Per- and polyfluoroalkyl substances (PFAS) were originally introduced into the market in the late 1940s after the accidental synthesis of polytetrafluoroethylene (PTFE) in 1938. The discovery that PTFE had unique surfactant and heat-resistant properties made it a valuable chemical for industrial processes and products. The chemical was first used in military equipment, but after a short time, PTFE became a critical component in the production of nonstick coating for bakeware. Since that time, the development of new species and the use of PFAS have grown. At the time of this writing, the Environmental Protection Agency (EPA) had recorded over 14,000 different types of PFAS.

PFAS are used in various products and manufacturing processes, including electronics, biotechnology, textiles, aerospace, food packaging, cosmetics, firefighting foams, plastics, and others.

The molecular structure of PFAS varies, but generally all PFAS contain a hydrophobic chain of carbon atoms attached to fluorine atoms, and many have a functional group or “head” at the end of the chain. The unique chemical structure of this chemical provides the family with highly desirable qualities such as thermal and environmental stability and the ability to repel oil, water, and stains, which have led to widespread use in manufacturing and consumer products. PFAS are generally grouped into 2 categories: long and short chain. This designation refers to the length of carbons that make up the hydrophobic chain. Chain length is important to note, as longer-chain PFAS were the first to be widely used in consumer products and are often associated with greater bioaccumulation.

The adverse health effects from PFAS exposure came to light in the 1980s when a farmer in...
West Virginia filed a claim against a nearby manufacturing plant for causing his family’s illness and the morbidity and mortality of animals on his farm. The concern was that effluent from the Dupont Washington Works Plant in Parkersburg, WV, was contaminating the water supply and making animals and people sick. The Washington Works Plant had been using one of the long-chain PFAS, perfluorooctanoic acid (PFOA), referred to as C8 because of the 8 carbons that made up its carbon-fluorine chain, to smooth out the Teflon® coating on pans. This accusation set off a nearly 20-year legal battle that ultimately demonstrated a probable link between PFOA and the illness experienced by the community. The case resulted in a health assessment and biomonitoring for the town of Parkersburg, WV, and tougher restrictions on the use of long-chain PFAS species in manufacturing.

The legal investigation against Dupont and subsequent health studies were a critical step for beginning government oversight of PFAS. Since that time, there have been thousands of studies conducted around the world to better understand the consequences of PFAS use and exposure. In the 2021 PFAS toxicological profile, the Agency for Toxic Substances and Disease Registry (ATSDR) lists increased cholesterol levels, changes in liver enzymes, decreased immune response, small decreases in birth weights, increased risk of kidney or testicular cancer, and increased risk of high blood pressure as a few of the growing number of potential human health effects following exposure to PFAS. Growing evidence demonstrates that the adverse health outcomes seen in people may also apply to the animal population.

In this paper, the authors present a summary of current literature regarding PFAS exposures in animals and discuss potential health risks for livestock, wildlife, and pets.

Methods

Sources included in this review were found by searching PubMed, Web of Science, and ScienceDirect databases using relevant search terms and by reviewing EPA and ATSDR documents. Additionally, the reference sections of relevant research articles were used for further discovery of publications. To gain a better understanding of how PFAS affect different animal groups outside the laboratory, searches focused mainly on studies and papers that involved food animals, wildlife, or companion animals. An effort was made to identify exposure pathways, toxicological processes, and pathology related to the various animal groups.

Results

For this review, we will discuss exposure in terms of the following overarching categories: exposure due to contaminated water, diet, and dust; dermal absorption from PFAS-containing products; and maternal transfer (Figure 2).

