Review

Overview of Per- and Polyfluoroalkyl Substances (PFAS), Their Applications, Sources, and Potential Impacts on Human Health

Zunaira Habib [1,*], Minkyung Song [2], Sadaf Ikram [3,4] and Zahra Zahra [5,*]

1 Institute of Environmental Sciences and Engineering, School of Civil & Environmental Engineering, National University of Sciences and Technology, Islamabad 44000, Pakistan
2 Plamica Labs, Batten Hall, 125 Western Ave., Allston, MA 02163, USA
3 Department of Chemistry, Quaid-i-Azam University, Islamabad 44000, Pakistan
4 Chemistry Department, Rawalpindi Women University, Rawalpindi 46300, Pakistan
5 Department of Civil & Environmental Engineering, University of California-Irvine, Irvine, CA 92697, USA
* Correspondence: zunaira.habib@yahoo.com (Z.H.); zahra.nust@gmail.com (Z.Z.)

Abstract: Per- and polyfluoroalkyl substances (PFAS) belong to a group of synthetic compounds that have recently raised concerns about human health and environmental quality due to their great prevalence, degradation resistance, and potential toxicity. This review focuses on the applications of PFAS and their effects on human health. Specific emphasis has been laid on (i) the application/use of PFAS, (ii) sources and distribution of PFAS in diverse environmental compartments, and (iii) the impact of PFAS on human health. Significant health effects on humans are associated with exposure to PFAS, i.e., immunotoxicity, thyroid and kidney disorders, cancer, etc. Conclusions obtained from PFAS studies demonstrate that inadequate evidence should not be used to justify delaying risk reduction steps for PFAS alternatives. PFAS can be determined in different environmental matrices using both traditional analytical approaches, i.e., liquid chromatography coupled with mass spectrometry (LC-MS/MS) and semi-quantitative and passive sampling, and advanced analytical methods with colorimetric, spectrofluorimetric, and electrochemical detection. Traditional methods are costly and not broadly available, while the emerging, cost-effective methods are less sensitive and unable to meet regulatory exposure limits. There is still a significant number of studies to be performed to fully comprehend the real contamination by PFAS.

Keywords: Per- and polyfluoroalkyl substances (PFAS); environmental contaminants; PFAS applications; impacts of PFAS; human health

1. Introduction

Per- and polyfluoroalkyl substances (PFAS) are a group of emerging pollutants that include at least one aliphatic perfluorocarbon component [1]. PFAS include approximately 5000–10,000 compounds, and the majority of them are highly resistant to decomposition in the environment under natural circumstances, due to which they are referred to as "forever chemicals" [2]. The presence of inert carbon–fluorine (CF) bonds and high polarity make PFAS persistent, highly thermal, chemically stable, and recalcitrant chemicals. These properties make it challenging to manage their presence in different environmental compartments, including air, water, and soil. However, their distribution in the environment significantly depends on geographic location based upon their production method and inherent chemical characteristics. In contrast, the structural difference affects their mobility in the environment. For example, branched isomers mostly exist in aqueous media as compared to linear ones, which prefer sediments and soil for existence. Among branched isomers, the long-chain hydrophobic PFAS usually bioaccumulate in fish tissues, and short-chain hydrophilic PFAS make their way towards surface water [3]. PFAS have become a severe hazard to public health and the environment due to their ubiquitous prevalence in the environment and potential toxicity [4]. They have been immensely produced and extensively used in a wide

variety of industrial, domestic, and consumer products, like fireproofing, waterproofing, or anti-staining agents. They are released into the environment and have been commonly found in human blood serum in volumes up to hundreds of μg/L [5–8]. According to a report by The Centers for Disease Control and Prevention (CDC), PFAS were detected in the blood of almost all Americans (98%) [9]. Estimates showed that many legacy PFAS have half-lives in humans for years, indicating that they have alarming bioaccumulation and biomagnification potential [10]. Emerging PFAS, such as hexafluoropropylene oxide dimer acid (HFPO-DA) and 6:2 chlorinated polyfluoroalkyl ether sulfonic acid (Cl-PFESA) (trade name "F–53B"), are extremely persistent in the environment and common in global surface waters [11]. To date, among emerging PFAS, F–53B is the most biopersistent, with a half-life that is even longer (15.3 years in humans) than that of perfluorooctane sulfonic acid (PFOS) [11]. Numerous detrimental health risks, including impaired immune functions, chronic autoimmune disorders [12], hepatotoxicity, cancer, decreased fertility, and toxic developmental effects, are associated with exposure to PFAS [13].

Due to the high toxicity of single perfluorinated substances, i.e., PFOS and perfluorooctanoic acid (PFOA), their use has been banned in the EU since 2006 and 2019, respectively, based upon the agreement in the Stockholm Convention. As a result, alternative PFAS, including short-chain lengths or fluorotelomers (partly fluorinated), have been in use [14]. Both short- and long-chain PFAS can be determined based on the length of the fluorinated carbon chain (C_nF_{2n+1}). The term "long-chain PFAS" refers to a carbon chain length of C8 and higher for perfluorocarboxylic acids (PFCAs), including perfluorooctanoic acid (PFOA), and carbon chain lengths of C6 and higher for perfluoroalkane sulfonic acids (PFSAs), including PFOS and PFHxS [15]. In contrast, the term "short-chain PFAS" refers to perfluorosulfonic acids (PFSAs) with $n < 6$ and perfluorocarboxylic acids (PFCAs) with $n < 7$ [15,16]. The shorter-chain PFAS are less toxic as compared to longer chains; however, they (short-chain PFAS) are more mobile and move swiftly in the case of soil pollution [17].

The degradation of short-chain compounds is difficult and needs further scientific research to remove these from the environment. Several PFAS removal techniques have been developed in response to the increased emphasis on removing PFAS contamination at levels ranging from parts per billion (ppb) to parts per trillion (ppt). The techniques are classified as destructive or non-destructive techniques. The destructive techniques include incineration, electrochemical oxidation, advanced oxidation/reduction, sonochemical photolysis, and biodegradation. However, the non-destructive techniques include activated carbon, ion-exchange resins, polymeric adsorbents, in situ foam fractionation or ozo-fractionation, etc., which remove PFAS momentarily [18].

Granular activated carbon (GAC) and ion-exchange resins (IERs) are the most widely used strategies among non-destructive techniques. GAC is considered an economical and efficient approach for long-chain PFAS due to their hydrophobic nature. However, their adsorption capability depends on the pore size, internal surface area, and surface charge [19]. As compared to GAC, ion-exchange resins can be used for a number of cycles, even after their adsorption capacity is reached. The functional groups on the ion-exchange medium are restored to their initial state during the regeneration process, allowing for the possibility of one more cycle of sorption. Therefore, without changing the filter material, the ion exchanger can be utilized for several adsorption cycles. After this separation, the concentrated PFAS can further be mineralized for effective degradation [14].

Among destructive techniques, sonochemical and advanced oxidation processes (AOPs) are valid options. Sonication is the main mechanism for sonochemical PFAS degradation. Using sound waves, PFAS are remediated at the water/bubble interface. Sound waves create bubbles that expand until they reach the quasi-adiabatic compression stage, after which they collapse. This procedure is not cost-effective, so it has not been scaled-up to the commercial level yet. However, sonication, as an initial pilot-scale and lab-scale technique, has been mentioned by Vo et al. [20] and Verma et al. [21] in review articles. AOPs represent an additional means of destruction that can be applied in two ways. Heterogeneous photocatalysis is one example, where PFAS are broken down by removing

CF$_2$ groups simultaneously through photo-oxidation and reduction routes. These groups have the potential to mineralize into fluoride and CO$_2$ ions later. Although it can break down PFAS fast, the AOP is still not able to break down short-chain PFAS efficiently. However, short-chain PFAS can be broken down by defluorination [22]. Almost all destructive procedures involve defluorination, which frequently results in the undesired byproduct of short-chain PFAS being synthesized during breakdown [19,20,23].

Membrane-based separation of PFAS is a non-destructive and non-adsorption technique. Among various membranes, nanofiltration (NF) and reverse osmosis are superior due to their pore sizes of 1–2 nm and <1 nm, respectively. These membranes can tolerate high flow rates and have a good retention capacity for both short- and long-chain PFAS. However, NF membranes require less pressure than RO membranes, which means they use less energy, making them cost-effective approaches [24]. Conclusively, further research on PFAS removal through adsorption on GAC is pointless due to its failure to remove short-chain PFAS. However, IER and NF are promising approaches to remove short-chain PFAS as well.

This review article presents comprehensive information on PFAS and their widespread applications in our daily life, along with detailed information about their sources and dispersal route in major environmental compartments, including air, water, and soil. Human exposure to PFAS through any possible pathway, along with potential impacts on human health, is the highlighted realm of this paper. A detailed understanding of the mechanism of PFAS and methods for their complete mineralization must be evaluated in future studies.

2. PFAS Applications/Uses

Since the mid-20th century, PFAS have been used in many applications, including textile coatings, surfactants, food contact materials, pesticides, and fire-fighting foams [25,26]. They are also found in haircare products, hand sanitizers, and makeup removers. Water-repellent clothing, which includes fluorotelomer alcohols (FTOHs), perfluorinated carboxylic acids (PFCAs), and perfluoroalkyl sulfonic acids (PFSAs), is another important application of PFAS [27]. Due to their usage in a number of applications, PFAS have been detected in a wide range of products, such as food contact materials (FCMs), outdoor apparel, carpeting, carpet cleaners, floor waxes, and upholstery [28–30]. Table 1 summarizes the applications of PFAS, their purposes of use, and consumer products in which they are detected.

Table 1. Applications of PFAS in different domains.

