

Presented Before the 23rd Annual Convention
of the
National Wildlife Federation
Sheraton-McAlpin Hotel, New York
Feb. 27, 1959

Panel Discussion: "Chemical Pesticides and Conservation Problems."

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Although I accepted this assignment quite willingly it was not without many misgivings, I assure you. I realize that what I have to say today will be accepted as coming from someone speaking with authority, and yet I fully realize that no one is capable of speaking with authority about exact causal relationships of pesticides and human health. For this and other reasons I should like it to be understood at the onset that I am not speaking as a representative of the Mayo Clinic nor of my associates who practice medicine there. I am expressing my own personal opinion and no other. As an individual who has had considerable experience in the conservation field, a passing knowledge of farm and industrial practices, as well as twenty-five years in the practice of medicine during which time I have seen people from all walks of life and from all parts of the country I feel that I may have some advantage in correlating various aspects of the overall problem of pesticides in forming my opinions. However, such opinions do not necessarily make me an authority.

The "problem" of pesticides has generated considerable heat in the last few years and this largely stems from the unknown effect as yet upon human, animal, aquatic and other biological values. The difficulty has arisen largely because each of us is viewing the "problem" from his own particular sphere of personal interest and specialized knowledge. This understandable situation has given rise to widely divergent views which have never been correlated with the views of those working in different spheres and having different experience. Actually, I doubt that any of us is completely aware of the real magnitude of the problem, particularly when we use the term pesticide. The shorter Oxford English Dictionary defines pest as first, "any deadly epidemic disease or pestilence," or second, "anything or person that is noxious, destructive or troublesome." It is of interest that the term pesticide is not yet included in this all inclusive dictionary printed twenty-five years ago and therefore must be of recent origin. Since the suffix "cide" means to cut or kill, the term pesticide could be of the magnitude of your interpretation of what constitutes a pest. I believe that the present concept of a pesticide, however, is a lethal agent employed to destroy noxious insects and plants. Since the term noxious is also subject to individual interpretation, the problem grows in complexity. When one also realizes that the, as yet, relatively non-specific pesticides in use today cannot discriminate between noxious and beneficial the problem is further compounded. It is of little wonder that it becomes heated when the judgment of the one applying the pesticide must also be questioned as to his ability to so discriminate.

Before proceeding further, I believe that a scrutiny of the objectives of pesticide use is in order. Simply stated perhaps we could agree that our objective in pesticide use is that of providing a more abundant and a fuller life for the majority of involved people by controlling and altering the environment of our habitat. Here, of course, there will

be a wide divergence of opinion as to what constitutes a more abundant and a fuller life. However, I doubt that even in a group of this sort, dedicated as it is to the preservation of desirable natural environmental values, that there are many who would exchange their present day living standard for that of their prehistoric, cave dwelling ancestor. The problem of future change then becomes relative, both as to the means to be employed and the ends to be achieved. However, the past is an accomplished fact and everything that our ancestors did that was considered an advancement to the more abundant life was accomplished by the use of newly developed tools to alter the environment of their habitat. An often neglected or unrecognized corollary of this statement is that our ancestors were able to adjust to these environmental changes of their habitat. Conversely, and it would seem obvious without saying it, those who could not adjust perished and did not transmit their hereditary make-up to that of the surviving population. In other words, this was the survival of those best fitted to adjust to the new environment of the habitat. That fact is still true today and is, of necessity, the crux of my thesis. If, then, you will agree with me that there are certain inherent risks in manipulating our habitat environment by means of new tools, I believe that we could summarize those associated with pesticide use as follows:

1. There is a loss of certain existing environmental values and ecological relationships which are displaced by the resulting new ones, and only time and readjustment will prove which we may need for survival.
2. There is an acquired responsibility to maintain constant surveillance or policing protection of the resulting environment since the introduction of the pesticide must now be a constant operating check in the new ecological balance established by its use.
3. There is a health hazard to existing individuals in the habitat, both from the effect of actual personal contact with the agent and from the need for habitat readjustment.

Actually, because of the ecological implications of each of these three risks they can scarcely be separated, even for discussions sake. However, I will attempt to enlarge upon Risk #3, that is the health hazards or the jeopardy to survival experienced by the individual member of a population subjected to pesticide exposure. Before any such effort can be made it is necessary to attempt to clarify or define many terms or circumstances relating to cause and effect. I hope by this course to bring as much of the picture into focus as possible and avoid as best we can the half truths which can enter such a controversial discussion. There are enough half truths as it is, even when we marshal all of the scientific evidence which we have available, and half truths can lead to individual panic and mass hysteria. There is need to avoid supplying any more ammunition than possible to the ever present paranoid, but still mentally compensated, crank who is back of many of the hysterical crusades which periodically emerge in every period of civilization. While such an individual may serve a purpose, he can still cloud an issue in need of solution for the common good.

