第600次学术讨论会·生物气溶胶与人类健康、国家生物安全及大气污染

生命早期环境污染暴露增加儿童过敏与感染风险

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2017-12-22 收稿, 2018-02-02 修回, 2018-02-11 接受, 2018-03-22 网络版发表

国家自然科学基金(51576214, 21777193)和湖南省重点研发项目(2017SK2091)资助

摘要 近年来随着我国城市化与经济快速发展, 城市环境空气污染比较严重, 城市儿童哮喘与过敏症患病率迅速增加, 儿童肺炎等呼吸系统感染发病率较高。虽然环境污染暴露对儿童健康的影响受到广泛关注与大量研究, 但是对于“主要环境污染物、关键暴露窗口、是否导致疾病”等关键科学问题尚不清楚。本文总结了生命早期包括出生前(孕前一年、整个孕期、孕期三个围产期)和出生后(第一年、过去一年、整个出生后阶段)室内与室外不同环境污染物暴露对儿童过敏性与感染性疾病的影响, 并总结了关键暴露窗口对不同疾病的重要性, 分析了不同污染物与时间窗口暴露增加儿童过敏与感染的发病风险。本文通过对已有文献的综合分析, 进一步证明了“儿童疾病胎儿起源”假设, 揭示了孕期与出生后早期阶段室内、外环境污染物长期暴露对儿童过敏与感染性疾病的发生与发展具有显著性影响, 为有效预防与降低我国儿童过敏性疾病与呼吸道感染提供了科学依据与干预策略。最后总结了生命早期室内与室外环境污染物暴露对儿童过敏与感染疾病的不同影响, 展望有效预防与降低儿童相关疾病发病风险的问题与挑战。

关键词 儿童, 过敏, 感染, 空气污染, 室内装修, 早期暴露

随着我国社会经济持续快速发展, 城市环境空气污染日趋严重。近年来我国大部分地区持续出现严重雾霾天气、重度污染事件频发, 给人们的生活与健康带来了非常不利的影响, 因而引起了社会大众与政府部门的高度关注。另一方面, 随着我国城市化进程加快, 每年大量居民(特别是新婚夫妇或准父母们)迁入新建建筑, 室内新家具与装修污染的健康危害也因此备受关注, 因为人们一生中超过80%的时间是在室内度过的, 其中儿童与孕妇暴露时间更长^[1,2]。环境空气污染目前已被认为是导致全球疾病

负担(global burden of diseases)的十大主要因素之一^[3], 其中室内、外空气污染分别位列第4、9位^[4,5]。

面对我国严重的室内外环境空气污染, 如何最有效地预防与降低其健康危害是关键。因此, 本文将系统总结国内与国外环境空气污染对儿童健康危害方面的文献, 论述生命早期环境污染物暴露的重要性, 并识别环境污染物暴露对儿童过敏性疾病与呼吸道感染最为关键的时间窗口, 从而为相关疾病的早期预防与有效控制提供科学依据与关键策略。针对以下4方面问题, 本文作者提出了有效预防与控制

引用格式: 路婵, 胡旭, 缪玉峰, 等. 生命早期环境污染暴露增加学龄前儿童过敏与感染风险. 科学通报, 2018, 63: 954–967

Lu C, Hu X, Miao Y F, et al. Early life exposure to environmental pollution increases childhood asthma, allergy and infection (in Chinese). Chin Sci Bull, 2018, 63: 954–967, doi: 10.1360/N972017-01346

空气污染健康危害的研究路线图(图1)。

1 环境空气污染对儿童健康影响的关键问题

1.1 什么污染物危害最大?

尽管以往研究已经证明环境因素,如室外空气污染、室内环境烟草(ETS)、霉菌/潮湿、过敏原、以及一些新型化学物质^[6-8]均与过敏症及感染性疾病的发展相关,但究竟哪种环境因素才是导致我国儿童过敏与感染患病率显著增加的主要原因尚不清楚。一方面,我国严重的室外空气污染具有多污染源特性。随着经济的快速发展,中国正面临着全世界最严重的工业空气污染^[9];与此同时,由于近年来汽车数量大幅增加,交通排放污染物日趋严重。因此,我国室外空气污染具有高浓度水平与多污染源特征,与国外大气污染明显不同。另一方面,由于快速的城市化进程,近十年来大量新婚夫妇与年轻父母迁居到城市并成为新建筑的主要居住人群。新建筑材料、装饰材料、家具能够增加室内有害化学物质浓度,例如挥发性、半挥发性有机化合物(VOCs, SVOCs)^[6,10],然而长期暴露于这些潜在的室内环境污染物对年轻夫妇及其新生后代的健康影响还不清楚。

1.2 污染物对谁的危害最大?

