before and during treatment, persisting until the lesion healed; this persistence apparently did not influence clinical recovery.

Discussion

Judged by the results obtained in the two main series of cases it would appear that an equally satisfactory response can be obtained in the treatment of out-patients by the use of either daily injections of 300,000 units of procaine penicillin in arachis oil or twice-daily injections of 300,000 units of penicillin in saline. It would therefore seem that for treatment of infections of the kind described a continuous bactericidal level of penicillin in the blood is not necessary.

Our experience of the use of 300,000 units of procaine penicillin with 2% aluminium stearate was not extensive, but it appeared that while clinical improvement took place it did not occur as rapidly as in the patients treated with procaine penicillin or with penicillin in saline. This suggested that persistence in the blood had been obtained at the expense of adequate blood concentration. The preparation containing aluminium stearate may well provide excellent treatment for infections caused by more sensitive organisms than staphylococci, but for the treatment of staphylococcus infections there would seem to be a place for a preparation of procaine penicillin, with or without aluminium stearate, which also incorporated crystalline penicillin to provide a high initial blood concentration.

The number of cases with resistant staphylococci was too small to allow of their being placed in a separate group, and, although it would have been highly desirable, no comment can be made on the response of such cases to treatment with penicillin. At present the number of infections in out-patients due to penicillin-resistant staphylococci is small, but in view of the growing number of reports of the increasing proportion of resistant strains in hospital wards it is likely that these infections may in time present a serious problem.

The number of lesions in which Gram-negative bacilli were present was also small, and there was no evidence in this series of cases that infection with Gram-negative bacilli played any major part in delaying healing.

Summary

The results of a clinical investigation are presented in which 116 patients with acute septic infections of the skin and subcutaneous tissues, mainly staphylococcal, were treated with daily injections of 300,000 units of procaine penicillin and a similar number of patients were treated with twice-daily injections of 300,000 units of penicillin in saline.

No significant difference between the response to treatment of these two groups was detected.

We would like to thank Professor Sir James Paterson Ross and Professor L. P. Garrod for the advice and encouragement they have given us; Miss Deal, sister in charge of the surgery, and the nursing staff for their co-operation; and Miss M. Rhodes and Mr. R. Andrew for technical assistance. The procaine penicillin used was supplied by Messrs. Glaxo Laboratories, to whom we are indebted for the supply of procaine penicillin with 2% aluminium stearate.

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"NEO-EPININE" IN THE DYSPNOEA OF COAL-MINERS

BY

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The most outstanding symptom of the pneumoconiosis of coal-miners is dyspnoea. This symptom occurs in mild degree in the earliest stages of the disease, but progresses over a period of years to such an extent that it may wholly incapacitate. In the advanced stages of anthracosilicosis gross pulmonary fibrotic changes have taken place, and in order to compensate for such loss of healthy functioning lung tissue respiration is speeded up and therefore dyspnoea becomes marked. In the beginning, however, the breathlessness is more difficult to explain. It could be attributed to various factors such as early bronchitis, focal emphysema, the psychic outlook of the patient, or a possible bronchospasmodic effect of siliceous matter.

As it was considered probable that some of the dyspnoea might be due to bronchospasm, alone or associated with emphysema, it was decided to try the effect of the most potent modern bronchodilator available.

Konzett in 1940 described the pharmacological actions of homologues of adrenaline and noted that the isopropyl derivative had a powerful relaxing effect on bronchial muscle spasm. The relaxant power of this derivative was considered to be 10 times stronger than that of the parent substance adrenaline. Little or no clinical application of this knowledge was made in this country until last year, when Herxheimer (1948) recorded his favourable findings with "aleudrine" (isopropyl adrenaline) in cases of asthma, although satisfactory reports had been forthcoming in the intervening years from the Continent (Stolzenberger-Seidel, 1940; Quitschal, 1942) and the United States (Segal and Beakey, 1947; Charlier, 1947).

Present Investigation

In order to assess the merits of such a bronchodilator in this disease 58 colliers, all complaining of shortness of breath in some degree or other, were investigated. The preparation used in the experiment was isopropyl-nor-adrenaline sulphate, "neo-epinine" (Burroughs Wellcome and Co.), which is chemically *dl*- α -3:4-dihydroxyphenyl- β -isopropylaminoethanol sulphate, and which is known to have the therapeutic quality of enhancing vital capacity. The neo-epinine had for convenience to be used in tablet form, each tablet containing 20 mg. of the drug. Strict instructions were given regarding slow sublingual dissolution and the swallowing of as little saliva as possible. Inert tablets of exactly identical appearance were also supplied by Messrs. Burroughs Wellcome and were used in all cases for the first week of treatment and when it was thought that functional factors were clouding the issue.

