Polio vaccines and polioviruses

SIR,—In your leading article "Polio vaccines and polioviruses" (25 June, p 1617) you rightly note some of the disadvantageous aspects of the oral live poliovirus vaccine (dissemination in the community, reversion to virulence, and occasional paralysis or death in vaccinees and contacts).^{1 2} I feel impelled to write to you because you imply, nevertheless, that a live virus vaccine is to be preferred to one made of inactivated or killed viruses because "immunity lasts longer." This statement is not correct so far as killed poliovirus vaccine is concerned, since it has been proved to establish durable immunity.³ Moreover, it produces a herd effect and, properly used, can result not only in eradication of disease but in elimination of poliovirus from a population.³

If a goal of poliomyelitis vaccination is "to eradicate disease and to control the spread of—and eventually to eliminate—the causative agents from the population"⁴ this goal can only be approximated but not obtained with the use of the live virus vaccine. Where the killed virus vaccine has been used such a result has been achieved (Finland, Sweden, and other countries).

In a paper³ that may not have come to your attention you will find a discussion of details, data, and mechanisms related to the control of poliomyelitis via the proper use of the killed virus vaccine.

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¹ Assaud, F A, Cockburn, W C, and Perkins, F T, *Bulletin of the World Health Organisation*, 1976, **53**, 319.

² Schoenberger, L B, McGowan, J E, jun, and Gregg, M B, *American Journal of Epidemiology*, 1976, **104**, 202.

³ Salk, J, and Salk, D, *Science*, 1977, **195**, 834.

⁴ Nightingale, E O, *New England Journal of Medicine*, 1977, **297**, 249.

Lithium and thyrotoxicosis

SIR,—In your leading article (6 August, p 346) "Adverse effects of lithium treatment" it is stated that "there is at least one report of lithium-induced thyrotoxicosis."¹ I wish to report another case of thyrotoxicosis associated with lithium treatment.

In January 1975 a 54-year-old man was admitted to the alcoholism unit of this hospital for the third time since 1973. On re-examination it was considered that he was suffering from depression as well and he was included in a current trial involving the use of lithium in the treatment of chronic alcoholics with depression.² In fact he had lithium carbonate (1200 mg daily) throughout the trial, which in his case began in January 1975. He was discharged from the alcoholism unit in March 1975 and was maintained on lithium. In May 1976 he began to feel unwell, and among his symptoms at times were shakiness and slight dizziness. His general practitioner considered that these symptoms might be a sign of lithium toxicity and so the lithium was discontinued and he was referred to me.

When I saw him he said that for the past two months he had had aching of the muscles of the thighs, buttocks, and calves and very slightly in the arms and neck. For the same period he had noticed shaking for 5-10 min at a time in the form of a fine tremor. He had also noticed that his heart was pounding and at times appeared irregular, and this occurred two or three times a day for periods of about 5 min. He also mentioned that his gait was unsteady and that he was clumsy with his hands. Over this period of two months he had lost about a stone (6½ kg) in weight, despite the fact that he had an enormous appetite.

On examination his weight was 67 kg (10 st 8 lb). His voice was husky (this was later found to be due to hyperkeratosis of the cords). He was sweating, his pulse was 100 min and regular, his blood pressure 130/50 mm Hg, and there were no signs of cardiac failure. His ankle jerks were brisk. The thyroid gland was not palpable. Investigations on 9 June 1976 revealed the serum thyroxine concentration to be more than 257 nmol/l (20 µg/100 ml) (reference range 51-154 nmol/l (4-12 µg/100 ml)), T3 uptake 1.47 (reference range 0.8-1.5), and free thyroxine index >20 (reference range 4-12).

Treatment was started with carbimazole and on 24 November his serum thyroxine level was 9 nmol/l (0.7 µg/100 ml), T3 uptake 0.74, and free thyroxine index 0.5. On 23 February 1977 the thyroxine level was 36 nmol/l (20 µg/100 ml), T3 uptake 0.81, free thyroxine index 2.3, thyroid microsomes positive 1 in 40, blood calcium 2.35 mmol/l (9.4 mg/100 ml) (reference range 2.25-2.6 mmol/l (9.0-10.5 mg/100 ml)), and his weight was 160 kg (11 st 5 lb). He felt well subjectively and there were no symptoms or signs of thyrotoxicosis. There was no relapse into acute alcoholism.

