SCIENCE REVIEW:

PFAS, COVID-19, and the Immune System

In the midst of a global COVID-19 pandemic, the fact that there is almost universal exposure to PFAS chemicals that can harm the immune system is troubling. The potential links between these twin crises was summed up by Congressman Harley Rouda, House Oversight and Reform Environment Subcommittee Chairman:

"We know that PFAS exposure, which weakens immune systems, causes diseases like cancer, and is reported to reduce antibody responses to vaccines, could create the perfect COVID-19 storm in communities across the United States." 1

The reasons why some individuals get COVID-19 and experience few or no symptoms while others fall gravely ill or die from the disease are complex. It is not yet clear whether high PFAS exposure may be playing a role in some cases, though there is now some preliminary evidence that this may be happening.² What we do know is that one effect of PFAS exposure is weakening of the immune system, and people with weakened immune systems are likely to have worse outcomes from COVID-19 infection.

This document is intended to provide a high-level overview of the science around PFAS and how it intersects with the major public health threat posed by COVID-19.³







Immune System Basics

The immune system is how the human body prevents and limits infection from pathogens such as viruses, bacteria, and fungi that can cause disease. It also plays an important role in identifying and killing mutated cells that can become cancer. It is a highly complex and important system made up of organs, cells, and proteins that work together throughout our bodies.⁴ If the immune system is not functioning properly, this can lead to health problems.

People with weakened immune systems are more likely to get sick from infectious diseases and can experience lowered responses from vaccines. A hypersensitive immune system can lead to allergies, asthma, or autoimmune diseases. FAS exposures have been linked to each of these immune system disorders, all of which pose unique concerns as we face the COVID-19 global pandemic.

PFAS can lower resistance to infectious diseases

PFAS can weaken the immune system and make people more likely to catch infectious diseases like colds, stomach bugs—and potentially COVID-19. This is suggested by several studies that have reported that people with higher exposures to PFAS are at increased risk of communicable diseases.

In one study of Norwegian families, children born to mothers with higher levels of some PFAS chemicals had more colds and more gastroenteritis (stomach flu) in early childhood. In Japan, mothers with higher blood measurements of some PFAS chemicals during pregnancy reported more infectious illnesses among their children, and young girls whose mothers had higher levels of certain PFAS also had more infectious illnesses.

In Denmark, mothers with higher levels of some PFAS were more likely to have children who developed fever during the study period, which is notable since fever is a marker of a variety of kinds of infections.⁹ The authors of this study also noted that this "finding is in agreement with an immunosuppressive effect of prenatal exposure to PFAS. The wider implications for childhood infectious disease deserve attention."¹⁰

There has been enough concern around how PFAS chemicals impact the immune system that the Centers for Disease Control and Prevention (CDC) issued a statement on the "Potential Intersection between PFAS Exposure and COVID-19", which acknowledged that PFAS exposure "may reduce infectious disease resistance."

While we don't have direct evidence that PFAS exposure increases people's risks of coming down with COVID-19, there is real reason to believe that this is likely, and we urgently need more research into this question.

PFAS can reduce vaccine effectiveness

Antibody production is an important component of the immune system. Vaccines work by training the immune system: when the body senses the presence of a virus, bacteria, or other pathogen that it has been primed to fight through vaccination, it produces proteins known as antibodies that attack that particular type of foreign invader (the measles virus, for example). If the body consistently produces enough effective antibodies after vaccination, then that person is considered "immune" and very likely won't get sick from a disease; or if they do get sick, it will be greatly reduced in severity and transmissibility.

However, not everyone who is vaccinated will become immune. According to the World Health Organization, most routine childhood vaccines are effective for 85% to 95% of recipients. People whose bodies don't launch a robust response to vaccination are more likely to fall ill from that particular disease.

The COVID-19 vaccines, for example, have been shown to be highly effective in protecting the general population against severe disease but have been found to be somewhat less effective for and immune compromised individuals.¹³ For this reason, the Food and Drug Administration is authorizing booster vaccines to increase protection for people most at-risk of severe COVID-19.¹⁴

What is highly concerning is that nearly a dozen studies of non-COVID vaccines have found significant decreases in antibody production in people with higher levels of PFAS exposure. These studies measure antibodies a person produces in response to common vaccines, and consistently find people with higher PFAS measurements have lower antibody levels—by as much as a 78%—for a number of different vaccine-prevented illnesses such as tetanus, diphtheria, rubella, mumps, and the flu. (See the table below for a summary of some of the key research.)

