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Horticulturists and others interested in the fruit industry are all acquainted in a general way with the attitude of the officials of the United States Food and Drug Administration toward spray residues, and with their activities and powers. It seems, nevertheless, that we should take this occasion to state the residue problem from their standpoint, as they have stated it. We should also consider the attitude of state and city health officials toward spray residues. Finally, we should consider the present and probable future attitude of the consuming public, which is, in the final consideration, first in importance.

The attitude, activities, and powers of the federal government have been described recently in an article by W. B. White,^{2/} United States Food and Drug Administration. The article is part of a symposium on insecticides held by the Division of Agricultural and Food Chemistry at the 85th Meeting of the American Chemical Society. The title of the article is "Poisonous Spray Residues on Vegetables," but the article itself is not confined to vegetables. The principles apply to all horticultural crops and to foods in general. I shall quote somewhat at length, but, because most of you are fruit growers, I shall quote nothing that is not strictly relevant to the fruit growing industry and to the subject with which this paper deals.

"Coming from this laboratory," says Dr. White, "it is natural that the whole problem of poisonous spray residues on vegetables should be discussed from the standpoint of the Food and Drug Administration. The Food and Drug Act was drawn to protect American consumers against harmful, revolting, debased, and misrepresented foods. We are concerned here with the harmful aspect. Vegetables carrying amounts of poisonous spray residues which may render the food injurious to the health of any citizen are within the ban of the statute. It is thus our clear duty in the interest of public health to impound all interstate shipments of sprayed or dusted vegetables which are capable of causing the slightest measurable derangement in the health of any consumer. Economic disturbances resulting from such regulatory action must be subordinated to this aim. The spray residue problem is no new one, having grown in the last fourteen years until it is now absorbing about one-third of the total appropriation of this bureau.

"There is a prevailing misapprehension, especially in the minds of those whose interests are involved, that because they themselves have never been seriously injured by contact with spray materials or by eating sprayed vegetables, that there is no danger to human health involved. What chiefly concerns regulatory officials is not immediate acute effects easily diagnosed and resulting in serious illness or death, but rather those more remote and insidious chronic effects which follow the frequent administration of small amounts of poison over a period of several years. Many rumors of death or serious illness from spray residues have been run down, but it is only in rare instances that the cause has been traced to this source.

^{1/} From a paper presented before the American Pomological Society and the Connecticut Pomological Society, meeting together at Hartford, Connecticut, December 12, 1935.

^{2/} W. B. White. Poisonous Spray Residues on Vegetables. Ind. and Eng. Chem. 25, 621, 1933.

"From the abstract public health standpoint, there can be no quarrel with the view that the safest course is the complete abandonment of poisonous sprays. However, since we are not operating under the Napoleonic code, the nature of American criminal law is such as to render it difficult to prove the potential danger to human health of traces of certain substances well known to be poisonous when present in relatively large amounts. The liberal Supreme Court opinion in the celebrated bleached flour case goes far, in that it is required to prove only that the harmful ingredient must be present in such amounts as to have the possibility or probability of affecting the health, not only of those in the vigor of youth, but the young, the aged, and the sick.

"The present so-called world tolerance for arsenic, of 0.01 grains of arsenious oxide per pound of food, dates back to 1900, when in England and Wales more than six thousand persons were made ill, and seventy of them killed by the consumption of beer containing traces of arsenic-----Whether the recent work of Myers, Thone and their co-workers may set an even more drastic limit remains to be seen. We have prepared the following brief summary of a paper by Wright, Sappington and Rantoul based on the findings of the Industrial Clinic of the Massachusetts General Hospital.