Because I believe that the following concepts are either based upon established facts or clinical evidence hard to deny, I present them for your consideration.

1. Pesticidal agents may be of many types such as the inorganic elements of arsenic, lead, sulfur and mercury or the various plant glucosides such as strychnine, curare and digitalis or bacterial by-products such as dicoumarin. The toxicological effects of these agents are well known and will not be discussed. The pesticide of today's discussion is the hydrocarbon both aliphatic and aromatic, and its modified chloro, bromo and nitro forms as well as the saturated and unsaturated and cyclic chain compounds. In fact the multitude of possible chemical combinations is almost beyond imagination and the pesticides of the future potentially would seem to hold promise of great specificity of action putting tremendous power of selective destruction in the hands of the user.

2. It may come as a surprise to many of you to find out that petroleum and the petroleum distillates are the most commonly used, as well as the oldest pesticides of the day. While petroleum, asphalt and tar have been used for centuries it was only about one hundred years ago that kerosene or "coal-oil" was combined with soap as an emulsifying agent and used as a pesticide, especially for the control of the various mites, scales and other pests that damage fruit trees, shrubs and bushes.

The implications of this statement are tremendous from a medical point of view since this categorically puts our gasolines, fuel oils, cleaning fluids, lubricants, solvents and a multitude of other petroleum agents into the class of pesticides whether we like it or not. Consequently, when we begin to look to "pesticides" and their effect upon human health you can see that we are surrounded by potential hazards and it is difficult to differentiate between the multiple exposures as to which might be responsible for any particular pathologic state.

3. The problem of multiple exposures is inherent in petroleum and its distillation products. It has been shown by careful distillation of a single sample from one oil well that more than two hundred different hydrocarbons are present in that sample. It is further recognized that no two oil fields yield a product of the same composition and that many crude oils are rich in the aromatic hydrocarbons, that is, the benzol series notorious in producing such blood dyscrasias as aplastic anemia, leukemia and the lymphomas.

The problem is further complicated by today's refinery change--over to thermal cracking and reforming and more lately to catalytic cracking and reforming which tremendously increases the percentage of aromatic, cyclic and unsaturated compounds. This gives us our high octane fuels, fuel oils, solvents, thinners and multiple basic compounds for a rapidly expanding petro-chemical industry to purify and fabricate into innumerable new products which contribute to today's more "abundant life."

4. When we speak of a pesticide we seldom refer to a single pure compound such as DDT, chlordane, lindane, dieldrin, 2-4-D or others. The next time that you look at an insecticidal aerosol or a can of fly spray I suggest that you read the label. Not only will you find that there is 2 to 5 per cent of one or more of the chlorinated hydrocarbons but that they are suspended in 10 to 14 per cent of "petroleum distillate" together with some suspending or dispersing agent. In the can of bulk spray the "petroleum distillate" may be 99+ per cent with a repellent such as pyrethrines added. It is possible that the aromatic, cyclic and unsaturated hydrocarbons of the "vehicle" may be more important as a toxic agent when inhaled by the human bystander than the DDT or other agent that

is being suspected of mischief. We forget, for example, that in the so-called Gypsy Moth Program one pound of DDT is suspended in one gallon of petroleum distillate (lightly glossed over as "one gallon of light oil") to which is added one quart of zylene which is dimethyl benzene.

5. In spite of toxicological work with animals it is still entirely possible that aromatic hydrocarbons, such as commercial zylene, when added to pesticidal mixtures may be potent cytotoxic agents to the hypersensitive human who inhales them.

6. When dealing with poisons of any sort most of us think in quantitative terms for any given substance. For example, the physician prescribes an accepted quantitative dose of drug to this patient and expects to get a result about in proportion to the mass or quantity given; the toxicologist determines the quantity of a poison which will kill 50 per cent or 70 per cent or 95 per cent of a test animal or insect and expresses his results as LD₅₀, LD₇₀ or LD₉₅; the layman thinks quantitatively when he says "there was enough there to kill a horse." Such quantitative arguments are continually being used to reassure the public regarding the safety of pesticides and toxicological experiments on animals (including human volunteers) are being used as a yardstick for such measurement of safety. Such quantitative reassurance is of small comfort to the hypersensitive individual who reacts qualitatively and dies in spite of the reassurance.

