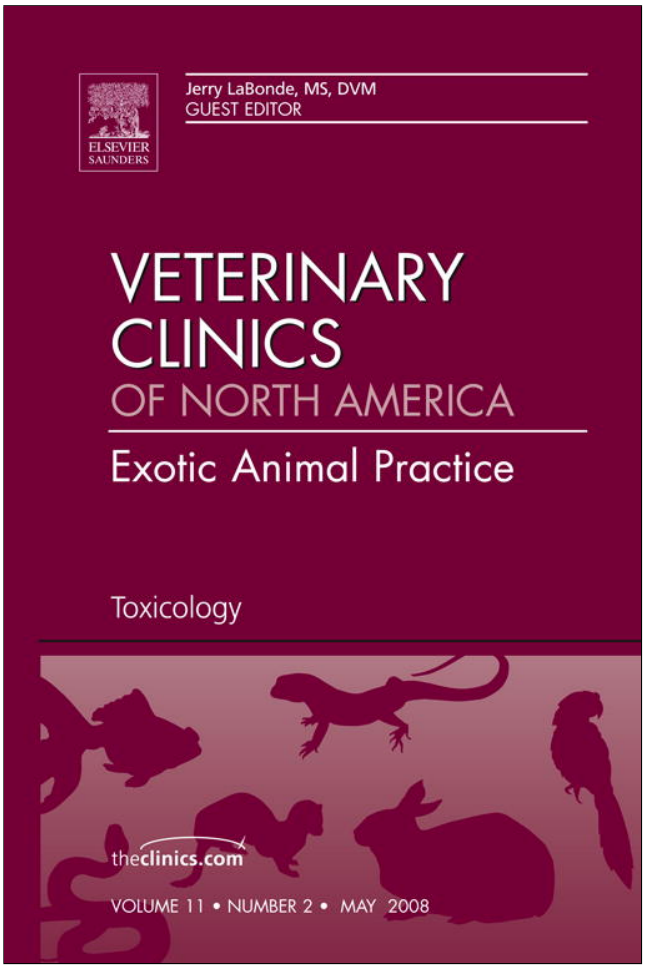

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Toxicology of Aquarium Fish

Helen Roberts, DVM[a,*], Brian S. Palmeiro, VMD[b]

[a]*Aquatic Veterinary Services of WNY, PC, 5 Corners Animal Hospital, PC, 2799 Southwestern Blvd, Suite 100, Orchard Park, NY 14217, USA*
[b]*PetFishDoctor.com, 645 Pennsylvania Ave, Prospect Park, PA 19076, USA*

Fish have a very intimate relationship with their surrounding aquatic environment, surrendering them vulnerable to waterborne toxicities. Most aquarium fish live in a closed system (water has to be manually removed and added to be renewed), so the effects of such toxins can be cumulative and devastating. Most cases of toxicity are due to deficiencies in husbandry and tank maintenance. Poor water quality kills more fish than infectious agents, making client education a very important preventive tool for aquatic practitioners. This article includes a discussion of toxicities related to water quality, chemotherapeutics, pesticides, and household substances.

Water quality–related toxicities

Toxicities in pet fish are most commonly due to abnormalities in water quality; poor water quality is one of the most common causes of morbidity and mortality in pet fish. Therefore, a complete water quality evaluation should be performed in every case presenting to the fish veterinarian. Acute exposure to poor water quality can result in sudden and significant mortality. Chronic exposure to suboptimal water quality conditions can cause immunosuppression and predispose fish to a variety of infectious diseases that ultimately lead to mortality. Common water quality–related toxicities in aquarium fish include pH, ammonia, nitrite, nitrate, chlorine/chloramines and hydrogen sulfide.

pH toxicity

pH is the measure of hydrogen ion concentration in water. It is measured on a logarithmic scale: a change in 1 pH unit represents a tenfold difference

* Corresponding author.
E-mail address: nyfishdoc@aol.com (H. Roberts).

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in concentration of hydrogen ions [1,2]. The pH can range from 1 to 14; values less than 7.0 are considered acidic, values greater than 7.0 are basic (alkaline), and a value of 7 is neutral. Optimal water pH varies with species. Most aquarium fish live in water with a pH ranging from 5.5 to 8.5. Fish in freshwater aquariums generally do best with a neutral pH, whereas marine fish typically require higher pH values (8.0–8.5). Some freshwater tropical fish such as discus (*Symphysodon discus*) prefer acidic water, whereas African cichlids prefer more alkaline water. A pH outside of the optimal range may not immediately result in acute mortality; however, chronic exposure may lead to stress and subsequent immunosuppression, predisposing the fish to disease.

