Updating Treatment of Pesticide Poisoning

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Except in life-threatening emergencies, it is advisable if not essential to obtain a reasonably complete history and perform a physical examination before making a final diagnosis, much less treating any illness. It sounds perhaps silly to start talking this way, but few medical practitioners require or obtain a sufficiently thorough and accurate history of exposure and clinical course of pesticide poisoning before instituting treatment. They accept the diagnosis of the patient's family or other informers. Even before it became popular amongst ecologists, environmentalists and other exaggerationists (including a few physicians) to blame poliomyelitis, neuropathies, blood dyscrasias, cancer, psychiatric and other diseases upon pesticides, there was and there still exists a tendency to accept pesticides as a cause of illness without sufficient confirmatory medical evidence. Faced with history of exposure to pesticides, they ignore the incidence of the same diseases expected in non-exposed population. Moreover there exists no good all-inclusive definition of pesticide poisoning.

The majority of original reports of illness suspected to be caused by pesticides in my twenty-five years of pesticide practice have not been confirmed as pesticide poisoning when carefully scrutinized by thorough history, physical examination, adequate laboratory work, good differential diagnosis and - if need be - therapeutic trial. Too often the primary physician accepts half-way or reasonable plausible association of time sequence of <u>sometimes insignificant</u> pesticide exposure with onset of illness not otherwise explained. Diagnosis <u>by default</u> or making pesticides a scapegoat in half-complete differential diagnoses has resulted <u>too</u> often.[1, 2] There has even been the tendency to attribute symptoms and signs of illness totally unrelated to the known modes of action of pesticides without any effort being made to explain why this aberrant phenomenon should be attributed to pesticides. This is especially frequent in cases covered by occupational insurance. Some

clinicians feel no obligation to make their diagnoses fit what is known about illnesses caused by pesticide formulations. They have acted as if the M.D. degree or some other doctorate confers some halo giving them a right to make any diagnosis they choose irrespective of its clinical or epidemiological merits and defensibility - and perhaps in the past they have had this right legally. Moreover, some careless editors of otherwise reputable journals published these bizarre case reports of disease attributed to pesticides without clinical toxicological editing. Some have been totally inconsistent with known or even reasonably speculated pharmacologic or toxicologic modes of action. Most such articles have failed the test of time. It is interesting to speculate on whether peer review by the Professional Standard Review Organizations will partially rectify this malpractice.

In the theme of this occupational conference, it is sad to report that my own Washington State Industrial Insurance Program has adopted the financially sound management policy of trying to refute all proven or strongly presumptive pesticide poisonings and attribute findings to some non-occupational syndrome. What is worse morally, the state insurance will not pay for differential diagnoses that rule out pesticide poisoning even after significant exposure. This has of course caused many physicians to diagnose poisoning following exposure whether they really believe it was causative or not. Otherwise, their services may not be compensated. Such poor practice must go on in other states that have the same policy.

The foregoing negativistic statements should not be construed as failure to recognize that there has to be a first time for every prior unknown mode of action to be diagnosed and/or published. However, in most of these new findings, the author was usually constrained to offer reasonable new proof or plausible presumption to explain his findings and interpretations.

The foregoing must also not be construed as failure to recognize that it is also necessary to institute treatment in emergencies or with inadequate history until the additional data can be collected either by the diagnostician, his staff, or other helpers.

The history-taker must listen carefully to the patient or other informant expecting this history to be incomplete or wrong in the majority of cases but tragically or classically correct and complete in a significant minority percentage of instances. Possibly in the industrial setting, the majority of illnesses blamed originally on pesticides can be substantiated diagnostically.

