CHAPTER 8

Pesticides

Chapter outline

In this chapter the toxicity of different types of pesticides will be studied:

- Introduction and types of pesticides
- DDT
- Organophosphorus compounds
- Paraquat
- Fluoroacetate

Introduction

Pesticides are substances which have been designed or chosen for selective toxicity to certain organisms. Although their toxicity *is* selective, they are often also toxic to other species although usually to a *lesser* degree. As well as being of interest in terms of their mode of action they are of concern to toxicologists for two reasons: **(1)** they may be **toxic to man** either in **acute poisonings** or after **chronic exposure**; and **(2)** they have toxic effects on some **non-target organisms** in the environment. This latter point was highlighted in 1963 by Rachel Carson in her book *Silent Spring*.

Human poisonings from accidental exposure to pesticides have occurred since they were first used and in some cases many people have been poisoned, sometimes fatally in single incidents. Many of these cases have been due to accidental contamination of food with pesticides or their inappropriate use (Table 8.1). For example, the use of organic **mercury fungicides** to treat seed grain which is then used to feed animals has resulted in several mass poisonings of humans. Occupational poisoning has also occurred in agricultural workers through accidental contamination or inappropriate use. The careless use of pesticides, such as spraying without adequate protection, may also lead to exposure of the operator.

Chronic toxicity due to the pesticides present in our environment is more difficult to identify although with the development of improved analytical techniques the detection of residues has become easier. Such techniques have

TABLE 8.1 *Mass poisonings due to pesticides*

Pesticide involved	Material contaminated	Number affected	(died)	Location
Endrin	Flour	159	(0)	Wales
Endrin	Flour	691	(24)	Qatar
Parathion	Flour	600	(88)	Colombia
Parathion	Sugar	300	(17)	Mexico
Hexachlorobenzene	Seed grain	>3000	(3–11%)	Turkey
Organic mercury	Seed grain	321	(35)	Iraq
Pentachlorophenol	Nursery linens	20	(2)	USA

Source: *Report of the Secretary's Commission on Pesticides and Their Relationship to Environmental Health* (Washington, DC: US Governmental Printing Office, 1969).

shown that most people in the Western World are indeed exposed to and may have detectable levels of certain pesticides. However, pesticides have become a very important part of our society especially in terms of agricultural economics and, although their use may be curtailed in some instances, it is unlikely to be completely halted when risk/benefit considerations are made.

Pesticides can be divided into several groups, such as **insecticides**, **fungicides**, **herbicides** and **rodenticides**, depending on the target organism. Those that have been specifically designed for a purpose often utilize a particular biological, metabolic or other feature of the target species, but unfortunately such features are *rarely entirely unique* to that species so other similar species may also be affected. A simple example of selective toxicity in a pesticide is the use of **warfarin** as a rodenticide. This depends on the *lack* of the vomit reflex in rats so that they are unable to vomit after ingesting the poison.

Other pesticides depend on more sophisticated biochemical differences. For example, the insecticide **malathion** is metabolized by *hydrolysis* in mammals to yield the acidic metabolite, which is readily excreted (Figure 3.9). In insects, however, the preferred metabolic route is *oxidation* to yield **malaoxon** which is toxic by inhibition of **cholinesterase** (see below). Although pesticides may all be perceived by the general public as equally hazardous to man, they vary in their toxicity to mammals, and other non-target wildlife, and in their effects on the environment

Some examples of the major pesticide types are as follows:

Insecticides: Organophosphorus compounds, carbamate and organochlorine compounds. Natural products such as pyrethrins.

Herbicides: Chlorophenoxy compounds, dinitrophenols, bipyridyls, carbamates, triazines, substituted ureas, aromatic amides.

Fungicides: alkyl mercury compounds, chlorinated hydrocarbons, dialkyldithiocarbamates, organotin compounds.

Rodenticides: inorganic agents, natural products, fluorinated aliphatics, α-naphthylthiourea.

It is clear from this list that pesticides comprise a wide range of chemical types and their modes of action will be very different. However, their

toxicity to man and other mammals may be due to a different mechanism from their pesticidal action.