The incidence of thyroid deficiency in patients taking lithium is now well established.^{3 4} The case described by Franklin,¹ to which you referred in your leading article, was "a case of thyrotoxicosis developed in the fourth year of lithium treatment in a 45-year-old woman who had had a pre-existing non-toxic goitre." The author also indicated that "there is no proof that lithium caused thyrotoxicosis" in that case. The case described here is of interest in that symptoms of thyrotoxicosis occurred during lithium therapy in a patient who had no pre-existing goitre.

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¹ Franklin, L M, *New Zealand Medical Journal*, 1974, **79**, 782.

² Merry, J, et al, *Lancet*, 1976, **2**, 481.

³ Schou, M, et al, *British Medical Journal*, 1968, **3**, 710.

⁴ Lazarus, J H, and Bennie, E H, *Acta Endocrinologica*, 1972, **70**, 266.

The grateful patient

SIR,—I would like to try to restore the balance upset by Mrs J Anderson's Personal View (27 August, p 573).

I have been a general practitioner for 28 years which I, unlike her, enjoy remembering. For the past seven years I have practised from a health centre. Certainly things have changed in this time, but not in the way described by Mrs Anderson. My partners, receptionists, and I continue to receive tokens of gratitude from our patients which take the form of verbal thanks, letters, presents, and even small legacies. Yesterday I returned home with three separate presents of home-grown vegetables, and this is by no means unusual. I do not keep a count but I am certain that not a week goes by without a present. Last Christmas my presents, over 70 in number, contributed to our cheer at Christmas and throughout the year, not least because of the sentiment which I knew had inspired their gift.

My practice, though fortunately situated, is by no means unusual. My practice administrator is not a dogsbody but a respected colleague and our whole team works to achieve a mutually confident relationship between the patients and their doctors. Of course there are many difficulties, but the important fact remains that I enjoy seeing the vast majority of my patients, including those who have had

the misfortune to acquire a fat record envelope, and they seem to enjoy seeing me.

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Effect of abortion on obstetric patterns

SIR,—Mr A F Pentecost (27 August, p 578) raises an important point that is still unresolved when commenting on the published account of an interview with one of us (RWB) on changes in obstetrics in the 'seventies (23 July, p 251). In that interview it was implied that the reported decline in the numbers of babies of low birth weight born in Sheffield might be in some measure due to the removal of high-risk pregnancies by legal abortion. Mr Pentecost suggests that such a beneficial effect is likely to be outweighed by the increase in premature labours as a direct consequence of abortion.

His statement that "it is an established fact that one or more terminations of pregnancy are liable to result in more women coming in at 26 weeks with ruptured membranes" must be challenged. In the study he quotes¹ to support his view seven out of eight women who had premature rupture of the membranes had previously been aborted of pregnancies of more than 10 weeks' gestation, and it is likely (as the authors comment) that they had been terminated by the traumatic techniques in use at that time. Stallworthy *et al*,² reporting the results of legal abortion in Oxford in the late '60s, commented that Hegar dilators of larger than size 12 were used in the majority of cases and in a fair number they were larger than size 14. Dilatation to such a degree is likely to result in frequent damage to the internal os leading to subsequent cervical incompetence and premature rupture of the membranes. Modern aspiration techniques rarely require the cervix to be dilated to more than Hegar 10, so that subsequent premature labour due to cervical incompetence is unlikely to occur. Johnstone *et al*³ studied the diameter of the internal os six weeks after induced abortion and found values similar to those of the nulliparous cervix if the dilatation at the time of abortion did not exceed 10 mm.

Evidence is often quoted⁴ from a number of papers^{5 7} in support of Mr Pentecost's view. In one of these, by Jurukovski and Sukarov,⁵ the only evidence presented is a statement, ascribed to Dr Potts, that there is a positive correlation between cervical incompetence and previous abortion.⁵ The second paper⁶ (from Denmark) does not mention damage to the cervix specifically and gives no long-term follow-up results. In the third paper (from Hungary) Klinger⁷ gives no data to support his statement that part of the increase in the prematurity rate in Hungary was due to legal abortion. The increase from 7.0% in 1954, when abortion was prohibited, to 10.5% in 1968 was during a time, as the author admits, when there were major changes in age, parity, and social class among pregnant women in Hungary. Low birth weight is known to correlate strongly with poor living conditions, irrespective of the prevalence of induced abortion.

