remain opposed to breast-feeding despite full propaganda should be allowed to bottle-feed their babies and receive instruction in the correct technique for doing this. (3) If breast-feeding is stopped, lactation should be vigorously suppressed under medical supervision. We would suggest that stilboestrol be given in a dosage of 45 mg. three times a day. The breast should be emptied regularly by manual expression and lumpy collections dispersed by gentle centripetal massage. (4) An antibiotic should be given if infection is suspected. If there is no local response after 48 hours the antibiotic should be stopped. Prolonging antibiotic treatment in the absence of a response leads to excessive fibrosis and protraction of the disease. (5) The antibiotic of choice in this series was chloramphenicol.

Summary

One hundred consecutive cases of puerperal breast abscess requiring hospital treatment were studied. It was shown that the duration of the disease has increased compared with earlier reports from the same hospital (Macpherson, 1943). This increase seems to be due to the widespread use of antibiotics.

Very high resistance rates to antibiotics were shown. The failure of antibiotic treatment was largely due to this resistance.

The modification of the pathology of the disease when treated with antibiotics to which the organism is not fully sensitive is discussed.

The importance of adequate suppression of lactation and of avoidance of breast engorgement in the prevention of infection in those who stop breast-feeding is stressed.

Recommendations to reduce the incidence and duration of the disease are made.

This work was made possible by the help and co-operation of Sister Gordon and the medical and nursing staff of the surgical out-patient department of the Royal Infirmary, Edinburgh; Dr. Richard Scott and his colleagues of the General Practice Teaching Unit of Edinburgh University; and Dr. J. H. Bowie and Dr. J. C. Gould, who performed the bacteriological examinations. We also thank Mr. D. McIntosh and Mr. A. I. S. Macpherson for permission to study cases in their charge.

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Medical Memoranda

Xanthocillin Cream for Local Treatment

The type of dermatological case for which local antibacterial treatment is required has altered considerably in recent years. Impetigo contagiosa and other relatively straightforward superficial infections of the skin are now quite uncommon in the hospital clinic. The eczematous eruptions and cheiropompholyx with gross pyogenic secondary infection often combine lymphangitis, cellulitis, lymphadenopathy, and some degree of systemic disturbance, and in these cases a systemic antibiotic is usually indicated; local treatment then aims at drainage of pus and anti-eczematous rather than antibacterial measures.

There remains a third group of very difficult conditions comprising some types of seborrhoeic dermatitis, particularly those with a tendency to flexural distribution, to weeping, and to superficial folliculitis; intertrigo, particularly with weeping and the development of fissures in the flexures; and varicose (stasis) dermatitis in which infection often plays an important though not the primary part. The role of bacterial infection in these disorders is difficult to assess, but antibacterial applications often produce striking improvement. Indeed, it is in this type of case that local antibiotic treatment is most used at the present time.

Cultures made from the affected surfaces yield pathogens the antibiotic sensitivities of which can be determined. The application of the appropriate antibiotic will frequently be followed by improvement, but all too often the condition relapses after a week or two. Further cultures now reveal a fresh pathogen, this time resistant to the antibiotic which has been used. Because of this the choice of antibiotic according to the results of cultures does not always give the best therapeutic results although it seems logical. Indeed, the use of the "wrong" antibiotic sometimes gives better clinical results than the "right" one.

It is common for these eruptions to become very much worse when a new treatment is applied. This aggravation is sometimes due to allergic hypersensitivity to a fresh antibiotic, but more often it appears to be a non-specific intolerance which at another time, in the same patient, would not occur. This unpredictable non-specific intolerance of treatment makes the management of these cases so much the more difficult.

A clinical trial of a new antibiotic cream therefore presents considerable difficulties. The cream has to be used chiefly in cases of the third group, mentioned above, where the therapeutic results are seldom immediate or clear-cut. Individual cases vary a great deal and may be difficult to classify, so that the selection of cases for treatment is difficult and the arrangement of controls even more so. Presumably, in order to overcome the difficulty of repeated superinfection, the antibiotic should have as wide a range of action as possible with the least tendency to allow the development of resistant strains. It should also have a low sensitizing index—a property which can be expected to emerge only after use in a considerable number of cases; the likelihood of sensitizing 1 to 2% of patients treated would be a serious drawback, and it may be necessary to treat 100 to 200 people before this can be appreciated.

XANTHOCILLIN

Xanthocillin is an antibiotic derived from *Penicillium notatum* (Rothe, 1954) and has been isolated in the form of yellow crystals which contain two components, x and y, in the proportion of about 4:1. The chemical properties of the two components are very similar: they are sparingly soluble in water, alcohol, ether, and other common solvents, and stable in normal conditions.