Rapid fluctuations in pH are generally more problematic for fish than specific individual pH values. Water with low alkalinity (buffering capacity) is more likely to undergo pH fluctuations. Slow pH changes (no more than 0.3–0.5 units/d) are usually tolerated well by most fish [1]. The pH can increase during algal blooms and in heavily planted ponds/aquaria due to carbon dioxide usage [1–3]. A buildup of organic debris/organic acids can also decrease the pH of an aquarium.

Suboptimal pH or pH fluctuations can result in lethargy, stress, skin irritation/lesions, behavioral changes (such as attempting to jump out of the aquarium, flashing), corneal edema, skin color changes, gill irritation with increased mucus production, respiratory signs, and mortality [1–3]. pH swings can result in decreased immune system function, predisposing the fish to various infections (parasitic, bacterial, viral). Blood acidosis can result from decreases in pH, whereas increases in pH can result in blood alkalosis [2,3].

Regular maintenance of aquaria, including routine water changes and regular cleaning of gravel beds, is essential. In closed systems such as home aquaria, water pH gradually decreases over time due to the metabolic processes that take place.

''Old tank syndrome'' is a common clinical finding that occurs in mature systems that have infrequent water changes and, often, overall neglect. A common historical finding is fish deaths after a water change. The client may also report intermittent fish deaths for no apparent reason. The tank may appear dirty or cloudy. Water chemistry testing reveals low or no alkalinity (buffering capacity), a low pH (often <5), elevated hardness, and high levels of nitrogenous waste products [1–3]. A pH crash is a term used to describe an acute decrease in water pH, and is often preceded by a drop in alkalinity. pH crashes may result in high fish mortalities (Fig. 1).

Treatment of pH abnormalities involves increasing or decreasing the pH (depending on the pH value and species involved) and improving the buffering capacity of the system. Water changes can be performed to normalize pH (the pH of the source water must be taken into consideration). Many commercial preparations/buffering compounds are available for adjusting pH. Sodium bicarbonate (baking soda) can be added at a rate of 3 mg/L

Fig. 1. A Chagoi koi (*Cyprinus carpio*) with traumatic injuries due to a pH crash. The water pH was 6.0. The black lines show area of injuries.

to temporarily improve buffering capacity/alkalinity of the system [1,2]. Long-term management of low alkalinity can be helped by the use of crushed coral, crushed oyster shells, or limestone [3]. Old tank syndrome treatments also include the use of ammonia binders, treatment of any secondary health problems, and client education in husbandry practices.

More ammonia is present in the toxic form at higher pH levels, resulting in increased ammonia toxicity. Increased toxicity of heavy metals and some medications (choramine-T, copper sulfate, formalin, malachite green) may be seen at lower pH levels [2].

Ammonia toxicity

Ammonia is the primary nitrogenous waste product of fish and also originates from the decay of complex nitrogenous/protein compounds [1,2]. Non-ionized ammonia is excreted from the gills by diffusion. Environmental increases in non-ionized ammonia decrease the rate of diffusion from the gills, resulting in elevated blood and tissue ammonia levels. Ammonia toxicity is one of the most common water quality problems affecting aquarium fish and can cause acute mortality or chronic sublethal stress. Nitrifying bacteria oxidize ammonia to nitrites and nitrites to nitrates. New tanks or ponds that lack nitrifying bacteria (an "immature" biofilter) have an increase in nitrogenous compounds ("new tank syndrome") that resolves as the biofilter matures.

Ammonia is present in two forms: ionized (NH_4^+) and non-ionized (also called un-ionized, NH_3). Non-ionized ammonia is the most toxic form. The portion of total environmental ammonia that is present in the non-ionized form is dependent on pH and, to a lesser degree, on water temperature

and salinity. Ammonia is more toxic in warmer water, at higher pH, and at lower salinity [1–3]. The higher the pH, the more ammonia is present in the non-ionized form; therefore, ammonia toxicity is worsened in aquaria that have higher pH. For every 1-unit decrease in pH, there is a tenfold decrease in non-ionized ammonia [2].

Ammonia toxicity can result from overcrowding, overfeeding, buildup of organic debris, infrequent water changes, immature/inadequate biologic filtration as seen in new tank syndrome, or damage to existing biofiltration (vigorous cleaning, certain medications). Clinical signs of ammonia toxicity include mortalities, neurologic and behavioral abnormalities, lethargy, anorexia, poor growth, secondary infections, injected fins, and respiratory signs due to gill hyperplasia/hypertrophy [1–3]. The precise mechanism of ammonia poisoning in fish is unknown; however, high aqueous ammonia increases blood and tissue ammonia levels, causing elevated blood pH, osmoregulatory disturbance, increased tissue oxygen consumption, and decreased blood oxygen transport [2]. Ammonia toxicity causes branchial irritation resulting in gill hyperplasia, hypertrophy, and hypoxia [2,4]. Neurologic signs can develop, likely due to interference with neurotransmitters in the brain [4].

