Conclusion

The scalene syndrome is of commoner occurrence than cervical rib in producing pain in the upper limb, and when symptoms are persistent it is not enough merely to divide the scalenus anticus, because the lowest trunk of the brachial plexus may still be stretched over and from time to time chafed by an underlying rib or band, or by the medial and tendinous lower fibres of the scalenus medius or an abnormal scalene muscle. It is necessary to divide any such structure so as to free completely the lowest trunk of the plexus, exploration of which is therefore the indication and not merely anterior scalenotomy. Similarly, where the subclavian artery is elevated over and compressed between an abnormal rib behind and the scalenus anticus in front, the part of the abnormal rib lying below and behind the artery must be removed so that the vessel is free to sink down on to Sibson's fascia. Only if these principles are applied in operating on cases of pain in the upper limb due to lesions of the thoracic operculum may we expect results that are wholly satisfactory.

Summary

Pain in the upper limb due to lesions of the upper thoracic opening may be the result of compression of the subclavian artery (the costoclavicular syndrome), or irritation by a band, rib, the scalenus medius, or an abnormal scalene muscle of the lowest trunk of the brachial plexus stretched over it and compressed from in front by the scalenus anticus (the scalene syndrome).

Similar pain does not occur in the lower limb, because acute angulation of the nerve trunks leaving the pelvis does not occur as in the case of the neurovascular bundle leaving the thorax. This angulation in the case of the upper limb and its absence in the case of the lower limb is due to the upright posture.

Elevation of the limb to a right-angle will usually relieve symptoms, indicating that similar relief can be obtained from operation.

Operation is best performed through an incision above the clavicle crossing the posterior triangle of the neck.

Anterior scalenotomy is not enough. The under surface of the lowest trunk of the plexus must be cleared so that no further chafing action of this nerve trunk can occur.

I am indebted to my friend and colleague Mr. Cecil Lewis, F.R.C.S., for the accompanying drawings.

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The Scottish Society of the History of Medicine, which was founded in April, 1948, has just issued its first annual report. There are already 75 members of the Society, and it is hoped that this number will increase. The sixth meeting, and the first annual meeting of the society, was held in the council room of the University of Edinburgh on October 1, 1949. It took the form of a discussion on "The Teaching of the History of Medicine." The subject was introduced by the president, Dr. Douglas Guthrie, followed by Dr. W. D. D. Small, P.R.C.P.Ed., and Mr. Denys Hay, lecturer on history and director of studies in the Faculty of Arts. A large number of members took part in the discussion, and the honorary secretary, Dr. H. P. Tait, brought the meeting to an end with a brief review of the opinions which had been expressed.

THE COMPARATIVE MERITS OF SODIUM AND PROCAINE PENICILLIN GIVEN INFREQUENTLY

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Penicillin is widely used in general practice and in the out-patient departments of hospitals for the treatment of acute staphylococcal infections of the skin and subcutaneous tissues, but as yet the dosage employed in different hospitals varies widely.

One school, of which the chief protagonist has been Eagle, believes that the aim should be to maintain a bactericidal level of penicillin in the blood, and hence in the tissues, continuously throughout treatment. This belief is based (Eagle, 1948) on the principle that the frequency of penicillin administration should depend on the generation-time of the micro-organism concerned. If too long a period after administration is allowed the blood will become free from penicillin and surviving organisms will be able to multiply. If this is permitted for only a brief period the effect of treatment will merely be counteracted in part; if, however, too long an interval is allowed the effect of treatment may be counteracted by the supervening multiplication of organisms. This view receives tacit support from the fairly general practice of treating out-patients with large doses of penicillin once or twice a day, and admitting to the wards serious cases, or those which do not improve, for treatment with three-hourly injections.

On the other hand, clinical reports in ever-increasing numbers suggest that penicillin given in large doses daily or twice daily is effective for staphylococcal infections.

For instance, Wheatley (1947) treated seven cases successfully, in six of which single daily doses of not more than 200,000 units of penicillin were employed. D'Abreu, Flood, and Hewitt (1947) and Barclay (1949) report some benefit from the use of spaced doses in the treatment of septic hands, although in the last group systemic penicillin was combined with local penicillin.

The object of this paper is to describe a clinical investigation in which acute septic infections of the skin and subcutaneous tissues, mainly staphylococcal, have been treated by one of two methods, the first designed to keep a low penicillin concentration in the blood throughout most of the 24 hours, the second to produce two high concentrations of penicillin in the 24 hours, allowing the blood to become free from penicillin during an appreciable part of that period. The opportunity has also been taken to make some general observations on the treatment of infections of this type.

Methods of Treatment

The first group of patients was given a single daily intramuscular injection of 300,000 units of procaine penicillin in arachis oil, an amount which has been shown to produce low concentrations throughout most of a 24-hour period

in the majority of patients (Jones and Shooter, 1948); the second group received two intramuscular injections of 300,000 units of sodium penicillin in saline in the day. In the latter method penicillin was given when the patient was first seen, and subsequently between 9 and 10 o'clock in the morning and at 5 o'clock in the afternoon. In this way two high penicillin levels were produced each day and there was a total period of 8 to 14 hours in which no penicillin would be detectable in the blood. Both forms of treatment were continued for five days. In a small number of cases the treatment was continued for a few extra days.

