naïal bed rest may actually have a deleterious effect upon fetal growth and well-being and that until this basic problem is settled it is not possible to say whether the better results obtained by Dr. Varma and Professor Curzen in their decompressed patients are more likely to have been effected by the decompression itself or by the lesser amount of enforced bed rest to which they were subjected.—I am, etc.,

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- 1 Varma, T. R., and Curzen, P., *Journal of Obstetrics and Gynaecology of the British Commonwealth*, 1973, 80, 1086.
- 2 Mathews, D. D., and Loeffler, F. E., *Journal of Obstetrics and Gynaecology of the British Commonwealth*, 1968, 75, 268.
- 3 Greene, J. W., Duhring, J. L., and Smith, K., *American Journal of Obstetrics and Gynecology*, 1965, 92, 1030.
- 4 Mathews, D. D., Patel, I. R., and Sengupta, S. N., *Journal of Obstetrics and Gynaecology of the British Commonwealth*, 1971, 78, 610.

Effects of Exertion on Hormone Secretion

SIR,—Physical activity or exercise is a stimulus to the secretion of many hormones, including cortisol¹ and testosterone.^{2,3} However, the response may depend on the physical fitness of the individual and the degree (or type) of exercise.

In order to study the response during very strenuous exercise we determined plasma testosterone by radioimmunoassay in 13 Finnish amateur sportsmen aged 30–40 years who were participants in the second non-competitive marathon run in Athens on 20 October 1973. Some determinations were also made on a Greek participant (no. 14), a former marathon prizewinner. All were in good physical condition before the event and had trained regularly, running as part of a programme to increase physical fitness. Eleven of the participants (nos. 1–11) ran the marathon (42.2 km) in 210–285 min. One of the participants (no. 12) took only 180 min, and because his physical condition after the run was exceptionally good he is considered separately. Participant no. 13 collapsed after having run 15 km in 66 min, and he also is considered separately. It must be emphasized that the temperature was very high, about 30°C in the shade. Water was available ad libitum every 5 km and at the finish, before blood sampling. The samples were obtained within 30 min of completion of the run. Control samples were taken at 1200 and 1600 hr (approximate times of start and finish of the marathon) some days before or after the run.

The results of the plasma cortisol determinations ($\mu\text{mol/l.}$) are shown in table I.

The results of the plasma testosterone determinations (nmol/l.) are shown in table II.

As was to be expected, the mean plasma cortisol value increased highly significantly ($P < 0.001$); however, in the participant who collapsed the value did not increase. Surprisingly, the plasma testosterone values fell

TABLE II—Results of the plasma testosterone determinations (nmol/l.)

Participant No.	Control Samples		After Marathon
	1200 hr	1600 hr	
1–11	21.6 $\pm$ 11.5 (S.D.)	23.4 $\pm$ 11.8 (S.D.)	14.1 $\pm$ 9.4 (S.D.)
12	27.4	33.2	36.0
13	13.9	11.0	3.0
14	—	19.9	11.4

significantly ($P < 0.001$) in all participants with the exception that participant no. 12, who was better trained than the others, had a slightly increased value. The participant who collapsed had a very low value—in fact within the normal female range. Thus these results show that strenuous physical exercise has different effects on hormone secretion in different individuals. Because some of the results cannot be explained at present the investigation will be continued during the next marathon run in Athens.—We are, etc.,

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- 1 Sutton, J., et al., *Medical Journal of Australia*, 1972, 2, 127.
- 2 Sutton, J. R., et al., *British Medical Journal*, 1973, 1, 520.
- 3 Lipsett, M. B., et al., *Recent Progress in Hormone Research*, 1966, 22, 245.

Amitriptyline and Imipramine Poisoning in Children

SIR,—Drs. H. W. Asbach and H. W. Schüler (18 May, p. 386) report the use in two children of haemodialysis in imipramine poisoning. The conclusion is that compared with conservative management “the duration of coma seems to be favourably shortened.” No information is given as to the amount of imipramine recovered by dialysis, but the authors cite Harthorne *et al.*¹ as reporting “successful haemodialysis treatment after imipramine poisoning.” Harthorne *et al.* in the reference cited stated in fact that “dialysis did not remove significant amounts of imipramine” and that out of a total of 5,375 mg of imipramine ingested only 30 mg was recovered after 5½ hours of dialysis.

