implications of this is that logical replacement therapy should probably be based on the production rate; this amounts to approximately 15 μg/kg/day.

(2) Although it is obvious that clinicians should want to reduce the number of injections given to children to the minimum, this should not be allowed to compromise the efficacy of treatment. The situation is similar to that with insulin in diabetic children, and it is never advised that this be given only twice weekly. Since growth hormone can be given subcutaneously it is logical that children with growth hormone deficiency should be taught to give their own injections of growth hormone in the same way as diabetic children. By the very nature of their problem it will be necessary to continue only until epiphyseal fusion occurs and not for life. This treatment schedule, if it were shown to be effective, would mean a considerable saving in growth hormone and could make it more widely available for countries not quite so fortunate as our own.

(3) All new therapeutic substances go through a stage of assessment of efficacy and safety before being made generally available. With growth hormone we feel that this stage was passed several years ago and that treatment and assessment of response to the hormone can now be carried out by a much larger group of hospitals, especially those with recognised paediatric and endocrine units with facilities for diagnosing growth hormone deficiency. This would involve making supplies of the growth hormone available to these units (perhaps the participation of the DHSS in growth hormone production is a signal that is about to happen) and would improve the convenience of follow-up and ensure continuity of care for the patients.

This does not mean that the growth assessment centres are no longer necessary; there remains much to learn about the best ways of treating these patients. We would like to see a trial of growth hormone treatment given by frequent and smaller dosage regimens assessed both by development and measurement of somatomedins. This is a trial that could conveniently be arranged through the existing Medical Research Council structure but would allow paediatricians and endocrinologists to treat their patients without having to refer them to the few and unevenly distributed "recognised" assessment centres.

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¹ Owens, D, et al, *European Journal of Clinical Investigation*, 1973, 3, 284.

Psychiatric aspects of shoplifting

SIR,—Dr M Segal's long list of psychiatric causes for shoplifting in his thoughtful letter (28 February, p 523) is impressive. Unfortunately, he has omitted the commonest cause of all—namely, simple stealing for gain. I prefer to call it stealing rather than shoplifting, a term which has developed an aura of respectability, and is almost a medical diagnosis. Whether rich or poor, famous or unknown, we all have the desire to obtain something for nothing. The fact that someone has a large sum of money in her purse or £50 000 in his bank when caught shoplifting does not imply (as many probation officers seem to think) that he or she must be mentally ill. He is simply doing what the modern supermarket openly invites us all to do—help ourselves. It is a basic impulse which has even been given the dubious honour of being called "the acquisitive instinct."¹ However, greed does not justify dishonesty.

In many years experience of psychiatry I have seen a steady stream of these cases referred by the courts. Very rarely indeed have I found any psychiatric disorder in these cases. True, there is the occasional case of a depressed menopausal woman, the odd schizophrenic, and the infrequent confused organic dementia. In over 30 years I can recall only one case of true compulsive stealing.

The truth about shoplifting seems to lie not so much in an esoteric diagnosis but more in Oscar Wilde's comment that the simplest way of dealing with temptation is to yield to it.

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¹ McDougall, W, *An Outline of Psychology*, 6th edn, p 161. London, Methuen, 1933.

Not so double-blind?

SIR,—Professor T W Anderson and his colleagues (21 February, p 457) suggest that a clinical trial can be called double-blind only if active and placebo preparations are indistinguishable and that evidence by a "taste committee" or similar group should be included before editors accept the description of "double-blind" for published trials. This implies that trials are double-blind only if all medicaments under test appear to be identical, which is just not true.

May I refer to the recent report on clinical trials by the Medico-Pharmaceutical Forum,¹ which states: "Double-blind Trials—A double-blind trial must ensure that neither patient nor observer recognises a treatment and preferably does not identify a treatment as being the same that he or others receives or prescribes or has received or prescribed in the past. Such lack of recognition (blindness) avoids bias by either patient or clinical assessor. . . . 'Identical' Medicaments—The simplest way of preventing recognition of medicaments is to make them appear identical for both test and control groups. While this is an established method, it may involve some risk of an increased carry-over effect in cross-over trials for an active treatment to a matching dummy or vice versa, resulting in a potential loss of sensitivity."

This makes it quite clear that the use of "identical" medicaments is just one method of organising a double-blind trial. Any method that prevents recognition of a preparation under

test by patient or doctor permits a valid double-blind trial and it is not essential for active treatment and placebo to appear to be identical.

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¹ Medico-Pharmaceutical Forum, *A Report by the Forum's Working Party on Clinical Trials*. London, Medico-Pharmaceutical Forum, 1974.

SIR,—Professor T W Anderson and his colleagues (21 February, p 457) express concern at the loose way the term "double-blind" is often used in reports of clinical trials and consider that "active and placebo preparations should be indistinguishable (short of chemical analysis) by any patient, nurse, or physician of average intelligence and curiosity." They recommend that the active and placebo preparation should be examined by a "taste committee" of 20 or 30 colleagues.

