NEOMYCIN IN PYOGENIC SKIN DISEASES

BY

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Pyogenic infections are the commonest cause of skin disease, and cure of the acute case can be simple, but even impetigo, when mishandled, may persist for many weeks. Although the local use of antibiotics has considerably shortened the duration of these illnesses, it presents two disadvantages which some have thought contraindicate their use: (1) the danger of sensitizing the patient and thus preventing future systemic treatment with the antibiotic in what might be a serious illness; and (2) the encouragement of antibiotic-resistant organisms.

A stable and effective antibiotic which is not used systemically, which causes little cutaneous reaction, and which has a low incidence of bacterial resistance would overcome the most valid objections to local antibiotic therapy. Neomycin appears to fulfil these requirements in infections with *Staphylococcus pyogenes*.

Neomycin was discovered by Waksman and Lechevalier in 1949. It is produced by a strain of streptomycetes related to *Streptomyces fradiae*. It is water-soluble and thermostable, and maintains its effectiveness in practically any vehicle, including both acid and alkaline aqueous solutions. The drug is bactericidal *in vitro* against a wide variety of Gram-negative and Gram-positive organisms. Toxic effects causing kidney damage and deafness have prevented the parenteral administration of the drug, and its present use is limited to oral administration as an intestinal antiseptic and to local application. The effectiveness of neomycin as a local application in pyogenic skin eruptions has been reported in America (Kile *et al.*, 1950, 1952; Livingood *et al.*, 1952; Kimberly, 1952).

Present Investigation

A series of 93 cases were treated. They included: impetigo, 48; sycosis barbae, 18; ecthyma, 10; infected eczema and dermatitis, 8; furunculosis, 5; infective eczematoid dermatitis, 3; and blepharitis, 1. In none of these cases was irritation or sensitization of the skin caused by the ointment.

Neomycin was used in a concentration of 5 mg. per g. in an ointment base consisting of

White mineral oil	..	..	25%
Wool fat	..	..	20%
White petrolatum	..	..	54.4%

For purposes of comparison of bases, the same concentration was used in a water-miscible base:

Emulsifying wax, B.P.	..	..	20%
White petrolatum	..	..	20%
Phenoxyethanol	..	..	2%
Borax	..	..	0.6%
Boric acid crystals	..	..	1.2%
Water	..	..	to 100%

The two bases were used on the impetigo cases, half the series being treated with the water-miscible base. In contrast to the experience of Forbes (1952), no appreciable difference in the clinical results was found.

The patients were instructed to apply the ointments three times daily, cleaning the affected areas and removing crusts with liquid paraffin. In the few cases of furunculosis treated the ointment was also applied once daily into the nostrils.

Bacteriology

The organisms were cultured from each case and their sensitivity to penicillin, streptomycin, chloramphenicol, aureomycin, and neomycin was estimated. From practical experience it was found that a *Staph. pyogenes* which was insensitive to less than 25 units of penicillin per ml. or to 50 µg. of chloramphenicol or aureomycin could be regarded as resistant to the respective drug as a local application.

Staph. pyogenes was found in 91 cases—46 were penicillin-resistant, 2 aureomycin-resistant, 18 chloramphenicol-resistant, and 1 was resistant to less than 16 µg. of neomycin. All other staphylococci were sensitive to less than 4 µg. of neomycin; in 70 cases the staphylococci were sensitive to less than 0.015 µg. of neomycin. A haemolytic streptococcus was found alone in two cases and in association with *Staph. pyogenes* in 20 cases. The only other organism isolated was *Pseudomonas pyocyanea* in one case of impetigo. This was resistant to penicillin, aureomycin, and chloramphenicol, but sensitive to streptomycin and neomycin.

In the 48 cases of impetigo a *Staph. pyogenes* was found alone in 37, a haemolytic streptococcus in association with *Staph. pyogenes* in 10, and a haemolytic streptococcus alone in 1. The staphylococci were resistant to penicillin in 34 cases and to chloramphenicol in 11.

