The Toxicity of Pesticides for Livestock

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A NEW PESTICIDE may be registered by the U. S. Department of Agriculture for shipment in interstate commerce after evidence has been presented showing that it is effective for the proposed usage and is reasonably safe when so used. The required information may be supplied by any responsible individual or organization, including other USDA agencies. State laws provide similar protection for products marketed within their borders.

Only a few chemicals can meet these requirements. This is obvious in that of more than 17,000 new chemicals proposed as insecticides or repellents since 1947, about 3,000 were tested for use against livestock parasites. Because of ineffectiveness, toxicity hazard, residues in meat or milk, manufacturing difficulties, and other problems, most of the 3,000 were eliminated, leaving only a dozen synthetic organic insecticides recommended by agencies of the USDA for use on livestock during 1960. This severe process of elimination functions in the investigation of all new pesticides, being carried out by industrial, commercial, private, and governmental research units.

The manner in which a chemical is used governs its toxicological hazard for livestock. Materials applied directly to the animals represent the greater danger for acute poisoning, while those applied to feed crops usually represent the greater danger for subacute or chronic poisoning.

A pesticide may be put into interstate commerce on the basis of data which indicate that it is reasonably safe and effective under prescribed conditions of use, but misuse will inevitably occur. Some misuse is generally anticipated and is considered in both the recommendations and the registration for use; but it is simply not possible to anticipate the varieties and extremes of misuse which certain individuals can devise.

The vast majority of livestock losses due to pesticides have been the result of either deliberate misuse, failure to read the label, or careless exposure of dangerous chemicals where animals could drink or eat them.

Our discussions of pesticides are usually dominated by insecticides because they may be sprayed on animals, may be injected or otherwise introduced into them, may be put on the animals' feed as a part of normal plant protection, and may be left carelessly exposed. Herbicides represent a smaller part, because their use is generally limited to the destruction of undesirable plants in crops not grazed by livestock, or pasture plants not normally eaten by livestock. Therefore, the opportunities for exposure of livestock are usually severely restricted. Defoliants and fungicides are even more restricted in use.

The Meaning of Toxicity and Hazard

Before going deeper into a discussion of the toxicological hazard of pesticides it is important to understand the relationship of the terms "toxicity" and "hazard." It is axiomatic in the science of toxicology that virtually any chemical or physical entity will have harmful effects upon living organisms if applied or consumed in excessive amounts. Such daily accepted essentials as sunlight and rain are perfect examples; too much of either will destroy plant and animal life. A substance is more or less toxic according to the amount, by weight, required to do damage. The most toxic substance we know is probably the botulinus toxin, while some of the least toxic ones are the staple foods we eat. A substance becomes a hazard if the normal use, or minor misuse of it, is likely to harm desirable organisms, regardless of the amount of the substance required as compared to other toxic materials.

Because of this relationship, the less toxic of a pair of compounds is sometimes found to be the more hazardous in use. Remember that toxicity can be measured for a compound in terms of grams or ounces, but the hazard of its use depends entirely upon the manner in which it is used.

There is a natural tendency to emphasize the relative toxicity of an insecticide rather than its relative hazard. A spray that is toxic at 0.1% concentration in a spray appears to be more dangerous than one toxic at 1.0%. In practice, this must be correlated with the concentration actually employed. For example, if the more toxic compound is used at 0.025% and the less toxic at 0.5%, the less toxic compound represents the greater hazard because of a twofold increase would produce poisoning, while a fourfold increase would be required for the more toxic material.

In the same manner, forage treated with 0.1 lb of insecticide producing toxicity in cattle at 10 mg/kg is less hazardous than one applied at 4 lb per acre with toxicity to cattle at 100 mg/kg.

Classification of Pesticides

Compounds capable of destroying one form of life must be suspected of being capable of at least injuring other forms. Stopping life processes, whether in an animal or a plant, involves the immobilization of essential enzymes, or in some other way blocking the essential functions of individual cells. When the essential cells of the organism die or stop functioning, then so must the organism.

