专栏：新污染物发育毒性
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氯化多氟烷基醚磺酸母婴暴露水平及对其健康的影响

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摘要：

氯代多氟烷基醚磺酸（Cl-PFESA，商品名 F-53B）是全氟辛烷磺酸（PFOS）的替代品，主要成分为 6:2 Cl-PFESA 和 8:2 Cl-PFESA，是目前已知的最具生物持久性的全氟及多氟烷基物质（PFASs）。自 1975 年中国首次合成并将其用作电镀工业的抑雾剂，F-53B 已经被使用了 40 多年。近几年随着对该物质的深入研究，许多基质和人体样本中均已检测到 F-53B 的存在，且在中国已成为流行病学研究中母体和脐带血清中浓度排名前三的 PFAS。目前，有限的流行病学研究提示了 F-53B 对母婴健康具有多种不良的影响。因此，本文对 F-53B 的母婴暴露水平以及其对健康的不良影响进行综述，旨在为评估 F-53B 母婴毒性效应和确定安全限值提供一定的参考。

关键词：全氟及多氟烷基物质；氯化多氟烷基醚磺酸；6:2 氯代全氟醚磺酸盐；8:2 氯代全氟醚磺酸盐；母婴健康

Levels and health effects of maternal and infant exposure to chlorinated polyfluorinated ether sulfonic acid

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Abstract:

Chlorinated polyfluoroalkyl ether sulfonic acid (Cl-PFESA, trade name F-53B), a substitute for perfluorooctane sulfonate (PFOS), notably featuring 6:2 Cl-PFESA and 8:2 Cl-PFESA as its primary components, are the most biologically persistent per-and polyfluoroalkyl substances (PFAS) currently known. Since its initial synthesis in China in 1975, F-53B has served as an antifogging agent in the electroplating industry for over four decades. Recently, F-53B has been detected across various matrix and human samples, ranking among the top three PFAS concentrations in maternal and umbilical cord blood sera in China, according to available epidemiological studies. Current limited epidemiological studies indicate that F-53B poses multiple adverse effects on maternal and infant health. Therefore, this article reviewed the exposure levels of F-53B in mothers and infants, along with its adverse health effects, thereby providing insights for evaluating the toxic effects of F-53B on maternal and infant health and establishing safety thresholds.

Keywords: per- and polyfluoroalkyl substances; chlorinated polyfluorinated ether sulfonic acid; 6:2 chlorinated polyfluorinated ether sulfonic acid; 8:2 chlorinated polyfluorinated ether sulfonic acid; maternal and infant health

全氟及多氟烷基物质（per- and polyfluoroalkyl substances, PFASs）是一类人造化学品，全氟辛酸（perfluorooctanoic acid, PFOA）和全氟辛烷磺酰基化合物（perfluorooctane sulfonate, PFOS）为其中暴露最为广泛的两类化合物。由于其化学结构稳定且具有独特的疏水、疏油性，因此被广泛应用于工业和消费品中，如不粘锅涂层、防油纸、消防泡沫等[1]。PFASs 在环境中具有高度持久性，目前在许多物质中均已检测到其存在，包括水、土壤、植物、动物、食品、人血清和母乳等生物样本[2–3]。人群流行病学研究表明，妊娠期暴露于 PFASs 可增加不良妊娠结局的风险，并影响子代的生长发育[3]。随着 PFASs 的生产和应用得到