环境污染对不同人群健康危害具有差异性,尤

其儿童属于典型的易感人群,更容易受到空气污染的影响。一方面与成人相比,儿童活动量更大、呼吸频率更快,从而导致单位体重呼吸的空气污染物更多^[11];另一方面,由于儿童处于身体与器官快速生长发育阶段,其呼吸系统、免疫系统、及器官功能尚未发育完善且比较脆弱,对环境有害物质与风险因素十分敏感,相比成人更容易受到环境暴露的影响^[12,13]。我国以往大多数研究主要关注学龄儿童或成人,但对于环境空气污染对学龄前儿童的健康影响研究很少,然而我国儿童人数众多且近十年来儿童过敏与感染患病人数激增,因此,深入研究我国严重的室外与室内环境空气污染对学龄前儿童的健康影响及其暴露风险十分必要、意义重大。

1.3 什么时期暴露危害最大?

近年来,越来越多证据表明,早期环境暴露对儿童疾病的发展具有重要甚至决定性影响^[14-16]。国际著名流行病学专家巴克教授David Barker(1938~2013年)1995年提出巴克假说(Barker hypothesis)^[17]:出生前与出生后早期阶段环境污染物暴露可以影响胎儿与新生儿的发育可塑性(developmental plasticity),并能够影响胎儿发育编程(fetal programming)或导致基因程序改变,产生永久性结构功能改变,从而使儿童对环境污染敏感性显著增强,诱发过敏与感染性疾病风险增加,甚至能够导致成年后一系列相关疾病的发生与恶化^[18]。近年来,基于“巴克假说”,越来

图1 空气污染健康危害研究路线图

Figure 1 Framework of health effect of air pollution

越多研究关注早期环境暴露与儿童和成人疾病之间的相关性,提出了“疾病胎儿起源(fetal origins of disease)”学说^[19]从病因学认识疾病发生与发展诱导因素及其关键时期^[15,20].

1.4 最可能导致什么疾病?

环境污染物暴露与儿童哮喘等过敏症及呼吸系统感染等疾病密切相关^[7].一方面,过敏性疾病是儿童最常见的慢性病(<http://www.who.int/topics/asthma/en/> / Accessed July 17, 2017),现已成为导致全世界儿童入院的主要原因^[21].20世纪以来,世界范围儿童哮喘及过敏症发病率显著增加,尽管近年来一些发达国家哮喘和过敏发病率已经趋于稳定甚至缓慢下降,但儿童哮喘、鼻炎、湿疹等过敏性疾病患病率在全球大部分地区仍在不断增长,尤其发展中国家发病率快速上升^[22].我国2010~2012年全国主要城市的最新调查研究^[23]表明,我国学龄前儿童哮喘发病率在过去10年由1.5%迅速增加至6.8%.另一方面,肺炎作为儿童最普遍的感染性疾病之一,是世界上导致5岁前儿童死亡的第一杀手^[24],而其中绝大多数(99%)的儿童死亡分布在发展中国家^[25,26].尽管我国儿童长期以来普遍使用肺炎疫苗,但其肺炎发病率在全世界仍然居高不下^[27].流行病学证据显示:“一个呼吸系统一个疾病”,因此,儿童呼吸系统感染与过敏性疾病理论上具有许多类似性^[28],并且前者也是导致后者的重要因素.近10年来,我国迅速增加的儿童过敏与频发的感染性疾病不仅导致了严重的家庭经济与社会医疗负担,而且对儿童身体与智力发育、甚至以后生命质量及其发展具有重要、长远影响^[29].越来越多研究表明,除基因外,环境空气污染是导致儿童过敏与感染性疾病最主要的因素之一^[30].

从我国目前情况来看,总体上降低空气污染还需要一个较长的时间过程,而有针对性、有选择地降低对人体健康危害大的污染源则有非常重要的科学价值与意义.但是,我国相关课题研究尚且十分缺乏.2011~2012年,我国开展了“中国室内环境与儿童健康(CCHH)”调查^[23],调查问卷基于中国室内、外环境的特殊情况,对国际儿童哮喘与过敏症研究协会(ISAAC)调查问卷^[22]与瑞典建筑潮湿与健康(DBH)调查问卷^[6]进行了少量修改,旨在研究中国室内、外环境污染物与学龄前儿童过敏与感染性疾病之间的相关性,其中环境因素主要包括:室外主要空气污染

物、室内新家具和装修、室内霉菌/潮湿.近期,这一课题的相关系列研究^[31~34]假设不同发育、成长阶段环境污染物暴露对儿童疾病及症状影响不同,将调查儿童的生命早期分为出生前(孕前一年、整个孕期、孕期三个围产期)与出生后(第一年、过去一年、整个出生后)两个阶段,评估不同阶段室外与室内环境污染暴露对儿童过敏(哮喘、鼻炎、湿疹)与呼吸系统感染(肺炎、耳炎、感冒)的影响.例如,2011年9月~2012年1月Deng等人^[31]在我国长沙市36个幼儿园对其所有儿童进行了问卷调查,这些幼儿园覆盖了长沙市5个主要的行政区:芙蓉区、天心区、岳麓区、开福区、雨花区,且每个行政区所调查的幼儿园数目较为均匀,因此调查问卷中获得的信息能够代表长沙市整体情况,同时也能体现区域之间的差异性.问卷包括儿童健康状况、住宅环境中潜在化学物质、儿童及其家庭成员生活方式等信息数据.其中,室外污染物主要考虑3种主要的空气污染物:PM₁₀, SO₂, NO₂;室内污染物主要研究新家具和装修暴露导致的健康效应.对于不同时间段的暴露处理,本课题组^[34]的近期研究将出生前怀孕期间和出生后(包括1岁与1岁后)是否购买过新家具/重新装修作为定性暴露,即出生前与出生后是否存在室内污染物暴露;对于新家具的暴露程度采用问卷中的问题进行定量评估“在怀孕期间或出生后阶段,您的住处是否购买过新家具(是,少量/是,大量/否)”,其中少量定义为低暴露,大量为高暴露,否为无暴露^[32].通过以上室内与室外儿童个人暴露与健康数据的分析,研究生命早期室内与室外环境风险因素暴露对儿童过敏性疾病与呼吸道感染的影响.