We have undertaken a study¹ using a panel of four observers to compare the matching qualities of 22 pairs of agents which have been employed in double-blind investigations. Our study demonstrates that Dr Anderson and his colleagues' concern is fully justified but also shows the adequacy of a small panel of assessors. Five pairs of substances were virtually indistinguishable, but in seven there were differences obvious to all the panel members. For this reason we recommended that matching properties should not be evaluated casually, but should be investigated in a formal way along the lines of our study, as Joyce² has also suggested.

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¹ Hill, L E, Nunn, A J, and Fox, W, *Lancet*, 1976, 1, 352.

² Joyce C R B, in *Psychopharmacology Dimensions and Perspectives*, ed C R B Joyce, p 215. London, Tavistock, 1968.

Progression and regression of atherosclerosis

SIR,—Your leading article on this subject (28 February, p 481) omits all mention of important experimental work carried out over the past 20 years on non-human primates. Recent visits to Chicago and to Iowa were immensely impressive, and it is very difficult to believe that anyone familiar with this work could doubt its relevance to man.

Rhesus monkeys are very similar to man in cardiovascular anatomy and cardiopulmonary physiology and in their lipoproteins and are not susceptible to spontaneous atherosclerosis. By feeding an ordinary American diet prepared by the chief medical nutritionist of the Chicago University Hospital and containing a mixture of 25 of the most commonly eaten constituents, such as beef, pork, fish, poultry, eggs, butter, margarine, cheese, cereals, cake, potato, vegetables, fruit, orange juice, and so on, Wissler and Vesselinovitch¹⁻⁸ have produced severe atherosclerotic lesions, both in their earlier and later stages, which closely resemble those seen in humans. Characteristic complex changes occur, with proliferation of collagen, fibroplasia, central necrosis, ulceration, thrombosis, and calcification, followed by "clinical" complications, including coronary occlusion,

myocardial infarction, and ischaemic gangrene. By immunohistochemical techniques, electron microscopy, and tissue culture the evidence indicates that the underlying mechanisms include migration of low-density β -lipoproteins through the arterial wall and stimulation of multipotential smooth muscle cells in the media, with their resultant proliferation and migration into the intima.

Previously, in Iowa, Armstrong *et al*^{7,8} demonstrated that, in more cellular lesions produced by a stronger dietary stimulus, considerable lipid depletion, condensation of fibrous tissue, and widening of the lumen resulted after returning to a natural diet. This has now also been shown in Chicago.

Interestingly and very importantly, if these primates are fed on what is now termed a "prudent" diet and recommended by many physicians for patients with coronary disease and those at high risk very little atherosclerotic change develops. The difference between the normal and the prudent diet is a reduction in total calories, saturated fat, and cholesterol, with partial replacement of saturated by polyunsaturated fat. Interestingly too, there is individual variation in susceptibility, as in man, and some animals are immune.

What more could one want? Surely, to doubt the relevance of this work to man is stretching incredulity beyond reasonable bounds. Of course, observations such as these in groups of humans are impossible. New techniques may be developed, but at present there is no possibility at all of conclusive evidence being obtained in man by long-term prospective intervention studies in free-living populations on account of the logistics, let alone the prohibitive costs.

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- ¹ Wissler, R W, and Vesselinovitch, D, in *Advances in Lipid Research*, vol 6, p 181, New York, Academic Press, 1968.
- ² Wissler, R W, and Vesselinovitch, D, *Annals of the New York Academy of Sciences*, 1968, **149**, 907.
- ³ Wissler, R W, *Journal of Atherosclerosis Research*, 1968, **8**, 201.
- ⁴ Wissler, R W, and Vesselinovitch, D, in *Pathology Annual*, 1969, New York, Appleton-Century-Croft, 1969.
- ⁵ Wissler, R W, *et al*, *Circulation*, 1971, **44**, 57.
- ⁶ Wissler, R W, in *The Myocardium: Failure and Infarction*, ed E Braunwald, New York, H P Publishing Co, 1974.
- ⁷ Armstrong, M K, Warner, E D, and Connor, W E, *Circulation Research*, 1970, **27**, 59.
- ⁸ Armstrong, M K, and Megan, M B, *Circulation Research*, 1972, **30**, 675.

These papers contain references to the work of many others in this field.

Antenatal diagnosis of the mucopolysaccharidoses

SIR,—In 1973 I was co-author of a method for the measurement of glycosaminoglycans (acid mucopolysaccharides) in amniotic fluid and urine.¹ While we appreciated that the ultimate diagnosis should depend on demonstration of the specific enzyme defect, it was hoped that analysis of glycosaminoglycan cell-free amniotic fluid would offer a more practical means of diagnosis.

In two cases with hysterotomy fluids taken respectively at 25 weeks' and 24 weeks' gestation the technique yielded results consistent with a San Filippo syndrome² and a Hurler syndrome. In the second case, however, a previous amniotic fluid sample analysed at 16 weeks' gestation gave normal results. Enzyme analysis and sulphate uptake studies

performed by other workers on cultured amniotic cells from the earlier amniocentesis revealed that the fetus was affected by Hurler's syndrome. I therefore consider that the only possible value of the method for glycosaminoglycan analysis described would be in later gestation samples where enzyme and sulphate uptake studies might not yield results soon enough. Currently it appears that the best means of diagnosis is by enzyme analysis and sulphate uptake studies undertaken on cultured amniotic cells obtained at 16 weeks' gestation.

