Correspondence

Letters to the Editor should not exceed 500 words.

Buccal Oxytocin

SIR,—Oxytocin can have a powerful effect upon the pregnant uterus, however it reaches the blood-stream. The intravenous "pitocin drip" was at first regarded by some as a dangerous technique; and so it was until experience had made plain the pitfalls and careful investigation had shown how these could be avoided. To-day it can only be accepted as safe and efficacious when used "under careful control in hospital practice" (19 September, p. 705). Even then the intravenous method has disadvantages for both the patient and her attendants. It behoves us therefore to continue to investigate other ways of administering the drug.

The buccal route has recently been shown to be an effective and convenient method. Just how safe it is compared with the intravenous method is not yet established. One thing, however, is quite clear; oxytocin should not be given buccally in circumstances which would preclude its use intravenously. This has been said over and over again by the manufacturers and by those who have most experience of the method. Nevertheless, judging by the case histories reported in your columns recently the lesson has not yet been learned. Up till the present I know of six uterine ruptures in association with the use of buccal oxytocin. And in four of these there were clear contraindications to the use of oxytocin by any route—namely, previous caesarean section for disproportion; hydrocephalus and disproportion; history of previous uterine sepsis, previous forceps delivery and manual removal of the placenta, and poor facilities for supervision; delivery in a "private hospital" apparently without adequate supervision or facilities.

In the other two cases the rupture occurred during labour in association with an abnormally rigid cervix several hours after the oxytocin had been discontinued, and may have had no direct relation to the method of induction at all.

I agree with Drs. J. A. Chalmers and J. L. Ng (24 November, p. 1070) that it would be a great pity if a potentially valuable method were to be abandoned prematurely and unnecessarily. Therefore, in view of our present relative lack of detailed information about the method, which will only gradually be overcome as experience accumulates, it is imperative not only in the interests of the method but also of our patients that buccal oxytocin should only be used where its effects can be recorded accurately and studied fully until it is certain that it is safe, and until the optimum dosage has been determined. In particular, I would agree with Professor MacGillivray,¹ that "a practitioner should only contemplate using buccal oxytocin in its present form if he can devote as much time and care to the patient as he would if she were on a continuous intravenous infusion and if he is prepared to do a

caesarean section should some abnormality develop."—I am, etc.,

J. H. M. PINKERTON.

Department of Midwifery
and Gynaecology,
The Queen's University of Belfast,
Belfast 12.

REFERENCE

- ¹ MacGillivray, I., *Practitioner*, 1964, 193, 415.

Urinary Infection in Childhood

SIR,—There seems good reason to believe that much of chronic pyelonephritis has its origin in childhood even although it may not reveal itself until adult life. The paper by Dr. Jean M. Smellie and her collaborators (14 November, p. 1222) is valuable in focusing attention on this.

There are many variables to be considered in examination of the urine of children as a diagnostic measure in suspected urinary tract infection, and these have not been fully evaluated. Dr. Smellie and her co-authors state, "In our experience, laboratory confirmation of the diagnosis rarely presents difficulty provided a fresh clean specimen of urine is collected before treatment is started," and again, "in young children urine may be collected into adhesive plastic bags . . . [and] . . . plated within two hours of voiding." Our experience has led us to be less confident about the bacteriological diagnosis of urinary tract infection in young children based on such methods of collection. We have found that under 2 years of age bacteriological examination of urine collected into plastic adhesive bags or as "clean catch" samples of mid-stream urine can be quite misleading. From equal numbers of randomly selected, apparently normal, male and female children under 2 years of age who had no suggestion of urinary tract infection we have examined 218 specimens of urine collected into adhesive plastic bags and 190 mid-stream (clean catch) specimens. These were collected from different patients and all were examined and plated for culture within half an hour of voiding, or, where delay in bacteriological examination was unavoidable, were immediately refrigerated. A significant growth of potentially pathogenic organisms (10³ organisms per ml. or more) was found in 48% of the bag-urine specimens and in 33% of the mid-stream urines. Only 20% of bag urines and 30% of mid-stream urines showed no growth. There was little difference between males and females. Further, no matter how rapidly the urine was examined bacteriologically after voiding into the bag similar bacterial counts were obtained, indicating that the initial inoculum of contaminant organisms from the skin and perineum was very heavy. Both with plastic bags and with mid-stream specimens cleans-

ing of the perineum and genitalia with sterile water did not significantly reduce the bacterial count.

