months. At that time she had had a histologically confirmed squamous cell carcinoma of the left ear treated by radiotherapy, which resulted in total deafness in that ear.

During 1984 she presented with a polypoid mass in the right external ear canal. Histological examination confirmed a squamous cell carcinoma. CT failed to show any bony involvement and no brain metastases were demonstrated. No neck glands were palpable.

Exploratory mastoidectomy revealed that the tumor had eroded the posterior portion of the bony canal wall, reached as far as the dura, and infiltrated the lateral semicircular canal. The facial nerve was widely exposed but not yet obviously infiltrated.

It was decided to give the patient radiotherapy because of her age, concomitant diabetes mellitus and controlled congestive cardiac failure. Two years later she is doing well, according to her family physician. Unfortunately she is not able to return for assessment but she apparently has reasonable hearing with the help of the hearing aid she had been using previously.

REFERENCES

Chorea and psychiatric changes in organophosphate poisoning
A report of 2 further cases
J. JOUBERT, P. H. JOUBERT

Summary
The acute muscarinic and nicotinic side-effects of organophosphate poisoning are well known. Less commonly encountered are neurological symptoms such as chorea and psychiatric disturbances such as psychoses and depression. Two patients with organophosphate poisoning are described, both exhibiting marked choreiform dyskinesias and one experiencing severe depression and emotional lability. Both responded well to the appropriate treatment. Because of the widespread use of organophosphate insecticides in agriculture, the neurological and psychiatric effects of chronic low-dose exposure to organophosphates in farmers and their employees deserves attention.

Since 1952, when Schrader1 synthesised approximately 2000 organophosphate compounds, they have been used as agricultural insecticides world-wide. Their toxicity in man is well documented.2 The usual cause of intoxication is accidental exposure of agricultural workers. Organophosphate compounds, being lipid-soluble,3 are readily absorbed by the alimentary tract, respiratory tract and skin.4 Because of their easy availability, suicidal or homicidal use of these substances may also occur.4

The deleterious effects are caused by the potent anticholinesterase activity of these compounds. The most commonly encountered toxic effects in man are peripheral. Muscarinic effects such as pupillary constriction, excessive secretions and gastro-intestinal symptoms are common in acute intoxication. Nicotinic symptoms include muscle fasciculations, weakness and even paralysis. Respiratory paralysis may lead to death.4 The chronic effects on the peripheral nervous system are mainly those of a demyelinating neuropathy as described after ingestion of organophosphate-contaminated Jamaica ginger during the prohibition years in the USA.5 The central nervous system effects of organophosphate intoxication have received less attention in the medical literature than peripheral effects. Animal studies have revealed cerebral oedema after acute organophosphate exposure,4 whereas persistent electro-encephalographic (EEG) abnormalities7 and spasticity7 can occur after chronic exposure. Acute manifestations of central nervous system involvement are convulsions, which can be antagonised by atropine,1,5 and mental disturbances such as anxiety, restlessness and emotional lability.6

Psychiatric symptoms. Tabershaw and Cooper10 noted that certain patients displayed vague mental changes such as irritability, memory disturbances and dream abnormalities for several months after their apparent recovery from organophosphate poisoning. In 1950, Rowntree et al.11 described an increase in depression and an amelioration of the manic symptoms in manic-depressive patients after exposure to organophosphates. Gershon and Shaw12 described the development of schizophrenic or depressive symptoms after exposure to organophosphate insecticides.

Chorea. To our knowledge, before the report in 1984 of a patient presenting with chorea after ingestion of organophosphate insecticide,12 this symptom had not been recorded as a manifestation of organophosphate intoxication. Two further cases of chorea occurring after ingestion of organophosphate insecticides are reported.

Case reports
Case 1
A 15-year-old black youth was admitted to hospital on 24 January 1986 from a rural area with a history of having accidentally ingested organophosphate insecticide. On examination the patient was confused, the pupils were constricted and choreiform movements of the right arm and leg were present.

Departments of Neurology and Pharmacology and Therapeutics, Medical University of Southern Africa and Ga-Rankuwa Hospital, Pretoria
J. JOUBERT, M.B. CH.B., M.R.C.P.
P. H. JOUBERT, M.MED. (SC.), F.C.P. (S.A.), D.M.

Accepted: 12 Aug 1987.
The most profound me
mose balance of transmitter systems
= 2000
me
Hb)
of patient 2.

Major neurotrans-

symptoms present in Gershon and Shaw's^ 1985

of the extremities were noted. Both serum and red blood cell

cause irreversible inactivation of cholinesterases in the central

neurotransmitter. Neostigmine and physostigmine that bind acetylcholinesterases irreversibly. Organophosphate insecticides fall into the latter

are, in general, highly lipid-soluble,3 and may

as neostigmine and physostigmine that bind acetylcholinesterases irreversibly. Organophosphate insecticides fall into the latter

nervous system resulting in prolonged effects, as described by

Gershon and Shaw.3

Mental changes

Patient 2 developed severe psychiatric symptoms for the

first time during the recovery phase after poisoning. She had

good insight into her condition, and was more concerned

about her changed mental state than the choreiform move-

ments. She complained spontaneously of severe depression,

emotional lability, forgetfulness, irritability, insomnia and

headache. She said all the symptoms dated from the ingestion

of the insecticide.

