Section of Comparative Medicine

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Hazards of Antibiotics in Milk and Other Food Products [*Abridged*]

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Sources and Hazards to Man of Antibiotics in Foods

There are two principal ways in which antibiotics may come to be present in human food: they may be added to the food itself as preservatives, or they may have been used for the benefit of the animal – or plant – from which the food is derived. These uses, with one important exception, are severely restricted by regulations. This subject was fully reviewed and recommendations were made on it in a recent WHO report (World Health Organization 1963).

Food Preservation

Nisin: This is a polypeptide antibiotic formed by some strains of *Streptococcus lactis*, the addition of which is now permitted in this country to processed cheese and under certain conditions to canned foods. It inhibits the growth of clostridia and thermophilic spoilage organisms. There is no evidence whatever that its consumption can do any harm; this is fortunate, since it is often present as a natural product in cheese.

Tetracyclines: These have been found the most suitable antibiotics for delaying spoilage in flesh foods. The most important of these applications is to fish, whether in trawlers on long voyages or to fillets after landing. Several countries permit the use of chlor- and oxy-tetracycline for this purpose: the United States and Canada also permit similar treatment of poultry, and Argentina is alone in including meat. The situation in this country is ludicrous, and illustrates both the confused state of our legislation about drugs and the slow tempo of proceedings in Whitehall. The Preservatives in Food Regulations 1962 permit the preservation of fish with tetracyclines, but the Therapeutic Substances Act debars the supply of these antibiotics to the fishing industry, and until an order is made under this Act the 1962 Regulations are without practical effect. This absurd situation has now existed for nearly two years.

I know of no evidence that the minute amounts of tetracyclines which may still be present in fish after cooking can be harmful. As regards any direct effect of the antibiotic on the consumer the same may be said of poultry or even meat, but an altogether different hazard may be involved here. Tetracyclines are also used as feed supplements or therapeutically in poultry and young animals, and Williams Smith (1957) has shown that this has led to the appearance of resistant strains of intestinal bacteria; these may include *Salmonella* spp. (Garside, Gordan & Tucker 1960). If these exist in a carcase its treatment with a tetracycline, by suppressing spoilage bacteria, may actually favour the growth of a resistant *Salmonella*. It seems, therefore, a sound principle that the same antibiotic should not be used both for the treatment of an animal during life and for the preservation of its carcase.

Administration to Animals

For growth promotion: It is well known that the addition of small amounts of antibiotics to the feed of young stock accelerates their growth although, strangely enough, the mechanism of this effect is still in dispute. In the amounts used, which should not exceed 20 ppm in the dry feed, there can be no detectable residues in the meat, even if administration were continued until the time of slaughter.

General therapeutic: Larger amounts of antibiotics may be given to animals for the treatment of intestinal and other infections, and here it is desirable that administration should have stopped at least four days before slaughter. Either of these forms of treatment may lead to a build-up of

antibiotic resistance in *Salmonella* spp. and staphylococci, but how far the existence of such organisms in the animal world is a hazard to man is at present uncertain.

Treatment of bovine mastitis: This presents a special problem, because the antibiotic is usually injected directly into the teat canal, and much of it is subsequently eliminated in the milk. A recent report (Milk and Milk Products Technical Advisory Committee 1963) reveals that 11% of samples of milk in England and Wales contained penicillin, and recommends a series of measures to prevent this, from the better control of mastitis by hygiene to the imposition of penalties on farmers for marketing milk before the antibiotic has been excreted.

Attention has been almost wholly concentrated on penicillin, but other antibiotics are also used for treating mastitis. Only about 1% of samples in the recent survey were shown to contain them, but the organism used in the assay was chosen for its high sensitivity to penicillin, and the test might fail to detect much higher concentrations of other antibiotics. There is in fact no method by which these substances can be assayed or even identified.

Among those in use for treating mastitis are tetracyclines, streptomycin and chloramphenicol. There are objections to the involuntary consumption of any of these in milk, but chloramphenicol stands apart from the others in being the occasional cause of fatal aplasia of the bone marrow. No one knows why a small proportion of patients treated with this antibiotic develop this complication. It has been suggested that in some way they become sensitized to it: if so, could they not have been sensitized by its previous consumption in milk?

With only one exception at present, nisin, the addition of antibiotics to foods is prohibited. Yet there is nothing to prevent the presence in milk of any antibiotic, other than penicillin, which the veterinarian may choose to inject into the cow's udder. This position is at least illogical, and might be termed intolerable.

I believe that unless and until we have all the necessary means for excluding from the market milk containing these other antibiotics, the Ministry of Health should demand of the Ministry of Agriculture that their use be stopped. It would be of great interest to know how far this would handicap the treatment of mastitis. Is there good evidence, from well-controlled trials, of the efficacy of streptomycin, tetracyclines or chloramphenicol? The problem is the penicillin-resistant staphylococcus, and none of these antibiotics is highly regarded in the medical field for dealing with such an organism, since it can become resistant to all of them, and their intrinsic activity is in any case less than that of penicillin. The choice falls rather on one of the semi-synthetic penicillins – methicillin or cloxacillin – which are resistant to staphylococcal penicillinase, and thus just as effective against resistant as against sensitive strains. If these are effective in mastitis, the restriction of its treatment to penicillins should present no hardship, the control of antibiotics in milk would be greatly simplified, and the medical profession would know it has only one hazard to fear in this connexion, instead of a series of unknowns the magnitude of which no one can yet assess.

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The Use of Antibiotics in the Control of Mastitis

When antibiotics first became available for the treatment of mastitis, the predominant infection was caused by *Streptococcus agalactiæ*. A survey of nearly 2,000 clinical cases on a country-wide basis has shown that *Str. agalactiæ* was associated with 44% of the cases of mastitis in 1942.

Penicillin

The first antibiotic used in treating mastitis was tyrothricin, but this was extremely irritant in the udder and was not used to any great extent. Penicillin was particularly suitable for the treatment of *Str. agalactiæ* infection, being non-irritant, non-toxic and it did not induce the emergence of resistant strains *in vivo*.

Initially, aqueous solutions, prepared immediately prior to injection into the udder, were used, but this was time consuming and introduced the possibility of cross-infection, and therefore single-dose collapsible tubes were employed. To maintain the stability of the penicillin a non-aqueous base had to be used and the original choice was arachis oil with beeswax as suspending agent. These substances were chosen because they are naturally occurring foodstuffs, normally con-