circulating. This would account for the tendency to the generalized form of sensitivity reaction. All the cases from the literature cited in this paper showed significant tissue damage related to general reactions.

REFERENCES

- Burckhardt, W. (1948). *Dermatologica, Basel*, 96, 280.
 Clark, T. W. (1943). *J. Amer. med. Ass.*, 123, 958.
 Davidson, T. C. (1943). *Curr. Res. Anesth.*, 22, 52.
 Epstein, S. (1939). *J. Invest. Derna.*, 2, 43.
 Hewer, C. L. (1939). *Recent Advances in Anaesthesia*. London.
 Hunter, A. R. (1943). *Lancet*, 1, 46.
 Knauss, A. C. (1946). *Anesthesiology*, 7, 84.
 Lundy, J. S. (1942). *Clinical Anaesthesia*, p. 542. Saunders, Philadelphia.
 Moore, P. H. (1946). *British Medical Journal*, 2, 340.
 Moore, R. H. (1946). *Ibid.*, 2, 209.
 Park, R. G., and Platts, W. M. (1942). *Ibid.*, 2, 308.
 Peterkin, G. A. G. (1945). *Ibid.*, 2, 1.
 — (1946). *Ibid.*, 2, 52.
 Rimington, C., and Hemmings, A. W. (1938). *Lancet*, 1, 770.
 Stryker, G. V. (1939). *J. Mo. med. Ass.*, 36, 484.
 Urbach and Godlieb (1946). *Allergy*.
 Warren, M. D. (1946). *British Medical Journal*, 2, 172.
 Watkinson, G., and Hillis, B. R. (1947). *Ibid.*, 2, 609.

TERRAMYCIN IN INFECTIONS IN INFANTS AND CHILDREN

BY

B. WOLMAN, M.D., M.R.C.P., D.C.H.

AND

A. HOLZEL, M.D., D.C.H.

(From the Department of Child Health, University of Manchester)

"Terramycin" is a new antibiotic obtained from *Streptomyces rimosus*, an actinomycete isolated from the soil (Finlay *et al.*, 1950). Its physical and chemical properties have been studied by Regna and Solomons (1950), and it has been shown to be a stable, amphoteric substance of high potency (Linsell and Fletcher, 1950). Preliminary experimental studies (Hobby *et al.*, 1950) have shown that it is active both *in vitro* and *in vivo* against a wide variety of pathogenic organisms. It is effective against Gram-positive and Gram-negative bacteria, spirochaetes, rickettsiae, and certain of the larger viruses, yet is distinguished by its low toxicity (Finlay *et al.*, 1950; King *et al.*, 1950; Herrell *et al.*, 1950).

Terramycin is supplied in 50, 100, and 250-mg. capsules of the crystalline hydrochloride salt, and as a yellow crystalline powder which dissolves easily in a specially prepared cherry-mint-flavoured liquid to make an elixir ("terrabon") suitable for administration to infants and children. A special solution containing 25 mg. of terramycin as the crystalline hydrochloride, made up with 62.5 mg. of sodium chloride and 25 mg. of sodium borate, dissolved in 5 ml. of distilled water, is available for ophthalmic use.

This report is based on a study of the use of terramycin in various infections of infancy and early childhood. Sixty-six children were treated with this drug, no other therapy being given during its administration. The dosage was 50 mg. per lb. (450 g.) of body weight per day, the elixir being given by mouth at six-hourly intervals for a period of seven days to each of 54 patients. It was found to be extremely palatable, and no difficulties were encountered in its administration. In fact, ward sisters preferred its use to other antibiotics because it was taken so readily by infants and children. Routine white-cell estimations during the course of treatment did not show any depressant action on the total

count or on the polymorphonuclear elements. The special ophthalmic solution was used for the treatment of 12 newborn babies, and was instilled into the eyes in the following manner: one drop every minute for five minutes, followed by one drop every two minutes for ten minutes, the whole procedure being repeated three times a day.

Terramycin was used for the treatment of pneumonia (35 cases), upper respiratory tract infections (10 cases), tonsillitis (6 cases), pyuria (3 cases), and purulent conjunctivitis (12 cases).

Pneumonia

The 35 cases of pneumonia, all confirmed radiologically, showed the following age distribution:

0-5 months	..	..	6 cases	2 years	..	..	6 cases
6-11 "	..	..	7 "	3 "	..	..	5 "
1 year	..	..	11 "				

Nasopharyngeal swabs were cultured in every case, the predominating organism being shown in Table I.

