Unintentional Intoxications of Nonhuman Primates: Phytotoxins and Pesticides

Subjects: Toxicology

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Wild and captive nonhuman primates (NHP) are exposed and potentially vulnerable to many natural and man-made toxic threats. Nevertheless, wild NHP are capable of coping with these threats using strategies, namely avoidance, dilution, gastrointestinal degradation, or detoxification, which require genetic potential, learning from parents and conspecifics in their social group, or prior experience through random food sampling and experimentation. Captive NHP are also at high risk for intoxications when they are often housed in an outdoor enclosure in a vivarium or zoo that is in or close to a large urban and industrial city. These NHP are potentially exposed to urban-industrial air pollution due to industrial and vehicle exhausts, waste incineration, and the domestic and industrial use of petroleum-based products, cleaners, pesticides, and paints, amongst others.

nonhuman primates poisoning

1. Phytotoxins

Phytotoxins are natural compounds that are inherently abundant in plants and are synthesized by plants to protect themselves against predators, insects, and microorganisms or in response to environmental stress. Phytotoxins can also underlie a plant's characteristics, such as its aroma, color, and flavor. The chemical or molecular structure of phytotoxins is diverse and encompasses alkaloids, terpenes, phenylpropanoids, and polyketoids. Poisonous plants are classified according to the chemical nature of their phytotoxin(s), their phylogenetic relationships, or their botanical characteristics.

Although NHP are omnivores, they spend most of their waking time foraging and searching for and processing food. Phytotoxin poisoning in NHP occurs after ingesting plants that are not intended for eating. Accordingly, NHP can be poisoned after ingesting a toxic plant because (a) hunger may cause them to graze a plant that would not be eaten under normal circumstances, or (b) they are undernourished and ingest a toxic plant to provide caloric intake. The consequences on the health of NHP after ingesting a toxic plant can range from none to sudden death. This large in-between range of adverse consequences comprises clinical signs of liver or kidney damage, cardiovascular, nervous system, musculoskeletal or gastrointestinal problems, allergic reactions, birth defects, and reproductive failure.

Most reports of phytotoxin poisoning describe such poisonings in captive NHP (**Table 1**). Descriptions of phytotoxin poisoning in wild NHP have not been reported because they have developed strategies to cope or avoid this toxic threat, namely avoidance, dilution, gastrointestinal degradation, or detoxification. For example, Zanzibar red colobus monkeys (*Procolobus kirkii*) eat the charcoal from burnt trees. This behavior is thought to be a learned behavior for counteracting the toxicity of phenols in the Indian almond and mango leaves, which constitute a major part of their diet [1]. Black-and-white colobus monkeys (*Colobus guereza*) frequently come to ground to eat water plants and clay [2]. Although water–plant consumption may remedy mineral deficiencies [3], the clay may be consumed to adsorb plant toxins (usually noxious phenols) and promote their excretion, in addition to adjusting the pH of the forestomach.

Table 1. Cases of unintentional phytotoxin poisoning in captive NHP.

NHP Species	Plant Species	Phytotoxin	Clinical Signs	Clinical Signs	Reference
Cebus apella	English ivy (*Hedra helix*)		Severe gastroenteritis resulting in acute death	Not performed	Fowler, 1981 [4]
White mantled-black colobus (*Colobus guereza*)	Alleghany (*Viburnum x rhytidophylloides)*		Pain, lethargy, inappetence, unable to climb, vomiting, diarrhea resulting in death	Small spicules of plant material were present in the inflammatory exudate associated with the stomach's mucosa	Irlbeck et al., 2001 [5]
François' langurs (*Trachypithecus francoisi)*	Hybrid yew shrub (*Taxus baccata X T. cuspidata*)	Taxine alkaloids	Found dead without previous clinical signs	Multiple yew fragments in gastric content and taxine alkaloids were detected by gas chromatography and mass spectrometry of the gastric contents	Lacasse et al., 2007 [6]
Alaotran gentle lemur (*Hapalemur griseus alaotrensis*)	Russian vine (*Polygonum baldschuanicum*)	Oxalate	Varying degrees of lethargy, inappetence, abdominal discomfort and diarrhea progressing to signs of renal insufficiency (hematuria, proteinuria, and severe uremia) resulting in death	Chronic renal failure, presence of calcium oxalate crystals in the renal tubules	Scott, 1996 [7]
black and white ruffed lemurs	Hairy nightshade (*Solanum*	Alkaloid glycoside	Acute death or less active and partial	acute, severe, diffuse hemorrhagic	Drew & Fowler,