The 10 cases of ecthyma yielded a *Staph. pyogenes* alone in three cases; in the remaining seven the infection was a mixture of *Staph. pyogenes* and a haemolytic streptococcus. The staphylococci were resistant to penicillin in one case and to chloramphenicol in two cases.

The 18 cases of sycosis barbae yielded pure growths of *Staph. pyogenes* alone. The staphylococci were resistant to penicillin in eight cases, to aureomycin in two, and to chloramphenicol in five.

The miscellany of eight cases of infected eczema, five cases of furunculosis, three cases of infective eczematoid dermatitis, and one case of blepharitis yielded a haemolytic streptococcus alone in one case, *Staph. pyogenes* in 14, and a combination of these organisms in two cases. Penicillin-resistant staphylococci numbered three and the organisms were sensitive to the other antibiotics.

Results

Impetigo.—Three cases were treated with base alone as a control; as expected, the impetigo spread rapidly. Of the remaining 45 cases treated with neomycin, 27 healed in less than one week, 11 in less than two weeks, and 7 took longer than two weeks, but were quite healed in three weeks. There were no failures. The cases varied in severity and duration. Twenty-one had resisted previous treatments by their own practitioners for over three weeks. Twenty-five cases were definitely known to have been treated with penicillin cream and six cases with chloramphenicol without response.

Sycosis Barbae.—The 18 cases are classified according to the severity and chronicity of the condition, those which had lasted less than nine months being referred to as folliculitis barbae. Eight cases of folliculitis barbae were seen whose duration varied from one week to eight months. Four of these cases are known to have been treated with penicillin cream, two with chloramphenicol cream, and one with aureomycin cream, all without success. On treatment with neomycin ointment four cases healed completely—two in less than one week, and two in a fortnight—and have remained healed for four months. One severe case improved to the extent of having only a few pustules left, and there was no response in three cases. The 10 cases of sycosis barbae varied in duration from two to 31 years. Six cases are known to have been treated with penicillin, five with chloramphenicol cream, and five with aureomycin cream, without cure. Four cases responded well to neomycin ointment, healing in periods ranging from two to four weeks, two of them having slight residual erythema but no pustulation while using the ointment. Two further cases healed in a fortnight, but relapsed

two and four months later while still using the ointment, although the organisms remained sensitive to the antibiotic. Two cases were much improved and two showed no response.

Ecthyma.—Of the 10 cases of pyoderma and ecthyma treated, 3 healed in less than one week; these were all cases in which *Staph. pyogenes* alone was cultured. The remaining seven cases had a mixed infection of staphylococci and streptococci, two healing in less than a fortnight and the other five showing no response.

Miscellaneous.—Eight cases of infected skin conditions, including seborrhoeic dermatitis, contact dermatitis, and eczema, were all treated without any sensitization reactions. Three cases healed in less than one week, four in two to three weeks, and one case showed no response. One case of chronic blepharitis healed in three days. Three cases of retro-auricular infective eczematoid dermatitis healed in less than two weeks. The five cases of furunculosis had resisted a variety of treatments for this condition, and only one case ceased to have boils on treatment with neomycin ointment.

Comment

In the treatment of impetigo contagiosa, neomycin ointment is effective and rapid in action. In view of the advantages of using neomycin as a solely local antibiotic it might with advantage be adopted as a routine treatment for this condition.

In this series 60% of cases of impetigo cleared in less than a week, and many of these took only three to four days. Forbes (1952) treated 67 cases of impetigo with neomycin, 62 clearing in less than a week; he remarks that the type of patient was of high standard, most of them being university students and able to follow instructions. It might be assumed that there is some difference in this capacity between American college students and the industrial population of Sheffield. In the treatment of impetigo, chloramphenicol cream (Newman and Feldman, 1951), aureomycin ointment (Solomons, 1951), and bacitracin (Miller *et al.*, 1949) all give comparable results, most cases healing in less than a week, though Solomons found two cases aggravated by aureomycin cream.

In the treatment of sycosis barbae, aureomycin cream seems to have given the best results. Solomons treated 22 cases, all of which responded, only three being left with a few scattered pustules. Chloramphenicol cream (Newman and Feldman, 1951) cured only one case in five, improved two cases, and gave no result in two. Bacitracin (Miller *et al.*, 1949) cured 5 of 16 cases, the other 11 showing no response. Neomycin ointment in this series cured eight cases, and improved five; there was no response in five. Neomycin therefore seems to be superior to all antibiotics except aureomycin in the treatment of this condition.