Applications	Purpose	Consumer Products	References
Paints, coatings, wax, and varnish	To reduce surface tension for dispersing agents, substrate wetting, penetration, and smoothing. To improve gloss, uniform surface treatment, and antistatic and antifouling properties. Oil and water repellent.	Agricultural glass and plastic covers (used as greenhouses) Automotive finishes Cellulose Cements Ceramics Chemical processing industry equipment (for example, reactors, ducts, pipes, tanks, and impellers) Transparent coats Cookware/bakeware Fishing rods Glass (i.e., mirrors, eyeglasses, windshields of automobiles and their headlights, etc.) Plastics Sport equipment strings Musical instrument strings Piano parts Resins and sealers Paints, polishes, and pigments Ink, varnish, and waxes	[31–35]

Table 1. *Cont.*

Applications	Purpose	Consumer Products	References
Cosmetics and personal care	PFAS are used in cosmetics as emulsifiers, lubricants, or oleophobic agents. A polyethylene wax containing PTFE called Clariant's Ceridust 3920 F is used in cosmetic waxes for creams and powders. Aliphatic PFCAs are used in dental preparations, i.e., toothpastes, tooth powders, dental flosses, chewing gums, and tablets.	Acne treatment Blush/highlighter Dental floss and plaque removers Eye shadow Foundation Hair conditioner, creams, and shampoo Hand sanitizer and lotions Lip sticks/balm Mascara/lash products Nail polish Shaving cream Sunscreen	[36–39]
Electronics	PFAS are used because of their dielectric property, low flammability, chemical and heat resistance, and other mechanical properties. Electronics frequently make use of fluoropolymers. It is known that PFOA is utilized to create the fluoropolymers used in computer network cable and wire insulation.	Aerospace and automotive applications Cables and wires associated with communication and facilities Cell phones, Digital cameras Disk drives Electrical wiring insulation Zinc and lithium batteries Magnetic recording devices Optical fibers Printers Radar and satellite communication systems Scanners Solar collectors and coatings	[34,40,41]
Medical applications	Perfluoro-organic compound emulsions with gas-transporting characteristics are used for arterial administration in emergency situations of blood loss, as well as to treat numerous disorders accompanied by hypoxic or ischemic lesions. PFAS are renowned at increasing effective reattachment.	Bags Surfaces with blood contact Blood substitutes Containers Contact lenses Catheters Cannulae Drainage tubes Fistulas Fabric liners Grafts Gaskets Guide wires Hernia patches Inhaler propellant Joint repair and replacement Joint spacers Needles Oral capsules or tablets Ports Pericardial patches Seals shunts Space-filling or growth-increasing devices Surgical sheets Stylets Stent grafts and suppositories	[42,43]
Packaging material	PFAS are used to make paper products oil- and water-resistant for food, as well as nonfood usage.	Anti-corrosion liner Baking paper and wallpaper Coated raw paper and kraft paper, Food plates, bowls, containers, and wraps Folding cartons and pizza boxes Food bags for pets Paper food straws General liner, Paper combined with metal and raw paper for plaster board Wood-containing paper.	[35,44,45]

Eyeglass lenses, restrooms, and automotive windshields often get fogged in humid conditions; however, PFAS can efficiently be used as an anti-mist coating on the surface of plastic, glass, metals, etc., in order to avoid blurring/fogging [31,35]. This anti-mist film can also be helpful in agricultural activities, especially on glass and plastic cover sheets [35,44,45]. They are usually termed as perfluoro(polyether silanes) when we blend PFAS esters or alcohols with silanes to clean bathroom ceramics and shower panels [40]. When used in oral composition, PFAS Zonyl FSA is an active antiplaque component either alone or in combination with water-solvable fluorides. Therefore, it is declared that any oral products containing perfluoroalkyl surfactants can efficiently be used against gingivitis and plaque [46]. As surfactants, PFAS might be used to increase the oil-and-gas recovery rate from wells [31]. Owing to their stable nature at high pressures and temperatures, liquid fluorinated combinations might be used in workover operations, well drilling, and related completion processes [47].

3. PFAS Analytical Techniques

The determination of PFAS in various environmental media is critical, which means that several analytical techniques must be developed to analyze traces of PFAS with varied levels of selectivity and sensitivity. Among traditional analytical methods, LC-MS/MS is used to analyze PFAS quantitatively with low detection limits at the ppt level [43]. In cases in which the targeted PFAS concentration is considerably lower and samples contain a variety of compounds, passive sampling methods are employed to concentrate the wide range of PFAS and develop standardized protocols for analysis. Essential improvement in sensitivity and selectivity is achieved using passive sampling. The fact that most of the environmental matrices contain traces of PFAS and their precursors makes their analysis more challenging. When standards and the precursor structure are unavailable, analysis becomes considerably more difficult. For this purpose, semi-quantitative analyses, i.e., the total organic fluorine content and total oxidizable precursors, have been developed that consider PFAS compounds and precursors of unknown structure, enabling a more complete analysis of PFAS contamination [48].

In the case of the proton-induced gamma emission technique, the sample is bombarded with a beam of protons, which are produced in a low-energy accelerator. As they pass through the sample, these protons cause inelastic collisions with a nucleus in certain instances and leave it in an excitation state. De-excitation of the nucleus emits gamma rays, which can be detected. The elements, along with their concentrations, can be determined based on the energy of gamma rays emitted and their intensity at a particular energy [49].

Combustion ion chromatography is commonly used for the determination of total fluorine in various environmental samples and consumer products. The samples are first burned in a combustion chamber after passing through an in-line chloride removal module. After that, the analytes are separated using isocratic separation and sodium carbonate/sodium bicarbonate buffer. A conductivity detector with a Metrohm IC system is used for analysis. The overall fluoride content of a sample is determined by measuring the fluoride ion that remains after burning [50].

Fluorine nuclear magnetic resonance (^{19}F NMR) spectroscopy exceptionally offers structural and quantitative data for both known and unknown compounds in a sample [51]. Unlike mass spectrometry, ^{19}F NMR shows decreased sensitivity to matrix components and generates clean spectra that are easy to read and do not require significant sample processing to remove matrix effects [52]. Other advantages include the ability to quantify PFAS without the need for reference standards, high reproducibility, and cost-effectiveness [53].

Advanced and emerging analytical methods include fluorescent and luminescence detection methods. Fluorimetric assays are based on measurements of the fluorescent signal of common fluorophores in solution or mounted on solid substrates before and after exposure to PFAS. Combining fluorescent dyes with molecularly imprinted polymers (MIPs) is an intriguing strategy. Usually, molecular imprinting is utilized to create polymeric materials with high affinity for a certain target and particular molecular recognition receptor

cages. MIPs have the special ability to identify non-electroactive compounds, including the PFAS family of chemicals. Although there are now more options for the development of fluorescent-based analytical assays and sensors due to these receptors' capacity to bind selectively to PFAS, the method's sensitivity still has to be greatly increased in order to fulfill practical application requirements [48].

In addition to the above-mentioned methods, electrochemical techniques and sensors are also used for PFAS detection, with the potential for increased sensitivity, in addition to being inexpensive, portable, and capable of being deployed on site [54]. Redox materials are commonly utilized as sensing probes to track changes in electron transfer resistance upon PFAS binding, since PFAS are not electrochemically active. The development of inexpensive sensors can help in the identification and prioritization of samples for PFAS analysis. To quantify PFAS contamination in situ, these low-cost, portable techniques that can be used remotely to assess individual or total PFAS would be extremely beneficial [55].

4. Sources and Their Dispersal into Environmental Sections

Humans have manufactured more than 4000 PFAS to date, among which hundreds of PFAS have been identified in environmental samples. The major PFAS contamination sources, as well as their possible environmental impacts, are presented in Figure 1. The major sources of PFAS in the environmental compartments are point and non-point sources. Point sources are stationary and discrete, including landfills, firefighting training places, wastewater treatment units, manufacturing, industrial amenities, etc., whereas, diffuse sources of unidentified location/origin mostly refer to non-point sources, including degradation precursor compounds, precipitation, surface runoff, atmospheric intrusion of volatile PFAS, etc. [56]. In the USA, aqueous film-forming foams (AFFFs) used for firefighting operations are widely documented as PFAS contamination in water bodies. The major consumer of AFFFs is the US military; airports and military bases are among the specific sites of these contaminants [3]. Upon release into the environmental compartments, chemically stable PFAS can be transported long distances and transform from one environmental medium to another through the processes of leaching, precipitation, partitioning, and deposition [57]. Therefore, their universal occurrence has been reported in various environmental milieus across the world [58,59]. After transportation, the PFAS pass through environmental compartments (e.g., air, soil, and water) and can be bioaccumulated by native fauna and flora [60–62]. This bioaccumulation of persistent PFAS could seriously affect multiple levels of the food web [63]. Air and landfill leachates are expected to be the most stable sources of PFAS, with average concentrations in the range of 10^{1-2} pg/m^3 and 10^{0-2} ng/L, respectively [64]. PFAS have been globally found in animals, plants, and aquatic environments [44]. For example, across the United States, PFAS are frequently found in freshwater fish. The median PFAS concentration in fish tested by the US EPA between 2013 and 2015 was 11,800 ng/kg [65].
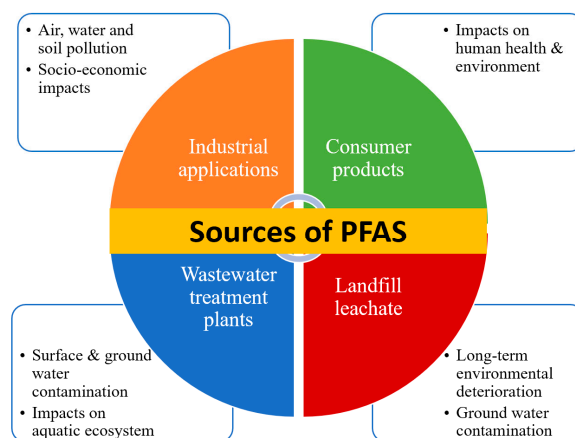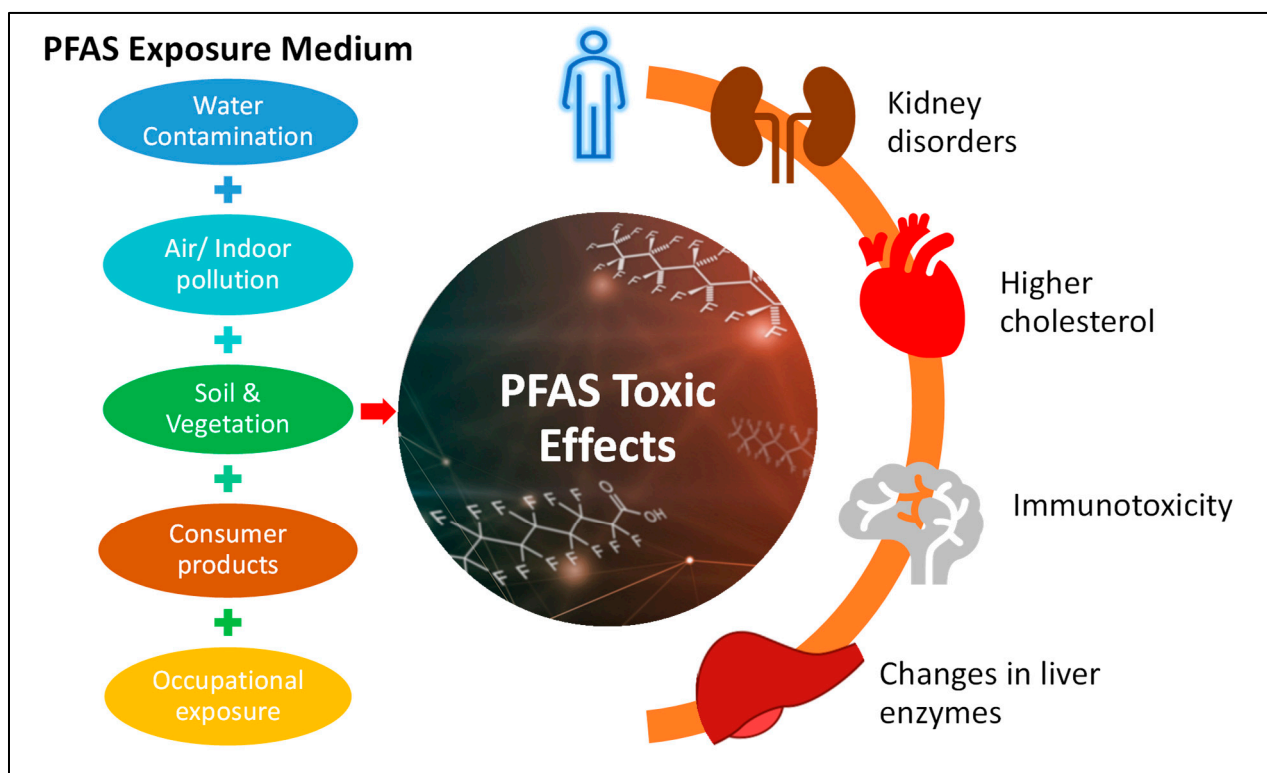

