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蠕虫及肠道原虫感染与肠道菌群关系研究进展

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[摘要] 肠道菌群是人体最大最复杂的生态系统，与肠道病毒和寄生虫等共同栖息在人或动物肠道内。已有研究表明，肠道菌群紊乱与多种疾病的发生、发展及预后密切相关。定植在宿主体内的寄生虫可直接或间接影响肠道菌群及其与机体的相对稳态，而肠道菌群结构及多样性的改变也会影响寄生虫感染及疾病的发生、发展和预后。本文就蠕虫及肠道原虫与肠道菌群相互关系研究进展作一综述。

[关键词] 蠕虫；肠道原虫；肠道菌群

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Progress of research on the interplay between helminth and intestinal protozoa and gut microbiota

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[Abstract] As the largest and most complex ecosystem in humans, gut microbiota resides in human or animal gastrointestinal tract with intestinal viruses and parasites. Previous studies have demonstrated that gut microbiota dysbiosis is strongly correlated with the development, progression and prognosis of multiple diseases. The parasites that are colonized in the host, may directly or indirectly affect gut microbiota and the gut microbiota-host homeostasis, and changes in the composition and diversity of gut microbiota may also affect parasitic infections and the development, progression and prognosis of parasitic diseases. This paper reviews the progress of research on the interplay between helminth and intestinal protozoa and gut microbiota. ;

[Key words] Helminth; Intestinal protozoa; Gut microbiota

寄生虫感染引起的寄生虫病一直是全球，尤其是发展中国家普遍存在的公共卫生问题，对人类健康与社会经济发展造成了严重危害[1]。目前尚无有效的寄生虫病疫苗[2]。因此，深入了解影响寄生虫病发生发展的因素，可以为寄生虫病防治提供参考依据。寄生在胃肠道系统内的蠕虫、原虫与肠道微生物群落共享一个肠道微环境，可通过改变肠道生理特征、渗透性以及抗菌肽产生等，直接或间接改变肠道菌群构成[3-4]；而肠道菌群的改变同样影响寄生虫在宿主体内的定植、感染状态及寄生虫病治疗等[5-9]。目前，寄生虫感染与肠道菌群相互关系研究尚处于早期阶段。本文主要就蠕虫及肠道原虫与肠道菌群相互关系研究进展作一综述。

1 蠕虫及肠道原虫概述

蠕虫主要包括吸虫、绦虫和线虫。据估计，全球约有4 500万人感染肝吸虫，7亿人存在肝吸虫感染风险；感染者中约3 500万人感染华支睾吸虫（1 500万人在中国），1 000万人感染麝猫后睾吸虫[10-11]。麝猫后睾吸虫与华支睾吸虫同属后睾吸虫科，主要因食用含有囊蚴的生的或者未煮熟的鱼而感染，成虫主要寄生在人体肝胆管内，慢性反复感染可致胆管癌，被国际癌症肿瘤机构列为I类致癌物[12-13]。泰国一项研究发现，肝吸虫感染可导致约70 745～138 221个伤残调整寿命年(DALYs)损失，其中33%～64%损失来

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自胆管癌[14]。后睾吸虫病及胆管癌可造成泰国每年至少1.2亿美元损失[15]，对国家社会经济造成严重损失。血吸虫病主要通过接触含有血吸虫尾蚴的疫水而感染，是全球性人兽共患寄生虫病，全球感染者约2亿例，超过8亿人面临血吸虫感染威胁，造成约153万DALYs损失[16-17]。线虫在自然界分布较广泛，据估计全球约有45亿人感染土源性寄生虫，其中约12亿人感染蛔虫、8亿人感染鞭虫、7亿人感染钩虫[18]。严重线虫感染者出现胃肠道不适症状和贫血，甚至引起儿童发育迟缓及认知障碍[19]。肠道线虫可通过直接或者间接方式损伤肠道黏膜，影响并改变肠道微环境[20]。

