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Per- and Polyfluoroalkyl Substances (PFAS): A Critical Threat to Human Health

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Abstract— Per- and polyfluoroalkyl substances (PFAS) are a group of chemicals extensively manufactured over the past few decades for various industrial and commercial applications due to their exceptional stability, as well as their hydrophobic and lipophobic properties. Because of their widespread use, PFAS have become pervasive in our environment, contaminating water, soil, air, and food, as well as materials in homes and workplaces, making human exposure nearly unavoidable. PFAS have gained significant attention due to their potential to cause a range of health effects, including endocrine disruption, liver diseases, kidney diseases, immune system dysfunction, lipid dysregulation, reproductive and developmental issues, and cancer. In this review, we examine the sources and pathways of human exposure to PFAS. We also explore the health implications associated with PFAS and the biological mechanisms involved. Furthermore, we discuss current research limitations and suggest future directions to better understand the relationship between PFAS exposure and human health.

Index Terms— Per- and Polyfluoroalkyl Substances, PFAS, PFOA, PFOS, Human Exposure, Health Concerns

1 Introduction

HUMANS are consistently exposed to a wide range of environmental chemicals that can significantly impact physiological functions and health. Per- and polyfluoroalkyl substances (PFAS) are particularly problematic due to their exceptional persistence in the environment [1]. PFAS are a group of emerging pollutants defined by the presence of at least one perfluorinated aliphatic component [2]. Their unique chemical structure, featuring a carbon backbone with perfluorinated methyl or methylene groups and various functional groups, grants them resistance to heat and the ability to repel water and oils. These characteristics have led to their widespread use in industrial and consumer products since the 1950s [3]. Estimates suggest there are between 5,000 and 10,000 different PFAS compounds, many of which are highly resistant to environmental degradation, earning them the nickname "forever chemicals" [4]. Their extensive application in products such as fire retardants, waterproof coatings, food packaging, household items, personal care products, and stain repellents has raised significant public health concerns. PFAS are now prevalent in the environment and are recognized for their potential toxicity [5].

High concentrations of PFAS have been detected in human blood serum, reaching several hundred μg/L [3]. Public concern over PFAS health effects intensified in the early 2000s when perfluorooctanesulfonate (PFOS) was discovered in the blood of Arctic polar bears and other remote wildlife [6]. Research by the Centers for Disease Control and Prevention (CDC) later revealed that PFAS were present in the blood of nearly all Americans (98%) [7]. From 2003 to 2014, more than 98% of U.S. adults had detectable levels of PFOS, perfluorooctanoic acid (PFOA), perfluorohexanesulfonic acid (PFHxS), and perfluorononanoic acid (PFNA) in their blood [8]. Between 2013 and 2015, PFAS levels above reporting thresholds were found in 194 of 4,864 tested public water supplies in the U.S. Approximately 6 million people served by 66 public water systems were exposed to PFOA and PFOS concentrations exceeding the Environmental Protection Agency's (EPA) recommended limit of 70 ng/L for these substances, either individually or combined. [9]. Many legacy PFAS compounds have long human half-lives, underscoring their potential for bioaccumulation and biomagnification [10].

Primary routes of PFAS exposure include contaminated drinking water, indoor dust, air, and food packaging. Inhalation of dust and air or direct skin contact also contribute to exposure. Once inside the body, PFAS have been detected in various tissues, with half-lives ranging from months to six years [11]. Research has linked specific PFAS exposures to a variety of health issues, including immune system suppression, endocrine disruption, lipid imbalances, cancer, liver disease, and adverse reproductive and developmental effects [1], [12], [13], [14]. For example, the similarity between PFAS and fatty acids has led to hypotheses that PFAS might interfere with lipid metabolism by binding to receptors and membranes, suggesting their relevance in studying cardiometabolic diseases such as dyslipidemia and cardiovascular conditions [1]. Additionally, prenatal and early-life PFAS exposure has been associated with various health problems in children, including impacts on immunity, infection susceptibility, asthma, thyroid and kidney function, obesity, cardiometabolic issues, and neurodevelopmental disorders like autism spectrum disorder and attention deficit/hyperactivity disorder [12]. This review aims to provide an in-depth examination of PFAS, focusing on their pervasive use, routes of human exposure, and potential health impacts and biological mechanisms related to PFAS exposure.