Figure 1. Major sources of PFAS and their potential impacts [66].

5. Exposure to Humans via Different Routes

PFAS usually belong to the class of water-soluble chemical compounds that have a wide range of applications. Actually, PFAS contain both hydrophilic (functional group) and hydrophobic (fluorinated carbon chain) parts [1]. However, the solubility of PFAS depends on functional moieties and chain length, which also determine their occurrence in the environment. PFAS with longer chains are less soluble in water and vice-versa. PFAS with short chains (C $\leq$ 8) usually occur in surface water, whereas PFAS with long chains (C > 8) tend to accumulate in sediments and fish tissues [3]. They may have a wide range of negative health impacts depending on the circumstances of exposure (such as magnitude, time, and route of exposure). Additionally, the characteristics of the individuals exposed—such as their age, gender, ethnicity, health, and genetic susceptibility—also affect how severe the negative consequences could be [67]. The major sources of PFAS release into ambient air are mostly characterized by industrial manufacturing of fluoropolymers, textiles, paints, food packaging, building construction, medical devices, printing inks, and firefighting foams [68]. However, consumer products including cosmetics, food processing and storage materials, and personal-care and household products contribute to the additional release of PFAS into the air [69]. Ultimately, the incineration and recycling of PFAS containing products also add emissions into the air [70]. The other environmental compartments (water and soil) become contaminated by PFAS through municipal wastewater treatment plants, which indirectly stimulate PFAS dispersal into soil by spreading filthy sludge, biosolids, and recycled effluent for agricultural purposes [71]. The landfilling application of these contaminants can also lead to leaching into soil and, ultimately, into groundwater, even under strict landfill regulations [72]. Figure 2 illustrates the various media of PFAS exposure to humans, along with their toxic effects. The details of human exposure to PFAS are further demonstrated in this section. Conclusively, considering these facts, it is an awful fact that PFAS have spread throughout the environment and become ubiquitous environmental pollutants. They are adversely affecting human health due to contamination via various human exposure routes, such as food sources, milk, vegetables, fruits, cereals, indoor air, and drinking water sources [73,74].

Figure 2. Overview of PFAS exposure media and toxic effects to humans.

5.1. Human Exposure to PFAS through Drinking Water

The major way humans are exposed to PFAS is through their dietary intake, followed by drinking water consumption, as illustrated by a comprehensive study conducted in Tarragona, Spain [75]. Groundwater, a major source of potable water in many areas, is significantly affected by PFAS contamination [76], which ultimately affects animals and humans upon consumption of this polluted water [44]. A study with the aim of identifying the potential source of PFAS contamination in Pennysylvania surface water found that the facilities to control water pollution and electronic manufacturing were the most likely potential sources of PFAS [77]. Both the influent and effluent from treatment plants of industrial wastewater are considered potential sources of short-, as well long-chain perfluoroalkyl acids (PFAAs). After treatment, an increase in the concentration of PFAAs was also reported [78]. Some PFAS are highly soluble in water, leading to their buildup in oceans and rivers, threatening fish and aquatic mammals. These PFAS also pollute groundwater reservoirs, ultimately contaminating drinking water and posing a threat to human health [13]. An elevated concentration (>10,000 ng/L in outgoing potable water) of PFAS was suddenly discovered in a municipal worker in Ronneby, Sweden. The source of contamination was a military airfield using AFFFs since the mid-1980s [79]. Upon these findings, the polluted water works were closed on an urgent basis, with an alternate water supply from other municipal waterworks. However, nearly one-third of the population of that area had been exposed to PFAS contamination for decades, unintentionally. A remarkable level of PFAS had been detected during biomonitoring of Ronneby residents, even 6 months after the exposure [80]. Conclusively, food, as well as drinking water, consumption is among the major conduits by which PFAS enter into humans [81].

5.2. Human Exposure to PFAS through Soil and Vegetation

PFAS pollutants enter the soil matrix, surface water, and groundwater from industrial waste, contaminated sludge, or foaming agents that ultimately enter the food chain through uptake by plants and drinking water consumption. The surrounding waterways also become polluted by the most PFAS present in industrial effluent and landfill leachate, ultimately causing severe environmental risks [82]. The main causes of PFAS contamination in soils are contaminated surfaces or groundwater used for field irrigation and the use of biosolids as fertilizers in agriculture [62,83,84]. When plants absorb PFAS, shorter-chain compounds collect in the leaves and fruits, while longer-chain compounds accumulate in the roots [85] and are, therefore, incorporated into food webs. A recent study reported that soil present in production, as well as storage sites, caused a potential hazard to field workers through exposure to perfluoro octane sulfonic acid [86].

5.3. Human Exposure to PFAS during Occupational Activities

Occupational exposure is a major concern because of the negative health effects of PFAS. Workers in certain occupations, such as professional ski waxers, firefighters, and fluorochemical plant workers, experience high PFAS serum concentrations based on their occupation. Because of the unique features of PFAS that increase product quality and performance, polyfluorinated alkyl compounds (PFAS) have been continuously employed in electronic products. However, the use of PFAS in electronic devices also raises the danger of PFAS exposure (through inhalation, ingestion, and skin absorption) for those managing and recycling e-waste. These recycling and scavenging steps are also among the occupational exposure routes for PFAS. In addition, e-waste collection, as well as processing and disposal, sites have been identified as potential PFAS exposure sites, since samples taken from these locations were contaminated with PFAS [87–89]. In another study, serum PFAS levels reported in various occupations were analyzed and compared to serum PFAS levels published on the general public exposed to PFAS-contaminated drinking water, and results indicated higher PFAS serum levels in professional ski waxers and firefighters [90]. Nevertheless, studies on PFAS exposure in workers have been limited to fluorochemical plant personnel involved in PFAS manufacture. Additional research on

occupational PFAS exposures through different occupations and industries is needed for future recommendations to protect workers from adverse health effects of PFAS exposure.

5.4. Human Exposure to PFAS through Consumer Products, Indoor Air, and Dust

PFAS in household items contribute to human exposure when they migrate into food, indoor air, and dust [91–94]. Papers, upholstery, carpets, outerwear, contact items, food, building materials, paints, cleaners, polishes, impregnation agents, and ski waxes have all been reported to contain them. PFAS can potentially seep into food from grease-resistant food packaging, increasing dietary exposure [95]. Furthermore, numerous precursor chemicals present in consumer goods, such as cosmetic products comprising powders, foundations, sunblocks, etc., can also be biotransformed into PFAS and ultimately accumulate in the human body. In experimental research, PFOA was mixed into a sunscreen and applied to the skin of a volunteer; this experimental approach demonstrated a significant uptake of PFAA via transdermal absorption in humans [96]. Another study also reported dermal penetration of PFAS. Accumulation of PFAS with moderate hydrophobicity in the body can be higher because of their favorable skin permeation and unfavorable urinary excretion [97]. In the category of outdoor air pollution, manufacturing plants and work facilities are the major sources of PFAS emissions into the air, resulting in the extensive contamination of both the ground and surface water in the vicinity [98]. According to computational research on atmospheric excellence, emissions of PFAS (5% of all) and GenX (2.5% of all) can easily settle in a circumference of 150 km of production sites [99]. Identifying the comparative significance of these several exposure routes is therefore crucial in understanding the reasons for progressive changes in blood and forecasting future exposure risks [100,101].

6. PFAS Potential Effects on Human Health

PFAS belong to the class of manmade, hazardous compounds that have the capability to bioaccumulate in humans, causing serious health issues like metabolic syndrome (MetS), a precursor to cardiovascular disease, which is the leading cause of mortality worldwide [102]. PFOS and PFOA are the most well-known and well-studied PFAS, owing to their long-lasting occurrence in major environmental compartments such as air, land, and water [75]. These long-chain PFAS (i.e., PFOA and/or PFOS) have also been associated with low birth weight, poor sperm quality, kidney and testicular cancer, thyroid disease, immunotoxicity, and pregnancy-induced hypertension in children [103–106]. Some of the toxic effects of PFAS on human health are briefly described here.

