that failure to respond to treatment was usually associated with the presence of insensitive strains of gonococci. It seems unlikely that these results with the higher doses of penicillin can be much improved, though the use of probenecid in divided doses rather than a single dose might repay study.

The increasing numbers of patients who are sensitive to penicillin has also emphasized the need for alternative methods of treatment. Streptomycin, at one time the drug of second choice, is no longer effective, because many strains of gonococci are now truly resistant to it, particularly those which are insensitive to penicillin. Tetracycline in a dosage of 0.5 g. four times daily for two days is usually effective; this method has the disadvantage that the patient has to be relied on to take the treatment at regular intervals. Strains with diminished sensitivity to tetracycline in vitro have also been encountered. Kanamycin in a single injection of 2 g. has given good results in the treatment of gonorrhoea in males. A. E. Wilkinson, J. W. Race, and F. R. Curtis[5] found only 2–3% of failures at this dosage and noted that the sensitivity in vitro of 212 strains of gonococci tested all fell within a narrow range from 0.39 to 3.125 μg./ml. W. F. Hooton and C. S. Nicol[6] found a failure rate of 3.6% in 138 female patients who were observed for at least one month after treatment with 2.0 g. kanamycin.

Combined treatment with antimicrobial drugs to discourage the emergence of resistant strains is an established procedure in other infections, and L. P. Garrod and P. M. Waterworth[7] have investigated the response of the gonococcus in vitro to three combinations. Penicillin and kanamycin were found to show a slightly additive effect on some strains, others being indifferent. Unfortunately this combination of two bactericidal drugs, which might be expected to act synergically, does not seem promising. Kanamycin and sulphafurazole have an additive effect which might permit reduction in the dose of kanamycin, an advantage in view of its potential ototoxicity, though this complication was not seen in the two series cited above. The combination of trimethoprim and sulphafurazole was found to produce a strongly synergic effect in tests of both bacteriostatic and bactericidal effect. These observations complement the results of a clinical trial of trimethoprim and Sulphatriad (sulphadiazine, sulphamerazine, and sulphathiazole) or sulphamethoxazole in the treatment of gonorrhoea in males reported by G. W. Csonka and G. J. Knight.[8] This gave a 7–11% failure rate, which was lower than that found after 1.2 mega units of penicillin during the same period. It was also found that 14 out of 15 patients who failed to respond to penicillin were cured by the trimethoprim–Sulphatriad combination.

No form of treatment can be guaranteed to give a 100% cure rate at present. In Great Britain a single dose of 1.2 mega units of aqueous procaine penicillin will usually be found effective. It should be increased to 2.4 mega units in cases with complications or if the rectum is infected, particularly in women—and this occurs much more frequently than is generally appreciated. If treatment fails with this dosage, patients can receive further treatment with 2.4 mega units of penicillin plus probenecid, or with kanamycin. There is no evidence at present that the upper level of resistance to penicillin among strains of gonococci being isolated in this country exceeds that first found in 1957. Nevertheless, it is desirable that periodical surveys of the sensitivity of randomly isolated strains of gonococci to penicillin and other antibiotics should be carried out to give an early warning of changes in sensitivity.

Orf

A specific poxvirus infection of sheep, orf sometimes affects man also. Shepherds and veterinary surgeons are more familiar with the disease than medical men, and in the patient who is not obviously and occupationally exposed to the infection it is often unrecognized.

Ecthyma contagiosum, to give its Latin name, is a disease of sheep in all continents. Most cases occur in spring and early summer. Vesicles, which soon become crusted, involve the sheep's hairless or relatively hairless gums, lips, and groins, and heal in three to four weeks. The gain in weight of infected lambs may be temporarily reduced, but the disease is of no great economic importance. It is often stated, but without proof, that lambs are infected from crusts which have persisted over winter in the pastures; most are infected from other lambs and from older sheep. Most human infections are contracted directly from lambs and are thus chiefly in shepherds, veterinary surgeons, and children. However, carcasses are an important source of infection, and cases have been reported in porters and butchers in Smithfield Market.[1] In one department of dermatology recent patients with orf have included a kennel-maid who prepared sheep's heads for her charges, a student who spent his vacation on a farm, a housewife, and a doctor's young daughter who enjoyed feeding the lambs on a neighbour's farm. The diagnosis must be suspected on the clinical appearance and confirmed tentatively by the history and irrefutably by virological investigation.

The clinical features of the infection are strikingly similar in man and in the sheep, but in man the lesions are commonly solitary or few, and are on hands, forearms, or face, while in the sheep they are usually multiple. Our knowledge of the course of the infection has recently been increased by the detailed studies of spontaneous and inoculated lesions by U. W. Leavell and colleagues.[2] After an incubation period of one to seven days a red macule appears and gradually becomes raised. During the second week the red centre is encircled by a white ring beyond which is a further ring of erythema. By the third week there is a nodule often 2 cm. or more in diameter, with a moist red surface. In the fourth week the lesion becomes dry and crusted, and it heals during the following two weeks. Lymphangitis and lymphadenitis are sometimes present, but they are seldom marked. There may be fever during the second and third weeks, but it is usually insignificant. A maculopapular eruption on the trunk, seldom mentioned in the literature, is present during the second week in many cases, though the patient is often unaware of it. Rarely the eruption is a florid erythema multiforme on the extensor aspects of the limbs.

A clinical diagnosis is not difficult if the possibility is considered and the patient is asked about contact with sheep, living or dead. The virus may be isolated in tissue culture but may be rapidly identified by electron microscopy of crusts or biopsy material.[3] In differential diagnosis poxvirus infections of other species may need to be excluded. In these days of air travel Britain's first case of camel pox may be waiting in any doctor's surgery.

[1] Hodgson-Jones, I. S., *Brit. med. J.*, 1951, **1**, 795.
[2] Leavell, U. W., McNamara, M. J., Muelling, R., Talbert, W. M., Rucker, R. C., and Dalton, A. J., *J. Amer. med. Ass.* 1968, **204**, 657.
[3] Nagington, J., *Brit. med. J.*, 1964, **2**, 1499.