Life-destroying compounds are generally somewhat selective in action, permitting us, by intelligent choice of material, to destroy one form of life without seriously harming the forms we consider desirable.

The classes of pesticides are not so well-defined as might be desired, and their members could be discussed under several classes. Most herbicides have some bactericidal or fungicidal activity. Similarly, many fungicides are herbicidal, but we can select many that can be safely applied to plants. One of the first systematically active animal insecticides 2-pivalyl-1,3-indanedione (Pival) found its better place as a rodenticide. Several insecticides, such as Bayer 21/199, Bayer L 13/59, Ruelene, and ronnel have been shown to have an anthelmintic action.

The specific data that have been obtained concerning the toxicity of pesticides by scientists of the Agricultural Research Service alone would require many hours to discuss; to include those from industry and the various state and commercial laboratories would require again as much time. My comments and illustrations have been selected to establish principles rather than to provide a complete set of toxicological data. For summaries of specific data, two publications are available to cover the livestock area. These are: The Nature and Fate of Chemicals Applied to Soils, Plants, and Animals ARS 20-9; and Pesticide Residues in Meat and Milk ARS-33-63.

Insecticides

The discovery of DDT as an insecticide by Müller in 1939 was a great advancement of our potential for insect control, and for it he received a Nobel prize. The low acute toxicity of DDT for most mammals suggested there would be no problems associated with its use. Several developments caused a revision of scientific attitudes toward the safety of DDT and toward several similar compounds then under development.

Appearance in Meat and Milk

Howell and co-workers found DDT in the milk of cattle sprayed with DDT. This was taken in many quarters to represent mechanical contamination of the udders by the insecticide, because at that time it was not an acceptable theory that such compounds could pass through the unbroken skin to the blood and be circulated. It was necessary for us, at Kerrville, to conduct similar studies and to devise closed systems for collection of milk from

within the udder to prove beyond doubt that excretion was taking place. It was then argued that the cattle were licking themselves and absorbing the DDT from their digestive tracts. The author and others at the Kerrville Laboratory then kept sprayed cattle in stanchions—muzzled except for a few minutes feeding time—and collected milk in sealed systems. Again, DDT was found in the milk. DDT was found in milk by a large number of workers in later studies.

During the same period, various scientists were appraising the effect of low level feeding of DDT. They determined that consistent effects upon rats could be produced with rather low levels of DDT in feed. Many workers, including those of the USDA, ARS at Kerrville and Beltsville, established that DDT and other chlorinated hydrocarbons were stored in the fat and excreted in milk of treated livestock, and were not likely to be destroyed in cooking whether exposure was by spraying or from ingestion. Other chlorinated hydrocarbons were found to be beset by the same problems.

As data and pressure accumulated against residues of chlorinated hydrocarbons in foods, it was more and more apparent that compounds that were not stored in tissues or excreted in milk were sorely needed. Industrial and governmental laboratories fell to the task. Soon, safer compounds appeared, with virtually no problems of storage in animal tissues. Most of these occurred in extremely low amounts in milk, eliminating them from use, but encouraging us to believe we would ultimately find materials that would not appear in milk.

There has been almost no evidence to indicate that the residues of insecticides on feed and forage, which occurred following recommended use, have poisoned livestock. This is due, of course, to careful preliminary study and evaluation of the toxicological hazards, to proper recommendations by industry and government, and to reasonable use by the consumers.

While poisoning has not been observed in animals consuming insecticides as normal residue on feeds, the consumption has usually led to storage in their tissues or excretion in their milk, or both. The storage of the insecticides in tissues has never seemed to have a harmful effect upon livestock. Obviously, I speak of residues following recommended applications. Higher levels could produce poisoning.

We could dispense with residues in animal tissues as usually being of no general significance to livestock health, and do so in clear conscience; but we are then confronted with their significance to people consuming animal products, as the level of residues in the tissues establishes the dietary level for people, and the level of intake for people is significant.

Our interest, then, in the appearance and disappearance of pesticide residues in tissues of livestock is primarily one of concern for the welfare of the consumer. The significance of these residues in human foods has been and will be discussed by experts in that field.