水源性肠道传染病目前仍是世界上影响发病率和死亡率的主要原因，每年造成超过220万人死亡，主要表现为腹泻和胃肠道疾病[20]。目前，腹泻每年可致842 000人死亡，是5岁以下儿童死亡的第二原因[21-22]。2014年WHO报告，在中低收入国家腹泻可致约33 793个DALYs损失[23]。水源性肠道原虫[如隐孢子虫和贾第鞭毛虫（简称贾第虫）等]可在肠道无氧环境中生存，是导致腹泻的主要原因[23]。隐孢子虫为世界六大腹泻病病原之一，被列为撒哈拉以南非洲和南亚腹泻病的第二大最重要病原[22]。贾第虫是“旅行者腹泻”的病原之一；埃塞俄比亚一项研究显示，13.8%的腹泻病人临床样本检测为贾第虫阳性[24]。2010年，由隐孢子虫、贾第虫和溶组织内阿米巴感染所致疾病约3.57亿人，致33 900人死亡以及294万DALYs损失[25]。已有研究发现，肠道原虫与肠道黏膜上的微生物群落及机体免疫系统相互作用，共同影响疾病发生、发展和宿主临床表现[26-27]。

目前，寄生虫病仍是一些国家，甚至全世界的公共卫生问题，造成较为严重的疾病负担，但是寄生虫具体致病机制至今仍不清楚。寄生虫病的发生主要与寄生虫毒力及宿主免疫状态及其两者的相互作用有关[28]。目前研究发现，肠道菌群也参与了寄生虫病的发生发展[29]。Ⅱ型免疫反应是机体抵抗肠道寄生虫感染的主要免疫反应，肠道菌群可通过Ⅱ型细胞因子、树突状细胞以及调节性T细胞影响Ⅱ型免疫反应[30]，进而影响宿主对肠道寄生虫的抵抗。此外，肠道菌群也影响肠道肠道寄生虫病的进展与结局，甚至可以抵抗某些肠道寄生虫感染[31]。

2 肠道菌群概述

微生态在20世纪80年代首次提出，肠道微生态是人体最大最复杂的生态系统。人体微生物群是由存在于人体不同部位（如皮肤、阴道、口鼻、食管和胃肠道）的微生物群落组成[32]，肠道微生物所编码的基因数量约是人体自身基因的150倍，其中99%以上来自肠道细菌[33]。肠道菌群是由数千种不同的微生物和15 000多种细菌组成，其数量约等于人体细胞总数量，构成肠道第一道保护屏障[34-35]，并在肠道免疫系统发育、营养物质代谢、吸收和人体必需维生素的产生等方面发挥着重要作用[36-37]。

人体肠道菌群在出生时开始建立，3岁左右肠道菌群结构及多样性达到成人水平，并在机体内构成微生态平衡，与机体保持相对稳定的状态，这种稳态会受到年龄、饮食结构和宿主基因型等因素的影响[38-40]。肠杆菌、肠球菌以及乳酸杆菌最早定植在肠道内，老年时肠道菌群组成及物种丰度会发生改变，包括肠杆菌丰度增加、拟杆菌与乳酸杆菌丰度降低[34]。不同饮食习惯的人群，肠道菌群结构也不相同。长期食用以蛋白质、脂肪为主的人群，其肠道内拟杆菌属的比例相对高；食用以糖类为主的人群，普氏菌占主导地位[38]。

肠道菌群失调是指肠道内正常菌群比例失调或者肠道菌群移位[41]。研究发现，肠道菌群失调与许多疾病的发生、发展密切相关[31]。肠道菌群通过微生物-肠道-大脑轴介导肠道炎症细胞增多，加快肠应激综合征发展[42-44]；肠道菌群结构改变会加快慢性炎症性疾病[45]、慢性非传染性疾病（动脉粥样硬化、Ⅱ型糖尿病和高血压等）[46]和肥胖等疾病进展；肠道菌群还可作为肠道炎症、糖尿病和肥胖等疾病辅助诊断以及预后的生物标志物[39, 45-46]。此外，肠道菌群失调与寄生虫感染状态及治疗预后密切相关[47]。枯草芽孢杆菌、鼠李糖乳杆菌和荧光假单胞菌形成的生物膜能诱导某些寄生虫的抗应激能力[49]。而肠道菌群的组成及结构改变也影响寄生虫感染定植、寄生虫毒力、宿主临床表现和治疗预后[6, 49-50]。

