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Toxins: New, Old, and Everywhere

"Nat," says Don Birnham (Ray Milland) to his bartender in *The Lost Weekend*, "You don't approve of drinking. Shrinks my liver, doesn't it? It pickles my kidneys. Yes, but what does it do to my mind?" We will consider the effects on his mind in later chapters. Here we will merely mention some effects prior to those on his liver and kidneys.

Don's rye whisky rewards him with a gentle burning sensation as it passes through his esophagus and on to his stomach. His nerves are signaling the deaths of millions of cells as alcohol diffuses rapidly through the usually protective barrier of mucus and enters those cells. If a cell gets more than a critical concentration of alcohol, it dies. Dead cells, or even those with damaged membranes, release *wound hormones* and *growth factors*, which diffuse to other cells held in reserve for just such an emergency. These reserve cells, deep in the protected crypts of the stomach lining, react to the chemical messages by migrating to the site of injury and dividing to produce new cells of the kind needed there. The most exposed layer of stomach cells can be replaced in mere minutes—but does Don allow them enough time before quaffing again?

Natural and Unnatural Toxins

High-proof alcohol is only one of the many novel hazards to which we are exposed. Agricultural pests are controlled mainly by insecticides that did not exist before 1940. Silos are perfused with poisonous vapors to protect grain from insects and rodents. Demonstrably toxic chemicals such as nitrates are used to extend the shelf life of our foods. Many workers inhale toxic dust or fumes, and suburbanites spray insecticides such as lindane into their trees, often with little regard to the possible effects on themselves or their neighbors. There are heavy metals in our water, pollutants in our air, and radon gas rising from our basements. Obviously our modern age is especially hazardous, with respect to poisons in the food we eat and the air we breathe. Right?

Wrong. While we are now exposed to many toxins that did not exist in even the recent past, our exposure to many natural toxins has greatly decreased since the Stone Age and early agricultural times. Recall from the chapters on infectious disease that the contest between consumer and consumed can generate an evolutionary arms race. Plants can't protect themselves by running away, so they use chemical warfare instead. People have always known that some plants are toxic. Gardening books routinely list plants known to have caused illness or death from being eaten. These lists merely deal with the worst offenders. Most plants contain toxins that would be harmful if eaten in more than a minimal amount. Scientists have only recently realized that the toxic substances are not by-products that just happen to be toxic to certain potential consumers; they are the plants' essential defenses against animals that want to eat them (herbivores), and they play a key role in the ecology of natural communities. People who live in the eastern United States needn't look far for an example. Most lawns there are of tall fescue, a grass species popular because it grows fast and resists pests. The fantasy of getting rid of our lawn mowers and letting horses graze our lawns once a week is appealing, but the horses would soon get sick. Most tall fescue is infected at its base with a fungus that makes potent toxins. The grass protects itself by transporting these toxins to the tips of the blades of grass, the perfect location for discouraging herbivores. Tall fescue and its fungus help each other.

Only very recently have a few pioneers, such as Timothy Johns and Bruce Ames and his collaborators, made us aware of the enormous medical importance of the plant-herbivore arms race. We can heartily recommend Johns's book *With Bitter Herbs Thou Shalt Eat It* for an introduction to the role of plant toxins in human history.

Here we are again dealing with an arms race, this time between animals such as ourselves, who eat plants, and the plants, which need to protect themselves from being eaten. When Stone Age inhabitants of central Europe died of starvation late one winter instead of happily filling up on oak buds and acorns, they were losers in the contest with oak trees. Oak buds and acorns are loaded with nutrients, but, unfortunately for potential consumers, they are also loaded with tannins, alkaloids, and other defensive toxins. Early Europeans who filled up on unprocessed oak tissues died even sooner than their starving companions did.

