

PAPERS AND SHORT REPORTS

Diagnosis of ophthalmia neonatorum

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Abstract

Ninety consecutively seen babies with eye discharge in the first three weeks of life were examined. Four babies had "sticky eyes" with no evidence of ophthalmia and had uniformly negative cultures and test results for antichlamydial antibody; these babies were excluded. Of the 86 babies with ophthalmia neonatorum, *Neisseria gonorrhoeae* was isolated from eight, *Chlamydia trachomatis* from 44, other bacteria alone from 20, and 14 had negative cultures. Three babies with negative cultures had longstanding conjunctivitis and had been treated with chloramphenicol eye ointment; all had antichlamydial IgM antibodies, indicating that the conjunctivitis was chlamydial. Hence the total number of babies whose conjunctivitis was chlamydial was 47. The result of the Gram stained conjunctival smear correlated well with that of culture and final assessment by the microimmunofluorescence test, enabling an immediate presumptive diagnosis to be made of gonococcal, chlamydial, or bacterial conjunctivitis. Prompt and effective treatment of babies was started. Explanation to the mother and contact tracing were carried out when the confirmatory cultures and antibody tests were completed.

The Gram stained conjunctival smear is a highly sensitive, specific, and predictive test for the aetiological agent of ophthalmia neonatorum. By virtue of its simplicity and rapidity the test may be useful in developing countries.

Introduction

Ophthalmia neonatorum is commonly due to the transmission of a sexually transmitted infection from the mother. Ophthalmias, particularly the persistent forms, are usually treated by general practitioners with local antibiotics such as neomycin or chloramphenicol. If there is no response to treatment the baby may then be referred to a paediatrician or to a sexually transmitted diseases or ophthalmology clinic. Accurate diagnosis is important, not least because ophthalmia neonatorum due to *Neisseria gonorrhoeae* or *Chlamydia trachomatis* indicates that the mother and probably also the father are infected.^{1,2} The mothers commonly suffer from pelvic inflammatory disease,^{1,3} which may cause one child sterility. In the baby the affected eyes may be damaged. Other sites such as the pharynx and rectum^{4,6} may also be colonised. Chlamydial ophthalmia may be complicated by pneumonia.^{7,8} Treatment, which must be systemic for gonococcal and chlamydial infections, depends on diagnosing the cause of the conjunctivitis. The initial diagnostic methods, however, should be simple, be accurate in experienced hands, and provide immediate results. Microscopy of the Gram stained smear is generally used for screening patients with urogenital and anorectal infections in sexually transmitted diseases clinics; less commonly it is used for the presumptive diagnosis of gonococci in the conjunctival material. The aim of this study was to assess the use of the Gram stained conjunctival smear in diagnosing the causes of ophthalmia neonatorum.

Patients and methods

We studied 90 babies who were referred consecutively to the Whitechapel Clinic with the onset of eye discharge in the first three weeks of life. Seventy seven (86%) of the babies had had local ocular treatment with neomycin or chloramphenicol before being seen. Inpatients at The London Hospital who were referred for advice about a "sticky eye" were investigated within the day of referral. Until seen they had either had no treatment or been given 1% neomycin eye ointment only. After a history and examination the following investigations were performed.

Scrapings were obtained from both conjunctivae with a sterile platinum loop for Gram stained smears, which were examined microscopically (1000 magnification) by the examining physician for polymorphonuclear leucocytes and bacteria.

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Sterile cotton tipped swabs were used to obtain material from both conjunctivae, throat, rectum, and vulval introitus (girls) or urethral meatus (boys) and plated on brain-heart infusion agar medium for isolating *N gonorrhoeae*. Additional swabs from these sites were placed in separate phials of 0.2M sucrose phosphate medium,⁹ which were stored in liquid nitrogen before inoculation on to irradiated or cycloheximide treated McCoy cells for chlamydial cultures.^{10 11} Sterile cotton tipped swabs were also used to obtain material from both conjunctivae and placed in Stuart's transport medium for bacterial cultures.

