The New England Journal of Medicine

Owned and Published by the Massachusetts Medical Society

CHANGING PROFILE OF PESTICIDE POISONING

SINCE 1945, some 15,000 individual compounds and more than 35,000 different formulations have come into use as pesticides. During this period, as a result of the widespread use of these agents, and particularly the organophosphorus insecticides, physicians have been called on to diagnose and manage a large number of poisonings. Most frequently, these present as life-threatening cholinergic crises, with miosis, sweating, and salivation, but with appropriate therapy, including the administration of atropine and pralidoxime, recovery usually follows within a few days.

In some cases of organophosphate pesticide poisoning, the cholinergic phase may be followed by a delayed peripheral neuropathy involving the distal muscles of the extremities. This neuropathy appears two to five weeks after a single exposure. The syndrome is distinct from the acute cholinergic-toxicity phase and involves phosphorylation and inhibition of an enzyme called neurotoxic esterase and then degradation of the phosphoryl–enzyme complex. A rapid onset of a distal and symmetrical sensorimotor polyneuropathy following a recent organophosphate exposure is considered diagnostic.[1]

In this issue of the *Journal*, Senanayake and Karalliedde[2] describe yet another manifestation of neurotoxicity following the cholinergic illness of organophosphate poisoning. A paralytic syndrome was observed in 10 of 95 patients with organophosphate poisoning that they treated. Muscle weakness developed 24 to 96 hours after the cholinergic illness, involving primarily the proximal limb muscles, neck flexors, certain cranial motor nerves, and the muscles of respiration. Because of weakness of the muscles of respiration, seven patients had difficulty breathing and three died from respiratory failure. This condition, which the authors call "an intermediate syndrome," was not responsive to atropine and pralidoxime and required urgent ventilatory support. The

PROSPECTIVE authors should consult "Information for Authors," which appears in the first issue of every volume and may be obtained from the *Journal* Editorial Office (address below).

ARTICLES with original material are accepted for consideration with the understanding that, except for abstracts, no part of the data has been published, or will be submitted for publication elsewhere, before appearing here.

NOTICES should be sent at least 30 days before publication date.

THE *Journal* does not hold itself responsible for statements made by any contributor. Statements or opinions expressed in the *Journal* reflect the views of the author(s) and not the official policy of the Massachusetts Medical Society unless so stated.

ALTHOUGH all advertising material is expected to conform to ethical standards, acceptance does not imply endorsement by the *Journal*.

FOR information on subscriptions, permissions, reprints, and other services see the "Business Information for Readers" page preceding the Classified Advertising section.

EDITORIAL OFFICES: 10 Shattuck St., Boston, MA 02115.

BUSINESS, SUBSCRIPTION OFFICES: 1440 Main St., Waltham, MA 02254.

chemicals responsible were fenthion in four cases, monocrotophos in two, dimethoate in two, and methamidophos in one.

For several reasons, this description of a new neurotoxicologic manifestation of organophosphate poisoning has features that are of substantial medical and public health importance. Most obviously, in order to avoid possible respiratory collapse in the early days after poisoning, patients who have recovered from the cholinergic illness should not be discharged too early and should stay within easy reach of ventilatory support. They should also be informed of the possibility of a relapse and told to contact the attending physician at once if breathing problems develop during the period of convalescence.

A second interesting point relates to the setting in which this new syndrome has been identified. Past surveys have shown that organophosphate poisonings have been common and severe in Sri Lanka. In a survey of patients hospitalized between 1975 and 1980, it was found that 79,961 patients were admitted because of pesticide poisonings and 6083 of them died. Thus, yearly attack rates in Sri Lanka approximated 13,000, and there were approximately 1000 deaths per year.[3] Organophosphate compounds caused most of these poisonings (76 percent). More detailed analysis of the data for 1979 showed that accidents and occupational exposures were responsible for about 25 percent of the cases, and attempted suicide about 73 percent. In an earlier report[4] on the delayed peripheral neuropathy after methamidophos poisoning in Sri Lanka, Senanayake and Johnson found that 7 of their 10 patients were poisoned in suicide attempts. Thus, not only were there many cases of organophosphate poisoning in the country, but most of them were clinically severe because they were the result of suicide attempts.

