

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.,

T. J. MUNTON
A. D. RUSSELL

Welsh School of Pharmacy,
University of Wales Institute
of Science and Technology,
Cardiff

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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.,

ERIK ASK-UPMARK

Sweden

- 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
\bar{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.,

JAMES GRIMWADE
DAVID WALKER
CARL WOOD

Department of Obstetrics and Gynaecology,
Queen Victoria Memorial Hospital,
Melbourne, Australia

- 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.,

P. P. MAYER
B. H. B. ROBINSON

Birmingham Regional Centre for Chronic Dialysis,
East Birmingham Hospital,
Birmingham 9

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.