3 蠕虫感染与肠道菌群相互作用

3.1 华支睾吸虫 华支睾吸虫成虫主要寄生在人体肝胆管系统，可改变胆汁组成成份，同时影响胆囊表面活性蛋白D合成[51]，流入肠道的胆汁成分改变及表面活性蛋白D缺失影响肠道菌群结构及多样性[52-53]。感染华支睾吸虫的脊椎动物肠道菌群变化主要表现为α多样性显著增加，乳酸菌、双歧杆菌数量减少以及致病菌肠杆菌、肠球菌数量增加[54-55]。拟杆菌与乳酸杆菌可刺激机体黏膜产生IgA抗体，乳酸菌还可调节树突状细胞，激活自然杀伤性细胞[56]；乳酸菌及拟杆菌丰度降低，影响肠道免疫对华支睾吸虫感染的抵抗。华支睾吸虫感染人群粪便样本中检测到存在于

外环境中的致病菌贪噬菌属[55]，该菌属在麝猫后睾吸虫感染与肠道菌群相互作用研究中发现，其可能会促进麝猫后睾吸虫感染所致的胆管癌发生[57-58]。这些存在于华支睾吸虫感染者体内的外环境菌群是否也具有促进胆管癌的发生，有待进一步研究和验证。此外，研究发现，华支睾吸虫感染的小鼠肠道菌群向肝脏器官移位，可能参与了华支睾吸虫所致肝损伤过程[59-60]。

3.2 麝猫后睾吸虫 与华支睾吸虫同属于后睾吸虫科的麝猫后睾吸虫成虫亦寄生于宿主肝胆管内，严重感染者可导致胆管癌，其感染所致肠道菌群变化与华支睾吸虫感染宿主肠道菌群变化相似。麝猫后睾吸虫感染仓鼠肠道菌群α多样性显著增加，菌群结构发生改变，潜在病原体肠杆菌科与李斯特菌科丰度增加[11]。此外，研究发现仓鼠体内感染的麝猫后睾吸虫菌群组成与其寄生宿主胆管内胆汁菌群组成相似，并且在感染组仓鼠粪便中检测到存在于水、土壤等外环境中的一些致病菌（如黄杆菌属、鼠球菌属以及贪噬菌属）丰度显著增高；有些研究认为麝猫后睾吸虫感染后所致肠道菌群紊乱可促进胆管癌发展[57-58, 61]。

3.3 曼氏血吸虫 曼氏血吸虫主要寄生于人或哺乳动物肠系膜静脉内，感染引起机体免疫系统改变，以及肠道、门静脉系统、肠系膜静脉系统损伤；结肠和肝脏是主要受损器官，严重可致肝硬化[62]。曼氏血吸虫虫卵在肠壁迁移，影响肠道菌群相对稳态。慢性曼氏血吸虫感染小鼠肠道菌群发生移位，在血吸虫感染肉芽肿形成、血吸虫特异性免疫反应中发挥重要作用[63-64]。同时，肠道菌群结构及多样性影响血吸虫虫卵排出及疾病进程[63, 65]。曼氏血吸虫感染宿主肠道菌群α多样性显著下降[63]。感染曼氏血吸虫28 d的小鼠肠道乳杆菌科丰度显著增加，该菌种的增加可能介导并促进曼氏血吸虫慢性感染的建立[63]。Reynolds等[9]也发现乳酸杆菌可提高具有免疫抑制功能的Treg细胞数量，以利于肠道蠕虫在肠道建立，并加重肠道蠕虫的易感性。此外，曼氏血吸虫感染小鼠肠道椰子菌丰度显著增加[63]，一般认为肠道椰子菌丰度与肠道炎症密切相关[66-67]，该菌种的增加可能是曼氏血吸虫感染引起的肠道炎症所致。也有研究发现，肠道菌群结构影响曼氏血吸虫病治疗，表现为感染曼氏血吸虫的儿童肠道梭菌属丰度越高，在治疗24 h后该细菌丰度的下降率越大，吡喹酮治疗效果越好[7,50]。