We will now consider some toxicologically important examples of pesticides.

DDT

Perhaps the best known organochlorine insecticide is DDT, (dichloro-diphenyl-trichloroethane; Figure 8.1). It was introduced in 1945 for the control of **malarial mosquitoes** and was extremely successful, being a major factor in the reduction in malaria after the Second World War. DDT is a contact poison which is highly potent against the insect nervous system but is relatively non-toxic to man. A dose of at least 10 mg kg^{-1} is required for toxic effects to occur in man and no human fatalities have been reported. Indeed human volunteers were induced to take 0.5 mg kg^{-1} (35 mg) daily for over a year and there was no demonstrable toxicity. Although some reports have suggested association between chronic disease and DDT, no causal relationship has been found and other reports have not found such associations. Large doses cause **tremors**, **hyperexcitability** and **convulsions**, **paresthesias**, **irritability** and **dizziness**. In experimental animals liver damage occurs after single large doses and **hypertrophy** and other histological changes in **liver** have been reported after chronic exposure. Toxic effects seem mainly to involve the nervous system in mammals as in insects. The mechanism of action is unknown but the primary site of action is thought to be sensory; **motor nerve fibres** and the **motor cortex** are possible targets. DDT may alter *transport* of Na^+ and K^+ across nerve membranes perhaps by interfering with the energy metabolism required for this transport.

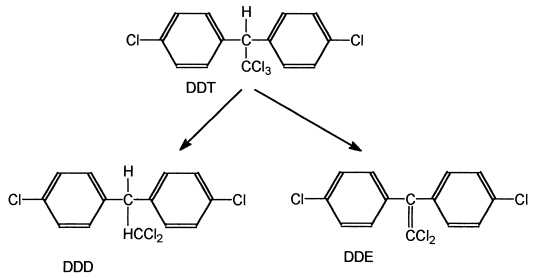


FIGURE 8.1 *Two of the pathways of metabolism of the insecticide dichloro-diphenyl-trichloroethane (DDT).*

DDT is chemically stable, highly insoluble in water, but soluble in body fat and is consequently very persistent in biological systems and the environment (Table 8.2). It is poorly absorbed through the skin and is metabolized in animals by a number of routes (Figure 8.1) but the metabolite DDE is more persistent than the parent compound (Table 8.2). There are other metabolites such as an acidic derivative which is more water-soluble but the conversion to these is slow and does not involve major routes. There are also microbial and environmental degradation to other metabolites.

TABLE 8.2 *Persistence of the insecticide DDT and its metabolites*

Compound	Half-life in pigeon (days)	Half-life in soil (yrs)
DDT	28	2.5–5
DDD	23	
DDE	250	

It is because of this persistence, that DDT levels in the environment have been increasing ever since it was first used. Furthermore, the DDT concentration in some of the exposed organisms increases at each higher trophic level of the **food chain** (see Chapter 9). For example, small organisms such as plankton or *Daphnia* absorb DDT passively or via filter feeding from river or lake water and this enters their body fat. The concentration in the tissues of these organisms may be several hundred or thousand fold greater than the concentration in the surrounding water. Then, either insects or small fish eat these small organisms and the DDT is transferred to their fat tissue (Table 8.3). These small organisms are in turn eaten by still larger organisms and so on up the food chain. As DDT is fat soluble it remains in the organism and is then transferred into the fat of the predator or animal at the top of the food chain which may be man. The result is that relatively high concentrations of DDT can occur in those animals at the top of the food chain by a continuous process of amplification or **biomagnification** despite the fact that the initial concentration of DDT in the water is low. This is illustrated by the following example: in one area of California, plankton were found to contain 4 ppm of DDT, while the bass found in the same area contained 138 ppm and the grebes feeding on them 1500 ppm. So what seems to be a negligible concentration of DDT in the river or lake water or at the bottom of a food chain may be biologically very significant at the top. Toxic concentrations of DDT appear to affect birds and fish particularly in the production of eggs. It can be shown, for example, that there is a relationship between shell thickness and DDE concentration in birds of prey such as the kestrel (Figure 8.2).

