

syphilis and rectal gonorrhoea. Swabs from the rectal mucosa were transported in Hanks medium, and herpes simplex virus (HSV) was cultured on human embryonic kidney cells.

HSV was isolated in seven patients. All 11 patients were asymptomatic and clinically well after 21 days, but the virus was repeatedly cultured at weekly intervals on three occasions from one patient. Two patients had recurrences of proctitis, and, though they experienced no urinary symptoms, HSV was cultured on each occasion.

### Comment

Herpetic infection of the anus and perianal region in homosexual men was first described by Astruc in 1736.<sup>1</sup> Hutfield<sup>2</sup> drew attention to the same condition in 1963 while Waugh<sup>3</sup> described 13 patients with anorectal herpes virus infection, five of whom had proctitis, in 1976. Neither described the associated urinary dysfunction.

Although HSV was recovered in only seven patients, the remainder pursued an identical clinical course and two also had ulcers typical of herpes present on the mucosa. The development of urinary dysfunction, which in some patients was associated with paraesthesiae, neuralgic pains, impotence, and scanty neurological signs, suggests a lumbosacral radiculomyelopathy or a localised sacral meningo-myelitis<sup>4,5</sup> as the most likely cause of these symptoms. Other explanations are unlikely as the urinary dysfunction developed at least two and sometimes as long as 14 days after the onset of rectal pain, and it persisted for an average of nine days while the rectal pain was subsiding.

During the period of the study 236 men with anogenital herpes were seen so the syndrome we have described was by no means rare. The problem of control of anogenital herpes as a sexually transmitted disease is well illustrated since at least six patients appear to have been infected by contacts who must have been "silent shedders" of HSV.

ADDENDUM.—Since writing this paper we have seen two further patients with herpetic proctitis and urinary dysfunction. HSV was found in both, and one patient needed catheterisation.

<sup>1</sup> Hutfield, D C, *British Journal of Venereal Diseases*, 1968, **44**, 241.

<sup>2</sup> Hutfield, D C, *British Journal of Venereal Diseases*, 1963, **39**, 181.

<sup>3</sup> Waugh, J, *Journal of the American Venereal Diseases Association*, 1976, **3**, 68.

<sup>4</sup> Caplan, L R, Kleeman, F J, and Berg, S, *New England Journal of Medicine*, 1977, **297**, 920.

<sup>5</sup> Oates, J K, and Greenhouse, P R D H, *Lancet*, 1978, **1**, 691.

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## Changes in blood pressure, heart rate, and plasma noradrenaline concentration after sudden withdrawal of propranolol

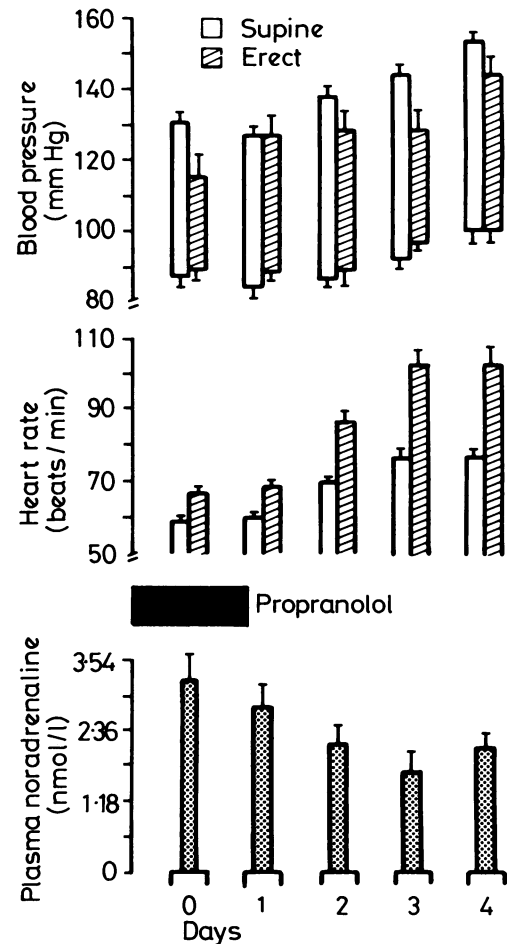
Patients with ischaemic heart disease may develop acute coronary artery syndromes within two weeks after stopping long-term propranolol treatment.<sup>1,2</sup> The underlying mechanism might be a period of rebound hyperactivity of the sympathetic nervous system after withdrawal analogous to that sometimes seen after interrupting clonidine treatment.<sup>3</sup> We have investigated this in hypertensive patients without ischaemic heart disease.

