admission she was hypothermic (93°F, 34°C, rectal), extremely dehydrated, blood pressure 120/80 mm Hg and pulse rate 66/minute. She was drowsy and confused. The plasma potassium was 5.2 mEq/l., urea 150 mg/100 ml, bicarbonate 5 mEq/l. and blood glucose 600 mg/100 ml. Arterial PO_2 was 92 and PCO_2 13 mm Hg with a pH of less than 6.8. The Ketostix test on undiluted plasma was negative. It was concluded that the patient had lactic acidosis with little or no ketoacidosis.

However, further analyses showed a blood lactate of 11.0 mmol/l. (normal, after an overnight fast, less than 1.0 mmol/l.), pyruvate 0.33 mmol/l. (normal, less than 0.1 mmol/l.), lactate/pyruvate ratio 33 (normal, 8-15), 3-hydroxybutyrate 4.8 mmol/l. (normal, less than 0.15 mmol/l.), acetoacetate 0.30 mmol/l. (normal, less than 0.07 mmol/l.), and 3-hydroxybutyrate/acetoacetate ratio of 16 (normal, 1.5-3). After drawing blood for analyses she was treated with soluble insulin (40 units intravenously and 40 units intramuscularly), intravenous bicarbonate and intravenous saline but 30 minutes later the patient suffered a cardiac arrest and, despite resuscitation, died four hours later.

The raised lactate/pyruvate ratio (an indicator of cytoplasmic NAD/NADH ratio)¹ and raised 3-hydroxybutyrate/acetoacetate ratio (indicating the hepatic mitochondrial redox state)² in both these patients suggests that a severe degree of hepatic anoxia was present. However it would be unlikely that ketone body production should continue at a significant rate in the presence of severe hepatic anoxia. An alternative explanation for the raised 3-hydroxybutyrate/acetoacetate ratio is that in the presence of rapidly deteriorating hepatic function the ratio of ketone bodies in the blood could be set by the preferential uptake of acetoacetate by peripheral tissues (Hawkins, personal communication). Against the suggestion that intracellular pH may determine the redox state and thus the ketone body ratio is the finding that in 30 patients with diabetic ketoacidosis the ratio was either normal or only mildly elevated (Williamson, Hockaday and Alberti, unpublished observation). The raised lactate/pyruvate ratio can reflect poor perfusion of peripheral tissues and need not necessarily imply hepatic anoxia. Thus the ketone body ratio is, with the proviso mentioned above, the more specific indicator of hepatic redox state.³

It is possibly that when lactic acidosis occurs in diabetic patients it will frequently be accompanied by a raised ketone body concentration although the redox state will not necessarily be altered. We cannot offer an explanation for the combined acidosis and redox disturbance found by Dr. Barnardo and his colleagues beyond suspecting tissue anoxia due to septicaemia, but we feel that many such cases will be revealed as more frequent measurements of blood metabolites are made in susceptible patients.

Finally, we should like to emphasize that the Ketostix test for blood acetoacetate can be negative even when total blood ketone bodies are grossly elevated.

We are grateful to Professor P. B. Beeson for permission to report the details of this case. —We are, etc.,

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¹ Hohorst, H. J., Kreutz, F. H., and Bücher, T., *Biochemische Zeitschrift*, 1959, 332, 18.
² Williamson, D. H., Lund, P., and Krebs, H. A., *Biochemical Journal*, 1967, 103, 514.
³ Brosnan, J. T., Krebs, H. A., and Williamson, D. H., *Biochemical Journal*, 1970, 117, 91.