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2 Chemical Properties and Human Exposure Routes

PFAS are widely produced chemicals extensively utilized in various consumer and industrial products due to their unique

surfactant properties and resistance to heat, oil, stains, and water [15]. These aliphatic substances are defined by their strong carbon-fluorine (C-F) bonds, which contribute to their environmental durability and gradual breakdown in both ecological systems and the human body. Structurally, PFAS feature a perfluoroalkyl group where fluorine atoms replace hydrogen atoms, accompanied by a functional group [16]. Based on their carbon chain length, PFAS are categorized as either short-chain or long-chain.

Short-chain PFAS contain fewer than eight or six perfluorinated carbon atoms, respectively. While often subject to less stringent regulation, short-chain PFAS also raise significant concerns due to their toxicity, persistence, and potential for long-range environmental transport [5], [19], [20]. Their lower adsorption potential makes them particularly difficult to remove from water sources [21]. Long-chain PFAS, by contrast, include perfluoroalkyl carboxylic acids with eight or more carbon atoms and perfluoroalkyl sulfonic acids with six or more carbon atoms. These compounds, such as PFOA and PFOS, are known for their bio-accumulative properties, with longer chains posing a higher risk of accumulation in biological systems [17] [18].

Since the 1950s, PFAS have been employed across a variety of industries and incorporated into numerous consumer products. These include sites related to the military and airports, cookware, food packaging, waterproof clothing, furniture, carpets, paints, and cosmetics [22], [23]. PFAS contamination has been detected globally in rivers, rainwater, soil, urban air, and even remote regions [24]. Despite the existence of over 4,700 known PFAS compounds, with at least 3,000 currently in use in various market products, only a few have been thoroughly studied for their health impacts [15].

Human exposure to PFAS primarily occurs through ingestion of contaminated drinking water and food, especially in areas near sites with high PFAS contamination from activities such as fluorochemical manufacturing or the use of aqueous film-forming foam. The relative source contribution, or the proportion of total daily PFAS exposure attributed to tap water, is critical in understanding its impact on serum PFAS concentrations. Other exposure pathways include dermal contact with cleaning or personal care products, inhalation of airborne volatiles and dust, and ingestion through food packaging [7], [25]. Figure 1 illustrates the primary sources of PFAS exposure. Most countries lack comprehensive safety regulations for PFOS and other PFAS in drinking water, and universally safe exposure levels have yet to be established, even at low doses [15].

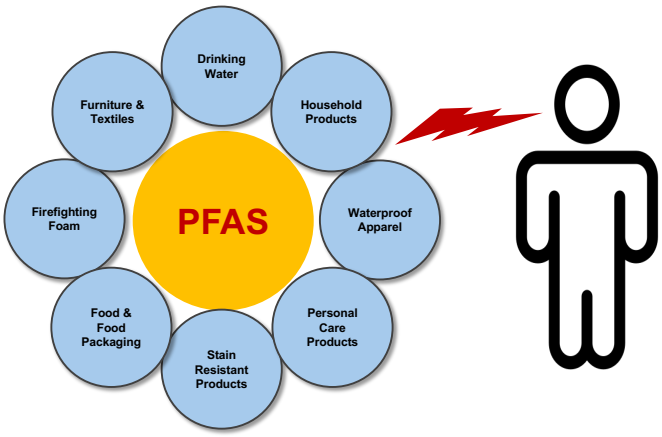

Fig. 1. Overview of the primary sources of PFAS exposure.

3 Significant Health Concerns Associated with PFAS

It is widely acknowledged that PFAS emissions, originating from both primary and secondary sources, can reach human receptors, including both professional workers and the general population, through multiple exposure pathways [26]. It is widely acknowledged that PFAS emissions, originating from both primary and secondary sources, can reach human receptors, including both professional workers and the general population, through multiple exposure pathways [15].