2 室外空气污染早期暴露对儿童过敏与感染的影响

2.1 汽车尾气暴露增加儿童过敏性疾病的风险

国外大量流行病学研究证明了整个生命时期或后期环境因素暴露对儿童过敏性疾病慢性发展的重要性^[30,35~38],但国内相关研究尚且十分缺乏.已有出生队列研究^[30]表明出生~4岁期间室外交通排放相关污染物暴露与哮喘、过敏及儿童呼吸道感染等疾病(如耳、鼻、喉、感染、严重感冒)显著正相关.此外,德国的一个出生队列研究^[38]发现出生~6岁期间交通排放污染物如PM_{2.5}, NO₂的暴露以及临近交通主干道

均能够显著增加儿童哮喘性支气管炎、花粉过敏、湿疹等过敏性疾病的患病风险。然而,由于靶器官及其系统在发育生长时期十分敏感,孕期和早期空气污染暴露比后期暴露影响更大^[39]。最近一些研究发现,早期空气污染暴露可以增加哮喘等过敏性疾病风险^[40~44]。近期一个西班牙出生队列研究^[40]发现,孕期与第1年室外交通排放污染物NO₂和苯的暴露与12~18个月婴儿下呼吸道感染和耳炎显著正相关。目前我国的大部分研究主要关注3种室外污染物:SO₂, NO₂, PM₁₀, 其中SO₂作为工业污染指标, NO₂作为交通污染指标, PM₁₀代表混合型空气污染^[9]。Deng等人^[45]的一项近期研究基于单个城市(长沙)不同环境监测站污染物浓度数据,采用反距离加权插值算法(IDW)^[46,47]评估了36个幼儿园学龄前儿童对室外这3

种大气污染物的个人暴露浓度,分析了不同污染物在不同时期暴露对儿童过敏性疾病的影响,研究结果发现孕期交通排放污染物(NO₂)暴露能够显著增加儿童过敏性疾病风险,而孕期传统工业污染物(SO₂与PM₁₀)暴露则与儿童过敏性疾病无显著相关性。此研究显示,孕期暴露NO₂每增加12 μg/m³,儿童哮喘、过敏性鼻炎、湿疹校正风险分别为1.64(1.22~2.21), 1.38(1.03~1.84), 1.20(1.02~1.41)。考虑到不同污染物之间具有相关性,我们进一步采用了多污染物相互校正模型,验证了NO₂孕期暴露风险。

尽管孕期不同窗口暴露十分重要,但至今只有少量研究分析了孕期不同围产期大气污染物暴露对儿童过敏与感染性疾病的影响(表1)。一些近期研究证明了孕期不同围产期大气污染物暴露能够增加儿

表1 不同国家/地区孕期三个围产期室外空气污染物暴露对儿童过敏性疾病的影响总结表^{a)}

Table 1 Summary for the effects of exposure to outdoor air pollution during three trimesters of pregnancy on childhood allergic diseases in different countries/areas