Provision of a grant from the Advisory Committee on Medical Research to this department has enabled the technique of enzyme analysis to be instituted on cultured amniotic cells supplied by Professor M A Ferguson-Smith, of the medical genetics unit at these hospitals. The analyses now available include those concerned in the diagnosis of mucopolysaccharidoses types I*, IIIa, IIIb, V*, VI, and VII. The opportunity to analyse cultured cells from known or suspect cases from outside Glasgow would be welcomed.

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¹ Duncan, D M, *et al*, *Clinica Chimica Acta*, 1973, **45**, 73.

² Harper, P S, *et al*, *Journal of Medical Genetics*, 1974, **11**, 123.

*Phenyl iduronide substrate kindly made available by Drs E F Neufeld and B Weissman (NIH-NIAMDD 73-2205).

First aid in acute myocardial infarction

SIR,—Your excellent leading article with this title (14 February, p 356) did not in fact discuss first aid. I believe that specific first-aid measures may reduce the mortality and morbidity caused by myocardial ischaemia and can be undertaken by anyone before the doctor arrives.

While working in a factory medical unit I have frequently seen patients within minutes of the onset of symptoms. Sometimes there is a resemblance to a vasovagal syncope episode with bradycardia, a weak, thready pulse, pallor or cyanosis, and collapse or even unconsciousness. Presumably these manifestations are caused by parasympathetic over-activity. Well-meaning friends and helpers usually prop up the patient in a chair or leave him slumped across a desk. Placing the patient on the floor and raising the feet, together with instructions to breathe deeply, often produce a remarkable improvement. Of course, the airway of an unconscious person must be ensured. Administration of oxygen (or Entonox if the pain is severe) also appears to help. It is not unreasonable to assume that by ensuring adequate venous return and full oxygen saturation of the haemoglobin, and possibly dissolving a small additional amount of oxygen in the plasma, fibrillation of the anoxic myocardium might be prevented.

In my experience most patients with acute chest pain from myocardial infarction or angina have shallow respiration. Indeed some of them appear to have respiratory depression, which could reduce oxygen saturation of the haemoglobin and the supply of oxygen to the myocardium. Therefore I believe that all patients with symptoms of acute myocardial ischaemia should lie flat with the feet elevated and be

instructed to take deep breaths. It is our usual practice to wait until the patient's condition stabilises before transporting him or her to hospital, and oxygen or Entonox may be administered during the journey.

Analysis of blood gases in the early moments following the onset of symptoms would make a fascinating study. Reduced oxygen tension of the blood from physiological factors could account for some of the early mortality.

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SIR,—In your leading article (14 February, p 356) you mention important recommendations for the early care of patients with myocardial infarction. However, the following statement could be misinterpreted: "For a patient in jeopardy from tachycardia . . . both intravenous practolol (5-10 mg) and verapamil (10 mg) are relatively safe drugs. . . ." This advice could possibly lead to the successive administration of both drugs if one of them was ineffective or even to the simultaneous administration of the two drugs.

Nayler and Szeto¹ reported that beta-adrenoceptor blocking agents and verapamil both possess calcium-antagonistic properties acting through different mechanisms, and both exert a mild negative inotropic effect. According to various authors the combination of a beta-blocker with parenteral verapamil may be harmful. Benaim² reported a case of asystole after administration of 20 mg of practolol intravenously followed within half an hour by 7 mg of verapamil intravenously. Krikler and Spurrell³ observed severe bradycardia and hypotension following administration of verapamil in patients receiving oral propranolol or practolol. In addition, a few cases of serious interactions of a similar type have been reported to our adverse reactions department in which pindolol was used in association with verapamil. These observations suggest that combined medication with beta-adrenoceptor blocking agents and verapamil should be avoided.

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¹ Nayler, W G, and Szeto, J, *Cardiovascular Research*, 1972, **6**, 120.

² Benaim, M E, *British Medical Journal*, 1972, **2**, 169.

³ Krikler, D M, and Spurrell, R A J, *Postgraduate Medical Journal*, 1974, **50**, 447.

Support for varicose veins

SIR,—Since publication of our article on this subject (31 January, p 254), our attention has been drawn to inaccuracies in the manufacturers' technical descriptions of the garments that we obtained for the study. The correct descriptions of the garments should read: (a) nylon-covered, elastane support tights, average denier 227; (b) nylon-covered, 0.2-mm rubber core, National Health stockings; (c) nylon-covered, elastane support stockings, average denier 150; (d) nylon-covered, elastane support tights, average denier 75; (e) non-supporting tights, average denier 20.

However, we must point out that the average denier of the different fibres used in the manufacture of a garment is only a crude guide to the relative strength of the garment.