Diagnosis of viral and chlamydial keratoconjunctivitis: which laboratory test?

Elfath M Elnifro, Robert J Cooper, Paul E Klapper, Andrew S Bailey, Andrew B Tullo

Conjunctivitis and keratitis are common forms of ocular morbidity seen in general practice and eye units.1,2 The aetiology of these diseases includes viral, bacterial, or parasitic infection as well as allergy, trauma, and dietary deficiency. Among the common microbial causes3–7 (Table 1) are adenovirus, herpes simplex virus (HSV), and Chlamydia trachomatis. Ocular adenovirus infections occur throughout the world in both sporadic and epidemic forms, and large scale outbreaks of epidemic keratoconjunctivitis can occur in hospitals, schools, military establishments, or factories.8 HSV type 1 ocular infection occurs in all countries with an annual incidence of up to 20.7 per 100,000 population and is the most common infective cause of blindness in developed countries. 9 Trachoma caused by C trachomatis serovars A–C is the leading infectious cause of blindness in the world and is a major public health problem in developing countries.10 Adult chlamydial conjunctivitis, caused by C trachomatis serovars D–K, is an ocugenital infection and up to 90% of patients have concurrent genital infection.11–13 Chlamydial neonatal conjunctivitis (ophthalmia neonatorum) develops in 18%–74% of babies born to mothers with genital chlamydial infection.7

This article reviews available diagnostic laboratory techniques for keratoconjunctivitis caused by adenovirus, HSV, and C trachomatis with special emphasis on modern molecular diagnostic techniques. For information on the clinical features, epidemiology, and treatment of these infections the reader is referred to a number of other reviews.8–10 14–17

The need for laboratory investigation

Owing to the limited reliability of clinical diagnosis of adenovirus, HSV, and C trachomatis induced keratoconjunctivitis,16–25 accurate laboratory investigation for these agents in conjunctival swabs is often valuable. Failure to diagnose ocular adenoviral disease can result in outbreaks of epidemic keratoconjunctivitis. Prompt recognition of the strains of adenovirus causing this condition in patients can, however, help to contain the development of a hospital based epidemic.24 C trachomatis infection (particularly with serovars D–K) is usually associated with asymptomatic genitourinary colonisation.25 Misdiagnosis of this ocular infection may represent a missed opportunity to detect infection of the genital tract which can ultimately result in a series of complications including pelvic inflammatory disease, epididymitis, ectopic pregnancy, and infertility in the patient and/or partner.11,13 25 In addition, delay in diagnosing chlamydial conjunctivitis and the use of inappropriate antibiotic treatment might trigger chlamydial persistence.24 The availability of appropriate treatment for chlamydia,18 HSV,20 and possibly adenovirus27 together with the potentially serious residual morbidity of these infections clearly justifies the need for accurate laboratory investigation in cases of keratoconjunctivitis.

Conventional laboratory techniques

The conventional techniques for diagnosing viral and chlamydial keratoconjunctivitis include conjunctival cytological investigation26–28; inoculation of susceptible cell lines followed by observation of cytopathic effect or visualisation