SIR,—I have recently estimated the blood levels of lactic acid in 110 patients in an intensive care unit (in press). This work suggested that inadequate perfusion of peripheral tissue was the most important cause of lactic acidosis. In shock, whether this is secondary to cardiac inadequacy or septicaemia, for example, the level of blood lactic acid is raised. When there is no additional disturbance of metabolism, catabolism of lactic acid may take place, especially in the liver. If however other metabolic disturbances such as diabetes, infection, raised blood alcohol levels, etc. are present unrelated independent lactic acidosis can develop. Under these circumstances, therefore, even a slight peripheral production of lactic acid may induce a severe "idiopathic" lactic acidosis, because the breakdown of lactic acid is inadequate. Furthermore, these studies point out that the level of pyruvate in the blood has no clinical significance, either alone or in relation to lactate as lactate-pyruvate-quotient.—I am, etc.,

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Fingerprint Changes in Coeliac Disease

SIR,—I should like to comment on the interesting paper by Dr. T. J. David and colleagues (5 December, p. 594). Although ridge atrophy may prove to be a diagnostic feature in new cases of adult coeliac disease, after a tentative diagnosis of the latter has been made the cause of associated fingerprint changes should be diagnosed with caution—perhaps until their response to a gluten-free diet has been observed.

The fingerprint changes described, particularly incomplete ridge atrophy and white lines, may on occasions be indistinguishable clinically from those quite commonly seen in dermatitis, including atopic dermatitis, in people with dry hands, and in those whose way of life involves frequent immersion of the hands in water—e.g., housewives. The lowering of ridges seen in dermatitis, housewives, and in some dry hands is reversible. I agree that commonly in dermatitis some fingers may be normal and others affected and that changes of a particular print may be patchy. However, ridge flattening (not usually with complete loss of visible ridges) and white lines of all digits (and often of palms also) may be seen in patients with atopic dermatitis even in the absence of dermatitis involving the fingerprint area.

It is, of course, also well known that skin changes including eczema may be associated with a gluten-sensitive enteropathy, so that one should not be surprised to find eczema present in some cases of coeliac disease. In wasting diseases, generally, ridged skin over finger tips often remains normal (as in the 40 patients mentioned by Dr. David and his colleagues), but it can certainly be dry, flattened, and wrinkled. The high incidence of ridge atrophy found in coeliac disease was clearly not necessarily associated with dry skin, but perhaps some reversible factor interfering with the nutrition of the papillary layer of dermis and epidermis will eventually be found to account for these changes.

The increase in height of skin ridges after treatment with a gluten-free diet is an exciting finding, and will prove of some importance if ridge changes do correlate closely with jejunal mucosal changes. It will also be interesting to see from further studies whether similar fingerprint changes to those described are seen in some patients with tropical sprue, ulcerative colitis, and dermatitis herpetiformis, in which conditions jejunal mucosal changes similar to coeliac disease may be present.—I am, etc.,

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Postoperative Leg Vein Thrombosis

SIR,—When we began our study of the effect of a major surgical operation under general anaesthesia on the rate of the venous return from the lower limbs, we were helped by Mr. L. T. Cotton's earlier investigations on the effect of posture and calf muscle activity on the venous return of conscious patients. Again we are indebted to him and his colleagues (28 November, p. 556) for demonstrating as a fact what we had guessed but not confirmed.

When designing the experiment which showed that during an operation electrical stimulation of the calf prevented the development of venous stasis, which otherwise occurred, we had to decide whether to stimulate the right or left leg in a random series, or always to stimulate the same one. Although there was no proof, rumour said that owing to the compression of the left common iliac vein by the right common iliac artery the venous return from the left lower limb was slower than the right. We therefore chose to always stimulate the left leg because to succeed over an initial disadvantage would strengthen the value of a positive result. We did succeed and our result was the stronger for our choice.

Similarly, when we designed the clinical trial to try and find out if electrical stimulation of the calf reduced the risk of deep vein thrombosis by reducing the risk of venous stasis in the theatre, we considered what effect the stimulation of one leg might have on the rate of the venous return from the other. As we were postulating that venous stasis disposed to deep vein thrombosis, then it followed that, if stimulating one leg accelerated the venous return in the other limb, then by reducing the difference in the rate between the stimulated and the unstimulated limbs it would again make it more difficult to demonstrate that calf stimulation did in fact reduce the risk of deep vein thrombosis. As before, we succeeded.² It is a relief to know that I no longer need worry about the off-chance that stimulating the calf of one limb might reduce the rate of venous return in the other.

