LETTERS TO THE EDITOR

Effect of a single dose of phentolamine and MJ 1999 on aspirin-induced gastric ulceration in rats

The preventive effect of α-methyldopa in two types of stress-induced gastric ulcer in rats has previously been demonstrated (Djahanguiri, Hemmati & others, 1967). These authors have also shown that the production of stress-induced ulcers is prevented by the pretreatment of rats by the α-blocking agent, phentolamine, and aggravated by the β-blocking agent, MJ 1999 {4-[1-hydroxy-2'-(isopropylamino)ethyl]methane sulphonanilide HCl} (Djahanguiri, Sadeghi & Hemmati, 1968).

I have now examined the effect of phentolamine and MJ 1999 on aspirin-induced gastric ulceration in rats.

Rats of either sex, weighing 90–110 g were given intraperitoneally 2 ml/100 g weight of normal saline to prevent dehydration. They were housed in individual cages and food was withheld for 24 h. The animals were divided into four groups. The first two groups (each of 20 rats) were injected intraperitoneally with 2 mg/kg of phentolamine and 10 mg/kg of MJ 1999 respectively. Thirty min later these two groups and a third group (20 rats) were injected with acetylsalicylic acid (150 mg/kg, i.p.) suspended in olive oil. The fourth group (10 rats) were given 1 ml/100 g weight of olive oil by the same route. Gastric damage was measured 5 h after the last injection. The rats were killed by a blow on the head and the stomachs were immediately removed, opened along the greater curvature, washed with water and examined by direct lighting (by an observer to whom the treatments were not known) for the presence of focal haemorrhagic erosions. Any haemorrhagic area 2 mm or greater in its largest dimension was considered as a positive. The frequency of these spots found in the glandular part of the stomach ranged from 2 to 12. Microscopic examination showed the presence of ulceration in the mucosal layer, rarely reaching the muscularis mucosa and always accompanied by oedema, necrosis and haemorrhage.

The results are summarized in Table 1. The percentage of gastric lesions after

Table 1. *The incidence of gastric ulceration in rats treated with adrenergic blocking agents and aspirin*

Drugs and doses (mg/kg body weight)	Number of rats	Number with ulcers	Percentage
Phentolamine 2 + aspirin 150	20	2	10*
MJ 1999 10 + aspirin 150	20	17	85
0 + aspirin 150	20	16	80
Olive oil (1 ml/100 g body weight) ..	10	0	0

* $P < 0.001$ when compared with the aspirin group value.

the administration of aspirin in the control group is similar to that obtained by Brodie & Chase (1967). The results also show that phentolamine, at a dose of 2 mg/kg, significantly prevented the occurrence of gastric ulceration in the rats. MJ 1999 did not affect the incidence of aspirin-induced gastric ulceration. The statistical significance was calculated by the χ^2 method.

The role of the sympathetic nervous system in the pathogenesis of acute gastric ulceration is supported by much experimental evidence. The role of sympathetic excitation has been demonstrated by the ulcerogenic action of noradrenaline injected into the left gastric artery of the dog (Nicoloff, Peter & others, 1965). Lynch, Highley

& Worton (1964) observed the ulcerogenic action of phenylephrine. Sun & Shay (1960) demonstrated that the late phase of gastric secretion produced by insulin hypoglycaemia could be blocked by an adrenergic-blocking agent and Emas (1964) found a decrease of gastric acid secretion after administration of guanethidine in the cat. By time-study experiments it has been claimed that the primary change, in the course of the development of stress-induced acute gastric ulcer, in which there is a high level of blood catecholamine (Euler, 1964), is a trophic disturbance which is produced under the influence of sympathetic excitation (Anichkov & Zavodskaya, 1965).

In the pathogenesis of aspirin-induced acute erosive lesions in the stomach, one of the more attractive mechanisms recently proposed is the loss of the mucus "barrier" of the stomach (Menguy, 1966). Kent & Allen (1966) found aspirin to produce deleterious effects on the protective mechanisms of the stomach by reducing the rate of synthesis of mucus. They observed that the biosynthesis of macromolecules in cells of the gastric mucosa was inhibited by a selective action of salicylate. Menguy (1966) has suggested that this loss of "barrier" permits the back diffusion of hydrochloric acid [the theory proposed by Davenport (1966)] into the aspirin-damaged gastric mucosa.

Whatever the pathogenic mechanisms of aspirin-induced gastric ulceration may be, the results of the present study would lend support to the theory that the sympathetic nervous system is implicated in the production of such lesions and that α-adrenergic receptors may be involved.

I wish to express my indebtedness to Dr. R. H. Salter in the preparation of this manuscript. The generous supply of phentolamine (Regitine) by Dr. Nik-Eteghad from Ciba Pharmaceutical Co. and of MJ 1999 by Mead Johnson Pharmaceutical Co. are acknowledged.

Department of Experimental Medicine & Pharmacology,
Faculty of Medicine,
University of Tehran, Iran.

B. DJAHANGUIRI

March 24, 1969

REFERENCES

ANICHKOV, S. V. & ZAVODSKAYA, I. S. (1965). *Actual pharmac.*, **18**, 1–18.

BRODIE, D. A. & CHASE, B. J. (1967). *Gastroenterology*, **53**, 604–610.

DAVENPORT, H. W. (1966). *Ibid.*, **50**, 487–499.

DJAHANGUIRI, B., HEMMATI, S., SADEGHI, DJ. & FIROOZABADI, A. (1967). *Medna Pharmac. Exp.*, **17**, 427–433.

DJAHANGUIRI, B., SADEGHI, DJ. & HEMMATI, S. (1968). *Archs int. Pharmacodyn. Thér.*, **173**, 154–161.

EMAS, S. (1964). *Acta physiol. scand.*, **60**, 57–69.

EULER, U. S. VON (1964). *Clin. Pharmac. Ther.*, **5**, 398–404.

KENT, P. W. & ALLEN, A. (1966). *Biochem. J.*, **101**, 43 P.

LYNCH, T. A., HIGHLEY, W. L. & WORTON, A. G. (1964). *J. pharm. Sci.*, **53**, 1077–1080.

MENGUY, R. (1966). *Gastroenterology*, **51**, 430–432.

NICOLOFF, D. M., PETER, E. T., LEONARD, A. S. & WANGENSTEEN, O. H. (1965). *J. Am. med. Ass.*, **191**, 383–385.

SUN, D. C. & SHAY, H. (1960). *J. appl. Physiol.*, **15**, 697– 703.