3.4 蛔虫 蛔虫成虫寄生于人体小肠中，可通过在宿主肠道分泌一些抗菌活性物质（如凝集素、抗菌肽和溶菌酶等）破坏肠道菌群形成的生物膜等方式改变肠道菌群结构，以利于其在肠道定植[68]。研究发现，给猪喂食富含多酚的食物可显著改变肠道菌群结构并增强宿主对蛔虫感染的免疫反应，但不能改变猪蛔虫在肠道的定植[6, 9]。Jang等[70]也发现给予猪喂食益生菌可调节肠道免疫系统对蛔虫的抵抗，延迟幼虫排出肠道。而目前尚未见人体蛔虫感染与肠道菌群关系的研究。

3.5 鞭虫 鞭虫是一种在哺乳动物体内较为普遍的线虫，主要寄生在宿主大肠内。研究发现，肠道菌群对小鼠体内鞭虫慢性感染的建立发挥着重要作用，并影响鞭虫虫卵的孵化及成功定植[6, 9]。Leonardi等[71]发现鞭虫虫卵可通过保护盲肠组织以及预防肠道菌群多样性降低，使无免疫抑制的新西兰大白兔免受硫酸葡聚糖钠所致结肠炎。鞭虫感染诱导的Th2型免疫反应可抑制拟杆菌定植，保护克罗恩氏病易感基因Nod2缺乏小鼠免受肠道失调，同时促进梭菌属增加；而进行鞭虫驱虫治疗后，小鼠肠道梭菌属降低，拟杆菌增加[72]。在鞭虫感染的厄瓜多尔儿童中，并未发现感染所致肠道菌群改变，但鞭虫与蛔虫合并感染儿童肠道菌群多样性降低、菌群结构也有变化[73]。

Myhill等[74]发现肠道菌群改变可能介导猪鞭虫与含有生物活性成分（如菊粉）的饮食相互作用的抗炎免疫反应增强；给感染猪鞭虫的猪喂食菊粉，可增加猪肠道拟杆菌门和厚壁菌门比例、降低肠道pH值、提高肠道益生菌数量。慢性腹泻猕猴给予鞭虫感染后，猕猴肠道菌群结构发生显著改变，木霉属丰度显著降低、厚壁菌门丰度显著增加，提示蠕虫可通过恢复黏膜屏障功能、减少细菌附着以及改变肠道菌群结构而改善肠炎[75]。

3.6 粪类圆线虫 粪类圆线虫主要寄生于人、犬和猫等宿主小肠内[76]。感染粪类圆线虫人群肠道菌群α多样性显著升高、β多样性显著降低、双歧杆菌、拟杆菌丰度降低，致病菌肠道杆菌丰度增加[77]。胃肠道寄生蠕虫感染可通过促进肠道菌群丰富度及均匀度增加而恢复肠道菌群稳态，被认为是寄生虫在慢性炎症中发挥治疗特性的一种机制[78-79]。在小鼠感染粪圆线虫丝状蚴前2周，给予喂食双歧杆菌菌株04450B可显著降低成虫负荷及虫卵排出量、降低感染所致肠道损伤，表明双歧杆菌可改善宿主感染粪圆线虫感染的情况[80]。

3.7 缩小膜壳绦虫 缩小膜壳绦虫成虫主要寄生于人或鼠类小肠内。感染缩小膜壳绦虫小鼠肠道菌群α多样性未见明显改变，但菌群结构发生显著变化[81]、菌群总数显著提高[82]；肠道乳酸杆菌目及芽孢杆菌目

丰度显著降低，而拟杆菌目与梭菌目丰度显著增加[83]。在感染缩小膜壳绦虫的狐猴肠道内发现，缩小膜壳绦虫感染与乳酸杆菌目及芽孢杆菌目丰度存在负相关[84]。但McKenney等[81]未发现缩小膜壳绦虫感染小鼠肠道乳酸杆菌变化，可能是由于感染严重程度及感染阶段不同所致。