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控制，新的替代品不断出现。

氯化多氟烷基醚磺酸（chlorinated polyfluorinated ether sulfonic acid, Cl-PFESA），商品名为 F-53B，是 PFOS 的常见替代品，具有与 PFOS 分子类似的-CF2-基团，但增加了醚键和一个氯原子，其主要成分为 6:2 Cl-PFESA 和 8:2 Cl-PFESA[4]。1975 年，中国首次合成了 F-53B，并将其用作电镀工业的抑雾剂，其在中国市场得以被广泛应用[5]。虽然 F-53B 已经被使用了 40 多年，但关于其对环境和人群潜在影响的研究仍相对较新。近几年来，人们在中国的饮用水、地表水、电镀废水、污泥和大气中检测到其浓度与 PFOS 相当或更高[6]，且在美国、德国、英国、荷兰和韩国的河流和湖泊中也普遍检测到了 F-53B[7]。根据 Globo-POP 模型推算，尽管 F-53B 远距离迁移潜力较低，但仍有少部分可以通过海洋平流到达北极[4]，因此 F-53B 对全球环境有可能造成威胁。F-53B 和 PFOS 的中位消除半衰期分别为 15.3 年和 6.7 年，作为替代品，F-53B 的生物累积性可能比 PFOS 更高。目前人群研究结果发现，过去十年中 6:2 Cl-PFESA 在人体中的检出频率增加，比例升高，已成为中国母体和脐带血清中第三大流行的 PFAS[8–10]，而且 F-53B 显示出较高的蛋白结合亲和力和人胎盘渗透性[7]，另外，根据中国第三次全国母乳调查的结果，6:2 Cl-PFESA 已成为中国母乳中主要的 PFAS 之一[1]。由此可见，F-53B 不仅能够导致母体的不良健康效应，还会进一步对子代的生长发育造成负面影响[11]。

孕妇和婴儿由于其特殊的生理状态，常常是环境污染物的易感人群，为了进一步探究和总结 F-53B 的母婴暴露水平及其对健康的影响，本研究在 PubMed 中检索了包含关键词“6:2 Cl-PFESA”“8:2 Cl-PFESA”“Cl-PFESA”或“F-53B”的论文，并进一步筛选了与母婴暴露水平及健康相关的文章纳入分析。

1 F-53B 母婴暴露水平

表 1 分别描述了 6:2 Cl-PFESA 和 8:2 Cl-PFESA 的检测水平。由于 F-53B 是中国所特有的环境污染物，绝大部分相关研究都在中国开展，仅有两项在中国以外的研究测量了 F-53B 的暴露水平，但浓度均低于检出限（limit of detection, LOD）[12–13]。

表 1 不同母婴生物样本中 F-53B 水平

Table 1 Levels of F-53B in various maternal and infant biological samples

地区(Area)	年份(Year)	样本(Samples)	样本量 (Sample size)	中位浓度(Median concentration)/(ng·mL^{-1})		参考文献(Reference)
				6:2 Cl-PFESA	8:2 Cl-PFESA	
血清(Serum)						
中国广州(Guangzhou, China)	—	儿童血清(Children's serum)	314	1.1	0.02	Liang L, et al.,2023[14]
中国上海(Shanghai, China)	2017—2019	母体血清(Maternal serum)	336	6.41	0.07	Mao D, et al.,2024[15]
中国杭州(Hangzhou, China)	2020—2021	母体血清(Maternal serum)	251	2.81	—	Tian Y, et al., 2023[16]
中国广州(Guangzhou, China)	2021	母体血清(Maternal serum)	302	1.53	0.04	Di J, et al.,2023[17]
中国北京(Beijing, China)	2017	母体血清(Maternal serum)	286	4.35	0.06	Hu Y, et al.,2023[18]
中国浙江(Zhejiang, China)	2020—2021	母体血清(Maternal serum)	340	3.64	0.18	Xu C, et al.,2022[19]
中国北京、山东(Beijing and Shandong, China)	2021	母体血清(Maternal serum)	124	2.37	<LOD	Hong A, et al.,2022[20]
中国四川(Sichuan, China)	2018	母体血清(Maternal serum)	60	0.8	—	Zheng P, et al.,2022[21]
中国广东(Guangdong, China)	2016	母体血清(Maternal serum)	94	1.78	0.02	Zhang B, et al.,2022[22]
中国天津(Tianjin, China)	2010—2012	母体血清(Maternal serum)	480	5.48	0.15	Liu J, et al.,2021[23]
中国广州(Guangzhou, China)	2013	母体血清(Maternal serum)	372	2.41	<LOD	Chu C, et al.,2020[24]
中国茂名(Maoming, China)	2015—2018	母体血清(Maternal serum)	424	0.8	0.01	Cai D, et al.,2020[25]
中国武汉(Wuhan, China)	2015—2016	母体血清(Maternal serum)	32	1.54	0.01	Chen F, et al.,2017[26]
脐带血清(Cord serum)						
中国北京(Beijing, China)	2020—2021	脐带血清(Cord serum)	109	0.57	0.03	Li X, et al.,2023[27]
中国(China)	2020—2021	脐带血清(Cord serum)	80	0.59	0.02	Yao J, et al.,2023[28]
中国武汉(Wuhan, China)	2013—2016	脐带血清(Cord serum)	324	0.95	—	Huang S, et al.,2023[29]
中国武汉(Wuhan, China)	2014—2015	脐带血清(Cord serum)	527	0.79	0.03	Huang H, et al.,2023[30]
中国武汉(Wuhan, China)	2014—2015	脐带血清(Cord serum)	908	0.76	0.03	Li X, et al.,2023[27]
中国武汉(Wuhan, China)	2013—2014	脐带血清(Cord serum)	1 015	0.76	0.03	Cao Z, et al.,2023[31]
中国广州(Guangzhou, China)	2021	脐带血清(Cord serum)	302	0.59	0.03	Di J, et al.,2023[17]

