Poly/Perfluorinated alkyl substances (PFAS) post-test counselling

Clinician advice

Principles of PFAS testing

Post-test counselling allows a joint decision-making approach between the FRV member and a clinician, providing opportunity to dispel myths and promote management options, aiming to reduce the risk of those health conditions that have been associated with elevated serum PFAS.

What is normal?

Total PFAS is an aggregate of a number PFAS substances tested by EnviroLab, specifically FRV uses the sum of PFOA, PFOS, PFHxS, and PFNA levels, which reflect those substances found in both the MFB Blood Donation study and the ANU PFAS study to reflect Legacy PFAS exposure. Total PFAS is preferred as there may be some effects of PFAS on health, suggesting that aggregates of the most common substances better reflecting current research. A total PFAS level of 10ng/mL has been selected by FRV, reflecting the mean value amongst the Australian population and is similar to other information overseas.

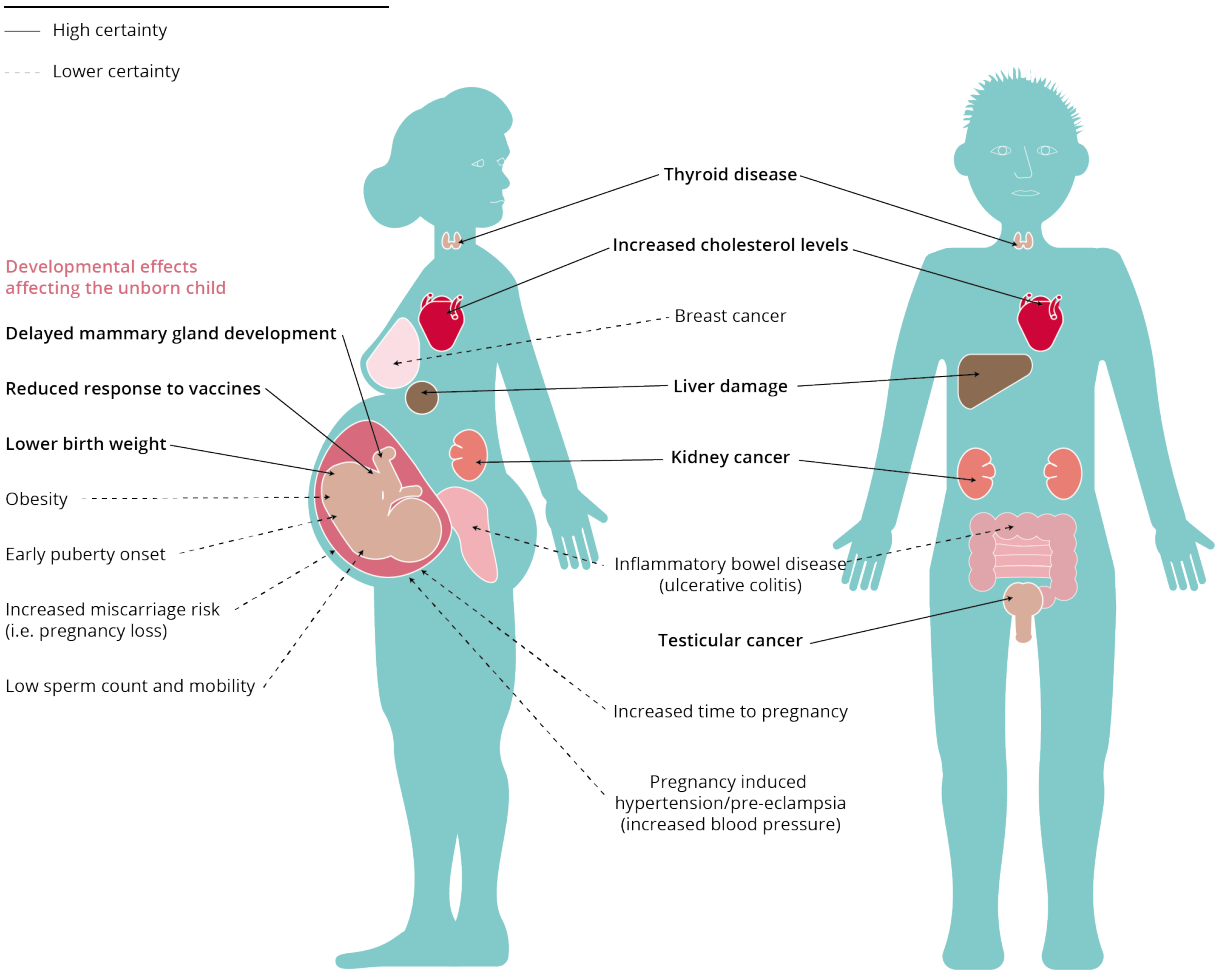
Total organofluorine testing is not undertaken as the components of occupational PFAS exposure has been established through the Macquarie blood donation study..

