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抗生素预测得到的准确值不同,例如现在对环丙沙星的敏感性预测有比较高的准确率^[28],可见耐药基因的研究与全基因组测序技术相互促进^[27]。

在全基因组测序之前,最常用的追踪耐药淋球菌的方法是NG-MAST基因分型,NG-MAST基因分型是根据高突变序列porB和tbpB对淋球菌进行编序,用于淋球菌的监测及追踪。但是随着全基因组测序的发展,全基因组测序将会有更高的分辨率,例如在英国布莱顿进行的一项研究发现,在28天内收集的淋球菌中有8.8%的淋球菌有相同的NG-MAST类型,但是根据全基因组测序结果只有3.6%的菌株有直接或间接的传播关系^[29]。

4 总结及展望

淋球菌耐药已不是一个新问题,抗生素刚开始被用于治疗淋病时,淋球菌就表现出了很强的耐药特性。近年来,随着淋球菌对头孢曲松的敏感性逐渐降低,以及H041、F89等“超级细菌”的出现,使得淋球菌的耐药形势越来越严峻。在对淋球菌的耐药研究中,发现淋球菌已形成了多种耐药机制:1)通过产生酶破坏抗生素或者对抗生素进行修饰;2)靶点修饰或者抗生素与靶点的亲和力降低;3)减少抗生素进入菌体内;4)增加抗生素的外排^[30]。另外,我们对淋球菌的耐药机制认识还不完全,还有许多未知需要我们去探索。

对于淋球菌的耐药问题,许多国家开始重视耐药淋球菌的监测并建立了“淋球菌耐药监测系统”^[31],欧美一些国家也开始推荐头孢曲松联合阿奇霉素用于淋病的治疗^[22]。同时,人们也在挖掘、探索新的治疗策略、新的敏感性检测技术。除了开发新的药物,人们也在尝试对已经存在的药物采用新的联合方式治疗淋病,例如一项临床随机多中心试验发现庆大霉素(240mg肌肉注射)加阿奇霉素(2g口服)作为潜在的替代治疗方案有很高的治愈率^[32]。另外,随着新技术的发展,如果能够快速及时的获得淋球菌的抗生素敏感性,那么根据淋球菌对不同抗生素的敏感性不同,我们的用药将会趋向于个体化,我们或许将会有更多的用药选择。

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