An analysis of the symptoms present in Gershon and Shaw's^ 3

series shows a remarkable similarity with those of patient 2.

Table II compares patient 2's symptoms with their prevalence

in the 16 cases described by Gershon and Shaw.3 Clinically,

our patient showed all the signs of severe depression and

emotional lability.

| TABLE II. COMPARISON OF SYMPTOMATOLOGY IN CASE 2 WITH PREVALENCE IN GERSHON AND SHAW'S^ 3 |
|-----------------------------------------------|-----------------|
| Case 2                                        | Gershon and Shaw's^ 3 |
| Loss of memory                               | 50              |
| Depression                                   | 44              |
| Irritability                                 | 25              |
| Headache                                     | 25              |
| Fatigue                                      | 13              |

The mechanism of mood changes and other psychiatric

symptoms is as yet unclear. In case 2, and in 50% of Gershon

and Shaw's^ 3 series, memory loss was a prominent symptom.

According to Davison,15 acetylcholine is the major neurotrans-
mittor for higher cortical functions and mentation, especially

memory. In senile dementia of Alzheimer type memory loss is

severe and the degree of reduction of acetylcholine synthesizing

enzyme (choline acetyltransferase) activity shown in autopsy

studies corresponds well with psychological tests before death16

and the degree of neuropathology present.14,15 It was also

found in autopsy studies that the areas with the most profound

reduction of choline acetyltransferase activity were the hippos-

campus and corpora mamillaria. These structures play an

important role in the co-ordination of memory processes.15

It may be that in organophosphate poisoning the excess

acetylecholine merely upsets the balance of transmitter systems

active in cortical functions or alternatively leads to presynaptic

inhibition of acetylecholine release via a negative feedback loop.

Another mechanism that may be postulated to explain the

psychiatric symptoms is dopamine receptor hypersensitivity as

seen after neuroleptic administration.16 In the corpus striatum,

a balance exists between dopamine as the inhibitory and

acetylecholine as the excitatory system. The balance is main-

tained via the nigrostriatonigral loop. The dopaminergic system

inhibits the cholinergic neurons and vice versa.17 Excessive

acetylecholine, as can occur in organophosphate poisoning,

suppresses dopaminergic activity, and hypersensitivity of post-

synaptic dopaminergic neurons may result.

In case 2 the psychiatric symptoms persisted long after the

serum and red blood cell cholinesterase levels had returned to

normal. It is therefore unlikely that simple accumulation of

acetylecholine at central synapses was the only pathogenetic

mechanism responsible for the psychiatric symptoms.
Choreiform movements

This symptom regressed gradually after administration of atropine in case 1 and improved only after haloperidol in case 2. The mechanism underlying the development of chorea in organophosphate poisoning may be dopamine receptor hypersensitivity, but a second possibility is that the initial excess of acetylcholine at central synapses may, by means of negative feedback analogous to presynaptic negative feedback at α-receptors, inhibit further acetylcholine release from cholinergic neurons. The relative dopamine excess may be manifested as chorea.

Seizures

EEG changes have been noted by several authors. Clinically these are reflected as generalised seizures. Atropine reverses both the convulsions and the cortical depression.

Overt seizure activity seems to be relatively rare in organophosphate poisoning. It was not present in either of our patients and was apparently not encountered in the 16 patients documented by Gershon and Shaw.

Conclusion

Organophosphate insecticides are widely used in agriculture in South Africa and consequently accidental poisonings are not rare. Analysing the admissions for acute poisoning to Ga-Rankuwa Hospital, Pretoria, over a 12-month period from May 1981 to April 1982, Joubert and Sebata found that 11% were pesticide poisonings and more than half of these were the result of organophosphate ingestion. Similarly, the incidence of organophosphate as a cause of death owing to acute poisoning among whites in the Bloemfontein area was 20.4% and that of blacks was 18.3% of all poisoning deaths per year. Thus the importance of organophosphates as a cause of acute poisoning in both the white and black communities of South Africa cannot be underestimated.

Although the acute muscarinic and nicotinic side-effects are well known and easily recognised, we have emphasised lesser-known symptoms — chorea and psychiatric changes. Drug-induced chorea is not uncommon, but chorea due to organophosphate poisoning was, to our knowledge, first reported in 1984. Organophosphate poisoning may now also be considered in the differential diagnosis of chorea.

Schizophrenic psychosis or depressive illness may occur after obvious acute organophosphate intoxication or may follow chronic subliminal exposure. This has far-reaching implications for any community such as the South African one, where agriculture forms a large part of the economy. It should be kept in mind that farmers and their employees who develop psychiatric symptoms may well be suffering from chronic repeated low-dose exposure to organophosphate insecticides.

REFERENCES