Health effects of elevated PFAS

Both local and international research has identified a wide range of health effects that are associated with elevated serum PFAS levels. A few of these health effects have been well established and found repeatedly in research studies showing robust evidence that the relationship cannot be questioned. For many more conditions, the evidence of association is less clear, with ongoing research increasing our knowledge, confirming some theories, and excluding others. For many health effects, we know little about why PFAS influences health, but observe a correlation, best summed up by the US National Academies of Sciences;

> *"This does not mean that health effects will occur, but likely relates to increased risk.*[i]*"*

The image below from the European Environment Agency shows our current knowledge, with dashed lines indicating effects that are less certain.



Health impacts of PFAS - European Environment Agency (eea.europa.eu)

Exposure tiers

A tiered approach to PFAS testing has been adopted using the Aggregate PFAS level[i] to stratify the risk of PFAS related disease. While no disease can ever be excluded with 100% certainty, the purpose of the tiered approach is to balance health risk, while considering avoiding excessive unnecessary tests, aiming for testing to be meaningful and used as a foundation for planning any additional needs.

The tiered approach is outlined in table 1 and shows recommended additional investigations, interventions and retest intervals.

Clinical management recommendations

Total PFAS level	Investigations	Interventions	Re-test interval
Tier 1 (0-10ng/mL)	Nil additional	Surveillance for sources of ongoing exposure	5 years service or greater - 8 years). Less than 5 years service - 5 years
Tier 2 (10.1-20ng/mL)	Health monitoring including cholesterols, blood pressure, cardiovascular risk factors (Framingham risk calculator) Cancer screening - Breast - Testicular (including self examination education)	Exposure reduction Consider voluntary plasma or blood donations Associated interventions for PFAS related disease - blood pressure management, - cholesterol management, - diabetes assessment Reduction of other cardiovascular risk factors (e.g. smoking cessation)	5 yearly, ongoing health monitoring including PFAS related disease monitoring biannually
Tier 3 (>20ng/mL)	Health monitoring including level 2 **and** - Thyroid function - Kidney cancer screen (screening questions +/- urinary cell analysis) - IBD screen ?UC – consider referral for colonoscopy	Including tier 2 **and** Consider deployment to safe work location) Specialist review for customised approach for management of disease risk and consideration of PFAS reduction measures as appropriate.	3 years to establish trend of interventions (if applicable) Then 5 yearly if interventions are effective Ongoing health monitoring or GP review yearly as indicated
Tier 4 (special considerations) PFOS >40ng/mL	Intervention or screening based on circumstance. HCC (OR4.5 at PFOS>55ng/mL)	As tier 3 .	As tier 3

Specific management

Liver enzyme derangement – strong evidence shows derangement of liver function tests, GGT, ALT and AST, as well as hepatic steatosis associated with PFAS exposure. Specific management for hepatic effects appear to be limited, however optimisation of serum cholesterol, and other factors in the traditional approach to steatosis should occur, particularly weight loss but including monitoring for associated co-morbidities (e.g. T2DM, HTN, Hypercholesterolaemia) and consider priority screening for HCC if PFOS>40ng/mL

Hypercholesterolaemia – Well established health effect of PFAS exposure, elevated cholesterol has been demonstrated to be effectively managed with standard cholesterol treatments (diet, exercise and statins), No particular statin has been identified in the literature as being more effective than others in the management of PFAS related hypercholesterolaemia.