3.1 Cancer

In 2017, the International Agency for Research on Cancer (IARC) classified PFOA as a potential human carcinogen [27]. Since then, research has increasingly linked PFAS exposure to various cancers, including those of the kidney, testis, prostate, liver, pancreas, bladder, and thyroid, though the evidence remains inconsistent [28]. For example, studies have found an elevated risk of bladder cancer mortality among workers in a PFOS production facility, yet other research, such as in the Danish population, found no significant correlation between PFAS levels and cancers like prostate or liver cancer [29], [30]. Similarly, research on PFOS has shown mixed outcomes—some studies associate it with increased thyroid cancer risk, while others suggest PFAS may influence liver function in lung cancer patients. Moreover, a large-scale study conducted in Appalachia indicated an inverse relationship between PFOS levels and colorectal cancer risk [14], [31], [32]. Sociodemographic factors, including occupation, geographic location, ethnicity, gender, income, and education, have been identified as influencing both PFAS levels and cancer risk. A. Ayodele and E. Obeng-Gyasi [33] identified significant sociodemographic factors—such as ethnicity, sex, occupation, geographical location, income, and education—that influence both PFAS levels and cancer risk. Stress has become a key factor in PFAS exposure and the risk of developing endometrial cancer, highlighting the importance of managing stress for overall health.

PFAS may contribute to cancer development through mechanisms such as epigenetic modifications, immunosuppression,

oxidative stress, and hormonal disruptions, thereby facilitating the initiation and progression of cancer. For instance, PFOS has been linked to changes in DNA methylation, while PFAS exposure is associated with oxidative DNA damage, both of which are related to cancer progression [34], [35], [36].

Recent studies have reported a correlation between PFAS exposure and an elevated risk of breast cancer, with higher PFAS concentrations observed in breast cancer patients compared to control groups [37], [38], [39]. Researchers propose that oxidative stress and endocrine disruption could be potential biological links. In vitro studies have shown that PFOA and PFDA can increase reactive oxygen species (ROS) and oxidative DNA damage, both of which are associated with breast cancer [40], [41]. Correspondingly, in vivo studies suggest that PFOA exposure can elevate markers of oxidative DNA damage, such as 8-OHdG and malondialdehyde [42]. Furthermore, metabolomics data suggest that high PFAS exposure disrupts the modulation of glutathione (GSH) and α-tocopherol, which are essential for maintaining oxidative stress balance. These findings imply that PFAS-induced oxidative damage could serve as a potential intermediary in breast cancer development [43]. Additionally, PFOA may enhance estrogenic effects in breast cancer cells and is associated with increased estrogen levels in population studies, indicating that PFOA might act as a xenoestrogen, altering estrogen production and effects, and potentially contributing to breast cancer [44], [45].

3.2 Endocrine Disruption and Metabolic Diseases Cancer

PFAS are known to disrupt endocrine functions in humans and animals, affecting various organs including the breasts, ovaries, brain, thyroid, pancreas, and uterus. Of particular concern is the relationship between PFAS exposure and metabolic syndrome, a cluster of cardiovascular-related metabolic abnormalities such as dyslipidemia, glucose dysregulation, insulin resistance, adiposity, and hypertension [46]. PFAS may interfere with lipid metabolism by binding to receptors and membranes, particularly targeting peroxisome proliferator-activated receptor-α (PPAR-α) and, to a lesser extent, PPAR-γ, which could influence lipid and glucose metabolism and promote adipogenesis [47].

