of endometrial cancer in this country. We could not recall having made any such suggestion, but memory is fickle and we reread our article with renewed interest. We found that the article contained a figure showing the trends in mortality attributed to cancer of the corpus uteri in England and Wales from 1955 to 1971 in three age groups. No comment was made on the data, which were included only to show that the reduction in mortality from cancer of the cervix uteri (which was the subject of the article) was not obviously due to more exact localisation of the site of origin of the cancer. Any "analysis" of the mortality rates would have required, first, a consideration of fatality (since we were dealing with mortality rather than incidence), and, secondly, as you rightly point out, some consideration of the prevalence of hysterectomy—which we noted was important for the interpretation of the trend in mortality from cervix cancer. Is it possible, perhaps, that you based your comments on Ziel and Finkle's misapprehension rather than on our original text?

In fact the latest available data on endometrial cancer in England and Wales show no increase in either mortality, up to 1973,² or in incidence, up to 1970,³ nor do the incidence data for residents of the old SE and SW Metropolitan Regions up to 1974.⁴ This, however, may not be surprising even if medically prescribed oestrogens do cause some cancers, as they have been prescribed here on a much smaller scale than in the USA. A study of prescriptions in a general practice population of approximately 40 000 people, which one of us is carrying out, shows that in the year preceding April 1975 the percentages of women who received at least one prescription for oestrogens other than oral contraceptives in the age groups 40-49, 50-59, 60-69, and 70-79 years were respectively 4.6, 5.9, 1.1, and 1.0%. The proportion of women who received regular repeat prescriptions is not yet available to us, but is likely to have been appreciably less.

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¹ Kinlen, L J, and Doll, R, *British Journal of Preventive Social Medicine*, 1973, 27, 156.

² Registrar-General's Statistical Reviews for England and Wales, Part I, Mortality Tables, 1960-73. London, HMSO.

³ Registrar-General's Statistical Review for England and Wales, Supplement on Cancer. London, HMSO, 1975.

⁴ Payne, P, 1976, personal communication.

Methaqualone and urinary steroids

SIR,—We should like to draw readers' attention to the possibility of spuriously high results of urinary 17-oxosteroid (17-OS) and 17-oxogenic steroid (17-OGS) estimations in patients receiving methaqualone therapy.

A patient taking two Mandrax tablets nightly was found to have apparent 17-OS excretion of 50 μ mol/24 h (14 mg/24 h) and 17-OGS excretion of 44 μ mol/24 h (13 mg/24 h). This was confirmed by analysis of a second urine specimen, but cessation of Mandrax treatment for a week resulted in lower values—28 μ mol/24 h (8 mg/24 h) for 17-OS and 30 μ mol/24 h (9 mg/24 h) for 17-OGS. This again was confirmed in a further specimen.

Each Mandrax tablet contains 250 mg of methaqualone and 25 mg of diphenhydramine. When solutions of these compounds were

separately subjected to the 17-OS and 17-OGS estimation procedures no effect was observed in the case of diphenhydramine, but methaqualone did produce considerable interference. The method of analysis for 17-OS was as described by Gray *et al.*¹ and for 17-OGS according to Metcalf.² Chloroform was employed as extraction solvent in both cases and the Zimmermann procedure of James and De Jong³ was used. When an alternative Zimmermann procedure⁴ was tried the interference seen with pure methaqualone was approximately doubled.

In view of these observations it seems prudent to stop methaqualone therapy at least several days before collecting urine for steroid estimations and we should like to endorse the recommendation¹ that, when possible, patients should not be receiving any drugs when such collections are made.

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¹ Gray, C H, *et al*, *Lancet*, 1969, 1, 124.

² Metcalf, M G, *Journal of Endocrinology*, 1963, 26, 415.

³ James, V H T, and De Jong, M, *Journal of Clinical Pathology*, 1961, 14, 425.

⁴ Beale, R N, Bostrom, J O, and Croft, D, *Journal of Clinical Pathology*, 1962, 15, 574.

