

气候变化对儿童过敏性疾病的影响

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摘要:

气候变化已被广泛认为是 21 世纪全球健康的最大挑战与机遇, 可直接或间接影响人群健康, 尤其是敏感人群如儿童。近年来, 无论是发达国家还是发展中国家, 儿童过敏性疾病患病率明显增加, 越来越多的证据表明气候变化会影响儿童哮喘、过敏性鼻炎和过敏性皮炎等过敏性疾病的发生发展。本文综述了国内外关于气候变化影响儿童过敏性疾病的研究, 阐述了全球气候变化和变化模式, 以及其对儿童过敏性疾病的影响和可能的机制。得出气候变化通过影响气象因素、空气污染以及空气过敏原等直接或间接影响儿童过敏性疾病的发生和发展。因此量体裁衣地制定和实施适宜的应对策略和措施尤为重要, 可以进一步提高儿童健康水平, 促进社会经济发展。

关键词: 气候变化; 适应性策略; 儿童; 过敏性疾病

Impact of climate change on childhood allergic diseases HU Ya-bin^{1a}, LIU Shi-jian^{1a}, JIANG Fan^{1b}, YIN Yong^{1c}, LI Sheng-hui², YAN Chong-huai³, YU Guang-jun⁴, TAN Jian-guo⁵, TONG Shi-lu^{1a} (1.a.Department of Clinical Epidemiology and Biostatistics b.Department of Developmental and Behavioral Pediatrics, Pediatric Translational Medicine Institution c.Department of Respiratory, Shanghai Children's Medical Center, School of Medicine, Shanghai Jiao Tong University, Shanghai 200127, China; 2.School of Public Health, Shanghai Jiao Tong University, Shanghai 200025, China; 3.Shanghai Key Laboratory of Environmental and Child Health, Xinhua Hospital, School of Medicine, Shanghai Jiao Tong University, Shanghai 200092, China; 4.Shanghai Children's Hospital, Shanghai 200062, China; 5.Shanghai Climate Center, Shanghai 200030, China)

Abstract:

Climate change has been widely recognized as the biggest challenge and opportunity for global health in the 21st century. It can directly or indirectly affect the health of people, especially vulnerable groups such as children. In recent years, the prevalence of childhood allergic diseases stays pretty high, and accruing evidence shows that climate change can affect the development of allergic diseases among children, such as childhood asthma, allergic rhinitis, and atopic dermatitis. This paper reviewed the domestic and foreign literature on childhood allergic diseases associated with climate change, described global climate change and patterns of the change, its impact on childhood allergic diseases, and possible mechanisms. It was concluded that climate change affects the development of childhood allergic diseases directly or indirectly through affecting meteorological factors, air pollution, and air allergens. Therefore, it is especially important to develop and implement tailored strategies to cope with climate impacts, to further improve children's health and promote social and economic development.

Keywords: climate change; adaptive strategy; child; allergic disease

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气候变化指气候系统和状态的变化, 这种变化可根据气候特征的均值和/或变率的改变进行识别 (如采用统计检验方法), 而且这种变化会持续几十年或更长时间。气候变化主要由自然因素 (如太阳活动周期的改变、火山喷发) 或/和人类生产生活活动所造成^[1]。气候变化已被广泛认为是 21 世纪全球健康

的最大挑战与机遇^[2-4]。大量研究表明气候变化可直接或间接影响人群健康,尤其是一些敏感人群(如儿童、老人和慢性病患者等)^[5-7]。最近几十年,过敏性疾病在全球范围内普遍增加。相比于成人,儿童过敏性疾病更常见^[8],这主要是因为儿童肺部不成熟,80%的肺泡在出生后形成,肺部持续发育至青春期,幼儿的呼吸系统易受到损伤而引起哮喘等疾病的发生^[9-10]。

