The great difference in incidence of this complication between males and females is another perplexing aspect. Undoubtedly, aggravating factors are not so prominent in the lives of most women, and they have much better opportunities for regular meals. But it would seem that there must be some fundamental difference.

Perforated gastric ulcers are a great deal less common than duodenal, which is fortunate, as their mortality in general is much higher; over the whole six years for which figures were given, the mortality rate for perforated duodenal ulcer was 10.7%, while for perforated gastric ulcer it was 20.8%. This agrees with Tidy (1945).

The late results with reference to alleviation of symptoms are in agreement with those of most recent authors. In the period 1920-30 several reports of very high "cure" rates were published—e.g., Stewart and Barber (1922) reported 28 cures out of 37 cases treated by simple suture. In 1925 Grey Turner in a Hunterian lecture recorded 81 cures out of 120 cases, and in the ensuing discussion R. P. Rowlands said that only 25% had further symptoms. Pannett, writing in 1928, thought 50% were cured by simple suture. But towards the close of this decade more critical appraisal of results showed that only 30 to 40% of cases so treated remained symptom-free. Gilmour and Saint (1932) reported 64 cases, with 38% satisfactory afterwards, Sallick (1936) 9 cases symptom-free out of 33 cases traced, and Scotson (1933) 42% symptom-free after 3 years.

In the present series 38% of such patients have remained symptom-free 12 or more years after operation. This confirms the work quoted, and tends to support the belief that recurrences usually betray themselves within two years of operation or not at all. There are exceptions to this rule, which appeared to be true in the present series, though patients' memories are not entirely reliable. Five years is the longest interval after which symptoms recurred.

An old-established belief that the more chronic the ulcer the less the likelihood of cure is challenged by the figures I have advanced. The "cure" rate in those whose symptoms had lasted less than one year was 43% (26 out of 60), while in those in whom symptoms had lasted more than one year it was 42% (43 out of 101). Brown (1925) also challenged this belief, and stated that patients with no previous history fared worse, as regards return of symptoms, than those with long-standing histories. But of the 38 patients who had had no symptoms beforehand, 22 (57.9%) remained symptom-free, which would seem to indicate that in this group the prognosis is relatively good. And Gilmour and Saint (1932) had excellent results in all their cases with short histories.

One further point requires some elaboration, and that is the effect of diet on the rate of recurrence. Most authors are agreed that perforation should be followed by a strict medical ulcer regimen, and doubtless this counsel of perfection is the ideal towards which we should strive. But, human nature being what it is, ideals are seldom attained, and the figures I have gathered seem to suggest that nothing less than a strict diet is of any value. Only 21% of those who remained symptom-free after operation had made any serious attempt to diet, whereas 44% of those in whom symptoms recurred had made such an effort. Scotson (1933) stated that diet post-operatively had a very definite effect in reducing recurrence of symptoms. Cutler has always stressed the importance of such measures, and undoubtedly they are most important. The point I wish to make is the uselessness of half-hearted measures: if results are to be worth while a strict regime is essential.

Summary

The general results of simple suture in treatment of perforated peptic ulcers have been traced in a series of 244 cases which had been operated on 12 years or more ago.

The mortality rate of perforated peptic ulcer has declined since the introduction of the sulphonamide drugs.

Symptomatic cures were obtained in 38% of cases.

The prognosis with regard to symptomatic cure is better in patients with no preceding symptoms and in those in whom perforation occurs after the age of 45.

Diet, unless rigidly supervised and enforced, exerts little effect on the late results.

Alcohol and tobacco, although tending to aggravate symptoms, continued to be enjoyed by most patients accustomed to them.

I would like to thank all the members of the surgical staff of the Royal Victoria Infirmary, Newcastle-upon-Tyne, past and present, for permission to use and publish their case records. I should also like to thank Mr. Rodney Maingot for much helpful advice in the preparation of this paper.