Blood was taken by heel prick on to a cellulose sponge (5 × 3 × 1 mm) which adsorbed 100 µl blood when saturated. This was used to estimate antichlamydial antibody titres to the D-K serotypes by the modified microimmunofluorescence method.¹²

A *chest radiograph* was taken if there were chest symptoms or chlamydial infection was suspected.

Results

The results of the Gram stained conjunctival smears were categorised in five groups and correlated with the culture results (table I). Table II shows the sensitivity (proportion of babies with positive cultures whose smears predicted the positive cultures), specificity (percentage of babies with negative cultures whose smears predicted the negative cultures), and positive predictive value (percentage of total true and false positive results

TABLE I—Correlation of conjunctival smears with cultures

Group*	No (%) of babies	No (%) with cultures positive for <i>N gonorrhoeae</i>	No (%) with cultures positive for <i>C trachomatis</i>	No (%) with bacteria grown	No (%) with negative cultures
1	8 (9)	8 (9)	0	0	0
2	45 (50)	0	38 (42)	2 (2)†	7 (8)‡
3	27 (30)	0	0	20 (22)	7 (8)
4	6 (7)	0	0	0	6 (7)
Total	86 (96)	8 (9)	38 (42)	22 (24)	20 (22)
5	4 (4)	0	0	0	4 (4)

*Group 1: smears contained polymorphonuclear leucocytes and Gram negative intracellular diplococci. Group 2: smears contained polymorphonuclear leucocytes and occasional or no bacteria. Group 3: smears contained polymorphonuclear leucocytes and many bacteria. Group 4: smears contained occasional or no polymorphonuclear leucocytes (all six babies initially culture positive for chlamydia but partially treated with chlortetracycline eye ointment before enrolment in study). Group 5: smears contained occasional or no polymorphonuclear leucocytes, excluding diagnosis of ophthalmia neonatorum (these babies excluded from study).

†Cultures also positive for chlamydia.

‡Three babies had IgM antichlamydial antibodies.

TABLE II—Sensitivity, specificity, and predictive value of Gram stained conjunctival smear in making presumptive diagnosis in groups 1-3

Group*	No of babies	Sensitivity (%)	Specificity (%)	Predictive value (%)
1	8	100.0	100.0	100.0
2	45	100.0	91.8†	91.1†
3	27	100.0	90.0	74.0

*See table I for definition of groups.

†Value corrected for three babies treated with chloramphenicol eye ointment who had IgM antichlamydial antibodies but negative cultures for *C trachomatis*.

TABLE III—Serum antichlamydial antibody titres of four babies with IgM antibodies compared with titres in their mothers

Baby	Babies		Mothers	
	IgG	IgM	IgG	IgM
A	128	64	256	0
B	256	128	256	0
C	256	128	256	0
D	128	32	256	0

Babies A-C were culture negative for *C trachomatis* from group 2. Baby D was from group 4 in which *C trachomatis* was isolated before local treatment was begun with chlortetracycline eye ointment.

which were true positives) of the Gram stained smear in each group in making a presumptive diagnosis.

N gonorrhoeae was isolated from the conjunctivae of eight babies; two isolates from a set of twins were due to a penicillinase producing strain. Of the 27 babies in group 3, bacteria were isolated from 20, all of whom had negative cultures for *C trachomatis* and *N gonorrhoeae*. The bacteria isolated were *Staphylococcus aureus* (three babies), *Staph aureus* mixed with *Haemophilus influenzae* (two), coliforms (three), *Pseudomonas* spp (one), *Streptococcus pneumoniae* (two), β haemolytic streptococci (one), *Str viridans* (two), *Branhamella catarrhalis* (one), *Staph epidermidis* (three), and *Staph epidermidis* mixed with coliforms (two). The remaining seven had negative isolates from the conjunctivae.

OTHER FINDINGS

A total of 18 babies had IgG antichlamydial antibodies with titres ranging from 1/16 to 1/256. Four of these babies also had IgM antichlamydial antibodies. Table III lists the antibody titres in these four babies and their mothers. Fifteen of the 18 babies were in group 2, all of whom were culture positive for *C trachomatis* except for three babies with IgM antibodies who had been treated with chloramphenicol eye ointment. The other three babies with IgG antichlamydial antibodies were in group 4.