续表 1

地区(Area)	年份(Year)	样本(Samples)	样本量(Sample size)	中位浓度(Median concentration)/(ng·mL^{-1})		参考文献(Reference)
				6:2 Cl-PFESA	8:2 Cl-PFESA	
中国四川(Sichuan, China)	2018	脐带血清(Cord serum)	60	0.42	—	Zheng P, et al.,2022[21]
中国广东(Guangdong, China)	2016	脐带血清(Cord serum)	94	0.73	0.02	Zhang B, et al.,2022[22]
中国山东(Shandong, China)	2017—2021	脐带血清(Cord serum)	326	0.27	<LOD	Xia X, et al.,2022[32]
中国武汉(Wuhan, China)	2013—2014	脐带血清(Cord serum)	942	0.7	—	Liu H, et al.,2021[33]
中国茂名(Maoming, China)	2015—2018	脐带血清(Cord serum)	424	0.38	0.02	Cai D, et al.,2020[25]
中国杭州(Hangzhou, China)	2016—2017	脐带血清(Cord serum)	110	0.73	0.02	Xu C, et al.,2019[34]
中国武汉(Wuhan, China)	2013—2014	脐带血清(Cord serum)	374	0.78	0.03	Liu H, et al.,2020[35]
中国武汉(Wuhan, China)	2015—2016	脐带血清(Cord serum)	32	0.6	0.01	Chen F, et al.,2017[26]
母乳(Breast milk)						
中国(China)	2020—2021	母乳(Breast milk)	1 151	2.63	13.59	Yao J, et al.,2023[28]
中国(China)	2017—2020	母乳(Breast milk)	3 531	0.025	—	Han F, et al.,2023[36]
中国四川(Sichuan, China)	2018	母乳(Breast milk)	60	0.01	—	Zheng P, et al.,2022[21]
中国杭州(Hangzhou, China)	2018—2019	母乳(Breast milk)	174	0.02	<LOD	Jin H, et al.,2020[37]
尿样(Urine)						
中国(China)	2020—2021	新生儿尿样(Neonatal urine)	80	<LOD	—	Yao J, et al.,2023[28]
卵泡液(Follicular fluid)						
中国北京、山东(Beijing and Shandong, China)	2021	卵泡液(Follicular fluid)	124	2.19	<LOD	Hong A, et al.,2022[20]
中国北京(Beijing, China)	2018—2019	卵泡液(Follicular fluid)	28	1.09	0.02	Kang Q, et al.,2020[38]
胎盘(Placenta)*						
中国广州(Guangzhou, China)	2021	胎盘(Placenta)	302	0.42	0.05	Di J, et al.,2023[17]
中国河南(Henan, China)	2016	胎盘(Placenta)	54	0.076	<LOD	Lu Y, et al.,2021[39]
中国山西(Shanxi, China	2009—2013	胎盘(Placenta)	519	0.34	—	Liu X, et al.,2020[40]
中国武汉(Wuhan, China)	2015—2016	胎盘(Placenta)	32	0.34	<LOD	Chen F, et al.,2017[26]