Animals that eat other animals may have to deal with venoms or other harmful materials manufactured by their prey, and they will certainly have to deal with at least traces of the plant toxins eaten by the prey. The monarch butterfly caterpillar, mentioned earlier, feeds on milkweed not only because it has machinery that makes it invulnerable to the milkweed's deadly cardiac glycosides but also because it becomes poisonous itself by consuming the plant and is therefore avoided by potential predators. Many insects and arthropods protect themselves with venoms and poisons. Many amphibians are poisonous, especially the bright-colored frogs that Amazonian peoples use to poison their arrowheads. The vivid colors and patterns of such poisonous animals protect them from predators, who have learned from bitter experience that such prey are not pleasant food items. If you are starving in a rain forest, eat the camouflaged frog that is hiding in the vegetation, not the bright one sitting resplendent on a nearby branch.

How do plant toxins work? They do whatever will keep herbivores from eating the plants. Why are there so many different toxins? Herbivores would quickly find a way around any one defense, so the arms race creates many different ones. The list of different toxins and their diverse actions is impressive. Some plants make precursors of cyanide, which is released either by enzymes in the plant or by the intestinal bacteria of the consumer. The bitter almond is noteworthy in this regard, but apple and apricot seeds use the same strategy, as do cassava roots, which are used for food in many cultures.

All adaptations, however, have costs, and plants' defensive chemicals have theirs. Toxin manufacture requires materials and energy, and the toxins may be dangerous to the plant that produces them. In general, a plant can have high toxin levels or rapid growth, but not both. To put it from the herbivore's point of view, rapidly growing plant tissues are usually better food than stable or slowly growing structures. This is why leaves are more vulnerable than bark and why the first leaves of spring are especially vulnerable to caterpillars and other pests.

Seeds are often especially poisonous, because their destruction would thwart the plant's reproductive strategy. Fruits, however, are bright, aromatic packets of sugars and other nutrients specifically designed to be attractive food for animals that can disperse the seeds contained in them. The seeds within the fruit are designed either to be discarded intact (like peach pits) or to pass safely through an intestinal tract (like raspberry seeds) to be deposited at some distant place surrounded by natural fertilizer. If the fruit is eaten before the seeds are ready, the whole investment is wasted, so many plants make potent poisons to discourage consumption of immature fruits, thus the proverbial stomachache caused by green apples. Nectar is likewise designed to be eaten, but only by whatever pollinators are best for the plant that makes it. Nectar is an elaborate cocktail of sugar and dilute poisons. The recipe has evolved as an optimal trade-off between the need to repel the wrong visitors and not discourage the right ones.

Nuts represent a still different strategy. Their hard shells protect them from many animals, and some, like acorns, are also protected by high levels of tannin and other toxins. Though many acorns are eaten, some are trampled into the ground, while others are buried by squirrels and thus have a chance to sprout into new trees. It takes such elaborate processing to turn acorns into human food that we wonder if the tannin may be too much even for squirrels. Perhaps it leaches out when acorns are buried in moist soil. If so, the squirrels are processing as well as hiding their food, a neat ploy in their arms race with the oak. If you find yourself starving in an unknown wilderness, seek your nourishment in soft sweet fruits, the nuts with the hardest shells, and perhaps some inaccessible tubers. Avoid seemingly unprotected fleshy plant materials like leaves; they are much more likely to be poisonous, as they must be to protect them from your own or any other hungry mouth.

Plants' escalations of the arms race are numerous and varied. Some plants make little defensive toxin until they are mechanically damaged, after which toxin rapidly accumulates in or near the injured part. Damage to a tomato or potato leaf induces production of toxins (proteinase inhibitors) not only at the site of the wound but throughout the plant. A plant has no nervous system, but it does have electrical signaling and a hormone system that can keep all its parts informed about what takes place in a small region. Some aspen trees have even more impressive communication. When a leaf is damaged, a volatile compound (methyl jasmonate) evaporating from the wound can turn on the proteinase response in nearby leaves, even those on other trees. The usual result of such defenses is that insects are discouraged after feeding even briefly. Some particularly adept insects, however, begin their meal by cutting the main supply vein to a leaf so the plant cannot deliver more toxins. And so the arms race goes on.

