Plants, their Predators and the Physician

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This article aims to give the view of an amateur botanist on some of the ways in which field botany, now called the study of plant ecology, continues to contribute to the understanding and treatment of disease. This pompous proposition would have been incomprehensible 250 years ago, when nobody could profess to be a physician without being a professional botanist and the materia medica was based almost entirely on plants. When, in 1709, Herman Boerhaave was appointed to the Chair of Medicine at Leiden[1], an appointment which can be thought of as the first Chair of Medicine in the modern pattern, it was regarded as right and normal that he should also be appointed Professor of Botany, working curator of the Botanical Gardens, and Professor of Chemistry.

On the chemical front the eighteenth century went on to see the foundation of modern inorganic chemistry, and the nineteenth an explosion of organic chemistry, the understanding of which was very largely based on the study of chemicals of plant origin. By 1914 it was estimated that the structure of more than 10,000 such compounds was known, and, for many, the steps by which they were synthesised. Similarly, the daughter sciences of human biochemistry and pharmacology originated in plant chemistry, as witness the nicotinic and muscarinic actions that tyrannised our youth, histamine, the physiological function of morphine, and muscle relaxants or the recent evolution of drugs based upon ergot. So it is remarkable how incurious doctors are about the origins of the drugs they use; the 1980 edition of Goodman and Gilman[2] contains not a single reference to the possible original reason for the existence of a drug of botanical origin, though it seldom leaves out the mythology that has attached to them. The materia medica is in danger of being relegated to folklore, and the debt of pharmacology to botany concealed behind the epithet 'semi-synthetic'.

The independent science of plant ecology began to diverge from chemistry before Boerhaave’s time, with the publication in 1682 of The anatomy of plants, by Nehemiah Grew, an Honorary Fellow of the Royal College of Physicians[3]. Grew recognised the sexual function of flowers, and that stamens contained the male element. He realised that plants, being immobile, required strategies to ensure the transport of that element. He also described what he called ‘saviours’, or what we would call volatile chemicals, as being common to certain groups of plants and potentially valuable in their taxonomy. Both these thoughts were taken further by John Ray in his Historia Plantarum, published in 1686[4]. Ray first suggested the role of insects as transporters of pollen and as determinants of the structure, colour and odour of flowers. He also remarked that where the caterpillars of one species of moth fed on more than one kind of plant, the plants concerned were likely to be closely related, and he speculated that the attractant they had in common might be their savour. The example he quoted was that of the Cinnabar moth feeding on ragwort and groundsel. Ray’s suggestions about the structure of flowers led, in the late eighteenth century, to the Linnean system of taxonomy, which was based on flower anatomy. The concept of chemical plant taxonomy is now commonplace, and is the rationale of the search for new forms of soil fungus, in the reasonable expectation that, if one species has produced an antibiotic, others yet to be found will produce similar ones.

Toxins and the Plant

Had enough chemists and pharmacologists kept up their interest in field botany, they might have speculated earlier that the existence of the chemicals they worked upon could be due to influences similar to those that had shaped the variety of flowers. It was recognised in the nineteenth century that chemicals of plant origin were metabolically costly to produce in that they were products of special synthesis and not merely by-products of excretory processes, and that they were usually not essential to the metabolism of the plant. Although this last concept has had to be much modified recently, these characteristics make it likely that such substances are serving some important external function. The nature of that function might well have been inferred from the results of the anthropological studies of the nineteenth and early twentieth centuries, which led to the discovery of many plant substances actually being used as poisons by man, or poisoning man and his domestic animals. The question of the function of such substances became even more compelling with the discovery of antibiotics.