As chemists developed more and more sensitive methods of analysis, experiments had to be repeated to prove or revise earlier conclusions concerning the amounts of residues present.

The analytical chemists were momentarily foiled by the animals in at least two cases. Aldrin was found to be converted by animals to its epoxide, dieldrin and heptachlor to its epoxide. Older methods, specific for aldrin and for heptachlor, had shown absence of residues of these compounds, but their epoxides were shown to be present in appreciable quantities. Chlordane also was reported stored as a metabolite.

It is interesting to note that while hundreds of tolerances have been established for fruits, vegetables, and feeds for a number of insecticides, only four compounds have tolerances in meat, these being DDT, methoxychlor, toxaphene, and malathion. DDT may be present at 7 ppm and methoxychlor at 3 ppm in fat of cattle, sheep, or hogs. Toxaphene may be present at 7 ppm in fat of cattle, goats, and sheep. Malathion may be present at 4 ppm in fat of cattle, hogs, and poultry. Insecticides may not be present in milk, although official tolerances of zero have been set only for malathion and methoxychlor. The tolerance is also zero for malathion in eggs.

A manufacturer, in complying with regulations may determine the maximum residues occurring in meat or milk after proposed use, show these quantities to be without hazard, and petition for a tolerance at that level. He might also establish the quantities remaining after a reasonable period of time, say 30 days, petition for a tolerance at that level, and then specify a 30-day delay between treatment and slaughter if the tolerance is granted. Alternatively, he can determine the time required for the residue to completely disappear, add a few days for safety, and make his recommendation include this time interval. When insecticides are not present, no tolerance is required.

Compounds that do not store and are not excreted in milk are at a premium. Very few can qualify without the protection of an interval of time between application and harvest or consumption.

The waiting period is not useful when producing dairy cattle are concerned. Complete absence of residues in milk is the rule. Therefore, direct application to lactating dairy cattle is virtually ruled out for all except dusts of methoxychlor and malathion, since the other materials available at this time are present in milk after treatment. The milk containing insecticides must be destroyed or enter commerce illegally. Neither alternative is desirable. The waiting period can be used in feed or pasture work by keeping cattle off the crop or by delaying harvest until the residues on the crop have disappeared.

Generally, these restrictions do not apply to dairy cattle not in production; even in this case, however, some residues could appear at the onset of lactation if appreciable residues developed in the fat depots of the animals' body during the dry period.

Biological Cycles

To a certain extent we have biological cycles involved in the use of pesticides. For example, we may treat a body of water for insect control and accomplish the objective, but organisms not killed by the treatment may absorb and store the chemical. They, in turn, according to their biological position, may be consumed as food by other species, and these in turn by others, until there is ultimately a removal from that water of a species serving as food for mammals or birds, or man. The cycle is then continued outside the original environment.

The accumulation of pesticide may be attenuated or concentrated within this cycle, depending upon the part the animal or plant may provide of the total diet of the consuming animal. The principle has been established by several workers in addition to the studies involving contamination of the ordinary daily diet.

Such a biological cycling has been the foundation for arguments against the use of insecticides, particularly by persons interested in the animal life included under the category of wildlife. Much harm has been done by unqualified persons who twisted basic knowledge to produce scares which would be beneficial to them financially. Other individuals made diagnoses of poisoning and harmful effects without proper evidence, or through improper interpretation of results of chemical analyses.

Diagnosis of Poisoning

Residues in Diagnosis. Much dissension has existed concerning the occurence of poisoning in livestock, as in wildlife, because of a tendency to diagnose without proper evidence. I know of no more pitiable a man than he who examines a dead animal, finds some insecticide in its tissues, runs five or six simple cultures, or none at all, and then states: "Insecticide X was found to be present. Tests for all other diseases were negative, therefore I conclude this animal died of poisoning by the insecticide X." Many chemists seem surprised to learn that chemical analyses are of no value in reaching a diagnosis.