国家/地区	人群	年龄	研究污染物	疾病	校正OR(95% CI)			文献
					第一围产期	第二围产期	第三围产期	
西班牙	2199	12~18个月	NO ₂	哮喘	1.06(1.00, 1.12)	1.08(1.02, 1.15)	1.00(0.93, 1.07)	[40]
				喘息	1.02(0.96, 1.09)	1.05(0.99, 1.11)	1.01(0.94, 1.08)	
				湿疹	0.97(0.89, 1.05)	1.01(0.92, 1.11)	1.01(0.92, 1.10)	
				耳炎	1.11(0.99, 1.24)*	1.16(0.98, 1.37)***	1.12(0.98, 1.29)**	
中国	2598	3~6岁	PM ₁₀	哮喘	1.07(0.84, 1.38)	0.96(0.76, 1.20)	0.85(0.69, 1.05)	[45]
				鼻炎	0.85(0.67, 1.09)	1.02(0.81, 1.28)	1.10(0.90, 1.35)	
				湿疹	1.03(0.89, 1.18)	1.04(0.92, 1.18)	0.98(0.87, 1.10)	
			SO ₂	哮喘	1.29(1.08, 1.55)**	1.26(1.05, 1.52)*	1.04(0.85, 1.26)	
				鼻炎	1.06(0.88, 1.27)	1.09(0.91, 1.31)	1.09(0.90, 1.32)	
				湿疹	1.09(0.98, 1.22)	1.05(0.94, 1.17)	1.00(0.89, 1.12)	
			NO ₂	哮喘	1.50(1.15, 1.96)**	1.70(1.26, 2.30)***	1.12(0.86, 1.45)	
				鼻炎	1.10(0.85, 1.43)	1.22(0.91, 1.64)	1.36(1.06, 1.75)*	
				湿疹	1.29(1.11, 1.49)***	1.24(1.05, 1.46)*	0.96(0.83, 1.10)	
美国	170	6~11岁	CO(24 h)	变异性致敏		1.52(0.93, 2.47)		[48]
			CO(日均最大值)			1.50(0.92, 2.45)		
			CO(8 h最大值)			1.45(0.90, 2.35)		
中国台湾	24200	0~3岁	NO ₂	特应性皮炎	1.17(0.95, 1.43)	1.02(0.83, 1.25)	1.02(0.80, 1.29)	[49]
			CO		1.51(1.16, 1.97)**	0.86(0.65, 1.15)	1.19(0.87, 1.64)	
			SO ₂		0.97(0.82, 1.14)	1.02(0.85, 1.24)	1.05(0.88, 1.26)	
			PM ₁₀		0.97(0.82, 1.14)	1.02(0.85, 1.24)	1.05(0.88, 1.26)	
			O ₃		1.04(0.91, 1.19)	1.14(0.98, 1.32)	1.11(0.95, 1.30)	
美国	736	0~6岁	PM _{2.5}	哮喘		显著正相关		[50]
中国	2598	3~6岁	PM ₁₀	湿疹	1.02(0.89, 1.18)	1.02(0.90, 1.16)	1.00(0.89, 1.13)	[51]
			SO ₂		1.05(0.94, 1.18)	1.06(0.95, 1.18)	1.00(0.89, 1.12)	
			NO ₂		1.26(1.09, 1.46)**	1.22(1.03, 1.43)*	0.97(0.84, 1.11)	

a) *, $P < 0.05$; **, $P < 0.01$; ***, $P < 0.001$

童出生后呼吸道感染等疾病风险^[40,48,52,53],但其结论尚不一致.例如,美国的一个研究^[48]发现整个孕期CO暴露与哮喘儿童的变应性致敏显著相关,并且孕期第二围产期CO暴露风险相对较大.一个西班牙出生队列研究^[40]发现12~18个月的婴儿湿疹与孕期第二与第三围产期交通排放污染物NO₂暴露相关;Hsu等人^[50]发现孕期第二围产期PM_{2.5}暴露与儿童哮喘显著相关;而中国台湾地区的一项近期研究则表明6个月的婴儿湿疹与孕期第一围产期CO暴露相关^[49].本课题组^[45,51]的一些近期研究也证明了孕期不同围产期甚至孕前阶段室外关键空气污染物暴露对不同过敏性疾病的影响存在差异性.例如,通过对孕期不同围产期污染物暴露风险的进一步分析表明:第一、第二、第三围产期汽车尾气污染物NO₂暴露分别增加儿童湿疹、哮喘、过敏性鼻炎疾病风险,其比值比(95%置信区间)(OR(95% CI))分别为1.54(1.14~2.09), 1.72(1.02~2.97), 1.77(1.09~2.89).这种不同围产期暴露导致不同过敏性疾病具有一定的生物学机理,即与胎儿时期的器官发育密切相关^[45].因此,上述研究表明孕期以及出生后早期阶段室外交通排放污染物暴露对儿童之后过敏性疾病与呼吸道感染的发生与发展具有显著性影响.

2.2 工业污染暴露增加儿童过敏与呼吸系统感染风险

发达国家大量研究认为汽车尾气(如NO₂, NO_x, CO, O₃等)是导致儿童过敏症与呼吸系统感染的关键污染物^[16,30,54~57],但忽略了传统污染物如工业排放污染物的暴露影响,这主要是由于发达国家的工业污染浓度水平十分低,室外空气污染类型单一化主要为汽车尾气.但是,发展中国家室外空气污染的浓度水平和污染类型与发达国家显著不同,但是其研究还十分缺乏.例如,我国室外环境空气污染具有浓度高与多元混合特性,对儿童健康影响与发达国家明显不同.如表2所示,以往大部分研究发现早期交通排放污染物(如NO₂/NO_x)与儿童哮喘之间的相关性较为显著与一致,但是对于早期传统工业污染物暴露对哮喘的影响及其致病风险尚无定论.本课题组一些近期研究结果发现,我国严重的工业空气污染如SO₂不仅能够显著增加儿童哮喘等过敏性疾病的风险以及加重交通排放污染物的健康效应^[31,33],还能够直接导致儿童呼吸系统感染^[64,65].通过分析不