Diagnosis of ammonia toxicity is easily attained using commercially available test kits (Fig. 2); these kits typically report total ammonia nitrogen. The concentration of non-ionized ammonia can be determined from a standard chart depending on temperature and pH. Any value of ammonia should be regarded as significant. Ammonia tolerance varies with species but it is generally recommended that ammonia levels measure 0 mg/L to maintain healthy aquarium fish.

Frequent water changes (30%–50%) are the mainstay of treatment of ammonia toxicity. Feeding should be decreased or temporarily stopped. In overcrowded aquariums, the stocking density should be decreased. The pH should be evaluated and maintained; an increase toward the alkaline range of normal pH should be avoided. Good oxygenation should be

Fig. 2. An example of a water test kit available from www.hach.com.

maintained. Commercial ammonia binders are available but may interfere with ammonia test kits that use Nessler reagent. In any case of ammonia toxicity, the life-support system (or systems) should be evaluated and improved if necessary [5]. If chemical treatment results in biofilter damage, then activated carbon can be used to remove the drug from the system. Low doses of salt increase the ionization of ammonia and decrease toxicity [1,2,5].

Nitrite toxicity (brown blood disease, methemoglobinemia)

Ammonia is oxidized to nitrite (NO_2^-) by *Nitrosomonas* and other microbes. Causes for elevated nitrite in aquaria are similar to those listed under ammonia toxicity, and elevated nitrite is common in new tank syndrome (with a maturing biofilter). Clinical signs of nitrite toxicity in fish are predominantly respiratory in nature and include increased opercular rate, piping (gasping at surface), gathering in well-aerated areas (eg, near filter input), and death [1–3]. Nitrite is absorbed by the gills and oxidizes hemoglobin to methemoglobin, resulting in methemoglobinemia and hypoxia. Gills may appear pale or tan in color. In severe cases, gills and blood may show brown discoloration due to the methemoglobin [1–3].

Nitrite toxicity is best diagnosed by finding elevated nitrite in the aquarium combined with elevated methemoglobin levels in the blood [6]. More commonly it is diagnosed with compatible clinical signs and elevated nitrite levels on commercial test kits. The optimal level of nitrite in aquarium water is 0 mg/L.

Treatment of nitrite toxicity is similar to treatment of ammonia toxicity (water changes, feeding and stocking density decreases, biofiltration improvement, and so forth). Oxygenation should be improved to improve the relative degree of hypoxia. Most freshwater fishes actively transport nitrite from the water by way of the chloride uptake mechanism on chloride cells of the gills. The rate of uptake can vary depending on the water temperature, pH, and chloride level. Toxicity can be prevented or treated by adding chloride (as sodium chloride) to the water [6]. Due to higher levels of chloride in seawater, marine fish are less sensitive to nitrite toxicity [2].

Nitrate toxicity

Nitrite is oxidized to nitrate (NO_3) by *Nitrobacter* and other microbes. It is the least toxic of the nitrogenous compounds, but eggs and fry may be more sensitive to toxicity than adult fish. The most common cause for elevated nitrates is infrequent water changes; other causes are similar to those listed for ammonia toxicity. Clinical signs of nitrate toxicity include poor growth, lethargy, anorexia, opportunistic infections, and injected fins [1–3]. One study suggested that prolonged exposure to elevated nitrate levels

might result in a pathologic response demonstrated by biochemical and hematologic changes [7]. Although the investigators could not conclusively prove that high nitrate levels were responsible for the changes, the results were highly suggestive [7]. High levels of nitrate can encourage algal blooms that can result in other water quality abnormalities (Fig. 3). The diagnosis can be confirmed with commercial test kits; nitrate levels should be maintained below 50 mg/L. Treatment for nitrate toxicity involves frequent water changes and removing organic debris. Aquatic plants can remove some nitrates from the water but do not eliminate the need for water changes and routine cleaning [1,3].

Chlorine and chloramine toxicity

Chlorine is added to municipal water to kill microorganisms and is highly toxic to fish [2]. The average level of chlorine in municipal tap water can vary between 0.5 ppm and 2.0 ppm. Chloramines (formed by a reaction between ammonia and chlorine) may also be used as disinfectants in municipal water supplies and are toxic to fish [2]. Chorine causes gill necrosis resulting in hypoxia [2]. Chlorine and chloramine can also result in hemolytic anemia [4]. Chloramine may result in methemoglobin formation by oxidizing hemoglobin to methemoglobin [4]. The most common cause of chlorine/chloramine toxicity in aquarium fish occurs when water is added without prior dechlorination. Fish affected by chlorine toxicity typically exhibit respiratory signs and acute mortality [1,2]. Chronic exposure to lower levels of chlorine may result in a history of sporadic mortalities. Sunken eyes have been reported as a possible clinical sign in cases of chronic exposure [6].