Defenses Against Natural Toxins

The best defenses are, of course, the sorts of avoidance and expulsion already discussed in relation to infectious diseases. We avoid eating moldy bread or rotten meat, which smell and taste bad, because we react with an adaptive disgust to the toxins produced by fungi and bacteria. We rapidly expel toxic substances by spitting or vomiting or diarrhea. We quickly learn to avoid whatever gives us nausea or diarrhea.

Many swallowed toxins can be denatured by stomach acid and digestive enzymes. The stomach lining is covered with a mucous layer that protects it from ingested toxins and stomach acid. If some cells become contaminated, the effect is temporary since stomach and intestinal cells, like those of the skin, are shed regularly. If toxins are absorbed by the stomach or intestine, they are taken by the portal vein directly to the liver, our most important detoxification organ. There, enzymes alter some toxic molecules to render them harmless and bind others to molecules excreted in the bile back into the intestine. Toxin molecules in sufficiently low concentration will be quickly taken up by receptors on cells in the liver and rapidly processed by the liver's detoxification enzymes.

For instance, our protection against cyanide depends on an enzyme called rhodanase, which adds a sulfur atom to cyanide to form a chemical called thiocyanate. Although thiocyanate is far less toxic than cyanide, it still prevents the normal uptake of iodine into thyroid tissue and thus can cause the overworked thyroid gland to enlarge—a condition called goiter. Plants from the genus *Brassica* (including broccoli, Brussels sprouts, cauliflower, and cabbage) get their strong taste from allylisothiocyanate. The ability to taste a related compound, phenylthiocarbamate (PTC) varies greatly, as is well known by generations of students who have tasted a bit of PTC-impregnated filter paper as part of an experiment to demonstrate genetic variation. While some people can't taste PTC, those with a different gene experience it as bitter. They may have an advantage in avoiding natural compounds that cause goiter. About 70 percent of individuals in most populations can taste PTC, but in the Andes, where such compounds are especially likely in the diet, 93 percent of the native people can taste it.

Oxalate is another common plant defense. Found in especially high concentrations in rhubarb leaves, it binds metals, especially calcium. The majority of kidney stones are composed of calcium oxalate, and doctors have for years recommended that such patients keep their diets low in calcium. However, a study of 45,619 men, published in 1992, showed a higher risk of kidney stones for those who had *low* calcium intakes. How is this possible? Dietary calcium binds oxalate in the gut so that it cannot be absorbed. If dietary levels of calcium are too low, some oxalate is left free to enter the body. If, as researchers S. B. Eaton and D. A. Nelson have argued, the amount of calcium in the average diet is now less than half of what it was in the Stone Age, our current susceptibility to kidney stones may result from this abnormal aspect of our modern environment, which makes us especially vulnerable to oxalate.

There are dozens of other classes of toxins, each with its own way of interfering with bodily function. Plants in the foxglove and milkweed family make glycosides (e.g., digitalis), which interfere with the transmission of electrical impulses needed for maintaining normal heart rhythm. Lectins cause blood cells to clump and block capillaries. Many plants make substances that interfere with the nervous system—opioids in poppies, caffeine in coffee beans, cocaine in the coca leaf. Are such medically useful substances really toxins? The dose of caffeine contained in a few coffee beans may give us a pleasant buzz, but imagine the effect of the same dose on a mouse! Potatoes contain diazepam (Valium), but in amounts too small even to cause relaxation in humans. Other plants have toxins that cause cancer or genetic damage, sun sensitivity, liver damage—you name it. The plant-herbivore arms race has created weapons and defenses of enormous power and diversity.

What happens if we overload our bodies with so many toxin molecules that all the processing sites in the liver are occupied? Unlike the orderly queues of shoppers in the supermarket, these molecules do not just wait their turn to be processed. The excess toxins circulate through the body, doing damage wherever they can. While our bodies cannot instantly make additional detoxification enzymes, many toxins stimulate increased enzyme production in preparation for the next challenge. When medications induce these enzymes, this may hasten the destruction of other medications in the body, thus necessitating dose adjustments. Timothy Johns's book notes the interesting possibility that inadequate exposure to everyday toxins may leave our enzyme systems unprepared to handle a normal toxic load when one occurs. Perhaps with toxins, as with sun exposure, our bodies can adapt to chronic threats but not to occasional ones.

