AETIOLOGY OF CONJUNCTIVITIS IN SEBOKENG HOSPITAL NEONATES WHO RECEIVED ROUTINE PROPHYLAXIS AT BIRTH AGAINST EYE INFECTION

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DECLARATION

I, Dr Cherian Thomas, hereby declare that this research report is my own work. It has not been submitted to any other University before for any degree or examination. It is being submitted for the degree of Master of Science in Medicine (Child Health), University of the Witwatersrand, Johannesburg.

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DATE : 8/05/99

DEDICATION

I dedicate this research report to my late parents, Dr M. Thomas and Dr (Ms) Alice Thomas, my dear wife Anita, my children Thomas Junior and Serra.

ABSTRACT

Introduction

Neonatal conjunctivitis remains an important cause of morbidity, particularly in developing countries, despite the widespread use of antibacterial prophylaxis.

Objectives

1. To establish the aetiology of conjunctivitis among Sebokeng neonates.
2. To assess the efficacy of the prophylaxis used at Sebokeng Hospital.
3. To propose an effective prophylaxis and treatment protocol for neonatal ophthalmia based on the study results.

Method

A prospective, observational study was carried out at Sebokeng Hospital, Gauteng. Hospital-born neonates presenting with conjunctivitis, between 0 – 30 days, who had routine prophylaxis (10% Spersamide) at birth were studied. . In addition, 10 home born infants who did not receive prophylaxis and presented with neonatal conjunctivitis were also studied.

The study was conducted over a 8 month period (November 1995- July 1996)

Two eye swabs were collected from each neonate, one for routine culture and susceptibility tests and the other for chlamydial culture. Results were statistically analysed using Chi-squared contingency table tests.

Mothers of affected infants were interviewed about the course of their pregnancy and about possible predisposing factors for their infant's illness.

Results

In the 105 hospital born infants with neonatal conjunctivitis, the commonest pathogenic organisms isolated were Staphylococcus aureus in 23.8%, Chlamydia trachomatis in 12.4%, Neisseria gonorrhoeae in 11.4% and Streptococcus pneumoniae in 9.5%. Gram negative bacilli were found in a total of 22 (20.9%) patients, the commonest being Klebsiella pneumoniae

The incidence of ophthalmia neonatorum was 3.66 cases per 100 live births; that of chlamydia 0.45 cases per 100 live births and the gonorrhoeae rate was 0.41 cases per 100 live births.

Though Spersamide (10% sulphacetamide) eye drops appeared to function adequately as a prophylactic agent, its efficacy in treating N. gonorrhoeae, S. aureus and C. trachomatis were inadequate. An overall 96% sensitivity rate to Chloramphenicol was shown by the commonest pathogenic organisms.

Home-born babies who did not receive any prophylaxis showed a higher rate of gonococcal and S. aureus infection rate (30% each) than hospital born babies. However, this was not statistically significant owing to the small number of neonates in this subset (10 neonates).

Only 25 (20%) mothers were married. A history of vaginal discharge was present in 78% of mothers, 68% of whom received some form of treatment antenatally.

Conclusions

S. aureus emerged as the most common cause of eye infection among Sebokeng Hospital born neonates followed by C. trachomatis and N. gonorrhoeae. Spersamide 10% eye drops was found to be inadequate as a prophylatic agent against eye infection. It is recommended that it should be replaced immediately by chloramphenicol eye drops or eye ointment. Recommendations are also provided on the optimal management of established neonatal conjunctivitis.

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1.0 INTRODUCTION

Neonatal conjunctivitis is defined as inflammation of the conjunctiva in an infant younger than 1 month old. It is characterised by redness and swelling of the eyelids and palpebral conjunctiva and a purulent discharge, with one or more polymorphonuclear cells per high power field in a gram-stained conjunctival smear [1].

In 1881, prophylactic treatment for neonatal conjunctivitis was introduced by Crede. He used silver nitrate to prevent infection with Neisseria gonorrhoeae. [1] Over the past century, this practice has been maintained to prevent neonatal conjunctivitis.

Although chemical and viral agents produce ophthalmia neonatorum, bacteria including chlamydia continue to play a major role in causing neonatal conjunctivitis [2-6].

The known causes of neonatal conjunctivitis have continued to expand and now includes Staphylococcus, Streptococcus, Neisseria species, herpes virus as well as chemical conjuctivitis. This expansion has brought to light a few organisms which were not responsive to silver nitrate and this has prompted a search for new and broader prophylactic agents, e.g. povidone iodine, tetracycline eye ointment, erythromycin eye ointment, etc.

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It has been reported that 42% of neonates exposed to N. gonorrhoeae during delivery and 31% exposed to Chlamydia trachomatis may develop conjunctivitis. Neonatal infection caused by herpes simplex virus develops in 40 - 50% of newborns exposed to active genital herpes virus [2].

1.1 CAUSES OF NEONATAL CONJUNCTIVITIS

1.1.1 Chemical conjunctivitis

Chemical conjunctivitis used to be the most common form of neonatal conjunctivitis, related to the prophylactic use of 1% silver nitrate. It is self-limiting and resolves in 24 to 48 hours [1-2].

1.1.2 Bacterial conjunctivitis

As noted earlier, various bacteria continue to cause neonatal conjunctivitis despite prophylaxis. Traditionally N. gonorrhoeae has been blamed as the cause of typical ophthalmia neonatorum with varying grades of clinical presentation [2-6]. Despite significant improvements in the prevention of conjunctivitis since antibacterial prophylaxis was introduced, N. gonorrhoeae still accounts for a significant number of cases. It presents as a hyperacute purulent conjunctivitis with a variable onset [2].

Other bacterial organisms can produce neonatal conjunctivitis because several types of bacteria can be found in the endocervix during early stages of labour [1, 7-9]. Gram positive organisms include Staphylococcus aureus, S. pneumoniae and groups A and B streptococci, gram negative

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Escherichia coli, Klebsiella pneumoniae, Serratia marcescens as well as Proteus and Enterobacter species.

The bacteria found in the conjunctiva of the newborn reflect the mode of delivery (whether vaginal or by caesarian section), In infants delivered vaginally, the bacteria are characteristic of the flora of the female genital tract [5, 10]. In babies born by caesarian section the conjunctival flora depends on the time elapsed between the membrane rupture and the operation [1].

In a study of 100 newborns, examining the bacteria isolated from conjunctival cultures taken within 15 minutes of delivery, anaerobic organisms accounted for 78% of the positive cultures and aerobic organisms for 22%. [1]

Frequently isolated anaerobes were Lactobacillus (41%) and Bifidobacterium species (19%) diphtheroids (6%), Propionibacterium acnes (6%) and Bacteroides species (5%). [2, 6] Of the aerobic organisms isolated, Staphylococcus epidermidis are the most common (9%) followed by Corynebacterium (6%), Streptococcus species (3%) and Escherichia coli (2%). [1]

A study conducted in 1984 in a Nairobi hospital where no prophylaxis was used gives useful information on the likely organisms causing neonatal conjunctivitis in an African setting. Twenty-three percent of the neonates developed ophthalmia neonatorum. Gonococci accounted for 12% of cases, chlamydia for almost a third (32%), and a combination of the two for 3%. In those cases of ophthalmia not caused by these two organisms, the most frequent organisms were Haemophilus influenzae , Staphyloccoccus aureus and Streptococcus pneumonia, each of which caused 6 - 7% of cases. [11]

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1.1.3 Viral conjunctivitis

Neonatal herpes simplex virus infection may affect the eyes as well as the skin with oral and vaginal lesions. If the mother has a history of a genital herpetic infection, neonatal herpes should be suspected. [1] In one reported series of 297 neonates with herpes simplex virus infection, ocular pathology was seen in 17% and conjunctivitis, specifically, in 10%. [1]

1.2 PATHOGENESIS AND PATHOGENETIC ROLE OF ORGANISMS CAUSING OPHTHALMIA NEONATORUM

The incidence and pattern of colonization depend on patient age, geographic location and ambient climatic conditions. Although some commensal organisms may produce an opportunistic infection, the pathogenic species are more likely to cause clinical disease, particularly conjunctival infection [2].

