THE SUSCEPTIBILITY OF 44 STRAINS OF SHIGELLAE TO ELEVEN ANTI-MICROBIAL AGENTS

By E. H. Sng and Selena Lam

(Pathology Department, Singapore)

The sensitivity patterns of Shigella species vary in different countries. In Japan, where the problem of drug resistance has been well studied, the proportion of resistant strains has risen over the last twenty years. In one recent study (Mitsuhashi *et al*, 1967), 58.4% of 2650 strains were found to be resistant. This problem has not been studied on our local strains, and the following results show that drugs resistance is present in a number of our strains.

MATERIALS AND METHODS

26 Shigella flexneri and 18 Shigella sonnei were isolated by the bacteriology laboratory from July 1968 to March 1969. These were primary isolates from routine specimens, all of which came from different patients.

The method of preparing media incorporated with the drugs, and assay for sensitivity is described elsewhere (Sng and Lam, in press). In the case of trimethoprim/sulphadiazine, the highest concentration used was 33.6 µg./ml.

RESULTS

Figs. 1 and 2 show that Sh. sonnei strains were more sensitive than Sh. flexneri to ampicillin, cephaloridine, chloramphenicol and tetracycline. All Sh. sonnei were inhibited by the four antibiotics at 12.5 µg./ml. On the other hand, tetracycline could only inhibit 23 (88.5%) Sh. flexneri at 25 µg./ml., whilst the other three drugs were active only against 25 (96.2%) strains at the same concentration.

The activity of cephaloridine and chloramphenicol were similar. In fact, against Sh. sonnei both drugs were equally effective, and their inhibition curves were identical. Against most strains of Sh. sonnei and flexneri both drugs were about two times more effective than ampicillin and tetracycline. However, against the more resistant strains, differences in activity were much less.

Gentamicin was the most effective aminoglycoside (Fig. 3) against Sh. flexneri. 6.2 µg./ml. of it was sufficient to inhibit every strain. Kanamycin, neomycin and streptomycin gave similar sensitivity patterns, though two strains were resistant to 25 µg./ml. streptomycin. One of the two strains was also insensitive to 25 µg./ml. kanamycin and neomycin.

Sh. sonnei (Fig. 4) were slightly more sensitive to the aminoglycosides than Sh. flexneri. All were sensitive to 1.6 µg./ml. neomycin and 3.2 µg./ml. gentamicin and kanamycin. Streptomycin was fairly active, though one strain was resistant to 25 µg./ml.

Polymyxin proved to be effective against all strains of shigellae at 3.2 µg./ml. (Fig. 5). On the other hand, sulphadiazine was found to be the least effective of the antimicrobial agents (Fig. 6). 38.5% Sh. flexneri and 33.3% Sh. sonnei were resistant to 100 µg./ml. of the drug. In contrast to the other drugs, many of the Sh. sonnei were less sensitive to sulphadiazine than Sh. flexneri. Thus at 50 µg./ml. only 33.3% Sh. sonnei were sensitive, compared to 53.8% Sh. flexneri.

Both species were susceptible to the combined effects of trimethoprim/sulphadiazine. At 4.2 µg./ml. the combination inhibited all Sh. sonnei and 25 of the 26 Sh. flexneri. One Sh. flexneri had a M.I.C. of 33.6 µg./ml.

Table I shows the percentages of strains sensitive to the different antimicrobial agents at the given concentrations. Sulphadiazine resistance was commonest in both species, and it was found that resistance to the other antimicrobial agents was always associated with resistance to 100 µg./ml. sulphadiazine. This meant that 38.5% Sh. flexneri and 33.3% Sh. sonnei were resistant to one or more drug. However, shigellae were generally sensitive to drugs other than sulphadiazine. 84.6% Sh. flexneri and 88.9% Sh. sonnei were sensitive to all the drugs other than sulphadiazine.

DISCUSSION

Many antimicrobial agents are available in the treatment of shigellosis, and the choice of a drug suitable to the patient can usually be made without much difficulty. Ampicillin and tetracycline (Patton *et al*, 1968), chloramphenicol (Aldova *et al*, 1967), kanamycin, streptomycin

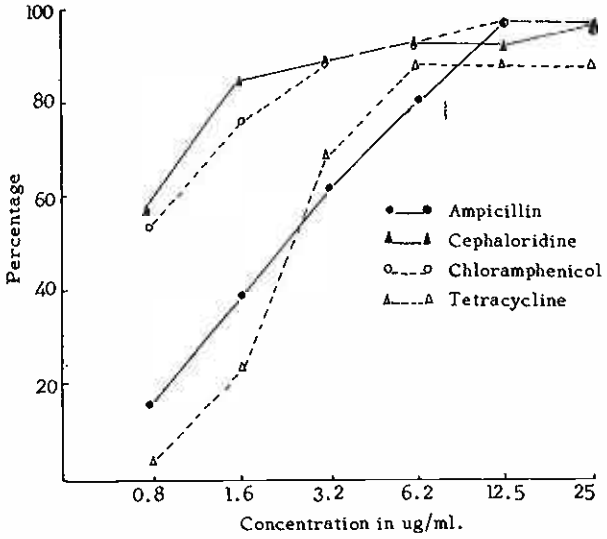

Fig. 1. Sensitivity of Sh. flexneri.