NHP Species	Plant Species	Phytotoxin	Clinical Signs	Clinical Signs	Reference
(*Varecia Variegate Variegate)*	*sarrachoides*)		inappetence for 48 h followed by depression, lethargy, ataxia, diarrhea, and slow pupillary reflexes prior to death	enteritis and typhlitis and a small volume of unidentifiable plant material was found in the stomach contents	1991 [8]

This plant has been conducted to substantiate the safety of browse species for captive NHP. The National Research Council of the National Academies has published a list of NHP-safe plants that can be used for browse [9]. However, the authors of the list do not guarantee the safety of ingesting these plants.

Table 1 summarizes the published reports of unintentional phytotoxin poisoning in captive NHP. No antidote or specific treatments for the poisonings were provided because the poisonings were not recognized before death.

2. Pesticides

A pesticide is a naturally occurring or synthetic chemical or biological agent that is used to control pests. About 700 pesticides are in current use and these pesticides can be classified according to (a) the type of target pest (organism), such as a herbicide, an insecticide, a nematicide, a rodenticide, a fungicide, and a bactericide; (b) the chemical structure, such as organophosphates, organochlorines, carbamates, and pyrethroids; and (c) the mechanism (mode) of action, such as enzyme inhibitors, disruptors of cellular signaling pathways, and generators of reactive molecules that destroy cellular components, amongst others. To be acceptable, a pesticide must be toxic to the intended target and not toxic to any non-target organism.

Wilderness areas are vital refuges where natural ecological and evolutionary processes can operate with minimal human disturbance. Humans have appropriated much land and altered terrestrial ecosystems for agriculture. Agricultural frontiers are dynamic environments that are characterized by the conversion of native habitats to agriculture and the highest incidence of species loss occurs on an agricultural frontier. Therefore, habitat loss is a burgeoning threat to a population of wild NHP and other terrestrial vertebrates that live on an agricultural frontier. Furthermore, the use of pesticides on an agricultural frontier has the potential to detrimentally affect wild NHP populations, the local biodiversity, and ecosystem’s structure and function.

An overview of the reported cases of pesticide poisonings in wild NHP are presented in **Table 2**A,B. Since these poisonings occurred mostly on agricultural frontiers, pesticides, which were used to control agricultural pests, were the suspected cause of these poisonings in non-target wild NHP. The main reported outcome of an acute poisoning by a pesticide was death (**Table 2**A). Continual exposure to a pesticide on an agricultural frontier may also be hazardous for wild NHP populations because of the possible teratogenic effects of the pesticide: birth (congenital) defects have been reported in the offspring of pesticide-exposed pregnant mothers (**Table 2**B). These effects were usually documented in the reports of research projects whose aims were to (a) determine the cause of the phenotypical harm to wild NHP and (b) understand whether these harms were linked to environmental pollution of their habitat. Unfortunately, no definitive links between pesticide exposure and reproduction or frequency of stillbirths could be made. Interestingly, many health authorities advise pregnant women or women who are planning to become pregnant avoid contact with or exposure to pesticides because some pesticides may cross the placental barrier and lead to miscarriages, pre-term births, infants with low birth weights, birth defects, and congenital anomalies.