<table>
<thead>
<tr>
<th>Causative agent (references)</th>
<th>Differential diagnosis</th>
<th>Epidemiology</th>
</tr>
</thead>
<tbody>
<tr>
<td>DNA viruses: Adenovirus (3)</td>
<td>EKC</td>
<td>Primarily types 8 and 19, but types 2–5, 7, 9, 11, 14, 16, 21–23, and 37 have also been associated with EKC. Highly contagious and transmitted by hand to eye contact, instruments, and solutions.</td>
</tr>
<tr>
<td>HSV (4, 5)</td>
<td>PCF</td>
<td>Primarily types 3, 4, and 7; occasionally type 5. Contagious; droplet transmission, particularly in families.</td>
</tr>
<tr>
<td>RNA viruses: Picornavirus</td>
<td>NSFC</td>
<td>A number of serotypes have been reported including 1–11, 14–17, 19, 20, 22, and 26.</td>
</tr>
<tr>
<td>Measles virus (6)</td>
<td>Conjunctivitis; keratitis or KC</td>
<td>HSV-1 or HSV-2; conjunctivitis is most common in adults and children 1–5 years of age; recurrent disease is common; leading infectious cause of blindness in developed countries.</td>
</tr>
<tr>
<td>Chlamydia: C trachomatis (7)</td>
<td>AHC</td>
<td>EV70; CA24; common (epidemic or endemic forms) in developing countries; highly contagious.</td>
</tr>
<tr>
<td>MVO</td>
<td>NCO</td>
<td>Common cause of childhood blindness in developing countries. HSK may complicate measles in developing countries.</td>
</tr>
<tr>
<td>LGV conjunctivitis</td>
<td>The most common form of infectious ophthalmia neonatorum today; occurs in babies born to mothers with genital infection serovars D–K.</td>
<td></td>
</tr>
<tr>
<td>Trachoma</td>
<td>Ocular conjunctivitis caused by serovars D–K, sometimes by B, and rarely by C; common in developed countries and urban areas of developing countries.</td>
<td></td>
</tr>
<tr>
<td>ACO</td>
<td>Most common cause of preventable blindness in the world and common in rural areas of developing countries particularly in Africa, the Middle East, and Asia; caused by serovars A–C.</td>
<td></td>
</tr>
</tbody>
</table>

EKC=epidemic keratoconjunctivitis; PCF=pharyngoconjunctival fever; NSFC=non-specific follicular conjunctivitis; KC=keratoconjunctivitis; AHC=acute haemorrhagic conjunctivitis; MVO=measles virus ophthalmia; NCO=neonatal chlamydial ophthalmia; ACO=adult chlamydial ophthalmia; LGV=lymphogranuloma venereum; HSK=herpes simplex keratitis; HSV=herpes simplex virus; EV=enterovirus; CA=Coxsackie virus type A.
Table 2  Sensitivities and specificities of antigen detection techniques for the diagnosis of adenovirus, HSV, and chlamydial keratoconjunctivitis in comparison with cell culture isolation

<table>
<thead>
<tr>
<th>Causative agent</th>
<th>Test format</th>
<th>Commercial name</th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adenovirus</td>
<td>EIA</td>
<td>Cambridge</td>
<td>86.0</td>
<td>100</td>
<td>42</td>
</tr>
<tr>
<td></td>
<td>Cambridge</td>
<td>Adenoclone</td>
<td>62.3</td>
<td>100</td>
<td>43</td>
</tr>
<tr>
<td></td>
<td>Cambridge</td>
<td>Adenoclone</td>
<td>77.0</td>
<td>100</td>
<td>44</td>
</tr>
<tr>
<td></td>
<td>Cambridge</td>
<td>Adenoclone</td>
<td>38.0</td>
<td>100</td>
<td>45</td>
</tr>
<tr>
<td></td>
<td>Cambridge</td>
<td>Adenoclone</td>
<td>50.5</td>
<td>100</td>
<td>46</td>
</tr>
<tr>
<td></td>
<td>ICP</td>
<td>SAS Adenotest</td>
<td>54.7</td>
<td>97.1</td>
<td>46</td>
</tr>
<tr>
<td>HSV</td>
<td>IF</td>
<td>IF</td>
<td>79.0</td>
<td>100</td>
<td>42</td>
</tr>
<tr>
<td></td>
<td>IDB</td>
<td>IDB</td>
<td>85.3</td>
<td>92.2</td>
<td>47</td>
</tr>
<tr>
<td></td>
<td>DIF</td>
<td>Syva Microtrak</td>
<td>67</td>
<td>93</td>
<td>48</td>
</tr>
<tr>
<td></td>
<td>DIF</td>
<td>Kodak Surecell</td>
<td>97</td>
<td>73</td>
<td>49</td>
</tr>
<tr>
<td></td>
<td>DIF</td>
<td>DuPont</td>
<td>65</td>
<td>100</td>
<td>53</td>
</tr>
<tr>
<td></td>
<td>DIF</td>
<td>Herpcheck</td>
<td>26</td>
<td>90</td>
<td>53</td>
</tr>
<tr>
<td></td>
<td>DIF</td>
<td>Syva Microtrak</td>
<td>100</td>
<td>99</td>
<td>54</td>
</tr>
<tr>
<td></td>
<td>DIF</td>
<td>Kodak Surecell</td>
<td>100</td>
<td>97.5</td>
<td>55</td>
</tr>
<tr>
<td></td>
<td>DIF</td>
<td>Syva Microtrak</td>
<td>57</td>
<td>81</td>
<td>56</td>
</tr>
<tr>
<td></td>
<td>DIF</td>
<td>Syva Microtrak</td>
<td>83.3</td>
<td>96.6</td>
<td>57</td>
</tr>
<tr>
<td></td>
<td>DIF</td>
<td>Syva Microtrak</td>
<td>52</td>
<td>98</td>
<td>59</td>
</tr>
<tr>
<td></td>
<td>DIF</td>
<td>Syva Microtrak</td>
<td>100</td>
<td>95</td>
<td>55</td>
</tr>
<tr>
<td></td>
<td>IPO</td>
<td>IPO</td>
<td>46</td>
<td>96</td>
<td>29</td>
</tr>
<tr>
<td></td>
<td>EIA</td>
<td>Abbott</td>
<td>71</td>
<td>97</td>
<td>56</td>
</tr>
<tr>
<td></td>
<td>EIA</td>
<td>Clamydiazyme</td>
<td>88</td>
<td>99</td>
<td>58</td>
</tr>
<tr>
<td></td>
<td>EIA</td>
<td>Clamydiazyme</td>
<td>97</td>
<td>96</td>
<td>56</td>
</tr>
<tr>
<td></td>
<td>EIA</td>
<td>Kodak Surecell</td>
<td>40</td>
<td>100</td>
<td>59</td>
</tr>
</tbody>
</table>