The clinical disease and the severity of symptoms, signs and complications depend on the pathogenesis of the disease process. This is determined by the growth characteristics of the organism, the production of toxins or enzymes by it and the type and degree of inflammatory response mounted by the host [2, 3].

Bacteria usually need to adhere to the epithelial surface before they can initiate clinical disease. The intact epithelium is an effective barrier to most organisms with the exception of N. gonorrhoeae, Corynebacterium diphtheriae, Listeria and Haemophilus aegyptius, that can, through specialized surface attachments, penetrate an intact epithelium [2, 4].

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The specialized surface attachments of organisms like the pseudomonas and gonococci enable biologic adhesion to occur, to the glycocalyx of injured epithelium, which then allows entry of diffusable toxin or bacterial products into the stroma [2].

A variety of enzymes can be produced by bacteria (e.g. proteases, coagulases, nucleases, elastases, lipases and fibrinolysins, etc). They also produce various toxins e.g. α, β and γ toxin of Staphylococcus. Disruption of the underlying tissue by the digestive effect of the released enzymes then allows further access of the organisms into tissue where they protect themselves from host defenses [2, 4].

In the conjunctiva the pathogenetic options produce a broad spectrum of diseases from self-limiting infections, such as a modest symptomatic conjunctival injection and chemosis, to severe inflammatory membranes that slough causing pain and photophobia.

1.3 DIAGNOSIS

Because of the potentially disastrous outcome of untreated neonatal conjunctivitis, the diagnosis of the aetiological agent and appropriate treatment must be initiated as soon as possible [1].

Though clinical signs and symptoms give minimal clues about the organism responsible for the infection, the time of onset may give some clues, e.g. conjunctivitis due to N. gonorrhoeae usually has its onset during the first two to

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five days of life. Chlamydia trachomatis conjunctivitis usually has its onset during the second week. Signs and symptoms of conjunctivitis are obvious and vary in intensity with the organism responsible. In the case of N. gonorrhoeae, within a day eyelids become oedematous, with prominent chemosis and the emission of thick purulent discharge. In cases of C. trachomatis, and other bacteria, symptoms and signs are highly variable, ranging from mild to severe oedema of the eyelids with minimal or copious purulent discharge [7].

Viral conjunctivitis due to herpes simplex virus may present within two weeks after birth and may be preceded by vesicular skin rashes. It may be unilateral or bilateral. Presence of microdendritic or geographical ulcers in the cornea are the hallmark of neonatal herpes conjunctivitis [1].

However, because of the variability in clinical presentation, symptoms and signs are unhelpful in making an aetiological diagnosis. Thus, microbiological culture and susceptability remains imperative for the identification of the causative organism as well as establishing the most effective therapy.

Culture specimens of the conjunctival surface should be obtained without the use of topical anaesthetic using a calcium alginate or dacron swab inoculated onto blood agar, chocolate agar and thioglycollate broth. If gonococcal infection is suspected it is wise to inoculate it onto a Thayer – Martin agar. [2]

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Conjunctival smears can then be obtained after using topical proparacaine anaesthesia by gently scraping the everted palpebral conjunctiva with a platinum spatula. Scraping can then be evaluated using Gram's and Giemsa stains.

A smear from an infant with chemical conjunctivitis would be characterized by the presence of neutrophils and occasional lymphocytes: whereas bacterial conjunctivitis would contain bacteria and neutrophils.

Intracellular Gram negative diplococci are identifiable in up to 95% of Gram stains in eye culture positive cases of gonococcal conjunctivitis [2]. The smear from chlamydial conjunctivitis would show neutrophils, lymphocytes, plasma cells and basophilic intracytoplasmic inclusions in epithelial cells [10]. In the case of a viral conjunctivitis the smear would show lymphocytes, plasma cells, multi-nucleated cells and eosinophilic intranuclear inclusions [1, 12-14].

Thus, prior to the culture results being available, a preliminary diagnosis can be made from the examination of a smear. Viral cultures are only taken if the smears suggest it, and if there is evidence of herpes infection in the mother, since they are expensive.

1.4 PROPHYLAXIS

The use of 1% of silver nitrate instilled in the conjunctiva shortly after birth has been the mainstay of prophylaxis for neonatal conjunctivitis over the past century.

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Concerns about the emergence of organisms resistant to silver nitrate and the chemical conjunctivitis caused by it are reasons to look for alternatives [1, 12-13, 15].

Various studies have been carried out in different parts of the world using 0.5% erythromycin ophthalmic ointments, a 1% tetracycline ophthalmic ointment and povidone iodine (2.5% solution). The reports indicate that they are all as effective, or better than, silver nitrate as they do not cause chemical conjunctivitis and are as cost effective [1, 12-13]. Nevertheless none of them are 100% effective even when administered appropriately. See table 1,1.

TABLE 1.1 : OPHTHALMIA NEONATORUM : TABLE SHOWING STUDIES PUBLISHED AROUND THE WORLD COMPARING THE EFFICACY OF VARIOUS PROPHYLACTIC AGENTS

COUNTRY.	YEAR	SUBJECT NO	ORGANISM	SILVER NITRATE *%	TETRA-CYCLINE %	ERYTHRO-MYCIN %	NIL. %	POVIDONE IODINE %
USA (16)	1981	171	All organisms	Not effective	Not effective	-	-	-
ZAIRE (17)	1988	450	All organisms	0	0	-	-	-
KENYA (18)	1995	3117	All organisms	17.5	-	15.2	-	13.1
USA (19)	1980	559	Chlamydia	33	-	0	-	-
USA (20)	1989	230	Chlamydia	20	11	14	-	-
TAIWAN (13)	1992	425	Chlamydia	1.7	1.3	1.7	1.6	-

* Percentage represents effectiveness of the drug to organisms cultured from eye swabs.

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In the prevention of neonatal ocular infection, four levels of intervention can be used [11, 21-22].

The first involves the prevention of sexually transmitted diseases. The emergence of the human immunodeficiency virus has led to new health promoting strategies. These programmes may reduce the prevalence of sexually transmitted diseases, which in turn could reduce the risk to infants of exposure to the agents that cause neonatal conjunctivitis.

The second approach consists of antenatal screening. Ophthalmia neonatorum can be prevented by screening pregnant women for genital infection, particularly those at high risk for disease. Foul-smelling vaginal discharges must be treated aggressively, following culture of the organisms. [12].

The third approach is ocular prophylaxis at birth, which is simple and inexpensive. It consists of cleaning an infant's eyelids with a dry swab as soon as possible after birth and then instilling a safe, available and affordable antimicrobial agent.

Tetracycline eye ointment 1%, povidone iodine solution 2.5%, or chloramphenicol eyedrops are all equally effective as silver nitrate and cause less side effects (e.g. chemical conjunctivitis) [6, 9, 12, 15].