Dyslipidemia and Cardiovascular Diseases

There is substantial epidemiological evidence linking PFAS exposure to elevated cholesterol levels, with dyslipidemia being the most consistently observed metabolic outcome [7]. Both European Food Safety Authority (EFSA) and population studies have demonstrated associations between PFOS, PFOA, and PFNA exposure and increased serum cholesterol levels [11], [48], [49]. A pharmacokinetic model suggests that approximately half of the population exposed to PFOS might experience more than a 20% increase in serum cholesterol [50]. Moreover, studies have found that plasma PFAS concentrations are associated not only with elevated cholesterol levels but also with changes in apolipoproteins and composite profiles of fatty acids and phospholipids [51]. The lipid changes observed in humans due to PFAS exposure are consistent with experimental findings, including decreased CYP7A1 enzyme activity, impaired bile acid metabolism, and adipogenesis, which can lead to intracellular lipid accumulation and steatosis [12]. Dyslipidemia is a well-established independent risk factor for cardiovascular disease (CVD), and PFAS exposure has been linked to an increased risk of CVD, atherosclerosis, and thrombus formation [52], [53]. PFAS may contribute to the development of atherosclerosis-related vascular diseases and arterial thromboembolism, with sex-specific differences observed in the relationship between PFAS levels and cardiovascular outcomes [54].

Diabetes

Emerging research suggests that PFAS exposure might contribute to insulin resistance and dysregulated lipogenesis, potentially increasing the risk of type 2 diabetes [55], [56], [57]. However, the evidence linking PFAS to diabetes remains inconsistent across different studies [58], [59], [60]. Experimental studies indicate that PFAS may activate G protein–coupled receptor 40, a membrane receptor on islet β cells, stimulating insulin secretion and potentially influencing the development of diabetes [61].

Obesity and Hypertension

Research has demonstrated positive correlations between PFAS exposure, particularly PFHxS, PFOS, and PFOA, and the occurrence of hypertension and obesity across various life stages [62], [63]. Several studies have observed an association between elevated PFAS levels, particularly PFOA, and higher rates of obesity in adolescents. For instance, one study found that higher PFOA levels were linked to increased obesity rates in children aged 12-18 years [64]. Similarly, another study reported a positive association between PFHxS and PFHpS concentrations and obesity in Norwegian adolescents [62].

Thyroid dysfunction

PFAS are thought to affect thyroid hormones and disrupt thyroid homeostasis, including hormone production, transport, and metabolism. One proposed mechanism is that PFAS lower circulating thyroxine (T4) levels by competing with thyroid hormone transport proteins for binding sites [66], [67]. A meta-analysis encompassing 12 studies revealed a negative correlation between PFAS exposure and serum total thyroxine levels, suggesting potential thyroid dysfunction [68]. Additionally, early exposure to PFAS has been associated with reduced thyroid-stimulating hormone (TSH) levels and elevated free thyroxine (FT4) or triiodothyronine (T3) levels in young children [69]. Boys with low iodine intake have shown increased free T4 levels when exposed to PFAS, either alone or in combination [70]. These observations are further supported by meta-analyses demonstrating a negative relationship between PFAS and total T4, with the impact varying based on PFAS concentrations [71]. Experimental studies indicate that PFAS may interact with thyroid hormone-binding proteins, thereby disrupting the feedback mechanism between free thyroid hormones and the hypothalamic-pituitary-thyroid axis [12]. Furthermore, in vitro research has revealed that PFAS exposure can inhibit the activity of the thyroid peroxidase (TPO) enzyme [72]. Several studies indicate that disruptions in thyroid hormone levels, particularly in maternal and neonatal outcomes, are more pronounced in individuals with high circulating anti-TPO antibodies. For example, a case-control study on congenital hypothyroidism found significantly higher serum concentrations of PFOA, PFNA, PFDA, and PFUA in diagnosed newborns, with correlations observed between PFAS levels and thyroid autoantibodies

[73].

3.3 Immunotoxicity

The U.S. National Toxicology Program (NTP) has flagged perfluorooctanoic acid (PFOA) and perfluorooctane sulfonate (PFOS) as immunotoxicants for humans, supported by evidence from various studies, including epidemiological, animal, and mechanistic research [74]. Laboratory studies suggest that perfluorinated chemicals influence immune cells by modulating cytokine expression, with peroxisome proliferator-activated receptors (PPARs) playing a crucial role in regulating these cellular processes [75], [76]. Notably, PFOS and PFOA interact with PPAR alpha, a transcription factor involved in regulating lipid metabolism, mitochondrial function, cell growth, inflammatory responses, and glucose metabolism [77], [78].