Exposure pathways

Water—PFAS can enter the water system in multiple ways. Runoff from contamination sites (ie, manufacturing plants, fields treated with biosolids, landfills) can either directly flow into lakes and rivers or soak into the ground to contaminate wells and aquifers. Clouds, which have developed over PFAS-contaminated sites, can carry contaminants hundreds of miles away from the source before precipitating, and ocean currents can transport PFAS from one part of the world to another.
Like humans, drinking contaminated water may be a significant source of PFAS exposure in animals. A study\(^{15}\) was initiated on an Australian farm in 2015 after it was discovered that the runoff from a neighboring facility, which used PFAS, had contaminated a culvert and dam used as the farm’s water source for livestock. Researchers collected samples of trough water, grass, and soil from the farm as well as blood from cattle and sheep that were raised there, from 2 distinct time points before remediation. Total perfluorooctane sulfonic acid (PFOS) levels in the trough water measured at 6,170 and 6,690 parts per trillion (ppt) in 2015 and 2016, respectively (EPA’s recommended drinking water limit ranges from 0.04 to 2,000 ppt depending on the type of PFAS measured\(^{14}\)). The team found no measurable PFAS in any grass samples and very low concentrations of PFAS in soil. Serum PFAS in cattle measured at the 2016 time point resulted in total PFOS concentrations ranging from 609 to 1,944 ng/mol (animals < 6 months of age had significantly less PFOS than older animals). After remediation of water supply, PFOS concentrations in water dropped in half, and cattle serum concentrations of PFOS ranged from 274.5 to 507.7 ng/mL with a mean of 370 ng/mL. In a separate Australian study, Braunig et al\(^{10}\) also found that cattle living in an area where firefighting foams had contaminated groundwater had significantly elevated blood PFAS levels compared with those of cattle living outside the area.

The US Geological Survey has found PFAS in surface water and groundwater in numerous sites across the US.\(^{15}\) One site is the former Wurtsmith Air Force Base on the eastern shores of Michigan’s Lower Peninsula. Researchers sampled adjacent waterways and measured total PFAS concentrations ranging from 17.0 to 12,266 ppt\(^{16}\) in the Au Sable River and Clarks Marsh, respectively. Contamination is attributed to the base’s known use of aqueous film-forming foam in firefighting training exercises\(^{17}\) and has led to restrictions on hunting and fishing in the area.

**Air, dust, and soil**—Though PFAS can be detected in outdoor air, Shoeib et al\(^{18}\) demonstrated PFAS concentrations inside could be 100 times greater than that measured outside. This is assumed to be largely because of the widespread use of PFAS in manufacturing and in stain-resistant coatings for furniture, flooring, and fabrics. For example, Shoeib et al\(^{18}\) measured 1 species of PFAS (methyl perfluorooctane sulfonamidoethanol [MeFOSE]) at 31.7 pg/m\(^2\) in an outdoor air sample but then found concentrations ranging from 667 to 8,315 pg/m\(^2\) within homes. In a 2013 study of dust in homes across the US, Shoeib et al\(^{16}\) found that bedrooms with flooring made from plastics had significantly higher levels of PFAS than those made from wood. To date, there have been no studies reviewing the risk of animals to PFAS-contaminated indoor dust.

Soil can be contaminated with PFAS-containing rainfall, runoff, irrigation, or biosolid and pesticide application and can act as a significant reservoir of the chemical. In a systematic review published in 2020, Brusseau et al\(^{21}\) evaluated data for > 30,000 samples collected from > 2,500 sites across the world to quantify PFAS concentrations in sites that do not have known PFAS contamination (background sites) and contaminated sites where PFAS was made, used, or disposed of. The study found that PFAS was present in soil samples across the world with total PFAS concentrations in background soils ranging from 0.001 to 237 µg/kg. PFAS in contaminated sites, however, ranged from 0.4 to 460,000 µg/kg. Animals can be directly exposed to PFAS in contaminated soils through foraging or burrowing habits and indirectly exposed when the chemical becomes airborne via wind, leached into groundwater, or has runoff into surface water.

