Meetings

Antibiotics in Agriculture

The 2nd international conference on antibiotics in agriculture was held at the University of Nottingham School of Agriculture, Leicestershire, England, from 2 to 6 April. The University of Nottingham has conducted eight previous "Easter School" conferences on specific research activity of interest to agriculturists.

During the 9th Easter School there were 20 lectures in five specific areas relating to research progress in the uses of antibiotics in agriculture: veterinary medicine, crop production, stimulative effects in animal feeds, food preservation, and public health. The participants spent one afternoon on field trips to nearby laboratories and research centers.

P. E. Macey (Boots Ltd., Nottingham) presented the initial lecture, on the present status of antibiotics. He gave a comprehensive review of the history of these important compounds and discussed the current trend of chemically manipulating standard antibiotics in the hope of eliminating objectionable characteristics such as toxicity and allergenicity.

S. J. Edwards (ARC Field Station, Compton, Berkshire) introduced the subject of antibiotics in veterinary medicine. He discussed the pathogenesis of mastitis and indicated that this most common of diseases affecting the mammary gland of the cow was formerly caused by streptococcus but now is caused by staphylococcal species and *Escherichia coli*. He illustrated the problem of resistance to antibiotics and commented on the usefulness of synthetic penicillins. He stated his opinion that current trends toward an immunologic approach to the problem of mastitis would not be as successful as chemotherapy.

R. Lovell (Royal Veterinary College, University of London) noted that changes in pathogens occur simultaneously with changes in human social patterns and that it was to be expected that some microbial changes would be fostered by the use of antibiotics. He discussed epidemiological changes in infectious diseases of animals and the shift of microbial populations to forms resistant to streptomycin and the tetracyclines, significant during the period 1950 to 1960.

G. Woolfe (Boots Ltd., Nottingham), commenting on the activity of antibiotics against protozoa, concluded that the antibiotics are not likely to be available in amounts that make them economically competitive with synthetics.

The lecturers interested in the impact of antibiotics on crop production—J. E. Crosse (East Malling Research Station, Kent), A. Rhodes (Glaxo Laboratories, Buckinghamshire), R. N. Goodman (University of Missouri), and the convener of the session, P. W. Brian (I.C.I. Ltd., Welwyn)—observed that the systemic activity of antibiotics in plant tissues differed markedly in the species to which the antibiotics were applied. Transcuticular penetration had been demonstrated with these compounds, but internal adsorption and inactivation seemed to limit their effectiveness. The speakers observed that the bacteriostatic nature of streptomycin at the levels achieved in plant tissues further limited the efficacy of this drug as an agent in the control of plant disease. Streptomycin could not be counted upon as an eradicant, as it was soon overwhelmed by the pathogen. Its effectiveness was limited to prophylaxis, with application to the plant in anticipation of infection.

Rhodes reported that his group had been able to produce over 300 structural analogues of griseofulvin. Of these, the propoxy-substituted ones showed increased activity against a number of plant fungal pathogens. D. M. Spencer (Wye, Kent) described antimicrobial agents from seeds and seedling plants. These were of considerable interest but not within the current definition of antibiotics.

According to K. L. Robinson (Northern Ireland), the use of antibiotics in livestock feeds was an absolute necessity in the United States because of "dry lot feeding." This gave the United States the lead in the technology of antibiotic feeding of farm animals for therapeutic purposes as well. This work has since been undertaken around the world, and the benefits have been definitely established. The mode of action of the observed stimulative effects is still not clear, and a number of theories have been advanced, with varying amounts of evidence. Foremost among these is the theory that low levels of antibiotics directly affect the microflora of the animal, and that this results in the elimination of subclinical infections, or perhaps in a nutrient sparing action on some growth factor, with improved efficiency of food conversion as the net result. More difficult to establish are proposed direct effects of antibiotics upon the animal, such as toxin elimination and improved absorption of nutrients due to an alteration of the gut wall. Clarification may be provided in the near future through research described by M. E. Coates and M. Lev (National Institute for Research in Dairying, Reading). They suggest that under germ-free or good sanitary conditions the stimulative effect of antibiotics on the growth of animals is difficult to elicit, and they therefore feel that the mode of action must be related to microbes.