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MENINGITIS DUE TO A PENICILLIN-SENSITIVE, SULPHONAMIDE-INSENSITIVE PITTMAN b STRAIN OF *H. INFLUENZAE*: RECOVERY

BY

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In a previous publication (McIntosh and Drysdale, 1945) a case of recovery from *H. influenzae* meningitis (Pittman b type) in a child aged 2½ years following treatment with penicillin and sulphamezathine, to both of which the organism was sensitive, was described. The following case is of interest since (a) the causal Pittman b type of *H. influenzae* was penicillin-sensitive but sulphonamide-insensitive; (b) recovery ensued after prolonged treatment with penicillin.

Case Report

A male child aged 20 months was admitted to King's Cross (Infectious Diseases) Hospital, Dundee, on Dec. 18, 1945, with a three-days history of stiffness of the right leg, tenderness of the spine, and vomiting. Examination revealed head retraction, presence of Kernig's sign, absence of abdominal reflexes, absence of knee-jerks, indefinite plantar reflexes; temperature 100.8° F. (38.2° C.), pulse rate 128, respiration rate 60. Lumbar puncture yielded a turbid fluid under increased pressure containing 383 cells per c.mm., of which 260 were red blood cells, and 75 mg. of protein per 100 ml. Sugar was absent. On Dec. 20 the preliminary bacteriological report stated that a micro-organism, probably *H. influenzae*, which was sensitive to penicillin and very slightly sensitive to sulphathiazole, but insensitive to sulphapyridine, sulphamezathine, and sulphadiazine, had been cultured. Detailed examination proved that the bacillus was a *H. influenzae* Pittman b type and quite insensitive to the above sulphonamides and also to sulphamerazine. *In vitro* tests showed that growth was noticeably inhibited in haematin broth containing 0.6 unit of penicillin per ml., and completely inhibited in a concentration of 0.7 unit per ml. Until the diagnosis had been established and full sensitivity tests completed 25 g. of sulphonamide (7 g. sulphapyridine, 5.5 g. sulphamezathine, 12.5 g. sulphathiazole), 125,000 units of Seitz-filtered penicillin intrathecally, and 900,000 units of penicillin intramuscularly were administered during Dec. 18-26. Thereafter penicillin alone was given. During the period Dec. 18-Jan. 21, 1,005,000 units were given intrathecally and 10,237,500 units intramuscularly (see Chart). The child's condition gave rise to anxiety until Jan. 10, when, with his reserves of strength almost depleted, and having made a good recovery from a convulsion (Jan. 8), probably induced by penicillin, he remained apyrexial, except for a slight elevation of temperature on Jan. 21 and 22, until he was discharged, recovered, on March 1. Clinically the most notable features of the illness were: head retraction (Dec. 18-23); the persistence of neck rigidity (Dec. 18-Jan. 14); intention tremors of

head and upper limbs (Dec. 18-Jan. 23); the occurrence of broncho-pneumonia (Dec. 24-30) despite the antecedent penicillin administration; the daily recurrence of a blotchy erythematous rash about two hours after the intrathecal injection of penicillin—appearing first on the thighs, then on the lower abdomen, followed by some blotchiness of the face, next morning found only on the thighs (Jan. 13, 16-18). The persistent nature of the meningeal infection is reflected also by the results of examination of the C.S.F. shown in the Chart. After the fluid had become clear and the culture sterile on Dec. 24, omission of lumbar puncture on Dec. 25 and 26 was followed by the recurrence of turbid C.S.F. on Dec. 27-Jan. 2 and by positive cultures on Dec. 27, 29, 30, and Jan. 3. Thereafter the pleocytosis diminished and a series of negative cultures was obtained. From Dec. 29 the daily intrathecal dose of penicillin was increased to 50,000 units until Jan. 8, on which date, owing to the occurrence of a convulsion about three hours after the injection, the dose was reduced to 30,000 units (Jan. 10) and to 25,000 units (Jan. 11-20). It is to be noted, however, that, using the method

2.0 units per ml. (with an average of 1.7 units per ml. for four days). While this concentration was adequate, as judged by the *in vitro* tests, for the inhibition of the causal strain, a reduction of the intrathecal dose to 25,000 units daily, despite the continuance of 500,000 units daily systemically, resulted in a concentration of penicillin in the C.S.F. which was in excess of the minimum *in vitro* level on only two of the nine occasions on which estimations were made (average for nine days, 0.6 unit per ml.)