### Patients, methods, and results

Four men and a woman entered the study, which was conducted in hospital over five consecutive days. All were attending the hypertension clinic at Hammersmith Hospital. Propranolol was the only medication, and no patient had clinical or electrocardiographic evidence of ischaemic heart disease on admission. During the first 24-hour, control period (day 0) the patients received their usual oral dose of propranolol (mean daily dose 344 mg, range 240-640 mg). They had been taking propranolol for a mean of

41 months (range 18-60 months). No further propranolol was given after the last morning dose at 0600 on the second day (day 1). Blood pressure was measured in duplicate by Arteriosonde (Roche) and pulse rate by radial artery palpation. Measurements were made supine after 15 minutes' rest and erect after two minutes' standing at 0900, 1100, 1300, 1500, and 1700 daily. Urine was collected over 12-hour periods during the whole withdrawal phase. Blood for estimating plasma noradrenaline concentrations was drawn by venepuncture after 15 minutes' resting supine at 0900 and 1700 daily. Concentrations were estimated in duplicate in 2 ml samples of plasma by a radioenzymatic assay.<sup>4</sup> Urinary catecholamines were measured fluorometrically<sup>5</sup> and expressed as ng/g urinary creatinine. Individual values for blood pressure, heart rate, and plasma noradrenaline were pooled for each day and significant differences assessed with Student's *t* test. One patient failed to complete the study, and the results are therefore based on the remaining four.

Blood pressure and heart rate rose steadily during the four days after the last dose of propranolol (see figure). Supine systolic blood pressure increased



Mean ( $\pm$ SE of mean) blood pressure, heart rate, and plasma noradrenaline concentration in four patients after stopping propranolol. Last dose given at 0600 on day 1. (Plasma noradrenaline: 1 nmol/l  $\approx$  0.17 ng/ml.)

from a mean of 131.2  $\pm$  SE of mean 3.2 mm Hg on day 0 to 153.0  $\pm$  3.3 mm Hg on day 4 ( $P < 0.001$ ). Supine diastolic pressure increased from 87.5  $\pm$  2.7 mm Hg to 100.2  $\pm$  2.7 mm Hg ( $P < 0.001$ ). Standing systolic blood pressure increased from 116.1  $\pm$  5.7 mm Hg to 144.5  $\pm$  5.6 mm Hg ( $P < 0.001$ ) over the same period, and standing diastolic pressure increased from 89.6  $\pm$  1.9 mm Hg to 100.0  $\pm$  2.7 mm Hg ( $P < 0.001$ ). Supine heart rate increased significantly from a mean of 59.3  $\pm$  1.4 beats/min on day 0 to 77.8  $\pm$  1.9 beats/min on day 4 ( $P < 0.001$ ). Standing heart rate increased from a mean of 67.4  $\pm$  1.8 beats/min to 103.2  $\pm$  4.3 beats/min over the same period ( $P < 0.001$ ). The greatest increase in heart rate occurred within 48 hours after propranolol withdrawal. Plasma noradrenaline concentrations fell after withdrawal. There was a 47% reduction in mean plasma noradrenaline concentration from 3.25  $\pm$  0.35 nmol/l (0.55  $\pm$  0.06 ng/ml) on day 0 to 1.71  $\pm$  0.3 nmol/l (0.29  $\pm$  0.05 ng/ml) on day 4 ( $P < 0.02$ ) (figure). Twenty-four-hour total catecholamine excretion during days 0-1 inclusive was 26.4  $\pm$  1.5 ng/g creatinine ( $n=8$ ) compared with 21.2  $\pm$  4.4 ng/g creatinine ( $n=12$ ) during the period after withdrawal.

Three of the four patients completing the study noted a pounding or forceful heart beat during the third and fourth days after withdrawal

immediately on standing after a period of rest or when walking about. These symptoms disappeared between the fifth and tenth days after the last dose of propranolol. There were no associated complaints of angina, sweating, tremor, or agitation.

### Comment

Long-term treatment with propranolol lowers the blood pressure and increases the plasma noradrenaline concentration, probably due to baroreflex stimulation resulting from the fall in cardiac output. Sudden withdrawal of propranolol produced a steady reversal of these features over four days. There was no evidence of excessive sympathetic activity during the withdrawal phase. Our results do not rule out a moderate degree of receptor hypersensitivity on withdrawing long-term beta-blockade, which may have been partly responsible for the heart rate increase 48 hours after the last dose, but these changes were slight.

<sup>1</sup> Alderman, E L, *et al*, *Annals of Internal Medicine*, 1974, **81**, 625.

<sup>2</sup> Miller, R R, *et al*, *New England Journal of Medicine*, 1975, **293**, 416.

<sup>3</sup> Reid, J L, *et al*, *Lancet*, 1977, **1**, 1171.

<sup>4</sup> Henry, D P, *et al*, *Life Sciences*, 1975, **16**, 375.

<sup>5</sup> von Euler, U S, and Lishajko, F, *Acta Physiologica Scandinavica*, 1961, **51**, 348.

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## Penicillamine causing acute colitis

We report a case of acute colitis in a patient with rheumatoid arthritis who was being treated with penicillamine.

### Case report

A 61-year-old woman with a 30-year history of classical, seropositive rheumatoid arthritis began taking penicillamine, 125 mg twice daily, in April 1978 because of active, progressive disease. Other treatment consisted of indomethacin suppository, 100 mg at night, and methyl dopa, 250 mg twice daily, for mild hypertension. In May the penicillamine was increased to 125 mg thrice daily and by June she had improved considerably, with no signs of active disease or adverse side effects from the penicillamine. On 7 August 1978, four and a half months after starting penicillamine, she developed colicky abdominal pain relieved by defecation, tenesmus, and profuse diarrhoea containing fresh blood and mucus with increasing frequency by day and night. She stopped the penicillamine three days before being admitted to hospital on 21 August.