Commercial test kits for chlorine and chloramines are available and aid in the diagnosis of chlorine/chloramine toxicity. Chlorine is easily removed from water with dechlorinators such as sodium thiosulfate (3.5 mg/L) or by aeration of water for 24 hours in an open-topped container [1,2].

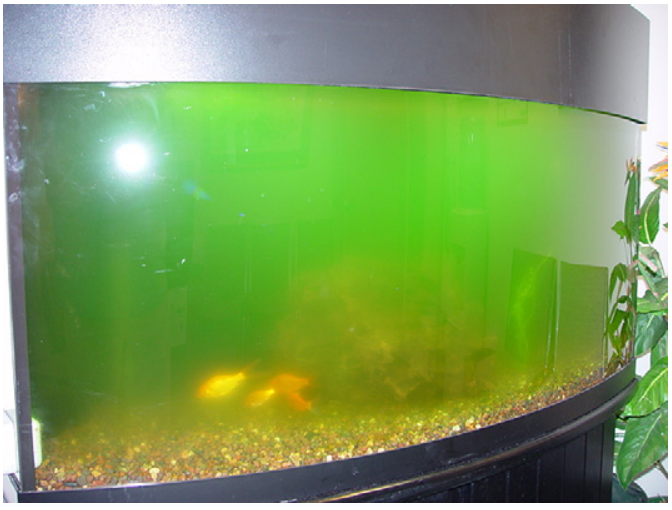

Fig. 3. Algae accumulation in a tank due to high nitrate levels.

Dechlorinators (like sodium thiosulfate) remove the chlorine from chloramines and release ammonia into the water [2]. The resulting ammonia is usually handled by the biofiltration in life-support systems unless the biofilter is immature, such as in a new aquarium setup. Fish treated for acute chlorine toxicity have improved survival if the water is supersaturated with oxygen; lowering the water temperature may also be beneficial [2].

Hydrogen sulfide toxicity

Hydrogen sulfide (H_2S) is produced from the reduction of sulfate ion under anaerobic conditions [2]. It can occur at the bottom of aquaria that have excessive organic debris or in deep gravel or sand filter beds that are not completely aerated (Fig. 4). Hydrogen sulfide toxicity is more of an issue in brackish and marine systems due to increased concentration of sulfate ions [2]. Disturbing the filter media or bottom substrate, which can occur when an owner vigorously cleans the gravel bed after a long period of neglecting routine maintenance, can release hydrogen sulfide into the water column. The owner may report a "black cloud" released into the water during this cleaning. Hydrogen sulfide may also be present in well water. Hydrogen sulfide interferes with respiratory function and results in hypoxia [1–3]. Affected fish demonstrate lethargy, anorexia, respiratory signs, and sudden death [1–3].

Presence of hydrogen sulfide can be detected by its characteristic rotten egg odor and can be confirmed with commercial test kits. Any levels detectable with commercial test kits should be considered detrimental [2]. Aggressive aeration and water changes remove hydrogen sulfide from the water. Maintaining aerobic environments in the tank and filter by removing decomposing detritus and allowing for thorough aeration of the filter bed prevents hydrogen sulfide accumulation. A degassing tower can be used to remove hydrogen sulfide from the water before it comes into contact with the fish. Potassium permanganate (2 mg/L) oxides/detoxifies hydrogen

Fig. 4. A deep layer of gravel in a 180-gal tank. Unless maintained, the gravel bed can develop pockets of hydrogen sulfide gas.

sulfide but cannot be used in marine systems [2]. Increasing the pH and lowering the temperature also decreases hydrogen sulfide toxicity [2]. Caution should be taken when restarting filters that have been turned off, because anaerobic environments may have been created.

Chemotherapeutic toxicities

Improperly administered chemical treatments can be a cause of toxicity in aquarium fish. In many cases, treatment dosages are based on empiric and anecdotal information; toxicity may therefore occur at recommended dosages. Pharmacokinetic data are seldom available for agents used to treat ornamental fish. Susceptibility to chemotherapeutic toxicity varies with species, water quality, and medication used. Chemotherapeutics can damage the biofilter, the fish, and other organisms that inhabit the aquarium. Common chemotherapeutics that can result in toxicity in aquarium fish include copper, formalin, potassium permanganate, malachite green, quaternary ammonium compounds, organophosphates, and antibiotics such gentamicin, sulfonamides, and oxytetracycline.