Grazers and browsers limit their consumption of certain plants to avoid overloading any one kind of detoxification machinery. This dietary diversification also helps to provide adequate supplies of vitamins and other trace nutrients. Left to our own devices in a natural environment, we do the same. If your favorite vegetable is broccoli and you were given an unlimited supply of it and nothing else, you would not eat as much as you would if given both broccoli and cucumbers. Many weight-loss diets are based on the principle that we eat less if given only a few foods than we would if we had access to a well-stocked cafeteria. We minimize the damage caused by dietary toxins by this instinctive diversification, as well as with our own special array of detoxification enzymes. These enzymes are not as potent or diverse as those of a goat or a deer, but they are more formidable than those of a dog or cat. We would be seriously poisoned if we ate a deer's diet of leaves and acorns, just as a dog or cat would quickly sicken on what we might regard as a wholesome salad.

We can also, more than any other species, protect ourselves from being poisoned by learning about how to avoid it. Only we can read about the dangerous plants in our gardens and woodlands, and we are the species whose diets are most shaped by social learning. A food our mothers fed us can usually be accepted as safe and nourishing. What our friends eat without apparent harm is at least worth a try. What they avoid we would be wise to treat cautiously.

More broadly, there is great wisdom in our innate tendency to follow the seemingly arbitrary dictates of culture. The rituals of many societies require that corn be processed with alkali before it is eaten. Can't you just imagine prehistoric Olmec teenagers ridiculing their elders for going to all the bother? But those teenagers who ate only unprocessed corn would have developed the skin and neurological abnormalities characteristic of pellagra. Neither rebels nor elders could have known that boiling corn with alkali balances the amino acid composition and frees the vitamin niacin, which prevents pellagra, but the cultural practice accomplished what was needed, despite the lack of scientific understanding.

Or consider the prehistoric residents of California, whose main sustenance came from acorns. The abundant tannins in acorns are astringent and combine strongly with proteins, properties that make them especially useful as leather-tanning agents. As noted above, they are highly toxic as they come from the tree. Whether the tannins evolved to protect the acorn against large animals or against insects and fungi is uncertain, but dietary concentrations of over 8 percent are fatal to rats. The tannin concentrations in acorns can reach 9 percent, and this explains why we cannot eat acorns raw. The Pomo Indians of California mixed unprocessed acorn meal with a certain kind of red clay to make bread. The clay bound enough of the tannin to make the bread palatable. Other groups boiled the acorns to extract the tannin. Our enzyme systems can apparently cope with low concentrations of tannin, and many of us like its taste in tea and red wine. Small amounts of tannin may even be helpful by stimulating production of the digestive enzyme trypsin.

Human diets expanded after fire was domesticated. Because heat detoxifies many of the most potent plant poisons, cooking makes it possible for us to eat foods that would otherwise poison us. The cyanogenetic glycosides in arum leaves and roots are destroyed by heat, so that arum could be cooked and eaten by early Europeans. Unfortunately, some toxins are stable at high temperatures, while other new toxins are actually produced by cooking. That tasty char on barbecued chicken contains enough toxic nitrosamines for several authorities to recommend restricting our intake of grilled meat to prevent stomach cancer. Have we been cooking meat long enough to have developed specific defenses against the char toxins? Cooking may have been invented hundreds of thousands of years ago, and it must have started with barbecues on open fires. It would be interesting to know if we are more resistant to heat-produced toxins than our closest primate relatives are.

Since the invention of agriculture we have been selectively breeding plants to overcome their evolved defenses. Berry bushes were bred for reduced spininess and the berries for reduced toxin concentrations. The history of potato domestication, as described in Johns's book, is especially instructive. Most wild species of potato are highly toxic, as you might expect, given that they are an otherwise unprotected, concentrated source of nourishment. Potatoes are from the same plant family as deadly nightshade and contain harmful amounts of the highly toxic chemicals solanidine and tomatidine. Up to 15 percent of their protein is designed to block enzymes that digest proteins. Still, a few wild species can be eaten in limited quantity, and edibility can be increased by freezing, leaching out the toxins, and cooking. We enjoy thoroughly edible potatoes today thanks mainly to many centuries of selective breeding by native farmers in the Andes.