" 'About 11 percent of all the cases of lead poisoning in the Industrial Clinic of the Massachusetts General Hospital, over the period of 1911-1933, were non-industrial in origin. One hundred and two cases were from families consuming drinking water flowing through lead pipes. Of all persons exposed, about 25 percent showed gross symptoms of lead poisoning--namely, a blue line about the gums, stippled blood cells, and in many instances, pallor, weakness, and digestive disturbances. Fourteen persons ingesting as little as 0.1 milligrams (about .0015 grains) daily of lead over an average period of $8\frac{1}{2}$ years, exhibited these symptoms. It is pertinent to observe that one moderately sprayed apple might readily contain more than 0.1 milligrams of lead unless subjected to appropriate cleansing treatment.' " (This is a conservative statement. Washed apples carrying the present tolerated amount of lead, if each apple weighed one-third of a pound, would carry .0027 milligrams of lead.)

To continue my quotation: "Because of the presence in such amounts of a cumulative poison like arsenic in foods against which regulatory officials are powerless to proceed (i.e., foods naturally containing arsenic, which has certainly not been added, such as codfish, which contains .014 to .038 grains per pound) these officials must be doubly vigilant against those foods, such as sprayed vegetables, where the arsenic is unquestionably an added substance." (The same attitude applies, of course, to lead.)

Dr. White concludes his article by describing federal authority and procedure. This is the final statement, "Foods carrying spray residues of arsenic, lead or fluorine cannot be impounded unless it can be established in court that food carrying the amounts actually found may be, beyond a reasonable doubt, dangerous to human health."

My statements above are quoted from a symposium held by chemists. I wish to quote now from a symposium held by public health officials. This symposium took up one session of three sections of the American Public Health Association at its annual convention this year at Milwaukee. My quotations are from a summary of my own notes, taken at the meeting. Points not already covered which describe the

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attitude of the Federal Food and Drug Administration were presented in a paper by W. S. Frisbie, Chief, Division of State Cooperation, Food and Drug Administration. They are as follows:

"Medical expert testimony has been necessary. Court verdicts have been favorable to the Food and Drug Administration. A large number of pharmacological experts have been consulted, which has assured the officials that their course was not arbitrary. Acting as a committee, these experts assured the officials that lead was more undesirable than arsenic. A lead tolerance was not applied until 1933, when the development of a rapid method of lead analysis made enforcement possible.

"Federal tolerances are not entirely effective without state tolerances and the Federal government is not at all happy about the reluctance of states to apply intrastate tolerances. There is no general disposition in this direction in the East. Toxicologists recognize the danger of minute amounts of lead, but the industry has not yet recognized the seriousness of the danger. Just recently two states, one in the East and one in the Middlewest, have taken steps to make analyses for apples in interstate shipment and have broadcast a warning that state tolerances are contemplated. The Federal government will continue to exercise vigilance against all toxic materials."

I believe that the attitude of Federal officials has been adequately described. At the same symposium several state and city officials presented papers. Typical statements were these, made in a paper, entitled "Spray Residues from the Viewpoint of the City Health Officer," by Dr. George H. Becker, of San Francisco.

"Acute poisoning seldom occurs, but chronic diseases are sometimes produced after a series of years. The demand for evidence of toxic effects is due to ignorance of chronic effects. Enforcement must be more rigorous. Tolerances in themselves are not necessarily sufficient protection."

Other typical statements, by Dr. Williams, Commissioner of Public Health, Baltimore, were that "officials around Baltimore have studied the literature, they conclude that the slogan that an apple a day keeps the doctor away is misleading, and they favor a slogan to the effect that an apple a day leads the doctor astray."

During the discussion which followed the papers, the question of "sub-chronic effects" was raised.

Unless the tolerance can be met, none of this is good news for the apple grower. It will be observed that the attitude of officials in general is consistent. We know that federal officials are successful in enforcement. Also, judging by the above statements and by past events, they have enough expert backing and court support to go still further.