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Finally, early diagnosis and adequate treatment after identification of the causative organism can prevent corneal ulceration and blindness. Elimination of childhood blindness due to ophthalmia neonatorum needs an interdisciplinary approach involving gynaecologists, neonatologists, ophthalmologists and most importantly primary care workers. All primary health care workers should be educated about the cause, prevention and treatment of neonatal conjunctivitis.

1.5 TREATMENT

1.5.1 Bacterial Conjunctivitis

The standard therapy recommended for gonococcal neonatal conjunctivitis consisted of frequent topical aqueous penicillin and also systemically administered penicillin. With the emergence of penicillin resistant gonococcal strains, this treatment has fallen out of favour [1, 4, 12, 23].

Ceftriaxone in a single-dose intramuscular injection at 50mg/kg per 24 hours works extremely well, is quick and cost-effective. This also treats extra ocular gonococcal infection [24].

Co-infection with C. trachomatis is not unusual in gonococcal conjunctivitis. Treatment of chlamydial conjunctivitis must be aimed not only at ocular colonization but also toward eradication of the nasopharyngeal carriage [3, 5, 15]. Oral erythromycin estolate or ethyl succinate suspension, 25-50 mg/kg/day for 10 - 14 days is the treatment of choice [7-8, 10, 25].

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1.5.2 Viral Conjunctivitis

Although the efficacy of treatment of herpes simplex conjunctivitis and blepharitis has not been fully established [1], the use of topical trifluorothymidine should be considered. If there is no response, other anti-viral agents like acyclovir should be initiated locally and parenterally.

1.6 COMPLICATIONS

Complications of untreated neonatal conjunctivitis caused by N. gonorrhoeae were common prior to the institution of ocular prophylaxis in the late nineteenth century. Until then neonatal conjunctivitis was the leading cause of blindness in children [1].

Usual complications include corneal ulceration, perforation, iridocyclitis, anterior synechiae and panophthalmitis.

Long term complications of chlamydial conjunctivitis are rare, but this should be considered as a presenting sign of chlamydial infection in the newborn, which may cause chlamydial pneumoniae, rectal and vaginal infection, etc.

2.0 THE RESEARCH PROBLEM

It has been an established routine at Sebokeng Hospital to instill Spersamide 10% eye drops (a combination of sodium sulphacetamide and mercuric borate), into the eyes of all the hospital born neonates (3–5 drops in each eye). Despite this, many neonates continue to present at the hospital with conjunctivitis during their initial stay or after discharge. This results in the re-admission of babies and their mothers. A belief prevalent among the doctors in the casualty department, is that all cases of neonatal conjunctivitis are caused by gonococci. This results in the empirical use of intravenous crystalline penicillin and penicillin eye drops for all cases of neonatal conjunctivitis.

In many instances, this treatment regime has proved to be ineffective, inconvenient for the baby and the mother and has resulted in an unnecessarily prolonged stay in the hospital, which ultimately leads to a strain on the hospital budget. Treatment is often commenced without any eye swabs being taken for culture. This has resulted in poor understanding about the aetiology of conjunctivitis among these neonates and has impeded the establishment of an effective ocular prophylaxis and treatment protocol.

The aim of this study was to establish the organisms causing neonatal conjunctivitis in the Sebokeng area. It would also evaluate the efficacy of Spersamide 10% in preventing ophthalmia neonatorum. This would also assist in establishing a more effective treatment protocol.

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2.1 OBJECTIVES

2.1.1 Primary objectives

1. To establish the aetiology of conjunctivitis in neonates born at Sebokeng Hospital.

2. To assess the efficacy of the prophylaxis used at Sebokeng Hospital (Spersamide 10%).

2.1.2 Secondary objectives

1. To estimate the incidence of neonatal conjunctivitis in the Sebokeng area

2. To devise and propose a more cost-effective treatment protocol.

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3.0 METHODS

3.1 DESIGN

This was a prospective, descriptive, observational study.

3.2 DEFINITIONS

Neonate: A patient between 0 to 30 days of age.

Conjunctivitis: Redness and swelling of the eyelids and palpebral conjunctiva, sticky eyelids and an associated purulent discharge.

3.3 SELECTION OF PATIENTS

3.3.1 Inclusion criteria

- Any neonates who developed a conjunctivitis during their stay in the hospital (after birth)
- Any neonate who presented with conjunctivitis at the paediatric out-patient department at Sebokeng hospital between 08h00 and 16h00 from Monday to Thursday. Infants born outside the hospital but in the Sebokeng area, e.g. at home, were eligible for study, but were analysed separately (as they did not receive ocular prophylaxis).

3.3.2 Exclusion criteria

- Neonates with conjunctivitis who presented at the out-patient department after 16h00 each day from Friday to Sunday or on public holidays
- Parent unwilling to complete patient questionnaire.

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3.4 SAMPLE SIZE

It was decided to enroll all patients presenting over a 8-month period (November 1995- July 1996). It was estimated that this would include 100 patients.

3.5 COLLECTION AND STORAGE OF SPECIMENS

3.5.1 Specimen collection

At the initial visit, two eye swabs were collected, using sterile swabs, from each infected eye. The first swab was sent for microscopy and bacterial culture and susceptibility testing to the local, hospital laboratory. The second swab was placed in a chlamydia transport medium, packed in ice, and sent to a central laboratory in Johannesburg (South African Institute for Medical Research [SAIMR]) for chlamydial culture.

It was decided to confine the collection of swabs to office hours from Mondays to Thursdays since the laboratory facility at Sebokeng Hospital was only available from 08h00 to 17h00 each day and not at all during weekends and public holidays. In addition, the chlamydial eye swabs had to be transferred to the central SAIMR laboratory which was 78 km away. Transport of specimens between this facility and the hospital were recognised to be poor on weekdays and non-existent on weekends.

The researcher collected all specimens and took them immediately to the local laboratory where a laboratory technician performed routine microscopy, culture and susceptibility tests. Slides for microscopy were prepared from the swabs and were stained with Gram's stain.

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3.5.2 Specimen processing

The following media were used for inoculation:

1.	Blood Agar 5%	-	For streptococci, staphylococci, pneumococci
2.	Chocolate Agar	-	For Haemophilus spp and N. gonorrhoeae
3.	Thayer Martin Agar	-	For N. gonorrhoeae
4.	Serum Broth	-	For sub-culture for fastidious organisms
5.	MaConkey Agar	-	For Gram negative bacilli, e.g. Pseudomonas

Organisms cultured on the media were identified by standard methods.

For antibiotic susceptibility studies, disc susceptibility tests were used.

In cases where N. gonorrhoeae and H. influenzae were isolated Beta-lactamase strips were used.

For C. trachomatis culture, a cell culture technique (McCoy cells) was used by the SAIMR laboratory [26].

3.5.3 Questionnaire

Each infant's mother was interviewed. The questionnaire (a copy of which is attached) recorded information on the baby's place of birth, clinical history, including the receipt of ocular prophylaxis, and the mother's antenatal and perinatal history and its management.

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3.5.4 Collection of incidence data

To allow an estimate of the incidence of neonatal conjunctivitis in the Sebokeng area, a record was kept of all neonates who presented to the paediatric polyclinic, outside the study enrollment hours. All mothers, on discharge, from the hospital were also requested to come directly to the hospital if their child developed signs of conjunctivitis.

A printed notice, authorised by the Superintendent, was sent to the peripheral clinics to be displayed on the notice boards of these clinics. The content of this letter was mainly an appeal to the Primary Health nurses to refer cases of neonatal conjunctivitis to Sebokeng Hospital's paediatric Polyclinic, without commencing any treatment.