Vaccination against meningitis

SIR,—In your excellent leading article on vaccination against meningitis (17 April, p 919) the name of Arstenstein is mentioned. In fact he is the only research worker mentioned specifically in the editorial. Your readers who are interested in this disease and its prevention will be sad to be informed that this brilliant and still comparatively young investigator has just died.

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Herpesvirus and cancer of the uterine cervix

SIR,—We note with interest your leading article on this subject (20 March, p 671).

It is well known that some women with dysplasia of the uterine cervix will develop carcinoma-in-situ or invasive cancer while in others the lesion remains stationary or regresses. The work of Skinner and his colleagues¹ at the University of Birmingham has shown that neutralising antibody activity against herpes simplex virus type 2 increases with the severity of cervical neoplasia—that is, from dysplasia through carcinoma-in-situ to invasive cancer. These observations suggest to us that the women with increased antibody activity against herpesvirus type 2 may be those with the dysplasias which progress to carcinoma-in-situ.

In conjunction with Dr G R B Skinner in Birmingham and Dr S D Gardner at the Central Public Health Laboratory, Colindale, we are carrying out a study to test this hypothesis by regular follow-up of women with dysplasia detected during routine cervical screening at venereal disease clinics and gynaecological clinics at this hospital. The women are being investigated by cytology, colposcopy, and virology at 3-monthly intervals to determine whether present or past infection with herpes simplex virus type 2

alters the risk of progression of dysplasia to carcinoma-in-situ. In this way we hope to establish a role for herpesvirus in cervical carcinogenesis and thus identify a group of women who are at particular risk.

The design of this study is, we feel, more effective and less costly than that proposed by Kessler² or Nahmias,³ who recommend close regular cytological and virological surveillance of 10 000 well women for 5-10 years. We estimate that close surveillance of 700-1000 women with mild or moderate dysplasia over a period of 3-5 years will provide valid results, assuming that approximately 10% of minor dysplasias progress to carcinoma-in-situ in this time.

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¹ Skinner, G R B, Thouless, M E, and Jordan, J A, *Journal of Obstetrics and Gynaecology of the British Commonwealth*, 1971, 78, 1031.

² Kessler, I I, *Cancer Research*, 1974, 34, 1091.

³ Nahmias, A J, *et al*, *Cancer Research*, 1973, 33, 1491.

Suppressor cells and human malignant disease

SIR,—It is most impressive to read the report by Drs I T Magrath and J L Ziegler (13 March, p 615) of a clinical trial of human tumour immunotherapy that contradicts the now widely held tenet that non-specific immunostimulation is clinically beneficial in the treatment of almost any human neoplasm. Among the possible mechanisms that invalidate non-specific immunostimulation is the activity of suppressor lymphoid cells.

At least two pathological conditions are known in which overactive suppressor cells play an aetiological role: one form of hypogammaglobulinaemia¹ and Hodgkin's disease.² Since the suppressor activity directed against the blastogenic response to Hodgkin's lymphocytes of normal lymphocytes parallels the clinical activity of the disease² it is possible that the neoplastic cells in Hodgkin's disease are a clone of suppressor T lymphocytes.

At least two physiological conditions could be listed whose maintenance depends in part on normal suppressor-cell function: self-tolerance and pregnancy with an allogeneic conceptus. As tumours imitate fetal growth morphologically and biochemically it is plausible to assume that the mammalian immune system responds to tumours as the mother responds to paternal antigens of the fetus.³ In a former, unpublished, study we observed enhanced growth of a virally induced murine lymphoma in mice pretreated with murine embryo cells. We propose that the physiological function of early-phase embryonic antigens is the activation of suppressor-cell clones in order that tolerance to (or even enhancement of) the allogeneic conceptus be mediated. Further, we propose that oncofetal antigen expression in tumours serves the same purpose: activation of appropriate suppressor cells and thus the induction of one type of immune tolerance towards the tumour. This immunosuppression may encompass a broad spectrum of reactivities or it may be limited to tumour-specific reactivity only. Thus the profound immunosuppression of patients with colorectal or bronchogenic carcinomas may be the result of excessive oncofetal antigen production. Patients with much less production of oncofetal