Forty-five per cent. of Dr. Smellie and her co-workers' cases of urinary infection were under the age of 1 year. The diagnosis in these cases, in so far as it was based on bacterial counts on urine collected in plastic bags, or by mid-stream specimens, might be in some doubt. It is our impression that contamination can be so gross at this age period that bacterial counts on non-catheter specimens of urine can often lead to conclusions of doubtful validity.—We are, etc.,

H. BRAUDE.

J. O. FORFAR.

J. C. GOULD.

Western General Hospital,
Edinburgh, and Department of
Child Life and Health,
University of Edinburgh.

Systemic Embolism in Mitral Stenosis

SIR,—Systemic embolism is a major hazard in patients with rheumatic heart disease, and successful mitral valvotomy reduces this risk. We feel embolism should be regarded as only one aspect of the assessment of patients for surgery. The recent articles on systemic embolism and mitral valve disease (7 November, pp. 1167 and 1169) have prompted this brief account of our experience with some comments.

From 1953 to 1961, 850 patients with mitral valve disease were seen in this centre, and 533 had a closed mitral valvotomy. Analysis of these cases showed:

(1) The pre-operative incidence of systemic embolism was 20%, increasing to 24% in patients over 40, and 31% in patients with atrial fibrillation.

(2) Operative systemic emboli occurred in 5.8% of patients; 3.5% at finger-split and 6.5% at instrumental valvotomy. Operative embolism occurred in 16% of patients with both valve calcification and atrial fibrillation compared to 1.5% in patients with sinus rhythm and no calcification.

(3) The operative mortality was 3% for finger-split valvotomy, and 9% for instrumental valvotomy, increasing with worsening disability.

(4) An average follow-up of 4½ years for 445 patients revealed a 5.6% post-operative embolic incidence; 3.7% with sinus rhythm; 12.3% with atrial fibrillation. 21 of 25 embolic incidents occurred in patients after an atrial appendagectomy.

Our patients fall into four main groups:

Group I.—Mitral stenosis judged operable with symptoms. In these cases we advise operation independently of systemic embolism.

Group II.—Mitral stenosis, judged operable, minimal or no symptoms. With sinus rhythm, no operation should be undertaken. With atrial fibrillation, no symptoms, and the patient below 35 years decision is more difficult. We generally recommend surgery, and certainly over 35 operation is advisable as the embolic risk is high.

Group III.—Mitral stenosis, judged operable, trivial or no symptoms, and systemic embolism. With atrial fibrillation operation is advised. Sinus rhythm is uncommon; if present we generally recommend operation.

Group IV.—Systemic embolism has occurred, but closed valvotomy will not improve valve function. (a) Patients with heavily calcified disorganized valves which are probably more stenotic than incompetent. Operative embolism is a grave risk, occurring in 16% with atrial fibrillation. There is a 12% risk of post-operative emboli. An operative mortality of 13% is considerably higher than for non-calcified valves. (b) Dominant mitral incompetence. 20 such patients had closed surgery, 6 died at operation, and three had recurrent emboli despite atrial appendagectomy.

Atrial appendagectomy alone does not protect against future emboli, especially if valve function cannot be improved. With a heavily calcified valve, a high surgical mortality rate, risk of operative embolism, and limited benefit make it difficult to recommend closed surgery despite previous embolism. In this situation anticoagulant treatment might be considered.

