

Molecular epidemiology and ophthalmology

Molecular epidemiology is the application of sophisticated laboratory techniques to analytical epidemiology and is used to identify, at the molecular or biochemical level, specific exogenous agents or host factors that play a role in disease causation. This is a relatively new research field that first appeared in the late 1970s and developed rapidly over the past decade. Molecular epidemiology is now set to make inroads into ophthalmology.

What contributions can molecular epidemiology make to ophthalmology? Currently, one of its most important contributions is to our understanding of the epidemiology of trachoma and other communicable eye diseases. Trachoma is the world's leading infectious cause of blindness.¹ At least 100 million children suffer from active trachoma and 30 million adults, mainly women, have trichiasis.² In several countries, including Kenya and Tanzania, trachoma is particularly prevalent and ranks alongside cataract as one of the leading causes of blindness. The infectious agent responsible for trachoma is *Chlamydia trachomatis* of which serotypes A, B, Ba, and C have a propensity for the conjunctiva. Person to person transmission, particularly among children and the women who care for them, occurs when infected ocular discharges are transmitted by flies, clothing, and fingers.

In this issue of the journal, Bailey *et al* report on the application of molecular techniques to an epidemiological investigation of trachoma in a village in the Gambia. The key findings of their study are that the molecular techniques supported the clinical findings, that two serotypes A and B, plus two variants of the B serotype were present in the village, and that these showed strong household clustering.

This study nicely highlights some of the potential contributions that molecular epidemiology can make to ophthalmology. It could have a marked impact on infectious disease diagnosis. Techniques such as polymerase chain reaction (PCR) and restriction fragment length polymorphism (RFLP) provide a rapid method of determining the molecular subtypes (genotyping) of strains of pathogens circulating in a population. The ability to assess a pathogen's genotype directly bypasses the need to culture the organism, which could reduce diagnostic delays particularly for fastidious organisms.

Applying the typing of micro-organisms to epidemiological research could enhance the identification of patterns of disease transmission, the geographical relation of isolates, the origins of outbreaks, the role of different vehicles of transmission, and the chain of transmission. The study by Bailey and colleagues has demonstrated that while two genotypes of *C trachomatis* were present in the village, most individuals with trachoma were infected with a single genotype only, and that members of a household tended to have the same genotype. Interestingly, members of one household could have one genotype, while their neighbours would have a different genotype, with little evidence of cross infection. This finding suggests that in the village studied, infection is mainly transmitted within the household, and that the spread of trachoma within the village is probably caused by the independent transmission of the two strains. The application of molecular techniques has strengthened the epidemiological investigation and provided a better understanding of the occurrence of trachoma in the village. It seems unlikely that the use of traditional epidemiological methods only would have resulted in the geographical pattern being discovered.

Molecular epidemiology could be combined with antimicrobial susceptibility testing to identify drug resistant strains of pathogens. A clear lesson can be learnt from current

research into drug resistant strains of *Mycobacterium tuberculosis*, the organism that causes tuberculosis. Multidrug resistant strains of *M tuberculosis* have appeared in several countries, resulting in major problems in providing effective treatment of drug resistant cases and preventing subsequent transmission of disease. Genotyping of isolates from drug resistant patients has reduced the delay in providing effective treatment. While drug resistant strains of pathogens which cause infections of the conjunctiva are not a major problem, molecular techniques could enhance current practices.

The uses of molecular epidemiology need not be limited to communicable disease. It could play a role in numerous areas of ophthalmic research. Molecular techniques could be used to provide biological markers of exposure to exogenous agents. Such markers could provide an alternative to the traditional methods of assessing exposure. Biological markers of exposure are now widely used in medical research, including such diverse measures as glycosylation of serum proteins as a molecular marker of diabetes, cotinine as a marker for exposure to nicotine in cigarette smoke, and oncogene activation as a marker of exposure to chemical carcinogens.

One area of ophthalmic research that could benefit from such a marker is assessing ocular exposure to solar ultraviolet radiation (UVR). Epidemiological studies have shown that several eye conditions are associated with exposure to UVR, including cataract, pterygium, and climatic droplet keratopathy. Unfortunately, studies to date have been limited in their ability quantitatively to measure lifetime ocular exposure to UVR. Studies have generally based exposure assessment on information collected by interview on a person's exposure to sunlight at different stages of their life. Clearly exposure assessments based on such methods have inherent limitations which may reduce their validity. A biological marker of UVR exposure is needed to further research efforts in this area. A marker, which was, for instance, a measure of UVR damage to a particular molecule, would provide a far better measure of cumulative lifetime exposure to UVR than is currently available to ophthalmic epidemiologists.

However, caution in the use of molecular techniques in ophthalmology is warranted. The field is rapidly evolving with new techniques constantly replacing existing methods. Often it is not known which is the best method for a particular situation. Close attention must be given to the sensitivity and specificity of molecular technique. Using genotyping of *C trachomatis* as an example, most methods have good specificity (giving a negative result for cases without active trachoma).^{3,5} Unfortunately, they generally have poor sensitivity (giving a positive result for cases with active trachoma), typically around 50%. The PCR method used by Bailey *et al* also has a sensitivity of around 50%. These techniques should not be viewed as replacements for traditional research methods but as innovative techniques to be used in parallel with them.

International Centre for Eye Health,
Institute of Ophthalmology,
Bath Street, London EC1V 9EL

PAUL J DOLIN

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