[注] *表示该样本类型中 6:2 Cl-PFESA、8:2 Cl-PFESA 的浓度单位为 ng·g^{-1}。

[Note] *: The concentration unit for 6:2 Cl-PFESA or 8:2 Cl-PFESA in the samples is ng·g^{-1}.

如表 1 所示，F-53B 在易感人群——孕妇和婴儿的各类生物样本中被广泛检出，在母体血清、脐带血清、胎盘、母乳、新生儿尿液、卵泡液等生物样本中，最常用于内暴露测量的是血清（包括母体血清和脐带血清），其中母体血清的 6:2 Cl-PFESA 中位浓度水平最高，且不同研究之间差异较明显；与 6:2 Cl-PFESA 相比，8:2 Cl-PFESA 的浓度很低，但不同研究的各类生物样本中，其中位浓度普遍相当。

进一步比较 6:2 Cl-PFESA 的浓度在不同时间点和地区是否有较大区别。同一地区，在不同时间点测量的同类型生物样本中未观察到 F-53B 暴露水平有明显的时间趋势，如 2013—2016 年中国武汉地区共有 5 项研究测量了脐带血清 6:2 Cl-PFESA 浓度，结果显示均在 0.6~0.9 ng·mL^{-1} 之间，并无明显差异[27, 29–31, 33, 35]。然而，6:2 Cl-PFESA 的暴露水平在不同地区之间差异较大，其中上海的母体血清 6:2 Cl-PFESA 暴露水平最高[15]，其次是天津、北京、浙江[18–19, 23]。F-53B 地区间暴露水平差异较大可能受多种因素影响，例如摄入较多海鲜的饮食习惯可能是上海和浙江地区母婴人群高暴露水平的促成因素[41]。另外，许多氟化学品生产设施和电镀厂都在天津等城市，也可能造成该地区人群的 F-53B 高暴露[7]。

2 F-53B 暴露对母婴健康的影响

表 2 总结了 F-53B 暴露可能对母婴健康造成的不良影响，目前的研究表明，孕妇和婴儿的 F-53B 暴露可能会引起一系列的妊娠并发症、导致不良妊娠结局并影响子代的出生结局和生长发育等。

2.1 糖脂代谢与妊娠并发症

研究表明，F-53B 会干扰孕妇的糖代谢和脂代谢过程，从而对母体的健康状况造成不良影响[15, 19, 42]。一项在上海开展的针对辅助生殖人群的队列研究发现母体血清的 6:2 Cl-PFESA 水平与妊娠糖尿病患病风险和 2 小时血糖水平显著相关[15]。两项浙江的病例对

照研究也显示出类似的结果，即 6:2 Cl-PFESA 的暴露与血糖水平、妊娠糖尿病风险呈正相关[19, 42]。另外一项北京的队列研究关注了妊娠期妇女的 PFAS 暴露水平与血脂的关系，结果显示 6:2 Cl-PFESA 在妊娠早期与孕妇血清总胆固醇、高密度脂蛋白胆固醇升高呈边缘显著相关，可能对脂代谢造成影响，表明妊娠早期是 F-53B 暴露对母体脂质代谢产生影响的关键脆弱窗口[18]。