Pre-operative embolism in a random group of 104 patients in this series was no commoner with a large than with a small appendage, as assessed radiologically. Conversely, in 105 patients with systemic embolism large appendages were as common as small appendages. Our findings differ from those of Dr. W. Somerville and Dr. Jane Chambers (p. 1167), and in our opinion a large atrial appendage is not an additional reason for operation.—We are, etc.,

N. COULSHED.
E. J. EPSTEIN.
E. WALKER.
R. W. GALLOWAY.

Liverpool Regional
Cardiac Centre,
Sefton General Hospital,
Liverpool 15.

Histamine Metabolites in Asthma

SIR,—Dr. J. W. Kerr is to be congratulated on his identification of the histamine metabolite 1-methyl,4-imidazole acetic acid in human urine and his demonstration that this substance is absent from the urine in allergic patients in status asthmaticus (5 September, p. 606).

In the discussion to his paper, Dr. Kerr quotes the observation of Rose, Rusted, and Fownes¹ that in a single case of asthma the histamine content of lung tissue (106 $\mu\text{g./g.}$)

was higher than the average histamine content of normal lung (20 $\mu\text{g./g.}$). We have studied the histamine in a number of lungs from asthmatic patients and have found no consistent difference in the histamine content of normal and asthmatic human lung. We should like to present some data on this point.

The group of patients described as "allergic asthma" had a personal or family history of allergy, had strongly positive skin reactions to one or more typical inhalant antigens, and were shown to develop bronchospasm on inhalation of aerosols of antigens. Isolated lung tissue from all these patients released histamine and isolated bronchial muscle contracted when brought into contact with the appropriate antigen *in vitro*, as in the cases described by Schild *et al.*² The group of patients described as "asthma" had some history of spasmodic bronchospasm but none of allergy. Though most of them had weakly positive skin reactions to one or more antigens, they did not respond to the inhalation of antigen, and isolated lung tissue and bronchi did not release histamine or develop bronchospasm, respectively, when brought into contact with appropriate antigens. The "control" cases had no history of allergy or spasmodic bronchospasm.

Fresh surgical specimens of lung were obtained from biopsies, lobectomies, and pneumonectomies. Samples (150–600 mg.) were cut from macroscopically normal areas of lung parenchyma, washed briefly in Ringer solution, and extracted for histamine by the method of Feldberg and Kellaway.³ In a number of cases some samples were also studied employing Code's extraction.⁴ The histamine content of the extracts was determined biologically using isolated guinea-pig ileum preparations. The results are shown in the Table. Where three or more samples were taken, the mean and standard deviations are given, and the number of samples is shown in parenthesis.

The histamine content of samples taken from different parts of the same lung varied considerably—for example, in Case 6 the range was 28 to 100 $\mu\text{g./g.}$ The mean histamine content of individual human lung specimens varied from 16 to 74 $\mu\text{g./g.}$ The content was not obviously elevated in patients with allergic asthma or patients with spasmodic bronchospasm but no allergic diathesis.—We are, etc.,

D. F. HAWKINS.
J. L. MONGAR.

Department of Pharmacology,
University College London.

REFERENCES

- Rose, B., Rusted, I., and Fownes, J. A., *J. clin. Invest.*, 1950, **29**, 1113.
- Schild, H. O., Hawkins, D. F., Mongar, J. L., and Herzheimer, H., *Lancet*, 1951, **2**, 376.
- Feldberg, W., and Kellaway, C. H., *J. Physiol. (Lond.)*, 1937, **90**, 257.
- Code, C. F., *ibid.*, 1937, **89**, 257.

Studies on Glucose Metabolism

SIR,—In our investigations on coronary heart disease in South African Bantu and Indian populations one aspect being studied concerns prevalences of glycosuria, glucose-tolerance abnormality, and diabetes. Among the Bantu, coronary heart disease is extremely rare; it is very common among Indians and South African Whites, as common as in

U.S.A. Whites.^{1,2} Diabetes occurs less frequently among urban Bantu compared with Whites.³ It is very unusual for Bantu diabetics to die from coronary heart disease.³ Among Indians, however, diabetes is very common.^{4,5}