Finally, what is the attitude of the layman? By layman I mean the man who is neither a horticulturist nor a health official. If he has read "100,000,000 Guinea Pigs" by Kallet and Schlink, of Consumers' Research, and there is a good chance that he has, his attitude toward consuming apples, either personally or by members of his family or by his friends, is probably not favorable. In that widely read, frequently quoted, and attractively written book, arsenic and lead on apples is mentioned repeatedly and discussed at length. Public health officials are severely taken to task for their leniency. On the second page where it can scarcely be missed

we find this attention-compelling question: "That big, juicy apple you have at lunch--do you know that indifferent Government officials let it come to your table coated with arsenic, one of the deadliest of poisons?" It would be a waste of time to speculate on the effect of this book and similar publications upon apple consumption except, perhaps, to say that it must be considerable. One can assume, also, that it will have an effect upon legislation. Because of the force with which its authors make their statements, the book is likely to be accepted in its entirety. It is not too much to say that this book would be likely to sway medical opinion, even without such forceful statements in the medical literature as the following, which is quoted from a current issue of the Journal of the American Medical Association:¹

"Lead poisoning may well be thought of as a counterpart of syphilis, not only in the variety of its effects on the human system, but in the manner in which it may be dormant and unsuspected in the tissues for years, apparently innocuous, until some alteration in the metabolic processes liberates it with unimpaired venom. Like syphilis, it is a contributing cause of many a death for which it does not receive its rightful share of blame."

I do not need to discuss at length the general necessity for residue removal to meet the present tolerances, or the extreme difficulty in meeting the present tolerances in certain parts of the country. In only one state that has published residue studies that I have seen has it been found unnecessary to wash to remove residue. This state is Connecticut, where of nineteen samples of sprayed apples taken in 1932 from sorting tables and shipping containers in different parts of the state, only one sample contained as much as one-half the tolerance.

It is also unnecessary to describe in this paper the search for other sprays, which may, of course, solve the problem. Predictions of failure or success in this search are futile. We can only accept the situation as it is, with lead arsenate the only insecticide generally recommended for commercial codling moth control.

The question which, I hope, naturally arises at this point is: What is the actual evidence of danger to the consumer from eating apples carrying the amounts of lead and arsenic now tolerated? Is the general attitude of public health officials, physiologists, toxicologists, and physicians justified? If it is, it should also be our attitude. If it is, the use of lead arsenate should be abolished, and the least that the states could do at present would be to parallel the present Federal tolerances. Is there any evidence that lead can be ingested in minute amounts without accumulation and without harmful effects, either acute, chronic, or "sub-chronic"? In that case, tolerances are justified.

I will answer these questions in order. First, there is no direct evidence that apples carrying the amounts of lead arsenate now tolerated are harmful to the consumer. The case against lead arsenate rests upon indirect evidence, which has many sources. It is built upon the effects of lead in drinking water, in drinks fermented in utensils glazed with a lead compound, in flour, in snuff, in house paint, in face powders, and upon the effects of lead in certain lead-using industries. The toxicity of lead arsenate to humans is a biological problem. Because it is biological, inferences, no matter how plausible, are not evidence. In the form of biology with which I am acquainted, it is not uncommon to find hypotheses built upon inference upset by direct experiment; moreover, the experiment must be as direct as possible. If the toxicity to humans of lead arsenate on apples were to be tested, the weathered lead arsenate that remains on sprayed apples would be used instead of unweathered lead

¹ Epidemiology of Lead Poisoning, A. J. Lanza, M. D., Assistant Medical Director, Metropolitan Life Insurance Co., Jour. Amer. Med. Assoc., 104, 85, 1935.

arsenate or lead arsenate made in the laboratory; the experimental subjects would be human beings, not animals, and the apples would be fed, as well as the lead arsenate.

The slightest need for inference would be ruled out, because inferences invariably involve uncertainties. Because of this lack of direct evidence, the common attitude toward lead arsenate cannot be said to be justified. Moreover, not all physiologists believe that minute quantities of toxic materials are toxic.

The following paragraphs are quoted from an article in "Science" for January 26, 1934, by Dr. John J. Abel, Emeritus Professor of Pharmacology and Director, Laboratory for Endocrine Research, the Johns Hopkins University.