TABLE I.—Predominating Organism on Culture of Nasopharyngeal Swab

Organism	No. of Cases
<i>Streptococcus viridans</i>	7
<i>Streptococcus haemolyticus</i>	5
<i>Pneumococci</i>	6
<i>Staphylococcus pyogenes</i>	2
<i>Haemophilus influenzae</i>	1
Friedländer's bacillus	1
Normal flora—no predominating organisms	13

In 23 cases the temperature fell to normal within 24 hours, in seven cases fever disappeared in 48 hours, and in one case in 72 hours. Improvement in appetite, colour, and general condition coincided with the settling of the temperature. Radiological clearing of the lungs usually took a few days longer than the disappearance of clinical signs.

One child, aged 3½ years, with a right lower lobe pneumonia, presenting characteristic clinical and radiological findings, showed no response to treatment until the dose was doubled and 100 mg. per lb. (450 g.) body weight per day was given. In this case the defervescence occurred by lysis over a period of eight days. No response to the drug was obtained in three patients (Table II), one of whom died.

TABLE II.—Details of Three Cases Not Responding to Terramycin

Case No.	Sex	Age	Dose	Diagnosis	Nasoph. Swab	Result
1	F	5/12	125 mg. 6-hrly for 7 days	R.L.L. pneumonia	<i>Staph. pyogenes</i>	Responded to "aureomycin"
2	F	3 yr.	250 mg. 6-hrly for 7 days	Broncho-pneumonia (coeliac disease)	<i>Pneumococci</i>	" "
3	M	6/52	100 mg. 6-hrly for 7 days	Broncho-pneumonia	Friedländer's bacilli; <i>pneumococci</i> ; <i>Str. haemolyticus</i>	Death. Necropsy showed collapse of left lower lobe, consolidation of right middle and lower lobes with abscesses. Pus: Friedländer

Upper Respiratory Tract Infections

Ten children with upper respiratory tract infections, classified as rhinopharyngitis, laryngitis, and otitis media, responded similarly to those in the pneumonia group, with an improvement in the clinical condition and a return of temperature to normal in 24 hours. In one child with otitis media, the discharge from the ear ceased within 24 hours, but the other ear then suppurated. Both ears were completely dry within five days of the onset of therapy.

Tonsillitis.—Six children with tonsillitis improved within 24 to 48 hours of treatment.

Pyuria

Three children with pyuria were treated. One, aged 8 weeks, with a staphylococcal perinephric abscess, had improved after surgical drainage and penicillin therapy. Three weeks later, however, he developed an acute febrile illness due to a *Bact. coli* pyuria. Sulphonamide therapy produced a temporary improvement, but during the subsequent five months he showed two further episodes of urinary infection, each controlled by sulphonamides and streptomycin. A further recrudescence at the age of 8 months, due to a coliform infection superimposed on a non-functioning left kidney, was treated with terramycin, and after seven days' treatment the urine showed no pus on microscopy or organisms on culture. During a follow-up period of four months he has had no recurrence of pyuria.

The second patient, aged 2 years 10 months, had suffered for two years from recurring bouts of pyuria associated with a left megaloureter. Sulphonamides, streptomycin, and chloramphenicol in turn had produced only temporary improvement. Terramycin therapy has so far maintained the urine bacteria-free for the longest period to date, about six months.

The third patient, aged 2 years, developed recurrent attacks of pyelitis associated with a congenital abnormality of the left kidney. The infecting organism, *Bact. coli*, responded at first to streptomycin, but became resistant after one course of therapy. Three further episodes of pyuria cleared up quickly with terramycin, but improvement was maintained for short periods only. The organism, however, is still sensitive to this antibiotic.

Conjunctivitis

Twelve newborn babies with purulent conjunctivitis were treated with terramycin. Swabs of the purulent material were cultured. In each case a coagulase-positive *Staphylococcus aureus* was grown, and its sensitivity to penicillin, streptomycin, and terramycin determined. Six out of seven cases classified as mild, three classified as moderate, and two severe cases improved within 48 hours, as shown by cessation of discharge and disappearance of injection of the conjunctivae. Although many of the mild cases of conjunctivitis will clear up without antibiotic therapy, terramycin is useful in those cases requiring antibiotics but in which the organism has become resistant to penicillin and/or streptomycin. No evidence of clinical irritation due to the drug was noted.

TABLE III.—Cases of Conjunctivitis

Case No.	Type	Organism	Sensitivity			Results
			Penicillin	Streptomycin	Terramycin	
1	Mild	Coag.-pos. <i>Staph. aureus</i>	Resistant	Sensitive	Sensitive	Improved
2	"	" "	Sensitive	"	"	"
3	"	" "	"	"	"	"
4	"	" "	Resistant	"	"	"
5	"	" "	"	"	"	"
6	"	" "	Sensitive	"	"	"
7	"	" "	Resistant	"	"	"
8	Moderate	" "	Sensitive	"	"	Improved
9	"	" "	"	"	"	"
10	"	" "	Resistant	Resistant	"	"
11	Severe	Coag.-pos. <i>Staph. A. Str. viridans</i>	"	"	"	"
12	"	Coag.-pos. <i>Staph. aureus</i>	Resistant	"	"	"

* Did not improve on terramycin. Responded to streptomycin.