6.1. Immunotoxicity

PFAS exposure can suppress the human immune response. In vitro studies show that perfluorinated substances influence immune cells by changing cytokine expression. The activation of peroxisome proliferator-activated receptors (PPARs) is the major mechanism of action for prefrontal cortex (PFC)-induced regulation of cellular functions [107,108]. PFOS and PFOA both attach to the PPAR (peroxisome proliferator-activated receptor alpha). These transcription factors are abundant and regulate gene expression by altering lipid pathways; increasing mitochondrial membrane permeability, cell proliferation, and inflammatory processes; and influencing glucose control [109,110]. PFC activation of PPAR has been a prominent focus of mechanistic research, with an emphasis on interceding toxicity [109,111].

The detection of immunotoxicity is relatively easier even at lower levels of exposure than others. For example, Grandjean et al. studied the influence of PFAS concentrations in blood on the production of serum antibodies in children of 5 to 7 years of age after routine tetanus and diphtheria vaccines [112]. A 50% decrease in antibody concentrations was observed by doubling the PFOS, PFOA, and perfluorohexane sulfonate (PFHxS) concentrations at age 5. If this effect is causative, average blood values in most nations with biomonitoring data far surpass the 0.3 ng/mL for PFOA and 1.3 ng/mL for PFOS—values computed based on immunotoxicity in children [113].

6.2. Carcinogenicity of Perfluoroalkyl Compounds

The International Agency for Research on Cancer (IARC) has classified PFOA as possibly carcinogenic to humans. Community members whose drinking water was contaminated with PFOA were observed to be at greater risk of cancer [13]. Human occupational and community exposure to PFAS has been linked to numerous malignancies, including kidney, testicular, prostate, and liver cancers. Multiple PFAS have numerous carcinogen-like properties, such as inducing oxidative stress or modulating receptor-mediated effects. While research suggests that PFAS are not directly mutagenic, numerous other carcinogenic mechanisms have been proposed. Three major proposed pathways of PFAS action are metabolism, endocrine disruption, and epigenetic perturbation [114]. They cause a wide range of biological changes in numerous carcinogenicity-related molecular pathways [115]. Among different classes of PFAS, long-chain PFAS are the most potent due to the presence of additional C–F bonds. Those containing sulfonic acid derivatives such as sulfonamide and sulfonate PFAS have also been reported as more toxic compounds in terms of carcinogenicity [116]. Investigations found perfluorohexanoate (PFHxA; another type of PFAS) in 100% of whole blood samples, while it was not found in any of the other blood matrices. This implies that whole blood is the only adequate blood matrix for PFHxA assessment and that PFHxA exposure can be disregarded while examining serum or plasma alone. These findings are consistent with those of numerous recent studies in which PFHxA was either not detected or detected in very few samples when screening serum/plasma [117–120].

6.3. Endocrine Disruptors and Kidney Disorders

Perfluorooctanoic acid (PFOA) is a member of the PFAS compounds and has been linked to endocrine disruption in humans and other animals. PFOA might affect a variety of endocrine organs, including the ovaries, breasts, testes, brain, pancreas, adipose tissue, uterus, and thyroid. Thyroid hormones and various biological mechanisms that are involved in thyroid homeostasis, such as generation of thyroid hormones, as well as their transportation, metabolism, and interaction with thyroid receptors (present in target tissues), are thought to be affected by PFAS. [121]. According to one of the proposed mechanisms of PFAS action, they reduce circulating T4 levels by competitively binding to transport proteins of thyroid hormones [122]. A toxicology investigation found links between PFAS contact and decreased kidney function and kidney cancer. Furthermore, pharmacokinetic investigations revealed the significance of the kidney's elimination pathways, and PFAS exposure was found to affect these pathways, causing various kidney diseases. PFAS contact can also distort several other pathways, such as the peroxisome proliferator-activated receptor, nuclear factor erythroid 2-related factor (Nrf2), epithelial mesenchymal transition, oxidative stress, and improved endothelial permeability through actin filament modeling. [123]. The link between thyroid hormones and the glomerular filtration rate (GFR) may play a role in the relationship with serum PFAS. Hypothyroidism causes decreased GFR, whereas hyperthyroidism causes increased GFR [124].

To understand the binding mechanism between PFAS and transport proteins, various experimental techniques and computational studies have been used to calculate the binding constants of different PFAS [125–127]. Molecular docking studies have revealed the involvement of hydrophobic and hydrogen-bonding interactions of PFAS with proteins. Acidic PFAS have a long, fluorinated hydrophobic chain and terminal acidic functional group that structurally resembles fatty acids. Due to this structural resemblance, PFAS can competitively bind to various transport proteins following the same binding mechanism as fatty acids [125]. They can directly bind to the binding pocket of proteins through Van der Waals interaction of hydrophobic chains and the formation of ionic/hydrogen bonds with negatively charged terminal acidic groups. They can also bind to allosteric sites, inducing structural changes in proteins. This can potentially affect the normal functioning/regulation of different proteins. For example, Yang Liu reported various spectroscopic and molecular docking experiments to gain insights into the interaction mechanism of different PFAS with human serum albumin (HSA). The study revealed that PFAS bound

to the arginine (Arg-410) residue of the active site in HSA and affected esterase activity; however, no change in the backbone and secondary structure of HSA was observed [128].

6.4. PFAS Exposure and Fetal Growth

PFAS are bioaccumulative contaminants, and it is suspected that prenatal exposure to PFAS affects the development of human fetuses and that these effects can also have prolonged negative impacts in later life. A study observed the quantities of five PFAS molecules (PFDA, PFNA, PFOA, PFOS, and PFUnDA) in fetuses of humans, maternal plasma, and placentas. The quantity of PFAS that can be transferred from mother to fetus was also studied, and it was found that the PFOS concentration is higher in maternal plasma than in placentas and fetal organs [129]. This indicates that all PFAS have a tendency to pass from mother to fetus, demonstrating the risk of prenatal exposure to these chemicals, even if not to the same degree of hazard. In most studies, higher PFOS and PFOA concentrations were associated with lower average birth weight; prenatal PFAS exposure may also play a more important role in growth variability during infancy and early childhood [130,131]. The degree of hazardous effects of these chemicals varies, as these molecules travel from mother to fetus with varying efficiency [132–134]. Another study, however, carried out in China, discovered no significant link [135].

7. Future Outlooks

PFAS are released from a range of sources and pathways; therefore, source distribution must be investigated to assess the comparative contribution of diverse PFAS forms in the environment. Furthermore, identifying sources and analyzing the impact and severity of specific sources is essential in order to construct and prioritize appropriate mitigation measures for the eradication or reduction of PFAS [66]. New PFAS research is needed to achieve a better understanding of their behavior and possible hazards to human health and the environment. The degradation mechanism of new PFAS is not yet confirmed; therefore, in order to quantify the exposure of the population to these chemicals, it will be necessary to acquire new methodologies or adapt existing techniques [57].

Future research must consider lifestyle factors (such as nutrition and physical exercise) and measure the influence of PFAS mixtures on metastatic cancer symptoms and clinical illnesses. Finally, doctors must use newly created clinical advice to screen patients for PFAS exposure, measure their levels, provide further clinical care, and advise patients accordingly [102]. Preliminary research suggests that emerging PFAS exposure causes serious health impacts. Lessons from legacy PFAS show that insufficient evidence should not be used to justify the postponement of risk reduction procedures for PFAS replacement.

Conflicts of Interest: The authors declare no conflict of interest.

List of Abbreviations

AFFFs: aqueous film-forming foams; AOPs: advanced oxidation processes; CDC: Centers for Disease Control and Prevention; CF: carbon–fluorine; Cl-PFESA: chlorinated polyfluoroalkyl ether sulfonic acid; FCMs: food contact materials; FTOHs: fluorotelomer alcohols; ^{19}F NMR: fluorine nuclear magnetic resonance; GAC: granular activated carbon; GFR: glomerular filtration rate; HFPO-DA: hexafluoropropylene oxide dimer acid; IARC: International Agency for Research on Cancer; IER: ion-exchange resin; MIP: molecularly imprinted polymer; NF: nanofiltration; Nrf2: nuclear factor erythroid 2-related factor; PFAS: per- and polyfluoroalkyl substances; PFOS: perfluorooctane sulfonic acid; PFSAs: perfluoroalkyl sulfonic acids; PFCAs: perfluorinated carboxylic acids; PFAAs: perfluoroalkyl acids; PAPs: polyfluoroalkyl phosphate esters; PFOA: perfluorooctanoic acid;

PPARs: peroxisome proliferator-activated receptors; PFC: prefrontal cortex; PFHxA: perfluorohexanoate; PFHxS: perfluorohexane sulfonate.