1 气候变化及变化模式

全球气候变暖是毋庸置疑的,而且主要是由人类生产生活活动所造成^[11]。自20世纪50年代以来,观测到的许多变化在几十年乃至几万年时间里都是前所未有的。大气和海洋变暖,积雪和冰川减少,海平面上升^[1]。2017年与工业革命前水平相比,人为导致的全球变暖已达到约1℃,最近几十年以来每十年约增加0.2℃^[11]。

气候变暖导致积雪和冰川融化,使得海平面上升。并导致降水模式改变,使得部分地区发生强降水,继而引发洪水;而在另外一些地区可能会造成降水减少、天气炎热,从而引发干旱、热浪以及森林火灾等极端天气事件的频发^[1, 4-5, 12-16]。气候变化还会增加部分地区雷雨天气的频率^[6]。欧洲最近的研究表明,全球变暖2℃会导致欧洲中部和北部冬季平均降水量明显增加,从而使得洪水频发;夏季只有北欧降水量增加,中欧和南欧则明显减少^[17-19]。自1950年以来,全球温度逐渐上升,大多数世界上较大河流的水流量变化趋势虽不具有统计学意义,但是一些区域洪水发生频率和极端流量显著增加^[20]。同时还有研究表明地中海和西非地区干旱的发生明显增加,而北美中部和澳大利亚西北部则减少^[21-22]。温室气体浓度升高导致的气候变化会增加城市热岛效应,并造成部分区域空气污染加重。气候变化还会引起花粉、尘螨、霉菌孢子等的改变^[23-24]。

“巴黎协定”的核心目标是保持21世纪全球气温上升不超过工业化前水平的2℃。气候变化对全球范围内的社会经济和人口健康产生负面影响,且随着气候变化的增加,风险将增加。据估计,到2030年,气候变化将导致每年25万人死亡^[25]。一项在23个具有不同气候区国家的451个地区进行多区域分析,假设人口分布和脆弱性没有变化,并在符合“巴黎协定”目标(1.5℃和2℃)和更极端全球平均温度增加的情景(3℃和4℃)下评估了热和冷相关死亡率的变化,

研究表明将变暖限制在2℃以下可防止全球大多数地区温度相关死亡率大幅上升^[26]。气候变化导致洪水、干旱和森林大火等极端自然事件发生以及海平面上升而迫使移民增加,直接造成生命和财产的损失^[27-31]。气候变化还可通过影响人类疾病(尤其是敏感人群如儿童)的发生发展,间接造成家庭和社会巨大的经济负担,影响儿童健康和社会经济发展^[32-36]。

2 气候变化对儿童过敏性疾病的影响

哮喘、过敏性鼻炎和过敏性皮炎(也称湿疹)是儿童的主要过敏性疾病。越来越多的研究证据表明气候变化直接或间接影响儿童过敏性疾病的发生和发展^[5-7]。儿童哮喘和过敏性疾病的国际研究(International Study of Asthma and Allergies in Childhood, ISAAC)第一阶段调查了世界各地不同人群中哮喘、过敏性鼻炎和湿疹的症状和严重程度,并确定了影响这些疾病的因素,发现相比于遗传因素,环境因素可能是儿童过敏性疾病最重要的驱动因素^[37-39]。目前,无论是发达国家还是发展中国家,儿童过敏性疾病越来越多,因此受到广泛关注和重视。加拿大一项针对一年级儿童的横断面研究显示,哮喘、过敏性鼻炎和湿疹患病率分别为15.9%,6.8%和20.5%^[32]。亚洲人群(全人群,包括儿童)的哮喘、过敏性鼻炎和湿疹的患病率在过去的二十年中显著上升^[34]。我国一项多中心横断面研究分析了中国八大城市(上海、广州、武汉、西安、哈尔滨、成都、呼和浩特和乌鲁木齐)6~13岁的儿童哮喘、过敏性鼻炎和湿疹等过敏性疾病,发现平均患病率依次为3.3%(95%CI:3.1, 3.6)、9.8%(95%CI:9.4, 10.2)和5.5%(95%CI:5.2, 5.8)^[40]。ISAAC第一阶段至第三阶段研究均发现无论是不同经济水平的国家之间还是同一国家不同地区之间,儿童过敏性疾病都存在显著的地区差异^[33, 38]。同时,气候因素和过敏性疾病密切相关,全球气候变化也存在显著的区域性差异。因此,探讨引起全球儿童过敏性疾病负担增加的危险因素,明确气候变化在其中发挥的作用,进而制定有效的预防和控制儿童过敏性疾病的干预策略,对保护儿童健康,贯彻健康中国的战略国策至关重要^[41]。