Rothe reported that xanthocillin was not suitable for systemic therapy because of its toxic properties and poor absorption, and so its use is limited to topical application. *In vitro* tests have shown that most of the common Gram-positive and Gram-negative pathogens, including *Proteus* and *Pseudomonas pyocyanea,* are sensitive to xanthocillin, and there is also some suppressive action against *Mycobacterium*

tuberculosis and certain pathogenic fungi and yeasts. Bacterial resistance to the antibiotic develops very slowly and no cross-resistance with other antibiotics has been reported. The sensitizing power of xanthocillin is said to be low.

The present trial with xanthocillin cream was carried out over a period of some months on a group of in-patients with a variety of eczematous and intertriginous eruptions, in all of which bacterial infection was thought to be playing a part. Most of these patients had already been treated with other antibiotics or with antiseptic applications; in some cases the eruption was symmetrical and permitted simultaneous comparison to be made between xanthocillin and other methods in routine use; these included iodochlorhydroxyquinoline, neomycin, and various other antibiotics.

At the same time xanthocillin cream was applied in the form of patch tests for 48 hours to the normal skin of 20 other subjects.

RESULTS

The patch tests carried out on normal skin were all negative and thus failed to show any primary irritant or toxic property in the cream.

When applied to the inflamed and eczematous skin there was no case in which aggravation of the eruption appeared to result. This in itself is encouraging, for the patients being treated were those in whom non-specific aggravation from treatment is rather often seen.

As to the therapeutic efficiency of the cream it is not possible to give more than a clinical impression. There were some cases in which the cream was of no apparent benefit; there were some in which rapid and striking improvement was produced after other antibiotics had failed. Generally speaking, the impression was that xanthocillin cream produced results which were on a par with other treatments with which it could be compared.

One may sum up these results by saying that xanthocillin did not show irritant or other objectionable properties and that these preliminary results warrant a more extensive trial. If the antibiotic action which has been demonstrated *in vitro* is exerted also on the surface of the skin, xanthocillin cream should prove to be a very useful local application in suitable cases.

I am indebted to Dr. C. N. Brown, of the Distillers Company, for supplies of xanthocillin cream and for information regarding xanthocillin.

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Preliminary Communications

The Physiopathology of Acute Haemolytic Shock

This paper summarizes the results and conclusions derived from the observation of a number of cases of transfusion reaction in patients, and from about 1,000 experiments on animals and on ourselves.

Distilled water was injected intravenously into dogs (5 to 10 ml./kg. body weight) and into ourselves and patients suffering from anaemia (100 to 150 ml.), in all cases with no detectable effects. Intravenous reinjection of our own haemolysed blood (100 to 130 ml.) and haemolysed autotransfusion into dogs (2 ml./kg.) also had no detectable effect. Haemolysed blood of group O also can be safely injected into recipients of any other group.

Haemolysed blood of group A can be transfused into individuals of any other blood group, provided it is freed from its stroma; in experiments in dogs no haemolytic shock was found to occur after the transfusion of heterospecific blood, if this had been previously freed of stroma. Stroma itself, on the other hand, does produce shock. Experiments on ourselves showed that the injection of blood of a different group, containing stroma, causes haemolytic shock, while the same blood freed of stroma has no effect.

We consider haemolytic shock to be closely related to anaphylactic shock. Our investigations in this connexion gave the following results:—In both we observed the same serological effects: diminution of complement, of haemolysins, of agglutinin titre, and of bactericidal properties. The haematological effects were also identical: primary leucopenia followed by leucocytosis, granulocytopenia followed by granulocytosis, lowered sedimentation rate of the red corpuscles, lowered Sabrarés index, polycythaemia, eosinopenia, thrombocytopenia, and disturbance of coagulation. The biochemical changes, too, were the same: alteration of the refractive index, lowering of the polarographic wave, increase of the serum potassium level, fall in calcium level and alkali reserve, and diminished intestinal absorption of glucose. In some of the experiments hyperglycaemia was noted, and a fall in the cholinesterase level.

One attack of haemolytic shock affords protection against a subsequent one, and prophylactic histamine treatment has a similar effect. Physostigmine, on the other hand, aggravates the shock.

The consequences of haemolytic shock are the same as those of the anaphylactic variety: biliary obstruction, contraction of the peripheral capillaries, and an increase of lymph flow in the thoracic duct. The muscle fatigue which Eppinger observed in histamine shock is also to be seen in haemolytic shock.

The simultaneous injection into the carotid sinus of blood from another person and of the recipient's own plasma produces shock.

We are able to bring about conditioned reflexes in haemolytic shock as well as in histamine shock. In the former, both the pressor and the depressor reflexes are diminished. The heart damage observed is not the result solely of disturbance of the peripheral circulation, but also occurs in Starling's heart–lung preparation, even when an adequate venous in-flow has been ensured.

Drugs effective in anaphylactic shock (antazoline, calcium, procaine, nicotinamide, chlorpromazine) also alleviate haemolytic shock.

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