Prolonged local application of any antibiotic encourages the growth of resistant organisms, and in this series the only aureomycin-resistant staphylococci were found in two cases of sycosis barbae. The routine use of a purely local antibiotic would therefore seem desirable as the first line of attack in the treatment of this condition.

As a local application to infected skin conditions and infective eczematoid dermatitis, neomycin showed no tendency to irritate the skin. Over a large number of cases this harmlessness is unlikely to continue, but Kile *et al.* (1952) applied neomycin to 869 cases and obtained only one sensitivity reaction. In the same paper the authors remark that some patients with haemolytic streptococcal infections did not respond well to neomycin. This was also found in this series in the cases of ecthyma, though impetigo with streptococci responded well. In the cases of sycosis barbae which did not respond or which relapsed the organisms had not developed resistance to the drug. This state is unlikely to last, although it has been the experience of all other investigators of neomycin. Nevertheless, antibiotic therapy is literally becoming a process of hurrying to use the new drug before it ceases to cure.

Summary

Ninety-three cases of pyogenic skin disease were investigated bacteriologically; *Staphylococcus pyogenes* was isolated and found to be resistant to penicillin in 46 cases, to chloramphenicol in 18 cases, and to aureomycin in 2 cases. None were resistant to neomycin.

The cases were treated with neomycin ointment in a strength of 5 mg. per g. In the treatment of impetigo the drug gave results comparable to those of aureomycin, chloramphenicol, and bacitracin. In sycosis barbae the results were superior to those of all other antibiotics except aureomycin. In other skin conditions, with the exception of the deeper infections with haemolytic streptococci, infection was controlled and sensitization reactions were not encountered.

Neomycin ointment is suggested as a routine treatment for impetigo and as the first line of attack in sycosis barbae.

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REFERENCES

- Forbes, M. A. (1952). *Sth. med. J.*, **45**, 235.
Kile, R. L., Rockwell, E. M., and Schwarz, J. (1952). *J. Amer. med. Ass.*, **148**, 339.
— Welsh, A. L., and McAfee, G. D. (1950). *Arch. Derm. Syph., Chicago*, **62**, 911.
Kimberly, L. W. (1952). *J. Iowa St. med. Soc.*, **42**, 221.
Livingood, C. S., Nilasena, S., King, W. C., Stevenson, R. A., and Mullins, J. F. (1952). *J. Amer. med. Ass.*, **148**, 334.
Miller, J. L., Slatkin, M. H., and Johnson, B. A. (1949). *Arch. Derm. Syph., Chicago*, **60**, 106.
Newman, B. A., and Feldman, F. F. (1951). *Ibid.*, **64**, 212.
Solomons, B. (1951). *British Medical Journal*, **2**, 525.
Waksman, S. A., and Lechevalier, H. A. (1949). *Science*, **109**, 305.

STORAGE OF TESTICULAR TISSUE AT VERY LOW TEMPERATURES

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The discovery that glycerol has the property of protecting the spermatozoa of certain species (Polge, Smith, and Parkes, 1949; Smith and Polge, 1950) and also red blood cells (Smith, 1950; Sloviter, 1951a, 1951b) against the otherwise fatal effects of freezing and thawing was extended by Smith and Parkes (1951) to ovarian tissue. The latter work was recently recorded in more detail (Parkes and Smith, 1953), and it is clear that rat ovarian tissue, soaked in glycerol-containing media and subsequently frozen slowly and stored in liquid air, suffers only slight loss of its capacity to form an endocrinologically active graft. Moreover, the loss is not increased by prolonging very greatly the period of storage.

Method

Analogous observations have now been made on the preservation and grafting of rat testis tissue. The testes were taken from male rats 7 to 9 days old, at which age the organ is firm and easy to handle. The tunica was slit and the contents were slightly teased out. The capacity of such preparations to form functional grafts, after treat-