3.5.5 Spersamide 10% ®Eyes drops

The agent used for ocular prophylaxis in this study was Spersamide 10%®. Each 100 ml of this substance contains sodium sulphacetamide 10g, hydroxypropyl-methylcellulose 0.2g, phenylmercuric borate 0.001%, and sterile water to 100ml.

3. 6 ETHICAL CLEARANCE

Permission to do the study was obtained from the Senior Superintendent of the hospital and Head of the Department of Paediatrics at Sebokeng Hospital.

The study protocol was submitted on 16.01.1996 to the University of the Witwatersrand Committee for Research in Human Subjects. It was approved unconditionally on the 22.03.1996.

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The protocol was approved by the Postgraduate Committee on 14th Nov 1996. Copies of both approval letters are attached herewith.

3.7 PILOT STUDY

A pilot study of 15 cases of neonatal conjunctivitis was carried out from the 24th November 1995 to 2nd January 1996. The study was done according to the protocol steps explained previously. It was encouraging to note that using the study design, two cases of positive chlamydial culture and several positive cultures, including Staphylococcus aureus, Staphylococcus epidermidis, Haemophilus influenzae and Neisseria gonorrhoeae were obtained. Relevant information was also collected using the questionnaire.

A problem in transportation of the specimens was identified during the pilot study. It was noted from a few of the laboratory reports that the central SAIMR laboratory were not always culturing chlamydia owing to the fact that some specimens reached them 24 hours after collection and that many specimens had also not been transported on ice. This failure occurred because the hospital transport system only delivered the specimens on two days (Monday and Thursday) to the central SAIMR. It was also found that collecting specimens on Fridays was futile since there was no one to deliver them the next day (Saturdays). In response to this Sun Couriers were contacted who agreed to transport specimens from Vereeniging Hospital t Johannesburg on weekdays.

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This meant that the researcher had to deliver the specimens to Vereeniging Hospital each day. Moreover, all specimens were placed in plastic bags containing ice cubes so that when they reached SAIMR they were suitable for culture.

3.8 ALLOCATION OF TASKS

A formal request for co-operation (referral of patients) from colleagues and nurses in and around the hospital was made in writing. All other tasks were done by the researcher. This included the examination of neonates, interviewing of the mother, filling in of the questionnaire, the collection of eye swabs, ensuring the transportation of specimens to the laboratory and the collection of results. The medical technologist at the hospital SAIMR laboratory offered his support in ensuring the prompt processing of the specimens.

3.9 STATISTICAL ANALYSIS

Most data were analysed manually. Dr J.B. Galpin from the Department of Statistics at the University of Witwatersrand helped with the statistical analysis. Chi-square contingency table tests were used when appropriate.

3.10 BUDGET

There were no additional costs to the hospital as the study methodology formed part of the routine management of neonatal conjunctivitis. All other costs (eg. printing costs) were paid for by the researcher. No financial assistance was obtained from outside sources.

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4.0 RESULTS

A total of 105 hospital-born neonates who received prophylaxis at birth over a period of 8 months, from November 1995 to July 1996, were included in the study. Ten neonates, born at home during this period, and who did not receive any prophylaxis, were also included into the study.

Initially, a pilot study of 15 cases was carried out. Since the methods used and results obtained were not significantly different from those of the main study, these 15 cases were included in the analysis of results.

The problems relating to the proper transportation of specimens to central SAIMR, identified in the pilot study, were rectified in the main study. Only 95 of the 105 hospital-born neonates were used in the calculation of the percentage of cases attributable to chlamydia. This was because in 5 cases, specimens reached the central SAIMR too late for culture and in other 5 cases, chlamydia could not be cultured due to contamination by other organisms.

The 10 home-born neonates were excluded from all the analyses of aetiological causes of neonatal conjunctivitis. They were included in the study mainly to compare the organisms causing their conjunctivitis with hospital -born neonates who received prophylaxis.

In summary, the incidence percentage of chlamydia was calculated using 95 cases and that of the other organisms are calculated out of 105.

4.1 ORGANISMS ISOLATED

Table 4.1 shows the bacteria isolated from the 105 hospital- born neonates, and their day of presentation.

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TABLE 4.1: BACTERIA ISOLATED ON CULTURE OF SWABS FROM HOSPITAL BORN BABIES

CASE NO	CHLAMYDIA CULTURE	OTHER BACTERIAL ISOLATES ON ROUTINE CULTURE	DAY OF PRESENTATION WITH CONJUNCTIVITIS AFTER BIRTH
Case 1	Positive	Staphylococcus epidermidis	8th day
Case 2	Negative	Staphylococcus aureus, Neisseria gonorrhoeae (Beta-lactamase negative)	4th day
Case 3	Negative	Haemophilus influenzae	30th day
Case 4	Negative	Staphylococcus aureus Klebsiella pneumoniae	2nd day
Case 5	Negative	Staphylococcus epidermidis Neisseria gonorrhoeae (Beta-lactamase negative) Bacillus species	13th day
Case 6	Specimen un-suitable for culture due to late arrival	Streptococcus pneumoniae and Staph epidermidis	3rd day
Case 7	Negative	Staphylococcus epidermidis Streptococcus pyogenes	11th day
Case 8	Negative	Staphylococcus epidermidis	8th day
Case 9	Specimen un-suitable for culture due to late arrival	Staphylococcus epidermidis	1st day
Case 10	Negative	Staphylococcus epidermidis Streptococcus pneumoniae	2nd day
Case 11	Specimen un-suitable for culture due to late arrival	Staphylococcus epidermidis	4th day

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CASE NO	CHLAMYDIA CULTURE	OTHER BACTERIAL ISOLATES ON ROUTINE CULTURE	DAY OF PRESENTATION WITH CONJUNCTIVITIS AFTER BIRTH
Case 12	Specimen un-suitable for culture due to late arrival	Staphylococcus aureus	9th day
Case 13	Positive	Staphylococcus aureus Streptococcus viridans	15th day
Case 14	Negative	Neisseria gonorrhoeae (Beta-lactamase positive)	7th day
Case 15	Negative	Staphylococcus epidermidis Streptococcus viridans	3rd day
Case 16	Negative	Haemophilus influenzae (Beta-lactamase negative)	4th day
Case 17	Negative	Neisseria gonorrhoeae, (Beta-lactamase negative) Staphylococcus aureus	2nd day
Case 18	Negative	Staphylococcus aureus	10th day
Case 19	Negative	Staphylococcus epidermidis	15th day
Case 20	Negative	No growth of any bacteria	9th day
Case 21	Negative	Staphylococcus epidermidis Bacillus species Streptococcus viridans	6th day
Case 22	Negative	Neisseria gonorrhoeae, (Beta-lactamase negative)	2nd day
Case 23	Negative	Staphylococcus epidermidis	7th day
Case 24	Negative	Staphylococcus epidermidis	7th day
Case 25	Negative	Staphylococcus aureus	2nd day

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CASE NO	CHLAMYDIA CULTURE	OTHER BACTERIAL ISOLATES ON ROUTINE CULTURE	DAY OF PRESENTATION WITH CONJUNCTIVITIS AFTER BIRTH
Case 26	Negative	Neisseria gonorrhoeae, (Beta-lactamase negative)	4th day
Case 27	Negative	Klebsiella pneumoniae	2nd day
Case 28	Negative	Staphylococcus epidermidis	14th day
Case 29	Negative	Enterobacter species	10th day
Case 30	Negative	Staphylococcus epidermidis	5th day
Case 31	Negative	Staphylococcus epidermidis Streptococcus viridans	3rd day
Case 32	Negative	Staphylococcus epidermidis	3rd day
Case 33	Positive	Staphylococcus aureus Streptococcus pneumoniae	10th day
Case 34	Negative	Staphylococcus epidermidis	12th day
Case 35	Negative	Staphylococcus epidermidis	2nd day
Case 36	Negative	Staphylococcus epidermidis	16th day
Case 37	Negative	Staphylococcus epidermidis	7th day
Case 38	Positive	Staphylococcus epidermidis	8th day
Case 39	Positive	Staphylococcus aureus	25th day
Case 40	Negative	Staphylococcus epidermidis Neisseria gonorrhoeae (Beta-lactamase negative)	4th day
Case 41	Specimen un-suitable for culture due to late arrival	Staphylococcus aureus	15th day