4 肠道原虫感染与肠道菌群相互作用

4.1 隐孢子虫 隐孢子虫病由隐孢子虫感染所致，主要经水传播，人因摄入被卵囊污染的水或食物而感染，常见于卫生条件有限的地区，是导致婴幼儿腹泻的主要原因[85-86]。狐猴感染隐孢子虫的初始阶段，其肠道菌群多样性降低[83]；感染隐孢子虫3 d后的小鼠，出现肠道黏膜受损及炎症加重的情况[87]。研究发现，刚出生小鼠肠道菌群具有保护小鼠抵抗隐孢子虫的作用，并且肠道菌群与聚肌胞苷酸可协同作用，保护刚出生小鼠或者新生儿小鼠抵抗隐孢子虫感染[88-89]。梭菌属、肠杆菌是腹泻者肠道内较丰富的菌种[89]，研究发现感染隐孢子虫的人群粪便中肠杆菌、芽孢杆菌和梭菌丰度是未感染者的2.5倍以上[90]；感染隐孢子虫的马达加斯加狐猴肠道内的肠杆菌、肠球菌及脱硫弧菌的数量显著增加[83]。

肠道中一些产吲哚的细菌或者吲哚可影响隐孢子虫感染力，隐孢子虫感染状态由肠道中吲哚量、隐孢子虫卵囊数量及机体免疫水平共同决定[90]。此外，肠道菌群可影响隐孢子病治疗[91]、隐孢子虫在肠道内定植、以及隐孢子虫的耐药性[92]。给予隐孢子虫感染小鼠喂食含有益生菌制品的饮水后，小鼠肠道微生态环境改变，进而间接改变小鼠肠道微环境或肠上皮结构，有利于隐孢子虫的定植，加重小鼠感染程度[93]。

4.2 贾第虫 贾第虫主要寄生在宿主十二指肠及小肠上段，主要因摄入含有感染性包囊的水或食物而感染，可导致腹泻及肠道外并发症等[94-95]，是2岁以下儿童肠道中的重要病原体[96]。贾第虫感染是肠应激综合征及慢性疲劳综合征的一个重要危险因素[97-98]，而贾第虫感染小鼠出现持续性肠黏膜紧密连接损伤、细菌渗透和肠黏膜炎症可能是感染后易发生其它肠道疾病的重要原因[99-100]。已有研究表明，贾第虫感染与肠道菌群密切相关[95, 100-101]，贾第虫病患者表现出的不同临床症状可能与宿主肠道菌群差异导致贾第虫感染后免疫反应有关[5, 102]。

贾第虫可直接破坏宿主肠道微环境稳态、激活肠道菌群潜伏的毒力基因、破坏微生物组成的生物膜、促进生物膜中病原体释放[103]，导致肠道菌群改变，进而影响感染状态及免疫病理变化[104]。贾第虫感染后7 d，小鼠肠道黏膜受损、肠道细菌过度增殖，乳酸杆菌、芽孢杆菌和葡萄球菌等多种细菌侵入肠道黏膜[99]。体外研究发现，益生菌乳酸杆菌的代谢物可将无毒的胆汁转化成对贾第虫有毒的含有去结合型胆盐的胆汁，进而阻止贾第虫发育[105]。大肠杆菌暴露于贾第虫后，会转化成对秀丽杆菌具有致命的有毒状态[106]。研究发现，贾第虫感染会导致肠杆菌和肠球菌等致病菌显著增长、乳酸菌丰度降低[107-108]，肠道菌群的这种改变有利于贾第虫在肠道中的定植。此外，贾第虫感染还会导致好氧菌变形菌门丰度增加，厌氧菌厚壁菌门丰度降低，这种改变可能是贾第虫感染致肠道菌群失调、贾第虫独特厌氧发酵代谢或感染所诱导的肠道炎症所致[109]。贾第虫感染小鼠还可发生肠道共生菌在脾、肝组织移位现象[94]。Keselman等[5]发现在进行贾第虫抗生素治疗过程中发生肠道菌群移位，这种移位现象可能与抗生素引起的肠道菌群紊乱抑制了$CD8^+$T细胞活化有关，并认为$CD8^+$T细胞活性降低是导致贾第虫感染治疗过程中发生肠道菌群移位的原因。虽然肠道菌群与贾第虫相互作用机制尚不明确，但已有研究表明肠道菌群影响宿主对贾第虫的易感性以及感染程度[5]。

