within the synovium or joint cavity, symptoms and signs of joint inflammation fluctuate in intensity, mimicking the intermittent synovitis common in early rheumatoid arthritis.

Histological examination of the synovial fluid precipitate is usually neglected in the investigation of rheumatic disorders. Though it is rarely informative in patients with polyarthritis, it is a pertinent investigation in those with monoarthritis, where failure to recall an initial penetrating injury does not exclude the diagnosis of persistent synovitis induced by foreign material.

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Controlled trial comparing De-Nol tablets with De-Nol liquid in treatment of duodenal ulcer

De-Nol (tri-potassium di-citrato bismuthate) is effective in the treatment of duodenal ulcer,[1] but its usefulness is limited by the unpleasant taste and smell of the liquid formulation. We compared the effectiveness of a new tablet preparation of De-Nol with the established liquid preparation in the treatment of duodenal ulcer.

Patients, methods, and results

Forty patients with duodenal ulceration proved endoscopically were allocated at random to treatment with De-Nol liquid (5 ml four times daily) or De-Nol tablets (1 four times daily) for one month. Patients symptoms were then reassessed and an endoscopic examination conducted by a clinician unaware of their treatment. Bismuth concentrations in blood and urine were measured in all patients before and immediately after treatment and again two weeks after the course of treatment had finished. Patients with renal failure, and those who had undergone surgery for their ulcer or had been treated with cimetidine, De-Nol, or carbenoxolone in the three months before endoscopy were excluded. Patients noted symptoms daily during the course of treatment.

Twenty patients (mean age 43) were treated with De-Nol tablets and twenty (mean age 38) with De-Nol liquid. Groups were comparable in age, severity, and duration of symptoms. In the group taking tablets 16 noted improvement of symptoms, and 15 of the ulcers had healed after one month's treatment. Mean time to the relief of symptoms was 18 days. Seventeen patients found the treatment acceptable or pleasant, and three found it unpleasant. In the group treated with De-Nol liquid 16 noted relief of symptoms, and 17 of the ulcers healed. Mean time to the relief of symptoms was 17 days. There were no significant differences between the groups for these indices. Thirteen of those taking liquid found it pleasant or acceptable, and seven found it unpleasant ($p<0.05$), but none failed to complete the course of treatment. No patient complained of major side effects. Two taking tablets complained of constipation, and one in each group complained of a sore mouth. Two patients taking tablets complained of mouth staining, which was found on questioning to have affected 15 patients taking tablets and six taking liquid ($p<0.05$). Serum bismuth concentrations rose slightly in only two patients and fell after treatment had stopped. The highest concentration recorded was 120 nmol/l (25 μg/l) in one patient. There was no difference between the groups.

Details of patients and results of treatment with De-Nol tablets and liquid

Treatment:	De-Nol tablets	De-Nol liquid
No of patients:	20	20
Male	14	16
Female	6	4
Mean (±SD) age (range) (years)	44·8±16·75 (22-69)	36·2±13·63 (21-60)
Average duration of symptoms (months)	85·4±98·5 (6 mth-26 yr)	56·7±58·9 (2 mth-17 yr)
Severity of symptoms:		
Mild	9	8
Moderate	6	6
Severe	5	6
Symptomatic response:		
Improved	16	16
Not improved	4	4
Mean time to relief of symptoms (days)	18	17
Endoscopic response:		
Healed	15	17
Not healed	5	3

Comment

De-Nol tablets are as effective as the established liquid preparation of De-Nol in the treatment of duodenal ulcer, and the proportion of ulcers healed in each group compares favourably with other agents. De-Nol in both the liquid[2] and tablet[3] forms has been shown to be as effective as cimetidine in the treatment of duodenal ulcer, and a recent report suggests that the relapse rate after De-Nol treatment may be lower (D F Martin, *et al*, British Society of Gastroenterology meeting, 1980).

