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点 评

大气颗粒物对健康的影响

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近年来研究发现, 大气颗粒物严重影响人体健康, $PM_{2.5}$ 每年造成 80 万人死亡, 排在所有致死因素的第 13 位[1]. 大气颗粒物是悬浮于空气中颗粒的总称, 按照其空气动力学粒径分为总悬浮颗粒物(TSP, 空气动力学直径小于 100 μm, 下同)、可吸入颗粒物(PM_{10})、细颗粒物($PM_{2.5}$)和超细颗粒物($PM_{0.1}$)[2]. 不同粒径颗粒物随呼吸分布在呼吸道不同位置[3,4]. PM_{10} 通常沉积在上呼吸道、气管和主支气管中, $PM_{2.5}$ 主要沉积到细支气管、肺泡[2], $PM_{0.1}$ 经嗅球进入中枢神经系统, $PM_{0.1}$、颗粒物可溶组分及诱导肺部产生的炎症因子进入血液循环[5], 作用于其他组织器官, 引起氧化应激和炎症反应, 导致机体损伤[6]. 因此, 大气颗粒物对健康的影响受到社会各界的密切关注. 本文主要综述大气颗粒物对健康的影响及其作用机制.

1 大气颗粒物对健康的影响

(1) 大气颗粒物对呼吸系统的影响. 大量流行病学研究表明, 大气颗粒物暴露与慢性阻塞性肺病、支气管炎、哮喘等呼吸系统疾病发生密切相关[7], 尤其是老人、儿童以及哮喘患者等易感人群对大气颗粒物十分敏感[8~10]. 近期研究显示, 大气颗粒物也与肺癌的发生相关[11~13]. 2013 年国际癌症研究机构已将大气污染确定为致癌物[14].

(2) 大气颗粒物对神经系统的影响. 颗粒物的急性暴露影响植物性神经功能, 降低副交感神经的信号传导, 影响心血管等器官的运动[15]. 急性颗粒物暴露还与中风发病率相关, PM_{10} 每增加 10 μg/m^3, 中风的住院率增加 1%[16].

长期高浓度颗粒物暴露影响机体认知能力. Ranft 等人[17]发现, 交通源颗粒物损伤老年人的认知能力. 高浓度颗粒物暴露易导致儿童、成人和老年人的认知能力下降、嗅球功能紊乱、听力损伤、抑郁等[18,19]. 此外, 自闭症与交通源颗粒物的暴露相关[20~22]. 儿童长期暴露颗粒物后, 其与神经退行性疾病相关的β淀粉样肽、Tau 蛋白磷酸化和α-突触核蛋白的水平显著升高[23,24]. 动物实验结果也显示, 小鼠暴露 $PM_{2.5}$ 10 个月后, 其学习能力和记忆能力受到明显影响, 出现焦虑和抑郁行为[25].

(3) 大气颗粒物对心血管系统的影响. 颗粒物急性暴露后心率、心率减速能力和心率变异性发生显著改变[26]. 颗粒物影响血压和血管直径, PM_{10} 增加 34 μg/m^3, 志愿者的收缩压增加 0.47 mm Hg[27], 暴露于 200 μg/m^3 柴油机尾气颗粒物(diesel exhaust particles, DEP) 2 h 后, 志愿者肱动脉直径减小 0.11 mm[28]. 此外, 颗粒物升高血小板黏稠度[29], 缩短凝血时间[30], 上调凝血因子水平[31].

长期高浓度颗粒物暴露降低血管舒张能力[32]和促进动脉粥样硬化的形成[5]. Wilker 等人[33]发现 $PM_{2.5}$ 增加 1.9 μg/m^3, 血管舒张能力减小 0.16%, 血流速度降低 0.72 cm/s. Kunzli 等人[34]发现, $PM_{2.5}$ 浓度每增加

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10 μg/m^3, 颈动脉的血管内膜增厚 5.9%. 4494 例长期暴露机动车尾气 $PM_{2.5}$ 的人群研究显示, 10.2%个体出现冠状动脉钙化[35]. 载脂蛋白-E 基因缺陷型小鼠和 Watanabe 高脂兔长期暴露 $PM_{0.1}$ 和 $PM_{2.5}$ 或经支气管灌流 PM_{10} 后, 动脉粥样硬化斑块体积显著增加[36~38].