7. In the human race there is undoubtedly a more heterogeneous mixture of protoplasmic characteristics than in any other species. Certainly no two of us react alike to an emotional disturbance and I am sure there is as much variation in our protoplasmic reaction to noxious agents. If this were not true there would be little need for a physician because it is the susceptible individual who "catches cold," contracts pneumonia, gets poliomyelitis, rheumatic fever, acute nephritis, hay fever and asthma, poison ivy, arteriosclerosis, heart disease, high blood pressure and ulcers to name a few. I might add that since modern medicine, in its broad sense, is saving more and more of these susceptible individuals from an early death we can expect an increasing number of them in our expanding population since their protoplasmic variations will be transmitted to their offspring.

In my opinion it is this susceptible or hypersensitive individual who runs the greatest risk of reacting adversely to the various hydrocarbons used as pesticides. It has long been known that chronic intoxication by benzol will produce aplastic anemia, leukemia or lymphomas in certain susceptible individuals while not doing so in their exposed associates. In medicine, practically every new drug that appears is first tried on a hundred or five hundred patients without severe "side-effects." However, by the time thousands or hundreds of thousands of patients have used it, reports begin to appear of susceptible individuals developing severe "side-effects" such as liver damage, hemorrhagic disease, bone marrow failure or other conditions which may end fatally. In fact there is hardly a drug which does not have to be used without assuming a calculated risk and in my opinion the same thing must be said of the pesticides.

8. With many noxious agents intermittent exposures, or exposures repeated after variable lapses of time, may permit the susceptible individual to develop a marked degree of sensitivity so that the next exposure may precipitate a disastrous consequence. Our periodic spray program would be an ideal mechanism to precipitate such a disaster.

9. Multiple exposures complicate our problem tremendously. Not only do our pesticides come mixed in a commercial form for more effective killing power but we are supplied with all of the separate ingredients in our environment to eat and inhale and do our own internal mixing. Reputedly we ingest a goodly amount of chlorinated hydrocarbon in our food and store it in our body fat. Consider then the possibilities of inhaling very significant quantities of the fat solvents while working with gasolines, fuel oils, dry cleaning agents, paint and varnish vehicles and thinners, solvents in the rubber and metal industries, vapors of gasoline and diesel motors constituting a major portion of city smells and smog and perhaps the problem takes on a new complexion as well as greater complexity.

10. In view of the multiple exposures there is the very good possibility, and probability, that many of these agents may have synergistic effects, that is, one greatly enhances the effect of another. For example, in the Merck Index one finds that Piperine "has been used to impart pungent taste to brandy. (It is a) useful insecticide: Harvill, Hartzell, Arthur - - - have shown that Piperine is more toxic to house flies than Pyrethrum, and that a mixture of 0.05 per cent Piperine and 0.01 per cent Pyrethrines is more toxic than 0.10 per cent Pyrethrines."

There is considerable experimental evidence to show that some agents have the ability to block protective mechanism in the mammalian body permitting a second agent to destroy the animal during this refractory state. I believe that such mechanisms are probably in operation when the pesticides impair human health.

In presenting this partial list of factors which have to be taken into account when one talks about the "Health Hazards of Pesticides" I trust that I have shed some light upon the problem and not simply confused it more. It seems to me that both opponents and proponents of pesticide use must be tempered by the responsibility that such complexity conveys.

However, just because one cannot categorically give exact causal relationships of pesticides and health at the moment, it must be remembered that there is always a beginning with every new or novel experience when observation and circumstantial evidence must be used in making decision for action and for opening up areas for research. So far as the pesticides are concerned, we in medicine are largely at the observation and circumstantial evidence stage. I often envy the entomologist who can raise hundreds or millions of insects for controlled experimental laboratory investigation while I struggle with successive patients, each with his own individual protoplasmic variations, piecing together a story of multiple exposures in an uncontrolled environment, and trying to come up with a causal relationship of pesticides and disease states. Little wonder I get irritated when he writes and asks what experimental evidence I have to substantiate my beliefs.

Since I am still in the observation stage, I should like to present a few thumbnail sketches of typical case histories which I feel contain considerable circumstantial evidence.

A man came to the Mayo Clinic because of a severe toxic pruritus which he had had for a period of about four years. Numerous medications had been used but none had seemed to be of any help. Lymph node biopsy finally revealed Hodgkin's granuloma

and his skin complaint was that of an associated toxic pruritus. It was determined that at the onset of his illness, the patient was engaged in a research project at one of the large United States government experimental farms working on the nutrition of hogs. The hogs developed a severe dermatitis during the experiment and the patient had repeatedly and intensively sprayed these animals with an aqueous solution of Lindane.