DIF=direct immunofluorescence; IPO=immunoperoxidase; EIA=enzyme immunoassay; ICP=indirect immunoperoxidase; IF=immunofiltration; IC=immunochromatography; IDB=immune dot blot.

*Compared with PCR.
†Compared with clinical diagnosis.
‡Compared with DIF.

using various chemical or immunological staining techniques; examination of blood and/or tears for various classes of antibodies; and detection of viral or chlamydial antigens in conjunctival and corneal specimens. The technique has been shown to be more sensitive than immunoassay in detection of ocular adenovirus infections. For example, Kinchington et al. evaluated the application of PCR in 107 ocular swab samples and correlated the results with those obtained with tissue culture and a commercial immunoassay (Adenoclone). The PCR was positive in 46 of 58 adenoclone negative, culture positive swabs, and in 11 of 11 adenoclone positive, culture positive swabs. Only one of 38 non-adenoviral ocular swab samples was positive by PCR giving an overall specificity of 97.3%. These results demonstrate the superiority of PCR in terms of speed over tissue culture isolation and in sensitivity over immunoassay.

In our own laboratory, the overall sensitivity of PCR for detection of adenovirus in eye swabs was similar to that of cell culture and superior to that of antigen detection by immune dot-blot test. More recently, using a newly designed adenovirus primer pair, we have a PCR which is significantly more sensitive than culture. Of 415 eye swabs positive by culture and/or PCR, 386 (93%) were positive by PCR compared with 248 (59%) by cell culture.

**HERPES SIMPLEX VIRUS**

Few studies have compared PCR with conventional techniques. This is probably because the clinical features of herpetic eye disease are often strongly suggestive and culture results are available much sooner (3 days) than those of adenovirus (up to 4 weeks) and chlamydia (5 days). Nevertheless, owing to its speed and sensitivity, PCR is a useful diagnostic tool for HSV infection of the ocular surface. Yamamoto et al. utilised PCR for the detection of HSV genomic sequences in tear film from patients with clinically diagnosed HSV keratitis. The PCR was positive in 12 of 12 epithelial keratitis specimens, two of six stromal keratitis, but in none of 20 normal specimens. In another study by Kowalski et al. utilising cell culture as a gold standard test, PCR was shown to be reappraisal of the use of conventional methods of diagnosis. Nucleic acid amplification techniques currently available or under active development include the polymerase chain reaction (PCR), the ligase chain reaction (LCR), transcription based amplification system, Qβ replicase amplification, cycling probe reaction, strand displacement amplification, and branched DNA signal amplification. Of these techniques, PCR, the first of the nucleic acid amplification methods to be described, is the most developed.