As Grew commented rather obviously, plants are immobile. This not only puts constraints on their sex life, but also on their methods of defence. They cannot run away, nor can they hide, except temporarily, as seeds or bulbs, in a state of suspended metabolism, since, with the exception of fungi, they depend directly upon sunlight for
their energy and must be exposed to it. Physical defences they obviously have, but the ones that one immediately thinks of, those of being out of reach or prickly or armed with stings, do not protect from creatures that can fly or slip between such obstacles. Plants have, therefore, specialised in chemical defence against insects, parasitic fungi, bacteria and viruses. They have been defending themselves against such creatures at least since the Carboniferous era, that is for over 300 million years, but against mammals only in the last 30 million years, and against man for very much less than that. All the modern families of flowering plants had evolved 120 million years ago, and animals that came later on the scene must themselves have evolved against the background of an already existing range of chemicals first designed for a different use. One must therefore be very cautious in extrapolating from known effects on man or his domestic animals to the original purpose for which any toxic plant substance evolved.

One can conceive of chemical defences as a spectrum, with instant toxins at one end, where the relevant plant or part of the plant cannot afford even limited damage, and much less dramatic deterrents at the other end of the spectrum where tissue that is grazed or browsed can relatively easily be replaced. The deterrents in the latter case serve mainly to spread the burden of damage between species or individuals or to prevent the build-up of predators to plague proportions on any one population of a plant[5].

The Whole Plant

Under what circumstances might a plant require really strong and fast-acting poisons? First, when the whole plant is vulnerable. This applies particularly to annual or biennial herbs which have to reproduce quickly and cannot easily repair damage or spare resources for compensatory growth. Again, the pressure would be expected to be greatest on herbs that are transients in plant successions or those that grow in places where there is little else for animals to eat. The foxglove, the source of digitalis, is an opportunist where fire or fallen trees have briefly exposed the woodland floor to sunlight; tobacco plants, opium poppies and the annual chrysanthemums which produce pyrethrum, the source of knock-down sprays for flies, are temporary colonists of disturbed ground, and die out when grasses and shrubs take over. So do plants of the genus Senecio, to which belong groundsel, ragwort and the Oxford ragwort which colonised the bombed sites of London, as well as many tropical species. Common ragwort (Senecio jacobaea), to which John Ray referred, is a plant that takes over heavily grazed pasture and dies out in high grass. As a result it has very good reason to be both poisonous and instantly recognisable to grazing animals. The genus specialises in producing pyrrolizidine alkaloids which function as alkylation agents, producing necrosis and giant cell formation at the sites where they are metabolised. In man, this is mainly the central area of liver lobules, whence the clinical presentation of poisoning as veno-occlusive disease. These alkaloids are also of wider botanical and genetic interest since those few moths and beetles that have evolved with them to become parasites on the genus Senecio do not metabolise them, but sequester them in their bodies, thus, in their turn, making themselves poisonous. Their bright colours, in combinations of black and yellow or red, black and white, as exemplified by the stages of the Cinnabar moth, led to the concept of warning coloration and, later, to the recognition of mimicry. Desert plants provide many striking examples: oleander is universally known; Calotropis is a highly poisonous plant conspicuous all round the Sahara. Calotropis procera is a member of the family Asclepiadaceae, named after Aesculapius, which produces lethal glycosides. Goats do not touch it but the grasshopper does, and again, the species concerned is brightly coloured and is itself poisonous.

Other plants are at particular risk because they are forced to compress their growth into a short season between snow and drought and spend most of the year dormant. Colchicum, the autumn crocus and source of colchicine, is an example. Its large leaves appear in spring and are shunned by animals, and as the leaves die down colchicine is transferred to the corms for the winter. The same is true of species of Scilla, the genus that provides squill, the cholinergic constituent of the traditional Brompton cough mixture. Both colchicine and squill are active underground against molluscs, caterpillars or fungi.

The fly agaric (Amanita muscaria) produces muscarine, and is historically interesting as the agent that sent the Vikings berserk, and as a traditional fly poison. Toadstools and mushrooms bear the spores of the next generation; they can either mature very fast (as does the field mushroom) and disperse their spores early, thereafter being eaten by maggots, or they can grow more slowly and be very toxic, especially to flies.