On examination she was afebrile and had a pulse of 80/min, sinus rhythm, and blood pressure 150/90 mm Hg. There were signs of chronic, severe rheumatoid disease that was clinically inactive. Abdominal examination disclosed a distended caecum with tenderness over the descending colon. Bowel sounds were increased. Rectal examination was extremely painful, but no other abnormality was detected.

Investigations showed haemoglobin 11.7 g/dl; white cell count  $7.3 \times 10^9/l$  ( $7300/mm^3$ ), normal differential; platelets  $210 \times 10^9/l$  ( $210\,000/mm^3$ ); erythrocyte sedimentation rate 30 mm in first hour; differential agglutination test for rheumatoid factor positive at titre of 1/64. Liver function tests showed albumin 30 g/l but were otherwise normal. Analysis of urea and electrolytes showed potassium 3 mmol(mEq/l) but was otherwise normal. Tests for occult blood in faeces were positive. No pathogens were isolated on faecal culture. A plain abdominal x-ray film taken on admission was normal. Sigmoidoscopy to 10 cm showed a friable, inflamed mucosa with contact bleeding and flecks of pus. Mucosal biopsy showed inflammatory changes. Double-contrast barium enema gave normal results.

Indomethacin suppositories were stopped on admission but the methyl dopa was continued, and dextropropoxyphene and paracetamol (Distalgesic) was used to control her pain. Her diarrhoea settled, and a repeat sigmoidoscopy one week after admission was entirely normal. Her rheumatoid arthritis became active again, and on 2 September she restarted penicillamine, 125 mg twice daily. Eleven days later she developed bloody diarrhoea and stopped the penicillamine after suffering symptoms for three days. Her bowel

function recovered completely over the next two days, but in the ensuing three weeks her rheumatoid disease became active and she began intramuscular gold, 50 mg weekly. Her bowel symptoms have not returned, and her rheumatoid disease is coming under control after three months of chrysotherapy.

### Comment

Acute colitis occurring in patients taking penicillamine has not been reported. The drug has many common gastrointestinal side effects, including nausea and vomiting, hypogeusia, indigestion, and possibly upper gastrointestinal bleeding<sup>1</sup> and diarrhoea.<sup>2</sup> The temporal association between taking the drug and developing the colitis, and the fact that symptoms recurred after rechallenge with penicillamine suggest strongly a direct causal relation. Although indomethacin suppositories cause rectal bleeding<sup>3,4</sup> and ulcerative colitis may be associated with oral indomethacin,<sup>5</sup> we think that indomethacin was not responsible for the symptoms in this patient, as she had been using indomethacin suppositories for many years without ill effect and did not resume using them after the initial episode, yet the colitis still recurred. She has subsequently restarted indomethacin suppositories and had no return of her acute bowel symptoms, but she still complains of occasional loose motions. Sigmoidoscopy and rectal biopsy performed in April 1979 were entirely normal. We conclude, therefore, that this was a case of penicillamine-induced acute colitis that remitted rapidly when the drug was stopped.

<sup>1</sup> Lyle, W H, *Lancet*, 1974, **2**, 285.

<sup>2</sup> Lyle, W H, personal communication.

<sup>3</sup> Walls, J, Bell, D, and Schorr, W, *British Medical Journal*, 1968, **2**, 52.

<sup>4</sup> Levy, N, and Gasper, E, *Lancet*, 1968, **1**, 577.

<sup>5</sup> Merck, Sharp and Dohme, data sheet, April 1978.

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## Relief of causalgia in limbs by regional intravenous guanethidine

Causalgia is a rare and intractable complication of injury to major peripheral nerves characterised by severe burning pain. Sympathetic block is the only consistent way of relieving this type of pain, and I have found that using guanethidine in an intravenous regional technique after applying a tourniquet has considerable advantages compared with repeated local-anaesthetic ganglion blocks. I report using guanethidine in 10 consecutive patients with causalgia affecting the upper limb.

### Patients, methods, and results

Causalgia was associated with damage to the ulnar nerve in five patients (four after surgery for ulnar-nerve transposition and one after a bullet wound); the median nerve in four patients (two after slashing wounds, one after a bullet wound, and one after surgery for carpal-tunnel decompression); and the brachial plexus in one patient after radiotherapy. The patients were aged between 21 and 70 and had failed to respond to various kinds of treatment before their referral to this centre.

Routine guanethidine blocks were carried out,<sup>1,2</sup> each patient receiving two blocks at an interval of three weeks. Pain relief was scored on a simple scale of 0-3 and the figure summarises the results. Though the first block produced considerable relief, the effects of the second were better and lasted longer. The patients fell conveniently into two equal groups according to the duration of their causalgia, the average durations being five months and 15 months from onset. Pain relief was superior in those treated earlier.

### Comment

None of the patients treated early required further blocks, whereas those treated after an average of 15 months did. All patients, however, affirmed that life had become tolerable by the end of the period of