takeuchi, K., *Endocr. jap.*, 1957, **4**, 17.
- 4 Conney, A. H., Schneidman, K., Jacobson, M., and Kuntzman, R., *Ann. N.Y. Acad. Sci.*, 1965, **123**, 98.
- 5 Bernstein, S., and Klaiber, E. L., *J. clin. Endocr.*, 1965, **25**, 293.

SIR,—I have read with interest the paper by Dr. S. D. Mohamed and colleagues on hypokalaemia (25 June, p. 1581) and the letter of Dr. T. N. Morgan and others (2 July, p. 48), in which the authors attribute side-effects to carbenoxolone sodium.

In view of the high dosage of carbenoxolone used in these two cases and the undue length of treatment, I feel we must, in the interests of your readers, bring to their attention the recommended dosage of Biogastrone brand of carbenoxolone sodium tablets in the treatment of gastric ulcers. This is: two 50 mg. tablets three times daily after meals (300 mg./day) for the first week, followed by one tablet three times daily (150 mg./day) for subsequent weeks until the ulcer has healed. It is normally expected that the ulcer will be healed within four weeks, when radiological examination should be made to ascertain this. If it is found necessary for the treatment to be continued beyond this period it is recommended that Biogastrone be given for five days a week only at the reduced dose.

There is also a warning that sodium and water retention may occur in a proportion of patients, resulting in ankle and pretibial oedema or hypertension. These side-effects normally disappear on discontinuing Bio-

gastrone for two or three days or by administering a thiazide diuretic together with potassium supplements. Hypokalaemia may occur in some patients and may require treatment with potassium supplements.

This information has been sent to all doctors on a number of occasions in the past.—I am, etc.,

London E.C.1.

M. H. KHAN,
Research Division,
Biorex Laboratories Ltd.

Male Sterilization

SIR.—Your admirable leading article on sterilization in man (25 June, p. 1553), will not, I hope, be taken as a final judgement on this subject. The need for population control is agreed by almost everybody. The various methods, however, have not been so universally agreed.

(1) The occlusive devices, such as the diaphragm, are disliked by many women and fail in others at a critical time when they already have a sufficient family. These women seek other methods.

(2) "The Pill" is known to be completely effective, and most specialists believe its continued use is not accompanied by any serious complications. But this is not agreed by all investigators, and it is known that many women do not feel well after taking the pill for one or more years.

(3) The intrauterine devices of various shapes and sizes seem little different in principle from the ring first introduced over 40 years ago, and are even less acceptable to many patients and gynaecologists.

(4) Vasectomy, being a simple operation, which if carefully performed should not be accompanied by any complications, would appear to merit as serious consideration as the pill and the intrauterine devices.

It is true that reversal cannot be guaranteed, but if the original operation has been properly performed, especially as regards site, the success rate should be 80% or over. With percutaneous coagulation occlusion, which leaves the continuity of the vas uninterrupted, the rate will, I trust, be better; and the silicon plug introduced by high-pressure syringe promises an even higher percentage of efficient reversible artificial sterility. It is, however, too early to evaluate this method, which was invented and elaborated only recently by Dr. George Hrdlicka at Columbia University,¹ where experiments are still proceeding.

In any case the operation should not be sought for convenience or with the intention of subsequent reversal, and is best suited for "failed contraception" cases, and especially where frustrations and fears are affecting the health of a couple and the welfare of a marriage. I have only twice received a frivolous request—the last time a few weeks ago when a young student sought it as a means of convenience until he and his girl friend could get married and afford a family. Typical of the usual request is the one I received from a doctor on 28 June 1966:

"This man is happily married with three children. He and his wife do not want any more children, yet she finds the more usual forms of birth control repugnant, and this includes the "pill." As this is leading to friction between husband and wife, he has come to me to know if he can be sterilized by vasectomy,

and I am writing to ask if you would see him with a view to performing the operation."

I submit that this letter presents adequate and proper reasons for doing a vasectomy.—I am, etc.,

London W.1.

REYNOLD H. BOYD.

REFERENCE

- 1 Personal communication.

SIR,—One of the difficulties to be faced in the performance of sterilization of the male (23 June, p. 1553) is the real risk of psychological trauma leading to psychological impotence. On these grounds I advise the couple seeking my advice that the safety of the marriage is better preserved by sterilization of the woman. I well remember that during the war years, when considering the provision of body armour for soldiers, it was felt that armour for the face and genital areas could be recommended because of the possible grave psychological danger carried by wounds in such areas.—I am, etc.,

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M. JEFFREY.

Rectal Ether in Intractable Status Asthmaticus

SIR,—Death from intractable status asthmaticus is usually due to asphyxia from respiratory obstruction. The majority of cases respond to treatment with bronchodilator drugs, antibiotics, and steroid therapy, and may require correction of acidosis. Ether is a time-honoured bronchodilator independent of arterial blood pH, but the administration of an effective dose by inhalation is extremely difficult because of the patient's small tidal volume and the physical properties of the gas. Hence the administration by the rectal route in the following case.

A man of 45 years was admitted to hospital in severe status asthmaticus. He had suffered from infrequent attacks of bronchial asthma during the preceding 10 years easily controlled with sublingual isoprenaline until one year ago, when he first required admission to hospital. He recovered fairly quickly on that occasion with mild sedation and bronchodilator drugs. Four months ago he was admitted for a second time. This attack did not respond to conventional bronchodilators and he was given a 16-day course of steroids, on which he soon improved.

On his present admission he was dyspnoeic and had marked expiratory wheezing. He was given aminophylline and 100 mg. of hydrocortisone intravenously, a second course of prednisolone was started, and he was given antibiotics. He was doing well until the fourth day, when he had a relapse. His condition deteriorated over the next eight hours despite aminophylline and six 100-mg. doses of intravenous hydrocortisone. He was cyanosed, his chest was fixed in inspiration, pulse rate was 160 per minute, and blood pressure 80/?. It was decided, therefore, to give him rectal ether, and a solution of anaesthetic ether 65% was well mixed with olive oil 35% warmed, and 100 ml. of it slowly administered. He improved enough in 30 minutes to accept 30% oxygen by face mask. Cyanosis disappeared, pulse rate dropped to 120/minute, and blood pressure rose to 100/60. His recovery thereafter was uneventful.

In cases of status asthmaticus not responding to standard treatment, general anaesthesia and intubation using thiopentone, suxamethonium, nitrous oxide, and oxygen has