In man, as in other animals exposed to DDT, most is located in the body **fat**. The concentration in fat is proportional to the intake, reaching a plateau with a half-life of around six months. The estimated intake for humans in the USA was around 35 mg $year^{-1}$ in 1969 but the level in food is declining as is the amount in human fat. The acceptable yearly intake for humans as given by the **FAO/WHO guidelines** is 255 mg $year^{-1}$. The DDT either comes from eating food of animal origin where the animal itself or another lower in the food chain has been exposed, or from vegetables or fruit

TABLE 8.3 *Example of a food chain*

Organism	Tropic Level
Pine trees	1st Producers
Aphids	2nd Herbivores
Spiders	3rd Insectivores
Tits and Warblers	4th Insectivores
Hawks	5th Carnivores

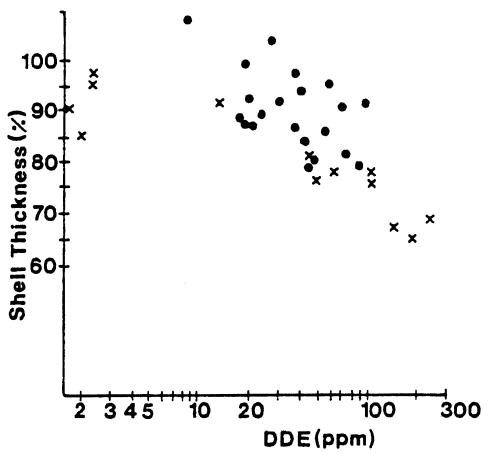


FIGURE 8.2 *The relationship between shell thickness and residues of the DDT metabolite DDE. The data is from kestrel eggs collected in Ithaca, New York in 1970 (●) or experimentally induced with dietary DDE (X). The data is the mean clutch thickness expressed as percent of control egg thickness collected before DDT use. Data from Lincer, J. L. (1975),* Journal of Applied Ecology, **12**, *781.*

which have been sprayed or otherwise contaminated.

The DDT in fat does not appear to be harmful to animals, however, and there is no correlation between adipose tissue levels and signs of poisoning. It is the concentration circulating in the **blood** which is more relevant to the toxic effects, and more particularly the level in the brain. However, if there is a reduction of the fat content of the body, the blood level will *rise*. Experiments with rats have shown that this increase in blood level can lead to toxicity. It has been found recently that bats in the southern USA have high levels of DDT even though it is no longer used. This is probably because the bats eat large quantities of insects and there is sufficient *residual* DDT in the environment for it to appear in **food chains**. In a particular species of bat this has been a problem because the DDT is passed via the milk to young bats and this then enters their fat tissues. When the bats go on mass long-distance migration, they start to mobilize this fat and so their blood levels of DDT increase until they become sufficient to cause toxicity and death.

Human milk may also contain **DDT** and as with other food chains there is a concentration effect. For example, lactating mothers exposed to 0.0005 mg kg^{-1} day^{-1} were found to produce milk containing 0.08 ppm DDT, hence their infants were exposed to 0.0112 mg kg^{-1} day^{-1}, an exposure some twenty times greater than the mothers.

There is no real evidence that DDT under such chronic exposure conditions is overtly toxic in man although there is some evidence that it is carcinogenic in mice. Consequently continuous exposure to low levels of DDT may constitute a long-term hazard. Chronic exposure to DDT does lead to induction of the microsomal enzymes involved in the metabolism of foreign compounds. It may be this effect that causes the **hormonal imbalance** seen in birds, as some hormones are also metabolized by the microsomal enzymes.

The story of DDT illustrates the problems of using chemicals in our environment and the assessment of risks and benefits. DDT is a very cheap and effective insecticide. Unfortunately it was used rather indiscriminately in agriculture in the USA in the early years after its introduction. The result of this was a marked decrease in the wild bird population. This was presumably partly due to the decrease in the number of insects on which the birds fed but was also a result of the direct toxic effect of DDT on the birds themselves. Improvements in analytical techniques allowed residues of DDT to be easily detected in many of the carcasses of the dead birds and other animals found.