Recent findings indicate that PFAS exposure is associated with changes in circulating inflammatory and immune markers. For instance, research has demonstrated shifts in blood cell subpopulations, including natural killer (NK), T-helper (Th), and cytotoxic T (Tc) cells [79]. Additional studies have reported increased frequencies of NK cells and their activated subsets, as well as higher levels of activated T memory cell subsets expressing Th2-associated chemokines, Th2/Th17 cytokine-producing T effector memory (TEM) Th cells, and markers such as Foxp3 and CD25 on central memory T cells (TCMs) and T helper cells [80]. These findings suggest that PFAS exposure may alter key immune cell subpopulations, potentially affecting immune function.

Moreover, calcium (Ca^{2+}) signaling is vital for immune responses, particularly in the activation and function of various immune cells like NK cells, mast cells, dendritic cells, and macrophages [81]. Studies have shown that PFOA can increase intracellular Ca^{2+} levels in mast-like cells in vitro [82], while PFOS has been observed to elevate cytosolic Ca^{2+} in human and mouse macrophages, leading to activation of the AIM2 inflammasome through a Ca^{2+}-dependent pathway involving PKC-NF-κB/c-Jun N-terminal kinase (JNK)-BAX/BAK. This pathway triggers the production of proinflammatory cytokines, induces endoplasmic reticulum (ER) stress, causes cellular damage, and leads to tissue inflammation [83]. Furthermore, PFAS are known to exacerbate oxidative stress by elevating levels of reactive oxygen species (ROS), which can result in mitochondrial DNA damage [81], [84]. Evidence of oxidative damage has been observed in human lymphocytes and primary mouse hepatocytes [85], [86]. Figure 2 illustrates the pathways by which PFAS modulate inflammatory responses.

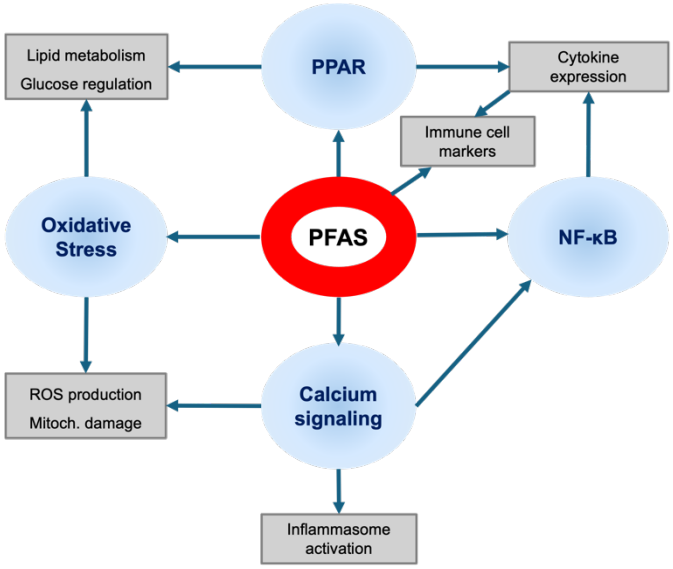

Fig. 2. The pathways of inflammatory modulation induced by PFAS.

Epidemiological studies have explored the relationship between PFAS exposure and immunosuppression in humans, particularly concerning prenatal and early childhood exposure [81], [87], [88], [89], [90]. For example, one study found that PFAS levels in blood were associated with reduced serum antibody production in children following routine vaccinations [91]. Similarly, another study observed immunosuppression, indicated by reduced antibody responses, particularly with PFOS, PFOA, and PFHxS exposure [89]. Additionally, PFAS have been shown to suppress trophoblast cell function, reducing the production of inflammatory proteins essential for placental blood flow, which may increase the risk of preeclampsia [92], [93]. Research also suggests that prenatal PFOA levels are linked to elevated IL-1beta, a pro-inflammatory cytokine, which has been associated with larger waist circumferences in exposed children, indicating a connection between inflammation and adverse metabolic profiles.