Copper toxicity

Copper (most commonly as copper sulfate) is used in the treatment of various ectoparasites in aquarium fish. It has a narrow therapeutic index, and accurate dosing is critical to prevent toxicity. Free copper ions must be maintained between 0.15 mg/L and 0.20 mg/L [2]. Copper is primarily toxic to the gill tissue, resulting in osmoregulatory dysfunction and hypoxia [2,3]. It may also damage the kidney and liver and result in immunosuppression [2]. Copper is extremely toxic to invertebrates. Copper toxicity can also result from the use of copper piping or decorations. Toxicity is most common in systems with low alkalinity, especially with low pH [5]. Copper treatments are not recommended in systems with a total alkalinity of less than 50 mg/L; in general, the authors do not recommend copper treatment in freshwater systems, especially when safer alternatives exist.

Clinical signs of copper toxicity include lethargy, anorexia, and respiratory signs [2,3] in addition to abnormal behavior, gill edema, disorientation, and scale protrusion [6]. Some species of fish may also show intense coloration before death [6]. Diagnosis of copper toxicity is made by way of history and commercial test kits. When copper toxicity occurs, large water changes and oxygenation of the water should be performed. Copper toxicity can be prevented by carefully monitoring copper levels and by avoiding its use in systems that have low alkalinity.

Formalin toxicity

Formalin is an aqueous solution of 37% formaldehyde gas [2,3]. It is used to treat a variety of ectoparasites in ornamental fish, most commonly at the

concentration of 25 mg/L (1 mL/10 gal). Formalin decreases dissolved oxygen in the water and can cause irritation of the gills; therefore, water should be oxygenated well during treatment. Formalin is more toxic in soft, acidic water and at higher temperatures [2]. A recent study evaluating the tolerance of various disinfectants in common aquarium fish found that goldfish (*Carassius auratus*) are more sensitive to the effects of formalin than zebrafish (*Danio rerio*) [8]. Exposure to formalin at a reported therapeutic dosage (250 ppm for 1 hour) resulted in toxic effects in goldfish but not in zebrafish, and prolonged exposure increased toxicity in goldfish but not in zebrafish [8]. The median lethal dose (LD_{50}) was 648 ppm for 1 hour in zebrafish and 272 ppm for 1 hour in goldfish [8].

Fish affected by formalin toxicity typically illustrate respiratory signs (eg, piping), decreased activity, loss of equilibrium, erratic swimming, excess mucus production, color changes, and mortality [2,3,8]. Treatment of formalin toxicity involves water changes, removing excess formalin with activated carbon, and aggressive aeration of the water. Formalin should never be used when the preparation appears cloudy or has a white precipitate. Formalin is a carcinogen and should be handled carefully [2].

Potassium permanganate

Potassium permanganate (K-P) is an oxidizing agent used to treat a variety of ectoparasites and external skin/gill bacterial infections in freshwater fish [2]. Effective treatment concentration requires 2 mg/L of active chemical; permanganate ion imparts a light pink or purple color to the water that fades as it becomes inactive [2]. Exposure of goldfish and zebrafish to lethal concentrations of potassium permanganate resulted in decreased activity, loss of equilibrium, erratic swimming, and death [8]. Goldfish were less sensitive to the effects of potassium permanganate then zebrafish; the LD_{50} was 5.75 ppm for 1 hour in zebrafish and greater than 25 ppm for 1 hour in goldfish [8]. Prolonged exposure increased toxicity in zebrafish but not in goldfish [8]. Potassium permanganate is toxic in water that has high pH because manganese dioxide may precipitate onto the gills; therefore, it should not be used in marine systems [2]. Potassium permanganate is extremely toxic when mixed with formalin [2].

Malachite green

Malachite green is a diarylmethane dye that is effective in the treatment of water mold infections and some ectoparasites in fish [2]. It is also a respiratory poison, teratogen, and suspected carcinogen and should be handled with caution [2]. Toxicity in fish typically presents as respiratory distress, given its activity as a metabolic respiratory poison [2]. Malachite green is reported as being hepatotoxic and implicated in causing developmental abnormalities when used to treat fish eggs [3]. Signs of malachite green toxicity in

zebrafish and goldfish include decreased activity, loss of equilibrium, erratic swimming, and death [8]. Extending the treatment time enhanced toxicity in goldfish but not in zebrafish [8]. The LD_{50} was 8.68 ppm for 30 minutes in zebrafish and 9.23 ppm for 30 minutes in goldfish [8]. The toxicity of malachite green increases with higher temperatures and with lower pH [2]. Some species such as tetras, catfish, and loaches are reportedly more sensitive to malachite green toxicity [2]. Young fry and near-hatching eggs are also very sensitive to toxicity [2]. Malachite green can be removed from the system with water changes and activated carbon.