These findings were meticulously documented by an American zoologist, Rachel Carson and published in her book *Silent Spring*. The book became a bestseller and consequently DDT was soon a notorious pollutant and was banned from use in many countries. The assumption was made that if this substance was responsible for such devastating effects on birds and other wildlife it must be bad for humans. However, this story illustrates a number of important points.

1 The finding that the carcasses of birds and other animals contained detectable levels of DDT does not prove that this was the cause of death.

2 DDT can be detected at very low concentrations in biological samples with sophisticated analytical techniques but this does not mean that such concentrations are dangerous or poisonous.

3 Birds are very different creatures to humans and other mammals.

DDT is very toxic to insects and consequently it is used as an insecticide but insect biochemistry and physiology is also different from that in humans.

The problems arose with DDT because of the indiscriminate use of the insecticide in agriculture. If it had been used more carefully then the problems with the wildlife might not have occurred. There have been two effects of banning DDT:

a Other insecticides have been developed and used and many of them are much more toxic to mammals than DDT and some have resulted in a significant number of human deaths.

b The control of the malarial mosquito for which DDT is very effective has been hampered and hence malaria is still prevalent in some parts of the world.

Furthermore, it should be noted that DDT has not been responsible for a single human death and there is very little evidence that it is toxic in humans.

The risk–benefit argument therefore is that the benefits of DDT used *responsibly* for the control of *disease-carrying* insects far outweigh the risks to humans. Unfortunately, misuse and public hysteria have clouded the rational scientific arguments.

Most other organochlorine insecticides such as **heptachlor**, **gamma-HCH**, **dieldrin** and **aldrin**, have similar problems of persistence to DDT.

Organophosphorus compounds

The use of organochlorine insecticides has decreased recently because of their persistence and because of fears about their long-term effects. The case against DDT is mainly due to its environmental impact on wildlife rather than its toxicity to man, which seems to be low. However, the organophosphorus compounds which have replaced the organochlorine type of insecticide are often *more toxic* to mammals (maybe as much as one hundred times more toxic), if less persistent.

There have been a significant number of human poisonings from organophosphorus compounds which are the major cause of poisonings in agricultural workers in California.

Case study *In Pakistan in 1976 in a programme to eradicate malarial mosquitoes a significant number of workers using* ***malathion*** *suffered poisoning (2800 out of 7500 sprayers) and there were five deaths. The malathion was used as a water dispersable powder. The components of the powder and the storage caused the malathion to change. The temperature was too high in some storage facilities and some of the malathion was converted into isomalathion. This contaminant then made the malathion very much more toxic in the exposed humans.*

There are many organophosphorus compounds now used as insecticides and their mode of action and toxicity is similar. As already indicated organophosphorus compounds are more toxic and have been responsible for more human deaths and illness than the organochlorine type of pesticide. **Parathion**, first synthesized in 1944 (Figure 8.3), is one widely used organophosphorus insecticide which has featured in a number of documented **mass human poisonings** (Table 8.1) and probably in many isolated incidents. Parathion has high mammalian toxicity and consequently it has been superseded by other less toxic organophosphorus compounds for certain uses. One such insecticide is **malathion** (Figure 3.9) which is more **selective** in its **toxi-**

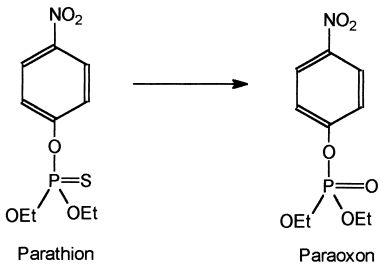


FIGURE 8.3 *The oxidative metabolism of the insecticide parathion.*
From Timbrell, J. A., Principles of Biochemical Toxicology, *Taylor & Francis, London, 1991.*

city mainly because of differences in its metabolism between mammals and insects. However, the effects of organophosphorus compounds are qualitatively similar and can be considered collectively.