References

1. Buck, R.C.; Franklin, J.; Berger, U.; Conder, J.M.; Cousins, I.T.; De Voogt, P.; Jensen, A.A.; Kannan, K.; Mabury, S.A.; van Leeuwen, S.P. Perfluoroalkyl and polyfluoroalkyl substances in the environment: Terminology, classification, and origins. *Integr. Environ. Assess. Manag.* **2011**, *7*, 513–541. [CrossRef]

2. Manojkumar, Y.; Pilli, S.; Rao, P.V.; Tyagi, R.D. Sources, occurrence and toxic effects of emerging per-and polyfluoroalkyl substances (PFAS). *Neurotoxicol. Teratol.* **2023**, *97*, 107174. [CrossRef] [PubMed]

3. Kurwadkar, S.; Dane, J.; Kanel, S.R.; Nadagouda, M.N.; Cawdrey, R.W.; Ambade, B.; Struckhoff, G.C.; Wilkin, R. Per-and polyfluoroalkyl substances in water and wastewater: A critical review of their global occurrence and distribution. *Sci. Total Environ.* **2022**, *809*, 151003. [CrossRef] [PubMed]

4. Adu, O.; Ma, X.; Sharma, V.K. Bioavailability, Phytotoxicity and Plant Uptake of Per-and Polyfluoroalkyl Substances (PFAS): A Review. *J. Hazard. Mater.* **2023**, *447*, 130805. [CrossRef] [PubMed]

5. Xiao, F.; Simcik, M.F.; Halbach, T.R.; Gulliver, J.S. Perfluorooctane sulfonate (PFOS) and perfluorooctanoate (PFOA) in soils and groundwater of a US metropolitan area: Migration and implications for human exposure. *Water Res.* **2015**, *72*, 64–74. [CrossRef] [PubMed]

6. Shan, G.; Wang, Z.; Zhou, L.; Du, P.; Luo, X.; Wu, Q.; Zhu, L. Impacts of daily intakes on the isomeric profiles of perfluoroalkyl substances (PFASs) in human serum. *Environ. Int.* **2016**, *89*, 62–70. [CrossRef] [PubMed]

7. Bräunig, J.; Baduel, C.; Heffernan, A.; Rotander, A.; Donaldson, E.; Mueller, J.F. Fate and redistribution of perfluoroalkyl acids through AFFF-impacted groundwater. *Sci. Total Environ.* **2017**, *596*, 360–368. [CrossRef] [PubMed]

8. Poothong, S.; Thomsen, C.; Padilla-Sanchez, J.A.; Papadopoulou, E.; Haug, L.S. Distribution of novel and well-known poly-and perfluoroalkyl substances (PFASs) in human serum, plasma, and whole blood. *Environ. Sci. Technol.* **2017**, *51*, 13388–13396. [CrossRef] [PubMed]

9. National Center for Health Statistics. National Health and Nutrition Examination Survey. Available online: https://www.cdc.gov/nchs/nhanes/index.htm (accessed on 10 February 2024).

10. Baker, E.S.; Knappe, D.R. Per-and polyfluoroalkyl substances (PFAS)—Contaminants of emerging concern. *Anal. Bioanal. Chem.* **2022**, *414*, 1187–1188. [CrossRef]

11. Pan, Y.; Wang, J.; Yeung, L.W.; Wei, S.; Dai, J. Analysis of emerging per-and polyfluoroalkyl substances: Progress and current issues. *TrAC Trends Anal. Chem.* **2020**, *124*, 115481. [CrossRef]

12. Guillette, T.; Jackson, T.W.; Guillette, M.; McCord, J.; Belcher, S.M. Blood concentrations of per-and polyfluoroalkyl substances are associated with autoimmune-like effects in American alligators from Wilmington, North Carolina. *Front. Toxicol.* **2022**, *4*, 1010185. [CrossRef]

13. Sunderland, E.M.; Hu, X.C.; Dassuncao, C.; Tokranov, A.K.; Wagner, C.C.; Allen, J.G. A review of the pathways of human exposure to poly-and perfluoroalkyl substances (PFASs) and present understanding of health effects. *J. Expo. Sci. Environ. Epidemiol.* **2019**, *29*, 131–147. [CrossRef] [PubMed]

14. Riegel, M.; Haist-Gulde, B.; Sacher, F. Sorptive removal of short-chain perfluoroalkyl substances (PFAS) during drinking water treatment using activated carbon and anion exchanger. *Environ. Sci. Eur.* **2023**, *35*, 12. [CrossRef]

15. OECD. Portal on per and Polyfluorinated Chemicals. Available online: https://www.oecd.org/chemicalsafety/portal-perfluorinated-chemicals/ (accessed on 10 February 2024).

16. Zhao, P.; Xia, X.; Dong, J.; Xia, N.; Jiang, X.; Li, Y.; Zhu, Y. Short-and long-chain perfluoroalkyl substances in the water, suspended particulate matter, and surface sediment of a turbid river. *Sci. Total Environ.* **2016**, *568*, 57–65. [CrossRef]

17. Trenkle, A. Transfer von poly-und perfluorierten Chemikalien (PFC) von kontaminierten Agrarflächen in Nutzpflanzen Transition of poly-and perfluorinated chemicals from agricultural areas in foodstuffs. *Tagungsbericht* **2015**, *2015*, 185.

18. Page, D.; Vanderzalm, J.; Kumar, A.; Cheng, K.Y.; Kaksonen, A.H.; Simpson, S. Risks of perfluoroalkyl and polyfluoroalkyl substances (PFAS) for sustainable water recycling via aquifers. *Water* **2019**, *11*, 1737. [CrossRef]

19. Yadav, S.; Ibrar, I.; Al-Juboori, R.A.; Singh, L.; Ganbat, N.; Kazwini, T.; Karbassiyazdi, E.; Samal, A.K.; Subbiah, S.; Altaee, A. Updated review on emerging technologies for PFAS contaminated water treatment. *Chem. Eng. Res. Des.* **2022**, *182*, 667–700. [CrossRef]

20. Vo, H.N.P.; Ngo, H.H.; Guo, W.; Nguyen, T.M.H.; Li, J.; Liang, H.; Deng, L.; Chen, Z.; Nguyen, T.A.H. Poly-and perfluoroalkyl substances in water and wastewater: A comprehensive review from sources to remediation. *J. Water Process Eng.* **2020**, *36*, 101393.

21. Verma, S.; Varma, R.S.; Nadagouda, M.N. Remediation and mineralization processes for per-and polyfluoroalkyl substances (PFAS) in water: A review. *Sci. Total Environ.* **2021**, *794*, 148987. [CrossRef] [PubMed]

22. Bentel, M.J.; Yu, Y.; Xu, L.; Li, Z.; Wong, B.M.; Men, Y.; Liu, J. Defluorination of per-and polyfluoroalkyl substances (PFASs) with hydrated electrons: Structural dependence and implications to PFAS remediation and management. *Environ. Sci. Technol.* **2019**, *53*, 3718–3728. [CrossRef] [PubMed]

23. Vu, C.T.; Wu, T. Recent progress in adsorptive removal of per-and poly-fluoroalkyl substances (PFAS) from water/wastewater. *Crit. Rev. Environ. Sci. Technol.* **2022**, *52*, 90–129. [CrossRef]

24. Kucharzyk, K.H.; Darlington, R.; Benotti, M.; Deeb, R.; Hawley, E. Novel treatment technologies for PFAS compounds: A critical review. *J. Environ. Manag.* **2017**, *204*, 757–764. [CrossRef] [PubMed]

25. Prevedouros, K.; Cousins, I.T.; Buck, R.C.; Korzeniowski, S.H. Sources, fate and transport of perfluorocarboxylates. *Environ. Sci. Technol.* **2006**, *40*, 32–44. [CrossRef] [PubMed]

26. Wang, Z.; Boucher, J.M.; Scheringer, M.; Cousins, I.T.; Hungerbuhler, K. Toward a comprehensive global emission inventory of C4–C10 perfluoroalkanesulfonic acids (PFSAs) and related precursors: Focus on the life cycle of C8-based products and ongoing industrial transition. *Environ. Sci. Technol.* **2017**, *51*, 4482–4493. [CrossRef] [PubMed]

27. Van der Veen, I.; Hanning, A.-C.; Stare, A.; Leonards, P.E.; de Boer, J.; Weiss, J.M. The effect of weathering on per-and polyfluoroalkyl substances (PFASs) from durable water repellent (DWR) clothing. *Chemosphere* **2020**, *249*, 126100. [CrossRef]

28. Kotthoff, M.; Müller, J.; Jürling, H.; Schlummer, M.; Fiedler, D. Perfluoroalkyl and polyfluoroalkyl substances in consumer products. *Environ. Sci. Pollut. Res.* **2015**, *22*, 14546–14559. [CrossRef]

29. Liu, X.; Guo, Z.; Folk IV, E.E.; Roache, N.F. Determination of fluorotelomer alcohols in selected consumer products and preliminary investigation of their fate in the indoor environment. *Chemosphere* **2015**, *129*, 81–86. [CrossRef]

30. Guo, Z.; Liu, X.; Krebs, K.A.; Roache, N.F. *Perfluorocarboxylic Acid Content in 116 Articles of Commerce*; US Environmental Protection Agency: Research Triangle Park, NC, USA, 2009.

31. Kissa, E. *Fluorinated Surfactants and Repellents*; CRC Press: Boca Raton, FL, USA, 2001; Volume 97.

32. Ebnesajjad, S. *Introduction to Fluoropolymers: Materials, Technology, and Applications*; William Andrew: Norwich, NY, USA, 2013.

33. Ober, C.K.; Käfer, F.; Deng, J. Review of essential use of fluorochemicals in lithographic patterning and semiconductor processing. *J. Micro/Nanopatterning Mater. Metrol.* **2022**, *21*, 010901. [CrossRef]

34. OECD. *UNEP Global PFC Group, Synthesis Paper on per-and Polyfluorinated Chemicals (PFCs)*; Environment, Health and Safety, Environment Directorate, OECD: Paris, France, 2013.

35. Gaines, L.G. Historical and current usage of per-and polyfluoroalkyl substances (PFAS): A literature review. *Am. J. Ind. Med.* **2023**, *66*, 353–378. [CrossRef]

36. Jensen, A.A.; Poulsen, P.B.; Bossi, R.; Miljøundersøgelser, D.; Technology, F. *Survey and Environmental/Health Assessment of Fluorinated Substances in Impregnated Consumer Products and Impregnating Agents*; Danish Environmental Protection Agency Copenhagen: Copenhagen, Denmark, 2008; Volume 99.

37. Fujii, Y.; Harada, K.H.; Koizumi, A. Occurrence of perfluorinated carboxylic acids (PFCAs) in personal care products and compounding agents. *Chemosphere* **2013**, *93*, 538–544. [CrossRef]

38. Brinch, A.; Jensen, A.; Christensen, F. *Risk Assessment of Fluorinated Substances in Cosmetic Products*; The Danish Environmental Protection Agency: Copenhagen, Denmark, 2018; pp. 1–116.

39. Whitehead, H.D.; Venier, M.; Wu, Y.; Eastman, E.; Urbanik, S.; Diamond, M.L.; Shalin, A.; Schwartz-Narbonne, H.; Bruton, T.A.; Blum, A. Fluorinated compounds in North American cosmetics. *Environ. Sci. Technol. Lett.* **2021**, *8*, 538–544. [CrossRef]

40. Dams, R.; Hintzer, K. *Industrial Aspects of Fluorinated Oligomers and Polymers*; Royal Society of Chemistry: Cambridge, UK, 2016.