Quaternary ammonium compounds

Quaternary ammonium compounds, such as benzalkonium chlorides and benzethonium chlorides, are disinfectants that may be used as antiseptics to treat external infections in fish [2]. Quaternary ammonium compounds are more toxic at higher temperatures and in softer water [2]. In one study, benzalkonium chloride was tolerated well by goldfish and by zebrafish [8]. There was no mortality in any of the fish exposed to benzalakonium chloride at or below the therapeutic dosage (2.0 ppm for 1 hour) [8]. Signs of toxicity occurred with greater than three times the therapeutic concentration and included decreased activity and loss of equilibrium [8]. The LD_{50} was 6.28 ppm for 1 hour in zebrafish and 5.80 ppm for 1 hour in goldfish [8].

Organophosphate toxicity

Organophosphates have been widely used for the treatment of ectoparasites in aquarium fish. These compounds are also potentially harmful to humans. In most cases, safer alternative treatments are available. Many species are sensitive to the toxic effects of organophosphates, even when therapeutic doses are used. Until the 1970s, dichlorvos (or dichlorvos mixtures) was used to control common carp populations by fisheries biologists [9]. The toxic effects of organophosphates in fish manifest primarily as neurologic signs. Clinical signs of organophosphate toxicity include vertebral fractures, convulsions, respiratory difficulty, erratic swimming movements, weakness or restlessness, and mortalities [2,10]. Because the use of trichlorphon, fenthion, and dichlorvos is extensively described in the literature and in hobbyist texts, the aquatic practitioner may still see toxicities from these agents. There is no specific treatment for organophosphate toxicity. Surviving exposed fish should be moved to clean water.

Antibiotics

Aquatic practitioners frequently use antibiotics to treat a variety of infectious maladies. In addition, antibiotics are readily available to hobbyists over-the-counter, potentially leading to inappropriate dosing and toxicity.

Pharmacokinetic data are not available for many drugs, and effective therapeutic dosing regimens can vary widely among fish species. Anecdotal data and extrapolation from the drugs used in other species may be used to treat fish patients. The potential for adverse side effects may also be extrapolated from use in other species. The common use of parenteral antibiotics and the frequent alterations in dosing regimens (usually shorter intervals and higher dosages) among laymen can increase the potential for toxic side effects. Questioning the owner on the use of previous therapeutants is an essential part of the historical data gathered on a sick fish consult. Aminoglycosides such as kanamycin, amikacin, and gentamicin have been documented to be nephrotoxic in several species. Nephrotoxicity may even occur at therapeutic doses, depending on the species [2,3]. Oxytetracycline can be immunotoxic in several species [2,11], and degraded products may be nephrotoxic [2]. In addition, the use of antibiotics as a prolonged immersion treatment may adversely affect biofiltration, leading to water quality concerns.

Pesticide toxicities

Aquarium fish are less likely to encounter pesticide toxicities than their farmed and wild cousins, but toxicities can still occur. Most household pesticides are highly toxic to fish. Organophosphates, chlorinated hydrocarbons, pyrethrins, and pyrethroids make up the most likely suspects in pesticide toxicity cases. Indoor pest extermination most likely involves aerosol spraying procedures, so it is important for the homeowner to turn off air pumps and cover the tank until the danger of pesticide introduction has passed. Although rare, curious household pets have been known to fall into tanks and indoor ponds. If these pets have had a recent application of a topical pesticide or are wearing an insecticide-impregnated collar, toxicity in the tank may occur. Clinical signs vary but are mostly neurologic in nature. Acute reactions include paralysis and death [3]. Chronic exposure has been associated with poor growth and deformities in fry [3]. Vertebral fractures have also been reported [2].

Household toxicities

In general, few household toxicities present with pathognomonic lesions. Some identification of the toxin may be gained by carefully questioning the owner. In situations in which accidental contamination of the aquaria is suspected, the goals of treatment are to move the fish to clean, uncontaminated water and to provide symptomatic therapy such as additional aeration, treatment of secondary infections, and reduction of stress. In cases in which the fish cannot be removed, frequent, ample water changes should be recommended. Water quality should also be monitored in case of filter failure. Education of the owner may help to mitigate potentially disastrous situations. Many owners are unfamiliar with proper breakdown, disinfection, and

cleaning procedures of used tanks and equipment (nets, decoration, siphon pumps, and so forth). Listed below are some common scenarios that may occur in home aquaria.

Nicotine

Cigarette smoke fumes containing several toxins, including nicotine, can be introduced into a fish tank by an air pump, whereby they are rapidly absorbed into the water. Nicotine is soluble in water and very toxic to fish [2,3,6]. Guppies exposed to a smoky room for 1 hour experienced high mortalities [6]. Clinical signs of nicotine toxicity include abnormal posture (rigid pectoral fins, clamped fins), muscular spasms, pale coloration, and death [6]. Chronic exposure to low doses can cause deformed fry and infertility [6]. Treatment is general and aimed at removing the fish from the toxic environment. Frequent water changes, fresh activated carbon, or placing the fish in a fresh tank may reduce the impact of nicotine.