The mechanisms of hypercholesterolaemia appear to be multifactorial, with rapid acceleration of serum cholesterols at PFAS levels up to 50ng/mL[i] do suggest that PFAS lowering interventions may provide a useful adjunct to usual lipid management

Hypertension – follow established hypertension management guidelines (e.g. Heart Foundation Hypertension Guidelines)

Cardiovascular disease – PFAS related CVD mechanisms may be a combination of cellular inflammatory responses as well as exaggerated cholesterol[i] and hypertension influences. Specific CVD or PVD screening (e.g. Chest pain on exertion, dyspnoea, claudication) and physical examination for congestive features (elevated JVP, oedema) should occur. Any concerning features should be referred as appropriate (e.g. cardiac stress testing and/or cardiology review). Counselling around cardiac risk factors and risk mitigation (e,g, smoking cessation), treatment of cholesterol and hypertension in accordance with established guidelines.

Reproductive health

Interpretation of elevated PFAS levels in pregnancy is difficult. Increased blood volume throughout pregnancy dilutes total body PFAS, while previous pregnancy is shown to significantly reduce PFAS levels through maternal blood loss and placental transfer. It is recommended that women who are already pregnant, discuss concerns with their treating obstetrician or midwife.

A number of reproductive concerns associated with elevated PFAS exposure in women continue to be the focus of research, including;

- Fertility effects

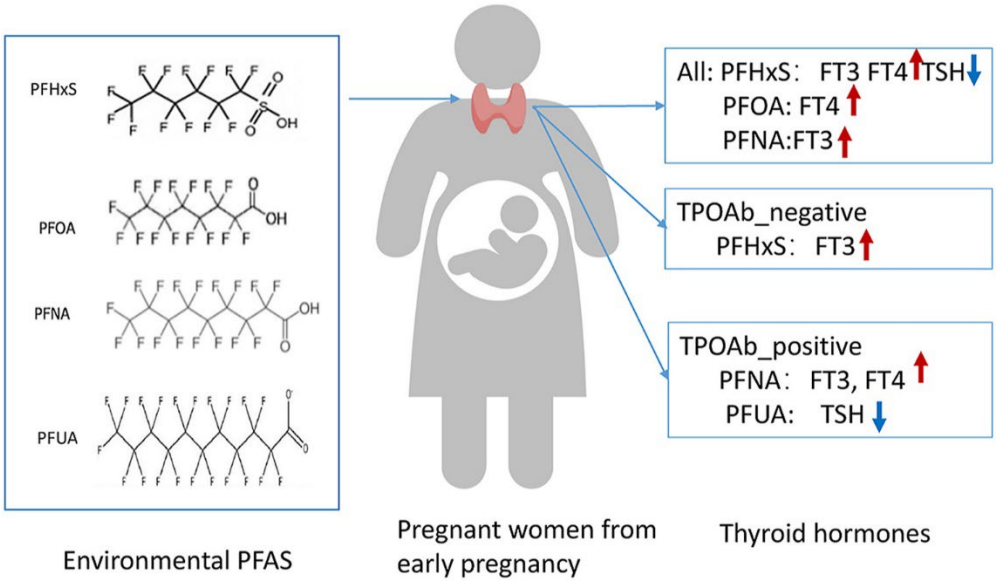
- Increased rate of miscarriage
- Gestational hypertension, late onset pre-eclampsia[i]
- Post-partum heamorrhage[i]
- Slight decreases in birth weight
- Mild developmental delay in some aspects of development
- Decreased response to vaccines in offspring
- Increased risk of obesity and type 2 diabetes in offspring

While some association appear to exist; direct links to PFAS are not understood, the strengths of these linkages appear to be limited, or where evidence has shown convincing relationships between PFAS exposure and adverse reproductive outcomes, results have not been able to be replicated in other studies, making the real effect difficult to apply to the broader community.

Breastfeeding

Addressing nursing mothers' concerns about PFAS in breast milk is complicated. While some PFAS exposure limits exist, the practicality of testing breastmilk, while avoiding reactionary responses during the challenges of the early post-partum period require careful, customised advice and should be referred to the members own obstetrician or midwife. Considering the important effects of breastfeeding on developmental and immunological support, early breastfeeding is encouraged. While the benefits of long-term breastfeeding of babies by mothers with known high PFAS levels is less clear, particularly in the context of decreased immune response to some vaccinations.