41. Van der Putte, I.; Murín, M.; Van Velthoven, M.; Affourtit, F. *Analysis of the Risks Arising from the Industrial Use of Perfuorooctanoic Acid (PFOA) and Ammonium Perfluorooctanoate (APFO) and from Their Use in Consumer Articles*; RPS Advies: Delft, NL, USA, 2010.

42. Tressaud, A.; Haufe, G. *Fluorine and Health: Molecular Imaging, Biomedical Materials and Pharmaceuticals*; Elsevier: Amsterdam, The Netherlands, 2008.

43. Zheng, Q.; Yang, S.; Zhang, Y.; Wu, R.; Pang, J.; Li, W. Vitreous surgery for macular hole-related retinal detachment after phacoemulsification cataract extraction: 10-year retrospective review. *Eye* **2012**, *26*, 1058–1064. [CrossRef]

44. Banzhaf, S.; Filipovic, M.; Lewis, J.; Sparrenbom, C.J.; Barthel, R. A review of contamination of surface-, ground-, and drinking water in Sweden by perfluoroalkyl and polyfluoroalkyl substances (PFASs). *Ambio* **2017**, *46*, 335–346. [CrossRef]

45. Wang, Z.; Cousins, I.T.; Scheringer, M.; Buck, R.C.; Hungerbühler, K. Global emission inventories for C4–C14 perfluoroalkyl carboxylic acid (PFCA) homologues from 1951 to 2030, Part I: Production and emissions from quantifiable sources. *Environ. Int.* **2014**, *70*, 62–75. [CrossRef]

46. Caslavsky, V.B.; Gron, P. Method of Inhibiting the Formation of Plaque. US5100649A, 31 March 1992.

47. Pasquier, D.; Driancourt, A.; Audibert, A. Well Fluid Comprising a Fluorinated Liquid Phase. U.S. Patent 8,383,555, 26 February 2010.

48. Rehman, A.U.; Crimi, M.; Andreescu, S. Current and Emerging Analytical Techniques for the Determination of PFAS in Environmental Samples. *Trends Environ. Anal. Chem.* **2023**, *37*, e00198. [CrossRef]

49. Langton, C. Development of Quantitative Methods to Study PFAS Using Proton Induced Gamma-Ray Emission. 2022. Available online: https://digitalworks.union.edu/theses/2555/ (accessed on 10 February 2024).

50. Yandrasits, M.A.; Marimannikkuppam, S.; Lindell, M.J.; Kalstabakken, K.A.; Kurkowski, M.; Ha, P. Ion chromatography and combustion ion chromatography analysis of fuel cell effluent water during open circuit voltage. *J. Electrochem. Soc.* **2022**, *169*, 034526. [CrossRef]

51. Gauthier, J.R.; Mabury, S.A. Identifying Unknown Fluorine-Containing Compounds in Environmental Samples Using ^{19}F NMR and Spectral Database Matching. *Environ. Sci. Technol.* **2023**, *57*, 8760–8767. [CrossRef]

52. Camdzic, D.; Dickman, R.A.; Joyce, A.S.; Wallace, J.S.; Ferguson, P.L.; Aga, D.S. Quantitation of Total PFAS Including Trifluoroacetic Acid with Fluorine Nuclear Magnetic Resonance Spectroscopy. *Anal. Chem.* **2023**, *95*, 5484–5488. [CrossRef] [PubMed]

53. Camdzic, D.; Dickman, R.A.; Aga, D.S. Total and class-specific analysis of per-and polyfluoroalkyl substances in environmental samples using nuclear magnetic resonance spectroscopy. *J. Hazard. Mater. Lett.* **2021**, *2*, 100023. [CrossRef]

54. Andreescu, S.; Vasilescu, A. Advances in electrochemical detection for probing protein aggregation. *Curr. Opin. Electrochem.* **2021**, *30*, 100820. [CrossRef]

55. Chen, L.D.; Lai, C.-Z.; Granda, L.P.; Fierke, M.A.; Mandal, D.; Stein, A.; Gladysz, J.A.; Bühlmann, P. Fluorous membrane ion-selective electrodes for perfluorinated surfactants: Trace-level detection and in situ monitoring of adsorption. *Anal. Chem.* **2013**, *85*, 7471–7477. [CrossRef]

56. Ruyle, B.J.; Pickard, H.M.; LeBlanc, D.R.; Tokranov, A.K.; Thackray, C.P.; Hu, X.C.; Vecitis, C.D.; Sunderland, E.M. Isolating the AFFF signature in coastal watersheds using oxidizable PFAS precursors and unexplained organofluorine. *Environ. Sci. Technol.* **2021**, *55*, 3686–3695. [CrossRef]

57. Brase, R.A.; Mullin, E.J.; Spink, D.C. Legacy and emerging per-and polyfluoroalkyl substances: Analytical techniques, environmental fate, and health effects. *Int. J. Mol. Sci.* **2021**, *22*, 995. [CrossRef] [PubMed]

58. Giesy, J.P.; Kannan, K. Global distribution of perfluorooctane sulfonate in wildlife. *Environ. Sci. Technol.* **2001**, *35*, 1339–1342. [CrossRef] [PubMed]

59. Sinclair, E.; Mayack, D.T.; Roblee, K.; Yamashita, N.; Kannan, K. Occurrence of perfluoroalkyl surfactants in water, fish, and birds from New York State. *Arch. Environ. Contam. Toxicol.* **2006**, *50*, 398–410. [CrossRef]

60. Pan, Y.; Zhang, H.; Cui, Q.; Sheng, N.; Yeung, L.W.; Guo, Y.; Sun, Y.; Dai, J. First report on the occurrence and bioaccumulation of hexafluoropropylene oxide trimer acid: An emerging concern. *Environ. Sci. Technol.* **2017**, *51*, 9553–9560. [CrossRef] [PubMed]

61. Lam, N.-H.; Cho, C.-R.; Lee, J.-S.; Soh, H.-Y.; Lee, B.-C.; Lee, J.-A.; Tatarozako, N.; Sasaki, K.; Saito, N.; Iwabuchi, K. Perfluorinated alkyl substances in water, sediment, plankton and fish from Korean rivers and lakes: A nationwide survey. *Sci. Total Environ.* **2014**, *491*, 154–162. [CrossRef]

62. Ghisi, R.; Vamerali, T.; Manzetti, S. Accumulation of perfluorinated alkyl substances (PFAS) in agricultural plants: A review. *Environ. Res.* **2019**, *169*, 326–341. [CrossRef]

63. Goodrow, S.M.; Ruppel, B.; Lippincott, R.L.; Post, G.B.; Procopio, N.A. Investigation of levels of perfluoroalkyl substances in surface water, sediment and fish tissue in New Jersey, USA. *Sci. Total Environ.* **2020**, *729*, 138839. [CrossRef]

64. Wang, Y.; Munir, U.; Huang, Q. Occurrence of Per-and Polyfluoroalkyl Substances (PFAS) in Soil: Sources, Fate, and Remediation. *Soil Environ. Health* **2023**, *1*, 100004. [CrossRef]

65. Barbo, N.; Stoiber, T.; Naidenko, O.V.; Andrews, D.Q. Locally caught freshwater fish across the United States are likely a significant source of exposure to PFOS and other perfluorinated compounds. *Environ. Res.* **2023**, *220*, 115165. [CrossRef]

66. Ehsan, M.N.; Riza, M.; Pervez, M.N.; Khyum, M.M.O.; Liang, Y.; Naddeo, V. Environmental and health impacts of PFAS: Sources, distribution and sustainable management in North Carolina (USA). *Sci. Total Environ.* **2023**, *878*, 163123. [CrossRef]

67. Fenton, S.E.; Ducatman, A.; Boobis, A.; DeWitt, J.C.; Lau, C.; Ng, C.; Smith, J.S.; Roberts, S.M. Per-and polyfluoroalkyl substance toxicity and human health review: Current state of knowledge and strategies for informing future research. *Environ. Toxicol. Chem.* **2021**, *40*, 606–630. [CrossRef]

68. Adamson, D.T.; Nickerson, A.; Kulkarni, P.R.; Higgins, C.P.; Popovic, J.; Field, J.; Rodowa, A.; Newell, C.; DeBlanc, P.; Kornuc, J.J. Mass-based, field-scale demonstration of PFAS retention within AFFF-associated source areas. *Environ. Sci. Technol.* **2020**, *54*, 15768–15777. [CrossRef]

69. Curtzwiler, G.W.; Silva, P.; Hall, A.; Ivey, A.; Vorst, K. Significance of perfluoroalkyl substances (PFAS) in food packaging. *Integr. Environ. Assess. Manag.* **2021**, *17*, 7–12. [CrossRef]

70. Hepburn, E.; Madden, C.; Szabo, D.; Coggan, T.L.; Clarke, B.; Currell, M. Contamination of groundwater with per-and polyfluoroalkyl substances (PFAS) from legacy landfills in an urban re-development precinct. *Environ. Pollut.* **2019**, *248*, 101–113. [CrossRef]

71. Panieri, E.; Baralic, K.; Djukic-Cosic, D.; Buha Djordjevic, A.; Saso, L. PFAS molecules: A major concern for the human health and the environment. *Toxics* **2022**, *10*, 44. [CrossRef]

72. Björklund, S.; Weidemann, E.; Yeung, L.W.; Jansson, S. Occurrence of per-and polyfluoroalkyl substances and unidentified organofluorine in leachate from waste-to-energy stockpile—A case study. *Chemosphere* **2021**, *278*, 130380. [CrossRef] [PubMed]

73. Shahsavari, E.; Rouch, D.; Khudur, L.S.; Thomas, D.; Aburto-Medina, A.; Ball, A.S. Challenges and current status of the biological treatment of PFAS-contaminated soils. *Front. Bioeng. Biotechnol.* **2021**, *8*, 602040. [CrossRef] [PubMed]

74. Awad, R.; Zhou, Y.; Nyberg, E.; Namazkar, S.; Yongning, W.; Xiao, Q.; Sun, Y.; Zhu, Z.; Bergman, Å.; Benskin, J.P. Emerging per-and polyfluoroalkyl substances (PFAS) in human milk from Sweden and China. *Environ. Sci. Process. Impacts* **2020**, *22*, 2023–2030. [CrossRef] [PubMed]