同室外空气污染物在不同暴露时期对低龄儿童(3~4岁)的耳炎影响,证明了儿童耳炎患病率与出生后空气污染物暴露无关,而仅与出生前(孕期)工业排放污染物SO₂暴露显著相关,浓度每增加27 μg/m³导致的耳炎风险OR(95% CI)=1.44(1.09~1.88)(图2)^[65].此研究^[65]进一步发现,孕期SO₂暴露主要显著增加耳炎发病风险(Onset),而对于耳炎的反复发作(Attacks≥3)无显著相关性.此研究结果显示,孕期SO₂暴露浓度每增加27 μg/m³导致的耳炎发病风险OR(95% CI)=1.47(1.10~1.96).由于感染性疾病如儿童耳炎是全球第5疾病负担,学龄前儿童发病率高、容易复发.据统计高达80%的儿童3岁前患过急性耳炎,其中40%的儿童7岁前经历过多次感染,因此辨识与研究导致儿童呼吸道感染发病与发展的主要空气污染物十分关键,而本课题组的上述研究不仅证明了工业排放污染物是导致儿童耳炎最主要的空气污染物,而且还识别出了孕期这一关键暴露窗口的重要性,对早期预防与有效降低我国儿童感染性疾病的发病率,减轻社会、家庭经济与疾病负担,均具有重要指导意义.

上述研究说明了我国空气污染对儿童健康效应与国外显著不同,一方面近年来由于我国快速的经济发展和以煤为主的能源利用方式,SO₂污染水平全世界最高^[66];另一方面SO₂对儿童过敏与感染性疾病的影响取决于其浓度水平.尽管由于SO₂污染很轻,发达国家忽略了它对儿童健康的影响^[67],但最近的研究却发现SO₂暴露尤其是早期暴露对儿童哮喘等过敏性疾病的影响十分显著.例如,Clark等人^[41]的研究发现3~4岁儿童哮喘风险与孕期和第1年SO₂暴露显著相关;其他一些研究^[62,68]也发现距离污染源较近地区其高浓度SO₂具有显著的健康风险.因此,与发达国家不同,我国城市高浓度的工业排放污染物(如SO₂)早期暴露对儿童的健康影响不容忽略.

3 室内污染暴露对儿童过敏与感染的影响

3.1 室内霉菌/潮湿暴露增加儿童过敏与感染风险

霉菌与潮湿被世界卫生组织(WHO)列为室内重要的环境风险因素之一(WHO 2009).近期一些综述研究^[35,36]表明室内霉菌/潮湿是引起哮喘患病率增加最重要的室内环境风险因素.其他一些综述研究^[69~71]

表2 不同国家/地区早期室外不同空气污染物暴露与儿童哮喘的相关性总结表

Table 2 Summary for the associations between early-life exposure to different outdoor air pollutants and childhood asthma in different countries

研究设计	国家	研究人群	年龄(岁)	校正OR(95% CI)			文献
				SO ₂	PM ₁₀	NO ₂ /NO _x	
出生队列	加拿大	37401	3~4	孕期暴露: 1.03(1.02~1.05) 第一年暴露: 1.03(1.02~1.05)	1.09(1.05~1.13) ^{a)} 1.07(1.03~1.12) ^{a)}	1.10(1.05~1.15) 1.12(1.07~1.17)	[41]
病例对照	美国	4320	8~21	第一年暴露: 0.99(0.90~1.08) 出生后三年暴露: 1.03(0.94~1.13)	1.13(0.98~1.29) 1.13(0.97~1.31)	1.17(1.04~1.31) 1.26(1.07~1.48)	[44]
横断面	美国	34073	3~17	1.03(0.99~1.07)	0.99(0.90~1.09) ^{a)}	0.97(0.91~1.03) 1.08(1.02~1.14) ^{b)}	[58]
横断面	中国	30139	3~12	1.19(1.06~1.33)	1.27(1.12~1.45) ^{a)}	1.19(1.06~1.34)	[59]
横断面	中国	3358	4~6	孕期暴露: 1.15(0.87~1.51) 第一年暴露: 1.22(1.01~1.49) 出生后两年暴露: 1.33(0.98~1.79) 出生后三年暴露: 1.48(1.11~1.98) 整个出生后暴露: 1.26(0.96~1.66)	0.99(0.78~1.25) 1.33(0.98~1.79) 1.13(0.92~1.39) 1.38(1.12~1.70) 1.38(1.02~1.88)	1.17(0.83~1.67) ^{c)} 1.55(1.26~1.92) ^{c)} 1.47(1.10~1.95) ^{c)} 1.40(1.04~1.88) ^{c)} 1.38(1.02~1.85) ^{c)}	[60]
队列	美国	2497	0~8		1.35(0.64~2.85) ^{a)}	2.17(1.18~4.00)	[61]
横断面	法国	6683	9~11	1.26(1.11~1.42)	1.28(1.06~1.51) ^{a)}	1.09(0.85~1.39) 1.21(1.03~1.54) ^{d)}	[62]
横断面	中国	7621	5~16	1.03(0.75~1.41)	1.33(0.80~2.19) ^{a)}	0.95(0.63~1.43)	[63]

a) PM₁₀; b) O₃; c) NO₂; d) CO

总结了家庭住宅环境中霉菌和潮湿暴露对过敏和感染性疾病影响,揭示了它们之间存在显著和统一的相关性(表3)。Mendell等人^[72,73]的最新综述研究还证明了室内霉菌/潮湿暴露与哮喘的发展和加剧均显著相关。芬兰的一项队列研究^[37]发现,早期室内霉菌暴露与哮喘的首次发作和发展密切相关。