(4) 大气颗粒物对生殖发育的影响. 研究表明, DEP 暴露后大鼠的精子数量和活性均降低[39], 受精能力受到影响. Slama 等人[40]研究显示, $PM_{2.5}$ 每升高 10 μg/m^3, 受精能力下降约 22%. DEP 引起小鼠 X 染色体失活和特异转录子表达[41]. 此外, 交通源 $PM_{2.5}$ 引起小鼠生育率下降和胎鼠体重减轻, 而且在怀孕前和怀孕期间暴露 $PM_{2.5}$, 胎鼠体重下降明显[42]. 人群研究结果也显示, $PM_{2.5}$ 的浓度每升高 5 μg/m^3, 低体重婴儿的出生率约为 1.18%, 如果 $PM_{2.5}$ 降低 10 μg/m^3, 低体重婴儿的出生率将减少 22%[43].

(5) 大气颗粒物对内分泌系统的影响. 流行病学调查结果显示, 大气颗粒物与 2 型糖尿病的发病相关. 研究表明, $PM_{2.5}$ 浓度升高与 2 型糖尿病的发病率上升呈正相关性[44~46]. 另外, $PM_{2.5}$ 可诱发 1 型糖尿病和妊娠糖尿病[47,48], 并升高糖基化血红蛋白水平[49]. 急性颗粒物暴露诱发酮症酸中毒等糖尿病急性并发症[50]. 亚急性低浓度 $PM_{2.5}$ 暴露引起机体胰岛素抵抗[51]. 动物研究结果也证实, 小鼠长期暴露 $PM_{2.5}$ 后, 其葡萄糖耐量水平下降, 肝糖原合成减少[52], 胰岛素抵抗指数显著升高[53].

糖尿病患者更易受到颗粒物的影响, 研究显示颗粒物暴露后糖尿病患者的心率变异性变化显著[54], 血液中炎症因子水平上调[55], 死亡率明显升高[56]. DEP 处理 1 型糖尿病小鼠后, 其肺泡灌洗液中肿瘤坏死因子-α、白蛋白和总蛋白水平显著较高, 超氧化物歧化酶活性和还原型谷胱甘肽浓度明显降低, 肺部出现大量凋亡细胞[57], 血液中血小板数量和聚集增加, 纤溶酶原活化因子抑制剂和血管性血友病因子明显升高[58].

颗粒物影响脂肪组织、垂体、下丘脑的分泌功能. 研究发现, $PM_{2.5}$ 降低脂肪组织分泌脂联素和瘦素, 减少脂肪组织的线粒体体积和数量[52], 引起小鼠白色脂肪组织内脂肪沉积[59], 内脏脂肪含量升高[60]. 此外, $PM_{2.5}$ 暴露改变了大鼠大脑垂体内皮激素和一氧化氮合酶基因表达量[61]. DEP 升高胎鼠下丘脑去甲肾上腺素分泌水平, 脑组织中多巴胺和 5-羟色胺含量也发生变化[62].

2 大气颗粒物对健康影响的作用机制

目前, 大气颗粒物诱导的氧化应激和炎症反应被认为是影响健康的主要作用机制. 颗粒物暴露后能够诱发多个组织产生炎症反应和氧化应激, 如肺部、血液、大脑、脂肪、肝脏等组织中炎性细胞数量增加, 炎症因子水平升高, 活性氧自由基(reactive oxygen species, ROS)生成增加, 氧化应激相关信号通路被激活, 超氧化物歧化酶、血红素加氧酶-1 等抗氧化酶活性改变[51,59,63~65]. 体外实验也证明, 大气颗粒物及其组分能够上调不同细胞内 ROS 水平, 引起氧化应激[66~68]. 研究发现, 炎症反应和氧化应激是相互诱导的, 炎症因子可增加细胞内 ROS 生成, 引起细胞氧化应激[69], 而氧化应激又可导致细胞炎症反应[70]. 因此, 颗粒物一方面可通过颗粒物及其可溶组分直接作用于组织器官, 引起炎症反应和氧化应激; 另一方面通过诱导肺部的炎症因子进入血液循环, 经血液分布到各组织, 引起氧化应激, 诱导组织炎症发生, 最终导致健康损害.

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