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CASE NO	CHLAMYDIA CULTURE	OTHER BACTERIAL ISOLATES ON ROUTINE CULTURE	DAY OF PRESENTATION WITH CONJUNCTIVITIS AFTER BIRTH
Case 42	Negative	Haemophilus influenzae (Beta-lactamase negative)	21st day
Case 43	Negative	Neisseria gonorrhoeae (Beta-lactamase negative) Staphylococcus epidermidis	5th day
Case 44	Negative	Haemophilus influenzae (Beta-lactamase negative)	2nd day
Case 45	Negative	Staphylococcus epidermidis	14th day
Case 46	Negative	Staphylococcus epidermidis	9th day
Case 47	Negative	Neisseria gonorrhoeae (Beta-lactamase negative) Staphylococcus epidermidis	3rd day
Case 48	Negative	Staphylococcus epidermidis Serratia marcescens	3rd day
Case 49	Positive	Streptococcus viridans Staphylococcus epidermidis	3rd day
Case 50	Negative	Neisseria gonorrhoeae (Beta-lactamase negative)	3rd day
Case 51	Negative	Staphylococcus aureus	8th day
Case 52	Negative	Staphylococcus epidermidis	2nd day
Case 53	Positive	Staphylococcus epidermidis	14th day
Case 54	Negative	Staphylococcus epidermidis	3rd day
Case 55	Negative	Staphylococcus epidermidis Bacillus species	5th day
Case 56	Negative	Streptococcus pneumoniae Klebsiella pneumoniae	5th day

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CASE NO	CHLAMYDIA CULTURE	OTHER BACTERIAL ISOLATES ON ROUTINE CULTURE	DAY OF PRESENTATION WITH CONJUNCTIVITIS AFTER BIRTH
Case 57	Negative	Staphylococcus epidermidis Haemophilus influenzae (Beta-lactamase negative)	14th day
Case 58	Negative	Neisseria gonorrhoeae (Beta-lactamase positive) Staphylococcus epidermidis Bacillus species	11th day
Case 59	Negative	Staphylococcus epidermidis Proteus mirabilis	2nd day
Case 60	Negative	Klebsiella pneumoniae	2nd day
Case 61	Negative	Staphylococcus epidermidis Bacillus species	15th day
Case 62	Negative	Staphylococcus epidermidis	5th day
Case 63	Could not be isolated due to contamination	Staphylococcus epidermidis	8th day
Case 64	Could not be isolated due to contamination	Klebsiella pneumoniae Proteus mirabilis Staphylococcus epidermidis	2nd day
Case 65	Negative	Staphylococcus epidermidis	2nd day
Case 66	Could not be isolated due to contamination	Staphylococcus epidermidis	18th day
Case 67	Negative	Bacillus species Staphylococcus epidermidis	14th day
Case 68	Negative	Bacillus species Staphylococcus epidermidis	2nd day

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CASE NO	CHLAMYDIA CULTURE	OTHER BACTERIAL ISOLATES ON ROUTINE CULTURE	DAY OF PRESENTATION WITH CONJUNCTIVITIS AFTER BIRTH
Case 69	Negative	Streptococcus pneumoniae Staphylococcus epidermidis	4th day
Case 70	Negative	Staphylococcus aureus	3rd day
Case 71	Negative	Streptococcus viridans Staphylococcus epidermidis	13th day
Case 72	Negative	Staphylococcus aureus	4th day
Case 73	Negative	Staphylococcus epidermidis	2nd day
Case 74	Negative	Staphylococcus epidermidis	2nd day
Case 75	Negative	Staphylococcus aureus	2nd day
Case 76	Negative	Staphylococcus aureus Bacillus species	5th day
Case 77	Negative	Staphylococcus epidermidis	7th day
Case 78	Negative	Staphylococcus epidermidis	nd day
Case 79	Negative	Neisseria gonorrhoeae (Beta-lactamase negative) Bacillus species Staphylococcus epidermidis	5th day
Case 80	Negative	Staphylococcus aureus Staphylococcus epidermidis	8th day
Case 81	Negative	Streptococcus pneumoniae	4th day
Case 82	Negative	Staphylococcus epidermidis Proteus mirabilis	7th day
Case 83	Negative	Staphylococcus aureus	20th day
Case 84	Negative	Pseudomonas aeruginosa Staphylococcus epidermidis	4th day

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CASE NO	CHLAMYDIA CULTURE	OTHER BACTERIAL ISOLATES ON ROUTINE CULTURE	DAY OF PRESENTATION WITH CONJUNCTIVITIS AFTER BIRTH
Case 85	Negative	Streptococcus viridans Staphylococcus aureus	3rd day
Case 86	Positive	Staphylococcus aureus Staphylococcus epidermidis	Not known
Case 87	Positive	Staphylococcus epidermidis	2nd day
Case 88	Negative	Pseudomonas aeruginosa Staphylococcus epidermidis	9th day
Case 89	Could not be isolated due to contamination	Klebsiella pneumoniae Escherichia coli	2nd day
Case 90	Positive	Klebsiella pneumoniae Staphylococcus aureus	8th day
Case 91	Negative	No growth of any bacteria	5th day
Case 92	Negative	Staphylococcus aureus	1st day
Case 93	Negative	Proteus mirabilis Staphylococcus aureus	1st day
Case 94	Negative	No growth of any bacteria	1st day
Case 95	Positive	Staphylococcus aureus	12th day
Case 96	Negative	Staphylococcus aureus Streptococcus pyogenes	6th day
Case 97	Negative	Staphylococcus epidermidis	3rd day
Case 98	Negative	Staphylococcus epidermidis	16th day
Case 99	Negative	Neisseria gonorrhoeae (Beta-lactamase negative) Bacillus species Staphylococcus aureus	10th day

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CASE NO	CHLAMYDIA CULTURE	OTHER BACTERIAL ISOLATES ON ROUTINE CULTURE	DAY OF PRESENTATION WITH CONJUNCTIVITIS AFTER BIRTH
Case 100	Positive	Staphylococcus aureus	3rd day
Case 101	Negative	Staphylococcus epidermidis Streptococcus pneumoniae	2nd day
Case 102	Negative	Streptococcus pneumoniae	10th day
Case 103	Negative	Escherichia coli Staphylococcus epidermidis	4th day
Case 104	Negative	Staphylococcus epidermidis Streptococcus pneumoniae Citrobacter freundii	5th day
Case 105	Could not be isolated due to contamination	Streptococcus pneumoniae Staphylococcus epidermidis	5th day

A variety of organisms were isolated and in 19 of 105 patients (18%) multiple pathogens were identified. A summary of the organisms isolated is given in table 4.2.

