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Decrease of Drug Resistance in *Salmonella* in The Netherlands

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Since 1974, tetracycline resistance in salmonellae of human and porcine origin has decreased nation-wide in The Netherlands. This decrease has coincided with the ban on incorporation of tetracycline in animal feeds.

Since 1959, all salmonella strains (about 20,000 per year) sent for serotyping to the National Salmonella Centre have also been screened for drug resistance (3, 8, 9). The majority of the strains (about 90%) that were found to be resistant to one or more drugs were typed as *Salmonella typhimurium*. About 60% of all human isolates and nearly 80% of all porcine isolates belong to this serotype. *S. typhimurium* may therefore serve as an indicator of the emergence of drug resistance in salmonellae in The Netherlands. The major changes in drug resistance in salmonellae concerned tetracycline (Tc) resistance. This note will therefore be limited to a description of the incidence of Tc-resistant *S. typhimurium* isolates.

Strains were tested for resistance with the tube dilution method, and were considered as Tc resistant when the minimum inhibitory concentration was ≥20 μg/ml (5). The main features of the emergence of Tc-resistant *S. typhimurium* isolates in humans, pigs, calves, and cattle are presented in Fig. 1. Tc-resistant isolates from humans and pigs were rare in 1959–1960, peaked at 40 to 50% in 1963–1966, and peaked again at 80 to 90% in 1973. After 1973, the incidence of Tc-resistant *S. typhimurium* isolates from these sources dropped.

With the introduction of a revised phage-typing system for *S. typhimurium* in 1971 (2), a comparison was made between the phage type and the antibiogram of each *S. typhimurium* strain (6, 7). Some relevant results are outlined in Fig. 2. The predominant *S. typhimurium* phage type in 1971–1974 was type 505; strains of this phage pattern were predominantly Tc resistant, due to the presence of a particular Tc resistance plasmid, pRI20 (5). In humans and pigs, the incidence of type 505 strains increased during this period. After 1974, the incidence gradually decreased. The percentage of Tc-resistant phage type 505 strains increased from 76% in 1971 to 99% in 1973 and then gradually dropped to 72% in 1978. A similar decrease of Tc resistance was also observed in *Salmonella panama* from human and porcine sources, but in this serotype the resistance dropped from about 55% in 1972 to 2% in 1977. In pigs and humans, Tc-resistant *S. typhimurium* strains were gradually replaced by Tc-susceptible strains with other phage patterns, such as phage types 650 and 260.

In calves, the incidence of Tc-resistant *S. typhimurium* isolates differed from that in pigs and humans. The absolute numbers of type 505 isolates remained rather constant from 1971–1978 (Fig. 2). From 1972 on, multiply drug-resistant strains with phage type 201 were found in increasing numbers. Their number dropped after 1974, but increased again in 1978. In 1977 and 1978, many multiply drug-resistant *S. typhimurium* strains with phage types other than 201 and 505 were isolated from calves. A small percentage (5 to 12%) of these strains belonged to phage types 204 and 193, which have been described in several outbreaks of calf salmonellosis in England (4). From 1975 on, an increasing number of multiply drug-resistant *Salmonella dublin* strains was encountered in calves. Multiply drug-resistant *S. typhimurium* and *S. dublin* strains cause a severe salmonellosis in calves. Such strains will frequently be exposed to therapeutic levels of antimicrobial drugs. This might explain the selection of multiply drug-resistant, virulent strains in calf herds.

Multiply drug-resistant strains were only sporadically encountered in humans. This can be explained by the fact that affected calves either die or, if they reach meat inspection, will not be considered fit for human consumption. The majority of the type 505 *S. typhimurium* strains, however, originate from healthy animals, especially slaughter pigs (1). Such animals pass meat inspection and thus reach the human consumer. In The Netherlands, pork is consumed in larger quantities than calf meat. These facts explain