A farmer with acute and fatal aplastic anemia who had used an insecticidal powder consisting of "75% naphthalen" and its analogues to "scrub" into the backs of his cattle and to put into the nests and litter of his large chicken house throughout the winter.

Farm wife---insecticide power containing "25% benzene hexachloride and its isomers" (actually hexachlorocyclohexane and not a benzol product) to kill flies and insects about the kitchen, back porch, outside toilet and other areas---"could sweep up the flies by the dustpanful"---leukemic reticulendotheliosis with marked bone marrow invasion and depression of all peripheral blood elements.

Ten year old boy--developed acute leukemia shortly after using an entire "bug bomb" "fighting bees" (wasps) in a closed garage.

A business executive--Three week "pack trip" into mountains September to October, -- tents sprayed with insecticides in the evening--Examination in December revealed severe suppression all blood elements. Liver dysfunction (14% dye retention BSP)---. "Disturbed" hyperplastic bone marrows consisting largely of leukoblasts and early erythroid cells. Sixteen months later---slowly improving.

Banker from a small town in Midwest found to have chronic myelogenous leukemia. His major interest outside of the bank was a 200 head herd of registered beef cattle which he continuously cared for---fitted for showing with petroleum distillate containing 40% chlordane.

Building contractor with fatal acute leukemia who, when inspecting his housing development each day, would commonly "varnish a door for exercise" before returning to his office. (Petroleum Distillate)

Farmer admitted to the Mayo Clinic with an acute leukemia---spent a great deal of time during the preceding winter refinishing his furniture--a varnish remover containing "less than 49% benzol plus paint and varnish."

A factory inspector who developed thrombotic thrombocytopenic purpura after a period of painting and decorating his house---seemingly complete recovery after several weeks of steroid therapy and multiple transfusions. Fatal relapse one year later after again painting in his house and garage (in spite of previous advice against it) as well as vacationing in a small closed tent heated by a gasoline lantern and stove because of inclement weather.

A carpenter---Admitted July, 1958---Acute leukemia of myelocytic type. Expired one month later---In his work he set a lot of formica and tile using an adhesive---Washed the excess adhesive off with gasoline after job of setting was complete---Had had two "big jobs" with formica year before with great deal of gasoline exposure---February 1958, had another such exposure followed by "the flu" from which he never recovered-- Undoubtedly the onset of his leukemic symptoms which progressed until his death in August.

A sales executive---diagnosis of acute leukemia. Patient actually was a paint chemist and manufacturer for the first 17 years after getting out of college. Following this experience---sales manager for another paint company. Illness started with redecoration of his own home---work done intermittently by some of his plant employees---painted outside in good weather, inside in bad weather (house closed). Following this, he developed present illness---brought him to the Mayo Clinic. A diagnosis of acute leukemia established--- 6-Mercaptopurine induced a very nice remission---went to Florida to rest and recuperate---did well until the city began to fog the streets and neighborhood with insecticides for mosquito and fly control. The patient returned to the Mayo Clinic with an acute exacerbation of his disease, died after several weeks of supportive treatment with multiple transfusions, steroids and 6-Mercaptopurine therapy.

A housewife---Patient abhorred spiders---in mid-August used an insecticide aerosol sprayer (D. D. T. and petroleum distillates) and very thoroughly sprayed the entire basement, under the stairs, in the fruit cupboards and in all the protected areas---got nauseated and quite ill at the end of this period of spraying---recovered satisfactorily within the next few days. September---repeated the performance on two occasions---got ill on each occasion---began to develop fever, joint pains and malaise---acute phlebitis in the left leg---hospitalized on my service---splenomegaly---blood picture of an acute myeloblastic leukemia---died within the ensuing month.

A lawyer admitted with an acute aplastic anemia. In the preceding few years exposed to considerable "fly spray" but just preceding the present illness the patient inhaled high concentrations of an insecticidal mixture consisting of 4 per cent chlordane in 96 per cent petroleum distillates a "cure" for an upper respiratory infection. With supportive care and avoidance of further exposure the patient seems to have made a complete recovery.