It is indeed unfortunate that you should have published Drs. Asbach and Schüler's letter which contained no facts to substantiate their claim that “the amount of imipramine recovered in the dialysate is not so small as has been supposed” (apart from a reference to unpublished work in vitro) and cited a reference which clearly proved the futility of using haemodialysis to remove imipramine in this form of poisoning.

It is to be hoped that haemodialysis or any other method attempting to increase elimination will continue to play no part in the management of patients poisoned by

tricyclic drugs until it can be demonstrated that worthwhile amounts of the drugs are indeed removed by the method advocated.—I am, etc.,

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- 1 Harthorne, J. W., Marcus, A. M., and Kaye, M., *New England Journal of Medicine*, 1963, 268, 33.

Sleeping Sickness

SIR,—Your leading article on this subject (4 May, p. 236) excellently draws attention to some new techniques becoming available for the “subspecific” differentiation of trypanosomes but calls for two comments, one major and one minor.

You mention the use of human volunteers for a “final test of infectivity to man” of strains already categorized by the blood incubation infectivity test (B.I.I.T.). It is not possible in a letter to discuss the serious doubts which attach to past experimentation with human subjects in Africa for this purpose, but I must record that to my mind it is ethically indefensible to inoculate B.I.I.T.-positive strains—that is, those indicated as infective to man—into humans to confirm that indication. This concordance between test result and infectivity to man may be studied by trial in the B.I.I.T. of strains isolated from naturally infected subjects. Only the opposite concordance, that of negativity in the B.I.I.T. with non-infectivity for man, calls for experimentation with humans; and the subjects used for such experimentation should be people who have never visited Africa and who may therefore be assumed not to have any acquired immunity to infection with *Trypanosoma brucei* subspecies.

The B.I.I.T. is dependent on the “neutralization” by human serum of the infectivity of *T. brucei brucei* (non-man-infecting) to laboratory rodents and on the absence of such “neutralization” effect in the case of *T. brucei rhodesiense* (man-infecting). It is not necessarily dependent, as you suggest, on the lysis of the organisms.—I am, etc.,

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Inversion of the Appendix

SIR,—In his letter reporting a unique late complication following the operation of inversion of the appendix Mr. G. H. Dickson (18 May, p. 385) invites accounts of other complications that may have been met with. I suspect that he will receive few replies as not many surgeons use this procedure and many are not even aware of what it implies. In addition, complications

TABLE I—Results of the plasma cortisol determinations ($\mu\text{mol/l.}$)

Participant No.	Control Samples		After Marathon
	1200 hr	1600 hr	
1–11	0.44 $\pm$ 0.19 (S.D.)	0.26 $\pm$ 0.10 (S.D.)	1.15 $\pm$ 0.36 (S.D.)
12	0.54	0.44	1.45
13	0.41	0.24	0.26
14	—	0.45	1.24

are very uncommon and are probably fewer than when other methods are used.

Reports advocating its use have been published including recent series of cases from the U.S.A.,¹ Uruguay,² Holland,³ and Britain.⁴ Complications have been negligible. One advantage of the operation, most commonly performed as a prophylactic measure during operations for other abdominal conditions, is that it avoids cutting across the appendix with the risk of infection that this entails, as when the ligated stump is buried in the wall of the caecum under a purse-string suture.

The principle of the operation is to turn the appendix completely outside in, as one does with the finger of a glove, so that it comes to lie in the lumen of the caecum. It is usually done by stripping the appendix of its mesentery and turning in its tip with a probe, which is advanced until the appendix has completely disappeared into the interior of the caecum, leaving only a tiny depression. This is oversewn with a non-absorbable cross-stitch which also includes any remaining blood vessels going to the appendix, which will then slough off and be digested. Radiographic studies show that this happens after a week or so. In any event appendicitis cannot occur because of the changed anatomy.