The value of antibiotics in the young ruminants was discussed by T. P. Preston (Rowett Research Institute, Aberdeen), who noted that the reduction of scours in calves was best accomplished by the tetracycline antibiotics and chloramphenicol. This finding seems related to the suppression of coliform bacteria, which in turn results in increased feed intake, decreased rate of fermentation, and a definite reduction in the production of gas. F. G. Clegg (Veterinary Investigation Centre, Sutton Bonington) reported on effects of antibiotics on the mammalian gut. He indicated that changes in toxicity, thickness, and volume might contribute to the direct effect of antibiotics in growth stimulation.

Perhaps the most provocative session of the conference was the one concerned with food preservation. The implications here for programs to provide food for the "developing nations," and

discussion of the possible untoward effects of preservation practices upon humans, heightened and sharpened discussion after each of the lectures in this session.

F. E. Deatherage (Ohio State) described the reluctance of regulatory agencies around the world, particularly in meat-deficient areas, to accept clear-cut data which seemed to show that the health hazards originally predicted have not to this time been substantiated.

Deatherage has, since 1953, studied the preservation of red meat with antibiotics and has reported repeatedly the effective suppression of spoilage bacteria with antibiotics, particularly with the tetracycline antibiotics. Spoilage in the lymphal system, referred to as "deep spoilage," has been significantly delayed in unrefrigerated meat with tetracycline (1 to 2 parts per million), with concomitant twofold and even threefold increases in keeping time.

The use of antibiotics in canned foods was discussed by H. B. Hawley (Somerset, England). It was pointed out that the major consideration in canning foods was the requirement for absolute elimination of spores of *Clostridium botulinum*. Hence, the canning industry is unable to consider treatment with antibiotics a substitute for heat treatment (treatment at 250°F for 3 minutes) but considers it an adjunct to heat treatment.

It has been shown that with the minimum heat treatment a number of thermophyllic bacterial spores persist and cause spoilage. For this reason, combinations of antibiotics and heat treatments have been evaluated. Heat treatments supplemented by treatment with the antibiotic subtilin delayed spoilage by the thermophile *Bacillus stereothermophilus*. Other studies have revealed that subtilin, penicillin, and a macrolide antibiotic, tylosin, sensitized spores of thermophiles with respect to heat so that they were killed either by lower temperatures or by shorter exposures to heat. There is some evidence to suggest that these compounds, as well as nisin, are only effective against heat-injured cells. Of further interest is the fact that tylosin and nisin have a low order of mammalian toxicity and may yet be cleared for use in canning.

J. M. Shewan (Torry Research Station, Aberdeen) outlined the British experience with antibiotics in fish preservation. On the basis of accumulated data on preservation, residues, and spoilage flora, parliamentary approval of the use of the tetracyclines (at levels not to exceed 5 parts per million) for preserving whole and filleted fish has been recommended.

A novel attempt to use antibiotics in bacterial classification was reported by A. Seaman and M. Woodbine (University of Nottingham). They concluded that such a technique was useful epidemiologically with organisms from similar environments.

E. H. Kampelmacher (Utrecht) reported on the nonmedical uses of antibiotics around the world, on the basis of a survey he made for the United Nations. He emphasized the proven value of antibiotics in food preservation and the potential value to developing nations of these techniques. Allusions to the theoretical public health hazards which might be precipitated arose and set the stage for the concluding session.

The final session was chaired by Sir Howard W. Florey, Nobel laureate and president of the Royal Society. H. Williams-Smith (Animal Health Trust, Essex) spoke on the emergence of antibiotic-resistant disease-producing organisms, and H. S. Goldberg (University of Missouri) discussed studies on humans exposed to antibiotics nonmedically. Williams-Smith concluded that although antibiotics in feeds did cause the emergence of antibiotic-resistant pathogens, the advantages of such use outweighed the disadvantages. Alterations of accepted chemotherapeutic techniques were often required, he said, but no public health hazard exists, since the emerging resistant animal pathogens are not pathogenic for man.

Goldberg discussed hypersensitivity studies on field workers spraying streptomycin for plant-disease control. In addition, he reported on antibiotic-resistant bacteria from humans given oxytetracyclin for 14 months at food-residue levels (5 to 10 parts per million). Streptomycin appeared to present no hazard in the amounts used in plant sprays. Long-term, low-level administration of oxytetracycline resulted in transient bacterial resistance. It was concluded that, in general, the public is not endangered by nonmedical uses of antibiotics.

The entire proceedings of the conference, including a summary of the discussions, will be published by Butterworths of London.

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