Thyroid – Multiple studies have shown elevated PFAS reduces serum Free T4 index levels in both mothers and male children[i]. Female children appear to be less affected. Different PFAS appear to have effects, while the situation become significantly more complicated with autoimmune thyroid antibodies (TPOAb) influencing impact[i].



PFAS influences on thyroid function in early pregnancy (Aimuzi etal, 2020)
Pregnancy associated hypertension and pre-eclampsia – PFAS related Pre-eclampsia appears to be specific to late pregnancy[i] and independent of the traditional pre-eclampsia biomarkers (tyrosine kinase-1 (sFLT-1) and placental growth factor (PlGF)). Handover of elevated risk due to PFAS exposure in FRV staff who are pregnant or considering becoming pregnant, is important.
Due to risk of anaemia and dilution of PFAS due to increased blood volume, lowering PFAS through blood or plasma donation is not recommended during pregnancy unless guided by the woman's usual treating obstetrician.

Surveillance

FRV are committed to the reduction of ongoing PFAS exposure. The rapidly increasing knowledge of PFAS exposure sources and health effects are increasing our knowledge daily. It is important that we continue to remain diligent in maintaining activities that reduce ongoing exposures within the environment we work and live in to maintain blood PFAS levels below levels of concerns as we currently understand them.

Exposure reduction

Ongoing exposure to PFAS is a concern for the organisation. Significant efforts have already been made to limit ongoing exposure, initially by ceasing the use of fluorinated foams, then the subsequent decontamination of appliances, through to the current and ongoing rehabilitation of PFAS contaminated fire stations.
Operational stations remain a potential risk for ongoing exposure to legacy PFAS, while other locations such as corporate sites are less likely to be sites of concern. For those of us with elevated PFAS levels, it is imperative that we limit any ongoing exposure, in conjunction with other measures to reduce blood PFAS levels.
Once blood PFAS levels reach 20ng/mL active steps to reduce ongoing PFAS exposure must be considered, such measures can include;

- Transfer to a location that has undergone PFAS remediation or has known low PFAS levels within the workplace. This may be another station or other work location.

- Consider other environmental exposures (e.g. contaminated groundwater or soils in the local area), both in the work and home environments

PFAS lowering interventions

Interventions to reduce serum PFAS levels are limited to blood and plasma donation as reflected in the MFB blood donation study, and no formal protocol outside voluntary donations with the blood bank have been established at this stage. While we know that lower PFAS levels can result in small changes in risk of health effects, research is yet to prove that removal of PFAS can reverse established health risks.

At this stage there is no restriction on donors with elevated serum PFAS providing blood or plasma donations to the blood bank, however any donation should occur in a way that does not impact on fitness for duty, in accordance with established policy. Some evidence exists that a medication (cholestyramine) increases PFAS excretion by reducing enterohepatic recycling, resulting in lower serum PFAS. At this stage, no clinical trials have been undertaken to demonstrate an appropriate regime of treatment and if considered as a treatment, would “off label” use and should be closely monitored by the prescribing practitioner.

Cancer screening

Research is showing increased evidence of cancer correlating with elevated PFAS levels. Cancer development is a complex interaction of exposures as well as a multitude of processes within the body. Some of these processes may be affected by PFAS, other exposures within firefighting and everyday life. While there is some correlation between elevated PFAS levels and cancer occurrence, the mechanisms that different cancers occur is not straight forward. Elevated PFAS levels are no substitute for an appropriate cancer screening program which is accessible through FRV Health. For individuals with elevated PFAS levels where evidence exists for association with cancers, then priority screening for those cancers will occur.

Clinical handover

Any concerning findings discussed in the post test counselling appointment should be forwarded to the staff members General Practitioner. If a staff member is unwilling to have information forwarded, this should be recorded in the patient file.

Further information

If you have any questions about PFAS testing or the FRV Health Monitoring program, feel free to discuss with FRV Medical Services (medicalservices@frv.vic.gov.au).