Oxygen Tension.—We were unable to confirm the recent suggestion (Katz *et al.*, 1971) that "oxygen transport" may be limited in subjects who develop exercise-induced bronchoconstriction. Though there was a higher arterial Po_2 during bicycle exercise in four patients, the mean arterial oxygen saturation did not fall below 96% in either study. In Case 1, in which oxygen saturation fell to 93·3% during treadmill exercise, the PEFR had also fallen (from 550 to 405 l./min) during the last two minutes of exercise. In the other patients, whose PEFR did not fall during exercise, the small differences in arterial Po_2 may be explained by relative hyperventilation during bicycle exercise, as discussed earlier. Arterial hypoxaemia, which has been reported after exercise in patients who develop exercise-induced bronchoconstriction, is likely to be the result of bronchoconstriction rather than its cause (Rebuck and Read, 1968).

Conclusion

As a result of the present study we are unable to propose any single factor which is responsible for the difference in exercise-induced bronchoconstriction after treadmill and bicycle exercise. We must speculate, as before (Anderson *et al.*, 1971), that neuromuscular effects arising from the mechanical difference between the two forms of exercise may be responsible for the difference in exercise-induced broncho-

constriction, either alone or in combination with other variables.

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Hypergastrinaemia in Chronic Renal Failure

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Summary

Fasting serum gastrin was measured by radioimmunoassay in 89 patients with chronic renal failure. When the serum creatinine level was used as an index of the degree of renal impairment serum gastrin rose proportionately with the degree of renal failure. Haemodialysis did not significantly alter serum gastrin levels but renal transplantation tended to return them towards normal. This study indicates that the kidney has a role in the degradation of gastrin.

Introduction

Though the precise sites of degradation or excretion of gastrin or both are unknown it has been suggested that the kidney may have a role in gastrin breakdown (Clendinnen *et al.*, 1970; Newton and Jaffe, 1971). If this is so, then patients with chronic renal failure may have raised circulating levels of gastrin. This paper reports serum gastrin levels, as measured by radioimmunoassay, in patients with chronic renal failure, some of whom were on chronic maintenance haemodialysis or had undergone renal transplantation.

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Material and Methods

Fasting serum was obtained from 89 patients with various types of renal disease. The degree of impairment of renal function was arbitrarily classified in relation to the serum creatinine—namely, normal function (serum creatinine <1·2 mg/100 ml), mild impairment (1·2-3·0 mg/100 ml), and severe impairment (>3·0 mg/100 ml). The distribution of the underlying renal disease and the mean age of patients in relation to impairment of renal function is shown in Table I.

TABLE I—*Distribution of Type of Renal Disease and Mean Age in Relationship to Serum Creatinine Level in 89 Patients*

	Serum Creatinine (mg/100 ml)		
	<1·2	1·2-3·0	>3·0
Glomerulonephritis	17	14	16
Renal allografts ..	12	19	2
Other renal diseases	0	1	8
Age in years (mean ± S.D.)..	31±12·6	33±13·5	35±12·1

Eight patients (mean age 36 years) on chronic maintenance haemodialysis were also studied and fasting serum gastrin levels were compared before and after a 14-hour Kiil haemodialysis.

Serum creatinine, urea, and calcium were determined by standard methods and serum gastrin was measured by radioimmunoassay (Hansky and Cain, 1969; Hansky *et al.*, 1971). The normal range is 0-120 pg/ml.

Basal gastric acid secretion was measured by using the method of Kay (1953).

Statistical comparison of groups was by "Student's" *t* test, and a χ^2 was constructed to compare normal and abnormal

gastrin levels in the severely impaired and less severely impaired groups (Snedecor and Cochran, 1968).