The use of chemical or biological determinations in the diagnosis of poisoning by insecticides is vastly complicated by their behavior. I doubt that sufficient emphasis can be given to this problem. It is not readily understood because the necessary explanations are apparently contradictory of our usual concept of the significance of the

presence of a foreign chemical in animal or human tissues. This lack of understanding has caused us particular difficulty when those concerned, after finding high residues, flatly state that these residues indicate death due to the material found.

Here are some examples: In feeding tests at Kerrville with heptachlor, using a diet containing 60 ppm of heptachlor, 52 ppm of heptachlor epoxide could be recovered from the fat of cattle at the end of a 16-week feeding period. The cattle at that time were in excellent health and condition. One of the cattle, when slaughtered immediately after the feeding period, contained as stated, 52 ppm in the fat, 1.2 in the thymus, and 1.5 in the liver. Other tissues, including brain, kidney, muscle, adrenal, heart, lung, and spleen contained none.

By contrast, a calf poisoned and killed by a single large dose of heptachlor revealed a residue of only 2.2 ppm in its fat.

In our feeding trials with lindane, using a level of 100 ppm in the feed for 10 weeks, a residue of 100 ppm existed in the fat at the end of the feeding period. This was reduced to 50 ppm in 4 weeks on control feed. These animals remained entirely normal throughout the test.

By contrast, three cattle of similar breed, age, and condition, deliberately poisoned by high concentrations of lindane in dips, revealed only 23 ppm one week later in their fat.

Let us assume that either of these animals with high residues had been found dead on pasture treated with the particular insecticide, and that no history other than this was available and the animals had been seen in good health a few days earlier. At necropsy, no lesions are observed other than a few petechiae on the heart, and cloudy swelling of various organs. Because of the prior use of insecticides, tissues are taken for analysis, with the results being at high levels. Unfortunately, many individuals would accept this as definite evidence of death caused by the insecticide and so render their diagnosis. Some have, only to have others prove the presence of rabies, Aujeszky's disease, or other diseases.

The chemist should be informed of the insecticide suspected, but here another difficulty is encountered. Animals fed treated forage or feed will show some residue in their fat in almost all cases. Therefore, finding a residue is not conclusive evidence. The person submitting the sample should keep his mind open to all other chemicals, including sprays and dips, to which the animal may have been exposed.

Unless the tissues are analyzed for all possible substances, the finding of one simply leads to erroneous conclusions. Above all, the presence of a residue of insecticide must never be taken to indicate anything more than exposure to that material. Presence of a residue must never be taken as a diagnosis of poisoning.

The Diagnostician. I feel I should emphasize my own feeling that all too many unqualified people have come to consider themselves as diagnosticians. I do not believe that an entomologist, zoologist, chemist, or conservationist has the training to determine the presence or absence of toxicological effect of a compound in livestock or in man. Obviously, almost anyone can note whether an animal becomes violently ill or dies immediately after a chemical exposure. This is not diagnosis as I use the term. Unfortunately some veterinarians and physicians have been guilty of assuming expert status without experience.

I feel that diagnosis of chemical poisoning should properly be left to those toxicologists with experience in this field and who can recognize the need for, and summon the aid of, other experts in the disease field.

Conclusion

In this discussion I have covered the relationship of toxicity to hazard, and I have argued that normally expected residues of pesticides on forage are practically never a hazard to livestock, but that some of the pesticides are stored in the tissues of livestock and excreted in their milk, creating a potential hazard to people. This hazard can be avoided by carefully following label instructions as to dosage and proper intervals which must occur between treatment and harvest of slaughter.

I have indicated that chemical analyses are of virtually no value for diagnostic purposes.

I have pointed out that all the toxicological information developed for a given compound can be utilized only if the manufacturer, formulator, and consumer contribute equally to safe, intelligent usage. The manufacturers and formulators must prepare the compounds in stable, readily usable form, and devise labels for the final product, which will clearly define the intended uses and limitations of the product. The consumer must read the label and adhere strictly to the suggestions found there.

I believe that the rational use of pesticides in agriculture is essential if we are to maintain maximum productivity in the face of constantly shrinking farm and ranch land and an exploding population. I believe that these materials can be, and are being, used with complete safety to man and animals when label instructions are followed.

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