Side effects in this trial were minor, and appreciable absorption of bismuth did not occur. Bismuth neurotoxicity occurs when serum concentrations exceed 479 nmol/l (100 μg/l),[4] concentrations below 239 nmol/l (50 μg/l) being considered safe, and no patient in our study reached these values. Neurotoxicity has never been reported in a patient taking De-Nol.

De-Nol treats duodenal ulcers effectively and does so without systemic absorption or side effects and without rendering the stomach achlorhydric. The development of an equally effective tablet formulation which more patients find acceptable is an important advance in the medical treatment of duodenal ulcer.

We are grateful to Brocades (GB) Ltd for supplies of De-Nol and to Mrs C L Baxendale for typing the manuscript.

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Successful treatment of D-penicillamine-induced breast gigantism with danazol

D-Penicillamine may cause sudden breast gigantism.[1] Danazol (17 α-pregna-2,4-dien-20-ynol [2, 3-d] isoxazol-17β-ol) has been used to manage benign breast disease.[2] This report describes the endocrine profile, regimen of danazol, and outcome in a patient with breast gigantism induced by D-penicillamine.

Case report

In January 1976 a 41-year-old nulliparous woman who suffered from rheumatoid arthritis began taking D-penicillamine 750 mg daily. In July 1977 she began to complain of breast enlargement. In June 1978 she discontinued the D-penicillamine for three weeks. There was no reduction in the size of her breasts and she had severe swelling of both knees. The D-penicillamine was restarted. In October 1978, after a further slight increase in the size of her breasts, the D-penicillamine was discontinued. Treatment with indomethacin was started and in January 1979 was changed to naproxen 250 mg three times a day. In February 1979, five months after the last exposure to D-penicillamine, the patient was admitted to hospital with

severe breast enlargement. She refused surgery. In March 1979 she attended the endocrine-infertility clinic.

The breasts were huge, tense, nodular, warm to palpation, and tender. The patient had begun to log her breast size regularly for four months before this visit. She agreed to accept experimental treatment with danazol, continue self-measurement, and submit to repeated blood sampling.

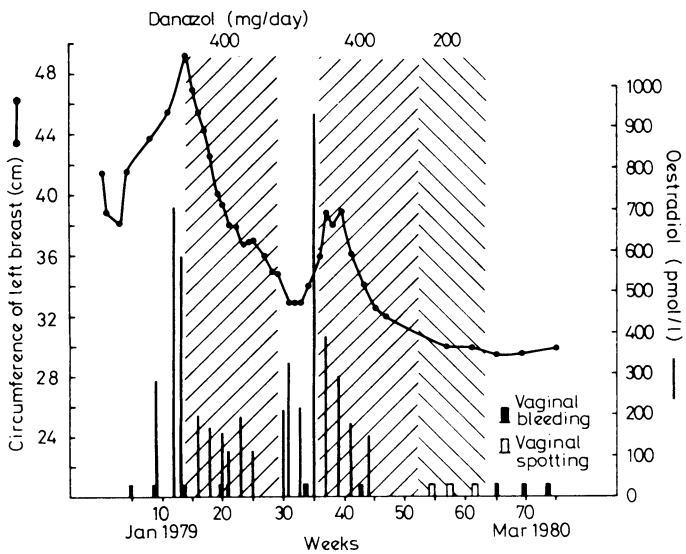
Serum oestradiol, luteinising hormone (LH), and prolactin concentrations were measured by double antibody radioimmunoassay. The intra-assay variation for oestradiol was 9·0%, for LH 4·9%, and for prolactin 7·9%. The circumference of each breast, measured from the lateral chest wall horizontally through the nipple to the medial chest wall, was recorded. Serum LH and prolactin values were consistently normal. Critical events are shown in the figure. Despite initial apparent success in reducing breast size with Danazol a second course of treatment was required to maintain a consistent effect.

Comment

How D-penicillamine induces breast enlargement is ill understood. An effect on sex hormone binding globulin might increase the amount of circulating free oestrogen.[1] Had D-penicillamine interfered with oestrogen binding the effects should have been apparent in other oestrogen-dependent tissues. The patient did not show changes in menstrual function while receiving D-penicillamine, nor during the time of maximal breast growth. It is more likely that D-penicillamine produced a local effect on the breast.