**Diet**—Plants grown in contaminated soils can absorb PFAS and, when consumed, expose animals to the chemical.\(^{22,23}\) Wang et al\(^{22}\) summarized the uptake and bioaccumulation of various PFAS in different plants and concluded that it is reasonable to assume that plant bioaccumulation leads to PFAS exposures in animals consuming these plants. A study by Palmer et al\(^{24}\) found that manatees in a Florida county had surprisingly elevated blood PFAS compared with other marine herbivores. The study authors proposed that the high chemical burdens of the manatees are potentially a result of consuming aquatic vegetation that contains high levels of PFAS, suggesting that PFAS accumulation could be an issue for both terrestrial and aquatic herbivores.

PFAS has been measured in livestock eating contaminated hay and feed. Vestergren et al\(^{25}\) detected PFAS in liver, blood, muscle, milk, and urine of the dairy cattle housed on a Swedish farm outside Stockholm. The cows were primarily fed silage and barley grown on the property and drank from the farm’s well. Of the food and water ingested, the silage had the highest concentration of PFAS followed by the barley. Only small amounts of PFAS were detected in the farm’s water source, indicating that the plants, rather than the water, were a significant source of exposure in this case. PFAS have been found in fish, muscle tissue, organs, and dairy products of livestock—all of which are used in the production of commercial pet foods. However, in a study\(^{26}\) of 11 different brands of popular dog and cat food sold within the US, researchers found only low levels of PFAS in a fraction of the food tested, suggesting that the food itself may not be a significant risk. The risk of PFAS contamination in livestock feeds from fishmeal was explored.
by Xiaomin et al,27 and PFAS was found in commercial fishmeal, with total concentrations ranging from 0.65 to 85.5 µg/kg. PFOS was detected in 98.9% of those samples. 27

Pet food packaging may also be a source of PFAS exposure, but more research is needed in this area. PFAS has been authorized for use in food contact surfaces since the 1960s to keep moisture and oil from soaking through food packaging and make cleanup of cookware easier.28 It has long been used to coat papers such as those used in microwave popcorn bags, pizza boxes, and fast-food wrappers. Research has demonstrated that small amounts of PFAS do leak from coated food-contact surfaces into human-grade food, particularly into oils or emulsified foods like butter.29

Dermal absorption—Four types of PFAS were found in an analysis of popular flea and tick products. A total PFAS concentration of 2,390 ppt was measured in Frontline Plus for Dogs, and 250 ppt was measured in Seresto Flea and Tick collars,30 which may have implications for our canine and feline patients.

Maternal transfer—Maternal transfer, both placental and oviparous, of PFAS has been documented in multiple species, including marine mammals31 and bald eagles.32 Evidence of PFAS secretion in milk also exists and has been documented in cattle.33 Based on these observations, maternal transfer in pets may also be likely. The authors suggest this is an area of future study.

Bioaccumulation

Studies have proven that PFAS bioaccumulate in many different animal species, with apex predators (eg, polar bears, bald eagles) at greatest risk.33,34 Bioaccumulation is dependent on multiple factors, including specific chemical properties (ie, functional group, carbon chain length) of the compound and variations within the animal population (eg, sex, species, habitat). In a study of rainbow trout exposed to PFAS of different chain lengths, Martin et al35 found that as PFAS carbon chain length increases, the ability of these chemicals to bioaccumulate also increases. This may be because shorter-chain PFAS are eliminated faster than longer-chain PFAS. Guruge et al36 found species differences while in investigations of PFAS levels in livestock and pets across Japan. In their study, PFAS levels (specifically the long-chain PFOS) were much higher in chicken livers compared with other samples sampled on the farm (cattle, horse, pig, goat, dog).35

Adverse health effects

Evidence from laboratory animal research indicates that hepatic, immune, and developmental processes are most often impacted following PFAS exposure.3 Adverse effects of the liver could include increased liver weight, hepatocellular hypertrophy, hyperplasia, necrosis, and decreases in serum cholesterol and triglyceride levels. Development outcomes may include reduced birth weights, prenatal loss, and delays in neurodevelopment and sexual maturity. Evidence of immune toxicity included decreased weight of thymus and spleen, changes in lymphocyte phenotypes, and reduced response to vaccination.36