Buds

Some parts of plants are in need of instant toxins even though the plant itself can usually replace any damage done to it. This applies to flowering tips and, to a lesser degree, to young leaf shoots, which are particularly at risk because of their high nitrogen and sugar content. A domestic example is the selective congregation of aphids on the young shoots of broad beans. Cannabidine comes from the growing tips of Indian hemp, and caffeine from the tips of Camellia sinensis, the tea plant. In nature, both are lethal to bugs. Eugenol, in clove oil from the buds of clove, is a specific inhibitor of beta-glucuronidase, and causes stripping of the gastric mucosa in rats. How or against what it acts in nature is not known.

Bark

To breach the bark of a tree or shrub by even a trifling hole may well kill it by allowing the entry of fungi or bacteria. The problem is solved in gardens by painting with tar wounds that have been made by pruning; the terpenoids in tar originally constituted the defensive resin of trees in the forests of the Carboniferous era. The
current epidemic of elm disease is due to a fungus and is
transmitted by an engraver beetle, Scolytus scolytus. Un-
der the bark is a mucilage that acts as a sealant of the
beetle holes. It also contains a variety of anti-beetle and
anti-fungal ingredients. The medical interest of elm bark
is limited, though in fact Dr Lettsom, an early President
of the Medical Society of London not otherwise renowned
for the rational nature of his treatment, did use Decoctio
Ulni, possibly as an anti-fungal ointment. The broader
medical importance of the beetle/fungus partnership is
enormous. It accounts, in part, for the presence of
polyphenols in coal tar, as in modern pine resin. The
forests of the coal measures must have been climatically
similar to today’s tropical rain forest, where fungi are
omnipresent. A formidable list of bark poisons comes
from this last source; for example, Cinchona, the Jesuit’s
bark, Cascara, the sacred bark, strychnine and curare.
An extreme example is the tree Dryobalanops camphora
from Sumatra. It has, literally, a pool of camphorated oil
under its bark, and was once a commercial source of
camphor. Many other trees have toxins under their bark;
salicylic acid and its methyl derivative came originally
from the barks of willows and birches. Cherries and
laurels contain under their bark cyanogenic glycosides
which serve the additional function of deterring rabbits or
deer from gnawing in winter.

The mention of cyanogenic glycosides raises a gen-
eral problem for plants that produce toxins. How does a
plant that often shares the relevant metabolic processes
with animals, and even more often with fungi or bacteria,
avoid the effects of its own poisons? In the case of the
cyanogenetic glycosides it does so in several ways. One is
by keeping the glycoside and the enzyme that hydrolyses
it to produce HCN apart in separate vacuoles, so that
they meet only when the tissue is damaged. The use of
chopped laurel leaves in schoolboys’ killing bottles pro-
vides an example. Alternatively, the enzyme may not be
present in the plant at all, so that hydrolysis can take
place only after ingestion, by the action of the animal’s
own enzymes. In addition, plants that produce cyanide
have the capacity to degrade it very rapidly and to allow
the nitrogen it contains to be recycled, unlike animals that
live on cyanogenetic plants, which merely degrade it
quickly, but derive no positive benefit from the process.
Alkaloids, as well as glycosides, are most often sequest-
ered in vacuoles, and are not usually found free in sap
except when held in preferential solution in latex. The
tobacco plant contains its nicotine in vacuoles in mature
leaves, but has none in the sap; the alkaloids of opium,
cannabis and euphorbias are held dissolved in latex.