Postmenopausal breast atrophy is partly a result of a relative decrease of oestrogen in the target tissue.[3] Danazol would appear to act by interfering with oestrogen receptors.[4] Such blocking in the breast would mimic the postmenopausal condition and has been successfully applied to the treatment of gynecomastia.[5]

The diminution in breast size (figure) during the first course of danazol occurred simultaneously with the reduction in circulating oestradiol concentrations. The rapid increase in breast size after



Breast size, oestradiol concentrations, danazol dosage, and episodes of vaginal bleeding from January 1979 to March 1980.

Conversion: SI to traditional units—Oestradiol: 1 pmol/l ≈ 0·272 pg/ml.

cessation of treatment indicates that the reduction in breast size was not simply a coincidental spontaneous remission. The second decrease in breast size with treatment once again accompanied a reduction in oestradiol values.

Our study did not determine whether the breast shrinkage produced by danazol was produced by a reduction in circulating oestradiol concentrations or by a local effect. Irrespective of the fundamental mechanism, this is the first case of successful non-surgical management of gigantism of the breasts induced by D-penicillamine treatment.

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Treatment of spontaneous priapism by embolisation of internal pudendal artery

There is no established standard and effective treatment for spontaneous priapism. Two cases of post-traumatic priapism successfully treated by embolisation of the internal pudendal artery with an autologous clot have been reported.[1 2]

We report a case of spontaneous priapism successfully treated by embolisation of the internal pudendal artery using gel foam.

Case report

A 26-year-old unmarried man was admitted as an emergency on 24 August 1977, two days after the onset of priapism. He had had one episode of painful erection five days before, but this had subsided spontaneously after a few hours.

No response was obtained with chlorpromazine 50 mg thrice daily, and the next day heparin and ancrod were started and a left corporosaphenous shunt performed under general anesthesia. No appreciable effect was noticed from these measures, and 24 hours later a right corporosaphenous shunt was carried out.

No improvement was observed over the next three days. Amyl nitrate was tried with no effect, and attempted aspiration and irrigation of the corpora cavernosa under general anaesthesia failed. With the aspiration needle still in place corporocavernosography was performed. This showed free drainage by the right corporosaphenous shunt, the left one being occluded.

The priapism persisted despite the effective venous drainage by the right corporosaphenous shunt. On the eighth day after admission percutaneous catheterisation of the right femoral artery was performed and a pelvic arteriogram obtained. The internal pudendal arteries were larger than normal with distinct staining of the base of the corpora cavernosa. Early venous filling was not seen in either corpus cavernosum. The right internal pudendal artery was embolised with a single shower of gelatin foam emboli. An autologous clot could not be used as the patient was fully anticoagulated.

An angiogram obtained after embolisation showed emboli within the pudendal artery with slowing of the circulation. Turgidity decreased, and 24 hours later the penis had returned to normal flaccidity. The penis remained flaccid without any evidence of induration, and he was discharged on 19 September, 27 days after admission. By May 1979 he had recovered full potency and was attaining normal intercourse and ejaculation.

Comment

The erectile tissue draws its arterial supply almost exclusively from the internal pudendal artery. Normal erection is a primary haemodynamic activity with arteriolar dilatation leading to filling and turgidity of the corpora cavernosa. Restriction of the venous outflow is less important. The return to flaccidity is initiated by arteriolar constriction and shunting into arteriovenous anastomoses.[3] In priapism the arterial inflow exceeds venous outflow. Prolonged erection with stasis in the corpora cavernosa leads to a rise in the viscosity of the blood in the corpora, impeding venous outflow. Oedema of the trabeculae reduces the vascular lumen and further impedes outflow. Eventually arteriolar occlusion occurs and later trabecular fibrosis develops, irreversibly disrupting the arteriolar mechanism and making adequate erection impossible.[3]

Our patient was treated rather late, after various ineffective treatments had been tried. We believe that medical methods of treatment are valueless,[4] and surgical treatments have complications.[1] It is