No reactions to the above were seen. On Sept. 9 a dose of 1 g. of sulphanilamide was given, and caused a pyrexia up to 100° F., with the same pains in the joints. This was confirmed by a similar reaction the next day to a dose of 2 g. On Sept. 12, 13, and 14 single doses of 3 g. each of sulphapyridine, sulphathiazole, and sulphanilic acid respectively were given, with no reactions. At this stage he had to leave hospital urgently for other reasons, and it was not possible to give him any further desensitization.

Discussion

To sum up, this patient developed a highly allergic state during sulphanilamide therapy, so that he reacted to as little as 0.25 g. with a sharp pyrexia. He was also allergic to sulphapyridine in a lesser degree, with a milder reaction to a dose of 1 g. Desensitization took six weeks, but succeeded in working him up to full doses without reaction. Nine months later he apparently had a reaction to further full doses.

Reinvestigation one year after desensitization showed mild reactions to doses of 1 g. and 2 g. of sulphanilamide, but none at all to doses up to 3 g. of other sulphonamides. His allergy had therefore partially returned, but only to a fraction of its original level.

If we may be allowed to theorize on the possible immunological mechanisms underlying this and other drug allergies, the following working hypothesis would fit the facts as they are at present known. In some people sulphonamides stimulate the formation of antibodies. These will then unite with future doses of the drug to cause allergic reactions. Their formation goes on after the drug has been stopped, but gradually tapers off and finally stops. Small desensitizing doses will use up these antibodies and abolish the allergic state. If desensitization is carried out before they cease to be formed, the allergy may partly recur; but if an interval is allowed to elapse before starting desensitization, it may be expected to be permanent. It now remains for this hypothesis to be tested in practice.

Summary

Desensitization to sulphonamides has been a consistent success by the method described.

An opportunity of following up a desensitized case showed that allergy had returned after one year to only a fraction of its former level.

There is theoretical reason to believe that if such cases are left for a time before being desensitized the benefit may be permanent.

I wish to thank the Director of Medical Services, 2 N.Z.E.F., for permission to publish this report.

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PENICILLIN IN CIVILIAN PRACTICE

BY

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Supplies of British-made penicillin have now been available for civilian use for three months, being distributed by the Ministry of Health to the Deans of Medical Schools and, through them, to their own and associated hospitals. An indication of the types of case which have received penicillin from one centre might be considered to be of general interest.

Forty million units of penicillin a month were allotted to this centre, and the administrative heads of 43 hospitals were circularized, but, largely owing to the publicity given in the Press to the fact that supplies were limited, the amount asked for in the first month was only 3 million units; in the second month it rose to 13.5 million units, and in the third month to 22 million units. No request for penicillin was refused in cases in which the infection was caused or was probably caused by a sensitive organism, and systemic treatment when needed was as a rule started before full laboratory investigations had been carried out, although in cases in which local treatment was indicated penicillin was usually withheld until a sensitive organism had been isolated. It was suggested that for systemic treatment the penicillin should be given as a continuous intramuscular drip, using 100,000 units a day dissolved in a pint of

saline and administered into the outer side of the thigh. In each case 5 days' supply was provided.

Conditions Treated

Cases receiving penicillin comprised 15 of osteomyelitis, 5 of staphylococcal pyaemia, 2 of brain abscess, 2 of sulphonamide-resistant gonorrhoea, and 1 case each of staphylococcal orbital cellulitis, staphylococcal jugular phlebitis after mastoidectomy, streptococcal puerperal septicaemia, septic abortion, actinomycosis, pneumococcal meningitis, staphylococcal meningitis, salpingitis of undetermined aetiology not reacting to sulphonamides, generalized staphylococcal pyoderma, post-operative pneumonia of doubtful aetiology not reacting to sulphonamides, staphylococcal pericarditis, suppurative pneumonitis with multiple small abscesses demonstrated in radiographs of the chest (this patient subsequently had a pneumonectomy performed with success), and a case of severe human bite which showed a mixed flora, including *Staph. pyogenes*, *F. fusiformis*, and an anaerobic streptococcus.

Local treatment was employed alone in 50 cases of staphylococcal skin infection, mainly sycosis barbae, 20 cases of staphylococcal infections of the hand, 5 cases of staphylococcal or pneumococcal conjunctivitis, 4 cases of pneumonectomy or lobectomy to prevent post-operative empyema, 4 cases of empyema—one being a case of tuberculous empyema with an associated staphylococcal infection—2 cases of staphylococcal carbuncle, and 1 case each of infected gangrene of the foot, streptococcal arthritis of the shoulder-joint, and generalized peritonitis secondary to a perforated gangrenous appendicitis.

