tested, but not justifiable that the best be condemned for the performance of the worst.

It is true that some of the most publicized trials have been statistically flawed because of high rates of "loss to follow-up," but the reservations this should occasion in our assessment of their results are by no means so sweeping as Dr. Hawkins suggests. Most recent trials, conducted in developing countries, have assessed results on the more correct basis of sample home follow-up studies, where the probabilities of important selection factors in untraced patients is very much lower than in consulting-room studies. These trials have yielded results in all ways comparable to those of Tietze's co-operative statistical programme.¹

While not necessarily the last word, the W.H.O. Scientific Group statement on infection,² "in general, pelvic infection is not a significant problem," represents an informed judgement of the information available in 1968. Incidences of pelvic inflammatory disease "up to 8%" are found only in studies where incidences of this order occur even in the absence of I.U.D.s or when extremely dubious definitions of inflammatory disease are used. The same consideration applies to menstrual disorder, where the incidence depends almost wholly on the criteria of definition employed. Minor menstrual changes, especially increased flow, are undeniably extremely common, especially in the first months of use. In assessing the safety and acceptability of I.U.D.s, our attention must be confined to the severe or persistent disturbances.

The survey of deaths and critical illnesses³ offers a further illustration of this point, for no definition of critical illness was included in the inquiry. This study in fact revealed only four deaths attributable to the I.U.D., with three doubtful associations and three quite unlikely ones. May I, in passing, correct the figure of perforations of the uterus, which is given in the report as 192, not 207. It is of interest for the assessment of clinical impressions and case reports to note that each of the deaths reported to the authors of the survey was reported by several physicians, and one case of perforation with intestinal obstruction was reported by no fewer than 21 doctors.

I find it regrettable that Dr. Hawkins has resurrected some of the old material which was used to "kill" the Gräfenberg ring. The 17 deaths reported in the *Journal of the American Medical Association*⁴ are something of a medical mystery. In that journal they are all attributed to a practitioner named Rust, and said to be the result of general peritonitis or septicaemia. In 1938, in an article by Howard Clark,⁵ they appear again, now attributed to Reist, and the result of perforation. Did these women ever die? Were they in fact wearing Gräfenberg rings? We shall never know.

No one will claim that I.U.D.s are entirely devoid of potential hazards. The extent of these hazards is under continuous careful scrutiny by persons skilled in the evaluation of data and wary of the traps of statistical analysis. Case reporting has its part to play in this process, but must not be allowed to derange our judgement. Sufficient data has been collected and analysed for us to be content that expulsion rates in the first year with accepted devices do not exceed 10% nor

pregnancy rates 3%, and that threat to life is of extreme rarity. Let us base our judgements on such sober figures.—I am, etc.,

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REFERENCES

- ¹ Tietze, C., *Co-operative Statistical Programme for the Evaluation of Intra-Uterine Devices, Eighth Progress Report*. New York, Population Council, June, 1967.
- ² W.H.O. Scientific Group on Physiological and Clinical Aspects of Intra-Uterine Devices, *W.H.O. Technical Report Series No. 397*, 1968, p. 21.
- ³ Scott, R. B., *Obstetrics and Gynaecology*, 1968, 31, 322.
- ⁴ American Medical Association Committee on Contraceptive Practices, *Journal of the American Medical Association*, 1937, 108, 413.
- ⁵ Clark, H. C., *American Journal of Surgery*, 1938, 39, 631.

Transferable Drug Resistance

SIR,—In her paper (17 May, p. 405) Professor Ellen Moorhouse quotes Miss Sheila Halls and myself (29 January, 1966, p. 266) as having isolated R factor-containing *Escherichia coli* from 15 of 24 adult human beings who looked after *farm animals* (my italics). This is not correct. In our paper we did mention that the ampicillin-resistant strains of *E. coli* found in this survey of human beings originated from human beings who looked after intensively reared calves. Although four such strains were examined they did, in fact, originate from two people only. None of the other 13 people with R factor-containing strains in their faeces actually looked after animals. It is therefore not surprising perhaps, as Professor Moorhouse states, that our results resembled those she obtained in her study of healthy infants.

Miss Halls and I never took the view that the 13 people referred to above had acquired their R factor-containing strains from the animal community. On the contrary, in our Discussion we mentioned that we thought the transfer of R factor-containing strains from one of the following species, man, ox, pig, and fowl, to the other was of limited importance because we had found a high incidence of R factor-containing strains in each species.—I am, etc.,

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Hypotensive Treatment

SIR,—There is of course much that I would agree with in your expert's contribution to your series on "Today's Drugs" in the treatment of hypertension (10 and 17 May, pp. 365 and 430). Some statements, however, are at least odd, and some require more detailed classification for the guidance of those who lack special experience in this field.