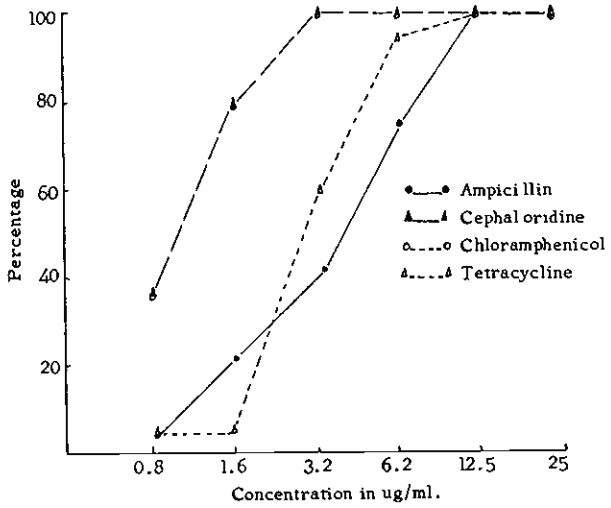

Fig. 2. Sensitivity of Sh. sonnei.

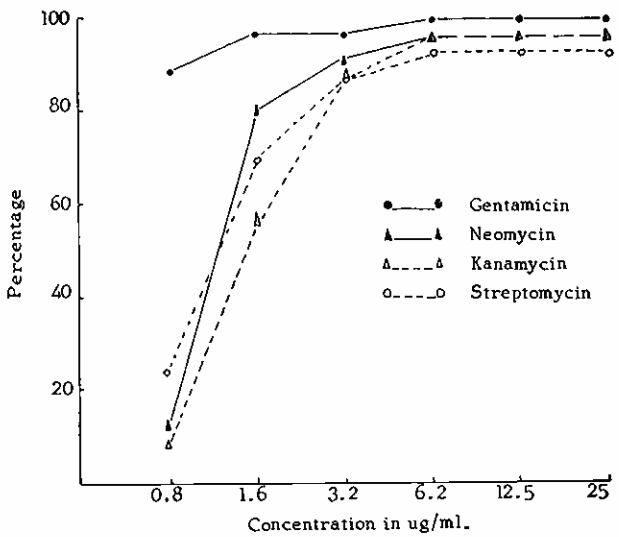

Fig. 3. Sensitivity of Sh. flexneri.

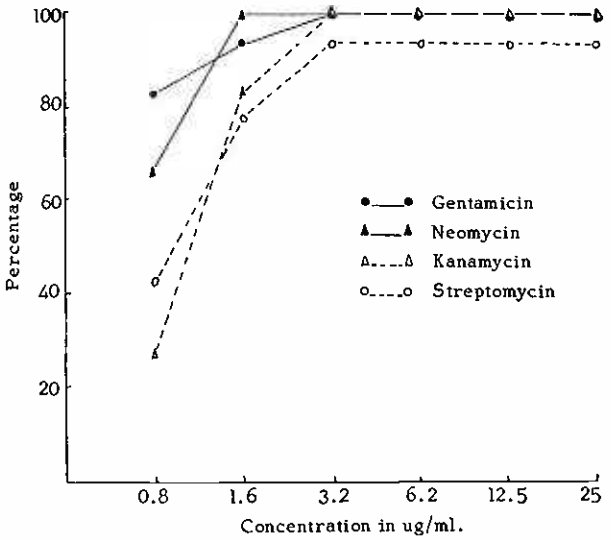

Fig. 4. Sensitivity of Sh. sonnei.

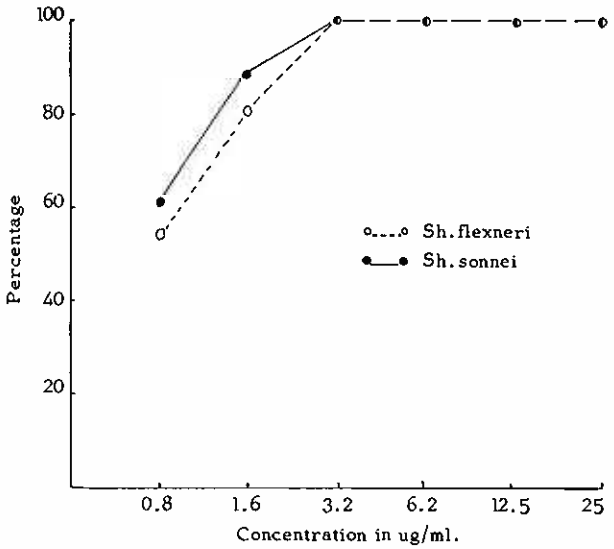

Fig. 5. Sensitivity of Shigellae to Polymyxin.