Seeds

Seeds are especially at risk from predators, as they
contain concentrated reserves for the seedling until its
independence, and so are necessarily nutritious. The
production of very small seeds and their early dispersal by
wind, as for example the dandelion, avoids the problem to
some extent, as no one seed is large enough and many
seeds are not together long enough to allow a generation
of insects to live on them or to tempt larger animals to
search hard for them, hence many seeds escape. Plants
that produce fewer and larger seeds often include toxins
in them. A decorative example is the morning glory
(Ipomoea purpurea), the large seeds of which are a source
of ‘LSD’, currently the most familiar plant hallucinogen.
There are obvious constraints on enclosing metabolic
poisons in a seed, both in terms of the risk to the embryo
seedling and of the cost of including unnecessary material
in a limited space[6]. They can be illustrated by reference
to leguminous plants, peas, beans, and pulses. These are
particularly important to man because of their high
nitrogen content, and are in fact strictly necessary if he is
to live successfully as a vegetarian. The high nitrogen
content in the legumes is feasible because of the additional
nitrogen such plants fix in their root nodules by the action
of symbiotic bacteria. This symbiosis, in turn, puts a
premium on the production of large seeds which can
sustain the seedling until its root nodules are established.
It is thus not surprising that leguminous plants are
particularly toxic. The Leguminosae, in common with
many families of plants, have their own attendant family
of parasitic insects, which has evolved with them. These
are Bruchid beetles whose larvae parasitise the seeds,
usually only one or two species for each species of plant,
and there are many hundreds of twin species of legumin-
ous plants and Bruchids. Under natural conditions the
beetles do not lay their eggs on the wrong species of plant,
but, in the laboratory, Bruchid larvae fed on any seeds
but the ones to which they are adapted are killed. Any one
species of seed contains a variety of toxins. Those perhaps
most characteristic of leguminous plants are atypical
amino acids and lectins[7]. Atypical amino acids are an
advantage to the plant because they constitute a nitrogen
store that is reusable by the seedling when it germinates,
but is not available to a casual predator. Canavanine is a
substituted arginine in the seeds of the tropical legume,
Dioclea megaparpa. The beetle concerned distinguishes
between canavanine and arginine and breaks down the
canavanine to urea, from which it resynthesises its own
amino acids. Other beetles fail to distinguish canavanine
from arginine and are killed. Several similar analogues of
glutamic acid occur in species of wild pea of the genus
Lathyrus in India. One of them causes neurorrhaphyism
in man, a fatal flaccid paralysis. This diseases occurs in
epidemics during times of famine when wild plants have
to be eaten. The abnormal amino acid is taken up in the
central nervous system instead of glutamic acid. There
is another form of lathyrism in domestic animals, in which
the abnormal amino acid is taken up in collagen, render-
ing its molecule abnormal, and causing aneurysm for-
mation and rupture of small blood vessels, a picture similar
to that of inherited abnormalities of collagen. The plant’s
ability to get the best of both worlds by producing a toxin
and using it as a storage medium allows very high
concentrations of these amino acids; about 90 per cent of
the nitrogen in the seed of Dioclea is held as canavanine.

Lectins or phytohaemagglutinins are proteins usually
found in the cotyledons of the embryo seedling. They
bind to specific sugars on animal cell membranes, par-
ticularly the cells of the gut wall. Exactly how they do
their damage is uncertain, though part of the explanation
may be that they remove the normal defence of the insect’s gut against bacteria. They are invaluable in laboratory medicine because of their mitogenic effects, and because some of them have specific affinity to animal or human blood groups, as, for example, the group H binding lectin of gorse seed and group A binding of Lima beans.

Many leguminous seeds contain anti-enzymes that inhibit beetle trypsins and chymotrypsins, with the invariable exception of those of the species adapted to that plant. Others contain anti-amylases, which seem to be more broadly specific and most effective against opportunist invaders through the holes that other beetles (such as weevils) have made. They are totally inactive against plant amylases, and so do not inhibit the hydrolysis of starch when the seed germinates. Many legume seeds also contain long-chain polysaccharides, which cannot be utilised by most animals but are available to the plant embryo at germination. They can also be broken down by bacteria in the mammalian gut, with flatulent effects, as noted by those who fly in an aeroplane after a meal of peas or beans. Another familiar non-leguminous example is the tuber of the Jerusalem artichoke. Leguminous seeds often also contain cyanogenetic glycosides and alkaloids, though the latter are usually in the seed coat or pod, where they are both separated from the embryo and cause instant death to any inappropriate beetle larva that tries to bore into it. A notoriously dangerous example in Britain is the laburnum.

