

acting penicillin. It will be important to decide to what extent each of these drugs is benefiting the treated group. We know that the chloroquine is effective (Table II), and we know clinically that whenever a patient has a positive slide for malaria it has either been preceded or followed by a fall of up to 2 g./100 ml. in the haemoglobin value.

In the meantime we feel justified in advocating that children with sickle-cell anaemia should be seen regularly, possibly at special clinics, and treated routinely with antimalarial chemoprophylaxis if they live in a malaria zone. For the present we reserve judgment on the place of long-acting penicillin.

SUMMARY

The results of a long-term chemoprophylactic trial of chloroquine and long-acting penicillin in homozygous sickle-cell anaemia at the Mulago Hospital, Kampala, show that those patients under 6 years old followed for 10 months or more who received chloroquine and long-acting penicillin had a significantly ($P < 0.01$) lower rate of dactylitis and higher average haemoglobin value ($P < 0.02$) than patients in a control group receiving only a placebo. In addition, the therapy probably reduced the tendency for the haemoglobin to fall.

It is recommended that children with sickle-cell anaemia in malarious zones should be treated with suitable chemoprophylactic doses of chloroquine and followed at special clinics, if possible, at least in the early years of life.

The role of long-acting penicillin is not yet clear and studies are in progress to try to clarify this.

(Note.—The full statistical analysis is available from Dr. M. A. Warley, Department of Paediatrics and Child Health, P.O. Box 2072, Kampala, Uganda.)

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Medical Memoranda

Alcohol-induced Pain Associated with Adenocarcinoma of the Bronchus

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The occurrence of pain immediately after the consumption of an alcoholic beverage was first described by Hoster (1950) in patients suffering from Hodgkin's disease. This phenomenon has recently been studied in this department in a patient who had an adenocarcinoma of the bronchus and who presented with shoulder pain.

CASE REPORT

A 42-year-old post-office sorter developed a dull ache in his left upper chest and shoulder radiating to the ulnar border of his left arm and hand. Three weeks after the onset of symptoms a miniature chest radiograph taken as part of the routine examination at that time was reported as normal. A few days afterwards the patient first noticed weakness of his left hand. When first seen in this department, four weeks after the onset of symptoms, a full-size chest radiograph revealed a very small left apical opacity, and tomographs of this region showed an erosion of the neck of the third

left rib. There was no history of cough, sputum, haemoptysis, alteration in voice, or dysphagia. The results of a barium-swallow examination and bronchoscopy (Dr. L. J. Grant) were normal, and cytological and bacteriological examination of bronchial washings at the time of bronchoscopy and subsequently of sputum obtained by positioning and chest percussion gave negative results. The haemoglobin was 14.3 g. per 100 ml., white blood count 15,600 (polymorphs 82%, eosinophils 1%, lymphocytes 14%, monocytes 3%). Erythrocyte sedimentation rate (Westergren) was 20 mm. in the first hour, blood urea 36 mg. per 100 ml., serum alkaline phosphatase 12.4 K.A. units. Urine analysis, direct and indirect Coombs test, and Wassermann and Kahn reactions were also normal.

Shortly after admission the patient remarked that his symptoms were made very much worse within minutes of drinking a glass of beer or cider. He had noticed this about a week after the onset of symptoms and had since avoided any form of alcohol.

The left supraclavicular lymph node became palpable within a week of admission and a subsequent biopsy of this showed a fairly well differentiated mucus-secreting adenocarcinoma. The patient was treated with supervoltage x-ray therapy. However, he developed further metastases in his lumbar spine within weeks and died at home six months after the onset of the first symptoms. There was no necropsy.

Experimental Study.—With his full co-operation and knowledge the patient was given 30 ml. of 70° proof brandy (equivalent to approximately 10.5 ml. of ethanol). After seven minutes he suddenly developed a very severe and peculiarly unpleasant pain over the

whole of his left upper chest wall anteriorly and posteriorly and radiating down the ulnar side of his arm as far as the wrist. So severe was the pain that he cried out, and 100 mg. of pethidine given intravenously gave only partial relief. No sensory defect could be demonstrated in the area of the pain, which lasted about 30 minutes and was then replaced by a sensation of numbness, soreness, and tingling. No change in size of the supraclavicular and left axillary lymph nodes (the latter was also examined by biopsy later and did not show carcinomatous invasion) was noted after the onset of the pain.

