Treatment of benign prostatic hyperplasia

SIR,—Professor Geoffrey D Chisholm's editorial[1] on the treatment of benign prostatic hyperplasia contained a sentence which cannot pass without comment: "The fact that a recent review has suggested that transurethral resection of the prostate may not be as good as urologists have claimed[2] does not detract from the important advantages of this technique in treating benign prostatic hyperplasia."

Surely all disadvantages detract somewhat from any advantages, however important? Moreover, readers may not be aware of the nature of the disadvantages that are being cited. These are an excess risk of reoperation and, most importantly, of death in the years after transurethral resection of the prostate when compared with open surgery of around 40%.

Obviously there are problems with interpreting the results cited, which are derived from observational and longitudinal data records from three countries among men with no serious concomitant illness and are adjusted as far as possible for case severity. But such data are suggestive and require further investigation by prospective randomised comparison, unless these differences can be unambiguously shown to be attributable to unmeasured aspects of selection or prognosis.

It seems slightly cavalier to dismiss implicitly these findings as if they amounted to nothing before such a demonstration.

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1 Chisholm GD. Benign prostatic hyperplasia: the best treatment. *Br Med J* 1989;**299**:215-6. (22 July.)
2 Roos NP, Wennberg JE, Malenka DJ, *et al.* Mortality and reoperation after open and transurethral resection of the prostate for benign prostatic hyperplasia. *N Engl J Med* 1989;**320**:1120-4.

AUTHOR'S REPLY,—I deliberately commented on the paper by Roos *et al*. Their observations are of great interest and concern to urologists but discussion on their paper was outside the scope of my editorial. The implications of this study are already being considered seriously by several urological groups. As Dr McPherson states, there are, however, problems in interpreting the data of Roos *et al*; it may be many years before the implications made in this paper are resolved. Meanwhile, the important advantages of a transurethral resection compared with open surgery remain true. If Dr McPherson is now suggesting that we should stop routine transurethral resections and set up a worldwide trial of transurethral resection of prostate versus open surgery then I will watch with interest how ethical committees, administrators, budget holders, and especially the patients handle this proposal. It might be relevant to note that in Scotland in 1987, 5236 transurethral resections of the prostate were performed compared with 315 open prostatectomies.

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Follicular stimulation and ovarian cancer

SIR,—Drs S Fishel and P Jackson correctly warned about the possible long term sequelae of ovarian stimulation, especially epithelial malignancies in the ovary, endometrium, and the breast.[1] Carcinoma of the breast in association with in vitro fertilisation has been described in a 34 year old woman.[2] We report on another young woman who achieved successful pregnancies after treatment with clomiphene citrate to induce ovulation and who later developed papillary serous cystadenocarcinoma in both her ovaries.

A woman aged 27 attended an infertility clinic in 1978 because she was unable to get pregnant after trying for two and a half years. A pelvic examination and laboratory investigations and her husband's sperm count were normal. She was advised to record basal body temperatures in the next two consecutive menstrual cycles. When she returned to the clinic the temperature chart showed no biphasic pattern and the serum concentration of progesterone in the latter half of the cycle suggested that she was not ovulating. She was given clomiphene citrate 50 mg for five days. This was increased to 150 mg in subsequent cycles because there was not an adequate response to lower doses. Because the patient developed severe nausea she was switched over to cyclofenil 400 mg daily for 10 days in each cycle. Eighteen months later she became pregnant and delivered a healthy girl at term.

Eight years after the patient was first seen in the clinic, when she was 35, she presented with severe abdominal pain and distension. On examination there was a pelvic mass: an emergency laparotomy showed a cystic right ovary of 22 cm. The left ovary and the uterus appeared normal. Right oophorectomy was performed and a serous papillary cystadenocarcinoma was reported on histological examination. The uterus and the other ovary were conserved because the patient wished to try for a further pregnancy. The patient was treated with chemotherapy and was apparently well until five months after her first operation when she again presented with abdominal pain and tenderness. A second laparotomy showed that the left ovary was cystic and was the size of a hen's egg. The uterus and other pelvic viscera were normal. Total hysterectomy and left salpingo-oophorectomy were carried out. Histology of the left ovary showed serous papillary cystadenocarcinoma without any spread into the uterus or the fallopian tube. Chemotherapy was continued, but in early 1989 a third laparotomy showed extensive metastasis of the tumour in the abdomen. The patient refused further chemotherapy and is now taking oral steroids only.

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1 Fishel S, Jackson P. Follicular stimulation for high tech pregnancies: are we playing it safe? *Br Med J* 1989;**299**:309-11. (29 July.)
2 Laing RW, Glaser MG, Barrett GS. A case of breast carcinoma in association with in vitro fertilisation. *J R Soc Med* 1989;**82**: 503.