As far as the relationship between venous stasis and deep vein thrombosis is concerned, therefore, I need not apologise for using one leg as the control for the other in each patient. To have used both legs so that patients whose limbs were stimulated had to be compared with those in which no stimulation was used at all would have been statistically clumsy and would have

required a very much larger clinical trial. This is exactly the cause of the equivocal results obtained by Mr. G. E. Moloney and his colleagues (24 October, p. 244).—I am, etc.,

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- ¹ Doran, F. S. A., Drury, M., and Sivyver, A., *British Journal of Surgery*, 1964, 51, 486.
² Doran, F. S. A., and White, H. M., *British Journal of Surgery*, 1967, 54, 686.

Cholera Again

SIR,—I venture to disagree with some of the points in your leading article on "Cholera Again" (3 October, p. 2). The 5/4/1 Dacca solution can be used only for cholera or choleraic dysentery. It is absurd to stockpile specialized fluid of this kind when equally good results are obtainable by the use of lactated Ringer (Hartmann's solution), provided that the extra potassium and alkali needed for full replacement therapy are given orally, either as a four-hourly or six-hourly dose of KC_7 , 3 g, and NaHCO_3 , 4.5 g. As lactated Ringer is used for the intravenous therapy of many conditions, it is widely available, and any stock of it can be sure to be turned over regularly as it is used and replaced, thus obviating deterioration as the result of lengthy storage.

It is unnecessary and often actually misleading to use the measurement of plasma specific gravity as an indication of the intravenous fluid requirements. So easy is it to see when the patient has been given enough fluid that we usually delegate the decision when to stop to the nursing staff—after they have had a little supervision over the first case or two—and they have no difficulty in deciding correctly. Surely what our nurses can do a physician in England can also do? I deprecate forsaking observing physical signs in exchange for reading laboratory reports.

My account¹ of the 1965 Brunei cholera epidemic may be of assistance to those who wish to know more of the practical aspects of cholera therapy. A second epidemic on a smaller scale has been dealt with subsequently in an identical manner, and we have yet to see one of our patients succumb to cholera. As a matter of practical experience, therefore, the simpler methods recommended in my article are difficult to improve on.—I am, etc.,

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State of Brunei, Borneo

- ¹ Hart, P. L. de V., *Medical Journal of Malaya*, 1966, 20, 281.

SIR,—In your excellent and most informative editorial on the topical subject of cholera (3 October, p. 2) you comment that "the usual vaccination at present is an injection of 0.5 ml of $4,000 \times 10^6$ each of killed cholera vibrios of Inaba and Ogawa serotypes per ml followed 7 to 28 days later by 1 ml of the same." Those practitioners who have used the Services' cholera vaccine may be interested to know that for many months now an El Tor component, in addition to the classical Inaba/Ogawa fractions, has been incorporated in the vaccine

prepared at the armed Forces own vaccine laboratory—the vaccine contains not less than a total number of $8,000 \times 10^6$ bacilli per ml as recommended by the World Health Organization, and can be used both for subcutaneous injection as described in your editorial and also in 0.1 ml doses for intradermal inoculation, which may suit those who suffer undue reactions after subcutaneous vaccinations.

In the past few years the ever-expanding frontiers of the El Tor epidemic have given good cause for alarm, as indicated so well by Professor B. G. Maegraith's letter (10 October, p. 114), and recently reported experience has shown that El Tor vaccines in a particular locality may have a marginal advantage over a classical-strains vaccine. One must remember that, despite the strikingly different appellation, under the facade of the biotype El Tor there really lurks one or the other of the two classical serotypes Inaba or Ogawa, and provided a vaccine contains the full quota of antigens from both these serotypes then some protection will be afforded against cholera by such a vaccine whether the prevailing strain or strains are Inaba, Ogawa, or El Tor Inaba/Ogawa. Obviously, however, nothing is lost by inclusion of an El Tor component. Another interesting facet to this problem is the indication that antigenic stability is not to be expected in members of this group, and changes from one serotype to another can apparently occur in the human gut.