One Bantu group selected for the glycosuria, etc., studies consists of elderly male schoolteachers. In the Johannesburg Bantu townships (including 700,000 Bantu) there are several thousand teachers, but only 50 of 45 years or more (average age 50.1 years). The selected group, in income and intellect, are much superior to average urban Bantu. Briefly, we found post-prandial glycosuria in one subject (2.0%), glucose-tolerance glycosuria in two subjects (4.0%); but no subject (0.0%) had "diabetic abnormality" (capillary blood sugar—"true" glucose—over 180 mg./100 ml. in 1 hour and over 120 mg./100 ml. in 2 hours⁶). In no case did urine-sugar concentration exceed 25 mg./100 ml. Among South African Indians, we have studied the male population (all middle class) in Rustenburg, aged 50 years or more (average age 56.1 years); 22 out of 24 subjects were available for examination. On these people the figures corresponding to the above were 36.4%, 45.5%, and 36.4%. Of the subjects with glucose-tolerance-test glycosuria sugar concentration exceeded 1 g./100 ml. in half of the cases. In the Birmingham study, for comparison, for the population of 50 years and over, the corresponding approximate figures were 3%, 16% (estimated), and 14.5%.⁷

The remarkable contrast between the South African Bantu and Indian groups, despite the slight difference in mean age, is striking. Both groups were almost equally overweight, had much the same mean blood-pressure, the same protein-nitrogen status (percentage urinary-urea nitrogen of total nitrogen), and much the same mean serum-cholesterol concentration. Both were equally physically inactive and had similar smoking habits. Both held positions of responsibility—the Bantu as inspectors, senior school principals, or teachers; the Indians as traders in competitive business. Yet these two racial groups have grossly different patterns of glycosuria and "diabetic abnormality," and, regarding coronary disease mortality, the Bantu, as stated, are scarcely affected, whereas the Indians suffer severely. We cannot help feeling, as suggested previously,¹ that there must be inherent metabolic factors, operating to the advantage of the one race yet to the disadvantage of the other, whose identity and mode of operation are largely unknown. Full details of the above studies will be published elsewhere.

Investigations are being supported in part by a grant (HE-04244-05) from the National Heart Institute, U.S.A. Public Health Service.

—We are, etc.,

ALEXANDER R. P. WALKER.
B. D. RICHARDSON.
S. D. MISTRY.

South African Institute
for Medical Research,
Johannesburg, South Africa.

REFERENCES

- Walker, A. R. P., *Amer. Heart J.*, 1963, **66**, 293.
- *S. Afr. med. J.*, 1963, **37**, 1155.
- Sefitel, H. C., Keeley, K. J., and Walker, A. R. P., *ibid.*, 1963, **37**, 1213.
- Campbell, G. D., *ibid.*, 1963, **37**, 1195.
- Walker, A. R. P., Mistry, S. D., and Sefitel, H. C., *ibid.*, 1963, **37**, 1217.
- Brit. med. J.*, 1962, **1**, 1497.
- Ibid.*, 1963, **2**, 655.

Histamine Content of Human Lung Tissue

Group	Case	Associated Pulmonary Condition	Histamine Content ($\mu\text{g./g.}$)	Mean
Allergic asthma	1	Bronchiectasis	61, 66	36
	2	Bronchiectasis	51 $\pm$ 9 (4)	
	3	Tuberculosis	16	
	4	Tuberculosis	28	
	5	Tuberculosis	18, 23	
Asthma	6	Bronchiectasis	50 $\pm$ 30 (6)	31
	7	Bronchiectasis	17 $\pm$ 1 (3)	
	8	Bronchiectasis	41 $\pm$ 10 (3)	
	9	Bronchiectasis	18 $\pm$ 4 (3)	
Controls	10	Carcinoma	27 $\pm$ 3 (3)	41
	11	Carcinoma	29 $\pm$ 3 (5)	
	12	Carcinoma	74 $\pm$ 13 (6)	
	13	Carcinoma	49 $\pm$ 10 (3)	
	14	Tuberculosis Lung abscess	23, 32	