# CORRESPONDENCE

*Correspondents are asked to be brief*



## One Thousand Vasectomies

SIR,—The article by the staff of the Margaret Pyke Centre on vasectomy (27 October, p. 216) is a timely and reasoned approach to a problem about which we as yet still do not have accurate information. This is an emotive subject because it affects the public at large in a most sensitive field and it has also been dragged into the political arena. I think the authors have been wise to confine themselves to objective analysis.

This publication has coincided with a review of a series of 223 patients of my own who underwent bilateral vasectomy and I would like the opportunity to comment through your columns. I undertake my own counselling, not because I do not have any ancillary help but because I believe that it is incumbent upon a surgeon who is carrying out an operation to be aware of the implications of that procedure and not merely to act as a technician. I emphasize that the operation I perform is absolutely irreversible, but I note that the authors use the words "virtually irreversible"; this indicates equivocation in their own mind and this will undoubtedly be transmitted to the patient, particularly if he is pressing. As with other programmes which are aimed at otherwise well people (cancer screening, etc.), I find that my patients consist of the more highly motivated members of the middle and artisan classes.

The burden of the article from the surgical point of view was concerned with the assessment of sterility and whether the presence of non-motile spermatozoa in the ejaculate was of significance. The authors state, however, that many of the specimens were examined up to 48 hours after ejaculation, and after this interval it would be surprising if any spermatozoa were motile; when fresh, however, they would still retain their potency. Much of the doubt about the after-effects of the operation in terms of fertility would be relieved by a different and more efficient surgical technique. My practice has been not only to resect a minimum of 2·5 cm of the vas on each side, but to double each end back on itself for a distance of 1·5 cm and double-ligate each end with a non-absorbable suture. This effectively destroys a minimum of 7·5 cm of the vas; I take care to replace the ends in the anatomical position so that the distance between them is maintained. I submit that the worrying sperm granulomata found in five of the published cases would not be possible under these circumstances. There is a disadvantage, however, in that efficient mobilization of the vas is painful and requires a general anaesthetic; there is more postoperative pain in these cases than those treated under a local anaesthetic, but this subsides within a few days. In no case have I found it necessary to reoperate for haematoma and there has been no incidence of scrotal infection; in one case the wound gaped owing to excessive tension on the skin sutures which cut through.

Assessment of sterility has been left to the end of the fourth month, by which time 91% of patients produce two specimens which contain no spermatozoa at all. The remainder have been reassessed monthly after producing two further specimens and all have become azoospermic within a further four months, except for three patients in whom this result was not achieved until 12, 14, and 15 months after operation, respectively. One of the latter patients was advised to undergo reexploration, but he refused and the semen later became negative.

I would agree with the authors that there is no such thing as a guarantee in medicine, but I believe that with a radical and efficient technique the possibility of conception is minimal, and certainly in this smaller series it has never arisen. The Margaret Pyke Centre obviously offers a valuable service which is based on volume and a large turnover; I would suspect, however, that a more individual approach to each patient, though more time-consuming and requiring more resources, may in the long run be more efficient.—I am, etc.,

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SIR,—May I comment upon the series of 1,000 vasectomies reported by the staff of the Margaret Pyke Centre (27 October, p. 216)?

It is stated that after vasectomy "within 48 hours of collection each [semen] specimen was . . . examined . . . for the presence of spermatozoa. . . ." As will be known by any doctor practising artificial insemination by donor for infertility, it is essential for semen to be examined within two hours of ejaculation in order to assess sperm motility and viability. I would expect no sperms to be motile after 48 hours and the great majority to be dead. Delay in examination may explain why some patients' wives subsequently

become pregnant: the semen was always fertile—and there is no question of non-motile sperms becoming motile, nor of the suggestion that non-motile sperms could cause pregnancy.