Under "general considerations" I feel that before lifelong treatment is started baselines should be obtained both as an aid to diagnosis and for reference in future manage-

ment. In addition, a full clinical examination is required which will take into account the appearance of the retinal vessels, the state of all the peripheral pulses, the presence of renal masses and of abdominal bruits, the character of the apex beat, and the quality of the heart sounds. The minimum investigations required are a urine analysis, estimation of blood urea and electrolytes, a chest x-ray to determine the size of the heart, the aorta, and the presence or absence of signs of pulmonary venous congestion, an E.C.G., and an excretion pyelogram. All these investigations should be available in district hospitals to the general practitioner. Ideally every patient should be screened for phaeochromocytoma by an estimation of catecholamine excretion (or of its degradation products) in the urine, but this is not always practicable.

With most physicians I would agree with your expert contributor that "increasingly complicated, expensive, and sometimes dangerous investigations" are uncalled for in most patients, but I would certainly not select as suitable for them "the younger patient with severe vascular disease or renal failure," as these are patients who are unlikely to profit from them. I agree that renal failure, with the exception of clinical uraemia, is no contraindication to hypotensive treatment even though the long-term outlook may not be favourable, but would add that the appearance of hypertension in the course of asymptomatic renal disease constitutes an urgent indication for hypotensive treatment.

As for the heart, how odd to state that "breathlessness on exertion is probably more a reflection of left ventricular failure with incipient pulmonary oedema than of hypertension per se." Certainly, but in most cases left ventricular failure is caused by work overload and it would seem logical to lessen the load with hypotensive treatment. In our urban society with its sedentary habits, symptoms such as breathlessness on exertion can precede physical signs indicative of left ventricular "strain." These comprise alteration of the pulse, a left atrial added sound, accentuation of the pulmonary component of the second sound, and reversed split of the second sound (even in the absence of left bundle branch block). These signs should be carefully sought for, and when present constitute an indication for hypotensive treatment, even in the absence of symptoms.

I personally have little doubt that hypertensive patients with angina benefit from hypotensive treatment, as this diminishes the work of the heart. However, it is probably wise to avoid drugs which can cause severe orthostatic and exertional hypotension, as this may lower coronary perfusion pressure below the critical point—therefore reserpine or methyl dopa with an oral diuretic would seem to be the drugs of choice in this situation. As for oral diuretics, one explicit recommendation must be made—that they be used daily, especially in conjunction with ganglioplegic and adrenergic blocking agents. Their intermittent use, which one has observed many times, is to be deplored because the blood pressure will be considerably higher on the days in which they are not used.

I agree with the preference expressed for bendrofluazide, because it is the cheapest diuretic and it is also of medium length of action. My distinct impression is that long-acting diuretics such as chlorthalidone and polythiazide lead to greater potassium loss. The short-acting diuretics such as frusemide and ethacrynic acid are both expensive and too violent in action—they should be reserved

for established left ventricular failure or given in the late afternoon to prevent paroxysmal nocturnal dyspnoea. The need for potassium supplements is governed by many factors, such as the potassium content of the diet, the presence or absence of primary or more commonly secondary hyperaldosteronism. It must be remembered that severe sodium restriction is a powerful stimulant to aldosterone secretion; therefore, if dietary sodium is restricted, potassium supplements are likely to be needed.

Finally, Dr. Susan Cotton and I¹ did not report occasional evidence of mild liver dysfunction in patients treated with guanoxan, but five cases of frank hepatitis with jaundice, one of them fatal, in addition to laboratory evidence suggestive of hepatic dysfunction in a third of the first 100 treated patients.—I am, etc.,

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REFERENCE

- ¹ Cotton, S. G., Lovel, T. W. I., and Montuschi, E., *Clinical Trials Journal*, 1967, 4, 707.

SIR,—The first article on hypotensive drugs, *Today's Drugs* (10 May, p. 365) will be of considerable value in guiding practitioners in the prescribing of drugs for the treatment of hypertension. It is unfortunate, therefore, that an error has crept into the Table indicating the daily doses of some of the more commonly used hypotensive agents. The dose of chlorthalidone (Hygroton, Geigy), is given as 100–200 mg. per day. This dose grossly exceeds that which is recommended—namely, 50 mg. per day. There is evidence¹ that little benefit is to be obtained in the use of a larger dose than 50 mg. daily in the maintenance of the majority of hypertensive patients.—I am, etc.,

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Geigy Ltd., Pharmaceuticals Division,
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REFERENCE

- ¹ Cranston, W. I., et al., *Lancet*, 1963, 2, 966.

* * We have shown Dr. Domenet's letter to our contributor who replies: "The daily dose of 100–200 mg. of chlorthalidone was based on a majority opinion taken from the literature. The observations of Cranston and his colleagues, cited by Dr. Domenet, were that 50 mg. daily produced a mean blood pressure fall of 17.9/8.9 (systolic/diastolic) mm. Hg, 100 mg. daily produced a mean fall of 27.5/13.9, and 200 mg. daily a fall of 29.8/14.7. The wide range of variation of individual patients and the relatively small numbers in the trial make statistics scarcely applicable, but the general trend of the results was the same for chlorthalidone as for the two thiazides tested. Most trials of chlorthalidone in hypertension have used daily doses between 100–200 mg. daily, but if one desires a slightly smaller hypotensive effect with a corresponding reduction in cost and possible complications of therapy then it is very reasonable to use 50 mg. daily, which certainly has a measurable and significant hypotensive effect, even though it is only about two-thirds of that achieved with 100 mg.