Scientific studies showing that PFAS reduces vaccine effectiveness

Population	Finding	Study
Faroe island children	Lower antibody response to tetanus and diphtheria vaccines	Grandjean 2012 ¹⁵
Norwegian children	Lower antibody response to rubella vaccine	Granum 2013 ¹⁶
German 1 year olds	Lower antibody response to flu, tetanus, and diphtheria vaccines	Abraham 2020 ¹⁷
West African children	Lower antibody response to measles vaccine	Timmermann 2020 ¹⁸
Greenlandic children	Lower antibody response to diphtheria vaccine, no such effect found in mothers	Timmermann 2021 ¹⁹
US adolescents	Lower antibody response to rubella and mumps vaccines	Stein 2016 ²⁰
US adults	Lower antibody response to flu vaccine	Looker 2014 ²¹
US adults	Lower antibody response to diphtheria and tetanus booster	Kielsen 2016 ²²
US adults	Lower antibody response to rubella vaccine in adults, no such effect found for adolescents	Pilkerton 2018 ²³

One scientific paper that looked at children in the Faroe islands concluded: "Our findings show that PFAS exposure may inhibit the formation of antibodies and cause more children to be unprotected despite a full regimen of vaccinations.... the strongly decreased antibody concentrations reflect a severe immunological deficit."²⁴

Another scientific study on children living in Greenland found that increased exposure to PFAS and other environmental chemicals was "associated with a decrease in post-vaccination antibody concentrations and with increased risk of not being protected against diphtheria despite appropriate vaccination." ²⁵

In a 2016 review of PFAS immunotoxicity, the National Toxicology Program concluded that two of the most studied members of the large class of PFAS chemicals, PFOA and PFOS, are "presumed to be an immune hazard to humans based on a high level of evidence from animal studies that PFOA and PFOS suppressed the antibody response and a moderate level of evidence from studies in humans. The evidence that these chemicals affect multiple aspects of the immune system supports the overall conclusion that both PFOA and PFOS have the potential to alter immune functions in humans."²⁶

Such findings raise concerns that similar effects from PFAS would be seen after COVID-19 vaccination, diminishing its effectiveness in some populations. As the former head of the National Institute of Environmental Health Sciences, Dr. Linda Birnbaum, stated in an interview in the Fall of 2020 about the impact of high PFAS exposure on COVID-19 vaccine effectiveness, "It's not that you won't get any response [from the vaccine], but that it could be decreased." Since antibody production is an important aspect of a healthy immune response, weakened antibody production could also have a direct

effect on a person's ability to ward off infection with the COVID-19 virus as well as their ability to recover quickly.

Historically, vaccines have been critical to protecting the public from communicable diseases,²⁸ and the COVID-19 vaccine is the latest example of their power. Research has shown the COVID-19 vaccine to be highly effective against preventing severe disease caused by the original virus as well as variants, with COVID-19 related hospitalizations and deaths among unvaccinated individuals being ten or more times higher than in fully vaccinated individuals.²⁹

At the same time, some vaccinated individuals are still ending up in the hospital or dying from COVID-19.30 The vaccinated people who are hospitalized with COVID-19 are often people with weakened immune systems.31 While we don't know whether there is a relationship between PFAS exposure and COVID-19 vaccine effectiveness, this is an area of active research.32 As the East Carolina University toxicologist Dr. Jamie DeWitt has noted, "I think that the risk is real, but we can't put definitive numbers on those risks right now."33 It is deeply concerning that pollutants like PFAS, which have such intense and lasting effects on our immune systems, have the potential to reduce the power of this important public health tool.

Experts emphasize the critical importance of vaccination regardless of any diminution in effect caused by toxic exposures. Dr. DeWitt has noted that even though some people have concentrations of PFAS that may be immunotoxic, people should still get vaccinated because vaccines give the immune system an additional tool to fight COVID-19 and other types of pathogens; it's like giving somebody who's fighting a battle a weapon.³⁴

In addition, people with high PFAS exposures should consider being extra cautious when it comes to COVID-19. As Philippe Grandjean, Harvard School of Public Health physician and PFAS researcher, noted in an interview: "My worry is that we vaccinate people with high PFAS exposures, and the vaccine is not protecting them, but they behave

differently... such as stop[ping] wearing masks and having more social interactions."³⁵ Until we better understand the relationship between PFAS and the vaccine effectiveness, additional care may be warranted. This is even more true given the spread of more transmissible variants of SARS Co-V2, the virus that causes COVID-19.

Can PFAS worsen the outcome of a COVID-19 infection?