Fruit

Distribution of its ripe seeds is very important to any plant, partly because it removes them from the environs of the parent where they are easily found and quickly consumed, and partly because young plants are dispersed to new habitats and away from the shade and competition of the parent. Fairly light seeds may be taken away by ants or catapulted from the plant, the latter a frequent device in leguminous plants as the pod dries, for example in gorse. Very large seeds and small seeds contained within large fruit are commonly taken by birds, bats or squirrels directly from the tree, or by ground-dwelling animals from under it. Such distributors have to be tempted to take the seed, but may have to be prevented from taking it before it is ripe. They have also to be given their reward without the loss of all the seeds, and pirate animals who fancy the reward but do not distribute the seeds must be put off. The whole exercise must be conducted within a merciless metabolic budget. These problems apply to almost any fruit so distributed. The ackee (Blighia sapida) is of particular medical and social interest. It was introduced from its native West Africa to the West Indies in 1778, and its generic name refers to Captain Bligh of the Bounty, whose ill-fated voyage had as a similar purpose the transport of breadfruit from the East to the plantations of the West Indies. The specific name sapida means savoury, and refers to the pleasant-tasting oily aril or flap on the seed within. The aril is a popular food in West Africa, and in Jamaica has become a national delicacy eaten with salt fish. The entire fruit when unripe contains a high concentration of a complex amino acid, hypoglycin, the effect of which in man is to produce profound hypoglycaemia. In ripe fruit the aril separates from the seed and its content of hypoglycin falls to a safe level. It is then eaten by birds, mainly parrots attracted to the red colour of the pod, who regurgitate the seed itself intact. There is an oral tradition in West Africa that the aril should not be eaten off the tree but only be taken from the ground, whereas in Jamaica it has too often been eaten unripe and caused fatal vomiting sickness. In this example the bird gets the aril as its reward. In other plants the distributor may get the fruit pulp. Pulp is usually inedible until the seed is ripe, and often contains tannins which are unpleasantly astringent, but are hydrolysed when the fruit ripens, as in grapes. The fruit also changes colour and odour to become conspicuous and attractive only when ripe. The distributing agent may eat the pulp and drop the seed as it flies off, as fruit bats do with the heavy seeds of mangoes. Alternatively, the distributor may eat the whole fruit and pass the viable seeds in faeces. This is especially the case when the fruit contains small seeds, as do currants, peppers or mistletoe, which are often spread by thrushes, or tomatoes, which are efficiently spread by man. Such pulp often contains laxatives that cause the seed to be expelled before it is digested. Familiar examples are prunes, figs, tamarind and, possibly, senna pods. Lastly, the distributor may be rewarded with the seeds themselves. Such seeds often contain dose-dependent emetics so that some at least of them are regurgitated while still viable. The castor oil bean contains ricinoleic acid which has this function, as probably do many of the long-chain fatty acids found in oil-bearing seeds.

Cereals

So far, I have discussed strong poisons. There are many plants that are well able to withstand grazing or browsing, for example, most shrubs or trees, or even depend upon it to maintain their dominant position in the plant community, as do many grasses. The problem here is not so much a need to produce toxins, though frequently they are produced, but to spread the burden of being eaten between species and individuals. This subject is very complex and mostly still obscure, and I dare not do more than discuss one example relevant to medicine. A feature of wild cereal seeds is their small size, early distribution by wind and the fact that they are all produced over a short period, enabling some to escape being eaten and compelling seed-eaters to move on to other seasonal sources of food. A similar function is served by a lack of nutritional quality in the seeds. Unlike seeds of legumes, they contain much less amino acid nitrogen than is required to sustain animals, especially when breeding, so that seed-eating birds, for example, are forced to augment their diet by being carnivores as well, often to the benefit of the plant. Large herbivores often provide extra nitrogen for themselves by keeping urease-producing bacteria in their rumen, or in diverticula of their gut, as does the goose. Many caterpillars are habitual cannibals, an ingenious way round the problem.