**Polymerase chain reaction (PCR)**

PCR allows the identification of extremely small quantities of DNA with a very high degree of specificity. The test has revolutionised the diagnosis of microbial diseases and since its first use in eye disease in 1990, the test is now being widely used in clinical ophthalmology. Owing to the sensitivity and speed of the PCR, and its use of small sample volumes, the technique has been shown to be of great value in the diagnosis of infections involving both the ocular surface and the orbit. A number of studies have evaluated the use of PCR as a diagnostic tool for the detection of adenovirus, HSV, and C trachomatis in conjunctival swabs.
Table 3  Applications of PCR in ophthalmic infectious diseases

<table>
<thead>
<tr>
<th>Causative agent</th>
<th>Ocular site</th>
<th>Clinical diagnosis</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Viruses:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adenovirus</td>
<td>Conjunctiva</td>
<td>KC</td>
<td>67–72</td>
</tr>
<tr>
<td>HSV</td>
<td>Tear film</td>
<td>keratitis</td>
<td>73, 74</td>
</tr>
<tr>
<td>EV70</td>
<td>Conjunctiva</td>
<td>keratitis or KC</td>
<td>21, 75, 76</td>
</tr>
<tr>
<td>CMV</td>
<td>Conjunctiva</td>
<td>uveitis</td>
<td>77, 78</td>
</tr>
<tr>
<td>EBV</td>
<td>Aqueous</td>
<td>retinal necrosis</td>
<td>78</td>
</tr>
<tr>
<td>HPV</td>
<td>Vitreous</td>
<td>ophthalmic zoster</td>
<td>80</td>
</tr>
<tr>
<td>Bacteria:</td>
<td></td>
<td>retina necrosis</td>
<td>81</td>
</tr>
<tr>
<td>C trachomatis</td>
<td>Aqueous</td>
<td>Vogt-Koyanagi-Harada syndrome</td>
<td>82, 83, 84</td>
</tr>
<tr>
<td></td>
<td>Aqueous, subretinal, and vitreous</td>
<td>chorioretinal inflammatory disease or retinitis</td>
<td>85</td>
</tr>
<tr>
<td>Parasites:</td>
<td>Aqueous and vitreous</td>
<td>conjunctival carinoma</td>
<td>85</td>
</tr>
<tr>
<td>T. gondii</td>
<td>Vitreous</td>
<td>endophthalmitis</td>
<td>96</td>
</tr>
<tr>
<td></td>
<td>Ocular tissue sections</td>
<td>retinochoroiditis</td>
<td>78</td>
</tr>
<tr>
<td></td>
<td>Conjunctiva</td>
<td>ocular toxplasmosis</td>
<td>97</td>
</tr>
</tbody>
</table>

CHLAMYDIA TRACHOMATIS

For *C. trachomatis*, the PCR has been shown to be as or more sensitive than conventional techniques.57 86–88 Bobo et al86 investigated the use of PCR in 234 Tanzanian children who were clinically classified as having no sign of trachoma (n=97), follicular trachoma (n=100), or intense inflammatory trachoma (n=37). The PCR detected *C. trachomatis* in 24%, 54%, and 95% of subjects, respectively, compared with detection by direct immunofluorescence of 1%, 28%, and 60%, respectively. The overall prevalence of chlamydial eye infection was 48% by PCR compared with 22% by direct immunofluorescence. In addition, this study showed the utility of PCR as a suitable method for field use owing to ease of specimen collection and transport.

In the United States, Talley et al88 screened ocular swabs from 30 consecutive patients with follicular conjunctivitis for adenovirus, HSV, and *C. trachomatis*. In this study, PCR was compared with cell culture and direct immunofluorescence for the detection of *C. trachomatis*. Only four patients were positive for *C. trachomatis* by PCR. Two of the four patients were positive by cell culture and one of four patients was positive by direct immunofluorescence. Thus, PCR appeared to be an equally specific and more sensitive method than cell culture or the direct immunofluorescence test. In another study Tabrizi et al90 compared culture and PCR techniques in the detection of *C. trachomatis* in 200 clinical samples including eye swabs (30%). A total of 173 specimens were assessable by PCR of which 24 (13.8%) were positive by both methods and four specimens were positive by PCR and negative by culture. Overall the PCR was 100% sensitive and 97.3% specific compared with cell culture, 79% sensitive and 87.1% specific by PCR. A more recent study91 compared cell culture and PCR in 341 specimens and found 96% sensitivity and 94% specificity for PCR.