This is a hard question to answer without conclusive data, but the answer is likely yes for several reasons. First, there is now one study from Denmark that has connected low levels of exposure to one type of PFAS to more severe disease, and at levels of PFAS exposure that are lower than they are in the US.³⁶ While more study is needed to confirm these results, this is a troubling finding.

Second, the CDC has stated that "people with weakened immune systems are at higher risk of getting severely sick" from COVID-19.³⁷ We know that people with high PFAS exposure often have weaker immune systems, which can make them less able to fight off viral infections and become more severely ill when they do get infected.

Third, some studies have also linked high PFAS exposure to autoimmune diseases such as ulcerative colitis and rheumatoid arthritis. The CDC has warned that people taking immune-suppressing medications for these kinds of autoimmune diseases are at increased risk for incidence and severity of COVID-19.

Fourth, while we are still waiting to see the results of ongoing studies looking at PFAS

exposure and COVID-19 mortality, it is becoming clear that some of the same diseases that are linked to PFAS are associated with higher death rates from COVID-19. For example, PFAS exposure is linked to liver damage, asthma, cancer, and certain kinds of cardiovascular conditions, according to a 2021 review of research conducted by the Agency for Toxic Substances and Disease Registry. A large study of more than 5,600 COVID-19 deaths in the United Kingdom found that people with liver disease, severe asthma, cancer, cardiovascular disease, as well as other health conditions were more likely to die of the infection. 43

The CDC has also acknowledged that these same diseases may increase the risk of severe illness from COVID-19.⁴⁴ While no research has evaluated these disease linkages, their similar patterns indicate that such studies are urgent. The concern is that people with high exposures to PFAS could be more likely to experience more serious infections or die of COVID-19 because they already are more likely to suffer from these aggravating conditions.

Fifth, PFAS can impact the fine tuning of the immune system, which can cause

hyper-sensitivities like asthma and food allergies, as well as increase risk of developing auto- immune diseases. ^{45,46} One type of immune overreaction experienced by many suffering from severe COVID-19 is a life-threatening systemic inflammatory syndrome called a "cytokine storm." ^{47,48,49}

While not very well understood, the tendency for PFAS to lead to immune system overreaction in some people and the fact that immune overreactions in COVID-19 patients can be deadly raises important questions. This is also an area where there have been no studies directly linking these health endpoints but is a key area for further study.

Concerns about the ability for PFAS exposure to worsen health outcomes for COVID-19 have also been raised by Dr. Philippe Grandjean who stated: "Given that PFAS are toxic to the immune system, exposure to these persistent chemicals may well worsen the consequences of a COVID-19 infection. Just like the studies which have shown that areas with more severe air pollution have more severe COVID-19 cases and greater mortality, we should also examine if the same applies to communities with PFAS-contaminated drinking water."50 Dr. Grandjean was the lead author on the study in Denmark that has suggested that there may be a link between PFAS exposure and more severe COVID-19 disease.51

PFAS immune system risks to the general population

People with high levels of PFAS chemicals in their bodies due to contaminated drinking water, their diet, or other intense exposures are more likely to experience immune system harm and other adverse health effects. Most human studies have focused on communities with elevated exposures, but the fact is that nearly all US residents have measurable amounts of PFAS in their bodies.52 While there are still many things that we don't know, several studies of the general population in the US or other places of presumably lower exposures suggest that PFAS-related immune system problems are not limited to those people who have been exposed to high levels of PFAS in drinking water or foods.

Two studies of large samples of US residents from the general population found lower

levels of rubella and mumps antibodies in people with higher concentrations of PFOS in their blood.53,54 Researchers who looked at PFAS levels in the blood of Norwegian mothers right after they had given birth and compared it to health outcomes in their children up to age three also found troubling results. The scientists found that "PFAS concentrations were associated with reduced antibody levels to the rubella vaccine and increased number of episodes of common cold and gastroenteritis, suggesting that prenatal exposure to various PFAS may lead to immunosuppression in early childhood."55 These two studies both point to PFAS-related immune system impacts in the general population.