本课题组^[74]的一项近期研究结果表明,儿童经常感冒不仅与出生时室内霉菌和潮湿(窗户凝结水汽)暴露显著相关,暴露风险分别为1.38(1.24~1.53)和1.23(1.13~1.33),而且与现在霉菌、潮湿、水损暴露也显著相关,暴露风险分别为1.36(1.22~1.52), 1.27(1.17~1.39), 1.34(1.20~1.49)。此外,该研究还证明了室内其他风险因素对儿童感冒的影响:孕期养狗能够显著延长儿童每次感冒周期,其风险为1.22(1.06~

1.41); 蟑螂暴露能够显著增加儿童经常感冒与延长感冒恢复周期的风险,而每天打扫卫生能够显著降低以上风险;南方儿童更易受养猫对经常感冒的影响,北方儿童更易受蟑螂暴露的影响,而霉菌与潮湿暴露对南、北方儿童的影响无显著性差异。

3.2 室内新家具/装修暴露增加儿童过敏与感染风险

近年来越来越多流行病学研究表明室内装修材料及其排放的有害气体与过敏和呼吸系统疾病显著相关^[35,75]。由于室内装修活动和新家具表面材料可以挥发出多种VOCs和SVOCs,从而被认为是过敏症与呼吸系统疾病的重要风险因素^[6,72,76,77]。表4中的结果显示,出生前与出生后早期阶段室内新家具/装修

图 2 孕期工业排放污染物SO₂暴露增加儿童耳炎风险^[65]
Figure 2 Prenatal exposure to industrial air pollutant SO₂ increases risk of childhood otitis media^[65]

表 3 室内霉菌/潮湿暴露对不同人群过敏与感染的影响总结表
Table 3 Summary for the effects of exposure to indoor mold/dampness on allergies and infections among different populations

疾病	研究人群	校正OR(95% CI)		
		文献[69]	文献[70]	文献[71]
上呼吸道感染	所有人群	1.70(1.44~2.00)		
咳嗽	所有人群	1.67(1.49~1.86)		
	成人	1.52(1.18~1.96)		1.30(1.22~1.39)
	儿童	1.75(1.56~1.96)		1.50 (1.31~1.73)
喘息	所有人群	1.50(1.38~1.64)		
	成人	1.39(1.04~1.85)		1.43(1.36~1.49)
	儿童	1.53(1.39~1.68)		1.49(1.28~1.74)
现在哮喘	所有人群	1.56(1.30~1.86)		
曾经诊断哮喘	所有人群	1.37(1.23~1.53)		
	儿童			1.35(1.20~1.51)
哮喘发展	所有人群	1.34(0.86~2.10)		
支气管炎	所有人群		1.45(1.32~1.59)	
	儿童			1.38(1.28~1.47)
呼吸道感染	所有人群		1.44(1.31~1.59)	
	成人		1.49(1.14~1.95)	
	儿童		1.48(1.33~1.65)	
呼吸道感染	儿童		1.50(1.32~1.70)	
花粉热	儿童			1.35(1.18~1.53)

暴露对儿童之后过敏与感染性疾病的发生与发展具有显著性影响。另外也有一些研究表明，孕期或第一年室内装修能够显著增加儿童呼吸系统疾病如阻塞性支气管炎^[82]、喘息^[76]、湿疹^[77]等过敏症风险；此

外还有一些研究结果发现哮喘与室内装修活动有关^[35,83]，但其早期暴露影响尚不清楚。近期一些综述研究^[35,36]证明了吸烟、临近交通主干道、室内霉菌/潮湿是引起哮喘患病率增加最重要的室内环境风险

表 4 不同国家早期室内新家具/装修暴露对儿童过敏与感染性疾病及其症状的影响总结表

Table 4 Summary for the effects of early-life exposure to indoor new furniture/redecoration on childhood allergic and infectious diseases and symptoms in different countries