Poisoning with organophosphorus compounds is an example of an **exaggerated pharmacological effect** rather than of direct toxic action and the toxicity may be either *cumulative* following chronic exposure or acute after a single exposure. Organophosphorus compounds exert their toxicity by interfering with the enzyme **acetylcholinesterase**. The organophosphorus compound binds to this enzyme because of similarities with the natural substrate for the enzyme, a neurotransmitter present in the nervous system called **acetylcholine**. Once its job at nerve endings is done, acetylcholine is hydrolysed by the enzyme, acetylcholinesterase and so removed. This terminates the action of the acetylcholine as a chemical transmitter at nerve endings. However, organophosphorus compounds inhibit this enzyme and so the acetylcholine accumulates leading to excessive stimulation of the nerve (Figure 8.4). This will lead to the death of the insect.

The same will occur in humans and other mammalian species. However, the organophosphorus insecticides have been devised so that the metabolism is different in mammals from insects and the organophosphorus compounds

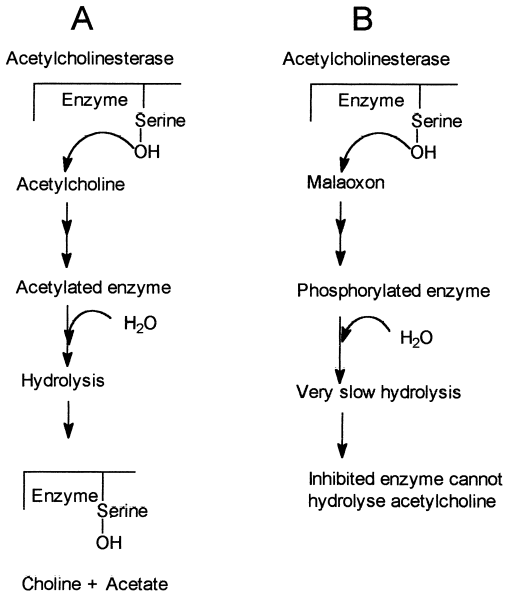


FIGURE 8.4 *The mechanisms of hydrolysis of acetylcholine by acetylcholinesterase (A) and the interaction of the malathion metabolite malaoxon with the enzyme (B).*

are detoxified in mammals. However, this is only efficient at low exposure levels and at higher levels humans will suffer the same consequences as insects. In the case of the poisoning in Pakistan, it was the alternative, detoxication route of metabolism, which was inhibited by the impurity and so the humans exposed became, like insects, much more susceptible.

Various different types of organophosphorus compounds inhibit cholinesterase enzymes and so cause a spectrum of similar toxic effects. These include headaches, nightmares, salivation and increased tear formation, diarrhoea and constriction of the passages in the lungs. These symptoms are all due to the increased levels of *acetylcholine*. Depending on the particular organophosphorus compound the inhibition may be *reversible* or *irreversible*. The **acetylcholinesterases** in different tissues such as plasma and nerves are different and so are not equally inhibited by organophosphorus compounds. There

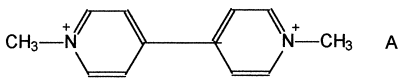
are degrees of inhibition of the total body acetylcholinesterase; in mammals a level of 50 per cent inhibition leads to toxic effects and 80–90 per cent inhibition will be lethal. The mechanism of toxicity of organophosphorus compounds relies on their similarity to the normal substrate **acetylcholine** (Figure 8.4). Thus, the organophosphorus compound is also a substrate for the enzyme but unlike acetylcholine, the product remains bound to the active site and the resulting complex may be only *slowly hydrolyzed*, if at all. With those organophosphorus compounds causing *irreversible inhibition*, resynthesis of the enzyme is necessary.

Malathion itself is not a substrate for cholinesterases but requires metabolism to **malaoxon**. This takes place readily in insects but in mammals hydrolysis is the preferred route and this leads to a readily excreted diacid (Figure 3.9). This is the basis of the selective toxicity.