The Services' cholera vaccine thus appears to get the best of all possible worlds in the present state of knowledge, until a much needed better cholera vaccine (bacterial with toxoid vaccine, or, say, attenuated oral/parenteral vaccine) arrives to supplant it.—I am, etc.,

WALLY VELLA

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Cataract Spectacles

SIR,—As an aphakic motorist I am writing to thank you for your leading article (12 December, p. 634) describing methods of overcoming the difficulties that we have because of the limitation of our visual fields. As you say, the full-aperture lens with its comparatively wide visual field does have an inconvenient peripheral ring scotoma, but this scotoma is so far out to the side that the motorist wearing full-aperture spectacles has no trouble at road junctions or in reversing.

Unfortunately, aphakic motorists are commonly prescribed "pebble" lenses which are only 3.2 cm in diameter. With these not only is the visual field very limited but their peripheral ring scotoma is dangerous as it lies so far forward that cars coming from the side suddenly appear without warning in front of the motorist approaching an intersection. Reversing is both difficult and dangerous with these small lenses. In my experience, pebble lenses do not give clearer vision than full-aperture lenses.

Full-aperture lenses should be prescribed for all aphakic motorists so that they will have as wide a visual field as possible.—I am, etc.,

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Vision and Accidents

SIR,—In your editorial (12 December, p. 634) you state that the Medical Commission on Accident Prevention says that available evidence suggests that defective visual acuity is not important in the causation of accidents. As accidents occur more frequently after dark, more frequently in foggy weather, and people are required to have approximately a visual acuity of 6/12 before being allowed to drive, it seems that a prima facie case is made out that good sight is necessary for safe driving and that present standards should not be relaxed whatever the "available" evidence is.

I feel that the "evidence" is likely to be unsound for various reasons, one being that eye tests are not performed on cadavers. An illustrative case occurred when a lady, knocked down as she stepped on to a crossing, complained ten days later that the accident had caused defective vision in her right eye. She had had no head injury, her vision in the right eye was less than 6/60, with what was obviously a cataract of some long standing present. It was clear that her previously unnoticed poor vision in the right eye, far from being the result of the accident, was contributory to it.

Unless the eyesight of all people involved in accidents, including those at night whose dark adaptation is known at the moment of impact, is recorded, I do not see how reliable statistics can be obtained.—I am, etc.,

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Gold in Rheumatoid Arthritis

SIR,—In your recent Current Practice article on rheumatoid arthritis (5 December, p. 603) the place of gold therapy was briefly reviewed. Reference was made to the possible value of estimating gold levels in biological fluids¹ and it was claimed that toxic effects are associated with excessive plasma gold values.²

In this connexion two patients who developed blood dyscrasias having received 810 and 780 mg Myocrisin (sodium aurothiomalate) respectively have been studied at the London Hospital. Both patients were receiving Myocrisin 50 mg by intramuscular injection at monthly intervals when the toxicity was observed. Each patient had received weekly injections of 50 mg to a total dose of 730 and 580 mg respectively, during which time serial serum gold estimations had been performed. The mean serum gold levels (taken one week after the previous injection and after the patients had received a total of 330 mg Myocrisin) were 339 and 248 $\mu\text{g}/100 \text{ ml}$, while in a group of nine patients who responded to gold without evidence of toxicity the mean level was 319 $\mu\text{g}/100 \text{ ml}$.

Clearly, in these two patients there was no evidence of significantly raised serum gold values. The levels of gold found in the serum vary widely depending on the size of the dose administered, the frequency of the injections, the interval after the last injection, and the total amount of gold given. If it is felt that a serum gold determination might be helpful in a patient with a genuine or suspected toxic reaction to gold a random blood sample estimation could not be interpreted correctly unless all these factors