

Oxytetracycline ("terramycin"). This gives slightly higher blood levels and has a longer half-life than chlortetracycline: it is about 20% bound to protein. It is more active than chlortetracycline or tetracycline against *Pseudomonas pyocyanea*.

Tetracycline ("achromycin," "tetracyclin"). When introduced in 1953 this drug was said to be better absorbed than either of its predecessors and to attain better levels in the cerebrospinal fluid, but much was also made of the claim that it caused less gastro-intestinal disturbance than either of them. A tendency towards lower dosage may have contributed to this difference. Protein binding and half-life are similar to oxytetracycline. It is not more active than either of its predecessors against any bacteria except perhaps *Proteus*.

Demethylchlortetracycline ("ledermycin"). This is the most chemically stable of these compounds. It is absorbed like tetracycline, but excreted much more slowly, giving a half-life exceeding that of any other tetracycline by several hours. It is about 40% bound to protein. It has about twice the activity of tetracycline against most bacterial species; hence a dose of 150 mg. is considered at least equivalent to 250 mg. of other tetracyclines. There is some suspicion that larger doses may cause more gastro-intestinal disturbances.

It should be understood that the differences in antibacterial activity referred to are minor in degree—two-fold or occasionally fourfold. There are no species sensitive to one tetracycline and insensitive to others. Moreover, an organism becoming resistant to one is resistant to all. These differences, and those in pharmacological behaviour—the prolonged action of demethylchlortetracycline possibly excepted—are thus of a minor character, and the choice of a tetracycline is usually based on personal preference and past experience rather than on any logical process of matching the drug with the precise requirements of a particular infection and patient.

Among other tetracyclines not so far available in this country are two intended particularly for parenteral injection. Parenteral forms of tetracycline and chlor- and oxytetracycline are available, but their low solubility presents difficulties. Pyrrolidinomethyl-tetracycline ("reverin") and tetracycline-L-methylene-lysine ("tetralysal") are soluble at >1 in 1, and intravenous or intramuscular injection of the former has been shown to produce very high blood levels. This compound is not exempt from the danger of causing staphylococcal enterocolitis in surgical patients, its action in the bowel evidently resulting from biliary excretion.

Therapeutic Indications

These are much more numerous than for any other antibiotic. To mention some of the less familiar, tetracyclines provide the standard treatment for *brucellosis* and *tularaemia*, and for *relapsing fever*. They have been used successfully in various forms of *typhus*, in *leptospiroses*, *lymphogranuloma inguinale*, and *granuloma venereum*. They have been shown to be effective in *anthrax* and *actinomycosis*, for which they afford an alternative to penicillin. Their use has been advocated for penicillin-resistant *gonorrhoea*, and for *syphilis* when penicillin cannot be used. They should theoretically be effective in the prophylaxis of *gas gangrene*, although adequate clinical proof of this is lacking, and penicillin is likely to be preferred. They even have some action

in *tuberculosis*, and rank as drugs of second or third choice when the bacillus is resistant to others.

The following are more commonplace indications.

Respiratory Tract

Tetracyclines are one alternative to penicillin for treating acute throat infections or their complications (otitis media, etc.), but since tetracycline-resistant Group A streptococci are now being encountered this involves some risk of failure. *Pneumonia*, particularly of unknown aetiology, has always been considered a strong indication, since all bacterial and other causes are sensitive. The prevention of pneumonia or of any bacterial complication of an acute virus infection such as *influenza* accounts for a large consumption, some of which may be effective. Owing to the unsuitability of chloramphenicol for prolonged administration, tetracyclines are standard treatment for *chronic bronchitis*: whether they should be given continuously throughout the winter or only for exacerbations is an open question. An average dose for continuous treatment is 250 mg. three times a day.

Alimentary Tract

Tetracyclines are ineffective in enteric fever. They have been used in acute enteritis and in both bacillary and amoebic dysentery, but their value in relation to other drugs is difficult to assess. *Peritonitis* due to a perforated viscus is a strong indication, almost all the numerous bacteria concerned being sensitive: the risk of staphylococcal enterocolitis must be borne in mind.

Among other uses may be mentioned **urinary tract infections** and **sepsis** of various kinds, superficial forms of which may be treated by local application. Two general warnings about these miscellaneous uses are appropriate. Resistance to the tetracyclines is common in staphylococci and coliform bacilli, and laboratory confirmation of their utility in a given case is therefore advisable. Secondly, in ordinary concentrations they are only bacteriostatic: where bactericidal action is imperative, as in endocarditis, they are contraindicated, however sensitive the organism may appear in the usual test.

Correction.—It was stated in "To-day's Drugs" (May 4, p. 1214) that no satisfactory preparations of novobiocin were available for intramuscular or intravenous injection. There is in fact a parenteral preparation of this drug under the name of "albamylin parenteral." It should be noted that this injection is apt to cause pain and the parenteral route is indicated only where oral therapy is impracticable.

W.H.O. is establishing two new schools of advanced nursing education—in Edinburgh, Scotland, and Lyons, France. In Edinburgh the school will be part of the University, and a consultant from W.H.O. will work with the staff of the Nursing Studies Unit at the University in planning the courses. At present, many European nurses must go to the United States or Canada for advanced training. With the establishment of these new schools more European nurses will have an opportunity for advanced study. The schools are not intended primarily for Europeans, but are open to nurses of all countries, provided they can qualify for entrance. It is expected that many nationalities will be represented, particularly from the African and Asian countries, when the schools are inaugurated.