The toxic effects of organophosphorus compounds centre around the *excessive* cholinergic stimulation with death occurring a a result of **neuromuscular paralysis** and **central depression**. Some organophosphorus compounds also cause another toxic effect where the nerves in the arms and legs die. This is known as **peripheral neuropathy** and the result is paralysis. However, not all organophosphorus compounds cause this and it is unrelated to the ability to inhibit the enzyme cholinesterase. One particular organophosphorus compound, **tri-orthocresyl phosphate** (TOCP), is a very potent agent in causing this effect. It is used in industry as a solvent. However, there have been a number of large-scale poisoning episodes generally in relation to food and these will be discussed under **Food additives and contaminants** (see above).

Paraquat

The examples mentioned so far have been insecticides which, as a group, are probably more important than other pesticides in terms of human and environmental toxicity. However, one particular **herbicide** is of particular importance and notoriety in terms of human toxicology. This is paraquat (Figure 8.5) which, during the more than twenty years of its use, has featured in several hundred cases of **fatal human poisoning**. Unlike the organophosphorus compounds, however, this has not been the result of accidental contamination of food and unlike the organochlorines there has been no particular environmental impact. Paraquat poisoning has mainly been the result of deliberate ingestion, usually orally, for **suicide** or **murder** with a few cases of **accidental** direct ingestion. Paraquat is a contact herbicide which binds very strongly to soil. Consequently it does not leach out of soil after being sprayed onto plants and does not have an environmental effect either on other plants or animals. Paraquat kills the plant by interfering with photosynthesis and its toxicity to animals may have some similarities at the biochemical level. When ingested by humans paraquat is usually fatal but even if it is not it may cause **serious lung and kidney damage**. The lung is the target organ because it *selectively* accumulates paraquat and consequently the concentration in the alveolar type I and II



$H_2N—CH_2—CH_2—CH_2—CH_2—NH_2$ B

$H_2N(CH_2)_3NH(CH_2)_4NH_2$ C

FIGURE 8.5 *The structure of the herbicide paraquat (A), and the polyamines putrescine (B) and spermine (C).*

lung cells reaches sufficient levels to cause toxic effects in those cells. The concentration in the lungs reaches a level *several times* that in the plasma and the paraquat is retained in the lung even when the plasma concentration is falling. Paraquat is taken up by the lung because of a structural similarity with **diamines** and **polyamines**, such as **putrescine**, **spermine** and **spermidine** (Figure 8.5). The presence of two nitrogens in paraquat, with a particular intramolecular distance, enables paraquat, but not the herbicide **diquat**, to be taken up by a selective active transport system in the lung for which polyamines are the normal substrate. The only other organ with an uptake system for polyamines is the brain which does not seem to accumulate paraquat.

Paraquat is believed to cause toxicity via its **free radical** form which is stable and results from an enzyme-mediated, one electron *reduction* which requires NADPH (Figure 8.6). In the presence of oxygen this generates **superoxide anion** and the paraquat cation reforms. This redox cycling continues to produce superoxide and deplete NADPH. The superoxide can lead to the production of **hydrogen peroxide** and **hydroxyl radicals**. Hydroxyl radicals are highly reactive and can cause **lipid peroxidation** which in turn causes further metabolic disruption. The presence of oxygen in the lungs is clearly an important factor in the pathogenesis of the lung lesion. The toxicity to the lungs is a direct result of the distribution of paraquat as the active uptake into lung cells gives rise to the relatively high and toxic concentration.

Paraquat causes a progressive **fibrosis** of the lungs and also damages the kidneys; once absorbed there is no antidote. The only treatments available are either an attempt to limit absorption by oral administration of substances such as **Fullers Earth** which *adsorb* paraquat or the use of **haemodialysis** or **haemoperfusion** to rid the blood of the paraquat. After the paraquat has accumulated in the lungs, however, there is no effective treatment currently available.