75. Domingo, J.L.; Nadal, M. Human exposure to per-and polyfluoroalkyl substances (PFAS) through drinking water: A review of the recent scientific literature. *Environ. Res.* **2019**, *177*, 108648. [CrossRef] [PubMed]

76. Pétré, M.-A.; Genereux, D.P.; Koropeckyj-Cox, L.; Knappe, D.R.; Duboscq, S.; Gilmore, T.E.; Hopkins, Z.R. Per-and polyfluoroalkyl substance (PFAS) transport from groundwater to streams near a PFAS manufacturing facility in North Carolina, USA. *Environ. Sci. Technol.* **2021**, *55*, 5848–5856. [CrossRef] [PubMed]

77. Breitmeyer, S.E.; Williams, A.M.; Duris, J.W.; Eicholtz, L.W.; Shull, D.R.; Wertz, T.A.; Woodward, E.E. Per-and polyfluorinated alkyl substances (PFAS) in Pennsylvania surface waters: A statewide assessment, associated sources, and land-use relations. *Sci. Total Environ.* **2023**, *888*, 164161. [CrossRef] [PubMed]

78. Lenka, S.P.; Kah, M.; Padhye, L.P. Occurrence and fate of poly-and perfluoroalkyl substances (PFAS) in urban waters of New Zealand. *J. Hazard. Mater.* **2022**, *428*, 128257. [CrossRef] [PubMed]

79. Xu, Y.; Nielsen, C.; Li, Y.; Hammarstrand, S.; Andersson, E.M.; Li, H.; Olsson, D.S.; Engström, K.; Pineda, D.; Lindh, C.H. Serum perfluoroalkyl substances in residents following long-term drinking water contamination from firefighting foam in Ronneby, Sweden. *Environ. Int.* **2021**, *147*, 106333. [CrossRef] [PubMed]

80. Xu, Y.; Jakobsson, K.; Harari, F.; Andersson, E.M.; Li, Y. Exposure to high levels of PFAS through drinking water is associated with increased risk of type 2 diabetes—Findings from a register-based study in Ronneby, Sweden. *Environ. Res.* **2023**, *225*, 115525. [CrossRef] [PubMed]

81. Cserbik, D.; Redondo-Hasselerharm, P.E.; Farré, M.J.; Sanchís, J.; Bartolomé, A.; Paraian, A.; Herrera, E.M.; Caixach, J.; Villanueva, C.M.; Flores, C. Human exposure to per-and polyfluoroalkyl substances and other emerging contaminants in drinking water. *Npj Clean Water* **2023**, *6*, 16. [CrossRef]

82. O'Connor, J.; Bolan, N.S.; Kumar, M.; Nitai, A.S.; Ahmed, M.B.; Bolan, S.S.; Vithanage, M.; Rinklebe, J.; Mukhopadhyay, R.; Srivastava, P. Distribution, transformation and remediation of poly-and per-fluoroalkyl substances (PFAS) in wastewater sources. *Process Saf. Environ. Prot.* **2022**, *164*, 91–108. [CrossRef]

83. Stahl, T.; Heyn, J.; Thiele, H.; Hüther, J.; Failing, K.; Georgii, S.; Brunn, H. Carryover of perfluorooctanoic acid (PFOA) and perfluorooctane sulfonate (PFOS) from soil to plants. *Arch. Environ. Contam. Toxicol.* **2009**, *57*, 289–298. [CrossRef]

84. Wen, B.; Zhang, H.; Li, L.; Hu, X.; Liu, Y.; Shan, X.-q.; Zhang, S. Bioavailability of perfluorooctane sulfonate (PFOS) and perfluorooctanoic acid (PFOA) in biosolids-amended soils to earthworms (*Eisenia fetida*). *Chemosphere* **2015**, *118*, 361–366. [CrossRef]

85. Krippner, J.; Falk, S.; Brunn, H.; Georgii, S.; Schubert, S.; Stahl, T. Accumulation potentials of perfluoroalkyl carboxylic acids (PFCAs) and perfluoroalkyl sulfonic acids (PFSAs) in maize (*Zea mays*). *J. Agric. Food Chem.* **2015**, *63*, 3646–3653. [CrossRef]

86. Jia, X.; Li, X.; Zhou, L.; Hui, Y.; Li, W.; Cai, Y.; Shi, Y. Variations of the Level, Profile, and Distribution of PFAS around POSF Manufacturing Facilities in China: An Overlooked Source of PFCA. *Environ. Sci. Technol.* **2023**, *57*, 5264–5274. [CrossRef]

87. Tansel, B. PFAS use in electronic products and exposure risks during handling and processing of e-waste: A review. *J. Environ. Manag.* **2022**, *316*, 115291. [CrossRef]

88. Zhao, L.; Cheng, Z.; Zhu, H.; Chen, H.; Yao, Y.; Baqar, M.; Yu, H.; Qiao, B.; Sun, H. Electronic-waste-associated pollution of per-and polyfluoroalkyl substances: Environmental occurrence and human exposure. *J. Hazard. Mater.* **2023**, *451*, 131204. [CrossRef] [PubMed]

89. Garg, S.; Kumar, P.; Mishra, V.; Guijt, R.; Singh, P.; Dumée, L.F.; Sharma, R.S. A review on the sources, occurrence and health risks of per-/poly-fluoroalkyl substances (PFAS) arising from the manufacture and disposal of electric and electronic products. *J. Water Process Eng.* **2020**, *38*, 101683. [CrossRef]

90. Lucas, K.; Gaines, L.G.; Paris-Davila, T.; Nylander-French, L.A. Occupational exposure and serum levels of per-and polyfluoroalkyl substances (PFAS): A review. *Am. J. Ind. Med.* **2023**, *66*, 379–392. [CrossRef]

91. Begley, T.; Hsu, W.; Noonan, G.; Diachenko, G. Migration of fluorochemical paper additives from food-contact paper into foods and food simulants. *Food Addit. Contam.* **2008**, *25*, 384–390. [CrossRef] [PubMed]

92. Tittlemier, S.A.; Pepper, K.; Seymour, C.; Moisey, J.; Bronson, R.; Cao, X.-L.; Dabeka, R.W. Dietary exposure of Canadians to perfluorinated carboxylates and perfluorooctane sulfonate via consumption of meat, fish, fast foods, and food items prepared in their packaging. *J. Agric. Food Chem.* **2007**, *55*, 3203–3210. [CrossRef] [PubMed]

93. Langer, V.; Dreyer, A.; Ebinghaus, R. Polyfluorinated compounds in residential and nonresidential indoor air. *Environ. Sci. Technol.* **2010**, *44*, 8075–8081. [CrossRef] [PubMed]

94. Beesoon, S.; Genuis, S.J.; Benskin, J.P.; Martin, J.W. Exceptionally high serum concentrations of perfluorohexanesulfonate in a Canadian family are linked to home carpet treatment applications. *Environ. Sci. Technol.* **2012**, *46*, 12960–12967. [CrossRef] [PubMed]

95. Schaider, L.A.; Balan, S.A.; Blum, A.; Andrews, D.Q.; Strynar, M.J.; Dickinson, M.E.; Lunderberg, D.M.; Lang, J.R.; Peaslee, G.F. Fluorinated compounds in US fast food packaging. *Environ. Sci. Technol. Lett.* **2017**, *4*, 105–111. [CrossRef]

96. Abraham, K.; Monien, B.H. Transdermal absorption of 13C4-perfluorooctanoic acid (13C4-PFOA) from a sunscreen in a male volunteer–What could be the contribution of cosmetics to the internal exposure of perfluoroalkyl substances (PFAS)? *Environ. Int.* **2022**, *169*, 107549. [CrossRef] [PubMed]

97. Chen, Q.; Yi, S.; Ye, Q.; Zhu, Y.; Zhong, W.; Zhu, L. Insights into the Dermal Absorption, Deposition, and Elimination of Poly-and Perfluoroalkyl Substances in Rats: The Importance of Skin Exposure. *Environ. Sci. Technol.* **2022**, *56*, 16975–16984. [CrossRef] [PubMed]

98. Gilmore, T.; Duboscq, S.; Genereux, D.; Pétré, M.; Solomon, D.; Knappe, D.; Hopkins, Z.; DeStefano, N. ^{3}H/^{3}He groundwater ages and discharge of PFAS from groundwater to a coastal plain stream in North Carolina. In Proceedings of the AGU Fall Meeting. 2020. Available online: https://ui.adsabs.harvard.edu/abs/2020AGUFMH096...01G/abstract (accessed on 10 February 2024).

