Per- and polyfluoroalkyl substances (PFAS) exposure might be a risk factor for thyroid cancer

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In the November 2023 issue of *eBioMedicine*, Maaike van Gerwen et al. presented their work "Per- and Polyfluoroalkyl substances (PFAS) Exposure and Thyroid Cancer Risk", which reports an association between PFAS exposure and thyroid cancer using both a cross-sectional and longitudinal study design.[1] The study found a 56% increased rate of thyroid cancer diagnosis per doubling of linear perfluorooctanesulfonic acid (n-PFOS) in plasma; importantly, a similar result was also observed when including papillary thyroid cancer cases only. Moreover, this positive association remained in subset analysis investigating exposure timing on thyroid cancer.

Thyroid cancer is the most common endocrine malignancy with incidence steadily increasing over past decades. Besides commonly known factors such as overdiagnosis, obesity, and ionizing radiation exposure, unavoidable environmental risks such as the exposure of persistent organic pollutants (POPs) affect thyroid hormonal homeostasis.[2] PFAS are a large class of man-made chemicals widely used in consumer products and industrial processes. As well-known "forever chemicals", PFAS are very persistent due to the stable carbon to fluorine chemical bond, and their adverse health effects, including thyroid hormone disruption, have been frequently investigated.[3] However, we still don't know whether PFAS are thyroid carcinogens. Obviously, van Gerwen's results provide strong epidemiological evidence to support the hypothesis that PFAS exposure might be a risk factor for thyroid cancer, especially for papillary thyroid cancer, which accounts for 80%–85% of all thyroid cancer cases.

Concerns about the adverse effects of PFAS on human health initiated in the late 1990s after the Parkersburg (West Virginia, USA) PFOA water contamination incident. From then on, PFAS have been frequently and widely detected in human biomonitoring, confirming the fact that people are universally exposed to PFAS. Recently, a growing number of laboratory and epidemiological studies have demonstrated that PFAS may disturb the hypothalamus-pituitary-thyroid (HPT) axis, interfere with thyroid function and contribute to the risk of thyroid cancer. A high-throughput screening found that many types of PFAS can inhibit iodine uptake by suppressing sodium iodide symporter (NIS) that regulates iodide uptake into the thyroid gland.[4] Animal and cell line studies found that PFAS could disrupt thyroid hormones, alter thyroid related gene expression, and change the transcriptome of central tissues of the HPT-axis.[5,6] Meanwhile, epidemiological studies also demonstrated that PFAS exposure can disrupt thyroid function.[7]

Chemicals that interfere with thyroid hormone homeostasis may increase the risk and severity of thyroid cancer, and therefore whether PFAS are thyroid carcinogens is a matter of great concern. Studies on the association between PFAS exposure and risk of thyroid cancer are still limited at present. In an ecological study, residents living in a community with heavy PFAS contamination in drinking water experienced a significantly higher risk of thyroid cancer.[8] A previous study from van Gerwen and colleagues reported significant correlation between certain PFAS in community water systems and thyroid cancer incidence.[9] These studies supported the hypothesis that higher PFAS exposure might link to thyroid cancer. However, inconsistent results were also observed. Two case–control studies from China reported negative associations between PFAS exposure and thyroid cancer risk.[2,10] Contradictory results may be related to dissimilar study designs, population heterogeneity, sample sizes, and statistical methods. Thus, further research is needed to collect more evidence.

van Gerwen's result suggests that the elimination of certain PFAS with high health risks should be accelerated. Some regulatory rules on PFAS have been introduced. A number of legacy PFAS have been added to the list of persistent organic pollutants under the Stockholm Convention. PFOA, PFOS, their salts and related compounds were added to *"the List of Strictly Controlled Emerging Pollutants"* set by the Chinese government. In February 2023, the European Chemicals Agency (ECHA) proposed that the manufacture and use of all PFAS must be banned immediately. Moreover, World Health Organization (WHO), the USA and EU have all set strict standards for PFAS in drinking water. Due to the implemention of these regulations in the past decade, decreasing contamination of PFAS can be observed. However, current rules only focus on legacy PFAS. Novel PFAS such as F-53B and GenX, which act as substitutes of legacy PFAS, haven't been evaluated and included in regulation due to the lack of data. Thus, more research is needed to fully reveal the health risks of PFAS, particularly on novel substitutes.

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Even though some PFAS have been proved to be harmful to the environment and human health, a blanket ban on all PFAS immediately may not be the most effective and sustainable strategy. PFAS are composed of a large group of chemicals with dissimilar molecular structures and properties. Current epidemiological studies, like van Gerwen's work, normally include a few PFAS simultaneously, and the results showed that most PFAS had no significant association with health effects. That is, it is too early to conclude that every PFAS will pose significant risks, and therefore it is unreasonable to ban all PFAS in a rush. Besides, alternative materials may not be safer. More time and effort are needed to gather epidemiological and toxicological studies on PFAS, and policymakers should carefully weigh up the evidence when considering PFAS regulation.

Contributors

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Declaration of interests

The authors have no conflict of interest to declare.

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