"Dr. Domenet, however, does us a useful service in emphasizing the way in which the

dose/response curves for diuretics in the treatment of hypertension tend to become relatively flat in the higher dose range, so it may well be correct that there is little virtue in giving the full dose of 200 mg. of chlorthalidone or 10 mg. daily of bendroflumazide when nearly as good blood pressure reduction can be achieved with considerably smaller doses."—Ed., *B.M.J.*

Miliary Tuberculosis

SIR,—In the article on miliary tuberculosis in adults (3 May, p. 273), the difficulty was stressed of making the diagnosis in elderly patients. This is also the case in young children. Bentley, Grzybowski, and Benjamin¹ showed there had been a failure to diagnose the condition radiologically in nine out of 28 children found to have miliary tuberculosis at post mortem. Occult or cryptic miliary tuberculosis can present considerable diagnostic difficulty in small children with tuberculosis complicating kwashiorkor. A high index of suspicion for the condition should be kept by those working in a famine area.—I am, etc.,

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(South Wales),
Cardiff.

REFERENCE

- ¹ Bentley, F. J., Grzybowski, S., and Benjamin, B., *Tuberculosis in Childhood and Adolescence*, 1954. London, National Association for the Prevention of Tuberculosis.

Metabolic Response in Ethnic Groups

SIR,—May we reply briefly to Dr. D. Craddock's criticism (26 April, p. 247) of our paper (22 March, p. 748)?

First-cousin marriages are very common among Moslem Indians in Johannesburg, occurring in about 60% of unions in one study,¹ and it is reasonable to postulate that genetic factors play some role in their metabolic responses, including the fact that they suffer from diabetes mellitus more frequently than do whites.

We have no wish to get involved in the "sugar controversy," but we must point out that sucrose is not absent from the diet of Johannesburg Africans. There are no accurate figures on the sugar consumption of these people, but there is no doubt that their intake of sucrose, both as such and in the form of jams, cold drinks, confectionery, etc., is substantial.

Our subjects were matched in respect of their physical characteristics, and at the same time were representative of their respective population groups, which explains why the whites were taller and heavier than the Africans. However, as indicated in our paper, when the weights were expressed as percentages of ideal body weight there was no significant difference between the groups.—We are, etc.,

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University of the Witwatersrand
Medical School,
S. Africa.

REFERENCE

- ¹ Seftel, H. C., *Medical Proceedings*, 1967, 13, 3.

Treatment of the Phobic Anxiety State

SIR,—I refer to the article "Anxiety Neuroses and Phobic States. II—Diagnosis and Management" by Professor Martin Roth and Dr. D. H. Myers (1 March, p. 559). There is clearly a difference of opinion between these authors and Dr. William Sargent (5 April, p. 49).

Professor Roth and Dr. Myers state "dangerous interaction may occur between a M.A.O.I. and any of the following drugs: the opiates, pethidine, local anaesthetics, sympathomimetic amines, methyl dopa, and the tricyclic antidepressants. M.A.O.I.s are inactivated slowly: for this reason these foods and drugs must be avoided both during treatment and for 14 days afterwards."

Dr. Sargent, on the other hand, specifically uses tricyclic antidepressants to establish a normal sleep pattern. "If the patient's sleep is impaired, specially by early morning waking, then we consider that monoamine-oxidase inhibitor drugs should be given during the day and a tricyclic antidepressant should also be given in the evening to try and get a return to normal sleep pattern."

When one specialist in psychological medicine advocates a method of treatment which is stated to be frankly dangerous by another, could a non-specialist like myself kindly ask for clarification?—I am, etc.,

GEORGE C. WILSON.

Kogarah Bay,
N.S.W., Australia.

Bilateral Posterior Dislocation of Shoulders

SIR,—In view of the low incidence of posterior dislocation of the shoulder, compared with that of anterior dislocation, it would seem justified to report an interesting case of bilateral posterior dislocation which recently presented in the accident room of this hospital.

The patient was a woman of 68 years who was otherwise healthy and gave no history of previous dislocation of the shoulder. She had been cleaning her electric fire the previous evening without having first taken the precaution of switching it off. While doing so she rested her left hand on the fire frame and then accidentally touched the element with her right hand. The shock she received made her fall backwards against her bed, and subsequently she found that she could move neither arm. She remained like this during the night, apparently in surprisingly little pain, before attending the infirmary the following afternoon.

On examination there was obvious deformity of both shoulders, and both arms were held immobile by her sides—a posture that would be instantly recognizable again. The only other physical signs were almost complete inability to move either shoulder and a small patch of erythema on her right hand, which was the site of contact with the hot element. She otherwise appeared healthy.

Radiographs subsequently demonstrated the presence of bilateral posterior dislocation of the shoulder, and she made a good recovery following reduction. The mechanism of dislocation here was presumably spasm of the posterior shoulder girdle muscles forcibly pulling the humeral heads posteriorly, owing to the electric current passing across the body from one arm to the other as one hand was