F-53B 除了会影响孕妇的血糖水平和脂代谢外，还可能与先兆子痫的几率增加有关[16]。一项浙江杭州的病例对照研究发现血清 6:2 Cl-PFESA 与先兆子痫风险呈正相关（OR=1.02，95%CI: 1.00~1.48，*P*=0.045），而 PFOS 与先兆子痫的相关性并不显著（OR=1.01，95%CI: 0.941~1.09，*P*=0.723），且分层分析表明，6:2 Cl-PFESA 暴露与产下女胎的妇女的先兆子痫风险有更强的正相关（OR=1.06，95%CI: 1.02~1.46，*P*=0.017）[16]，这可能与 6:2 Cl-PFESA 在人胎盘滋养层细胞内抑制芳香酶活性而产生的胎儿性别特异性效应相关[45]。

表 2　母婴 F-53B 暴露的不良健康效应

Table 2　Adverse health effects of maternal and infant exposure to F-53B

研究对象 (Study subjects)	样本类型 (Sample type)	暴露剂量 (Exposure dose)/(ng·mL^{-1})		结局(Outcome)	参考文献(Reference)
		6:2 Cl-PFESA	8:2 Cl-PFESA		
糖脂代谢与妊娠并发症(Glucose and lipid metabolism and pregnancy complications)					
辅助生殖技术妊娠孕妇(*n*=336，中国国家出生队列的一部分) (Pregnant women using assisted reproductive technology) (*n*=336, part of the China National Birth Cohort)	血清(Serum)	6.41	0.07	6:2 Cl-PFESA水平与口服葡萄糖耐量试验2小时血糖水平、妊娠期糖尿病风险有正向关联 (6:2 Cl-PFESA levels had positive association with 2-hour glucose levels during oral glucose tolerence test and the risk of gestational diabetes)	Mao D, et al.,2024[15]
孕妇(*n*=204，浙江) (Pregnant women) (*n*=204, Zhejiang)	血清(Serum)	2.58	0.02	6:2 Cl-PFESA水平与妊娠糖尿病风险间有正向关联 (6:2 Cl-PFESA levels had positive association with the risk of gestational diabetes)	Zhang Y, et al.,2023[42]
孕妇(*n*=118，北京) (Pregnant women) (*n*=118, Beijing)	血清(Serum)	4.35	0.06	6:2 Cl-PFESA在妊娠早期与孕妇血清总胆固醇和高密度脂蛋白胆固醇水平增高有关联 (6:2 Cl-PFESA had association with increasing total cholesterol and high-density lipoprotein cholesterol levels in pregnant women in early pregnancy)	Hu Y, et al.,2023[18]
孕妇(*n*=340，浙江) (Pregnant women) (*n*=340, Zhejiang)	血清(Serum)	3.64	0.18	6:2Cl-PFESA暴露与血糖水平和妊娠期糖尿病风险增加有关联 (6:2 Cl-PFESA exposure had association with increasing blood glucose levels and the risk of gestational diabetes)	Xu C, et al.,2022[19]
先兆子痫妇女(*n*=251，浙江杭州) (Pre-eclampsia women) (*n*=251, Hangzhou, Zhejiang)	血清(Serum)	2.81	—	6:2 Cl-PFESA与新生儿出身体重有负向关联 (6:2 Cl-PFESA had negative association with newborn birth weight)	Tian Y, et al., 2023[16]
不良妊娠结局(Adverse pregnancy outcomes)					
首次体外人工受孕治疗的妇女 (*n*=124，北京、山东) (Women undergoing first IVF treatment) (*n*=124, Beijing and Shandong)	血清(Serum) 卵泡液(Follicular fluid)	2.37 2.19	<LOD <LOD	6:2 Cl-PFESA和8:2 Cl-PFESA均与任何目标辅助生殖结果之间没有关联(6:2 Cl-PFESA and 8:2 Cl-PFESA showed no association with any assisted reproductive outcomes)	Hong A, et al.,2022[20]
复发性流产的妇女(*n*=464，山东、浙江) (Women with recurrent miscarriage) (*n*=464, Shandong, Zhejiang)	血清(Serum)	2.92	0.08	6:2 Cl-PFESA和8:2 Cl-PFESA均与复发性流产风险增加之间存在关联(6:2 Cl-PFESA and 8:2 Cl-PFESA showed association with increasing recurrent miscarriage risk)	Nian M, et al.,2022[43]
母子对(*n*=372，广州) (Mother-child pairs) (*n*=372, Guangzhou)	母体血清(Maternal serum)	2.41	<LOD	6:2 Cl-PFESA与早产风险增高有关联(6:2 Cl-PFESA showed association with an increased risk of preterm birth)	Chu C, et al.,2020[24]
孕产妇(*n*=519，山西) (Pregnant women) (*n*=519, Shanxi)	胎盘(placenta)	0.34	—	低水平6:2 Cl-PFESA暴露不会引起自发性早产，但与炎症生物标志物水平有关联(Low-level 6:2 Cl-PFESA exposure did not cause spontaneous preterm birth but had association with inflammatory biomarker levels)	Liu X, et al.,2020[40]

