life of this important chemosterilizer, investigations should be undertaken with the polymeric,⁴ rather than the monomeric, form of glutaraldehyde.

Full details of this work will be published elsewhere.—We are, etc.,

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- 1 Snyder, R. W., and Cheadle, E. L., *American Journal of Hospital Pharmacy*, 1965, 22, 321.
- 2 Stonehill, A. A., Krop, S., and Borick, P. M., *American Journal of Hospital Pharmacy*, 1963, 20, 458.
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Abdominal Swelling

SIR,—Mr. Wallace Barr (26 June, p. 758) has presented an excellent survey of abdominal swelling. May I be allowed to add three more conditions?

Hirschsprung's disease, in infants, gives a most characteristic almost quadrangular distension of the abdomen, roughly following the contours of the colon.

In rare instances polycystic kidneys may attain a size exceeding 10 kg for each kidney. In such cases a most pronounced abdominal swelling may be seen, dominant in the upper part of the abdomen "as if the patient had swallowed a chest of drawers."

What the Americans call "bloating" has been demonstrated to represent a special type of equivalent to migraine. It is characteristic that the distension may appear rapidly, most usually in the week preceding the period, and when the patient is for some reason tired. The mechanism has been dealt with elsewhere.¹ The distension may be so considerable as to masquerade as an advanced pregnancy (although confined to a few days). This syndrome is by no means uncommon.—I am, etc.,

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- 1 Ask-Upmark, E., and Frantzell, A., *Acta Radiologica*, 1950, 33, 104.

Morphine and the Fetal Heart Rate

SIR,—Increasing attention is being paid to measuring the fetal heart rate especially by monitoring, in order to minimize the development of asphyxia during labour. In particular, correlations have been found to exist between changes in the heart rate and the fetal pH and Apgar score of the infant at birth.^{1,2} These findings, while adding significantly to our management of at risk pregnancies, have not taken into account any effect that analgesics given to the mother during labour may have on the fetal heart rate. That morphine administered to the mother may result in a change in the fetal heart rate is illustrated by the following study.

The fetal heart rate was recorded in six antenatal patients at term for one hour by a Hewlett-Packard Cardiotocograph (8020A), and the mean baseline heart rate was estimated in each patient by averaging the rate observed at five-minute intervals. Morphine sulphate, 0.2 mg/kg, was then

given to each patient by intramuscular injection and the heart rate was again measured in a similar manner beginning one hour following the injection. The mean fetal heart rate in the six patients studied was found to be significantly less ($P < 0.001$) after maternal administration of morphine, an average change of 17 beats per minute being noted (Table).

Case	Fetal Heart Rate		Difference X
	Before Morphine	After Morphine	
1	136	123	13
2	136	124	12
3	140	125	15
4	153	133	20
5	136	116	20
6	146	126	20
X	141	124	17

Student paired 't' test.
 $t = 10.80 (> 6.87) p < 0.001$

It is not known whether these changes in the fetal heart rate in patients receiving morphine are due to an indirect maternal influence on the fetus, or to placental transfer which is known to occur. It is clear, however, that conclusions about the relation of the fetal heart rate to fetal wellbeing should in the future take note of prior drug therapy.—We are, etc.,

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- 1 Wood, C., Ferguson, R., Leeton, J., Newman, W., and Walker, A., *American Journal of Obstetrics and Gynecology*, 1967, 98, 62.
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Testosterone for Anaemia in Maintenance Dialysis

SIR,—We have read with interest the paper by Dr. S. Shaldon and colleagues (24 July, p. 212) recommending the prolonged use of large doses of testosterone for the treatment of anaemia in patients on chronic intermittent haemodialysis. We have been unable to confirm his observations in four males on regular dialysis for a total of 30 hours a week over a period of one to four years who were treated with Sustanon [a proprietary preparation of testosterone esters]. Blood transfusions were not given and residual blood loss in the Kiil dialyser was negligible. Each patient was on a liberal protein diet and received intravenous iron supplements as required.

Three patients received intramuscular Sustanon 250 mg weekly for a minimum of nine months, and one patient received 250 mg weekly for four months and 100 mg weekly for three months. The initial packed cell volumes (P.C.V.) ranged from 17–22% and there was no significant rise in the P.V.C. in any of these patients. In one individual a steady fall occurred in the P.C.V. which rose again only after cessation of therapy. Because of these disappointing results we have not felt justified in treating more patients with androgens.

These findings suggest that further evaluation of this therapy is necessary before it can be recommended for general use in

patients on dialysis in view of the possible side effects of this dosage.