A smaller group of patients, not included in the main series, was treated with 300,000 units of procaine penicillin in arachis oil with 2% aluminium stearate. These injections were given once every two days.

As local treatment, sodium sulphate (12½%) dressings and, in some cases, kaolin poultices were used, and immobilization of the affected part was advised. Lesions were incised only when necessary, with minimal incision. Boils and carbuncles were never so treated. In general it can be said that the local treatment in the two series followed exactly the same lines, without reference to the type of penicillin used.

All the patients were seen by one of us (E.G. or P.F.J.), usually at daily intervals, and never less frequently than once in three days. Clinical findings were recorded on a special form. As a rule swabs were taken from lesions before beginning treatment, but when the lesion was not open at the start it was swabbed as soon as possible after it had begun to discharge. Subsequent swabs were taken at five-day intervals until the lesions healed.

Conditions Treated

The patients treated were those attending the out-patient department of the hospital suffering from acute staphylococcal infections of the skin and subcutaneous tissues who required penicillin for treatment. Patients attending during the first month were allotted to the procaine penicillin series and those in the next month to the saline penicillin series, and this alternation was continued throughout the trial. In view of the ample evidence of the value of penicillin in the treatment of staphylococcal infections it was not considered justifiable to deprive patients of the antibiotic in order to provide a control series.

The types of infection treated are given in Table I.

TABLE I.—Types of Infection Treated (116 Patients in Each Group)

Condition	Procaine Penicillin	Saline Penicillin	Total
Boils	32	23	55
Cellulitis	15	13	28
All carbuncles except dorsal finger carbuncles	23	25	48
Dorsal finger carbuncles	6	8	14
Other conditions	40	47	87
Total infections	116	116	232

Patients who took their discharge while under treatment were not included in either series; neither were those patients with infected burns, chronic osteomyelitis, and hand infections (other than dorsal finger carbuncles) who were treated with penicillin while this trial was in progress. The final category in Table I, "other conditions," included those lesions which were not numerous enough to form separate groups, and comprised such conditions as lymphadenitis, abscesses, and erysipelas.

Comparison of Lesions in the Two Groups

Dealing with such a heterogeneous collection of infections, it has been difficult to ensure that the two series of cases were comparable, and some lesions were included in one series which had no strict parallel in the other. In an attempt to compare lesions in the two series the approximate diameter or greater transverse measurement of the area of redness and induration was recorded. These findings, together with the time interval between the patient's noticing any abnormality and his attendance for treatment (time to treatment), are given in Table II. Fig. 1

EXTENT OF INDURATION

Fig. 1

Table II. Fig. 1 shows diagrammatically the extent of induration. All three findings were not always recorded for each patient. In the table the means are based only on the patients for whom the findings were recorded.

TABLE II

	Mean Time to Treatment (Days)		Mean Redness (in.)		Mean Induration (in.)	
	Procaine Penicillin	Saline Penicillin	Procaine Penicillin	Saline Penicillin	Procaine Penicillin	Saline Penicillin
Boils	3.5	3.7	1.5	1.3	1.1	1.1
Cellulitis	6.7	4.1	2.6	2.9	1.3	1.6
Carbuncles of neck ..	7.1	7.9	1.7*	2.5	2.0*	2.1
All carbuncles except dorsal finger carbuncles	5.8	5.3	1.8	2.5	1.7	1.9
Dorsal finger carbuncles	6.0	3.9	1.8	1.7	1.2	1.0
Other conditions	4.8	4.6	2.1	2.1	1.6	1.4
All conditions	4.9	4.5	1.9	2.1	1.4	1.4

* The apparent inconsistency shown here is due to the fact that for one patient with a large indurated area the redness was not recorded.

Results of Treatment

As a criterion of the results of treatment, the time between onset of treatment and the relief of pain, and the healing time, which was defined as the time from the start of treatment to epithelization, have been taken. These times are given in Table III and diagrammatically for the individual groups of lesions in Fig. 2. Information was not recorded in every case, and the figures in parentheses indicate the number of cases on which the mean times were

TABLE III

	Mean Time to Relief of Pain (Hours)			Mean Healing Time (Days)		
	Procaine Penicillin	Saline Penicillin	All Cases	Procaine Penicillin	Saline Penicillin	All Cases
Boils	28 (19)	24 (17)	26 (36)	8.2 (29)	7.9 (21)	8.0 (50)
Cellulitis	35 (5)	24 (10)	27 (15)	8.4 (15)	7.3 (12)	7.9 (27)
Carbuncles of neck ..	—	39 (6)	38 (10)	13.1 (10)	12.3 (7)	12.8 (17)
All carbuncles except dorsal finger carbuncles	35 (9)	27 (22)	29 (31)	14.7 (22)	11.9 (23)	13.2 (45)
Dorsal finger carbuncles	28 (5)	19 (7)	23 (12)	12.0 (5)	12.3 (8)	12.2 (13)
Other conditions	28 (19)	27 (35)	27 (54)	8.9 (38)	7.5 (45)	8.1 (83)
All conditions	29 (57)	26 (91)	27 (148)	10.0 (109)	8.8 (109)	9.4 (218)

FIG. 2

based. Where this number was less than five no entry was made in the table.