It seems unlikely that it will ever be possible to carry out the clinical trial that will finally settle the matter because of the difficulty of obtaining matched controls, problems of follow-up, and variable techniques of abortion. However, two large trials^{8 9} in which careful

matching was attempted with total sample sizes of 2779 and 12 588 respectively showed no differences in birth weight or of the incidence of preterm (<37 weeks' gestation) delivery.

Thus the evidence that is available does not support the idea that modern legal abortion generally increases the risks of prematurity in a subsequent pregnancy. The question raised in the *BMJ* interview that still has to be answered is whether the reduction in the incidence of low birth weight can be ascribed to legal abortion.

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- ¹ Wright, C S W, Campbell, S, and Beazley, J, *Lancet*, 1972, **1**, 1278.
- ² Stallworthy, J A, Moolgaoker, A S, and Walsh, J J, *Lancet*, 1971, **2**, 1245.
- ³ Johnstone, F D, et al, *British Medical Journal*, 1976, **1**, 68.
- ⁴ Richardson, J A, and Dixon, G, *British Medical Journal*, 1976, **1**, 1303.
- ⁵ Jurukovski, J, and Sukarov, L, *International Journal of Gynaecology and Obstetrics*, 1971, **9**, 111.
- ⁶ Olsen, C E, Nielsen, H B, and Ostergaard, E, *International Journal of Gynaecology and Obstetrics*, 1970, **8**, 823.
- ⁷ Klinger, A, *International Journal of Gynaecology and Obstetrics*, 1970, **8**, 680.
- ⁸ Roht, L H, and Aoyama, H, *American Journal of Obstetrics and Gynecology*, 1974, **120**, 868.
- ⁹ Daling, J R, and Emanuel, I, *Lancet*, 1975, **2**, 170.

Women who regret sterilisation

SIR,—Mr R M L Winston's paper (30 July, p 305) provided much valuable information about women who regret sterilisation, although interpretation of the facts presented was restricted by the lack of a control group. This was inevitable because of the nature of the study, but perhaps some of my own figures may be found acceptable for comparison.

A total of 1081 women sterilised consecutively at the Women's Hospital, Liverpool, were followed up 24-42 months later and 614 (56.8%) of them were traced. The age and parity distributions of this group at the time of sterilisation are shown in tables I and II. It may be seen that the mean age (32.1 years) of patients sterilised at this hospital is 5.4 years older than the mean age of patients subsequently seen by Mr Winston for reversal of the procedure, which appears to support his

hypothesis that patients sterilised at a young age are more likely to regret the operation.

In answer to the question "Do you regret having been sterilised?" an affirmative answer was given by 54 (8.8%) patients. The reasons given for regret were often multifactorial and included the following: desire for further children, 18; loss of libido, 9 women and one husband; menstrual disorders, 6; dysmenorrhoea, 2; dyspareunia, 2; irritability and depression, 4; excess weight, 4; early menopause, 1; vague aches and pains, 5. The commonest reason for regretting the operation was a desire to bear children to a new partner. Although women who remained married to the same partner sometimes expressed transient yearnings for further children, none of them felt strongly enough about childbearing to regret having been sterilised. Many patients expressed dissatisfaction with the operation for bizarre reasons probably unrelated to the procedure. Trivial aches and pains were frequently blamed on the operation and one patient aged 45 years was convinced that it had brought on an early menopause. Many of these symptoms would probably have responded to explanation. The age distribution at the time of operation of patients who subsequently regretted the procedure (table I) also suggests that sterilisation performed at a young age is more likely to lead to regret than it is in older women.

Although these "regrets" did not all amount to requests for reversal of the procedure, the trend is in accord with Mr Winston's findings. The association between parity and subsequent regret of the procedure was less clear (table II). Although patients sterilised at a young age appear to run an increased risk of living to regret their decision, it would be unwise to refuse them sterilisation simply because of their age. The underprivileged grand multipara of tomorrow is the young woman of today who already has two or three children. Perhaps such a woman is the one most in need of sterilisation. Instead I would support Mr Winston's plea for careful counselling of the very young before sterilisation, particularly with a view to predicting the likely divorce.