Studies focusing on the health effects of PFAS exposures in animals outside the laboratory are scarce, and with different diets, habitats, and metabolism rates, it is difficult to extrapolate how different species may react to exposure. Limited studies37,38 have shown that some animals may tolerate higher levels of PFAS exposure or may eliminate PFAS more quickly compared with others. A few studies have hinted at the risks of PFAS in cats and dogs. A study39 in North Carolina found concentrations of various PFAS in blood samples of both domestic and feral cats. In the examination of 72 animals, the authors discovered a significant association between PFAS concentration and body weight. Cats with higher serum PFAS levels were more likely to weigh more. The authors also found associations (though weak) between PFAS concentrations and liver, thyroid, and kidney disease in the cats. In contrast, a study by Wang et al40 found a significant correlation between hyperthyroid cats and high total PFAS levels. High PFOS levels were detected among dogs in a veterinary clinic in Japan, but the health status and history of these animals and the effect of PFOS on their health were not evaluated.41 A study42 of police dogs exposed to PFAS-containing firefighting foams and laboratory Beagles exposed to PFAS in their diet found dose-dependent alterations in amylase (increased) and cholesterol (decreased). There were also links between PFAS exposure and certain blood chemistry parameters such as the albumin-to-globulin ratio, BUN, ALP, and creatinine.41 With additional research, possible associations between PFAS and certain disease states might be discovered, which would prove beneficial to veterinarians and clients in understanding the etiology of health conditions in pets.

In terms of livestock, multiple studies have found that PFAS can be found in the serum, liver, kidneys, and milk of production animals,43,44 but aside from an anecdotal report of cattle dying after drinking PFOA-contaminated water,7 there have not been any published adverse events in livestock.

Pharmacokinetics and toxicology

Upon ingestion, PFAS are almost entirely absorbed through the gastrointestinal tract.45 PFAS can be found in various body tissues, but primarily the serum, liver, kidneys, and milk of production animals,45,46 but aside from an anecdotal report of cattle dying after drinking PFOA-contaminated water,7 there have not been any published adverse events in livestock.
the half-life of PFOS in mice ranges from days to weeks, while in pigs it is almost 2 years (634 days).45 For PFOA, the half-life could be as short as 2 hours in mice, while in pigs the half-life of the same compound was 236 days.45 In dogs, the half-life of PFOA ranged between 8 and 30 days.46 At the time of this writing, there was no report for half-lives in cats. Activation of a nuclear receptor called peroxisome proliferator-activated receptor-α (PPARα) is thought to be responsible for liver toxicity, decreased cholesterol, and some of the developmental delays seen in exposed laboratory animals. This receptor is a transcription factor and a key component to regulating lipid metabolism, cellular growth, and differentiation. Exposure to PFOS changes the expression of genes in the PPARα pathway.5 In rodents, activation of PPARα by PFOA and PFOS has led to proliferation of peroxisome in the liver, resulting in accumulation of cholesterol in the liver and subsequent hepatocyte vacuolization and hyperproliferation and liver enlargement.5,47 More research is needed to learn the effects of serum cholesterol in livestock and companion animals. Peroxisome proliferator-activated receptor-α is also a key receptor of rodent and human embryos. Activation of the PPARα receptor during gestation was associated with reduced postnatal survival, delayed eye opening, reduced pup survival, and smaller body weights. One hypothesis is that metabolic disruption of lipids may also be the cause of decreased neonatal survival and reduced body weights.5 Suppression of the T-cell dependent antibody responses and antigen-specific IgM titers has been documented following in vivo and in vitro exposures to PFAS.5,36 In a study to understand the role of PPARα activation in immune suppression, DeWitt et al36 found that the presence of PPARα does result in the reduction of thymus and spleen weights but does not seem to have an impact on the activity of T-cell–dependent antigen responses and antigen-specific IgM titers. Instead DeWitt proposed that PFAS exposure depresses immune function by suppressing the B-cell and plasma cell function. PFAS are associated with altered thyroid function in both humans and animals, although the mechanisms of action and health outcomes appear to differ between species. Both Wang et al40 and Bost et al39 found significant positive associations between PFAS and hypothryoidism in cats. Human epidemiological studies are somewhat inconclusive. Some of the studies included in the 2021 ATSDR PFAS toxicological profile5 pointed to significant positive association between PFAS exposure and hypothryoidism, some showed significant positive association between PFAS and hyperthyroidism, and others didn’t find any linkages at all. No association between thyroid function in dogs has been made. Researchers hypothesize that altered thyroid function can occur either through PFAS-induced increase in thyroid hormones or by competing with active thyroid hormone (T3) and its precursor, thyroxine (T4), for binding sites on carrier proteins.46,48

