Letter From the Desk of David Challinor
June 2000

A question often asked by curious adolescents is why don't "poisonous animals" get poisoned by their own poison? The answer to this reasonable query is more complicated than first imagined. The toxins these animals produce seem to originate in what they consume; this mechanism is most clearly understood in toxic insects, although it evidently applies also to poisonous amphibians, fish, reptiles and at least one bird. This letter is about poisonous animals and what it takes for them to maintain the toxicity needed for protection against predators. I will not be discussing poisonous snakes whose venom is a chemically modified form of their saliva and is used less for protection than for capturing prey. Among all animals with saliva, those with venomous saliva are relatively rare and found only in some snake species, one lizard (gila monster), and one mammal (short-tailed shrew), as well as some invertebrates: an octopus, some cone snails, spiders, etc.

Perhaps the best known toxic insect is the monarch larva and butterfly. Its caterpillar feeds on milkweed leaves and is able to counteract in its body the plant's poisonous milky sap without ill effect. It uses this toxin for its own protection and passes it on to its butterfly stage. When monarchs are fed to hand-raised blue jays, they have such an emetic effect that the birds spit them out as soon as they touch them with their tongue. Taking advantage of the bad taste of monarchs, the viceroy (whose wing color and pattern closely mimics that of its monarch relative) uses its resemblance for protection against predators. Unlike the monarch, the viceroy does not migrate, but winters as a partially grown larva in a rolled up leaf fastened with silk threads. It is further protected from the cold by having an antifreeze component in its blood. When the larvae emerge in the spring, they quickly pupate to become a butterfly slightly smaller than the monarch, but faster flying and gliding with horizontal wings rather than on the dihedral as does the monarch. Scientists long thought that, if offered, birds would eat viceroys, but recently when this species was experimentally fed to birds, they also appeared to be distasteful. Scientists now ask, does the viceroy also have a mild toxin?

Professor Thomas Eisner and his colleagues at Cornell have long been interested in understanding how insects cope with the toxins in the plants they eat. Another well-studied, chemically protected insect is the rattlebox moth and its larvae. Rattlebox plants (Crotalaria spp.) are yellow-flowered common pasture weeds found in southeastern USA (krotalon = rattle in Greek). If eaten by a cow the plant can cause liver and breathing problems or even fatality. However, the bright black and yellow rattlebox caterpillar metabolizes the toxins in the plant's leaves to protect it and its moth from being eaten. Just as we humans consume plant alkaloids for extra energy (caffeine) or to fight malaria (quinine), other animals use plants for their own purposes. Most alkaloids are powerful, but if consumed to excess can be lethal.

Only the rattlebox caterpillar, not the moth, feeds on the rattlebox plant's leaves. After becoming a moth, however, only the males retain enough toxin from their caterpillar stage to be protected from predation. The female has to have her toxins "recharged" by copulation, an act taking about nine hours, during which time the male moth passes to the female a large packet of both sperm cells and the toxic alkaloid. This "inoculation" takes effect rapidly, so that within five minutes she is as fully protected as the male, as are her eggs and subsequent hatchlings.

Eisner was puzzled as to why this complex system would protect the unhatched eggs yet not the female. To learn more he brought both male and female moths that he had raised in his laboratory to the southeast where the rattlebox plant grows. He also used two local spiders known to prey on moths. He soon found that the laboratory moths which lacked the toxic alkaloid monocrotaline were immediately eaten by the spiders when presented to them. However, all wild moths and females that had recently copulated were fully protected from spiders; they were so repellent that when thrown into the webs of nephila spiders, the spiders speedily cut them loose from their webs.

Eisner then sought to learn how these insects could contain a toxin powerful enough to kill a cow yet be immune to it themselves. He discovered that monocrotaline in the rattlebox plant is not in itself toxic, but it becomes so when it moves through the enzyme system of almost all animals except the rattlebox moth. Enzyme systems normally help to detoxify whatever harmful substance an animal is eating by altering the structure of the poisonous alkaloid and converting it to a relatively harmless, unstable compound. Occasionally, however, the opposite effect occurs as in the rattlebox moth where its enzyme system keeps the alkaloid toxic. If we can understand how this insect stores the plant's poisonous alkaloid in non-lethal form, then scientists might be able to protect cows and horses from the potentially fatal consequences of unwittingly grazing on this plant.