续表 2

研究对象 (Study subjects)	样本类型 (Sample type)		暴露剂量 (Exposure dose)/(ng·mL^{-1}) 6:2 Cl-PFESA	暴露剂量 (Exposure dose)/(ng·mL^{-1}) 8:2 Cl-PFESA	结局(Outcome)	参考文献(Reference)
子代体格发育与神经发育(Offspring physical and neurological development)						
母子对(*n*=372，广州) (Mother-child pairs) (*n*=372, Guangzhou)	母体血清(Maternal serum)		2.41	<LOD	6:2 Cl-PFESA与新生儿出生体重降低有关联 (6:2 Cl-PFESA had association with decreasing in newborn birth weight)	Chu C, et al.,2020[24]
母子对(*n*=302，广州) (Mother-child pairs) (*n*=302, Guangzhou)	绒毛膜下胎盘 (Chorionic membrane placenta)*		0.42	0.05	出生体重与绒毛膜下胎盘中6：2 Cl-PFESA及8：2 Cl-PFESA有负向关联(Birth weight had negative association with 6:2 Cl-PFESA and 8:2 Cl-PFESA in the chorionic membrane)	Di J, et al.,2023[17]
	副基底胎盘(Subchorionic placenta)*		0.42	0.03		
	母体血清(Maternal serum)		1.53	0.04		
	脐带血清(cord serum)		0.59	0.03		
母子对(*n*=195，合肥) (Mother-child pairs) (*n*=195, Hefei)	母体血清 (Maternal serum)	正常胎龄儿组 (*n*=130) (Term infant group) (*n*=130)	1.89	—	与正常胎龄儿组相比，小于胎龄儿组的6:2 Cl-PFESA与胎盘转移效率下降之间有关联 (Compared with the term infant group, there was association between the decreased placental transfer efficiency and the 6:2 Cl-PFESA in the small-for-gestational-age infant group)	Fan Y, et al.,2023[44]
		小于胎龄儿组 (*n*=65) (Small-for-gestational-age group) (*n*=65)	1.6	—		
	脐带血清 (Cord serum)	正常胎龄儿组 (*n*=130) (Term infant group) (*n*=130)	0.77	—		
		小于胎龄儿组 (*n*=65) (Small-for-gestational-age group) (*n*=65)	0.67	—		
母子对(*n*=94，广东) (Mother-child pairs) (*n*=94, Guangdong)	母体血清(Maternal serum)		1.78	0.02	脐带血6:2 Cl-PFESA水平与出生体重有正向关联(Cord serum 6:2 Cl-PFESA levels had positive association with birth weight)	Zhang B, et al.,2022[22]
	脐带血清(Cord serum)		0.73	0.02		
母子对(*n*=174，杭州) (Mother-child pairs) (*n*=174, Hangzhou)	母乳(Breast milk)		0.02	<LOD	婴儿的身长增加率与母乳中6:2 Cl-PFESA的浓度有负向关联(Infant length increase rate had negative association with 6:2 Cl-PFESA concentration in breast milk)	Jin H, et al.,2020[37]
母子对(*n*=110，浙江) (Mother-child pairs) (*n*=110, Zhejiang)	脐带血清(Cord serum)		0.73	0.02	6:2 Cl-PFESA和8:2 Cl-PFESA与出生结果之间不存在关联(6:2 Cl-PFESA and 8:2 Cl-PFESA showed no association with birth outcomes)	Xu C, et al.,2019[34]
儿童(*n*=314，广州) (Children) (*n*=314, Guangzhou)	血清(Serum)		1.1	0.02	接触6:2Cl-PFESA 和 8:2Cl-PFESA与儿童威斯康星卡片分类测验表现不佳有关联 (Exposure to 6:2 Cl-PFESA and 8:2 Cl-PFESA had association with poor performance in the Wisconsin Card Sorting Test in children)	Liang L, et al.,2023[14]