Dr. Shaldon states that there are many uncontrollable variables, and it may be relevant that folic acid and vitamin B₁₂ supplements are not given routinely to our patients but only when serum levels of these factors are low or there is other evidence of deficiency.—We are, etc.,

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Oat-cell Bronchial Carcinoma and Catecholamine Production

SIR,—The report by Dr. J. G. Azzopardi and others (28 November, p. 528) on the relation of histological and functional properties of bronchial carcinoma shows a surprisingly low incidence of Cushing's syndrome in their series. In several earlier reports a greater frequency of production of ACTH-like substance in bronchial tumours seemed to be evidenced or at least postulated.^{1,2} The warning of the authors—in other words the mistaken diagnosis based solely on hypokalaemic alkalosis—is fully justified.

We would like to add a new combination to the list of multiple hormonal secretion of oat-cell bronchial carcinomas so far reported.³ A 49-year-old man with bronchial carcinoma exhibited overt signs of Cushing's syndrome, but he also had frequent hypertonic crises with palpitation and sweating, giving a somewhat different picture from the usual. Two days after admission the patient died in a hypertonic crisis, and laboratory confirmation of the assumed multiple hormonal production in the tumour could not be confirmed (except the low serum potassium content—2.5 mEq/l.). Necropsy showed an oat-cell bronchial carcinoma, weighing 170 g, and bilateral adrenocortical hyperplasia (the weight of both the organs was 50 g. The adrenal cortex had several whitish-yellow nodules on it. Histological examination proved the nodules to be multiple adenomas composed of cells of the zona fasciculata with great foamy lipid granules. No change whatever could be detected in the pituitary.

Extraction of the tumorous material yielded an ACTH activity of 250 mU/g. In the gel electrophoresis of the substance eight to ten peptide components could be observed; one of them had the same motility as natural porcine and synthetic human ACTH.³ These data make it appear likely that the peptides were identical or at least analogous with ACTH. The tumour tissue also contained 12,750 µg/catecholamines, while the whole adrenals contained 120 µg of them. The bronchial tumour had a serotonin content of 576 µg, which is the maximal serotonin concentration ever reported except in the case of Smith.⁴

To our knowledge this case would be the first instance of non-endocrine tissue tumour producing non-polypeptide hormone (the serotonin can be considered more as a degradation product⁵). The event could be ascribed, however, to hormonal secretion of dispersed chromaffin or argentaffin cells in the bronchial tumour, though the most thorough histological examination failed to detect them.

In any event, it seems that the multiplicity of hormone production in oat-cell tissue tumours is not exhausted with the combinations so far presented.

The detailed description of this case is to be published in the *Acta Medica Academiae Scientiarum Hungarica*.—We are, etc.,

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1 Liddle, G. W., Givens, J. R., Nicholson, W. E., and Island, D. P., *Cancer Research*, 1965, 25, 1057.

2 Sommers, Sh. C., in *Endocrine Pathology*, ed. J. M. B. Bloodworth, Jr. Baltimore, Williams and Wilkins, 1968.

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Hypoglycaemia in Infancy and Childhood

SIR,—It was with great relief that I read the leading article on "Hypoglycaemia in Infancy and Childhood" (17 July, p. 130). At last there is guidance on the "controversial" point of whether or not to treat asymptomatic hypoglycaemic infants. These infants warrant intravenous therapy until there is evidence to the contrary.

Can we now expect that requests for true glucose levels on neonates "at risk" will be recognized as urgent and necessary investigations by pathology departments throughout the country?

It may well be that these actions will help to reduce the number of school children with learning difficulties in the future.—I am, etc.,

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Cerebral Vasodilators

SIR,—I am writing to support Dr. C. G. Elliott's comments (17 July, p. 185) on your article on cerebral vasodilators in *Today's Drugs* (19 June, p. 702).

I entirely agree with Dr. Elliott that your article echoes the currently orthodox and rather nihilistic views on the treatment of cerebral arteriosclerosis, and that this is probably because the diagnosis of the condition is made at too advanced a stage rather than necessarily being due to the inefficacy of vasodilator drugs.