Now, with the recognition of another neurologic sequela of organophosphate poisoning in Sri Lanka — the intermediate syndrome — one must ask why neurotoxic sequelae seem to be observed so much more frequently in organophosphate poisoning there than elsewhere. Are there special unrecognized factors contributing to the different types of neurotoxicologic manifestations?

One possibility is contamination of the compound by an impurity. This seems an unlikely explanation for the intermediate syndrome since four different compounds were involved. Another possibility is that there is an interaction of the organophosphate pesticides with other pesticides. However, since a suicide attempt is the most frequent cause of poisoning, ingestion of the large doses of chemical that usually occurs with suicides, together with earlier atropine and oxime therapy for the cholinergic phase of the illness, may be the most plausible explanation for the unusual frequency of peripheral neuropathies. It has been shown experimentally that with certain organophosphate compounds, the potential for a delayed neuropathic reaction can be demonstrated only by first protecting and pretreating the animals with atropine and oxime and then challenging them with a dose of organophosphate that exceeds the mean lethal dose.[5]

Although reliable statistics on pesticide poisoning are hard to come by, there is growing evidence that this is a serious public health problem in many developing nations, and one that is not limited to persons attempting suicide.[6,7] On the other hand, the problem of suicide is a major concern in the Third World, and ingestion of chemical pesticides is probably one of the most common current methods of attempting suicide.

Much can be done by both pesticide-importing and pesticide-exporting countries to prevent poisonings by pesticides. In many Third World countries, it is easy to find potentially dangerous situations that set the scene for pesticide poisoning.[8] The sale of pesticides in shops, where anyone may purchase the most toxic chemicals, is one example, and others include the formulation and repackaging of pesticides by local vendors in whatever containers or unlabeled bottles are available, the use of pesticides to kill fish raised in fish farms for human consumption, and the sale and reuse of pesticide-contaminated drums. New methods of educating individual users, particularly small farmers, are also needed.

At the level of the exporter, the growing number of training programs on pesticide safety and the printing of pamphlets and brochures by the chemical industry are steps in the right direction.[9] Research into safer methods of packaging and disposal, and the blending of emetic or malodorous materials with the more hazardous agents are other measures that may ameliorate the situation. Only through such efforts can we reduce the problem of acute pesticide poisoning and, more specifically, the special problems associated with its neurotoxic sequelae.

University of Miami
School of Medicine
Miami, FL 33176

JOHN E. DAVIES, M.D., M.P.H.

REFERENCES

1. Davis CS, Richardson RJ. Organophosphate compounds. In: Spencer PS, Schaumburg HH, eds. Experimental and clinical neurotoxicology. Baltimore: Williams & Wilkins, 1980:527-44.
2. Senanayake N, Karalliedde L. Neurotoxic effects of organophosphorus insecticides: an intermediate syndrome. N Engl J Med 1987; 316:761-3.
3. Jeyaratnam J, de Alwis Seneviratne RS, Copplestone JF. Survey of pesticide poisoning in Sri Lanka. Bull WHO 1982; 60:615-9.
4. Senanayake N, Johnson MK. Acute polyneuropathy after poisoning by a new organophosphate insecticide. N Engl J Med 1982; 306:155-7.
5. Johnson MK. The delayed neuropathy caused by some organophosphorus esters: mechanism and challenge. CRC Crit Rev Toxicol 1975; 3:289-316.
6. Davies JE, Lee J. Changing profiles in human health effects of pesticides. Presented at the Sixth International Congress of Pesticide Chemistry, Ottawa, Canada, August 10 to 15, 1986. abstract.
7. Davies JE, Smith RF, Freed V. Agromedical approach to pesticide management. Annu Rev Entomol 1978; 23:353-66.
8. Bull D. A growing problem: pesticides and the Third World poor. Oxford: Oxfam Public Affairs Unit, 1982.
9. Litchfield MH. Measures for the prevention of accidental pesticide poisoning. Presented at the American Chemical Society Symposium of Safe Production and Use of Pesticide in Developing Countries, New York, April 16 and 17, 1986.