[注] *表示该样本类型中 6:2 Cl-PFESA、8:2 Cl-PFESA 的浓度单位为 ng·g^{-1}。

[Note] *: The concentration unit for 6:2 Cl-PFESA or 8:2 Cl-PFESA in the samples is ng·g^{-1}.

2.2 复发性流产和早产

F-53B 暴露显示出与复发性流产和早产之间的显著关联[24, 43]。一项在山东和浙江开展的病例对照研究发现，暴露于 PFASs 替代品 6:2 Cl-PFESA 与复发性流产风险增加之间存在显著关联（OR=1.18，95% CI: 1.00~1.39），且在年龄大的妇女中相关性更强（OR=1.39，95%CI: 1.04~1.84），这种年龄效应可能归因于年长女性 F-53B 暴露时间更长[43]。另外一项在广州开展的研究表明，母体血清中 6:2 Cl-PFESA 浓度越高，早产风险也越高，但早产风险仅在 6:2 Cl-PFESA 暴露的最高四分位数时更大（OR=5.42，95% CI: 1.70~17.29），且略高于 PFOS 所导致的早产风险（OR=4.99，95% CI: 1.34~18.56）[24]。山西的一项队列研究结果与该研究结果一致，其发现低水平 F-53B 暴露不会引起自发性早产，但与炎症生物标志物水平相关[40]。然而，与上述结果均相反的是，一项在北京和山东开展的针对首次体外受精妇女的

队列研究表明，血清和卵泡液 F-53B 水平与卵母细胞成熟率、受精率、优质胚胎率、生化妊娠、临床妊娠和临床前自然流产之间均没有显著关联[20]。造成研究结果不一致的原因可能是大多数研究的样本量较小，存在研究人群的人口统计学特征差异以及各种混杂因素的干扰[20]。

2.3 子代体格发育与神经发育

由于 F-53B 在脐带血清中的比例高于母体血清中的比例，其经胎盘转移效率高于 PFOS，提示 F-53B 可能具有更高的胎儿暴露水平[22]。现有的流行病学研究显示，F-53B 暴露会导致不良的出生结局，如影响出生体重、身长增加减缓、小于胎龄儿等[16, 17, 22, 24, 37, 44]。多项研究发现，F-53B 暴露水平增加会引起新生儿体重的显著变化[16, 17, 22, 24]。Tian 等[16]和 Chu 等[24]的研究均表明母体血清的 6:2 Cl-PFESA 水平升高会引起新生儿出生体重降低，Ji 等[17]研究也发现绒毛膜下胎盘中 6:2 Cl-PFESA（β=−80.04，95%CI: −139.5~−20.61）及 8:2 Cl-PFESA（β=−0.663，95%CI: −1.199~−0.126）水平与出生体重呈负相关。然而，一项在广东开展的队列研究发现脐带血 F-53B 水平与出生体重呈正相关（β=0.077，95%CI: 0.000 3~0.154），相反的结果可能与该项研究样本量较少以及研究对象均居住在电子废物拆解区附近有关[22]。Jin 等[37]在杭州开展的纵向出生队列发现婴儿的身长增加率与母乳中 6:2 Cl-PFESA 的浓度呈负相关，即通过母乳暴露于 6:2 Cl-PFESA 会导致婴儿出生后身长增加减缓，对其生长发育造成负面影响。关于小于胎龄儿与 F-53B 暴露的病例对照研究提示，小于胎龄儿组的母体血清 F-53B 水平与胎盘转移效率下降之间显著相关（r=0.90，P < 0.001），因此，小于胎龄儿分娩结局可能部分是由于 F-53B 暴露导致胎盘功能障碍，必需物质主动转运减少所引起的[44]。F-53B 引起不良出生结局的另一种可能机制与胎盘血流动力学及血管破裂有关，分析结果显示胎盘血管生物标志物（促血管生成素 2 和血管内皮生长因子受体 2）改变在胎盘和脐带血清 F-53B 水平与相关不良出生结局之间存在潜在中介作用[17]。