Smith, Duthie, and Cairns (1946), referring to the dangers of intrathecal treatment with penicillin, point out that excessive dosage (40,000 units and over at a single injection) may produce fits or other severe cerebral reactions when injected into the ventricles, or damage to the cauda equina or gumming of the subarachnoid space when injected by the lumbar route. In McIntosh and Drysdale's (1945) case myoclonic movements of

of Brodie (1945), the penicillin content of the fluid as estimated 20 to 24 hours after the previous intrathecal injection showed 2.0, 2.0, 1.7, 1.0 units, respectively, on Jan. 5-8 (average, 1.7 units). After the dose had been reduced to 25,000 units the daily values were only 0.5, 1.5, 0.25, 1.0, 0.5, 0.2, *nil*, and 0.5 units, respectively, for the period Jan. 11-19 (average, 0.6 unit).

Discussion

In vitro sensitivity tests conducted by Gordon and Zinnemann (1945) showed that with 2.5 units of penicillin per ml. of medium the growths of 16 of 18 meningeal strains of *H. influenzae* were completely inhibited and those of the remaining two strains showed marked inhibition. Accordingly they recommended that it would be necessary to administer penicillin intrathecally (in addition to systemic dosage) so as to obtain a concentration of at least 2.5 units per ml. in the C.S.F. at the outset. "Later, more exact determination of the penicillin sensitivity of the particular *H. influenzae* strain isolated and assay of the penicillin content of the cerebrospinal fluid should serve as a guide to the further dosage to be given." The results obtained in the present case indicate that, even with a dosage of 200,000-500,000 units systemically and 50,000 units intrathecally daily, the penicillin content of the C.S.F. is, at least towards the end of the 24-hour period, not greater than

the face, arms, and lower limbs occurred five minutes after an intrathecal injection of 50,000 units by the lumbar route, and in the present case a fairly severe convulsion took place about three hours after an injection of 50,000 units by the same route. In each of these cases the convulsion occurred after the meningeal infection had been brought under control, as evidenced by sterile cultures, and there seems little doubt that the reactions were directly due to the penicillin. Smith, Duthie, and Cairns (1946) suggest that a single daily intrathecal injection of from 3,000 to 16,000 units is usually adequate to achieve the 0.03 to 0.06 unit per ml. concentration in the C.S.F. necessary for the control of the pneumococcal infections they have encountered. The findings of McAdam *et al.* (1945) accord with the view that the passage of penicillin into the C.S.F. depends on the breakdown by inflammation of the blood-brain barrier. They were unable to demonstrate penicillin in the C.S.F. of any of seven normal subjects who received a dosage of penicillin intramuscularly varying from 100,000 to 500,000 units. In persons suffering from meningitis and post-meningitic encephalitis adequate amounts of penicillin passed into the C.S.F. The results are not expressed in units per ml., but it seems unlikely that the concentrations would have approached the levels required for the control of *H. influenzae* infections.

The findings in the present case suggest that the necessary concentration of penicillin required to inhibit *H. influenzae* may not be maintained unless dosages greater than 25,000 units intrathecally are given, daily.

Summary

A case of *H. influenzae* meningitis in a male child aged 20 months is described. The organism belonged to the Pittman b type, and was sensitive to penicillin in a concentration of 0.7 unit per ml. and insensitive to sulphapyridine, sulphamezathine, sulphadiazine, sulphathiazole, and sulphamerazine. Complete recovery followed prolonged treatment with penicillin.