"Let me say to begin with that no one has ever been able to give a concise and accurate definition of a poison that would apply to every one of the many thousands of known poisons. All attempts to do this have simply ended in offering definitions that do not define. The medical jurisprudence of this country and of England has never attempted to define the word poison.

"Nature has not affixed a poison label to any particular substance or class of substances. The pharmacist does that. I have met intelligent people who actually believe that once a poison always a poison, and that it continues to exert its noxious power in some degree to the last molecule. If ten milligrams of nitrate of strychnine be dissolved in five hundred cubic centimeters of sterilized physiological saline solution, each cubic centimeter will contain 0.02 mg of the strychnine salt, but no one in the world could demonstrate either a harmful or a beneficial action after the injection of a half or one cubic centimeter of this solution underneath a person's skin or when so small a quantity as this is taken by mouth.

"The experience of physicians throughout the ages has convinced them that even the most deadly of poisons are entirely innocuous when given in certain minimal quantities. Scientists have arrived at the same conclusion on the basis of their experimental work. To be quite accurate, however, we can only say that neither a harmful nor a beneficial influence can be detected after such minimal doses by any methods known to us at present.

"There is, however, another fact of fundamental importance for everything that is endowed with life, whether it be a plant or an animal or something that lies somewhere between the two. This fact may be expressed as follows: The harmful effects of a large dose of a drug or a poison do not fall off *pari passu* with the diminution in dose. The law of concomitant variation in respect to the two variables does not hold for the living cell. On the contrary, with the diminishing dose there may occur a turnabout in the action of the drug with the appearance of a highly beneficial action, one indeed that is indispensable for the continuance and maintenance of health, as is the case when we pass from the toxic dose of a hormone to its therapeutic dose. Examples of this beneficial action are seen daily in medical practice. Many powerfully acting drugs, to which the popular designation of poison is entirely applicable, such as strychnine, quinine, the digitalis glucosides, certain arsenicals, insulin, parathyroid extracts, the vitamins, and a long list of other drugs illustrate this principle when their dosage is restricted to a certain amount. This fact holds also for other agents of our environment that may be harmful in their action when they come in contact with our tissues in too high a concentration. Sunlight and other forms of radiation are instances in point. In ordinary concentrations

sunlight is beneficial, but it is deadly in its effect on many organisms when they are exposed to it for too long a time. Its scorching action on the skin of adults at high altitudes and in the tropics is well known, and it is also well known that very young children have died as a result of exposure for too long a time to the burning rays of the noonday sun without having been previously inured to its action.

Poisons in Our Bodies

"An excellent illustration of our principle that toxic substances may be highly beneficial and even indispensable to life is furnished by certain poisons that are produced in our own bodies and circulate in our blood, at a concentration below the toxic level. Many will be surprised to learn that we ourselves are walking drug shops, and that an experienced chemist or pharmacologist would have no difficulty in preparing arrow poisons from some of our own organs that would have delighted the heart of primitive man."

There is, moreover, direct evidence that lead itself can be ingested in minute amounts without accumulation; ingested in minute quantities it is not a cumulative poison. This evidence resulted from very extensive work at the Kettering Laboratory of Applied Physiology, which was established at the University of Cincinnati with the immediate object of studying the problem of lead accumulation. Tangible results, pertinent to this point, are summarized by Dr. Kehoe, the Director of the Laboratory, and his associates^{1/} as follows:

"A recent series of articles in another journal has detailed the method and the major results of our studies of lead absorption and lead poisoning during the past ten years. So far as they are concerned with normal lead absorption and excretion, the results may be summarized briefly as follows: 1. Two groups of native Mexican Indians, whose mode of life and environment were devoid of opportunities for contact with the lead-containing products of highly organized and industrial populations, were found to have lead in their blood and to excrete lead in their feces and urine, as a consequence of lead in the soil and hence in vegetation and animal products employed with food. 2. Various groups of healthy children and adults in the United States, with no occupational exposure, were shown to have lead in their tissues and in their excreta, chiefly because of the regular ingestion of lead with their foods. 3. The rate of lead excretion among Americans is higher than that observed in people living under simpler and more natural conditions (native Mexicans) in correspondence with the higher lead content of certain American foodstuffs. 4. Evidence was obtained that the ingestion of these "normal" amounts of lead did not result in steady accumulation of lead in the body. Apparently an equilibrium is reached after a time, so that a substantially constant concentration of lead remains in the tissues, and lead output becomes equivalent to lead intake." It is interesting that the mean normal daily lead intake was approximately 0.25 milligrams (.004 grains). The authors also conclude that the bulk of normal lead ingested with the food is passed through the alimentary tract unabsorbed.

Early last summer Professor Pickett, as President of the American Pomological Society, appointed a committee to formulate lead arsenate research. Certain members of the committee and certain other interested individuals visited the

^{1/} Kehoe, R. A., Frederick Thamann, and Jacob Cholak, Jour. Amer. Med. Assoc. 104, 90-92, 1935.

Kettering Laboratory early in September. Those who made the trip were Professor Talbert of the Missouri Experiment Station, Professors Greene and Kraybill of Purdue, Professor Howlett of the Ohio Station, and myself. Our purpose was to visit the laboratory, to make the acquaintance of the staff, and, if it was possible and desirable, to outline a plan for research at that institution. The laboratory, we found, is remarkably well-equipped and staffed. Physiological lead research with human subjects has been, for a long time, its principal activity. The staff was interested in our problem, and, together, we worked out a plan for research.

This plan calls for work with human subjects who would be fed apples commercially sprayed with lead arsenate. It would call for a very large number of analyses. The immediate object would be to determine the point at which lead arsenate becomes a cumulative poison. The minimum cost would approximate \$20,000 a year, and it would be best to anticipate three years' work.

The cost of the experiment is staggering if we lose sight of the fact that such experimentation offers the only possibility of solving the problem. The monthly cost can be reduced if less work is done, but less work means slower progress. So far, the committee and those of us who visited the Kettering Laboratory have concerned ourselves almost entirely with the formulation of a plan for research, which was the purpose for which the committee was appointed. The possibility of carrying on the experiment depends, of course, upon financing. One way to secure money would be to organize for this experiment all of the industries, societies, and individuals who are directly or indirectly interested, which the American Pomological Society could logically undertake. Representatives and officials of manufacturing companies to whom I have talked all see the need of the experiment, its logic, and its possibilities.

Finally, all of us are agreed, including the representatives of some of the most important manufacturing companies, that the purpose of the experiment is solely to find facts. We believe that it is only upon facts that state and federal tolerances can be intelligently based. We also believe that it is only facts that will satisfy the fruit industry, which criticises the enforcement official for setting the tolerances too low, and the type of critic who says that enforcement is too lax. We are not attempting to embarrass the United States Food and Drug Administration. We feel, in fact, that they will be as much interested in the experiment as state officials and the industries, and that they should be represented in its organization and progress.

I am taking the liberty to quote from a letter written by an official of one of the largest insecticide companies to one of the members of our committee. I am quoting the letter because it shows the attitude that industry is likely to take, if the plan is properly presented, and because it emphasizes what I have just said about the purpose of the experiment.

"You personally, and in fact your whole committee, as well as all of the right thinking producers of insecticides are first of all interested in getting the truth in regard to the possible harmful effect of arsenical residues. We are not merely concerned with proving that our products as now manufactured are harmful to insects but harmless to humans, nor in pointing out inaccuracies in U. S. Department procedure or regularities, but in supporting wholeheartedly any program, governmental or institutional, that will give to the grower a product of minimum cost and maximum efficiency and safety."

Finally, we are fortunate to have available at this time, for this experiment, a staff of men such as that of the Kettering Laboratory, which has a background of several years' experience in lead analyses and lead studies with human subjects, and a laboratory such as the Kettering Laboratory, which was designed and equipped for this specific work.

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