Results

A number of these cases will no doubt be reported in detail by individual clinicians, but certain general conclusions emerge from the series as a whole. The results of penicillin treatment have confirmed the findings of earlier clinical trials: very serious staphylococcal infections, such as meningitis and pyaemia with a high colony count in the blood culture, have been cured, but two patients with multiple lung abscesses died. In very early cases of osteomyelitis it was possible to bring about apparent cure without operative intervention, but in those seen late in the disease penicillin seemed to have disappointingly little effect. It is therefore more than ever necessary for practitioners to get cases of osteomyelitis into hospital at the earliest possible moment. The cases in which the bacteriology was unknown—viz., those of salpingitis, post-operative pneumonia, and septic abortion—all did badly; as would be expected, the result of the administration of penicillin without bacteriological control is likely to prove unsatisfactory. The case of human bite improved rapidly under general and local penicillin treatment. The patient was a negro who had been bitten on the thumb by a negro, and, as Boland (1941) showed, these bites carry a high morbidity rate due to spreading cellulitis. In this case the patient was treated with injections of 20,000 units every three hours and with local penicillin cream; the inflammation remained localized, and she was discharged from hospital in 27 days. One patient complained of considerable local pain when being treated with a continuous intramuscular drip; it was noted that blood concentrations of penicillin were lower than usual, and at necropsy there was evidence of considerable muscle damage.

Systemic Treatment.—The number of patients for whom penicillin was requested for systemic use was the same in the second and the third months in which supplies were available, although in the latter, owing to increasing supplies, greater individual doses were prescribed. It is probable, therefore, that, although spectacularly successful in suitable cases, the number of patients in hospitals needing systemic penicillin is by no means large, and the total quantity which will be used even when supplies are freely purchasable will be smaller than many of us expected.

Local Application.—The general practitioner will find local penicillin treatment of great value in suitable cases of conjunctivitis and staphylococcal skin diseases. For conjunctival instillation the solution of 1,000 units per c.cm. is less painful than the application of penicillin cream, but for sycosis the lotion was less effective than the cream; this was prepared according to the formula of Clark *et al.* (1943), and results from

all hospitals have been excellent. For infections of the hand the instillation of the solution at a concentration of 1,000 units per c.cm. seemed to be more effective than the cream; but dressings have to be done more often, and were more painful. Small boils were successfully aborted in 24 hours by injecting 0.1 c.cm. of a strong solution of 10,000 units per c.cm. into the boil; the treatment, however, is painful, and not more than 0.1 c.cm. should be injected at a time. Local application uses up comparatively small quantities of penicillin.

Comment

Penicillin cream is certain to be used very widely in civilian practice, and the difficulty that practitioners and pharmacists have encountered was largely in the preparation of the sterile lanette wax and castor-oil base, which has to be autoclaved. This can, however, be prepared in bulk, and will keep indefinitely; when needed, the appropriate amount can be melted, cooled to 60° C., and the penicillin solution added to make a final concentration of 200 units per gramme.

It would be a great advantage if supplies of sterile cream base were available from a central store so that pharmacists and practitioners in small hospitals could make up their own penicillin cream as they needed it. A self-sterilizing cream would be very desirable, but until this is available it is essential that practitioners supplying patients with penicillin cream for application at home to a skin lesion should be careful to provide them with precise instructions on how to remove the cream from the jar with reasonably sterile precautions. We have found it satisfactory to tell patients to immerse the blade of a metal-handled table-knife in boiling water for five minutes and then cool it under a freely running cold tap; the cream is removed without delay, and the knife is not replaced in the jar without resterilizing. The tablets of penicillin proved to be easier to handle and more economical in use than the ampoules in which American and Canadian penicillin is dispensed. If in the future British penicillin is to be sold in ampoules it would be of considerable advantage if the glass used were soft enough to be cracked without considerable effort or, better still, if the substance could be dried in a bottle or ampoule with a rubber seal in order that the reconstituted solution could be removed in small quantities with a syringe and needle.

Summary

The types of case in which penicillin is likely to be of value in civilian practice are indicated by the conditions treated in the first three months in which British penicillin was freely available.

The general practitioner will probably use penicillin cream locally more often than any other preparation of the substance.

Sterilized penicillin cream base should be available to practitioners and pharmacists, who will then be quite capable of making up the cream from penicillin tablets.

With adequate instruction patients can carry out treatment of skin conditions with penicillin cream quite successfully in their own homes.

The consumption of penicillin is largely conditioned by the number of cases needing systemic treatment, and this was smaller than was anticipated.