研究设计	国家	研究人群	年龄	新家具/装修	校正OR(95% CI)	文献
出生队列	德国	465	0~2岁	新家具	孕期暴露: 1.94(0.72~5.26) ^{a)} 第一年暴露: 2.26(0.83~6.17) ^{a)} 孕期暴露: 2.04(0.78~5.28) ^{a)} 第一年暴露: 1.89(0.71~5.06) ^{a)}	[76]
病例对照	德国	475	6周、1岁	装修	6周: 5.6(1.3~24.0) ^{b)} 1岁: 1.9(1.1~3.5) ^{a)}	[78]
病例对照	中国	3945	1~6岁	2年前装修	1.49(1.04~2.14) ^{c)} 1.40(1.11~1.76) ^{d)} 1.50(1.16~1.92) ^{e)}	[79]
横断面	俄罗斯	5951	8~12岁	新家具	过去12个月: 1.33(0.57~3.06) ^{c)} 1.62(1.17~2.24) ^{f)} 1.32(0.99~1.77) ^{d)} 更早时期: 1.27(0.64~2.51) ^{c)} 1.30(1.00~1.70) ^{f)} 1.16(0.92~1.47) ^{d)}	[80]
横断面	中国	3700	1~7岁	新家具	出生前: 1.23(1.03~1.48) ^{a)} 1.24(1.00~1.53) ^{d)} 第一年: 1.23(0.93~1.63) ^{a)} 1.47(1.08~2.00) ^{d)} 出生前: 1.15(0.92~1.45) ^{a)} 1.24(0.95~1.61) ^{d)} 第一年: 1.45(0.93~2.33) ^{a)} 1.40(0.82~2.40) ^{d)}	[81]

a) 曾经喘息; b) 肺部感染; c) 现在哮喘; d) 现在喘息; e) 医生诊断哮喘; f) 类似哮喘症状

因素,对于室内装修散发的(半)挥发性有机化合物(S)VOC等空气污染物对人们潜在的健康风险尚不清楚^[35].

本课题组^[32]的研究发现孕期室内大量新家具与

装修暴露能够显著增加儿童哮喘风险,调整相关协变量后OR(95% CI)分别为2.34(1.16~4.74)与2.21(1.29~3.81).由于室外环境空气污染物(特别是NO₂)也能够增加儿童哮喘风险,此研究进一步控制室外

污染物后发现孕期室内新家具和装修暴露与儿童哮喘的相关性具有非常好的稳定性. 一些近期研究证明了室内新家具与装修暴露对儿童呼吸系统感染疾病(耳炎)的影响. 例如本课题组^[65]研究发现, 与哮喘等过敏性疾病不同, 儿童耳炎风险仅与出生后室内新家具与装修暴露显著相关, 调整相关协变量后OR(95% CI)分别为1.62(1.05~2.49)与1.81(1.12~2.91). 本课题组的另一项近期研究^[84]结果发现, 出生后室内新家具与装修暴露能够显著增加学龄前儿童肺炎的发病风险, 其OR(95% CI)分别为1.30(1.02~1.64)与1.30(1.00~1.69).

另一方面, 有研究证明室外空气污染与室内过敏原之间具有潜在的交互作用, 能够进一步增加健康风险, 但此理论尚且没有受到广泛关注^[85]. 只有少量研究同时分析了室外与室内环境因素暴露对儿童过敏症的影响^[7,8,83,86,87]. 本课题组^[31]的近期相关研究表明, 孕期和第一年室外与室内空气污染暴露均与儿童哮喘密切相关, 并且研究还发现室外空气污染与室内新家具/装修污染能够协同作用, 从而进一步增加儿童耳炎的患病风险^[65]. 因此, 对于我国室内与室外空气污染均很严重的特殊环境, 应该特别关注早期暴露对儿童将来相关疾病的影响, 采取科学有效的防护措施, 比如当室外空气污染十分严重时, 人们在室内应尽量少开窗或者采用空气进化器以降低室内、外空气污染交互作用对人们的健康危害.

4 总结与展望

本文系统地总结了生命早期室外与室内不同空气污染物暴露与国内、外儿童过敏性疾病与呼吸系统感染的相关性, 分析了关键暴露时间窗口的重要性. 综上所述: (1) 国内与国外对于室外交通排放污染物与儿童过敏性疾病的相关性较为明确, 观点比较一致, 普遍认为出生前与出生后早期阶段高浓度的汽车尾气污染物暴露能够显著增加儿童哮喘与过敏症的发病率, 并且孕期不同围产期空气污染暴露对不同疾病的影响与重要性存在差异; (2) 对于工业排放等传统型空气污染物, 由于其在世界范围内浓度分布十分不均且污染源类型具有多样性, 早期暴露引起的健康效应研究相对较少, 且结论尚不统一. 发达

国家工业污染浓度很低不是主要污染源, 而发展中国家如中国工业污染很重但其早期尤其出生前如孕期和不同围产期暴露对儿童健康影响的研究十分缺乏, 国内现有文献认为工业排放污染物暴露主要与呼吸系统感染相关; (3) 孕期与出生后早期阶段室内新家具与装修导致的空气污染暴露与儿童过敏及感染性疾病的发生与发展显著相关, 并且室内与室外空气污染物能够协同作用从而进一步增加儿童过敏与感染的患病风险; (4) 本课题组的近期研究发现除了空气污染, 环境温度例如高温^[88]与温差^[89]的早期(孕期)暴露也能显著增加儿童之后呼吸道感染(肺炎)的风险. 此外我们^[74]的近期研究还发现在全国城市范围内, 相对高温是导致儿童经常感冒的重要风险因素. 本文结论支持了儿童过敏与呼吸系统感染的胎儿起源假设, 对于儿童过敏症与感染性疾病的早期预防和风险控制提供了科学依据与有效策略.