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Not only is the total amino acid content of cereals usually insufficient for them to be a sole food, but there is often a relative deficiency of methionine and cysteine, an important limitation for man if, as sometimes happens, the cereals are the only food offered to newly weaned children. Other mechanisms discourage concentration on one food source alone. Like legumes, cereals often contain anti-amylases effective against weevils, and phytic acid; the latter acts as a chelating agent, and may be medically important in immigrants from India to this country, who are in a state of border-line deficiency of vitamin D and so stressed for calcium. There are often other specific deficiencies in cereal seeds, for example of nicotinic acid in maize, which makes it a dangerous sole source of food.

Toxins and the Predators

The array of toxins and deterrents can be looked at from the point of view of the predator, primarily the human one. Virtually all herbivorous animals larger than insects are forced by the need to find sufficient food to be generalist eaters rather than parasites on one or very few plant species. As a consequence, they face two major problems. One is how to recognise, out of the huge variety of plants, what is good or bad for them, and the other how to metabolise so many substances economically.

Parasites of one kind of plant, such as caterpillars, aphids or mites, usually have specific receptors by which they recognise and are induced to feed on their own plant. These receptors may be to the toxic substance which they can circumvent, or to an attractant that is an indicator, analogous to the scent of a flower, which attracts an insect to the nectar. Generalist feeders seem to accept foods mainly because they lack deterrents rather than possess attractants, a process much modified by hunger, and, in higher animals, by learning or habit. It seems that nutritive quality is rarely recognised chemically, except by some grasshoppers and possibly aphids, and, if it is possible to dissolve out deterrent substances, many animals will eat a wide range of plants that they would not otherwise touch, and often grow well on them.

The enormous variety of deterrent substances in the plants to which general feeders are exposed clearly prevents any one animal having specific receptors to all of them, and the cues to their presence are non-specific. Visual warning transcends plant taxonomy and is of obvious value to the plant in that it avoids damage, and to the potential predator in that dangerous experimentation is prevented. Its limitation is the need for colour vision, and, in its main value is thought to be against birds and mammals. Tactile stimuli, such as the presence of hairs, stings or vesicants, and possibly the initiation of immediate hypersensitivity, as in poison ivy, are subject to the limitation that they are discontinuous on the surface of the plant, and hence effective only against relatively large animals. The sensations of smell and taste are built up by generalist eaters from a limited range of graded stimuli; the chemical conformations that activate the receptors concerned are only just beginning to be understood. With exceptions (for instance the death cap toadstool), most strong poisons taste very unpleasant to man, alkaloids and glycosides usually being very bitter, long-chain fatty acids and terpenoids burning (and even vesicant) and tannins feeling, as indeed they are, astringent and drying the mouth.

Most of man's food is by these standards innocuous, but has a distinctive taste which we find merely pleasant or otherwise. The only universal attractant to herbivorous mammals is sweetness, of very doubtful benefit to modern man. Otherwise, appreciation varies without obvious reason. The plants that wild gorillas choose to eat are all apparently unpleasantly bitter to man, and different human cultures and even individuals disagree endlessly about palatability. Did flavours in general evolve as toxins, primarily effective against plant parasites? Many undoubtedly did, for example mustard oil, the toxin common to Cruciferae, cabbages, rape and mustard itself; mustard oil is metabolised to thiocyanates, which are goitrogenic to mammals and lethal to unadapted insects. The substituted xanthines in coffee, tea, cola and cocoa, all attractive to man because of their analptic effects, are toxic to insects in their host plants. By their source many more can be guessed to be toxic or indicators of the presence of toxins. Ginger comes from the roots of a lily which are fragile and irreplaceable if damaged, and vanilla from all parts of an orchid. Some of the characteristic oils of citrus and of umbellifers, angelica, carrots, parsley or fennel, act as anti-fungal agents and can cause lethal photosensitivity in caterpillars. One has to be very careful not to over-extend guilt by association until much more is known about the natural role of such substances.