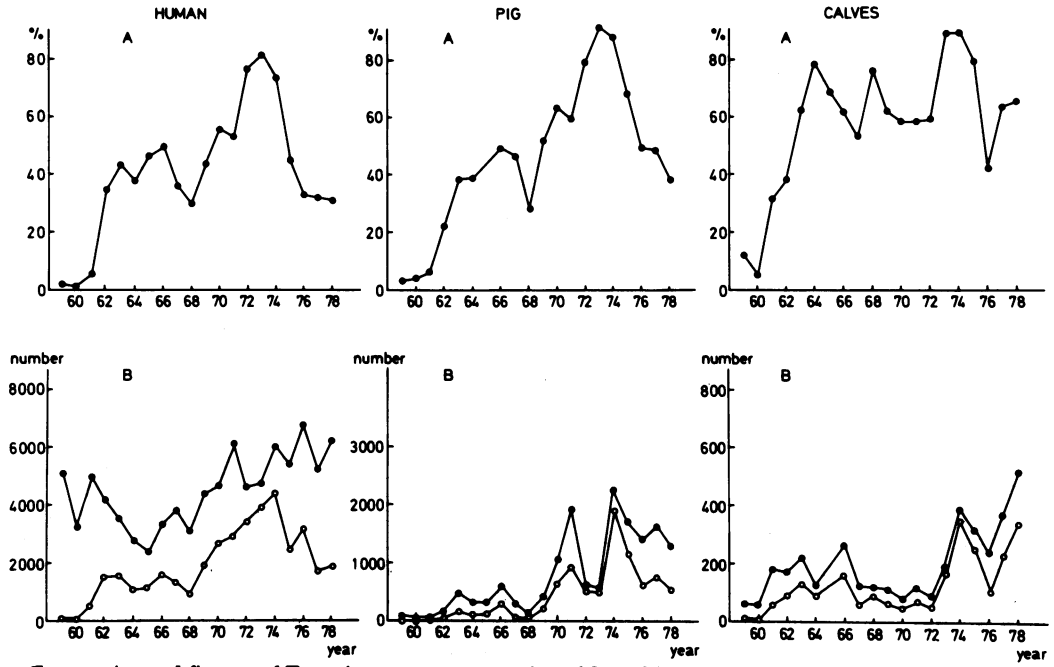

FIG. 1. *Annual figures of Tc resistance among strains of S. typhimurium isolated from humans, pigs, and cattle from 1959 to 1978. (A) Percentage of S. typhimurium isolates resistant to Tc. (B) Number of isolates investigated (●); number of Tc-resistant isolates (○).*

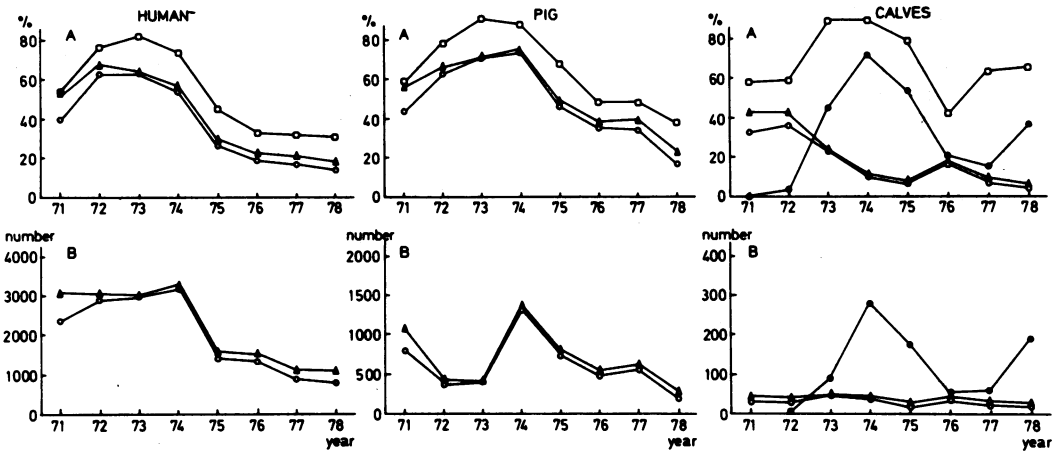

FIG. 2. *Relationship between Tc resistance and phage type of strains of S. typhimurium isolated from humans, pigs, and calves and cattle. (A) Percentage of isolates resistant to Tc (□); percentage of isolates of phage type 505 (△); percentage of isolates of phage type 505 and resistant to Tc (○); percentage of multiply resistant isolates of phage type 201 (●). (B) Absolute number of strains investigated; number of type 505 strains (△); number of Tc-resistant type 505 strains (○); and number of multiply resistant type 201 strains (●).*

the concurrence of the decrease of Tc-resistant salmonellae in pigs and humans. In January 1974, the European Common Market regulations on the use of antibiotics for nutritive purposes came into force in The Netherlands. Tetracyclines, which had been used for growth promotion in increasing quantities since the early sixties, were now no longer permitted for this purpose. Casual monitoring of animal feed since 1974 indicates that the ban has been executed. On the other hand, there is no indication that the use of Tc on veterinary prescription has been changed since 1974. The coincidence of discontinuing the use of tetracyclines for growth pro-

motion on one hand, and the nation-wide decreased incidence of Tc-resistant *S. typhimurium* and *S. panama* strains in pigs on the other hand, are highly suggestive for the role that nutritive doses of Tc have played in the emergence of Tc-resistant salmonellae in pigs and humans.

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