Gynaecologists have most opportunity of incidental elimination of the appendix, and it has been my routine to do so in all appropriate cases during pelvic surgery. I have employed the inversion technique exclusively since 1958 and have used it over 1,000 times. In no case has there been any post-operative complication whatever and I am unaware of any at a later date. Colleagues who have adopted the same procedure have had similar results. I therefore support the view of Edelbohl⁵ who in 1895 wrote: "Inversion of the normal appendix is so simple and easy a matter, withal in itself so devoid of danger, that the writer is prepared to advocate inversion of the appendix whenever for any reason the abdomen is opened. There are those surgeons who under the conditions just stated advocate ligature and removal of the normal appendix. How much more does their logic apply to the inversion of the entire appendix as contrasted with ligature and ablation."—I am, etc.,

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¹ Hallatt, J. G., *American Journal of Obstetrics and Gynecology*, 1958, 75, 1043.

² Lopez, M. B. R., *Archivos des Ginecologia y Obstetricia del Uruguay*, 1962, 20, 140.

³ Aartsen, E. T., *Nederlandsch Tydschrift voor Verloskunde en Gynaecologie*, 1966, 66, 100.

⁴ Young, H. B., and Goodhead, B., *Journal of the Royal College of Surgeons of Edinburgh*, 1972, 17, 55.

⁵ Edelbohl, G. M., *American Journal of the Medical Sciences*, 1895, 109, 650.

Multiple Prescribing

SIR,—It has been said that geriatrics is the art of taking patients off tablets. In the example I am reporting your readers may like to work out which tablets were treating the effects of others and in what order they were accumulated.

The patient, a 75-year-old woman whom I was asked to see at home because she was "arthritic and becoming unable to cope," was sitting in a chair, mildly confused, incontinent of urine, and un-

willing to walk because she had been falling often. The only physical abnormality of note was osteoarthritis of the knees. She said she was "on rather a lot of pills but was managing to get them all down." Inspection of her bedside table revealed tablets containing the following: (1) dextropropoxyphene and paracetamol; (2) phenylbutazone; (3) aspirin, codeine, and caffeine; (4) aspirin, magnesium carbonate, and aluminium glycinate; (5) aluminium hydroxide; (6) dicyclomine hydrochloride, doxylamine succinate, and pyridoxine hydrochloride; (7) alkaloids of belladonna leaf, ergotamine tartrate, phenobarbitone; (8) medazepam; (9) prochlorperazine; (10) calcium lactate; (11) sodium chloride; (12) Senokot; (13) ferrous sulphate; and (14) proteolytic liver and vitamin B₁₂. There were also liquid paraffin; chlorpromazine linctus; and a "vegetable treatment for rheumatism" containing watercress, celery, horse-radish, parsley, lettuce, and mint.

This patient was taking a total of 26 different drugs together with a liver paté and salad. Should this be entered in the *Guinness Book of Records*? She was admitted to hospital, all tablets were stopped, and she returned home fully mobile 10 days later.—I am, etc.,

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Intradermal Influenza Vaccination

SIR,—The possibility of achieving satisfactory immunization against influenza with a small intradermal dose of vaccine has obvious attractions, as Dr. J. D. Avison has pointed out (10 November, p. 358). Tauraso and others¹ showed that 0.1 ml of killed vaccine given intradermally with syringe and needle produced as good an antibody response as a standard 0.5-ml subcutaneous dose, but this method is unsuitable for mass vaccination. Jet injectors can be adjusted to deliver intradermally but the entire dose may not always be implanted in the skin, and their use in this way for vaccination with killed vaccines has been criticized.^{2,3} Recently we were able to assess this method using a Portojet gun. Though the results were not clear cut we think they are worth recording.