Of the 47 babies positive for chlamydia (44 conjunctival culture positive, three IgM positive), the agent was also isolated from the nasopharynx in 14, from both the nasopharynx and rectum in four, and from the rectum alone in one. The isolations from the nasopharynx included two of the six babies given local chlortetracycline eye ointment and referred after *C trachomatis* had been isolated. Twelve babies had abnormal chest x ray findings, suggesting chlamydial pneumonia of varying degree, and 10 of these had *C trachomatis* isolated from the nasopharynx. The three babies with IgM antichlamydial antibodies had negative isolates from all sites for *C trachomatis*. Twenty nine of the 38 babies from whom *C trachomatis* was isolated from the conjunctivae at the Whitechapel Clinic had been treated with neomycin eye ointment. The other nine had received no local treatment.

Discussion

All eight babies in group 1 with polymorphonuclear leucocytes and Gram negative intracellular diplococci in conjunctival smears were culture positive for *N gonorrhoeae*, making the smear a sensitive and specific test with a positive predictive value of 100% in diagnosing gonococcal ophthalmia in this small group. Nevertheless, difficulty may arise in interpreting such smears if the infection is due to *B catarrhalis*.¹³ The single case in this study did not give difficulty.

Thirty eight of the 45 babies who had Gram stained smears showing many polymorphonuclear leucocytes without bacteria or with occasional bacteria (group 2) were culture positive for *C trachomatis*. Smears in group 2 were 100% sensitive in predicting chlamydial ophthalmia. Three other babies in this group with negative isolates who were seen late in the disease with high IgM antibody titres should be accepted as having chlamydial infection. High antichlamydial antibody titres may be associated with negative chlamydial cultures. With the addition of these three babies to the 38 with positive cultures the specificity of the Gram stained smear in diagnosing chlamydial conjunctivitis was 91.8% and the positive predictive value 91.1%.

Rapid diagnosis of chlamydial conjunctivitis may be made with Giemsa stained conjunctival smears.¹⁴ This technique needs experience in staining and interpreting the smear and is not routinely performed in sexually transmitted diseases clinics. Fluorescein conjugated monoclonal antibodies against chlamydial elementary bodies may be used to obtain quick results, but this test requires a fluorescence microscope and particular skill. Confirmation by culture takes a few days and is not always available. The Gram stained smear is simple and rapid to perform and indicates gonococcal infection accurately and chlamydial infection with considerable accuracy if it shows polymorphonuclear leucocytes and very few or no bacteria. Instead of a platinum loop to obtain conjunctival material a sterile cotton tipped swab may be used.

Mycoplasma spp, which may possibly cause some cases of ophthalmia neonatorum,¹⁵ were not looked for in this study.

Finding polymorphonuclear leucocytes with many bacteria in the Gram stained conjunctival smear (group 3) correctly predicted the association with positive bacterial cultures in 20 of 27 cases (74%). Some of these organisms, such as *Staph aureus*, *Str pneumoniae*, and *Haemophilus* spp, were acknowledged pathogens in the eyes.

The presence of only an occasional polymorphonuclear leucocyte or its absence in the conjunctival smear from the babies in group 4 is important. The six babies in this group were referred to us by ophthalmologists after isolation of *C trachomatis* from the conjunctiva and local treatment with 1% chlortetracycline eye ointment for one to two weeks. Treatment was completed in our clinic with systemic erythromycin by mouth. If cultures for *C trachomatis* had not been taken when chlortetracycline was prescribed the diagnosis of this potentially systemic infection would have been missed. Negative cultures were also obtained in three babies with chlamydial ophthalmia neonatorum treated with chloramphenicol eye ointment.