2.1 哮喘

哮喘是一种最常见的慢性非传染性疾病,影响全世界约2.5亿人,造成持续性的疾病负担^[34-35],尤其对于儿童^[36]。暴露于大气环境中的过敏原如尘螨、

花粉、霉菌和动物皮屑等与哮喘密切相关,是儿童过敏性气道疾病发生发展、持续和加重的一个重要危险因素^[42-43]。

环境温度与儿童哮喘发生的关联越来越受到关注^[44-45],尤其是在气候变化的背景下^[46]。随着气候变化的进展,全球表面温度将升高^[1],炎热天气(如热浪)的频率、持续时间以及强度也会增加^[47]。这些均可能导致高温相关的儿童哮喘疾病负担增加,尽管低温相关的儿童哮喘疾病负担可能减少。众多学者采用绝对温度探讨对儿童哮喘的短期影响^[24, 44-45, 48-57],也有不少学者研究了日内或日间温度变化对儿童哮喘的短期影响^[58-62]。一项涉及美国3个州的研究显示,季节性哮喘症状加重时间多为秋季(尤其11月)和春季^[63]。研究证明雷雨天气与哮喘症状加重相关,导致急诊增加,死亡率升高^[64-66]。近期,香港的一项研究表明在寒冷季节,低温和低湿度更易引起哮喘住院人数增加^[45]。Pollock等学者^[67]对北美33篇文献进行系统综述表明,PM_{2.5}、CO和花粉与儿童哮喘发生密切相关。布鲁塞尔首都地区一项研究显示,暴露于草、桦树和角树的花粉可明显提高哮喘住院率,提高率依次为5.9%(95%CI:0.0~12.0);3.2%(95%CI:1.1~5.3)和0.7%(95%CI:0.2~1.3)^[68]。Sanchez等^[69]研究发现城市儿童哮喘患病率显著高于农村儿童。

2.2 过敏性鼻炎

过敏性鼻炎(allergic rhinitis, AR)是一类由IgE介导的鼻黏膜释放免疫细胞因子或炎症因子等的上呼吸道免疫疾病,主要表现为鼻痒、鼻塞、阵发性喷嚏和清水样涕,可伴有眼红、眼痒、流泪等症状。

AR已成为全球性的公共卫生问题,困扰全世界10%~40%的人口^[70-72]。一项包含世界4个地理区域(亚洲、欧洲、美洲和非洲)的横断面研究显示,AR患病率为15%~25%,儿童最易感。其中最常见的气体致敏原为花粉和螨虫,占67.3%^[73]。韩国一项涉及14 678名儿童的横断面研究发现,22%患有AR。其中室内尘螨致敏率最高,达86.8%;其次为花粉(38.7%)和霉菌(13.5%)^[74]。我国一项包含内蒙古6个不同地区的研究表明,AR患病率为32.4%,其中花粉诱导的AR为18.5%。城市区域花粉诱导的AR患病率高于非城区(23.1%比14.0%, $P<0.001$);同时,花粉诱导的AR临床症状与花粉量、温度和降水量呈正相关,而与风速和气压呈负相关^[75]。长春一项研究表明,SO₂、NO₂、PM₁₀和PM_{2.5}暴露会增加当天AR患病风

险,CO暴露与AR患病风险存在4d的滞后效应^[76]。与农村儿童相比,生活在城市地区的儿童患鼻炎的风险增加^[75, 77-79],尤其在空气污染暴露程度较高和车辆交通密集区域。最近的研究也表明暴露于高浓度PM_{2.5}与AR患病率升高显著相关^[76, 80-81],同时AR相关的住院率也增加^[82]。国内邹祺缘等学者^[83]对近15年来室内空气污染与过敏性鼻炎发病关联的文献进行meta分析,发现霉菌暴露会造成AR发病风险显著上升。