Concerns about pesticides have recently spurred programs to breed plants that are naturally resistant to insects. This protection is provided, of course, by increased levels of natural toxins. A new variety of disease-resistant potato was recently introduced that did not need pesticide protection, but it had to be withdrawn from the market when it was found to make people ill. Sure enough, the symptoms were caused by the same natural toxins the Andean farmers had spent centuries breeding out. An evolutionary view suggests that new breeds of disease-resistant plants should be treated as cautiously as artificial pesticides are.

NOVEL TOXINS

One reason to stress the prevalence of toxins in our natural environment, and our evolutionary adaptation to them, is to provide a perspective on the medical significance of novel toxins. Novel toxins are a special problem not because artificial pesticides such as DDT are intrinsically more harmful than natural ones but because some of them are extremely different chemically from those with which we are adapted to cope. We have no enzymatic machinery designed to deal with PCBs or organic mercury complexes. Our livers are ready and waiting for many plant toxins, but they don't know what to do with some novel substances. Furthermore, we have no natural inclination to avoid some novel toxins. Evolution equipped us with the ability to smell or taste common natural toxins and the motivation to avoid such smells and tastes. In psychological jargon, the natural toxins tend to be aversive stimuli. But we have no such machinery to protect us from many artificial toxins, like DDT, that are odorless and tasteless. The same is true of potentially mutagenic or carcinogenic radioisotopes. Sugar synthesized from radioactive hydrogen or carbon tastes as sweet as that made with ordinary stable isotopes, but we have no way of detecting its dangers.

It is not always easy to tell what the effects of a novel environmental factor may be. For instance, the debate about the possible dangers of mercury in dental fillings has gone back and forth, but Anne Summers and her colleagues at the University of Georgia have recently found that mercury fillings increase the number of gut bacteria that are resistant to common antibiotics, apparently because the mercury acts as a selective factor for bacterial genes that protect against mercury and some of these same genes confer resistance to antibiotics. The clinical significance of this finding is uncertain, but it nicely illustrates the unexpected means by which novel toxins can affect our health.

Since we can no longer, in our modern chemical environment, rely on our natural reactions to tell us which substances are harmful and which are not, we often rely on public agencies to assess the dangers and take measures to protect us from them. It is important to avoid unrealistic expectations of such agencies. Tests on rats are of limited reliability as models for human capabilities, and there are many political difficulties that can frustrate public action on environmental hazards. Scientifically illiterate legislatures can pass laws saying that no amount of any chemical that causes cancer can be allowed in food, even though many such chemicals are already present naturally in many foods. Conversely, political pressures can lead to inadequate controls on known toxins, from nicotine to dioxins. There is no such thing as a diet without toxins. The diets of all our ancestors, like those of today, were compromises between costs and benefits. This is one of the less welcome conclusions that arise from an evolutionary view of medicine.

MUTAGENS AND TERATOGENS

Mutagens are chemicals that cause mutations, which may cause cancer or damage genes and thus lead to health problems for many generations. Teratogens are chemicals that interfere with normal tissue development and cause birth defects. Mutagens and teratogens are not sharply separate from each other or from toxins with short-range effects. Ionizing radiation and mutagens such as formaldehyde and nitrosamines can all cause distress immediately or cancer or birth defects years later.

While it is important to learn which poisons harm everyone, people vary in their susceptibility to many substances, such that one man's meat may be another's poison. We will deal with special aspects of individual variability in the chapter on allergy. Vulnerability varies by age and sex. It seems particularly unlikely that detoxification capability is the same in both adults and the very young, especially during embryonic and fetal development. There are abundant theoretical reasons, as well as data from many experimental studies, that show that actively metabolizing tissues are more vulnerable to toxins than dormant ones, cells that divide rapidly more than quiescent ones, and cells that differentiate into specialized types more than those that merely reproduce more of the same.