The most courageous - and yet legally dangerous - tactic that a physician can practice is to withhold or delay treatment in mild to moderate illnesses that follow significant or uncertain exposures. Whenever he does this, he should of course be as thorough as practical in seeking to establish all other differential diagnoses. Too many handbooks or textbooks on diagnosis in toxicology fail to emphasize the need for exercising conservative judgment in attributing illness to pesticides.[3]

An additional problem, often overlooked in correctly diagnosing diseases caused by pesticides is that many formulations of pesticides cause diseases by chemicals <u>other</u> than the primary intended ingredients such as solvents, carriers, adjuvants, precursors, side reactants, interactants, decomposition products and even reconjugation of molecular moities of the pesticide. [3] Dr. Thomas Milby published a classical illustration in the instance of furfural, the precursor of malathion, causing dermatitis in various malathion formulations.[4] One of the most recently recognized potential hazards of poisoning by other than the active agent is that of carcinogenic asbestos up to 3% in many dusts, pellets and pills of pesticides and drugs.

Undertreatment by physicians inexperienced in poisoning has long been a problem of the consulting toxicologists especially in those cases requiring atropinization of severe anticholinergic crises. There seems simply no arbitrary limit to the single or total dosage of atropine required to titrate any given severe organic phosphorus poisoning especially after ingestion or massive occupational exposure. Neither has there been established any such arbitrary limit for the cholinesterase-reactivating antidote pralidoxime (2-PAM).

Overtreatment with atropine even to death has occurred where the therapist has used a single therapeutic response such as heart rate or miosis without recognition that the entire patient's vital signs and response must be followed, especially pupillary dilatation, heart rate, lung wetness, tearing and sweating to decide when atropinization is sufficient to taper off or discontinue.

There has also been overtreatment with pralidoxime after the drug has reactivated all the cholinesterase necessary to re-establish nerve conduction merely because all the signs and symptoms had not been relieved. Also in cases of ingested organic phosphorus pesticides dissolved in Xylene, continued use of higher doses of pralidoxime does no known good after cholinesterase has been reactivated to maximal levels during increasingly permanent phosphorylation by some of the organic phosphorus compounds.

In certain cases of massive ingestion of such things as parathion, malathion and paraquat, no one in this country has had the courage to surgically evacuate the gastro-intestinal system, but I am convinced this is the only way to save some lives.

One of the most inexcusable forms of overtreatment has been the use of atropine or pralidoxime in regionally anatomically restricted topical anticholinergic poisoning such as unilateral or bilateral miosis, brief bronchogenic constriction from breathing vapors or dilute dusts for short times. The only treatment these cases need is diagnosis of topical organic phosphorus poisoning, discontinuation of exposure, reassurance, and perhaps intelligent observation for the hours necessary to assure spontaneous recovery during judicious medical neglect.[5]

Failure to recognize psychogenic nausea and vomiting has caused many over-treated illnesses and much undue public, political, and economic concern. Washington and Texas have seen at least three outbreaks of psychogenic nausea, vomiting and even public hysteria in corn pickers, school

children, and others exposed to the nauseating odors of the mercaptan-producing formulations of disulfoton (Di-Syston) and Thimet (phorate).[6]

Some of the older pesticides like sulphur, the polysulphides, and nicotine have received so little attention in the literature that it was difficult to find appropriate references for the 1969 Report of the Secretary's (HEW) Commission on Pesticides.[7] Yet every older physician in areas of formulation and agricultural use of these pesticides has seen frequent chronic dermatitis from sulphur and polysulphides as well as classic nicotinic signs from over-exposure to nicotine.

Increasing reliance upon organic phosphorus compounds, carbamates, and carbamoyl oximes as substitutes has followed the limitations of usage of the chlorinated hydrocarbons with attendant greater occupational hazards from production, shipment, storage, and dispersal. This means physicians must expect greater frequency of anticholinergic poisoning even though it may be of briefer, self-limited duration if due to carbamates and more dramatic if caused by the carbamoyl oximes.

Propoxypur (Baygon or isopropoxy phenyl carbamate) has caused up to 100% attack rates of mild anticholinergic poisoning among the household spraymen of the World Health Organization and in about 1% of household residents. Their signs and symptoms disappear rapidly without treatment after exposure is terminated even when they can not decontaminate their skin and clothing as thoroughly as they should.[8] Usages of Baygon approved in the United States have not caused the expected occupational poisoning to my knowledge even though there has been growing reliance upon it.