There was an indication that the longer the period before the patient attended for treatment the longer was the healing time. Table IV gives the mean healing times for both series together, corresponding with days before patients sought treatment, where this information was recorded.

Two groups of lesions which responded similarly in both series merit further comment.

TABLE IV

Mean Time to Treatment (Days)	Number in Group	Mean Healing Time (Days)
-1	14	5.4
-2	43	7.6
-3	35	9.5
-4	22	10.2
-5	22	9.5
-6	16	9.8
-7	15	12.9
-14	20	13.0
14+	1	14.0

The correlation coefficient between mean time to treatment and mean healing time is 0.27, which is significant ($p < 0.05$).

Carbuncles

These have been among the most satisfactory infections to treat. In all cases treatment has been entirely conservative, and the relief of pain and toxæmia has been remarkable. Usually within two days, sometimes within hours, the surrounding area of redness disappeared and the induration softened. Finally, with separation of the slough the lesion was left as an area of healthy granulation tissue, with no reaction in the surrounding skin or connective tissue. Some carbuncles responded with exceptional speed and seemed to be completely absorbed, without slough formation. No complications of any kind were seen in this series.

Dorsal Finger Carbuncles.—The importance of the dorsum of the proximal phalanx as a site for carbuncular lesions seems to be insufficiently recognized. Donald (1948) and Pilcher *et al.* (1948) are among the few authors who specifically mention these lesions, which, we have found, are generally diagnosed as boils and sometimes treated by incision, with disappointing results. If not treated with penicillin they tend to pursue a chronic course and are apt to give rise to complications such as osteomyelitis, stiff finger, and tender scar (Pilcher *et al.*, 1948). No complications followed in the 14 cases treated.

Cases Treated with Procaine Penicillin and Aluminium Stearate

A small group of 24 patients was treated with 300,000 units of procaine penicillin in arachis oil with 2% aluminium stearate, this amount being given when the patient was first seen and repeated every two days. The

infections treated comprised boils, carbuncles, and abscesses. Although in 22 of the patients amounts of penicillin which could be assayed were present in the blood towards the end of the first 24 hours of treatment, and in the blood of 10 of the 11 patients tested towards the end of the second 24 hours, the clinical response was unsatisfactory. After six of the 24 patients had been transferred to treatment with procaine penicillin with successful results no further patients were treated with procaine penicillin containing 2% aluminium stearate.

Bacteriology

All the swabs were sown direct on to horse-blood agar plates from which two cups had been cut with a cork-borer. After inoculation the cups were filled with 1 unit per ml. and 10 units per ml. of penicillin respectively. Staphylococci which after subculture from the primary plate coagulated plasma in a tube were described as *Staphylococcus pyogenes*. Penicillinase production was noted from the primary plate by the method described by Waterworth (1948).

The results of the swab examinations when organisms were grown are given in Table V.

TABLE V

Organisms Isolated from Initial Swabs	Cases
<i>Staph. pyogenes</i> , penicillin-sensitive	180
<i>Staph. pyogenes</i> , penicillin-resistant	13
Gram-negative bacilli	8
Haemolytic streptococci	11

Of the eight Gram-negative bacilli isolated, two proved to be *Proteus* and one *Ps. fluorescens*; six were not identified. Of the 11 haemolytic streptococci, only two occurred in the absence of *Staph. pyogenes*.

A further 231 swabs were examined from patients during the course of treatment, and four more Gram-negative bacilli were recovered which were not present in the initial swabs. One of these was *Proteus* and one *Bact. coli* (intermediate type II); two were not identified. From only one of these subsequent swabs were haemolytic streptococci isolated when they had been absent originally.

General Observations on Treatment

During the course of this investigation it was our impression that the cases in the two series were responding in much the same way, and this has been confirmed by statistical analysis, there being no significant difference between any of the groups in either series. The two series were tested for differences in mean (t) and differences in distribution (χ^2) in all groups. The apparent consistency with which the healing times for the saline penicillin series were shorter than the healing times for the procaine penicillin series, shown in Table III, was also shown not to be significant.

Three observations were made which had no bearing on the main course of the investigation, as the facts observed occurred in both series. The first was that when the pain was relieved it sometimes went very quickly—at one moment it was there and within half an hour it had almost entirely gone. The second observation was that in many cases the original purulent lesion was replaced by apparently healthy granulation tissue in a fairly short time, and it took as long again for this comparatively small area to be covered by epithelium. This was particularly noted in the boils and carbuncles, and accounted for a considerable part of the healing time.

Thirdly, it was interesting that in some of the lesions coagulase-positive staphylococci could be demonstrated

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