All these perspectives suggest that embryonic and fetal tissues may be harmed by lower concentrations of toxins than adult tissues are. We regard Figure 6-1 as a likely picture of vulnerability through human prenatal development. Vulnerability rises rapidly from the level characteristic of a quiescent egg in an ovary to a peak in the critical stages of organ formation and tissue differentiation, then slowly declines to closer to the adult level of tolerance at full term.

We will return to this graph in a moment, but first let's look at a classic mystery of traditional medicine. So-called morning sickness is often the first reliable sign of pregnancy, especially for women who recognize it from prior experience. This nausea and its associated lethargy and food aversions are so common as to be considered a normal part of pregnancy, although they are quite variable in intensity. For some women they mean many weeks of misery, while others aren't bothered much. We may even think of morning sickness as one of the symptoms of pregnancy, as if pregnancy were a disease. The current clinical approach seems to be: pregnancy sickness makes

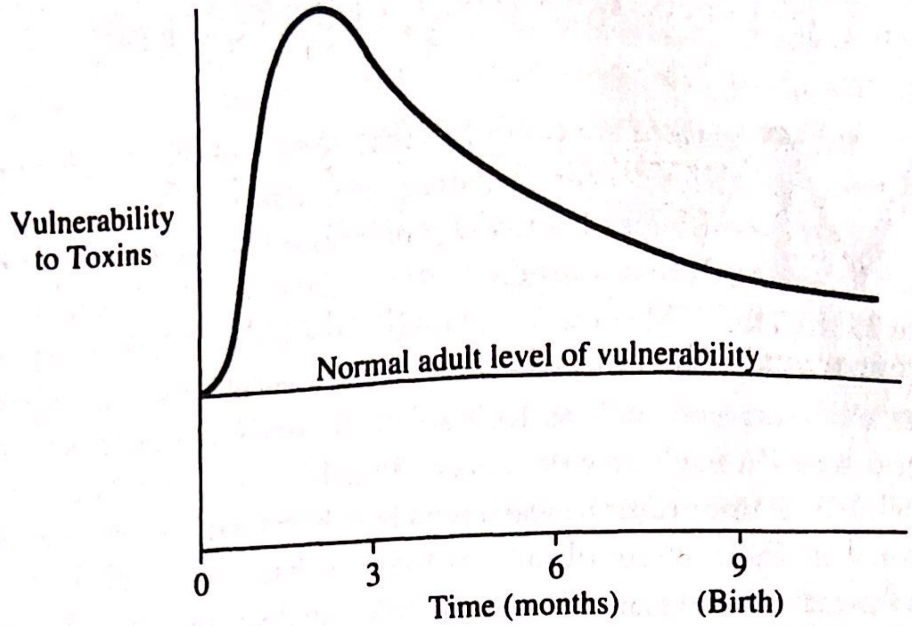

FIGURE 6–1. Toxin vulnerability at different prenatal ages.

women distressed, so let's find a way to alleviate the symptoms and make them feel better. Unfortunately, making people feel better does not always improve their health or secure other long-term interests. As pointed out in Chapters 1 and 2, natural selection has no mandate to make people happy, and our long-range interests are often well served by aversive experiences. Before we block the expression of a symptom, we should first try to understand its origin and possible functions.

Fortunately, a biologist thoroughly committed to the adaptationist program has recently wondered at the mystery of morning sickness and devised an explanation. Margie Profet, an independent scholar and biologist in Seattle, argues that a condition as common and spontaneous as pregnancy sickness is unlikely to be pathological. Note on the graph how fetal vulnerability corresponds almost exactly to the course of pregnancy sickness. This concordance provided Profet with a crucial clue. Nausea and food aversions during pregnancy evolved, she argues, to impose dietary restrictions on the mother and thereby minimize fetal exposure to toxins. The fetus is a minor nutritional burden on the mother in the early weeks of pregnancy, and a healthy, well-nourished woman can often afford to eat less. The food she is inclined to eat is usually bland and without the strong odors and flavors provided by toxic compounds. She avoids not only spicy plant toxins but also those produced by fungal and bacterial decomposition. A lamb chop that smells fine to a man may smell putrid and repulsive to his pregnant wife.