3.4 Liver Dysfunction

The liver is a major organ for the storage of long-chain PFAS, which has been associated with various toxic effects, including fat infiltration in hepatocytes, activation of specific CYP450 pathways, apoptosis, and the development of hepatocellular adenomas and carcinomas. PFAS exposure also disrupts fatty acid trafficking, which may be dependent on or independent of PPARα across different species [12].

Research has consistently linked PFAS exposure to alterations in liver function markers. [94]. Similarly, an analysis of National Health and Nutrition Examination Survey data (2003–2016) reported positive correlations between elevated alanine aminotransferase (ALT) levels and exposure to PFOA, PFHxS, and PFNA [95]. Other studies have also identified positive associations between PFAS concentrations and liver enzymes such as ALT, aspartate aminotransferase (AST), and gamma-

glutamyl transferase (GGT), with variations depending on factors like sex, obesity, and PFAS type [96]. Additionally, PFAS exposure has been linked to changes in Apolipoprotein B (APOB) and GGT, likely related to disruptions in amino acid and glycerophospholipid metabolism, as well as negative associations with total and direct bilirubin [97].

PFAS accumulation in the liver disrupts homeostasis, altering metabolic processes and potentially leading to conditions such as fatty liver disease and liver cancer [12], [98], [99]. Evidence from studies using nonalcoholic fatty liver disease (NAFLD) cytokeratin C18 biomarkers supports the role of PFAS in inducing steatosis [100], and metabolomic research suggests disruptions in glycerophosphocholine and fatty acid profiles [101], [102]. A clinic-based study found that obese children (85%) aged 7 to 19 had advanced disease linked to PFHxS and PFOS exposure, as well as related disruptions in amino acid and lipid pathways [103]. In a study of 462 heavily exposed workers, significantly higher mortality rates from cirrhosis and liver cancer were reported compared to the regional population [104].

3.5 Kidney disorder

The kidney is another primary site for PFAS accumulation, likely due to its high levels of phospholipids, liver fatty acid binding proteins (L-FABPs), and organic anion transporter (OAT) proteins [105], [106], [107]. Research has demonstrated that PFAS can lead to various forms of kidney dysfunction. For instance, research involving rats exposed to perfluorododecanoic acid revealed alterations in 12 proteins associated with amino acid metabolism, signaling potential renal dysfunction [108]. Furthermore, PFOS has been demonstrated to promote renal inflammation through the activation of the absent in melanoma 2 (AIM2) receptor [83].

Exposure to PFAS compounds may also affect urinary metabolism. Elevated levels of uric acid, a marker indicative of heightened renal disease risk, have been consistently linked to PFAS exposure in both adult and pediatric populations [12]. Serum PFAS concentrations exhibit an inverted U-shaped relationship with glomerular filtration rate: they increase as filtration decreases initially but decrease in the later stages of renal disease due to impaired reabsorption. This pattern is more pronounced in cases of albuminuria. However, studies suggest that PFAS levels related to uric acid may be underestimated because damaged kidneys excrete long-chain PFAS but retain uric acid, potentially obscuring links with conditions like hypertension and elevated uric acid in cross-sectional studies [109], [110].

A study conducted in Hubei Province, China, comparing occupational workers with local residents, found that higher urinary PFAS levels were positively correlated with key kidney molecules. The analysis identified eight metabolites involved in enterohepatic circulation , steroid biosynthesis, and amino acid metabolism [111]. Additionally, PFAS exposure disrupts several pathways, including those related to oxidative stress, PPAR, epithelial-mesenchymal transition, and endothelial permeability through actin filament remodeling [112].

3.5 Reproductive and developmental toxicity

Prenatal exposure to PFAS has been linked to significant effects on fetal development, particularly concerning fetal growth restrictions. This exposure has raised concerns about adverse outcomes such as reduced birth weight and an increased likelihood of infants being born small for gestational age due to maternal contact with PFAS [113], [114], [115]. Moreover, exposure to PFAS during prenatal and early life stages is associated with long-term health issues in children, such as obesity, endocrine disruption, neurodevelopmental disorders, and heightened cardiovascular risk [114], [116], [117].