Dr. Mary Harcup and I found in a detailed clinical study of a number of these patients that visual inspection of the electroencephalogram provided little in the way of early diagnostic features and, obviously, once clinical symptoms have appeared, these tend to be irreversible because of the absence of neuronal regeneration. It therefore seems highly desirable that some way of making the diagnosis before neurological signs appear is discovered, and we have currently completed a further study of these patients which we hope to publish in the near future, this time using a quantitative computer-linked analysis of the electroencephalogram by automated low frequency wave analysis as well as detailed clinical

scales. This study has involved assessment of cyclandelate (one of the cerebral vasodilators mentioned) under strictly controlled conditions. This drug has already been found to be effective in improving mental function and cerebral blood flow under controlled conditions² and a recent symposium on its use³ confirms the high probability of its effectiveness. Cyclandelate has been found objectively to increase cerebral blood flow, reduce arterial spasm, and to improve to a clinically very relevant degree many of these symptoms of cerebral arteriosclerosis.

It is, as Dr. Elliott remarks, extraordinary that its safety and apparently real, if perhaps modest, success in a common and extremely distressing and crippling malady has not caused more enthusiasm among some sections of the profession.—I am, etc.,

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1 Hall, P., and Harcup, M., *Angiology*, 1969, 20, 287.

2 Ball, J. A. C., and Taylor, A. R., *British Medical Journal*, 1967, 3, 525.

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Epilepsy and Driving

SIR,—I have read with interest the article on epilepsy and driving by Drs. R. D. H. Maxwell and G. E. Leyshon (3 July, p. 12). I must confess, however, that I have found their presentation of facts and figures somewhat difficult to follow and I have misgivings about some of their conclusions.

In particular, I find it hard to accept their assumption that "many and probably most epileptics have obtained driving licences by concealment of their condition." Assuming that there are annually 440 people with epilepsy in the West Riding licensing authority area who could apply for driving licences, do we really know what proportion of such people actually do so? The supposition that some 9 out of 10 male subjects with epilepsy may have concealed their disability in violation of the Road Traffic Act of 1961 does not therefore seem to me to have been very clearly established.

However, even if the authors' assumption were a valid one, it does not follow that relaxation of the regulations for the granting of a driving licence will lead to a perpetuation of such a state of affairs. Presumably it is more likely to operate in the opposite direction, but further facts and figures will be needed to establish whether or not this turns out to be the case.

With regard to the E.E.G. criteria as applied to the 855 patients in the authors' group 2, I cannot comment usefully upon them because these have not been defined in detail. I would however like to emphasize that in my experience there have only been rare occasions when the E.E.G. findings played a decisive role in the assessment of fitness to drive so far as the history of epilepsy was concerned. The utmost caution must at all times be exercised in assessing their clinical significance, and I have seen most unfortunate results accrue when this basic rule has not apparently been observed.

In my opinion the authors are right to stress the importance of patients' testimony, and the importance of obtaining corroborative evidence whenever possible cannot be over-emphasized. There is certainly some-

thing to be said for the provision of a certificate of fitness by people with past histories of epilepsy who wish to hold driving licences.—I am, etc.,

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Morbidity after Dental Anaesthesia

SIR,—The Society for the Advancement of Anaesthesia in Dentistry is sponsoring a survey to inquire into all known cases of morbidity after dental anaesthesia.

I shall be grateful if readers can inform me of any cases of which they have personal knowledge, or of authorities to whom my subcommittee can refer for further information of such cases.—I am, etc.,

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The Community Paediatrician

SIR,—I hope others feel as grateful as I do to Professor Ross G. Mitchell for his clear and convincing analysis of the need for, and the training of, the community paediatrician of the future (10 July, p. 95). But I have to take issue with two articles of his faith.

He asserts that "The present-day doctor . . . approaches a problem . . . with little real appreciation of the interplay of physical, emotional, and social factors which have created the difficulty." I must challenge the truth of this in respect of most general practitioners; they, par excellence, are aware of the said interplay (especially if well-trained health visitors are attached to the practice) and do an amateur's best to help the patient to achieve adjustment. I certainly hope that the gradual introduction of behavioural science into undergraduate and postgraduate medical education will help to improve the professionalism of all doctors in the wider aspects of patient care. Equally, I hope that too much will not be expected too quickly of the behavioural sciences and that meantime the value of experience in general practice will not be undervalued.

Professor Mitchell gives us a glimpse of the imaginative programme of training already under way in Aberdeen. But surely it omits one essential for the future community paediatrician? A period in general practice, even if it were no more than three months (the present trainee general practitioner scheme could be adapted to make this feasible), would give the trainee paediatrician some experience of the common illnesses of childhood, both physical and psychological, some insight into the interplay of personalities that can both cause and help to cure the problems, and a better understanding of the difficulties the general practitioner and his team have to face. Of course such a short exposure to general practice is far from ideal, but where a loaf cannot be had, a slice is better than nothing.

Just as vocational training for general practice looks to the paediatrician for help, so must the medical specialist acknowledge