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.,

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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 µg./g.)

was higher than the average histamine content of normal lung (20 µg./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 µg./g. The mean histamine content of individual human lung specimens varied from 16 to 74 µg./g. The content was not obviously elevated in patients with allergic asthma or patients with spasmodic bronchospasm but no allergic diathesis.—We are, etc.,

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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.

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Histamine Content of Human Lung Tissue

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