Discussion

The broad antimicrobial spectrum of terramycin, combined with its low toxicity, ease of administration, and rapid absorption from the gastro-intestinal tract, suggests that this new drug is a most useful addition to chemotherapy.

In contradistinction to penicillin and streptomycin, which have to be given by injection, and to aureomycin and chloramphenicol, which, although given by mouth, are distinctly unpalatable, terramycin can be given in a pleasant form by the oral route. It is therefore particularly valuable in paediatric practice. Although a large number of reports on its use have already appeared in the American literature, opportunity of using the drug in this country has so far been limited, and no account of its value against the common infections of infancy and childhood has yet appeared.

Friedländer's bacillus is highly sensitive to the action of terramycin *in vitro* (Gunnison *et al.*, 1950), but so far no report describing its clinical effects in this type of infection has come to our attention. Hobby (1950, personal communication) mentioned three of five adult patients who showed complete resolution of lung consolidation within five days of the beginning of therapy. In our series, one infant with a Friedländer bronchopneumonia died.

Wooding and Scott (1951) reported the successful use of terramycin in 10 cases of bacterial pneumonia in infants and children, while Graves and Ball (1951), comparing the action of aureomycin, chloramphenicol, and terramycin in a series of 143 children with atypical pneumonia, considered terramycin to be the drug of choice in the treatment of this disease.

Two patients developed a scarlatiniform rash mainly involving the trunk and accompanied by a slight rise of temperature on the third day after cessation of treatment. As no other drugs had been given, it is assumed that this was a drug rash due to terramycin. Vomiting, diarrhoea, glossitis, and moniliasis were not seen. The "ano-rectal syndrome" described by Willcox (1951) in male adults treated for gonorrhoea was not noted.

Summary and Conclusions

A group of 66 infants and children with various infections were treated with terramycin, using a dose of 50 mg. per lb. (450 g.) body weight per day. Thirty-four out of 35 patients with pneumonia responded rapidly to treatment, in most cases within 24 hours. One patient with a Friedländer's bacillus pneumonia died.

Ten patients with upper respiratory tract infections, six with tonsillitis, and three with pyuria also showed a rapid and dramatic response. Eleven out of 12 infants with purulent conjunctivitis responded rapidly to the drug.

There were no toxic reactions, and it is stressed that terramycin, because of its wide spectrum of antibacterial activity and, in the form of the elixir, its easy and palatable administration, is particularly valuable in paediatric practice.

Grateful acknowledgments are due to Dr. Gladys L. Hobby, of Messrs. Charles Pfizer and Co. Inc., Brooklyn, New York, for generous supplies of terramycin, and to the physicians at the Duchess of York Hospital for Babies, Manchester, for permission to treat patients under their care. We wish to thank Professor Wilfrid Gaisford for advice in the preparation of this paper.

REFERENCES

- Finlay, A. C., Hobby, G. L., Pan, S. Y., Regna, P. P., Routien, J. B., Seelye, D. B., Shull, G. M., Sobin, B. A., Solomons, I. A., Vinson, J. W., and Kane, J. H. (1950). *Science*, 111, 85.
 Graves, F. B., and Ball, W. O. (1951). *J. Paediat.*, 39, 155.
 Gunnison, J. B., Coleman, V. R., and Jawetz, E. (1950). *Proc. Soc. exp. Biol., N.Y.*, 75, 549.
 Herrell, W. E., Heilman, F. R., Wellman, W. E., and Bartholomew, L. G. (1950). *Proc. Mayo Clin.*, 25, 183.
 Hobby, G. L., Dougherty, N., Lenert, T. F., Hudders, E., and Kiseluk, M. (1950). *Proc. Soc. exp. Biol., N.Y.*, 73, 503.
 — Lenert, T. F., Pikula, D., Kiseluk, M., and Hudders, M. E. (1950). *Ann. N.Y. Acad. Sci.*, 53, 266.
 King, E. Q., Lewis, C. N., Welch, H., Clark, E. A., Johnson, J. B., Lyons, J. B., Scott, R. B., and Cornely, P. B. (1950). *J. Amer. med. Ass.*, 143, 1.
 Linsell, W. D., and Fletcher, A. P. (1950). *British Medical Journal*, 2, 1190.
 Regna, P. P., and Solomons, I. A. (1950). *Ann. N.Y. Acad. Sci.*, 53, 229.
 Willcox, R. R. (1951). *Lancet*, 2, 154.
 Wooding, C. H., and Scott, R. B. (1951). *J. Pediat.*, 38, 423.