2.3 过敏性皮炎

过敏性皮炎(atopic dermatitis, AD),是一种慢性炎性皮肤病,多发于儿童早期。近期研究表明,全世界儿童AD患病率为15%~20%^[84]。在发达国家和发展中国家,过敏性皮炎的患病率仍在增加^[85-86]。美国一项关于儿童的前瞻性队列研究发现,长期气候变化会造成AD患病率增加,尤其在高温和阳光暴露增强时^[87]。韩国一项5岁以下儿童的研究表明昼夜温差大于14℃时,每上升5℃会造成AD患病风险增加284.9%(95%CI:67.6%~784.2%)。低温和低湿度也会加重儿童AD症状^[88]。同时,PM₁₀、NO₂和O₃每增加10个单位,当天AD患病风险会分别增加3.2%(95%CI:1.5%~4.9%)、5.0%(95%CI:1.4%~8.8%)和6.1%(95%CI:3.2%~9.0%)^[88]。法国一项追踪儿童3年以上的研究也表明,PM₁₀、NO₂和CO等空气污染物与AD的发生密切相关^[89]。最近Bonamonte^[90]和Nguyen^[91]等人的系统综述表明,气象因素(温度、日照或紫外线暴露和湿度)以及气候变化导致的环境污染都与儿童过敏性皮炎的发生和发展关系密切。

3 可能机制

基因^[92]和环境因素^[93-94],以及基因-环境交互作用^[95-96]都与儿童过敏性疾病的发生有明显关联。人群中存在共有的哮喘遗传因子^[92]。室内外环境污染物和过敏原与儿童哮喘的发生直接相关^[93-94]。基因-环境交互作用与儿童哮喘的研究发现,腺苷酸环化酶2(adenylate cyclase 2, ADCY2)、 β -1,4半乳糖基转移酶V(β -1, 4-galactosyltransferase 5, B4GALT5)、鸟苷酸激酶DLG2(discs large homolog 2)与空气污染相互作用,可引发哮喘的发生^[95]。尘螨过敏原暴露改变了rs117902240对哮喘患儿FEV1的预测作用^[96]。如图1所示,气候变化对儿童过敏性疾病发生的可能作用机制主要包括直接和间接的路径。

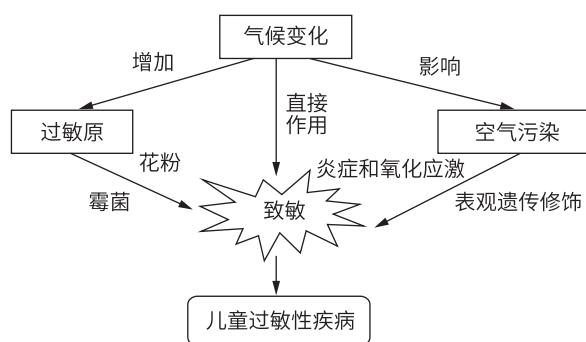


图1 气候变化对儿童过敏性疾病发生的可能作用途径

3.1 气候变化直接作用于儿童过敏性疾病

大量研究发现气温（高温、低温和温差）都会对儿童过敏性疾病造成影响^[44-62, 75, 88-89]。高温会激活迷走神经支气管肺纤维C-纤维感觉神经，引起反射性支气管收缩，影响呼吸系统。而低温通过降低肺功能和肺活量显著抑制人体免疫系统^[97]，有利于呼吸道病毒的存活和运输，增加呼吸道炎症，导致呼吸道狭窄等来影响哮喘的发生和恶化^[98]。温度变化主要通过炎症介质释放和影响体液或细胞免疫对儿童哮喘产生影响^[99]。Graudenz等学者^[100]观察到突然的温度变化会引起过敏性鼻炎患者更严重的炎症反应。温度过高、日照或紫外线暴露过多以及干燥的气候（湿度低）会引起皮肤屏障受损，导致人免疫系统水平下降，更易发生AD^[91]。而适量的日照或紫外线暴露有利于机体维生素D的产生，对AD患者起保护作用^[101]。

