Bezold-Jarisch reflex⁶ and help to explain the findings of this paper.

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Sulphinpyrazone in acute myocardial infarction

SIR,—The administration of sulphinpyrazone early after myocardial infarction was recently shown by Dr R G Wilcox and others (23 August, p 531) to be accompanied by a significant elevation of serum creatinine and urea. Moreover some of us had reported on four cases of acute renal failure within the first days after starting sulphinpyrazone therapy in patients with a recent myocardial infarction.¹

The mechanism of this renal functional deterioration has to be clarified. Little evidence supports the hypotheses of intratubular urate precipitation or of an immunologically induced interstitial nephritis. We propose that sulphinpyrazone impairs renal function by inhibiting synthesis of prostaglandins in the kidney, as it does in platelets.²

To test this hypothesis, we compared the effect of sulphinpyrazone and of indomethacin—a well-known inhibitor of prostaglandin synthesis—on the urinary excretions of prostaglandins E₂ (PGE₂) and F_{2α} (PGF_{2α}), which reflect the renal synthesis of PGE₂ and PGF_{2α}.³ Four healthy male volunteers with normal dietary salt intake collected their 24-hour urine during 10 consecutive days. Four doses of sulphinpyrazone 200 mg were taken on days 3 and 4 and three doses of indomethacin 50 mg on days 9 and 10; other days served as controls. Other medications, smoking, and sexual activity were withheld. Urinary PGE₂ and PGF_{2α} were measured by radioimmunoassay, as previously described.⁵ When compared with the mean of the values obtained during the two days preceding the drug therapies, the mean urinary PGE₂ concentration significantly decreased on the two days of sulphinpyrazone as well as of indomethacin therapy (see accompanying table). Both drugs produced a comparable effect on the urinary PGE₂. On the other hand, the mean urinary PGF_{2α} did not change under sulphinpyrazone therapy, but it was significantly reduced under indomethacin treatment. Neither drug produced a significant change in creatinine clearance; while sulphinpyrazone produced, as expected, an increase in the urate clearance.

The different handling of renal PGF_{2α} by the two drugs is not yet well understood. However, a drug such as sulphinpyrazone that reduces the formation of the vasodilating PGE₂ in the kidney and does not modify the formation of the vasoconstrictive PGF_{2α} could in certain clinical situations impair renal haemodynamics and even lead to acute renal failure. In the volunteers studied neither drug produced a consistent change in creatinine clearance. This contrasts with the decrease in renal function when sulphinpyrazone was prescribed soon after infarction reported by Dr Wilcox and his colleagues and by Boelaert *et al.*¹ It is possible, however, that sympathoadrenal activation and other vasoconstrictive stimuli characteristic of the post-infarction period lead to renal prostaglandin activation, withdrawal of which could result in decrease in renal blood flow and glomerular filtration. This is now under investigation.

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Salt and blood pressure in Scotland

SIR,—We read with interest the article by Dr D G Beevers and his colleagues concerning salt and blood pressure in Scotland (6 September, p 641). In the light of our results from a recent study of dietary salt intake and urinary sodium excretion in Swedish women with high and low blood pressure levels¹ we would like to comment on the results.

In our study 24-hour urine specimens were collected at five different occasions during a three-year period, and in connection with the last three collections food sampling was carried out by applying the duplicate portion technique.² Dietary sodium and potassium were highly correlated ($p < 0.001$) with the corresponding urinary excretion values in the two groups, indicating that the urinary excretion of sodium and potassium very well reflected the dietary intake of these substances. The reproducibility of the five different 24-hour

urinary collections was examined by analyses of variance for sodium and potassium excretion. These analyses did not show any significant differences between the five separate measurements of the 24-hour urinary excretion either for sodium or for potassium, despite the rather long period of time between the sampling occasions.

Thus it seems that urinary excretions of salt are highly reproducible and therefore that there is probably no need to "correct" for creatinine excretions. Like the data published by Dr Beevers and his colleagues, our data on salt intake do not support restriction of salt intake as a means of decreasing blood pressure in the population.

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Prevention or cure for stress-induced gastrointestinal bleeding?

SIR,—A recent leading article (6 September, p 631) has suggested that impaired coagulation may compound local lesions in cases of stress-induced gastrointestinal haemorrhage. It follows therefore that impaired platelet function may also be disadvantageous.

In order to establish whether cimetidine treatment could influence platelet function we studied its effect on platelet aggregation *in vitro*. Platelet-rich plasma was prepared from seven healthy volunteers and 400 μ l incubated for 10 minutes with 50 μ l of various dilutions of cimetidine in physiological saline (see table). 50 μ l of ADP or adrenaline

Mean percentage fall in optical density at various concentrations of cimetidine

	Final concentration cimetidine (μ mol/l)					
	0	160	240	320	400	480
ADP	76	72	67	53	50	32
Adrenaline	74	70	64	52	48	23
p*		NS	NS	0.05	0.01	0.01

NS = non-significant.
*Paired Wilcoxon's test.

(final concentration 2-5 μ mol/l) was added to initiate aggregation. Details of methods have been previously described.¹

Other workers² have shown that the average peak blood levels of cimetidine are 2.8 μ mol/l after a 200 mg oral dose and approximately 30 μ mol/l after a 100 mg intravenous bolus injection. On the basis of these data our

Urinary prostaglandin E₂ and F_{2α} excretion, serum uric acid and creatinine excretion, and creatinine and uric acid clearance before and during sulphinpyrazone or indomethacin (values are means $\pm$ standard errors of means)

	Time (days)	PGE ₂ (nmol/24 h)	PGF _{2α} (nmol/24 h)	Serum urate (mmol/l)	Serum creatinine (μ mol/l)	Creatinine clearance (ml/min)	Uric acid clearance (ml/min)
Control 1	Average of 2 days	0.66 $\pm$ 0.05	3.05 $\pm$ 0.50	0.37 $\pm$ 0.01	91.0 $\pm$ 7.1	109.8 $\pm$ 3.8	9.01 $\pm$ 1.14
During sulphinpyrazone	Day 1	0.35 $\pm$ 0.07†	3.75 $\pm$ 0.82				
	Day 2	0.26 $\pm$ 0.05†	2.64 $\pm$ 0.66	0.10 $\pm$ 0.01*	86.6 $\pm$ 4.4	122.8 $\pm$ 10.4	42.17 $\pm$ 1.30*
Control 2	Average of 2 days	0.76 $\pm$ 0.14	2.82 $\pm$ 0.27	0.34 $\pm$ 0.02	88.4 $\pm$ 5.3	113.6 $\pm$ 9.8	9.11 $\pm$ 1.74
During indomethacin	Day 1	0.26 $\pm$ 0.04†	1.68 $\pm$ 0.18†				
	Day 2	0.30 $\pm$ 0.07†	1.55 $\pm$ 0.23†	0.35 $\pm$ 0.02	91.0 $\pm$ 2.6	106.6 $\pm$ 8.0	9.02 $\pm$ 0.77

Conversion: SI to traditional units—Urate: 1 mmol = 16.8 mg; creatinine: 1 μ mol/l = 11.3 μ g/100 ml.

* $p < 0.001$
† $p < 0.02$
‡ $p < 0.05$ } compared with the average of the values obtained during the two days preceding sulphinpyrazone or indomethacin.