A Puerto-Rican---multiple abdominal masses causing partial bowel obstruction. Biopsy of supraclavicular nodes revealed a lymphoblastic lymphosarcoma for which he received treatment. Exposure history---most of his life he had slept under the protecting cover of a mosquito netting tent---three years ago, the mosquito netting tent had been displaced by a chlorinated hydrocarbon-petroleum distillate spray---several times a week the bedroom was sprayed and closed for a period of time before the patient retired. After three years of this exposure he appeared at the Mayo Clinic with his lymphoma.

A 33-year-old farm wife referred to the Clinic with essentially a pure erythrocytic aplasia. No exposure history to common farm or household agents was obtained. However, it was finally determined that in her music room where she played and practiced her piano for variable times each day, there was a Lindane "fumigator" to keep the room free of moths, flies and mosquitoes. This gadget is a recent addition to American life in which a small container is electrically heated to vaporize Lindane crystals into the air of the room. The patient had been inhaling these fumes intermittently for about a year.

A physician who came to the Clinic because of a severe jaundice and anemia which proved to be an acute hemolytic anemia and associated liver damage---exposure history is interesting since he operates a convalescent rest home which became infested

with roaches about mid-December of 1956. The patient attempted to rectify the situation by using aerosol insecticide spray and he used approximately a "bug bomb" a week working in all parts of the building, about the pipes, mopboards, bottoms of closets and other secluded areas of this 22-room sanatorium. Boxes of supplies coming to the sanatorium were also sprayed to prevent any new infestations. The doctor did all of this work himself and continued for approximately eight or nine weeks, progressively becoming more ill until he became so anemic that he collapsed and had to be hospitalized. He has since made a complete recovery and seems to show no ill effect from his near fatal experience.

Eleven years as pilot of crop dusting planes---numerous chlorinated hydrocarbons ---aqueous solution---worried about exposures---examination reveals early liver dysfunction with 12 per cent dye retention B. S. P.

A businessman---runs cotton gin and a contract crop dusting agency---buys insecticides by truckload and contracts pilots and planes to dust for his customers ---planes loaded near his warehouse---depressed bone marrow for several years.

Fifty-five year old M. D. ---office in old building---roach problem---Used a 25 per cent D. D. T. concentrate suspended in solvent containing "a high proportion of methylated naphthalene and found it to be no more irritating than kerosene" plus an emulsifier of unknown nature. Diluted in water and used as spray---worked most of a Sunday spraying basement and all secluded areas---within a short time began to bruise and bleed---Blood studies revealed severe marrow depression---25 blood transfusions in next 3 1/2 months---34 more transfusions in next critical two months plus treatment with steroid---slow recovery and year later still not back to normal.

I believe that this representative type of case history, of which I have a large number, will illustrate what I mean. In fact, I believe that the vast majority of patients suffering from the blood dysoracias and lymphoid diseases have a significant history of exposure to the various hydrocarbons which in turn includes most of the pesticides of today. A careful medical history will almost invariably establish such a relationship.

HENS-EGGS-AND FUNGICIDE-TREATED AND FUMIGATED GRAINS. -Tetramethylthiuram disulfide (TMTD), Arasan, is widely used as a fungicide in the treatment of commercial seed corn. Ethylene dibromide (EDB), Dowfume EB-5, is widely used to fumigate grains stored in commercial elevators and farm granaries for the control of weevils....In 1955, it was reported that feeding corn treated with TMTD to laying hens resulted in the production of soft-shelled and misshapen eggs....Workers in Israel reported that grains fumigated with EDB, when fed to laying hens as part of their ration, resulted in a gradual diminution in egg size and, in extreme cases, to complete cessation of egg production. ...During 1957, an egg producer in South Carolina, maintaining flocks totaling up to 10,000 birds, complained of a diminution in egg size and number after feeding oats as part of the laying hens' ration. The oats had been treated with the grainsfumigant EDB. The birds laid numerous so-called "pee-wee" (less than 18 oz. per dozen) and small (less than 21 oz. per dozen) eggs. The egg size improved when the fumigated oats were withheld but did not return to normal. ...Feeding trials (revealed that) corn containing tetramethylthiuram disulfide (TMTD) ...fed to laying hens may have disastrous effect on egg production even when such grains are heavily diluted with nontreated corn.-B.W. Bierer, V.M.D., and C.L. Vickers, D.V.M., The Effect on Egg Size and Production, of Fungicide-Treated and Fumigated Grains Fed to Hens, *Journal of the American Veterinary Medical Association*, May 15, 1959.-*J.A.M.A.*, Aug. 29, 1959, page 2159.

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Reprint No. 105
Price - .20¢

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Milwaukee 1, Wisconsin