除了对出生结局造成影响外，F-53B 暴露还可能进一步影响儿童后续的神经发育[14]，甚至对成年期健康产生深远的影响。有一项队列研究关注了 F-53B 暴露与儿童神经发育之间的关系，观察到接触 6:2 Cl-PFESA 和 8:2 Cl-PFESA 与儿童威斯康星卡片分类测验表现不佳有关，表明存在运动和学习障碍[14]。

F-53B 对子代体格发育和神经发育的毒性效应可能是通过影响性激素和甲状腺激素水平导致的[33, 46]。计算机模拟表明，与 PFOS 相比，Cl-PFAES 与雌激素和甲状腺激素受体间具有更大的化学亲和力[46]。多项流行病学研究发现，F-53B 暴露与新生儿雌激素水平、甲状腺激素水平具有显著相关性[31, 33, 35]，提示 F-53B 可能会通过影响新生儿雌激素的合成和甲状腺激素分泌影响子代的生长发育。

3 总结

目前的数据表明，F-53B 在孕妇和婴儿的各类生物样本中被广泛检出，在传统 PFAS 和替代物中，F-53B 的主要成分 6:2 Cl-PFESA 含量已成为母婴生物样本中排名第三的物质，且是所有已知 PFAS 中半衰期最长的。尽管流行病学研究相对有限，但现有证据表明，F-53B 暴露会导致孕妇妊娠糖尿病、脂代谢紊乱、先兆子痫等妊娠并发症的风险增加，与不孕、早产、复发性流产等不良妊娠结局相关。另外 F-53B 暴露还会对子代的生长发育造成负面效应，可能影响新生儿的出生体重、体格发育和神经发育等。F-53B 对母体的毒性效应可能是通过抑制芳香酶活性、干扰性激素合成、引发炎症反应等途径所导致的，而对婴儿的毒性作用的可能机制与胎盘血流动力学以及激素变化相关。暴露于 F-53B 可能会导致胎盘功能障碍，引起必需物质主动转运减少，或者引起胎盘血管破裂造成血流动力学变化，从而影响新生儿的出生体重和身长等指标。对后续生长发育的影响如神经发育毒性等，则可能是通过影响生命早期雌激素、甲状腺激素水平和造成端粒长度缩短所导致的。

然而截至目前，关于 F-53B 暴露对母婴健康影响的人群流行病学研究仍处于起步阶段，并存在一定的局限性：几乎所有研究仅在单一时点测量了 F-53B 的内暴露水平，尽管其半衰期较长但仍可能错误估计研究对象的暴露水平；部分研究为病例对照研究，暴露与结局的时序性无法确定，因此在推断暴露与结局间的因果关系方面受限；部分研究仅关注特定人群或样本量较小，不同研究存在人口学特征间的差异且同一研究中也存在一定的混杂因素。未来人群研究可以根据上述局限性进行改进和开展，例如多时点收集样本并测量内暴露水平，建立样本量充足的队列研究等。

F-53B 虽然作为 PFOS 的替代物进行使用，但仍存在一定的毒性，甚至在部分研究中展现出高于 PFOS 的母婴毒性，因此 F-53B 使用的安全性有待商榷，需要进一步的研究提供安全限值。

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