In two local boarding schools, one with 600 boys and the other with 240 girls, influenza immunization has been carried out each October for several years by the Schuco Jet Injection Service. In 1973, owing to manufacturing difficulties, there was insufficient vaccine to give both schools the usual 1-ml dose, so a decision was made to give a reduced dose intradermally. A volume of 0.15 ml was chosen on Schuco's recommendation, based on experiments showing that a leakage of 0.05 ml may occur with this method. Simultaneously a trial was conducted on 87 volunteers (51 boys, 8 girls, and 28 staff). They were divided into two groups—those born on odd dates were given 1 ml Admune vaccine subcutaneously, and those born on even dates 0.15 ml of the same vaccine or 0.15 ml Influvac intradermally. Each 1 ml Admune contained 400 IU A/England/42/72, 100 IU B/Vic. 98926/70, and 100 IU B/Hong Kong/8/73. Thus

0.15 ml Admune contained 60, 15, and 15 IU of the three viruses respectively. Each 0.15 ml of the Duphar vaccine contained 120 IU A/England/42/72, 60 IU B/Berkeley/1/71, and 60 IU B/Hong Kong/8/73. Blood samples from the volunteers were taken at the time of the inoculation and again three weeks later. Haemagglutination inhibition tests were run in parallel on the paired sera against three virus antigens: A/England/42/72, B/England/1/68, and B/Hong Kong/5/72. The method used was that described by Hoskins⁴ in which the reagents are used in 0.25-ml amounts in W.H.O.-type plastic agglutination trays.

Fewer people in the intradermal group showed a four-fold or greater rise of antibody to the three viruses than the subcutaneous group (table I), but the differences were not statistically significant. In the case of virus A preinoculation titres were generally high and this may have modified the overall antibody response, for even in the subcutaneous groups only about one-third of the subjects showed a four-fold antibody rise. Response to the B viruses was poor in both groups, even though initial antibody titres were low, and the proportion of the subcutaneous control group showing a four-fold rise was less than half that found by Schild and his colleagues.⁵ We can offer no explanation for this. Within the intradermal group responses to the Admune and Influvac vaccines were not significantly different, though surprisingly there seemed to be less response to the vaccine containing the larger amount of virus (Influvac). Reactions to intradermal inoculation were minimal and local discomfort less than with subcutaneous jet inoculation; also the need for preliminary skin testing of "allergic" patients was eliminated.

We believe that the economic and other advantages of this method merit its further assessment and that on existing evidence its use might well be justified when vaccine supplies are limited.—We are, etc.,

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¹ Tauraso, N. M., et al., *Bulletin of the World Health Organization*, 1969, 41, 507.

² *British Medical Journal*, 1970, 4, 64.

³ Roberts, T. E., *British Medical Journal*, 1973, 4, 738.

⁴ Hoskins, J. M., *Virological Procedures*, chap. 20. London, Butterworth, 1967.

⁵ Schild, G. C., et al., *British Medical Journal*, 1973, 4, 127.

Self-administered Clinical Questionnaires for Outpatients

SIR,—Reading Drs. J. M. Gumpel and A. M. S. Mason's interesting paper (27 April, p. 209) on medical questionnaires made me wonder again why they are so slow to catch on. Patients like them, and once one has used them in a clinic there is a real sense of deprivation if they are not available. It may be just conservatism that has delayed their more widespread acceptance, but I think the real reason is the feeling that forms equate with bureaucracy, a condition rightly

TABLE I—Antibody Responses

Vaccine Dose	No. of Persons Tested	No. (%) with 4-fold rise of H.I. Antibody		
		A/Eng/42/72	B/Eng/1/68	B/HK/5/72
1 ml subcutaneous ..	37	14 (38)	10 (27)	8 (22)
0.15 ml intradermal ..	50	12 (24)	10 (20)	7 (14)

TABLE II—Mean (Geometric) H.I. Antibody Titres before and after Vaccination

Vaccine Dose	No. of Persons Tested	A/Eng/42/72		B/Eng/1/68		B/HK/5/72	
		Before	After	Before	After	Before	After
1 ml subcutaneous ..	37	105	263	12	30	2.2	8.6
0.15 ml intradermal ..	50	81	175	14	36	2.6	8.9