One patient in the authors' series had a serious staphylococcal abscess and sinus "which continued to discharge until the silk suture was extruded from the wound." To use black silk in order to "permit subsequent identification" shows a lack of confidence in the operator's method. (I gave up using silk to ligate the vas after seeing several stitch abscesses with silk protruding from the wound.) In my series of 240 vasectomies, using catgut for ligating the vasae, I have never had a stitch abscess or skin infection.

Finally, may I venture an explanation for the large number of patients who were still producing sperms 6-18 months after vasectomy. Often the vas is long, tortuous, and very mobile, and it is quite easy to ligate and remove a section of the same vas twice. To avoid this it is essential to open the scrotum well away from the midline and to bear this possibility in mind.—I am, etc.,

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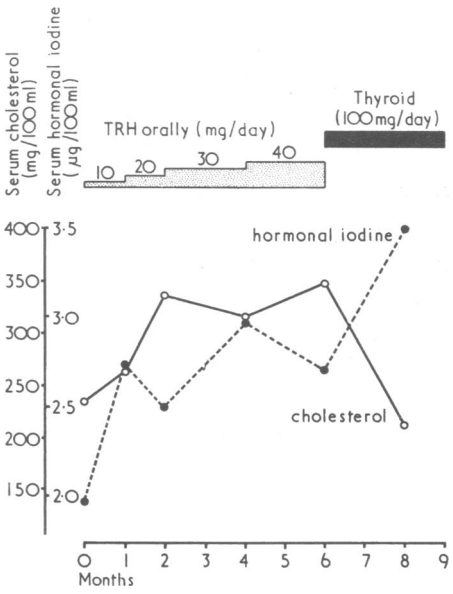
## Effect of Thyrotrophin-releasing Hormone on Serum Cholesterol

SIR,—In the past 1½ years we have treated eight patients with oral doses of thyrotrophin-releasing hormone (TRH) 10-40 mg/day for periods of 2-15 months. The patients had either mild hypothalamic hypothyroidism or an intractable depressive syndrome; one of the latter patients has been briefly reported on before.[1] Serum hormonal iodine[2] and cholesterol levels were determined serially.

In five of the eight patients a significant and generally marked increase in serum cholesterol concentration was observed during TRH treatment (see table). The effect did not appear to be dose-dependent. All patients were clinically euthyroid at the time the cholesterol values were increased and their hormonal iodine values were higher than before the treatment was started. In one of these five patients (case 6) thyroid tablets were substituted for the TRH therapy after six months. Within two months the serum cholesterol concentration had fallen to normal (see fig.).

It has been known for a long time that serum cholesterol values are normal in many patients with secondary (that is, suprathyroidal) hypothyroidism.[3] This has commonly been attributed to concomitant (often subclinical) hypoadrenocorticism. Reports on serum cholesterol in patients with *isolated* deficiency of thyrotrophin (TSH)—or TRH—are too few for the role of adrenocortical function in this respect to be assessed. In the light of the present observations it seems likely that at least part of the increase in serum cholesterol seen in primary hypothyroidism is mediated by the chronic hypersecretion of TSH or possibly TRH occurring in this disorder.




Whether the observed increase in serum cholesterol is a direct effect of TRH or is secondary to chronic stimulation of the secretion of TSH, or possibly prolactin, is as yet unknown. The possible influence of TRH on other serum lipids is now being studied.—We are, etc.,

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1 Vis-Melsen, M. J. E. van der, and Wiener, J. D., *Lancet*, 1972, **2**, 1415.
2 Backer, E. T., Postmes, T. J., and Wiener, J. D., *Clinica Chimica Acta*, 1967, **15**, 77.
3 VanArsdel, P. P., and Williams, R. H., *American Journal of Medicine*, 1956, **20**, 4.