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Oestrogen treatment for menopausal flushing

SIR,—Dr W H Utian (27 August, p 577) says that double-blind studies have shown that hot flushes respond to short-term oestrogen therapy. We have never claimed that flushes do not respond to oestrogens, but have pointed out that flushes also respond to other agents, including placebos, and that the superiority of oestrogen over placebo has yet to be established.¹

In the paper by Campbell *et al*² which Dr Utian cites the patients were studied for only four months, since the authors had already decided that patients with severe menopausal symptoms "did not justify a prolonged placebo trial." All patients were given oestrogen before being given placebo and the response to this subsequent placebo period was unimpressive. The poor placebo response found by these workers is unusual and contrasts sharply with the findings of Coope, which are reported in the same publication.³ She found that patients

made a striking improvement when given placebos and that over the first three months, when the women did not know whether they were receiving hormones or not, there was no statistically significant difference in the flush count between oestrogen and placebo groups. The study by Campbell *et al* cannot therefore be taken as proof of the superiority of oestrogen over placebo in the management of menopausal flushing. Well-conducted double-blind crossover studies must be done if the issue is to be clarified.

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- ¹ Mulley, G, and Mitchell, J R A, *Lancet*, 1976, **1**, 1397.
- ² Campbell, S, *et al*, in *Management of the Menopause and Postmenopausal Years*, ed S Campbell, p 149. Lancaster, MTP, 1976.
- ³ Coope, J, in *Management of the Menopause and Postmenopausal Years*, ed S Campbell, p 159. Lancaster, MTP, 1976.

Oestrogen treatment and endometrial carcinoma

SIR,—In your leading article on this subject (23 July, p 209) you adopt an unusually passionate tone, suggestive more of fervent evangelical zeal than of calm scientific appraisal. The editor of the *Lancet* may want to comment separately on the way his judgment has been impugned, but the rest of your tirade also requires rejoinder, particularly the strident cry that "each and every one of these criticisms is invalid and shows a misunderstanding of the case-control approach."

The latter contention is somewhat similar to the argument offered by alchemists that Lavoisier failed to comprehend the basic ideas of phlogiston. It is the advocates of the "case-control" approach, not the critics, who show a misunderstanding of elementary scientific reasoning. For the sake of simplicity, ease, and convenience, case-control investigators work backwards, examining an "effect" group (called *cases*) and a "non-effect" group (called *controls*). The antecedent rate of occurrence of the "cause" is then compared in these two groups. In defence of this reverse logic case-control investigators offer the ideological argument, as do you, that customary scientific standards can be ignored and that "what matters is comparability of cases with controls in terms of factors which may be related to the disease or the exposure being studied."

This argument is scientifically untenable for at least two reasons. Firstly, case-control investigators almost never pay suitable attention to demonstrating true comparability of the clinical (rather than demographic) factors that are related to disease and pharmaceutical exposure. Secondly, when a case-control study is completed the investigators want to conclude that a cause-effect relationship exists. Such a conclusion requires that the reasoning be logically acceptable in a forward, not backward, direction. Accordingly the investigators must demonstrate that the observed relationship was not biased by events that may have occurred, in a forward direction, between the imposition of the alleged cause and the occurrence of the alleged effect. In particular the compared patients who have received or not received oestrogens should be similar both in the clinical characteristics that serve as reasons why the drug may have been prescribed and in the procedures used to evoke

TABLE I—Age distribution at time of sterilisation

Age (years)	No sterilised	No regretting sterilisation (%)
<21	0	—
21-25	49	10 (20.4)
26-30	179	19 (10.6)
31-35	205	15 (7.3)
36-40	121	6 (5)
>40	60	4 (6.6)
Total	614	54 (8.8)
Mean age (years)	32.1	30.1

TABLE II—Parity distribution at time of sterilisation

Parity	No sterilised	No regretting sterilisation (%)
0	2	0
1 or 2	158	17 (10.7)
3-6	408	34 (8.3)
>6	46	3 (6.5)
Total	614	54

Mean parity of whole group 3.86.