DDVP formulated in one of the plastics has produced a chronic dermatitis beneath flea collars in dogs and reportedly in veterinarians or other dog handlers but details have not been published.[9] Neither has the skin irritant been even suggested. Some DDVP solid formulations were suspected to be suspended in polychlorinated biphenyl or polychlorinated terphenyl solids that may contain polychlorinated dibenzofurans.[10]

Parathion and certain carbamate applications have continued to cause since 1948 epidemics of mild or moderate and rarely severe poisoning in workers who enter treated crops either the same day or before the residues had sufficient hours to decay. In California this problem is somehow inexplicably clinically more frequent and more serious with valid reports of parathion poisoning in peach pickers extending out to 40-odd days or more after last application.[11] Also authorities in California and a few other states with similar climates, together with some national authorities, believe that some other organic phosphorus compounds alone or in combinations cause poisoning in those who enter crops too early after application. This so-called "Early Entry Poisoning" has been a great debatable issue in recently proposed legislation to eliminate this form of occupational poisoning. It is regrettable that this issue has been contended mostly in the political, legal, and judicial arena instead of in scientific circles where it should be settled. As far as I know, no one has published a diagnostic review of crop workers or early entry poisoning with great care given to critical confirmations of etiology. How can we expect our politicians and legislators to draft correct practical laws or regulations when there is no reasonable agreement among the physicians diagnosing, treating, and trying to prevent recurrence of early-entry poisoning?

Sometime prior to October, 1973, Dr. Joseph Holmes and his co-workers of the University of Colorado treated two cases of mevinphos (Phosdrin) poisoning[12] adding to those treated during the preceding decade or more.[13,14,15] One of these agricultural workers showed marked improvement following intravenous atropine as well as greater improvement following intravenous pralidoxime (2-PAM), the second not given 2-PAM. The younger worker had microscopic hematuria, but the clinical description indicates catheterization as the early cause of red blood cells. However, hematuria persisted for eight days following withdrawal of the catheter as was found in seven other cases of organic phosphorus poisoning previously reported by the senior author. This young greenhouse sprayman also complained in his Mexican Spanish of "burning of the eyes" that may be a newly observed symptom or an interpreter's

error. Hypercoagulibility was temporarily increased in one of these cases as reported by the senior author 13 years previously in other organophosphorus poisonings. Increased fibrinolysis was observed in the second case. Neither of these laboratory findings was directly related to the clinical picture. A satisfactory mode of action for the hematuria has not been proposed.

In preparation for this publication, your author has discussed with several other clinical toxicologists the future impact that peer review of all hospitalized illnesses by the Professional Standards Review Organizations (PSROs) is having or will have on the diagnosis and treatment of occupational pesticide poisoning. No significant suggestions were made except that there are insufficient physicians trained in clinical toxicology to treat or consult in diagnosis and treatment occurring in pesticide poisonings. In such a controversial field, it remains to be seen whether PSROs will require physicians <u>not specialized in toxicology</u> to judge the indication, adequacy, duration and therefore the cost of treatment procedures. I would appreciate referrals of records of all such paradoxical administrative procedures.

In August, 1974 after eight years of formative planning, the American Academy of Clinical Toxicology has just announced its first examination for Board Certification in Clinical Toxicology to take place in Denver, Colorado in February, 1975. Anyone interested this year may apply before a November date. Board Certification hopefully is to be recognized and sponsored by the American Medical Association. It should lend to diplomates a formal recognition of their training, experience, and qualifications in treatment of poisoning. This is expected to be one basis to warrant fee schedules and salary levels parallel to certain other Board Certifications above that of non-certified physicians. This should also clarify eligibility for peer review by PSROs of clinical toxicological management in all private hospitals and government-controlled diagnostic and treatment facilities.

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