S. epidermidis was the most common organism identified (57%). S. aureus was cultured in 25 cases (23.8%) and was the most important pathogenic organism isolated. . In 7 of 25 cases (28%) this was the only organism isolated. S. aureus also co-existed in 7 of the 12 chlamydia positive cases. Of 25 S. aureus isolates, 24 were sensitive to erythromycin and chloramphenicol. No growth of any bacteria was recorded in 3 cases where the possibility exists that a viral agent may have played a role in the aetiology of conjunctivitis.

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TABLE 4.2: SUMMARY OF ORGANISMS ISOLATED FROM EYE SWABS OF HOSPITAL BORN NEONATES (N - 105)

ORGANISM	NUMBER	PERCENTAGE
S. epidermidis	60	57.1
S. aureus	25	23.8
*C. trachomatis	12 of 95	12.4
N. gonorrhoeae	12	11.4
S. pneumoniae	10	9.5
S. viridans	7	6.6
K. pneumoniae	7	6.6
H. influenzae	5	4.7
P. aeruginosa	2	1.9
Enterobacter species	1	0.95
E. coli	2	1.9
S. pyogenes	2	1.9
P. mirabilis	3	2.8
S. marcescens	1	0.95
C. freundii	1	0.95
Bacillus spp	9	8.5
No growth of any bacteria	3	2.8

- **Ten cases excluded while calculating percentage for Chlamydia due to delayed transportation (5 cases) and contamination of cell cultures (5 cases)**

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N. gonorrhoeae was isolated in 12 cases. In 2 of the 12 (16%) the organisms were Beta-lactamase-positive, penicillinase producing N. gonorrhoeae (PPNG). All 12 isolates were susceptible to a combination of erythromycin and chloramphenicol. In 4 cases it co-existed with Bacillus spp and in 6 cases with S. epidermidis.

C. trachomatis was isolated in 12 of the 95 cases (12.4%). In the pilot study, a delay in transport prevented successful culture in 5 cases, and in 5 cases in the main study contamination by other organisms prevented the growth of chlamydia. Thus, 10 specimens were excluded from the analysis of chlamydia. Seven of the 12 patients presented during the 2nd week of life. The other 5, who had mixed infections, presented earlier.

S. epidermidis was isolated in 57% of cases. This organism is usually considered to be a contaminant. In the majority of cases it co-existed with other relevant and potentially pathogenic organisms. In 25 cases it was the only organism isolated. It is arguable whether S. epidermidis played any role in causing the conjunctivitis in these patients.

Streptococcus pneumoniae was the fourth most important pathogen and was detected in 10 (9.5%) of cases. The time of presentation varied from 2 days to 15 days. Streptococcus viridans were also identified in 6.6% of cases.

Several Gram-negative bacilli, the most important of which was Klebsiella pneumoniae (6.6%) were isolated. Isolation rates of E. coli, Enterobacter spp and Pseudomonas aeruginosa were low – less than 3% each. However, in total these organisms accounted for 16% of positive cultures.

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Haemophilus influenzae was found in 4.7% of cases. Haemophilus aegyptius was not isolated in this study. S. pyogenes was isolated in 1.9% of cases.

4.2 TIME OF PRESENTATION

The time of presentation in the hospital born infants is shown in Figure I. Only 104 cases were included in the analysis because one mother could not remember the day of onset of conjunctivitis. It shows that the largest number of cases presented on the second day of life; 72% of cases presented in the first week, 25% in the second and only 3% thereafter.

Among the important pathogenic bacterial conjunctivitis presenting after first week, there were 12 cases of S. aureus, 8 cases of C. trachomatis, 3 cases of N. gonorrhoeae, 2 cases of S. pneumoniae, 2 cases of S. viridans, 1 case of K. pneumonia, 3 cases of H. influenzae, 1 case each of P. aerogenosa, S. pyogenes and Enterococci .

Figure II focuses on seven important bacteria and their week of presentation. It is clear that all organisms most frequently caused infection in the first week after birth except for chlamydia which presented more often in the second week of life.

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Fig 1: Day of presentation of neonatal conjuctivitis after birth

Hospital born neonates
(n = 104)

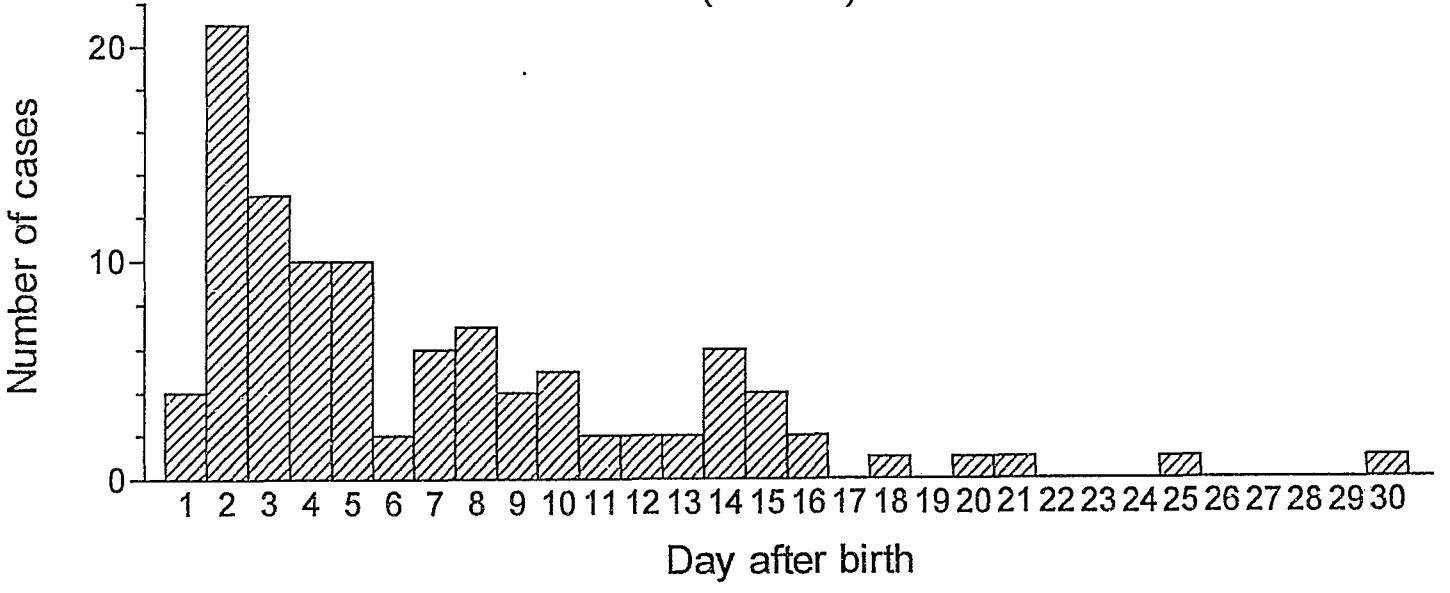
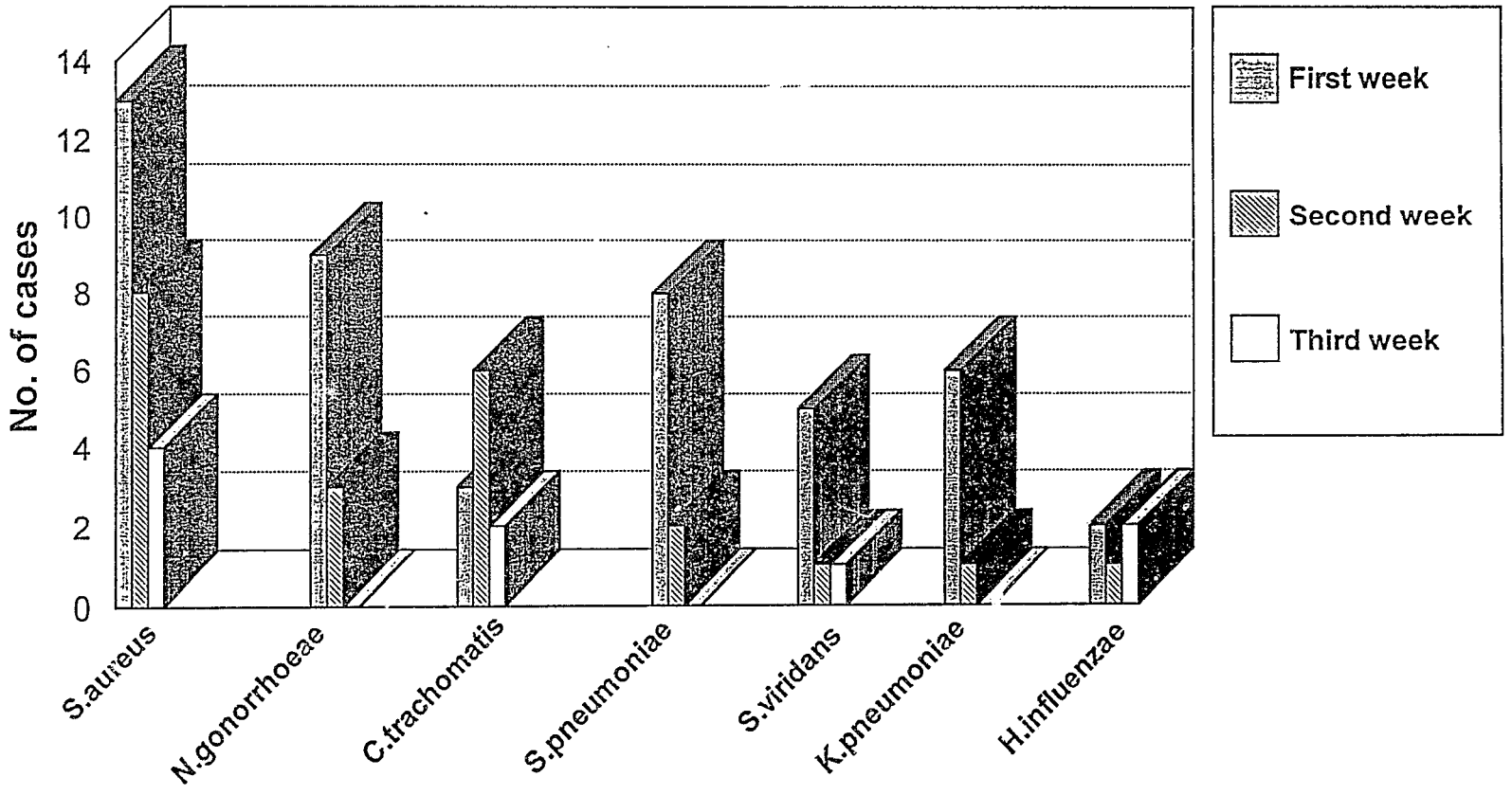