RELIABILITY

Because of its sensitivity, false positive results due to the carryover of small amounts of the products of previous PCR tests may be encountered. Such problems can be avoided by strict application of a variety of preventative measures.92 False negative results may arise as a result of failure of PCR amplification. The most common cause of PCR failure is due to the introduction of inhibitors with the test sample.93 A variety of sample preparation techniques are now available to help avoid such problems and control for sample inhibition can be accomplished by the inclusion of internal control molecules94 or by amplification of human DNA in the sample (for example, β globin gene).95

AUTOMATION

Nucleic acid amplification procedures may be automated to improve the reproducibility, speed, and overall cost of tests. An example is the Cobas Amplicor (Roche Molecular Systems) automated PCR system101 and the ligase chain reaction test kit (Abbott Diagnostics Ltd).102 While commercial test procedures and automation are, in relation to ocular disease, currently only available for *C. trachomatis*,62 90 the available test repertoire is increasing.

Discussion and conclusions

The ideal test for diagnosing ocular pathogens has been defined as one whose result is available before the patient leaves the doctor’s office.103 However, achieving sensitivity, specificity, low cost, long term shelf storage, and ease of performance by office staff without the need for expensive equipment or hazardous reagents currently presents a formidable technological challenge. Although PCR achieves the accuracy needed for diagnosis of ocular infectious agents, it still lacks the speed and simplicity required for an office based test. The anticipated introduction of effective treatment of adenoviral keratoconjunctivitis poses a real challenge to the applicability of the emerging tests discussed in this review. To allow dispensing of treatment and discharge of the patient from clinic (where cases of adenoviral keratoconjunctivitis pose a real threat to other patients and staff) test results would be required within 10–30 minutes. At the present time only immunochromatography can provide information within such a time frame but the low sensitivity of such tests is a major drawback.
Diagnosis of viral and chlamydial keratoconjunctivitis

625

procedures,98 including rigorous application of anti-cross contamination
cult communication with the

disadvantages. Particularly in relation to
positive and false negative results generated are serious
experienced microscopists and although commercial en-
specimens are submitted and examined by skilled and
HSV, and chlamydia. The direct immunofluorescence test
tics of enzyme immunoassay, culture, and direct
laboratories without access to PCR, the conventional tech-
ries. These techniques are evolving rapidly and are likely
to have an increasingly important role in therapeutic
management.

Diagnosis of viral and chlamydial keratoconjunctivitis

The choice of the optimal technique for diagnosing viral
and chlamydial keratoconjunctivitis depends upon the effi-
ciency, speed, and cost of the test. The performance of
conventional laboratory procedures is relatively poor and
the interpretative difficulties documented with these tests
are well recognised. Owing to their inherent sensitivity and
high specificity, nucleic acid amplification procedures, in
particular PCR, are recognised as the ultimate modern
diagnostic tool for the identification of adenovirus, HSV,
and C trachomatis in clinical eye swab samples. However, in
laboratories without access to PCR, the conventional tech-
niques of enzyme immunoassay, culture, and direct
immunofluorescence are useful for diagnosing adenovirus,
HSV, and chlamydia. The direct immunofluorescence test
can, however, only be recommended if a small number of
specimens are submitted and examined by skilled and
experienced microscopists and although commercial en-
zyme immunoassays have the advantages of low cost and
suitability for testing large numbers of specimens, the false
positive and false negative results generated are serious
disadvantages. Particularly in relation to C trachomatis
infection, inaccurate diagnosis in a patient being investi-
gated for conjunctivitis and not sexually transmitted
disease, can lead to difficult communication with the
patient and even litigation.