The Zoo has no rattlebox moths in its invertebrate exhibit, but does have brightly colored poison dart frogs of three genera (Dendrobates, Phyllobates and Epipedobates) in its Amazonia building. The Zoo's wild-caught frogs gradually lose the powerful toxins stored in their skin glands each time they molt until they are no longer poisonous to the touch. Evidently their failure to maintain a normal wild diet results in a lack of certain elements needed to metabolize their protective toxins. It would be difficult to track a detoxed frog in the wild to see if it could regain its toxicity. However, an experiment by Smithsonian scientist Stan Rand and his colleagues helped support the connection between diet and toxins. Wild, poison dart tadpoles were raised in a laboratory. Some of the resulting frogs were fed only fruit flies and others were fed small insects found on leaf litter near the tadpole collection site. Those fed fruit flies had virtually no alkaloids in their skin, whereas those raised on leaf litter arthropods showed substantial amounts of several kinds. Skin coloring evidently protects all poison dart frogs, especially those few small local populations that happen to be non-poisonous because there is a patchy distribution of essential prey insects.

Batrachotoxins (batrakhos = frog in Greek) and other substances from the skin of these frogs are being studied in hopes of developing a non-opiate pain-killing drug. A trace alkaloid (epibatidine) from the skin of an Ecuadorian frog (*Epipedobates tricolor*) is now being analyzed as a potentially powerful non-opiate painkiller. The toxin's paralyzing or even lethal effect is achieved by the alkaloid attaching itself to sodium channels in cell membranes which are important to the victim's nerve and muscle activity. The frogs can withstand the powerful toxin in their own skin glands because, for some still unknown reason, the toxin does not bind to the sodium channels of their cell membranes.

Recently an amazing discovery by Zoo researcher John Dumbacher broadened the list of toxic animals to include a bird, the Hooded pitohui. When collecting specimens for research in New Guinea, a pitohui became trapped in his mistnet. As he disentangled it, the bird bit him on his finger and when he automatically licked the cut, his mouth became numb. The local people knew about this bird and averted it. This human avoidance enabled pitohuis to forage around villages without avian competition, because most other local bird species had been killed for food. When Dumbacher returned to the United States, he sent a sample from the bird to Dr. J.W. Daly at the National Institutes of Health who had spent many years identifying arthropod alkaloids in the skin glands of frogs. Daly recognized the bird's poison as a homobatrachotoxin, one of the toxic compounds that had already been found in a poison dart frog. If this bird is an insectivore, the arthropods in New Guinea could contain alkaloids similar to those in insects eaten by the poison dart frogs in the Ecuadorian rainforest. It is more likely that pitohuis acquire their poisons from plants, but Dumbacher plans to return to New Guinea to monitor them with radio collars and thereby learn about their daily habits diet. He also is curious to know whether an incubating pitohui can transfer enough toxin from its feathers to its eggs to make them unpalatable to the arboreal brown tree snake, an egg eater that when accidentally introduced on Guam extirpated many of its endemic birds. In one experimental test, a tree snake, when fed a mouse with a drop of this toxin on it, dropped it immediately on tasting the poison.

Scientists in time may solve some of these "poison animal" mysteries, but I would be surprised if we ever have a complete understanding of exactly how these toxic alkaloids transfer from the plant or insect to the eater and then how the eater protects itself from the poison it consumes. There seems to be a race between those plants and animals that can produce protective toxins and their predators who are evolving ways to neutralize such defenses. Because the system is constantly evolving, scientists will be monitoring changing relationships, thus making their work endless. Competition of this nature has been going on since life began, but it is only in the last few decades that scientists have been able to explore the complicated paths that have evolved.

David Challinor
Phone: 202-673-4705
Fax: 202-673-4607
E-mail: ChallinorD@aol.com

P.S. Much of the material in this letter came from an excellent article by Elizabeth N. Lasley in BioScience 49(12) 945-950 (1999) and from Ed Smith of the National Zoo.