99. D'Ambro, E.L.; Pye, H.O.; Bash, J.O.; Bowyer, J.; Allen, C.; Efstathiou, C.; Gilliam, R.C.; Reynolds, L.; Talgo, K.; Murphy, B.N. Characterizing the air emissions, transport, and deposition of per-and polyfluoroalkyl substances from a fluoropolymer manufacturing facility. *Environ. Sci. Technol.* **2021**, *55*, 862–870. [CrossRef] [PubMed]

100. Dassuncao, C.; Hu, X.C.; Zhang, X.; Bossi, R.; Dam, M.; Mikkelsen, B.; Sunderland, E.M. Temporal shifts in poly-and perfluoroalkyl substances (PFASs) in North Atlantic pilot whales indicate large contribution of atmospheric precursors. *Environ. Sci. Technol.* **2017**, *51*, 4512–4521. [CrossRef] [PubMed]

101. Dassuncao, C.; Hu, X.C.; Nielsen, F.; Weihe, P.; Grandjean, P.; Sunderland, E.M. Shifting global exposures to poly-and perfluoroalkyl substances (PFASs) evident in longitudinal birth cohorts from a seafood-consuming population. *Environ. Sci. Technol.* **2018**, *52*, 3738–3747. [CrossRef] [PubMed]

102. Hall, A.M.; Braun, J.M. Per-and Polyfluoroalkyl Substances and Outcomes Related to Metabolic Syndrome: A Review of the Literature and Current Recommendations for Clinicians. *Am. J. Lifestyle Med.* **2023**. [CrossRef]

103. Barry, V.; Winquist, A.; Steenland, K. Perfluorooctanoic acid (PFOA) exposures and incident cancers among adults living near a chemical plant. *Environ. Health Perspect.* **2013**, *121*, 1313–1318. [CrossRef] [PubMed]

104. Fei, C.; McLaughlin, J.K.; Tarone, R.E.; Olsen, J. Perfluorinated chemicals and fetal growth: A study within the Danish National Birth Cohort. *Environ. Health Perspect.* **2007**, *115*, 1677–1682. [CrossRef]

105. Joensen, U.N.; Bossi, R.; Leffers, H.; Jensen, A.A.; Skakkebæk, N.E.; Jørgensen, N. Do perfluoroalkyl compounds impair human semen quality? *Environ. Health Perspect.* **2009**, *117*, 923–927. [CrossRef]

106. Lopez-Espinosa, M.-J.; Mondal, D.; Armstrong, B.; Bloom, M.S.; Fletcher, T. Thyroid function and perfluoroalkyl acids in children living near a chemical plant. *Environ. Health Perspect.* **2012**, *120*, 1036–1041. [CrossRef]

107. Andersen, M.E.; Butenhoff, J.L.; Chang, S.-C.; Farrar, D.G.; Kennedy Jr, G.L.; Lau, C.; Olsen, G.W.; Seed, J.; Wallace, K.B. Perfluoroalkyl acids and related chemistries—Toxicokinetics and modes of action. *Toxicol. Sci.* **2008**, *102*, 3–14. [CrossRef] [PubMed]

108. Rosen, M.B.; Thibodeaux, J.R.; Wood, C.R.; Zehr, R.D.; Schmid, J.E.; Lau, C. Gene expression profiling in the lung and liver of PFOA-exposed mouse fetuses. *Toxicology* **2007**, *239*, 15–33. [CrossRef]

109. Post, G.B.; Cohn, P.D.; Cooper, K.R. Perfluorooctanoic acid (PFOA), an emerging drinking water contaminant: A critical review of recent literature. *Environ. Res.* **2012**, *116*, 93–117. [CrossRef] [PubMed]

110. Starkov, A.; Wallace, K.B. Structural determinants of fluorochemical-induced mitochondrial dysfunction. *Toxicol. Sci.* **2002**, *66*, 244–252. [CrossRef] [PubMed]

111. Vanden Heuvel, J.P.; Thompson, J.T.; Frame, S.R.; Gillies, P.J. Differential activation of nuclear receptors by perfluorinated fatty acid analogs and natural fatty acids: A comparison of human, mouse, and rat peroxisome proliferator-activated receptor-α,-β, and-γ, liver X receptor-β, and retinoid X receptor-α. *Toxicol. Sci.* **2006**, *92*, 476–489. [CrossRef]

112. Grandjean, P.; Andersen, E.W.; Budtz-Jørgensen, E.; Nielsen, F.; Mølbak, K.; Weihe, P.; Heilmann, C. Serum vaccine antibody concentrations in children exposed to perfluorinated compounds. *JAMA* **2012**, *307*, 391–397. [CrossRef]

113. Grandjean, P.; Budtz-Jørgensen, E. Immunotoxicity of perfluorinated alkylates: Calculation of benchmark doses based on serum concentrations in children. *Environ. Health* **2013**, *12*, 35. [CrossRef]

114. Boyd, R.I.; Ahmad, S.; Singh, R.; Fazal, Z.; Prins, G.S.; Madak Erdogan, Z.; Irudayaraj, J.; Spinella, M.J. Toward a mechanistic understanding of poly-and perfluoroalkylated substances and cancer. *Cancers* **2022**, *14*, 2919. [CrossRef]

115. Temkin, A.M.; Hocevar, B.A.; Andrews, D.Q.; Naidenko, O.V.; Kamendulis, L.M. Application of the key characteristics of carcinogens to per and polyfluoroalkyl substances. *Int. J. Environ. Res. Public Health* **2020**, *17*, 1668. [CrossRef]

116. Singh, N.; Hsieh, C.Y.J. Exploring potential carcinogenic activity of per-and polyfluorinated alkyl substances utilizing high-throughput toxicity screening data. *Int. J. Toxicol.* **2021**, *40*, 355–366. [CrossRef] [PubMed]

117. Eriksson, U.; Mueller, J.F.; Toms, L.-M.L.; Hobson, P.; Kärrman, A. Temporal trends of PFSAs, PFCAs and selected precursors in Australian serum from 2002 to 2013. *Environ. Pollut.* **2017**, *220*, 168–177. [CrossRef] [PubMed]

118. Yang, L.; Wang, Z.; Shi, Y.; Li, J.; Wang, Y.; Zhao, Y.; Wu, Y.; Cai, Z. Human placental transfer of perfluoroalkyl acid precursors: Levels and profiles in paired maternal and cord serum. *Chemosphere* **2016**, *144*, 1631–1638. [CrossRef]

119. Salihovic, S.; Kärrman, A.; Lind, L.; Lind, P.M.; Lindström, G.; van Bavel, B. Perfluoroalkyl substances (PFAS) including structural PFOS isomers in plasma from elderly men and women from Sweden: Results from the Prospective Investigation of the Vasculature in Uppsala Seniors (PIVUS). *Environ. Int.* **2015**, *82*, 21–27. [CrossRef]

120. Christensen, K.Y.; Raymond, M.; Thompson, B.A.; Anderson, H.A. Perfluoroalkyl substances in older male anglers in Wisconsin. *Environ. Int.* **2016**, *91*, 312–318. [CrossRef]

121. Boas, M.; Feldt-Rasmussen, U.; Skakkebæk, N.E.; Main, K.M. Environmental chemicals and thyroid function. *Eur. J. Endocrinol.* **2006**, *154*, 599–611. [CrossRef] [PubMed]

122. Weiss, J.M.; Andersson, P.L.; Lamoree, M.H.; Leonards, P.E.; van Leeuwen, S.P.; Hamers, T. Competitive binding of poly-and perfluorinated compounds to the thyroid hormone transport protein transthyretin. *Toxicol. Sci.* **2009**, *109*, 206–216. [CrossRef]

123. Stanifer, J.W.; Stapleton, H.M.; Souma, T.; Wittmer, A.; Zhao, X.; Boulware, L.E. Perfluorinated chemicals as emerging environmental threats to kidney health: A scoping review. *Clin. J. Am. Soc. Nephrol. CJASN* **2018**, *13*, 1479. [CrossRef]

124. Basu, G.; Mohapatra, A. Interactions between thyroid disorders and kidney disease. *Indian J. Endocrinol. Metab.* **2012**, *16*, 204. [CrossRef]

125. Zhao, L.; Teng, M.; Zhao, X.; Li, Y.; Sun, J.; Zhao, W.; Ruan, Y.; Leung, K.M.; Wu, F. Insight into the binding model of per-and polyfluoroalkyl substances to proteins and membranes. *Environ. Int.* **2023**, *175*, 107951. [CrossRef]

126. Rajak, P.; Ganguly, A. The ligand-docking approach explores the binding affinity of PFOS and PFOA for major endogenous antioxidants: A potential mechanism to fuel oxidative stress. *Sustain. Chem. Environ.* **2023**, *4*, 100047. [CrossRef]

127. Peng, M.; Xu, Y.; Wu, Y.; Cai, X.; Zhang, W.; Zheng, L.; Du, E.; Fu, J. Binding Affinity and Mechanism of Six PFAS with Human Serum Albumin: Insights from Multi-Spectroscopy, DFT and Molecular Dynamics Approaches. *Toxics* **2024**, *12*, 43. [CrossRef] [PubMed]

128. Liu, Y.; Cao, Z.; Zong, W.; Liu, R. Interaction rule and mechanism of perfluoroalkyl sulfonates containing different carbon chains with human serum albumin. *RSC Adv.* **2017**, *7*, 24781–24788. [CrossRef]

129. Mamsen, L.S.; Jönsson, B.A.; Lindh, C.H.; Olesen, R.H.; Larsen, A.; Ernst, E.; Kelsey, T.W.; Andersen, C.Y. Concentration of perfluorinated compounds and cotinine in human foetal organs, placenta, and maternal plasma. *Sci. Total Environ.* **2017**, *596*, 97–105. [CrossRef] [PubMed]

130. Gao, Y.; Luo, J.; Zhang, Y.; Pan, C.; Ren, Y.; Zhang, J.; Tian, Y.; Cohort, S.B. Prenatal exposure to per-and polyfluoroalkyl substances and child growth trajectories in the first two years. *Environ. Health Perspect.* **2022**, *130*, 037006. [CrossRef]

131. Kashino, I.; Sasaki, S.; Okada, E.; Matsuura, H.; Goudarzi, H.; Miyashita, C.; Okada, E.; Ito, Y.M.; Araki, A.; Kishi, R. Prenatal exposure to 11 perfluoroalkyl substances and fetal growth: A large-scale, prospective birth cohort study. *Environ. Int.* **2020**, *136*, 105355. [CrossRef] [PubMed]

132. Spratlen, M.J.; Perera, F.P.; Lederman, S.A.; Robinson, M.; Kannan, K.; Trasande, L.; Herbstman, J. Cord blood perfluoroalkyl substances in mothers exposed to the World Trade Center disaster during pregnancy. *Environ. Pollut.* **2019**, *246*, 482–490. [CrossRef]

133. Midasch, O.; Drexler, H.; Hart, N.; Beckmann, M.; Angerer, J. Transplacental exposure of neonates to perfluorooctanesulfonate and perfluorooctanoate: A pilot study. *Int. Arch. Occup. Environ. Health* **2007**, *80*, 643–648. [CrossRef]

134. Winkens, K.; Vestergren, R.; Berger, U.; Cousins, I.T. Early life exposure to per-and polyfluoroalkyl substances (PFASs): A critical review. *Emerg. Contam.* **2017**, *3*, 55–68. [CrossRef]

135. Huo, X.; Zhang, L.; Huang, R.; Feng, L.; Wang, W.; Zhang, J. Perfluoroalkyl substances exposure in early pregnancy and preterm birth in singleton pregnancies: A prospective cohort study. *Environ. Health* **2020**, *19*, 60. [CrossRef]