Profet amassed diverse evidence in support of her theory. One example is the correlation between toxin concentrations and the tastes and odors that cause revulsion. Another is the observation that women who have no pregnancy nausea are more likely to miscarry or to bear children with birth defects. Much more evidence needs to be gathered on the evolutionary and related medical questions. We think it unlikely, for instance, that the phenomenon is uniquely human. Is it found in mammals in general, especially herbivores? Do newly pregnant rabbits eat less and choose their food more carefully than either before pregnancy or later on? Studies of wild animals would be the best way to answer these evolutionary questions. The medically more important research can be carried out on laboratory animals. An essential premise to be tested is that some toxins of trivial importance for normal adults have seriously deleterious effects on fetal development. We also need to know the common environmental toxins that are most likely to harm a fetus. We also need to look for associations between diet during pregnancy and the more frequent kinds of birth defects, as well as at individual variations in detoxification enzymes.

Some practical applications of this theory are illustrated by the history of the antinausea medication Bendectin. Pregnant women, understandably, often ask their physicians to do something about their nausea. Recognizing the dangers of drug administration during pregnancy, physicians were generally cautious, but the drug Bendectin was thought to be safe and was widely prescribed. After the thalidomide tragedy, there were many studies on the possible harmful effects of Bendectin, and the equivocal evidence has even been the topic of Supreme Court deliberations. Unfortunately, none of the studies has ever considered the possible functions of morning sickness. Perhaps anything that suppresses morning sickness may cause birth defects indirectly by encouraging harmful dietary choices.

If Profet's theory is correct, it means that pregnant women should be extremely wary of all drugs, both therapeutic and recreational. Fetal alcohol syndrome is perhaps the biggest current problem, affecting thousands of babies every year. Cigarettes can also cause problems, and coffee, spices, and strong-tasting foods may well best be avoided. Certainly, it would be wise to avoid taking any medications if possible. Studies can determine which medications cause major birth defects, but because others may have more subtle effects, it is better to be safe than sorry.

Other than avoiding toxins, what should a pregnant woman do about her nausea? The easy and obvious answer is "Respect it. Your reactions to food are probably adaptive for your baby. Do not succumb to the urgings of others to eat what you are inclined to avoid. Better to offend the host at the party than to risk imposing a long-term impairment on your child." But what about your own suffering? It would be easy enough for two male authors to say, "Accept your nausea; it contributes to your long-term desire for a healthy family." We realize that this is not a satisfactory recommendation. Relief of unpleasant symptoms is desirable as long as side effects are acceptable. We would hope that obstetricians someday will be able to provide their patients with a list of all the substances they ought to avoid. Armed with this knowledge, women could safely use a medication to prevent nausea if it is possible to find one that is effective and to have confidence that it is safe.

People in many cultures, especially pregnant women, eat certain kinds of clay. Although this clay has often been regarded as a mineral supplement, it can relieve gastrointestinal distress and for this reason is used in some modern antidiarrheal medications. Certain kinds of clay, as mentioned in the discussion about acorns, tightly bind soluble organic molecules, including many toxins. In other words, they may relieve symptoms in the best possible way—by removing the harmful cause. Unfortunately, we doubt that it is possible to patent clay. Our present system of drug marketing makes it unlikely that any company would invest the millions needed to test such a product and bring it to market if it could not control an exclusive patent. Regulatory agencies protect us, but they also constrain us.

As fetuses grow older, they become children who tend to hate vegetables. They especially dislike strong-flavored vegetables such as onions and broccoli, the very ones that contain high levels of plant toxins. The developmental course of these dislikes offers a clue to their explanation. Even finicky children often begin to experiment with new foods just as they mature into teenagers and their growth nears completion. The evolutionary explanation for this sensitivity may be the benefits, during the Stone Age, of avoiding the most toxic plants during childhood. Modern-day children and adults would both benefit from eating more of our modern low-toxin vegetables, but there may be a good evolutionary explanation for why children steadfastly resist eating their vegetables.

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