Estimations of the penicillin content of the C.S.F. showed that concentrations between 1.0 and 2.0 units (average, 1.7 units) were achieved by daily intrathecal injections of 50,000 units and daily systemic injections of 200,000–500,000 units, while concentrations between nil and 1.5 units (average, 0.6 unit) were achieved by daily intrathecal injections of 25,000 units and daily systemic injections of 500,000 units. These findings indicate that intrathecal doses greater than 25,000 units daily may be required to combat *H. influenzae* infections. The dangers associated with this dosage are discussed.

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ACUTE ENTERITIS IN SUBTROPICAL CLIMATES

BY

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Acute enteritis in subtropical climates is the cause of the loss of a great number of working hours, and is therefore a vital consideration in industry as well as to Forces in the field. It is, in fact, responsible for the loss of many times more man-hours than are lost from intestinal diseases such as typhoid or dysentery, which, though much more common than at home, do not normally reach a serious level, except in the event of a definite epidemic.

acute enteritis. The cases included in the statistics for upper respiratory infections were attacks of acute nasal catarrh and fresh cases of sinusitis. Cases of chronic nasal catarrh and chronic sinusitis with acute exacerbations were excluded for the reason stated later. The cases of acute enteritis taken were those of simple diarrhoea—i.e., those with loose frequent motions only, with no obvious blood or mucus. Microscopical examinations were carried out on the faeces of most of these cases, and the typical pathological report was: "Loose stool; no blood, mucus, or pus seen; culture, *B. coli* only"; or "Loose stool; some mucus with an occasional pus cell seen; no blood; culture, *B. coli* only." The occasional case the report of which proved it to be a true dysentery was withdrawn from the statistical figures. Pathological examinations were not carried out on swabs from the nose and nasopharyngeal cavities in either of the two conditions, as such swabs have frequently been investigated by other workers on upper respiratory infections and the common organisms usually present are well known to all.

The incidence of the two diseases in relation to climatic conditions and diet was also studied, and the following observations were apparent.

Climate

(a) Sandstorms and khamsins appeared to cause no increase in the incidence of acute enteritis or in fresh upper respiratory infections. This observation suggests that the pathology of subtropical acute enteritis is more complex than a mere irritation of the bowel. These storms did, however, produce a marked increase in the incidence of acute exacerbations of chronic rhinitis and sinusitis. It was this fact which induced me to exclude such cases from the statistical figures, as it appeared that there must be some slight difference in the pathology involved. Other observers have stated that sandstorms and khamsins have increased the incidence of acute enteritis, but this was certainly not so in this large series of cases.

(b) Climatic conditions conducive to the common cold—such as sudden cold spells after severe heat, a sudden fall in the night temperature after a very hot day—and men who admitted going to sleep on the top of the bed in the open air without pyjamas or bed-clothing, produced not only an increased incidence of acute respiratory infections but a corresponding increase in the number of cases of acute enteritis. This was most pronounced at the beginning of a hot season, when Service dress was changed from the winter uniform to the thin summer khaki drill. The period over which these observations were

Graph showing weekly incidence of upper respiratory infections and acute enteritis in subtropical climates.

My attention was first drawn to the possibility that the cause of these cases of acute enteritis may be in some way related to the causative organism of upper respiratory infections by the fact that, while serving with the Royal Air Force in the Middle East, I kept a graph indicating the weekly incidence of these two conditions. A careful study was made of the incidence of acute enteritis as related to upper respiratory infections, and the possibility of a correlation between these diseases became apparent (see Graph)—a rise in one being accompanied by a corresponding rise in the other, and vice versa.

Over a period of 80 weeks observation was made of this relationship, and during that time the figures involved no fewer than 455 cases of upper respiratory infections and 357 cases of

made included two such occasions, and on each of them the incidence of both conditions showed a marked increase.

Diet

The observations were made at a base station in Egypt where rations arrived regularly, were always plentiful, and were more or less standardized, with only slight variations from week to week. There appeared to be no connexion between the incidence of acute enteritis and any one specific ration issue, except an occasional and obvious epidemic of acute food-poisoning that was traceable to one particular commodity in the week's issues. The recognition of such epidemics was made even easier by the fact that I was medically responsible for three