Detergents

Most cleaning agents and detergents used in homes are extremely toxic to fish [3]. Several household cleaners contain detergents and several other compounds, including ammonia-based products. Detergents may find entry into home aquaria by way of aerosol dispersion, accidental spillage, and intentional use by the owner. Failure to thoroughly rinse aquaria equipment and tanks is a common problem that can lead to toxicity in fish. Cationic detergents may contain quaternary ammonium disinfectants, another group of toxic compounds to fish [6]. Detergents break down the protective mucus layer on fish skin, facilitating pathogen entry [6]. Clinical signs of detergent contamination include skin hemorrhages, flashing due to irritation, excess mucus production or ''dry skin'' due to epithelial disruption, and edema of the gill epithelium [2]. Foam and bubbles may still be visible on the water surface. Treatment involves moving fish to fresh, oxygenated water. Salt at 0.1% may be added to freshwater to reduce stress.

Food-related toxicities

Food-related toxicities occur due to spoilage of food, contamination of food, the addition of potentially toxic ingredients to food, improperly balanced diets, and an inadvertent excess (toxic) amount of a required nutrient. In light of the recent pet food recall scares of 2005 (aflatoxin-contaminated dry pet food) and 2007 (melamine and cyanuric acid toxic reaction), consumers are more conscious of what is being fed to their pets, including their pet fish. One only has to visit the pet store, read trade journals, or look online to see the huge variety of foods available for feeding pet fish. Pet fish food is available frozen, live, pelleted, flaked, baked, and soft-moist, among

other preparations. Despite the scrutiny, food-related toxicities still occasionally occur.

Aflatoxins are mycotoxins produced by *Aspergillus* spp, molds that occur commonly in the environment. Foods that are most susceptible to aflatoxin contamination are those containing oilseed crops (corn, cottonseed, and peanut meal), but other grains and feed are also susceptible [12]. The feed is more likely to have increased amounts of aflatoxin when stored at high temperature and humidity levels and when it has a high moisture content. Aflatoxin causes hepatotoxicity, and with prolonged feeding at sublethal levels, it can lead to hepatic neoplasia [2,4,12–14]. Sensitivity varies with species. Clinical signs of aflatoxicosis range from decreased growth or lack of weight gain, pale gills/anemia, and impaired coagulation (Fig. 5) [12]. Aflatoxin can also destroy important nutrients in food, such as thiamine and vitamins A and C [12]. Subsequent immunosuppression can lead to increased susceptibility to other diseases [12]. As part of an environmental assessment and complete history, the owner should be questioned on feeding habits for the pet fish. When there is a high index of suspicion for aflatoxicosis, a sample of food can be evaluated by a diagnostic laboratory. It is wise to contact the laboratory before sending any samples to verify whether the test can be performed and to determine the specifics of sample submission.

In 2007, a nationwide recall of dog and cat food occurred because of the addition of melamine and cyanuric acid. When both ingredients were present in the food, crystals formed that potentially impaired renal function, sometimes leading to renal failure and death [15]. One large pet product company also voluntarily recalled several varieties of fish food due to potential melamine contamination [16]. No fish toxicities were reported due to the use of commercial diets during this recall.

Some plant legume proteins that contain nonessential amino acids have been found to be toxic when fed to fish, resulting in reduced growth [13]. The essential amino acid leucine has been reported to cause toxicity in

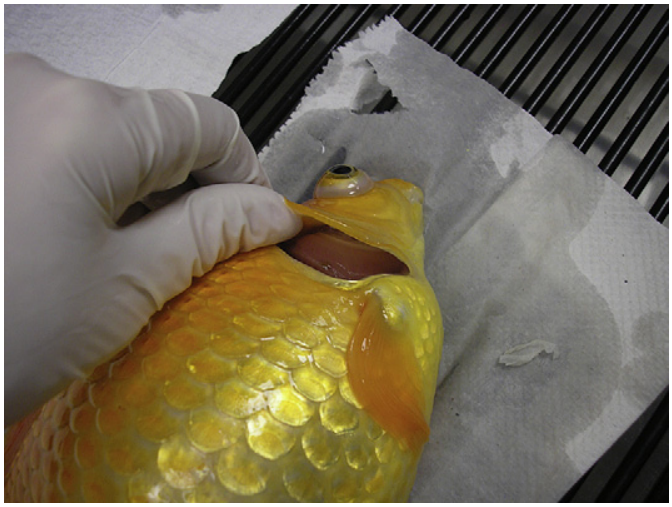

Fig. 5. Examination of pale gills in a goldfish (*Carassius auratus*).

rainbow trout. Clinical signs include scoliosis, deformed scales and opercula, and epidermal spongiosis [13]. The fat-soluble vitamins A, D, and E can cause toxicity when consumed in excess by fish. Salmonids were reported to experience decreased growth and reduced red cell counts [13]. In addition, toxic consumption of vitamin A resulted in necrosis of fins and tail, scoliosis, lordosis, pale yellow livers, and increased mortalities in salmonids [13].