Treatment of shingles and post-herpetic neuralgia

SIR,—Dr Jacqueline V Jolleys's response[1] to our letter[2] concerning her editorial on treating shingles and post-herpetic neuralgia[3] cites seven further controlled trials of acyclovir in herpes zoster that she did not originally reference. The studies of Wassilew *et al*[4] and Cobo *et al*[5] were of oral acyclovir 400 mg and 600 mg five times daily, lower doses than those licensed. Indeed, Cobo *et al* concluded: "While the effect of oral acyclovir at the doses studied is positive certain findings point to marginal antiviral effect" and suggested that higher doses should be used. The earlier studies of McGill *et al*,[6] Juel-Jensen *et al*,[7] and Bean *et al*[8] were primarily aimed at evaluating treatment with intravenous acyclovir in severe herpes zoster. Patient numbers, reflecting the required statistical power, were therefore smaller, but the trends observed for chronic pain were consistent with the experiences of others.[9,10]

The trial by Esmann *et al*[11] did not prove a lack of effect of acyclovir on post-herpetic neuralgia; it was designed only to identify any steroid mediated component, absence of which does not relate to an effect of acyclovir alone. The high incidence of post-herpetic neuralgia in both treatment groups more probably relates to the highly susceptible (>60 years) patient population and the authors' measurement and definition of pain.

Dr Jolleys acknowledges the effectiveness of acyclovir on post-herpetic neuralgia at three months in the studies by Huff *et al*[12] and Morton and Thomson.[13] The lack of a similar statistically significant effect at six months results from the lower incidence of post-herpetic neuralgia in the placebo group with consequent loss of statistical power. Analysis for the six month period showed a significant overall reduction in the incidence of post-herpetic neuralgia, hence our previous conclusion.

Further prospective controlled trials in large patient populations have been considered, but such placebo controlled studies may not be practicable now because of the consistent benefit of acyclovir in severe herpes zoster. Regarding the proposal to study the effect of longer courses of oral acyclovir,[14] an investigation in 400 patients of 7 *v* 21 days of treatment with acyclovir is ongoing.

The company may promote only on the basis of claims in the product licence. When the licence for oral zovirax as a treatment for herpes zoster was granted in 1986 clinical experience to that date was limited to the severe phase; no data were submitted on post-herpetic neuralgia. Hence the data sheet states "Studies have not yet shown an effect of zovirax on post-herpetic neuralgia." Completion of the more recent specifically designed studies for evaluating post-herpetic neuralgia suggest that a review of our licensed claims is now appropriate.

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1 Jolleys JV. Treatment of shingles and post-herpetic neuralgia. *Br Med J* 1989;**299**:393. (5 August.)
2 Crooks RJ, Bell AR, Fiddian AP. Treatment of shingles and post-herpetic neuralgia. *Br Med J* 1989;**299**:392-3. (5 August.)
3 Jolleys JV. Treatment of shingles and post-herpetic neuralgia. *Br Med J* 1989;**298**:1537-8. (10 June.)
4 Wassilew SW, Reimlinger S, Nasemann T, Jones D. Oral acyclovir for herpes zoster: a double blind controlled trial in normal subjects. *Br J Dermatol* 1987;**117**:495-501.
5 Cobo LM, Foulks GM, Liesegang T, *et al.* Oral acyclovir in the treatment of acute herpes zoster ophthalmicus. *Ophthalmology* 1986;**93**:763-70.
6 McGill J, MacDonald DR, Fall C, McKendrick GDW, Copplestone A. Intravenous acyclovir in acute herpes zoster infection. *J Infect* 1983;**6**:157-61.
7 Juel-Jensen BE, Khan JA, Pasvol G. High-dose intravenous acyclovir in the treatment of zoster: a double blind placebo controlled trial. *J Infect* 1983;**6**(suppl 1):31-6.
8 Bean B, Braun C, Balfour HH. Acyclovir therapy for acute herpes zoster. *Lancet* 1982;ii:118-21.
9 Klenerman P, Peto TEA, Luzzi GA, Juel-Jensen BE. Antiviral treatment and postherpetic neuralgia. *Br Med J* 1989;**298**: 832. (25 March.)
10 Bannister P, Crosse B. Severe herpes zoster infection in the United Kingdom: experience in a regional infectious diseases unit. *J R Soc Med* 1989;**82**:145-6.
11 Esmann V, Geil JP, Kroon S, *et al.* Prednisolone does not prevent post herpetic neuralgia. *Lancet* 1987;ii:126-9.
12 Huff JC, Bean B, Balfour HH, *et al.* Therapy of herpes zoster with oral acyclovir. *Am J Med* 1988;**85**:84-9.
13 Morton P, Thomson AN. Oral acyclovir in the treatment of herpes zoster in general practice. *N Z Med J* 1989;**102**:93-5.
14 Todd P, Thomson J. Treatment of shingles and post-herpetic neuralgia. *Br Med J* 1989;**299**:393. (5 August.)

SIR,—In response to the editorial by Dr Jacqueline Jolleys[1] and the recent correspondence we would like to comment on our experience with post-herpetic neuralgia.

We recently studied a large sample of patients with the condition in Liverpool and compared