A conceptual difficulty with all nucleic acid amplifica-
tion procedures is the finding of positive detection of
nucleic acid in the absence of viable organisms (as deter-
mained by culture) or of antigens. The current
sophistication of PCR means that provided due
attention is given to intralaboratory quality control
including rigorous application of anti-cross contamination
procedures,99 the finding of the nucleic acid of an
infectious organism in an ocular specimen is significant.
The presence of residual nucleic acid usually indicates
that infection persists well beyond the period indicated by
cell culture or antigen detection tests. Factors generated
in the course of the clinical response such as the
elaboration of antibodies, interleukin 1, interferon
gamma, and tumour necrosis factor (TNF) might inhibit
or alter the metabolic capacity, surface receptor expres-
sion, or infectivity and therefore culturability or the
antigenicity of the organism. In this way the infectivity
might fall while the organism, containing DNA, is still
detectable by PCR.

Nucleic acid amplification may, as has happened with
other non-culture diagnostic procedures, also detect an
infectious agent in circumstances which are not consistent
with the clinical features under investigation. Such findings
should not be dismissed because these diagnostic pro-
cedures have proved to be a powerful tool in elucidating
the aetiology of several ocular diseases previously classified
as idiopathic.

A further item of value in detection of nucleic acid in
ocular specimens is in the assessment of treatment failure.
Until recently, treatment failure was defined solely on the
basis of positive culture. For the reasons outlined above,
the lack of detection of infectious organisms may not signal
the end of a disease process. Non-culture test results,
particularly those of high sensitivity, are very probably a more
reliable indicator of treatment failure. The continued
development of nucleic acid amplification procedures will
lead to the wider availability of quantitative procedures
which will refine our ability to monitor the efficiency and
progress of therapeutic regimens.

The continued development of nucleic acid amplifica-
tion procedures will also lead to a reduction in the overall
cost of diagnosing viral and chlamydial keratoconjunctivi-
tis. Already PCR procedures are available to allow the
simultaneous investigation of several pathogens using one
test in which the three or more organism specific oligonu-
cleotide primer pairs are included (multiplex PCR). Such
tests allow the testing of a single sample and permit easy
identification of possible, albeit rare, concurrent
infection.106-107 In our own laboratory, for example, a multi-
plex PCR has been developed for the simultaneous investi-
gation of adenovirus, HSV, and β globin in ocular swabs76
and, currently, we are modifying the technique to include
C trachomatis detection.

In conclusion, nucleic acid amplification procedures are
valuable modern techniques for the diagnosis of infectious
ocular disease. The availability of automation and the
more widespread availability of commercial assays will
facilitate the use of these techniques in routine laborato-
ries. These techniques are evolving rapidly and are likely
to have an increasingly important role in therapeutic
management.

ELFATH M ELMIFRO
ROBERT J COOPER
Division of Virology, Department of Pathological Sciences,
University of Manchester

PAUL E KLAPPER
ANDREW S BAILEY
Clinical Virology Laboratory, Manchester Royal Infirmary,
Manchester

ANDREW B TULLO
Royal Eye Hospital, Manchester
Correspondence to: Mr Elfath M Elmifro, University Virology, 3rd Floor,
Clinical Sciences Building, Manchester Royal Infirmary, Oxford Road,
Manchester M13 9WL.