Paraquat has been used on many occasions for suicide and parasuicide attempts but unfortunately for the victim death is slow and painful,

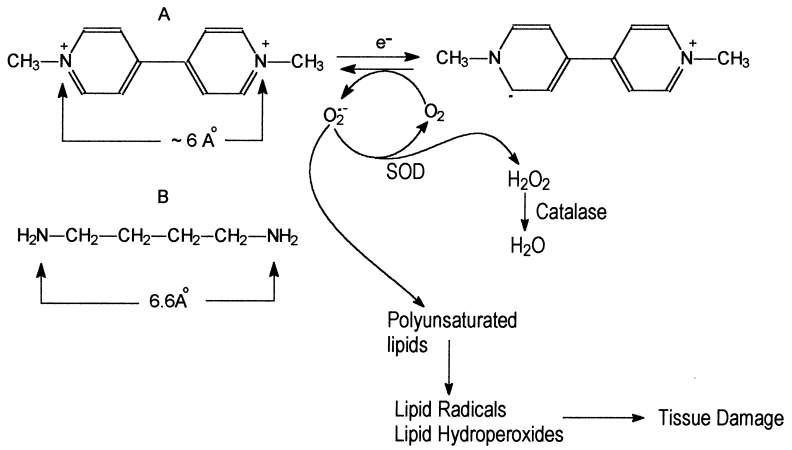


FIGURE 8.6 *The proposed mechanism for the lung toxicity of paraquat. The paraquat molecule, (A), readily forms a free radical by accepting an electron from cellular donors such as NADPH. The paraquat radical donates its unpaired electron to oxygen forming superoxide, which is reactive. It is detoxified by superoxide dismutase (SOD), but in excessive amounts overloads the enzyme and causes lipid peroxidation, leading to tissue damage. Paraquat has similarities to putrescine, (B), having two nitrogen atoms a similar distance apart. Therefore paraquat is a substrate for the putrescine active uptake system in the lung and so is accumulated there.*

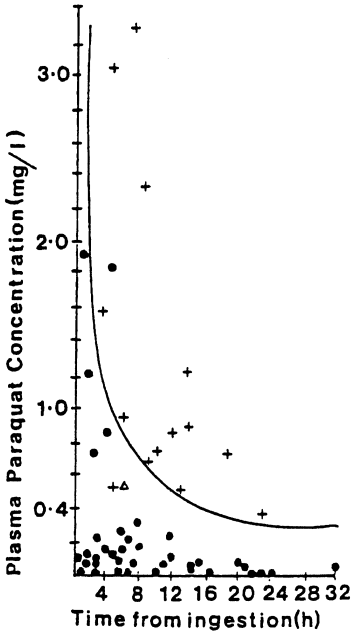


FIGURE 8.7 *The relationship between plasma paraquat concentration and the outcome of the poisoning, death (+) or survival (●). Δ is an aspiration death.*
Data from Vale, J. A. and Meredith, T. J., Paraquat Poisoning, pp. 135–141, Figure 21.4 in Poisoning – Diagnosis and Treatment, *Vale, J. A. and Meredith, T. J., (Eds) Update Books, London, 1981.*

occurring over a period of several days to a week or more with the progressive fibrosis of the lung leading to eventual suffocation. The prognosis is usually bad and the plasma level of paraquat indicates the likely outcome (Figure 8.7).

Fluoroacetate

Monofluoroacetate is an interesting example of a pesticide which is also a **natural product**. This compound is highly toxic by virtue of its very specific blockade of Krebs (tricarboxylic acid) cycle. Fluoroacetate is a **pseudosubstrate** and is successfully incorporated into Krebs cycle as **fluoroacetyl CoA**. The **fluorocitrate** produced will bind to the enzyme **aconitase**, but after binding the pseudosubstrate, the enzyme cannot remove the fluorine atom and so the enzyme is *blocked*. Therefore, Krebs cycle is unable to function and the cell and organism dies through lack of metabolic intermediates and energy.

Fluoroacetate is found naturally in some plants in Australia, Africa and South America. Some indigenous animals in Australia, especially the skink and emu have developed tolerance. However, introduced and unadapted animals, such as rats, mice, cats and dogs and those living outside the areas where fluoroacetate producing plants grow, are more susceptible to fluoroacetate toxicity (see Twigg and King, 1991). This is an example of what has been termed '**chemical warfare**' between plants and animals. The plants produce such toxic substances to stop animals eating them. However, fluoroacetate is also used as a pesticide for example in New Zealand, where it is known as **1080** and is used to kill **possums** which have become pests.