Table 2. (**A**) Summary of the reported cases of death in wild NHP due to acute pesticide poisoning on agricultural frontiers. (**B**) Summary of the reported birth defects and congenital anomalies in wild NHP due to suspected continual pesticide exposure on agricultural frontiers. * The clinical signs and main laboratory findings and pathology were often not performed and documented in the report.

(**A**)

NHP Species	Suspected Pesticide	Clinical Signs	Laboratory and Main Postmortem Findings	Reference
Not specified	Anticoagulant rodenticide	Not provided	Not performed	Bates, 2016 [10]
Vervet monkeys (Chlorocebus pygerythrus)	Aldicarb, carbofuran	Sudden death	Not performed	Botha et al., 2015 [11]
Golden Langurs (*Trachypithecus geei*)	Organochlorine insecticide	Sudden death	Insecticide was detected in the liver, kidney, and intestinal contents	Pathak, 2011 [12]
Bonnet macaque (*Macaca radiata*)	Carbofuran (a carbamate insecticide)	Sudden death	Cyanosis, severe pulmonary congestion, splenomegaly and dark purplish-blue granules, identified as carbofuran, in the gastric contents	Radhakrishnan, 2017, 2018 [13] [14]
Cynomolgus monkeys (*Macaca fascicularis*)	Anticoagulant bromadiolone and difenacoum	Sudden death	extensive subcutaneous and internal hemorrhages. Bromadiolone and difenacoum were detected in frozen liver samples	IJzer et al., 2009 [15]
Squirrel Monkey (*Saimiri sciureus*)	Fipronil	Ranging from sudden death to symptoms of	Fipronil and fipronil sulfone were detected in	Demir et al., 2021 [16]

		depression, inappetence, lethargy and body weight loss, which progressively disappear over time	cutaneous and brain tissue	
Tantalus monkeys (*Cercopithecus aethiops*)	Dieldrin	Sudden death	Not performed	Koeman et al., 1978 [17]
		(B)		
NHP Species	**Suspected Pesticide**	**Clinical Signs**	**Laboratory and Main Postmortem Findings**	**Reference**
Ring-tailed lemurs	Organochlorine pesticides	*	*	Rainwater et al., 2009 [18]; Dutton et al., 2003 [19]; Miller et al., 2007 [20]
Chimpanzees and baboons	Several different pesticides	(Congenital) facial and nasal deformities (i.e., reduced nostrils, cleft lip), limb deformities, reproductive problems, and hypopigmentation	*	Krief et al., 2017 [21]; Lacroux et al., 2019 [22]
Baboons, howler monkeys, chimpanzees, red-tailed monkeys, red colobus	Pesticides, halogenated flame retardants, and organophosphate flame retardants	*	*	Wang et al., 2020 [23]
Douc langurs (*Pygathrix* spp.)	Dioxins (i.e., Agent Orange, tetrachlorodibenzo-p-dioxin) and dioxin-related compounds	Two animals exhibited developmental consequences of possible dioxin exposure	*	Brockman et al., 2009 [24]; Brockman & Harrison, 2013 [25]
Baboons (*Papio* spp.), Tantalus monkeys (*Chlorocebus tantalus*), red tail	Pesticides	*	*	Ogada, 2014 [26]; Naughton-Treves, 1998 [27]; Eniang et al.,

monkeys (*Cercopithecus ascanius*), vervet monkeys (*C. pygerythrus*), Campbell’s monkeys (*Cercopithecus campbelli lowei*), Zanzibar red colobus (*Procolobus kirkii*), and chimpanzees (*Pan troglodytes*)				2011 [28]; Nowak et al., 2009 [29]; Sai et al., 2006 [30]
Japanese monkeys (*Macaca fuscata*)	Dieldrin and heptacholorepoxide	Congenital defects such as abnormal limbs in offspring	Elevated concentration of dieldrin and heptacholorepoxide in the liver and kidney of female monkeys whose babies were born with malformations	Minezawa et al., 1990 [31]

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