1 Dart JKG. Eye disease at a community health centre. BMJ 1986;293:1477–
80.
2 Jones NP, Hayward JM, Khaw PT, et al. Function of an ophthalmic accident
and emergency department: results of a six month survey. BMJ 1986;292:
188–90.
3 Appell PA, deLusie VP, Bartolomei A. Viral conjunctivitis. In: Tabbara
453–70.
4 Leitner TG, Melton J, Date PY, et al. Epidemiology of ocular herpes simplex
5 Ol JØ. Ocular infections of herpes simplex virus type 2 in adults. In: Darrel
6 Foster A, Sommer A. Corneal ulceration, measles, and childhood blindness
7 Tabbara KF, Chlamydia: trachoma and inclusion conjunctivitis. In: Tabbara
KF, Hyndriuk RA, eds. Infections of the eye. London: Little, Brown,
8 Ford E, Nelson KE, Warren D. Epidemiology of epidemic keratoconjunctivi-
9 Darougar S, Monnickendam MA, Woodland RM, Management and
prevention of ocular viral and chlamydial infections. CRC Crit Rev Microbiol
10 Tabbara KF, Ross-Degnan D. Blindness in Saudi Arabia. JAMA 1986;254:
3378–84.
11 Stenberg K, Mardh P. Genital infection with Chlamydia trachomatis in
patients with chlamydial conjunctivitis: unexplained results. Sex Transm Dis
12 Postema EL, Reijemer I, van der Meiwen JD. Epidemiology of genital
chlamydial infections in patients with chlamydial conjunctivitis: a
13 Garland SM, Malatt A, Tabrizi S, et al. Chlamydia trachomatis conjunctivi-
tis, prevalence and association with genital tract infection. Med J Aust
15 Gottsch JD. Surveillance and control of epidemic keratoconjunctivi-
16 Nakagawa H. Treatment of chlamydial conjunctivitis. Ophthalmologica
17 Lee SY, Laibson PR. Medical management of herpes simplex ocular infec-
18 Wishart PK, James C, Wishart MS, et al. Prevalence of acute conjunctivitis
caused by chlamydia, adenovirus, and herpes simplex virus in an ophthal-
19 Darougar S, Woodland RM, Walpita P. Value and cost effectiveness of
double culture tests for diagnosis of ocular viral and chlamydial infections. Br J
20 Fitch CP, Rapoza PA, Owens S, et al. Epidemiology and diagnosis of acute
immunoassay and polyme: nase chain reaction with the clinical examination
22 Rao SK, Madhavan HN, Radmanabhan P, et al. Ocular chlamydial
23 Kowalski RP, Romanowski EG, Cruz TA, et al. Immunnoassay, PCR or slit
lamp diagnosis: which is superior for detecting ocular herpes simplex virus
24 Ankers HE, Klapper PE, Cleeter GM, et al. The role of a rapid diagnostic
test (adenovirus immune dot-blot) in the control of an outbreak of aden-


---


Visitors to the world wide web can now access the *British Journal of Ophthalmology* either through the BMJ Publishing Group’s home page ([http://www.bmjpg.com](http://www.bmjpg.com)) or directly by using its individual URL ([http://www.bjophthalmol.com](http://www.bjophthalmol.com)). There they will find the following:

- Current contents list for the journal
- Full text of the issue
- Contents lists of previous issues
- Members of the editorial board
- Information for subscribers
- Instructions for authors
- Details of reprint services.

A hotlink gives access to:

- BMJ Publishing Group home page
- British Medical Association web site
- Online books catalogue
- BMJ Publishing Group books.

The web site is at a preliminary stage and there are plans to develop it into a more sophisticated site. Suggestions from visitors about features they would like to see are welcomed. They can be left via the opening page of the BMJ Publishing Group site or, alternatively, via the journal page, through “about this site”.

Downloaded from [http://bjo.bmj.com/](http://bjo.bmj.com/) on October 14, 2017 - Published by [group.bmj.com](group.bmj.com)
Diagnosis of viral and chlamydial keratoconjunctivitis: which laboratory test?

ELFATH M ELNIFRO, ROBERT J COOPER, PAUL E KLAPPER, ANDREW S BAILEY and ANDREW B TULLO

Br J Ophthalmol 1999 83: 622-627
doi: 10.1136/bjo.83.5.622

Updated information and services can be found at:
http://bjo.bmj.com/content/83/5/622

References
This article cites 96 articles, 27 of which you can access for free at:
http://bjo.bmj.com/content/83/5/622#BIBL

Email alerting service
Receive free email alerts when new articles cite this article. Sign up in the box at the top right corner of the online article.

Topic Collections
Articles on similar topics can be found in the following collections
- Conjunctiva (216)
- Ocular surface (618)
- Cornea (524)
- Eye (globe) (708)
- Epidemiology (1075)
- Choroid (565)
- Neurology (1355)
- Vision (627)
- Public health (479)

Notes

To request permissions go to:
http://group.bmj.com/group/rights-licensing/permissions

To order reprints go to:
http://journals.bmj.com/cgi/reprintform

To subscribe to BMJ go to:
http://group.bmj.com/subscribe/