On a second occasion the patient was given 50 mg. of diphenhydramine (Benadryl) orally 30 minutes before the administration of alcohol. He was then asked to take initially 10 ml. of brandy and when this had produced no symptoms within half an hour he was asked to drink a further 25 ml. This again had no effect within the next 10 minutes, and a further 15 ml. was given, making a total of 50 ml. of brandy. About 20 minutes after the last dose the patient reported only a mild discomfort in the usual area of distribution. Again no increase in size or tenderness of his palpable lymph glands was noticeable.

On a third occasion 30 ml. of brandy was given without antihistamine being administered beforehand, and half-hourly white cell counts and differential counts were done, but these showed no significant variations compared with a count taken before alcohol was given.

Vasodilators such as trinitrin gr. 1/130 sublingually and tolazoline (Priscol) 50 mg. orally, as well as the higher alcohol derivative methylpentynol 400 mg. orally, failed to reproduce the pain.

Shortly after the start of radiotherapy to the tumour site the patient lost all spontaneous and alcohol-induced pain. Further investigations at that time showed a normal 5-hydroxyindolacetic acid excretion, the serum protein electrophoresis showed a raised alpha-2-globulin, and a bone-marrow examination showed a few atypical blast cells, no excessive plasma cells, but was otherwise normal.

COMMENT

James (1960) estimated that when alcohol-induced pain is specifically asked or tested for in patients suffering from Hodgkin's disease it is found in 17% of cases, and it occurs more frequently in those under the age of 40 and in those patients whose nodes show an excess of eosinophils and fibrosis on biopsy.

Since its first description in 1950 alcohol-induced pain has been found in isolated instances in a wide variety of conditions. James *et al.* (1957) report its occurrence in a patient with carcinomatous invasion of the thymus and in a patient with pulmonary metastases from a presumably primary pancreatic carcinoma. Conn (1957), who tested for alcohol-induced pain in 98 patients, describes its occurrence associated with osteomyelitis, with traumatic fracture of the acetabulum, and in a patient with pyogenic lymphadenitis who also had sarcoidosis. In

addition alcohol-induced pain has been described in association with Brodie's abscess of bone (Alexander, 1953), eosinophilic granuloma of the skull (Lewes and Valentine, 1962), carcinoma of the cervix (Healey, 1959), as well as in a normal healthy physician who experienced this symptom for 15 years (Conn, 1957).

The symptoms can be produced by oral as well as by intravenous ethanol usually by both routes in the same patient, though sometimes only by one or the other. It has been reported in patients with and without bone involvement and it has been known to antedate clinical and radiological evidence of disease at the sites of pain. Quite minute quantities of alcohol such as a portion of sherry-containing jelly (Portman, 1950) can produce the symptoms and it has been reported with all forms of alcoholic beverage. Gros, Veillon, and Waeckel (1953) first noticed that alcohol-induced pain could be prevented by the administration of an antihistamine beforehand, and, as in the patient described here, Bichel and Bastrup-Madsen (1953) failed to reproduce the symptom with a vasodilator.

Though 14 years have elapsed since it was first described, there is still no explanation of the pathogenesis of the symptom. Most of the case descriptions have been of patients suffering from Hodgkin's disease, and as dilute alcohol is often used as a nutrient either in the form of a drink or intravenously in carcinomatosis the occurrence of the symptom in the latter condition must be very rare indeed.

I would like to thank Dr. A. St. J. Dixon for allowing me to report on this patient who was admitted to the Rheumatism Unit at St. Stephen's Hospital under his care, Mr. O. Tubbs for allowing me to follow-up and further investigate the patient at the Brompton Hospital, Professor D. W. Smithers for access to the relevant case notes at the Royal Marsden Hospital, and Dr. H. E. M. Kay for carrying out some of the investigations.

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Otogenic Tetanus: Report of a Case with Bacteriological Findings

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Tetanus associated with chronic ear infection has often been reported from India (Stonham, 1938; Shah, 1955; Hazra and Agnihotri, 1960; Apte, 1961), but only two cases in the British Isles are found reported in the literature to date (Corcoran, 1938; Wadsworth, 1962).

The following is a report of a case together with bacteriological findings.

CASE REPORT

A 49-year-old woman, who was employed in a factory manufacturing horse-hair upholstery filling, was admitted to hospital on 13 December 1963 with a three-day history of pain along the right side of the lower jaw and difficulty in opening her mouth. During the 24 hours before admission she had been able to take fluids only. She had no recollection of any recent puncture wound or abrasion, but did volunteer the information that she had had some blood-stained discharge from the right ear some three weeks previously, that both ears had felt "blocked up" for some time, and that there had been intermittent discharge from the left ear for several years. She had not attempted any more than superficial mopping of the ears.

Clinical examination revealed an apparently over-anxious little woman who was unable to open her jaws more than $\frac{1}{2}$ in. (1.3 cm.).