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EDITORIAL

An Impending European Ban on Per- and Polyfluoroalkyl Substances in Vascular Surgery: Little Environmental Benefit With Major Patient Harm?

The addition of endo to vascular has revolutionised the practice of vascular surgery and treatment of vascular disease on a minimally invasive basis. Integral to this are the requisite devices needed for endovascular procedures, from sheaths, catheters, and low friction wires to those used for procedures such as aneurysm repairs, angioplasties, or embolisation. These are necessarily synthetic, with a significant subgroup made from expanded polytetrafluoroethylene (ePTFE), which now has widespread commercial, industrial, domestic, and vascular applications since its accidental discovery in 1938, along with two other compounds, fluorinated ethylene propylene (FEP) and perfluoroalkoxy alkane (PFA). These are members of a class of chemical compounds denoted per- and polyfluoroalkyl substances (PFAS or PFASs), which have been recently highlighted as a matter of environmental concern. This editorial expounds the risks related to PFAS use in (endo) vascular surgery, as the vascular community at large needs to be aware of the significant implications around this issue.

Historically, ePTFE based membranes were used to develop experimental venous grafts in porcine models in 1972; these were improved and have been in widespread use in open vascular surgery as tube grafts and patches. More recently these were adapted to the endovascular era, particularly in the manufacture of endografts including for endovascular aneurysm repair, e.g., the Excluder AAA Endoprosthesis (WL Gore & Associates, Flagstaff, AZ, USA) and Ovation Alto and AFX systems (Endologix, Irvine, CA, USA), and also some off label venous indications.[1] Smaller stent grafts are available for peripheral use, as exemplified by the heparin bonded VBX/Viabahn Endoprostheses (Gore), Atrium Advanta (Getinge AB, Gothenburg, Sweden), and BeGraft (Bentley InnoMed GmbH, Hechingen, Germany) devices, used for peripheral arterial occlusive or aneurysmal disease and also salvage of arteriovenous fistulae for dialysis;[2] these are also used as branches during the repair of complex thoraco-abdomino-iliac aneurysmal disease. The MVP microvascular plug (Medtronic, Minnesota, MN, USA) for peripheral embolisation also employs PTFE. Such devices are thus employed in critical limb and lifesaving applications, and production of medical devices containing PFAS, more specifically ePTFE, is highly regulated (particularly as it is the precursor monomeric versions that have the potential to cause environmental effects) and their effects investigated.[3]

The use of ePTFE goes beyond vascular surgery and also encompasses applications in many other medical fields[4] such as orthopaedic (device coatings) and general surgery (meshes), urology (catheter coatings), reconstructive surgery (facial prostheses), and interventional cardiology,[5] to name a few, and even generic use such as surgical drapes and gowns.

PFAS include a heterogeneous group of $>$ 10 000 organofluorine compounds in global use existing in solid, liquid, and gaseous forms, with as yet no formal subclassification[6] that would guide understanding of manufacture, use, effects, and regulation.[3] Like many inventions, these were seen as beneficial in their multiple applications from fabric with inherent waterproof properties, as is well known, to paints and coatings. Two forms, perfluorooctanoic acid (PFOA) and perfluorooctane sulfonate (PFOS), were found to be widespread in ecosystems, triggering multinational efforts around regulation and management.[3] Dubbed forever chemicals, with over 4 000 PFAS in commercial use, molecular accumulation in humans raised concerns on environmental and health grounds. Thus, the perceived advantage of durability can be simplistically viewed as a disadvantage – although critically the vast majority of PFAS do not enter vascular or endovascular use.

The European Environment Agency issued an infographic (Effects of PFAS on human health ; https://www.eea.europa.eu/signals-archived/signals-2020/infographics/effects-of-pfas-on-human-health/view) detailing the toxic effects of PFAS but not providing directly accessible source details. There are worrying implications from the recent EU REACH (Registration, Evaluation, Authorisation and Restriction of Chemicals) PFAS restriction proposal, following on from a proposal prepared by bodies from Denmark, Germany, the Netherlands, Norway, and Sweden and published by the European Chemicals Agency (ECHA) on 7 February 2023 (https://echa.europa.eu/-/echa-publishes-pfas-restriction-proposal). This intends to ban the manufacture and sale of products containing PFAS (including PTFE and FEP) in the EU market either 18 months after entry into force (estimated 2026) or after a use specific, time limited derogation period (up to 13.5 years for medical devices) – the European Commission is yet to finalise the scope and provisions of the final restrictions. Currently there is no substitute matching the desirable PFAS characteristics that have brought them (particularly) into endovascular applications, and the restrictions do not consider that all PFAS are not the same or the impact this would have on life and limb saving procedures available to patients and physicians. The essential use concept by the EU Commission[7] itself needs to be applied.

The questions that arise from a vascular standpoint are around the above context. While a PTFE based implant

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remains within a patient it seems clear that it is non-toxic both to host and environment. Parallels therefore cannot be drawn against PFAS intake via ingestion or occupational exposure.[8] There is no focused research on the environmental effects of PFAS once the host has died and has then been either buried or cremated. Recent studies seem to indicate that controlled civic PFAS incineration does not generate toxic post-combustion levels.[9] Strategic use of landfill components themselves may stabilise or reduce PFAS leaching.[10]

Do medical PFAS create levels that are environmentally significant? Given the published hazard quotient for generic PFAS is < 1,[8] the same for medical PFAS would be conceivably low. Correspondingly, there has been no drive to assess PFAS levels in patients who have received relevant implants; also, the amount of ePTFE used in medical devices is significantly lower than what is used in consumer and industrial applications, and does not systemically enter hosts compared with occupational exposure of firemen to foams, for example.[8] Global human serum concentrations of legacy PFAS are seemingly decreasing,[11] suggesting that regulation is working. Such issues have therefore created a need for realistically looking at the concerns leading to subdivision of risk, namely the designation of polymers of low concern,[3,12] emphasising that the term PFAS alone does not indicate whether there is associated risk, and also that most PFAS in commercial use meet the criteria for low risk,[12] conforming to the 13 requisite Organisation for Economic Co-Operation and Development (OECD) criteria.[3] This implies that all PFAS should not be bundled together for regulatory purposes.

What would happen if we suddenly removed ePTFE containing devices from (endo)vascular applications? Relevant procedures using these devices would simply cease, become difficult to undertake, or need alternative approaches. Proven alternatives will probably take decades to develop. Vascular societies will need to collaborate with policy makers and industry on taking a more nuanced and scientific approach to avoid the serious potential outcomes described. Whilst sustainability and minimising environmental contamination is of great importance and must also influence our use of PFAS containing vascular devices, this should be based on scientific rationale, with consideration given to the need to find alternatives within a reasonable timescale.

CONFLICTS OF INTEREST STATEMENT AND FUNDING

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