Ingredients used to manufacture food may be contaminated with residues of pesticides, herbicides, and heavy metals [13]. Contamination by various toxins may also occur. These toxins are derived from protozoans, algae, fungi, and bacteria [13]. Pathogenic bacteria, parasites, and viruses are a risk when feeding live foods.

Heavy metal toxicities

Heavy metals that cause toxicity in aquarium fish include copper, zinc, mercury, cadmium, lead, and aluminum. Heavy metals usually originate in the water supply [3]. Older plumbing can leach metals into the water source of aquaria, especially after pipes have not been used for a period of time, allowing a higher concentration of metal to develop. Other sources include inappropriate tank décor, therapeutic agents (copper) [3], runoff, and contamination of ground water in wells. The level of toxicity depends on the water pH, hardness, temperature, and the presence of organic material and solids [2,3,6]. In general, heavy metals are more toxic at lower pH, at higher temperatures, in soft water, and at low alkalinity levels. Zinc toxicity may present in koi (*Cyprinus carpio*) that are wintered-over in galvanized tubs or live in indoor display ponds into which coins are thrown by the public. Copper and zinc toxicity effects are additive. High iron levels in water can lead to the precipitation of iron oxides. A heavy layer of iron oxides on the gills can lead to lamellar fusion and to severe gill disease [4]. Clinical signs of iron toxicity reflect the relative hypoxia (piping, gasping, and increased opercular rate). Rust-colored staining of tanks, gravel, and other aquarium equipment may be seen when performing an environmental evaluation. Lead toxicity may be caused by the use of lead plant weights, lead plumbing, lead paint, and lead solder joints [2]. Clinical indications of lead toxicity in some species of fish include scoliosis, anemia and stippling of the red blood cells, lordosis, and black tail (caudal cutaneous melanosis) [2,13]. Heavy metals affect the gills, kidneys, and liver [3], and clinical signs may reflect the extent of damage to these organs in exposed fish. Respiratory difficulty and osmoregulatory disturbances are the most common signs observed.

Definitive diagnosis requires submission of a water sample to an environmental or analytic laboratory. Source water should also be evaluated. Affected fish can also be submitted to analytic laboratories in cases of suspected heavy metal poisoning [2]. Specific handling instructions are required for processing the samples to prevent contamination or an inaccurate diagnosis [2]. Treatment of heavy metal toxicity requires identifying and removing

the source of exposure. No specific treatment with chelating agents or antidotes has been fully evaluated [6], although the use of EDTA has been recommended in the literature [2]. Water that has elevated iron levels can be pumped through an ion exchange filter before use in tanks [2].

Miscellaneous toxicities

Cyanide

Fish are very sensitive to the toxic effects of cyanide. Many species of common marine aquarium fish are collected outside the United States with the use of cyanide. Cyanide fishing has been reported to cause reef loss and deaths in smaller, nontarget fish [17]. Cyanide toxicity can also result from the use of salt containing yellow prussiate of soda (sodium ferrocyanide), an anticaking ingredient added to water conditioner. Clinical signs of acute toxicity include impaired swimming ability and relative performance, susceptibility to predation, muscle tremors, disrupted respiration, osmoregulatory disturbances, and altered growth patterns [18]. Clinical signs of hypoxia and stress can also be seen. The toxic effects from cyanide fishing may be further enhanced by hypoxic periods experienced during the transportation and handling of fish from the site of collection to wholesale distributors and, eventually, to the retailer [19]. Exposure to low levels of cyanide can cause poor reproductive performance and liver damage [19]. Owners may notice mortalities in cyanide-collected fish a short time after their introduction to the aquarium. Although clinical signs of toxicity may not precede the mortalities, hepatic necrosis, suggestive of cyanide exposure, can be detected on histopathologic examination.

Algicides (pseudo-poisoning)

Although not a true toxicity, the use of commercially available algicides can result in fish deaths. It is not unusual for an aquatic practitioner to receive a frantic phone call from an owner wondering whether the algicide used was toxic to the fish. Most fatalities can be attributed to acute low dissolved oxygen content following algal death. Decaying oxygen consumes a large amount of dissolved oxygen in the water [2]. If the pre-existing dissolved oxygen was borderline or low, then the resulting algal decay can wreak havoc in a system. An algae crash or widespread algae death for other reasons can also result in a similar situation.

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