The placenta, a complex organ critical to pregnancy, may be particularly vulnerable to PFAS exposure. In vitro studies indicate that PFOS and PFOA can interfere with placental vascular development, leading to observable morphological and molecular changes [118], [119]. Such disruptions can impair the placenta's ability to supply nutrients and oxygen to the fetus, potentially resulting in adverse birth outcomes [120]. Additionally, research has shown that PFAS exposure can alter gene expression related to crucial placental functions, including viability, transport, and invasion/mesenchymal transition [121].

There is also evidence to suggest that prenatal PFAS exposure may contribute to Alu DNA hypomethylation, a condition associated with genomic instability and various complex diseases [35], [122]. High levels of PFAS exposure have been linked to neonatal morbidity and mortality, while lower levels are associated with growth deficits and developmental delays [12]. For instance, studies in mice have demonstrated that PFOA exposure can impair lactation and increase offspring mortality, likely due to placental dysfunction. Even at low doses, PFOA exposure during pregnancy has been shown to cause lasting deficits in mammary gland development, though these levels did not appear to affect body weight, lactation, or neonatal growth [123], [124].

Systematic reviews consistently connect in utero exposure to PFOS and PFOA with reduced fetal growth in both animal models and human populations [125], [126]. PFAS exposure is also associated with reproductive issues, such as ovulation failure [127]. However, the relationship between prenatal PFAS exposure and neurobehavioral outcomes, including ADHD, ASD, and autism, remains uncertain, with studies producing mixed results. To better understand these associations, comprehensive meta-analyses are needed [128], [129].

4 Common Limitations of Previous Studies and Future OutlookCitations

Current research underscores the potential health risks associated with PFAS exposure, linking these chemicals to a range of adverse outcomes, including immunotoxicity, dyslipidemia, kidney and liver dysfunction, cancer, and reproductive and developmental issues. Notably, the NTP has categorized PFOA and PFOS as "presumed immune hazards to humans" [74].

Despite these findings, pinpointing the specific health effects of PFAS exposure is challenging due to several factors. First, the sheer number of PFAS compounds—each with varying effects and toxicity levels—complicates research, as most studies focus on only a few well-known PFAS. Second, the diversity in exposure pathways and life stages further complicates the assessment of their health impacts. Third, the evolution in the types and uses of PFAS over time makes it difficult to track exposure patterns and predict their long-term effects on human health

[130].

To improve our understanding, future research must address several critical areas. Investigating how variables such as physical activity, occupation, ethnicity, geographical location, stress, and sex influence PFAS-related health outcomes is essential. Additionally, employing mixture-based analyses alongside single pollutant assessments will provide a clearer picture of the cumulative effects of PFAS exposure. Longitudinal studies that track exposure over time and standardize health outcome measurements across different studies are also crucial for enhancing the consistency and reliability of findings. Moreover, integrating PFAS exposure testing and clinical follow-up into routine medical practice could help clinicians identify individuals at higher risk for PFAS-related diseases.

5 Conclusion

Per- and polyfluoroalkyl substances (PFAS) are widely utilized across various industries due to their unique chemical properties, which are crucial for the production of a broad spectrum of consumer goods. However, the pervasive pollution resulting from PFAS, coupled with their exceptional stability due to the strong C-F bond, presents significant environmental challenges. PFAS are persistent in the environment, resisting degradation and consequently accumulating in water sources (including drinking water and groundwater), air, and soil. Human exposure to PFAS can occur through the consumption of water, food, or consumer products. Long-term exposure to these substances is associated with various health risks, including thyroid dysfunction, several types of cancer, diabetes, dyslipidemia, liver and kidney disorders, inflammatory conditions, and other health issues. This review has provided a comprehensive overview of the pathways through which humans are exposed to PFAS, the potential health impacts, and the underlying mechanisms driving PFAS toxicity.

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