Fig 2: Week of presentation of conjunctivitis in hospital born neonates in relation to important organisms isolated (n= 104)



4.3 ANTIBIOTIC SUSCEPTABILITY

The antibiotic sensitivity patterns of the five most commonly isolated significant pathogenic organisms is shown in table 4.3. Not all the strains were tested against all the antibiotics. Only 4 of the 12 N. gonorrhoeae strains were tested against tetracycline. None of the chlamydia strains were tested for susceptibility to antibiotics by the SAIMR.

TABLE 4.3: SENSITIVITY RESULTS OF 5 MAJOR ORGANISMS ISOLATED IN THE STUDY TO VARIOUS ANTIBIOTICS

Organism	Number	Erythromycin n (%)	Chloram-phenicol n (%)	Penicillin n (%)	Tetracy-cline n (%)	Gentamycin N (%)
S. aureus	25	24 (96)	24 (96)	5 (20)	*NT	18 (72)
S. pneumoniae	10	10 (100)	10 (100)	6 (60)	8 (80)	NT
S. Viridans	7	7 (100)	6 (86)	7 (100)	1 (14)	4 (57)
K. pneumoniae	7	1 (14)	NT	0 (0)	4 (57)	6 (86)
N. gonorrhoeae	12	NT	12 (100)	10 (83)	4/4** (100)	NT
Overall	61	42/49 (85)	52/54 (96)	28 (45)	17/28 (61)	28/39 (71)

* NT - Not tested

** Only 4 specimens tested

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4.4 INCIDENCE

The average number of deliveries at Sebokeng Hospital during 1996 was approximately 480 per month. The actual number of hospital deliveries during the eight-month study period was 3 850.

A total of 105 cases of conjunctivitis were noted among hospital-born neonates. An additional 36 cases were noted among hospital-born neonates during the period of the study which had to be excluded from the study for reasons stated earlier, eg. presentation at times outside the study enrolment period. Thus the total number of hospital-born neonates suffering from conjunctivitis was 141.

Thus, the "true" incidence of conjunctivitis in the first month of life among hospital-born neonates at Sebokeng Hospital can be calculated as follows:

141 cases per 3 850 births = 3.66% of all births or 1 case per 27 births.

The chlamydial infection rate was 0.45 cases/100 live births and that of gonococci 0.41/100 births.

4.5 HOME BIRTHS

Ten babies who were born at home, and received no prophylaxis at birth, were enrolled into the study .

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A comparison was made between hospital and home-delivered babies regarding the pathogens responsible for eye infections. Organisms isolated from home-born babies are highlighted in table 4.4.

N. gonorrhoeae was cultured in three cases (30%) among the home delivery group. S. aureus was also isolated in another 3 cases (i.e. 30%).

TABLE 4.4: BACTERIA ISOLATED ON CULTURE OF SWABS FROM HOME BORN BABIES

CASE	DAY OF PRESENTATION	BACTERIA ISOLATED	CHLAMYDIA
Case 1	12th	N. gonorrhoeae, S. epidermidis, Bacillus species	Specimen arrived late
Case 2	8th	H. influenzae, S. epidermidis, Bacillus species	Negative
Case 3	2nd	H. influenzae	Negative
Case 4	21st	S. pneumoniae	Negative
Case 5	2nd	S. aureus	Negative
Case 6	5th	N. gonorrhoeae, S. epidermidis, Bacillus species	Negative
Case 7	1st	N. gonorrhoeae, S. epidermidis	Could not be isolated due to contamination
Case 8	18th	Enterobacter species	Negative
Case 9	21st	S. aureus	Negative
Case 10	3rd	S. aureus, Enterobacter species	Negative

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Of the total number of home born infants 50% presented in the first week and 70% in the first two weeks. There appeared to be no difference between the time of presentation of home and hospital-born infants.

4.6 MANAGEMENT OF CONJUNCTIVITIS

All babies enrolled into the study were treated at the time of presentation, and prior to the culture and sensitivity results being available, with erythromycin syrup 25 – 50 mg/kg four times/day for ten days and chloramphenicol eye drops (five drops four times daily) for seven days. In 15 cases (10%) this treatment failed and babies returned with persistently discharging eyes. The causative pathogens isolated in these 15 cases, at the time of first presentation, are shown in table 4.5. Treatment with a single injection of 50 mg/kg Ceftriaxone was given to all these infants.