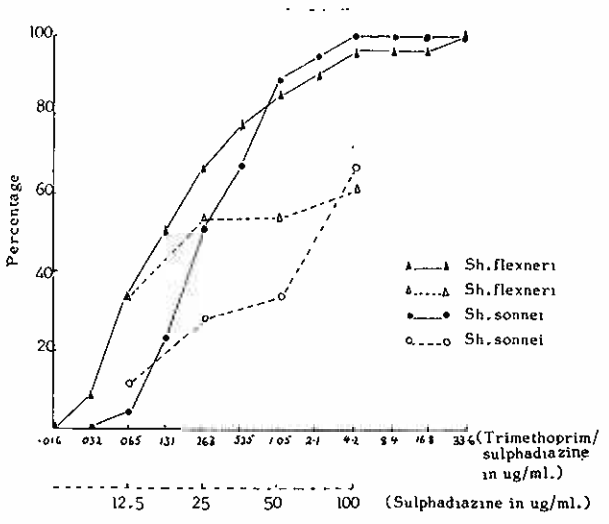

Fig. 6. Sensitivity of Shigellae to Trimethoprim and Sulphadiazine.

TABLE I

THE SENSITIVITY OF SHIGELLAE TO VARIOUS ANTI-MICROBIAL AGENTS

Drugs	Sh. flexneri	Sh. sonnei
Ampicillin (12.5 µg./ml.)	96.2%	100 %
Cephaloridine (12.5 µg/ml.)	92.3%	100 %
Chloramphenicol (12.5 µg./ml.)	96.2%	100 %
Tetracycline (6.2 µg./ml.)	88.5%	94.4%
Gentamicin (3.2 µg./ml.)	96.2%	100 %
Neomycin (12.5 µg./ml.)	96.2%	100 %
Kanamycin (12.5 µg./ml.)	96.2%	100 %
Streptomycin (12.5 µg./ml.)	92.3%	94.4%
Polymyxin (3.2 µg./ml.)	100 %	100 %
Sulphadiazine (100 µg./ml.)	61.5%	66.7%
Trimethoprim/Sulphadiazine	100 % (33.6 µg./ml.)	100 % (4.2 µg./ml.)

and nalidixic acid (Parry, 1967) have all been reported to give satisfactory results. On the other hand, sulphonamide (Haltalin *et al*, 1967) and neomycin (Haltalin *et al*, 1968) have not been found to be as satisfactory clinically.

In deciding on a drug of choice, a few factors like the sensitivity of the common species must be taken into consideration. In our study, Sh. sonnei were generally more sensitive than Sh. flexneri. All the Sh. sonnei were sensitive to the antimicrobial agents other than tetracycline, streptomycin and sulphadiazine. Sh. flexneri, in contrast, was fully sensitive only to polymyxin and trimethoprim/sulphadiazine.

On the whole most of the strains were sensitive to the drugs used. 84.6% Sh. flexneri and 88.9% Sh. sonnei were susceptible to all the drugs other than sulphadiazine. There does not, therefore, appear to be any lack of effective antimicrobial agents against most of the local strains.

The new drug combination trimethoprim/sulphadiazine proved to be effective at 4.2 µg./ml. against all strains except one Sh. flexneri, which had a M.I.C. of 33.6 µg./ml. It should be worth conducting a clinical trial on the effectiveness of this drug combination on shigellosis.

Aldova and Zavadsky (1966), studying strains isolated in Eastern Europe, found that antibiotic resistance was most commonly associated with resistance to sulphonamide. Only 4 of their 476 shigella strains resistant to 2 antimicrobial agents were susceptible to sulphonamide. In our series, all the resistant strains were insensitive to sulphadiazine. We are continuing our study on the presence of resistance transfer factors in these strains.

SUMMARY

26 strains of Sh. flexneri and 18 strains of Sh. sonnei, isolated from routine specimens, were tested for susceptibility to eleven antimicrobial agents. 84.6% Sh. flexneri and 88.9% Sh. sonnei were sensitive to all the drugs tested other than sulphadiazine. Sulphadiazine resistance was commonest in both species, being found in 38.5% Sh. flexneri and 33.3% Sh. sonnei. All strains resistant to two or more drugs were also insensitive to sulphadiazine. On the whole, Sh. sonnei were more sensitive than Sh. flexneri to the drugs, other than sulphadiazine.

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