Toxins and Human Activity

There are various ways in which man is adversely affected by plant defences. Instinct is fallible, and it is foolish to ignore warning coloration. Some urban mushroom hunters in the Highlands failed to appreciate why the fungus Cortinarius speciosissimus is as beautiful as its name indicates, and suffered permanent renal damage from the alkaloids it contains[8]. Loss of oral tradition with transportation into slavery allowed the vomiting sickness to occur in Jamaica. Overcrowding in relation to land resources leads to the planting of food in unsuitable places and to a need in unfavourable years to eat diseased crops. Ergotism, St Anthony's Fire, was a dreaded disease in peasant communities in Europe before the Black Death. Colourful fruiting bodies of the fungus Claviceps purpurea grow on the ears of rye in wet years, and were eaten out of necessity and despite their taste. Over-population is often accompanied by famine, which has been mentioned in the context of lathyrism, and notoriously by civil disorder, and this can cause trouble when fields are left unweeded or have hastily harvested. Veno-occlusive disease occurred in Afghanistan in 1967 and in Chad in 1977, when the Sahel drought coincided with a civil war. Slovenly preparation of crops can also cause trouble. The tubers of cassava contain cyanogenetic glycosides that are leached out by prolonged soaking in water. Sometimes inadequate leaching combined with
over-dependence on this undemanding crop combine to cause chronic cyanide poisoning in coastal areas of West Africa[9]. It is a locally important cause of poor vision in school children and of myelopathy in adults. Storage of inadequately dried groundnut meal for export has been associated with the growth of fungi of the genus *Aspergillus*. They produce aflatoxins that are lethal to the weevils which compete with the fungus for the groundnuts, and have caused hepatitis when fed to turkeys and hepatoma in rainbow trout. Whether they also cause liver disease in man is undecided. Human folly as a cause of contact with poisons is exemplified by addiction. Addiction, in turn, shades into ceremony, which has provided mescaline, cannabis, tea and coffee. Trial by ordeal used hemlock, the conine in which is an anti-cholinergic drug similar in its effects to atropine.

Such a series is formidable enough, but the main importance of plant defences to man is found in the economics of agriculture. Since the production of toxins is costly, the advantage that accompanies it is turned to disadvantage if a plant happens not to be exposed to predators. Most plant species are therefore polymorphic in the amount of any toxin they make, so ensuring the presence in the community of individuals producing the least concentration of the toxin appropriate to their circumstances. Cultivators have tended consciously to select such bland forms. This was notably the case with the Cucurbitaceae, melons, gourds and cucumbers, which were perhaps the earliest plants to be cultivated. The result has been that their own once closely specialised families of beetles and mites are now able to live on a broader range of cultivated species, and unspecialised insects, notably aphids, have moved in. Cultivated almonds, cherries and peaches were similarly selected for low concentrations of cyanogenetic glycosides, which may in part explain their susceptibility to fungi and aphids.

The selection of cereals, the staple food of man, for larger seeds has had a similar effect, in that the most productive strains have tended to lack toxins, especially those that confer resistance to rust fungi. With many cereals, too, strains whose seeds are not dispersed before threshing have been selected, thus providing a standing invitation to birds, generations of weevils, and fungi. The development of monocultures has allowed the build-up of plagues, and predators rather than soil exhaustion necessitate rotation of crops. The value of mixed crops in small stands is well known to peasant farmers the world over. Conversely, crops that have lost resistance factors and are grown as monocultures in climates periodically unfavourable to them are at continual risk of plagues. The social and political effects of the potato blight in Ireland in 1847 are still with us. The trouble with domestication is that it permanently transfers the responsibility for protection from the plants to the men who cultivate them. The predators that compete with us have unknown weapons and a long experience on their side, and we still have to face the curse of Adam: ‘Cursed is the ground for thy sake: in sorrow shalt thou eat of it all the days of thy life: thorns also and thistles shall it bring forth to thee, and thou shalt eat the herb of the field’[10].

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