Type of Case.—No special attempt was made to select any particular type of anthracosilicotic so far as age-grouping, radiographical grading, length of time in mines, etc., were concerned. The youngest man was 33 years old, the oldest 65, and the average age for the whole group 56.3 years. Radiographical grading, international classification (International Labour Office Studies and Reports, 1930), was: 29 showing partial distribution of linear shadowing and an early indication of nodulation (Ia), five more widespread shadowing (Ib), five generalized but still

discrete nodulation (Ic), and five increase in number and size of discrete shadows with a tendency to confluence (II). Those that could not be classified according to this standard were regarded as: emphysema, five; bronchitis, five; and negative, four. If, however, cardio-renal disease was thought to play any part in the development of the dyspnoea, then such patients were considered to be unsuitable for investigation. The criteria for the test were simply (1) that the man was or had been working in the coal-mines for many years, and (2) that his main complaint was shortness of breath which could be attributed to his work, no other cause being found.

Routine Adopted

At the first visit of the patient to hospital the following details were recorded: (a) careful medical and occupational history; (b) clinical examination; (c) urinalysis; (d) Hb percentage, leucocyte count, erythrocyte sedimentation rate, sputum examination, blood urea, and electrocardiography if considered necessary; (e) vital capacity estimation; (f) x-ray examination.

It was at this time explained to the man that as his chief complaint was shortness of breath we were going to try to improve this by means of tablets, but that we would need his careful co-operation and he would be required to report back to hospital each week for a period of five or six weeks so that we might assess his progress. He was then given a seven-days supply of inert tablets, being told to take one three times a day, with the already noted injunction about slow sublingual melting. On the succeeding visits the patients were given a weekly supply of neo-epinine after the vital capacity had been recorded. It was considered that the study of the vital capacity would be the most valuable estimate of the effect of the drug. Especial care was taken on all occasions to allow each man plenty of time to explain exactly how he felt and what effect, if any, the new drug had on his breathing and general feeling of well-being.

Results

It was found, during the test period when the patients were having the inert tablets, that there was on the average a slight increase in the vital capacity but not such as could not be ruled out by experimental error. With neo-epinine, however, there was an actual average increase of 236 ml. Irrespective of vital-capacity estimations, the comments of the patients were interesting, as 44 admitted improvement, 11 considered that their condition was unchanged, and one said that he felt worse; two did not complete the test. The 44 who felt better were further classified according to their expressions of well-being: 17 were enthusiastic about the effect of treatment, another 17 said they were better but thought that they could still make more of it, while the remaining 10 thought that they had improved a little, though they still complained of symptoms such as shortness of breath on hurrying, ascending hills, etc.

As was to be expected, the commonest side-effect complained of with neo-epinine was palpitation; this, however, was always a transient feature, lasting only a matter of 10 to 15 minutes after taking the tablets. Other passing complaints were shakiness, giddiness, and flushing.

The inert tablets did not give rise to any untoward symptoms. It has to be noted that no attempt was made to vary the dose of the drug according to the severity of the dyspnoea, and whether or not any degree of tolerance arises with the use of this drug in such cases cannot at present be stated.

Summary

On the assumption that dyspnoea in the earliest stages of pneumoconiosis might be due to bronchospasm associated with focal emphysema it was considered desirable to try the effect of a bronchodilator. It was thought that the iso-propyl derivative of adrenaline, a powerful bronchial antispasmodic, might prove useful in these cases.

Fifty-eight colliers complaining of breathlessness were given inert tablets for one week, followed by neo-epinine tablets for four weeks. It was found that there was little or no difference in vital-capacity estimations with the inert tablets, but after neo-epinine had been taken for four weeks there was an average increase of 236 ml.

Forty-four of the men commented upon a feeling of improvement in varying degree while under treatment. Although there was an average increase in the vital capacity with this drug, it is realized that some of the improvement could be "spiritual," as in Fletcher's (1948) classic description of such cases.

Toxic effects of the drug are noted.

I am indebted to Dr. A. Fergus Hewat for kind co-operation and permission to establish an out-patient pneumoconiosis clinic attached to his wards; also to Professor D. M. Lyon for much helpful criticism of this paper.

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RECTAL HAEMORRHAGE ASSOCIATED WITH INFECTIOUS MONONUCLEOSIS

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Rectal bleeding in the course of glandular fever is so rare an occurrence as to warrant a brief description.

Case Report

The patient, a man aged 34, gave no relevant previous history and had never manifested any haemorrhagic tendencies. He suffered a typical mild attack of glandular fever during which there was no jaundice or severe malaise and the temperature did not exceed 100° F. (37.8° C.) at any time. Generalized lymphadenopathy affecting the glands of the neck, axillae, and groins was first noticed on the fifth day, following an ill-defined influenza-like onset. On that day the patient sought medical advice at hospital, where a palpable spleen was found and the clinical diagnosis of infectious mononucleosis confirmed by a blood examination (see Table).

Subsequently the patient seemed to make a satisfactory recovery, becoming completely afebrile on the seventh day and getting up for a short period during the ninth. However, later in the evening of that day, while micturating, he passed some bright, partly clotted blood per rectum. The bleeding was not profuse and could be stopped by rest, but it was immediately brought on again by straining such as passing urine or flatus. This condition persisted during the night and the following morning (the tenth day), when the patient presented