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The third annual report of the North-Eastern Regional Hospitals Advisory Council contains as an appendix a report by Prof. J. C. Spence on the Durham University department of child health at the Royal Victoria Infirmary, Newcastle-upon-Tyne, which opened up in 1943. The main work of the children's clinic is the medical consultation service provided each afternoon in sessions held by experienced children's specialists. In collaboration with the health department of the Newcastle City Council a child welfare clinic was placed in the new department and opened in May last to serve as a training centre for doctors and nurses taking up this work. The main in-patient clinical work of the department is carried out in the children's wards of the Royal Victoria Infirmary, with additional wards in the Babies' Hospital. The teaching of undergraduate students in child health and clinical paediatrics is now established. It is intended that research shall become one of the chief features of the department's activities; already several important lines of research are being pursued.

Medical Memoranda

A Case of Exomphalos complicated by Acute Intestinal Obstruction

The following notes of a case of exomphalos which has come under my care may prove of interest.

CASE REPORT

At noon on Dec. 14, 1943, I was called to a ward where a Munyarwanda woman had just given birth to a male child with exomphalos. The proximal portion of the cord was in the form of a bag covered with translucent amniotic membrane. It was about the size and shape of a large lemon, and through the membrane covering coils of small intestine could easily be made out. The sac was attached to the abdomen by a skin-covered pedicle 1 in. in length and 1 in. in diameter. In all other respects the infant appeared normal and strong. The cord was ligated and severed distal to the sac.

At 3 p.m., three hours after birth, I performed an operation. Naturally the question of the most suitable anaesthetic arose. Langton Hewer states that in acute abdominal conditions in young children the techniques involving local and spinal blocks show a higher mortality than general anaesthesia. Lambert Rogers (1941) operated upon a very severe case of exomphalos 20 minutes after the birth of a baby. In this case the operation was so near the birth that he felt it might be considered a mere prolongation of normal birth trauma, and consequently used no anaesthetic. The child suffered no shock, respiratory distress, or other complication. Three hours was perhaps too long after birth to consider a severe operation as a prolongation of the physiological process of birth. Carman (1941), after operating on a 4-day-old baby for strangulated hernia, reported favourably on ether and oxygen as the anaesthetic agent, after premedication with atropine 1/200 gr. I had no ether or oxygen available. However, Ley (1942), in reporting a successful operation in a case of severe exomphalos on a baby 10 hours old, stressed the value of pure chloroform anaesthesia for abdominal sections in very young children. Accordingly I instructed my comparatively inexperienced native orderly to administer pure chloroform.

A transverse incision was made, as in Mayo's operation for umbilical hernia, through the skin and subcutaneous tissue. The inner layers of the neck of the sac consisted of tense, tight fibrous tissue, and so the superior-anterior surface of the sac itself was incised and the sac opened. It was seen to contain almost the whole of the small intestine, the coils of which were very congested indeed, and I was in doubt whether one of the coils was viable or not. The umbilical vessels were found on the inferior wall of the sac; these were carefully ligated and tied, and the sac was then opened completely. As the opening through the neck was so tight it was obviously impossible to attempt the return of the bowel through it. The fibrous ring was therefore cut. At this stage, the anaesthesia being light, the child strained and almost the rest of the bowel prolapsed. The normal pink colour of the freshly prolapsed coils was in marked contrast to those already seen. There was a distinct compression ring on the two coils which had been constricted in the neck.

Smellie, in Ley's case, was compelled to use "deep chloroform anaesthesia." As it was found impossible to replace the intestines under light anaesthesia I instructed the orderly to push the chloroform. This was done; but very soon, in spite of the constant use of towels wrung out in hot saline, the child became cold and clammy and its breathing very intermittent and gasping, like that of a baby just born with asphyxia neonatorum. I did not think it could survive the rest of the operation. With difficulty the bowel was replaced. The abdomen was closed with one purse-string suture through the peritoneum and fascia, and the skin with interrupted silkworm-gut sutures. The apparently moribund child was returned to the ward wrapped in cotton-wool, surrounded with hot-water bottles, and placed with its head low down. The operation had lasted about 1½ hours.

To my amazement the child rapidly recovered. That night it vomited only once. It almost immediately started taking the breast, passed water normally the first night, and had a normal action of the bowels the second night. With the exception of slight sepsis of the wound, which rapidly responded to fomentations and sulph-anilamide powder, it made a complete and speedy recovery. The weight of the baby was 6 lb.

DISCUSSION

Exomphalos, when a true sac is present, is a very rare condition, with a high mortality rate; but the above case, and more especially those reported by Lambert Rogers (1941) and Ley (1942), show that even marked degrees of this abnormality are viable if submitted to operation at once. Sheldon (1936) states: "Operative treatment is usually required, but, in the absence of intestinal obstruction, conservative treatment, by simply protecting the sac from injury, has been followed by slow natural repair." Intestinal obstruction is always a serious condition, and the younger the patient the more serious it is. Therefore a conservative treatment which awaits the signs of