以往流行病学研究存在一些不足与缺陷: (1) 由于流行病学通常采用问卷调查的形式, 这样会导致基于调查问卷的选择性偏差. 比如调查人群问卷回收率偏低或人群分布不均可能会导致相关疾病发病率存在一定误差; (2) 此类流行病学主要关注环境暴露与健康结局之间的相关性, 但对于可能存在的因果关系却没有从生物学机制上进行解释, 因此可靠性尚且存在质疑; (3) 以往研究主要关注环境污染物的暴露浓度(剂量)与疾病发病率之间的相关性, 但没有考虑不同来源污染物的毒性差异; (4) 此类流行病学研究对于早期污染物暴露究竟导致儿童体内哪些关键生物指标(生物标志物)明显超标, 从而显著增加发病风险尚不清楚, 且此类研究十分缺乏, 值得进一步深入研究.

根据当前关于早期环境空气污染物与儿童健康效应的研究现状, 建议如下: (1) 将来应拓展与深入研究不同来源颗粒物(如PM₁₀, PM_{2.5}, PM_{2.5-10}等)中各种化学组分的健康效应, 并进一步研究其致病机制; (2) 研究重污染(如雾霾)空气中生物组分特征对人们健康的影响, 为评估生物组分促炎症效应提供基础数据; (3) 研究能够与空气污染共同作用从而进一步增加过敏与感染发病风险的其他环境风险因素, 如气象参数(温度、湿度、降雨等)与极端气候的影响.

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Summary for “生命早期环境污染暴露增加学龄前儿童过敏与感染风险”

Early life exposure to environmental pollution increases childhood asthma, allergy and infection

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Allergy and infection have been exerted seriously adverse effect on children's health. On the one hand, asthma and allergy have become the most common chronic diseases in childhood and the leading cause of pediatric hospitalization worldwide. The prevalence of childhood asthma has considerably increased since the 1950s, with some suggestion of plateauing in developed regions but rapidly increasing in low- and middle-income countries over recent years. On the other hand, pneumonia as the most prevalent infectious disease is the leading cause of mortality in children under 5 years old globally. Approximately 99% of the pneumonia death occurs in developing countries. During recent decade, China has witnessed a rapid increase in the prevalence of childhood asthma and allergies and the morbidity of childhood infectious diseases such as pneumonia tend to be very high. Environmental exposure is thought to be the most important factor which is responsible for this rising trend and serious burden of childhood allergic and infectious diseases.

Ambient air pollution has been widely suggested to be associated with the incidence and prevalence of allergies and infections, and a distinct need is then to find out the key component of air pollution and the critical exposure window so as to develop more effective measures of prevention and intervention. A large body of evidence mainly from developed countries suggested that traffic-related air pollution (TRAP) plays a key role in the exacerbation and development of allergies and infections. However, differences in the chemical and physical composition of air pollution, both in level and source, between China and developed countries prompts the need for further investigation into the role of outdoor air pollution in the development of childhood allergic and infectious diseases.

On the other hand, due to the rapid urbanization progress in China, a huge number of people, especially the new couples and expected parents, migrated into new buildings in urban areas during the past decade. New building materials, decoration materials, and new furniture caused high indoor level chemicals, such as volatile and semi volatile organ compounds (VOCs and SVOCs). Due to lack of central air conditioning and heating systems, mold and dampness in dwellings is very serious in the southern China with subtropical climate. Thus, indoor environmental risk factors are also serious in China, which play important role in the rapid increase in the allergic diseases and high prevalence of infectious diseases in childhood.

Although the impact of environmental pollution on children's health has attracted wide attention and extensive research, some key scientific issues such as “main environmental pollutants, critical exposure windows, and whether the exposure cause diseases” still remain unclear. This paper summarizes the effects of prenatal (one year before pregnancy, entire pregnancy and three trimesters of pregnancy) and postnatal (first year, past year, and entire postnatal period) exposure to both indoor and outdoor environmental pollution on childhood allergic and infectious diseases, and also analyzed the relative importance of the critical exposure time windows for different diseases. We concluded that most studies mainly from developed countries found a positive association between traffic related air pollution and childhood allergic diseases. However, in China, early life exposure to classical air pollution (such as industrial air pollution) also exerts an adverse effect on childhood asthma and allergies. The recent studies identified relative importance of traffic-related air pollution exposure in different critical time windows (such as different trimester of pregnancy) in the development of different allergic diseases. This paper also concluded that early-life exposure to indoor mould/dampness and renovation significantly increased risk of childhood allergic and infectious diseases. According to the analysis of available literatures, this study proved the hypothesis of “fetal origins of disease” in children, and revealed that exposure to indoor and outdoor environmental pollution during pregnancy and early postnatal period played an important role in the onset and development of childhood allergic and infectious diseases, which provides a scientific basis for effective prevention and intervention strategies to reduce childhood allergies and infections. Finally, this study summarized the different influences, and expected the problems and challenges of effective prevention and reduction of childhood allergies and infections.

children, allergy, infection, air pollution, indoor renovation, early life exposure

doi: 10.1360/N972017-01346