4.3 溶组织内阿米巴 溶组织内阿米巴是一种寄生在小肠、结肠的单核细胞寄生原虫，摄入被污染的食物或水可导致感染[110]。溶组织内阿米巴病最常见临床表现为阿米巴痢疾或阿米巴结肠炎[111]。研究发现，溶组织内阿米巴与肠道菌群组成及多样性密切相关[107, 112-113]，肠道菌群失调被认为是感染溶组织内阿米巴的危险因素之一[108-109]。印度北部溶组织内阿米巴感染人群粪便菌群研究显示，肠道梭菌属、拟杆菌、乳酸杆菌及弯曲杆菌丰度显著降低，双歧杆菌丰度显著增加[114]；并在患有阿米巴肝脓肿的患者脓液样本中检测到与引起人脓肿和其他败血症感染相关的厌氧菌拟杆菌及消化链球菌，认为脓液中的这两种细菌可能是由于肠道细菌过度增生、肠道黏膜通透性增加以及宿主免疫力低下等原因导致[113, 115]，肠道厌氧菌在阿米巴肝脓肿发生机制中的重要作用，也在其他研究中得到证实[115-116]。

研究发现，肠道菌群与机体免疫系统可共同调节肠道阿米巴病临床表现[27, 111]，肠道微生物群可潜在影响溶组织内阿米巴感染[27]。在1～2岁儿童中，阿米巴感染引起的腹泻症状与普雷沃氏菌有关，且感染引起的临床症状与肠道菌群结构及多样性有关[117]。Morton等[112]通过对喀麦隆西南部部分人群粪便研究发现，个体肠道菌群的组成可预测宿主是否存在溶组

织内阿米巴感染，准确率达79%，而普雷沃氏菌是辅助检测阿米巴感染的一个重要菌种。普雷沃氏菌是一种肠道机会致病菌[118]，与肠道炎症、肠道产生的过度免疫有关，可促进溶组织内阿米巴感染建立，并影响侵袭性疾病进展[117, 119]。肠道中的梭菌属及分节丝状菌可保护小鼠免受溶组织内阿米巴的感染[27, 120-121]。因此，肠道微生物群在改变溶组织内阿米巴感染方面存在潜在影响[27]。

溶组织内阿米巴的毒力受寄生虫本身、宿主及环境因素等影响[122]，同时肠道菌群也会影响溶组织内阿米巴的毒力[123]，并且肠道菌群对溶组织内阿米巴毒力的调节是非特异性的[116]，如链球菌、葡萄球菌以及假单胞菌等革兰氏阳性菌，可刺激溶组织内阿米巴，使其毒性增加[116, 123-124]；当溶组织内阿米巴与益生菌乳酸杆菌及粪肠球菌共培养时，其存活率降低到80%[125]。肠道菌群不仅改变溶组织内阿米巴的毒力，还与溶组织内阿米巴耐药产生密切相关。研究发现，甲硝唑耐药相关基因与拟杆菌、消化链球菌相关[126-127]。阿米巴肝脓肿患者经甲硝唑治疗后，肠道细菌相关耐药基因迅速扩增，这种现象在给予甲硝唑治疗的健康对照组及肠应激综合征患者得到验证[113]。

4.4 人芽囊原虫 人芽囊原虫是一种寄生在人和大多数动物肠道内的寄生原虫，全世界超过10亿人感染[128]，在肠应激综合征和结肠癌患者中感染率较高[129-131]。健康人群肠道人芽囊原虫可通过与肠道有益菌群、免疫系统相互作用或直接维持肠道黏液层健康[132]。人芽囊原虫感染与较高的肠道菌群物种丰度有关[133]，且肠道菌群与人芽囊原虫感染者感染状态和临床症状密切相关[129-131, 134]。