3.2 气候变化通过影响空气质量作用于儿童过敏性疾病

环境空气污染和室内空气污染都会引发呼吸道感染。2016年环境空气污染导致420万人过早死亡；其中，5岁以下儿童死亡人数达54.3万^[102]。2016年室内空气污染导致380万人过早死亡，其中超过40万名是5岁以下儿童^[103]。儿童特别容易受到空气污染影响，尤其是胎儿发育期间和儿童早期。他们的肺、器官和大脑仍在发育，他们在户外污染空气中玩耍和活动时间较多，身高刚好处于一些污染物峰值浓度的水平，比成人呼吸更快，更多用嘴呼吸，随之吸入更多污染物。与此同时，新生儿和婴儿大部分时间都在室内，如母亲用污染的燃料和设施做饭，他们更容易受到室内空气污染的影响。

众多研究发现暴露于空气污染物（SO₂、NO₂、CO和PM_{2.5}等）都与儿童哮喘的发生呈正相关^[8, 57-58, 104-109]。

最近，我国一项涉及7个城市39782名参与者的研究表明，室外NO₂和PM₁₀可增加学龄前儿童（3~6岁）哮喘、喘息、鼻炎和湿疹的风险^[110]。气候变化可通过影响空气污染对个体产生刺激，使机体炎症反应和氧化应激反应加剧，产生不良健康效应^[111]。空气污染物的水平（如O₃）在高温天气可能会更高^[112]，高水平的空气污染可能直接触发儿童哮喘的发生^[113]。炎症和氧化应激是已知的空气污染有害影响的作用机制。通过减缓气候变化来减轻空气污染，可以改善人群健康和福祉。在一项生活在高污染环境中哮喘儿童的研究中，高浓度的SO₂、NO₂和苯与支气管炎、氧化损伤生物标志升高及哮喘症状加重相关^[114]。另一项研究表明，DNA的表观遗传修饰在空气污染和儿童哮喘中发挥重要作用^[115]。同时，DNA甲基化模式在哮喘儿童肺损伤与空气污染中的作用已被证实^[116]。也有研究表明DNA甲基化通过改变生命早期基因表达在产前暴露多环芳烃和儿童哮喘的发展中发挥作用^[114]。

3.3 气候变化通过影响过敏原作用于儿童过敏性疾病

全球变暖是显而易见的，主要由CO₂、CH₄和N₂O等温室气体排放和积累导致^[1]。现在有令人信服的证据表明，过去几十年由于全球变暖导致二氧化碳排放和降雨模式改变，从而造成一些植物花粉产量增加、致敏性提高和花粉季节延长，以及世界各地的室内霉菌浓度提高^[117-121]。

花粉和霉菌是主要的吸入性过敏原，可以促进过敏性疾病。气候变化会影响这些过敏原的水平和分布，从而影响儿童哮喘和过敏性疾病的发生和加重^[43]。高温和高浓度CO₂会引发众多植物开花提前、花期延长，导致花粉产量上升、分布更广，从而使致敏程度更严重^[23]。Hashimoto等学者^[24]发现高温可以促进室内空气过敏原生长和暴露，如霉菌孢子和蟑螂。澳大利亚的研究发现气候变化可以通过空气过敏原诱发哮喘和过敏性鼻炎等疾病发生^[23, 122]。

4 小结

过敏性疾病严重影响儿童的身心健康，并对家庭和社会造成巨大的压力。气候变化可直接或间接地影响这些疾病的发生和发展，但目前这一领域尚缺乏系统的定量化研究。因此，探索气候变化与儿童主要过敏性疾病的定量关系和可能作用机制，并据此提出和评估气候变化适应性应对策略，对进一步提高儿童健康水平，促进社会经济发展具有重要意义。

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