Chlamydial ophthalmia may be associated with secondary bacterial infection which may be controlled by neomycin eye ointment, facilitating culture of *C trachomatis*. Lack of response to local treatment should prompt referral for full investigations to exclude chlamydial infection. Because chloramphenicol may suppress *C trachomatis* and possibly cause blood dyscrasia, it seems advisable that when gonorrhoea has been excluded bacterial ophthalmia should initially be treated with neomycin eye ointment, though it is inactive against streptococci. Treatment may be changed according to response and bacterial sensitivities. No local sensitivity to neomycin occurred in this study. Neomycin, chloramphenicol, and tetracycline may all suppress gonorrhoea.

In the four babies in group 5 the absence of polymorphonuclear leucocytes and negative culture results enabled ophthalmia neonatorum to be excluded with confidence.

This study suggests that the Gram stained smear is a useful and sensitive test with a high positive predictive value for identifying the

aetiological agent of ophthalmia neonatorum. It may be useful in developing countries where more elaborate diagnostic tests are not available.

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SHORT REPORTS

Traditional Chinese acupuncture as an antiemetic

The problem of postoperative nausea and vomiting continues to confound anaesthetists, surgeons, and patients despite modern techniques and drugs.¹ Though the analgesic effect of acupuncture has been well studied, there have been few studies into an antiemetic effect. Dundee *et al* have recently shown an antiemetic effect of acupuncture at the P6 acupuncture locus (Nieguan),² which is a point recommended for the treatment of nausea in classical acupuncture and is located 2 cun (about 3 cm) from the distal palmar crease, at a depth of 1-2 cm. We undertook the present study to corroborate their findings.

Patients, methods, and results

Approval was obtained for the study from the hospital ethical committee, and written consent was given by all subjects. The investigation was designed as a double blind randomised trial. Consecutive patients scheduled for elective laparoscopy (for tubal ligation or diagnosis) were studied; one group received acupuncture at the P6 locus and the control group did not. The P6 acupuncture locus was identified and marked before operation; patients were allocated to each group by drawing a random number after inducing anaesthesia. All patients were anaesthetised by an identical technique; oral temazepam was given as premedication, and endotracheal anaesthesia was induced and maintained with thiopentone 5.0 mg/kg, 70% nitrous oxide, 0.5% isoflurane, oxygen, and morphine 0.1 mg/kg. Muscle relaxation was obtained with vecuronium 0.1 mg/kg and reversed with neostigmine and atropine.

Acupuncture was performed during surgery with a regular acupuncture needle, which was manually rotated 20 times each minute. After the operation the patients were not mobilised until the end of the study; metoclopramide 10 mg was prescribed and given intramuscularly at the discretion of the attending staff, who, like the subjects, were unaware if acupuncture had been used or not.

The occurrence of nausea and vomiting was assessed by interview at 30

minutes, 60 minutes, and six hours after surgery by an independent observer. The two groups were similar with regard to age of patients, nature and duration of surgery, and the number in each group requiring postoperative morphine. The table shows the prevalence of emetic events and the use of antiemetics during the six hours of the study. Twenty three (52%) of all the patients experienced nausea with or without vomiting, and 15 (34%) of all the subjects vomited. Acupuncture did not lead to a significant reduction in nausea or vomiting.

Prevalence of nausea and vomiting, and use of antiemetics*

	Acupuncture (n=20)	No acupuncture (n=24)
0-1 Hours:		
Nausea	5	5
Nausea and vomiting	4	1
Required antiemetics	3	1
1-6 Hours:		
Nausea	11	12
Nausea and vomiting	9	6
Required antiemetics	3	3

*Differences between groups not significant at $p=0.05$ (Fisher's exact test).

Comment

The overall prevalence of nausea and vomiting in our study was similar to that reported after similar surgery³ and underlines the magnitude of this "minor complication of anaesthesia." Randomised double blind trials of acupuncture are scarce, as it is difficult to blind both observer and subject to the treatment used⁴; in our study we avoided many of these difficulties by giving acupuncture under anaesthesia. It is not known if acupuncture under anaesthesia is effective in man, but there are several animal studies that show an analgesic effect of acupuncture given under anaesthesia.⁵