不同研究分析获得的人芽囊原虫对肠道菌群的影响结果不同。有研究发现，人芽囊原虫感染人群肠道菌群多样性增加，梭菌属丰度增、致病菌肠杆菌丰度降低，认为人芽囊原虫感染所形成的肠道菌群状态不同于炎症或其他疾病导致的菌群失调[135]。人芽囊原虫感染所致肠道菌群多样性增加在无肠道疾病或者炎症的人群中也得到证实，说明人芽囊原虫定植对肠道菌群有显著影响[136]。但是在肠应激综合征患者中发现，人芽囊原虫并没有显著改变肠道菌群结构及多样性[137]；在一组感染人芽囊原虫的学生中同样发现，人芽囊原虫对于肠道菌群的改变影响不大[138]。也有研究发现人芽囊原虫感染与肠道菌群多样性及肠道拟杆菌数量存在负相关关系[139]；与瘤胃球菌及普氏菌肠型的人群相比，拟杆菌肠型感染人群粪便中人芽囊原虫阳性数较少[140-141]。在人芽囊原虫阳性伴有便秘的肠应激综合征男性患者中，发现双歧杆菌丰度显著降低；与未感染者相比，感染人芽囊原虫人群肠道普氏菌属和梭菌属XIVa簇丰度显著增加，肠道粪杆菌与大肠杆菌比例显著升高[110]。人芽囊原虫感染后所致肠道菌群的不同变化可能与人芽囊原虫亚型相关。在人芽囊原虫ST4亚型感染人群肠道定植量与高丰度菌群存在正相关关系，与富含拟杆菌肠型成负相关关系，但人芽囊原虫ST3亚型感染人群与肠道菌群并未表现出明显相关关系[141]。

4.5 微孢子虫 微孢子虫主要寄生在人、动物或昆虫的消化道上皮细胞内，人因摄入被成熟孢子污染的水或者食物或者性接触途径而感染。目前，关于微孢子与肠道菌群相互作用的研究主要集中在蜜蜂肠道菌群与蜜蜂微孢子虫的相互作用。Koch等[142]发现感染微孢子虫的野生大黄蜂肠道菌群多样性增加，肠道乳酸菌丰度降低[143]，也有研究并未发现感染蜜蜂微孢子虫的蜜蜂肠道菌群发生明显改变[144]。有研究表明，通过饮食可改变蜜蜂肠道菌群，进而改变对微孢子虫的抵抗。给予感染微孢子虫的蜜蜂喂食含有乳酸杆菌及双歧杆菌的食物后，微孢子虫感染水平显著下降[145]；益生菌喂食会降低蜜蜂幼虫死亡率，增强成年蜜蜂对蜜蜂微孢子虫的抵抗[146]；给蜜蜂喂食蜜蜂饲料可增加蜜蜂肠道菌群稳定性，抵抗微孢子虫感染，降低死亡率[147]。目前，尚未见人微孢子虫肠道菌群的研究。

5 小结与展望

近年来，随着高通量测序技术的发展，关于肠道菌群与人类疾病之间相互关系的研究日益增多，越来越多的研究者认识到肠道菌群在人类疾病发生、发展及治疗和预后中的重要作用。肠道菌群已应用于一些疾病的诊断、治疗以及致病机制等方面的研究，如可基于肠道菌群开发疗效更好、不良反应更少的新型治疗策略。目前，粪菌移植已经应用于肠应激综合征、肥胖及便秘等疾病治疗，并取得了较好效果[148-149]。在寄生虫病领域，虽然尚处于早期研究阶段，但研究者已发现肠道菌群在寄生虫感染中表现出在非特异性临床症状、寄生虫感染定植、感染状态、慢性寄生虫病发展以及寄生虫耐药性的形成等方面均有重要影响，并且发现肠道菌群也可作为寄生虫感染诊断的辅助标志[121, 150]。但是，目前寄生虫感染与肠道菌群的具体作用机制尚不清楚。

因此，探讨肠道菌群与寄生虫相互作用的关系及其机制，将是寄生虫定植、感染、疾病发展和预后以及诊断靶标或治疗等方面进一步研究的新方向，也将为

寄生虫病致病机制、感染免疫及防控等提供新的研究思路。

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