## Breast Cancer Regression under Oestrogen Therapy

SIR,—In a recent article for debate Dr. B. A. Stoll (25 August, p. 446) puts forward a hypothesis concerning breast cancer regression and oestrogen therapy, the hypothesis being required since oestrogens had been shown to stimulate prolactin release. He suggests that inhibition or stimulation of tumour growth by oestrogens may depend on "the absolute and relative concentrations of prolactin and oestrogen activity available at the site" and that a theory of multiple clones in tumours cannot explain some observations made during treatment. Further he concludes that a tumour requiring both prolactin and oestrogen for maintenance of growth would be inhibited by *both* endocrine ablation *and* high-dosage oestrogen therapy. We would like to raise the following points, in debate.

(1) Evidence cited to support a stimulation of prolactin release by oestrogens was based on an experiment in rats[1] and unpublished findings in man. The scientific content of the latter cannot be assessed, while high doses of oestradiol in ovariectomized rats had a smaller effect on serum prolactin concentration than low doses. It is not always simple to equate results from animal experiments with expected results in man, and there are qualitative species differences in hormonal control of prolactin release and breast tumour induction by exogenous hormones.[2]

(2) Oestrogens at a dose similar to that described by Dr. Stoll are used to prevent or suppress lactation, an observation difficult to reconcile with a further increase in plasma prolactin concentration, especially since serum prolactin is increased in the third trimester by a factor of 30 over non-pregnant values[3] and remains elevated during early lactation.

(3) The incidence of abnormal mitoses detectable by light microscopy is increased in all malignancy.[4] It seems highly likely therefore that daughter cells with differing chromosome material are constantly produced, and that many clones are likely to be present in any particular tumour. While some daughter cells would perhaps be less fitted for survival, some might be more capable of surviving various environmental conditions.[5] This is supported by the observation that different sites and metastases of individual tumours in the same patient show marked variation in oestrogen-binding receptors (O.B.R.).[6 7] Further, one patient with an O.B.R.-containing tumour responded to endocrine manipulation, but after a subsequent relapse did not respond and O.B.R. were then absent.[8] Some animal tumours contain both cancer cells and cancer-host hybrid cells.[9]

(4) The alternating response in Dr. Stoll's first case can, in contrast to his hypothesis, be explained by the clone phenomenon. This eventual escape of tumour response from oestrogen therapy, coupled with inhibition of growth on oestrogen withdrawal, may be an example of selection of a clone requiring oestrogens for growth. It has been suggested that androgen-dependent breast cancer might be induced by prior androgen therapy stimulating a specific clone,[10] though this has been questioned.[11]

(5) The statement that a tumour might be inhibited by both an absence and a gross excess of oestrogen is difficult to understand. However, even if true it would again be evidence in favour of at least two clones, one sensitive to oestrogen lack and the other sensitive to oestrogen excess.

(6) The role of prolactin in human breast cancer requires some comment. Plasma prolactin concentration is reported to be the same in women with untreated breast cancer as in controls.[12] Levodopa, which reduces plasma prolactin, has relieved pain in some patients with extensive breast carcinoma,[13] but this drug induces extensive endocrine effects at many sites. Dr. Stoll induced one remission with levodopa com-

| Case | Sex | Age (years) | Dose of TRH (mg/day) | Serum Cholesterol (mg/100 ml; normal: 150-250 mg/100 ml) | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | before | 1 month | 2 months | 3 months | 4 months | 6-7 months | 9-10 months | 11-15 months |
| 1 | F | 52 | 10 | 244 | 279 | 290 | 298 | | | 325 | 437 |
| 2 | F | 42 | 10–20 | 186 | 201 | 197 | 201 | | | | 162 |
| 3 | M | 38 | 10–40 | 325 | 360 | | 402 | 321 | 468 | 410 | |
| 4 | F | 54 | 20 | 205 | 213 | 263 | | | | | |
| 5 | F | 23 | 30 | 174 | 174 | 283 | 259 | | | | |
| 6 | F | 21 | 10–40 | 236 | 263 | 337 | | 317 | 348 | | |
| 7 | F | 19 | 40 | 178 | 162 | 162 | 162 | | | | |
| 8 | M | 33 | 40 | 194 | 197 | 190 | 197 | | | | |