Results

NON-DIALYSIS PATIENTS

The mean serum gastrin levels ± S.E. of the mean in the three groups of patients with differing levels of renal function are shown in Table II. The difference between patients with

TABLE II—*Relation of Basal Serum Gastrin Level to Serum Creatinine Level in Patients with Renal Failure*

	Serum Creatinine (mg/100 ml)		
	<1·2	1·2-3·0	>3·0
No. of patients	29	34	26
Serum gastrin in pg/ml* (mean ± S.E. of mean)	38±8·9	51±9·1	220±79·6

* Normal range 0-120 pg/ml.

severe renal impairment and patients with normal function or mild impairment is significant at P <0·025. There was no significant difference in serum gastrin levels when patients were compared on the basis of underlying renal disease.

Two patients with severely impaired renal function had very high gastrin levels (>1,500 pg/ml) and may have unduly biased the mean values. A χ^2 was therefore constructed and is shown in Table III. There was a strong association between

TABLE III—*Relation of Degree of Renal Impairment to Serum Gastrin Levels in 89 Patients*

Gastrin Level	Serum Creatinine (mg/100 ml)	
	<3	>3
<120 pg/ml	54	15
>120 pg/ml	7	13

$\chi^2 = 13·46$; P <0·001.

the degree of impairment of renal function and the raised level of serum gastrin ($\chi^2 = 13·46$; P <0·001).

Basal gastric acid secretion was estimated in 14 out of 28 patients with a serum creatinine of 3 mg/100 ml or over. Acid output ranged from 0 to 8·6 mEq per hour and there was no correlation between basal serum gastrin and basal acid output ($r = 0·007$; P >0·1).

The serum calcium levels were all within the normal range, as those patients with severely impaired renal function were on oral phosphate-binding agents. There was no correlation between serum gastrin and calcium levels in these patients.

DIALYSIS PATIENTS

Serum gastrin levels before and after haemodialysis are shown in Table IV. In all but one of these patients the gastrin levels fell over the period of dialysis, but the differences were not significant for the group as a whole (P = 0·30).

DISCUSSION

This study shows that basal serum gastrin levels are significantly higher in patients with severe renal impairment than in those with mild impairment or normal renal function. This rise is independent of the type of renal disease present and reflects only the degree of renal dysfunction.

TABLE IV—*Serum Gastrin Levels before and after Haemodialysis in Chronic Renal Failure*

Case No.	Serum Gastrin (pg/ml)	
	Predialysis	Postdialysis
1	108	130
2	160	38
3	56	50
4	3,450	900
5	184	116
6	260	240
7	160	100
8	90	28
Mean ± S.E. of mean	554±414	200±103

$t = 1·1427$; P = 0·30.

It is generally agreed that the liver is not the major site of gastrin degradation or excretion (Gillespie and Grossman, 1962; McGuigan et al., 1970) and so alternative sites have been sought. Sequestration of significant amounts of intravenously administered radio-labelled gastrin in the renal cortex has implicated a renal role in gastrin degradation (Jaffe and Newton, 1969), yet the only report of gastrin levels in chronic renal failure has shown normal values in five patients and no difference after haemodialysis (Reeder and Thompson, 1971). The present results in a larger group of patients do support an important role for the kidney in gastrin metabolism, in that gastrin levels are raised in severe renal impairment. The results also indicate that gastrin does not pass the dialysis membrane in appreciable amounts.

Further corroborative evidence for a renal role in gastrin metabolism is given by preliminary studies of serum gastrin levels after renal transplantation. Three patients studied before and after renal transplantation have shown a return of raised gastrin levels to the normal range.

Other possible explanations of high gastrin levels in chronic renal failure include overproduction, which seems improbable, or increased release associated with achlorhydria. The absence of correlation between acid secretion and serum gastrin, however, indicates that hypergastrinaemia is not due to an associated gastritis and achlorhydria (Korman et al., 1971) and also suggests that the hypergastrinaemia is not associated with an increased acid output.

Further study of these patients, in particular the relation between serum gastrin, gastric acid secretion, and the histological status of the gastric mucosa, will shed some light on the role of the kidney in gastrin metabolism.

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