rRNA-based tests for chlamydial infection in trachoma

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Br. J. Ophthalmol. 2007;91;271-
doi:10.1136/bjo.2006.105270

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Trachoma, the worlds leading cause of preventable blindness, is the subject of worldwide control efforts via the SAFE (Surgery, Antibiotic Treatment, Facial Cleanliness and Environmental Improvement) strategy. The ''A'' component of this strategy antibiotic treatment of the active disease has been supported through the large scale donation of millions of doses of the antibiotic azithromycin by its manufacturers, Pfizer, for distribution in trachoma endemic areas by the International Trachoma Initiative.[1] Azithromycin, as a single 20 mg/kg oral dose is effective against *Chlamydia trachomatis* infection.[2] In the field the diagnosis of active trachoma may be made simply by examining the surface of the everted upper eyelid for clinical signs of trachoma: lymphoid follicles and inflammatory thickening.[3] Current recommendations are that communities in which the prevalence of active trachoma is greater than 10% of 1–9 year olds should be mass treated annually for three years.[4] So far, so good. A problem, however is that the clinical signs of trachoma are quite poorly predictive of the presence of ocular chlamydial infection. Wherever tests for infection have been carried out, there have been significant rates of mismatch between infection and clinical signs: infection without disease and disease without infection are very common. There are also examples of whole communities with substantial rates of active trachoma in whom not a single individual has been found to harbour *C trachomatis* infection,[5] and of communities where mass treatment has suppressed infection, but clinical signs of trachoma persisted at pre-treatment levels.[6] Distributing azithromycin repeatedly to such communities must be considered wasteful of scarce resources.

Thus there are at least three reasons why testing for infection in trachoma may be informative. Firstly it may tell us how to prioritise individuals or communities for treatment. Secondly it may indicate when treatment, or distribution ought to be discontinued, or resumed. Finally we may learn something useful about the biology of trachoma. In their paper, Yang *et al* present the first data using a commercial assay which detects chlamydial ribosomal RNA (rRNA) in subjects with trachoma (***see page 293***).[7] Because chlamydial rRNA, reflecting ribosomal activity, is typically present in infected cells at a multiplicity of hundreds to thousands of copies per chlamydial chromosome one would expect that, as demonstrated in their findings, rRNA based testing would be more sensitive than the more commonly applied Amplicor PCR, which detects the common chlamydial plasmid pCT typically present at a median multiplicity of about six per chromosome in ocular infection.[8]

The advent of rRNA based tests raises more questions in need of answering. Does the detection of rRNA without chlamydial DNA really indicate an infectious reservoir of epidemiological significance? What is the prognosis for infection in these subjects? Does rRNA disappear before or after DNA following treatment?[9] A previous study, albeit using a homebrew quantitative assay, found that high level rRNA expression was strongly predictive of clinical signs of active trachoma.[10] It would be interesting to know whether quantitative estimation of rRNA in trachoma subjects will reconcile these findings. Finally, trachoma habitually occurs in settings characterised by poverty and poor access to services and utilities. An ideal test for chlamydial infection would be specific, able to be performed at the point of care and to be interpreted by programme staff with minimal training, cheap and not requiring electricity or expensive technology. The high sensitivity conferred by nucleic acid amplification tests is likely not strictly necessary for community prioritisation and treatment-stopping decisions by programmes. A new test in dipstick format that detects chlamydial lipopolysaccharide antigen is currently undergoing evaluation and may fit the bill here.[11]

Br J Ophthalmol 2007;**91**:271.
doi: 10.1136/bjo.2006.105270

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