**PFAS regulations**

Interest in regulating PFAS production began in 1998 during the investigation into PFAS exposure at Parkersburg, WV. By the time the US Government began regulatory oversight, PFAS were widespread in the environment and found in human blood samples49 across the continent. In 2010, the EPA established the PFOA Stewardship Program to reduce the amount of long-chain PFAS produced within the US. Within 5 years, all companies participating in this voluntary program succeeded in phasing out PFOA production in the US.49,50 In July 2020, the European Union stepped forward toward stronger regulation of these chemicals by banning the sale of products that contain PFOA and related chemicals within Europe.11 The EPA recently announced that it would work toward regulating PFAS concentrations in drinking water in the US. Even though the newer short-chain PFAS do not bioaccumulate at the same rate as the long-chain species, a study by Gomis et al44 found that exposure to these chemicals can potentially result in similar adverse effects. The use of short-chain PFAS in industrial processes is likely to continue for years to come, as some species are essential to production of lifesaving items such as medical devices or flame retardants.

**Clinical Relevance**

From food packaging and cosmetics to drinking water and dust, PFAS have been found in virtually every corner of the world. Though the introduction and use of PFAS have improved many aspects of our lives, the chemicals are known to cause health problems in both humans and laboratory animals, and exposure to this family of chemicals is considered a significant public health threat. Elevated PFAS levels in indoor dust and air contribute to PFAS exposures among pets and people.3,37 The proximity of small children and household pets to PFAS-treated carpets and floors where dust accumulates, in addition to their mouthing behaviors, potentially place children and pets at similar exposure risk.39 Additionally, certain textiles produced for pets and children (eg, beds, toys) likely contain PFAS due to the wide usage of PFAS-containing stain-resistant treatments in textiles and plastics.3,38 As with water, contaminated dust can be carried long distances from PFAS contamination sites, making it difficult to pinpoint specific exposure sources for wildlife and other animal groups.

PFAS contamination and exposure are emerging issues in clinical practice, but understanding how PFAS impact our veterinary patients is complex. Laboratory studies, which often expose animals to much higher PFAS concentrations than typically found in the real world, are hard to interpret in the context of livestock, pets, and wildlife.

In addition to extrapolating laboratory animal data to their specific patient, clinicians need to consider the type of PFAS the animal was exposed to,
the magnitude of exposure, and the species of animal exposed. When considering a diagnosis of PFAS exposure, clinicians should first check with the state health department to see whether there is local PFAS contamination in the area. If PFAS are suspected, diagnostic tests may be offered by the state public health laboratories.

There are no treatments for humans or animals exposed to PFAS. Rather, current recommendations are to reduce the sources of exposure. For the veterinary patient, this could mean changing the source of drinking water from tap to filtered water, switching to an oral flea and tick preventive, or reducing the amount of contact of furniture or carpets treated with stain-resistant coatings.

The risks of PFAS contaminating animal products such as meat and milk, the impact of PFAS exposure on the health of pet patients, and the potential of pets to act as sentinels for human exposures (especially children) are questions that need to be considered. As the family of PFAS continues to grow, continued research will be critical to understanding their impacts on public health, animal health, and the environment.

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