Summary and learning objectives

Pesticides are chemicals that have been ***specifically designed*** to be toxic and generally lethal to a particular organism such as an ***insect, plant***, ***fungus*** or ***rodent***. Some pesticides show ***selective toxicity*** and only damage the target organ but others are less selective and therefore are toxic to non-target organisms, including man. The widespread and initially rather indiscriminate use of the insecticide ***DDT*** causing the death of large numbers of birds and other wildlife led to it being banned in a number of countries. Although relatively

non-toxic to mammals, DDT is a very effective insecticide for the control of the malarial mosquito. Insect nerve fibres are the biochemical target. DDT and its metabolites are lipophilic and undergo bioaccumulation in the food chain. Consequently, those animals at the top of that chain such as birds may be exposed to higher concentrations of the pesticide. The destruction of non-target insects also reduces the natural food supply. Toxicity, especially chronic toxicity due to pesticides in mammals such as man has occurred, particularly from those pesticides that replaced DDT such as the ***organophosphates*** (e.g. parathion, malathion). These act by inhibiting acetylcholinesterase, usually after metabolic transformation. However, in mammals, alternative detoxication pathways may be available. Inhibition of acetylcholinesterase may be irreversible and in mammals leads to accumulation of acetylcholine, which causes toxic effects which include salivation, diarrhoea, bronchoconstriction and respiratory failure. Some organophosphates (e.g. TOCP) also cause peripheral neuropathy. Pesticides may be highly toxic to humans, such as the herbicide ***paraquat***, which causes lung damage as a result of selective uptake and accumulation in lung cells and production of reactive oxygen species. Natural pesticides also exist such as the highly toxic plant product ***fluoroacetate***, which blocks Krebs' cycle and is lethal to mammals as a result of heart failure, except those wild species that have developed tolerance.

Questions

Q1. Indicate which are true or false.
DDT:

a is an organophosphate
b is very lipid soluble
c is toxic to mammals
d is metabolized by loss of HCl
e inhibits cholinesterase
f is a herbicide
g is toxic to eggs.

Q2. Indicate which are true or false.
Parathion is an insecticide which:

a has low toxicity to humans
b is not metabolized
c acts by inhibiting Na K ATPase
d causes excessive cholinergic stimulation
e causes bronchoconstriction.

Q3. Indicate which are true or false.
Paraquat:

a is an organochlorine insecticide
b is metabolized to diquat by SOD
c causes lipid peroxidation
d is concentrated in lung tissue
e causes liver fibrosis
f blocks uptake of putrescine into the brain.

SHORT ANSWER QUESTION

Q4. What is the underlying basis of fluoroacetate toxicity?

Bibliography

ALDRIDGE, W. N. (1996) *Mechanisms and Concepts in Toxicology*, London: Taylor & Francis.

ECHOBICHON, D. J. (Ed.) (1998) *Occupational Hazards of Pesticide Exposure: Sampling, Monitoring, Measuring,* Washington: Hemisphere.

HAYES, W. J. (1975) *Toxicology of Pesticides,* Baltimore: Waverley Press.

HAYES, W. J. (1982) *Pesticides Studied in Man,* Baltimore: Williams and Wilkins.

MATSUMURA, F. (1975) *Toxicology of Insecticides,* New York: Plenum Press.

MORIATY, F. (1999) *Ecotoxicology: The Study of Pollutants in Ecosystems*, 3rd edition, London: Academic Press.

RAND, G.M. (Ed.), (1995) *Fundamentals of Aquatic Toxicology*, Taylor & Francis. A large, comprehensive text.

SHAW, I. C. and CHADWICK, J. (1998) *Principles of Environmental Toxicology*, London: Taylor & Francis.

TWIGG, L. E. and KING, D. R. (1991) The impact of fluoroacetate-bearing vegetation on native Australian fauna: a review. *Oikos*, **61**: 412–430.

WALKER, C. H., HOPKIN, S. P., SIBLY, R. M. and PEAKALL, D. B. (2001) *Principles of Ecotoxicology*, 2nd edition, London: Taylor & Francis.