Due to widespread contamination of food and water with PFAS and other persistent

organic pollutants, the concern is that many people in the US and worldwide could have weaker immune systems, including potentially a poorer response to COVID-19 vaccines. Notably, about one-quarter of the US population has blood levels that exceed a safety level for PFOS and PFOA set by the German government to ensure exposures are low enough to protect people from PFAS-related health problems including risks to fertility and pregnancy, immune system problems, and thyroid disruption.56,57 (It should be noted, of course, that the US is not subject to the German safety level and has only set health advisories for drinking water that are quite weak.58)

An independent assessment also suggests that many Americans have had exposure to levels of PFAS that may put them at risk, with Harvard University scientist Phillippe Grandjean finding that PFAS "immunotoxicity in humans and toxicity in animal models suggests that current limits for drinking water contamination are too permissive and must be decreased substantially," and that the "current limits appear to be several hundred fold too high." ⁵⁹ Grandjean's more recent study on the relationship between PFAS exposure and COVID-19 severity among the general public in Denmark also

suggests that current levels of exposure could be causing health impacts, especially given that background exposure levels are quite low in Denmark.⁶⁰

It is also important to recognize that science evolves and often what used to be considered safe is later realized to be unsafe. For example, the "safe" blood level of lead was 60 µg/dl in the 1960s, but this was lowered to 10 µg/dl in 1991 after there was mounting evidence of harm at lower levels.⁶¹ This trend has continued: today there is no level of lead that is considered safe and a blood lead level of 5 µg/ dl is considered elevated.62 Therefore, what is considered to be a "safe" level of PFAS in our bodies today may not be considered safe a decade from now when we have had more time to study the impacts of current exposures. In fact, we have already seen this trend take place with certain PFAS chemicals over the last ten or twenty years: state and federal drinking water guidelines for PFOA and PFOS have decreased significantly over this time period.⁶³

The bottom line is there is scientific evidence that the immune system impacts of PFAS do extend to the general population and could make some people more vulnerable to COVID-19 and other infectious diseases.

COVID-19, toxic chemicals, chronic disease, and racial justice

PFAS aren't the only chemicals that have been shown to interfere with antibody responses to vaccines, correlate with higher rates of infectious diseases, or adversely affect the immune system in other ways. Such impacts have been detected in people with higher levels of exposure to heavy metals like mercury, arsenic and lead, and other persistent organic pollutants including PCBs, DDT, dioxins, and organochlorine pesticides. 64,65,66,67,68

Many of these same toxic chemicals affect people of color and low-income communities disproportionately. For example, a study of more than 30,000 women from the CDC's National Health and Nutrition Examination Survey cohort found significant racial disparities in exposure to heavy metals and pesticides.⁶⁹ Black communities tend to have poorer air quality and Black children are much more likely to have severe lead poisoning.^{70,71} A study by NRDC, Coming Clean, and the Environmental Justice Health Alliance for Chemical Policy Reform found that the rate of drinking water violations was higher in communities of color, low-income communities, and areas with higher numbers of non-English speakers.72 This analysis also showed that drinking water systems that had repeated violations year after year were 40 percent more common in places with higher percentages of residents who were people of color.

These findings, of course, are just the tip of the iceberg and mean that communities of color and low-income communities are often experiencing higher exposures to many different chemicals that can impact their immune systems and their health. Like other pollution hotspots, people in PFAS-impacted communities live in "fenceline communities" where some people bear the brunt of industrial pollution, facing many of the consequences and none of the benefits.

While many factors affect the spread of the COVID-19 virus, the data clearly show dramatically higher, disproportionate impacts to Black, Latinx, and Indigenous communities in the US.⁷³ Members of racial and ethnic minority groups are more likely to experience severe illness, be hospitalized, or die from COVID-19.⁷⁴ This is likely the cumulative toll of many factors, but many scientists are now pointing to the increased burden of exposure to pollution (particularly air pollution) experienced by communities of color as being

one important underlying reason for this pattern. 75,76,77

Native populations living in Arctic regions are at particular risk for cumulative effects given that persistent contaminants are concentrated in northern latitudes and accumulate in higher levels in the fat of seafood and marine mammals. The rate of infectious disease among Inuit children is guite high and there have been three studies showing that infants with higher exposures to organochlorine compounds are more likely to experience acute respiratory, ear, and gastrointestinal infections. 78,79,80 Since it is now known that exposure to PFAS chemicals are also elevated in the Arctic, one question worth noting is whether they could be causing additive or synergistic effects on the immune system as this was not examined in earlier studies looking at organochlorine exposure. There is much reason for concern given that one recent study found that exposure to both PCBs and PFAS increased the chances of children not being protected by the diphtheria vaccine due to lowered antibody levels.81

These findings underscore the need to look beyond just PFAS and prevent the continued use of toxic chemicals more generally. This is critical to protect the health of our communities, and the health of our immune systems. It is also a reminder that when it comes to persistent pollutants, highly impacted populations can extend to the furthest reaches of the globe and include indigenous communities.

Endnotes

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