TABLE 4.5: ORGANISMS ISOLATED FROM NEONATES NON-RESPONSIVE TO INITIAL THERAPY

ORGANISM	NO
K. pneumoniae	7
P. aeruginosa	2
E. coli	2
S. aureus	1
N. gonorrhoeae	1
Enterobacter species	2
TOTAL	15

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4.7 QUESTIONNAIRE RESULTS

The questionnaire analyses showed the following data. Of the 111 mothers interviewed :

1. Only 10 babies (9%) were born at home and none of them received any eye prophylaxis.

2. 25 mothers (22%) were married.

3. 90 mothers (78%) complained about vaginal discharge to the clinic sister.

4. 11 mothers (10%) who attended the clinic did not complain to the clinic sister about their vaginal discharge.

5. Only 3 mothers (3%) did not attend antenatal clinic.

6. 34 mothers (30%) gave a history of receiving some form of treatment from the clinic for their vaginal discharge.

5.0 DISCUSSION

5.1 INCIDENCE

The incidence of conjunctivitis in the first month of life among hospital-born neonates at Sebokeng Hospital was calculated to be 3.7% of all births in this study. This is lower than that reported from most other parts of the world.

In a published study by Laga et al in 1986, in Nairobi, the incidence of ophthalmia neonatorum was 23.2% of all live births [27]. No prophylaxis was offered to children in this cohort. In situations where prophylaxis has been used , rates are generally lower. A study done in Belgium in 1987 reported a rate of 11% (44) using Argyrol eye drops prophylaxis while Chen in Taiwan in 1992 found an incidence of 6.7 % when various different agents were used [13]. The lowest reported rate of neonatal ophthalmia is an American study performed in 1981 with an incidence of 3 per 1000 (0.3%) [16].

The relatively low incidence in the present study may be attributable to one of three reasons:

a) Sulphacetamide is a good prophylactic antibiotic, or
b) Many infants with neonatal conjunctivitis were not brought by parents to the health centres or hospital, despite the researcher's appeal to them to do so.
c) The incidence of ophthalmia varies geographically even where no prophylaxis is used.

The first explanation is the most likely.

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5.2 TIME OF PRESENTATION

A quarter of cases presented by the second day of life (21 cases) and almost three-quarters presented in the first week. Most cases (75%) of chlamydial conjunctivitis presented after the first week, but only a quarter of gonococcal conjunctivitis presented after the first week. Chlamydia comprised a quarter of all significant bacteria after 1 week of life.

The importance of this finding is that the treatment of neonatal conjunctivitis, after the first week of life, must include coverage for chlamydia.

5.3 DISTRIBUTION OF ORGANISMS

5.3.1 Staphyloccus epidermidis

S. epidermidis was isolated in 57 % of cases in this study- and was by far the commonest organism found. In the majority of cases (58%) it was found in addition to another organism. However, it is generally regarded as a contaminant and of no clinical significance by most authorities. [28].

5.3.2 Staphylococcus aureus

The commonest pathogenic organism isolated was S. aureus. It was present in a quarter (24%) of the cases. Many studies conducted elsewhere in the world also confirm S. aureus to be a significant pathogen in neonatal conjunctivitis. The following table shows the relative prevalence of S. aureus from various studies done in different parts of the world.

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TABLE 5.1: RELATIVE PREVALENCE OF S. AUREUS IN DIFFERENT PARTS OF THE WORLD

Country	Year	Relative Prevalence	Prophylaxis used
Sebokeng(RSA)	1996	24 %	Sulphacetamide
Sweden (29)	1987	48 %	None
India (30)	1992	37 %	Unknown
India (9)	1994	35 %	None
Thailand (5)	1993	29 %	S. Nitrate
Spain (23)	1993	14 %	None
Denmark (31)	1984	19 %	Unknown
Japan (32)	1993	3 %	Norfloxacin or gentamycin

This study's figures are lower than those reported from Sweden and India but more than those from Spain, Denmark and Japan S. aureus featured prominently among the home born babies also (30%), who did not receive any prophylaxis.

5.3.3 Zaragoza Study

A retrospective analysis of fifty conjunctival samples from infants less than one month with conjunctivitis done by Martine, et al in 1993 in Spain showed a 84% positivity for bacterial culture. In order of frequency, the organisms isolated were S. epidermidis (14%). S. aureus (14%), S. pneumoniae (12%), C. trachomatis (8%), H. influenzae (8%), et al. Most of the organisms showed a high level of susceptibility to most of the drugs tested, except for penicillin. [23] Pharmacological preparations tested for sensitivity to the organisms isolated included chloramphenicol, rifampicin, erythromycin, tobramycin and sulphonamide eye drop preparations.

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This study merits special attention owing to various similarities in their findings to our study.

The following table shows a comparison of both the studies.

TABLE 5.2 : COMPARISON BETWEEN SEBOKENG & ZARAGOZA STUDY

SIMILARITIES	DIFFERENCES
1. Both studies were conducted among neonates	Sample size was larger in Sebokeng study (105 vs 50)
2. Though pathologically insignificant S. epidermidis was the commonest isolate in both the studies	No prophylaxis was used in the Zaragoza study, while Spersamide was used in this study
3. S. aureus was reported as the most significant pathogen in both studies	Isolation of N. gonorrhoeae was common in Sebokeng whereas it was insignificant in the Zaragoza study
4. Many significant organisms identified in the Zaragoza study were seen at Sebokeng too e.g. C. trachomatis, H. influenzae, E. coli, S. pneumoniae etc	S. aureus and chlamydial rates were much higher in the Sebokeng study

The results of the Zaragoza study were statistically compared to the results of this study for five organisms, namely S. aureus, C. trachomatis, N. gonorrhoeae, S. pneumoniae and H. influenzae. Except for N. gonorrhoeae, no statistically significant difference was seen in the isolation rates of bacteria compared in the two studies.

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It is interesting to note that the susceptibility of S. aureus, S. pneumoniae and H. influenzae to sulphonamide were 100 %, 100 % and 50 % respectively in the Zaragoza study. Corresponding sensitivities are not available for this study.

5.3.4 Chlamydia

The chlamydial infection rate in this study was 4.5 cases per 1000 live births and that of gonococci 4.1 per 1000 live births. table 5.3 shows the incidence figures for Chlamydia and Gonococcus in different regions. It is apparent that the incidence in Sebokeng is lower than that reported in most other studies. The factors responsible for this are similar to those mentioned previously for the overall incidence figures.

TABLE 5.3: INCIDENCE OF CHLAMYDIA AND GONOCOCCUS IN VARIOUS PARTS OF THE WORLD

Country	Year	Chlamydia	Gonococcus	Prophylaxis used
Kenya (11)	1986	8.1%	3.6%	None
Kenya (27)	1988	0.7%	0.4%	Silver nitrate
Kenya (27)	1988	0.5%	0.1%	Tetracycline
USA (20)	1989	4.4%	0.6%	*S.N, Erythromycin, Tetracycline
Taiwan (13)	1992	1.6%	-	No prophylaxis
Taiwan (13)	1992	1.5%	-	Erythromycin
Taiwan (13)	1992	1.4%	-	2 doses erythromycin
Taiwan (13)	1992	1.3%	-	Tetracycline
Taiwan (13)	1992	1.7%	-	Silver nitrate
Sebokeng	1996	0.45%	0.41%	Sulphacetamide

* S.N. = Silver Nitrate

In recent years chlamydia trachomatis has replaced gonorrhoea as the most frequent cause of neonatal conjunctivitis in North America, Europe and Africa. [17, 21].

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The frequency of ophthalmia neonatorum depends on the prevalence of maternal genital infections and on the application of prophylatic agents to the eyes of newborns [12]. It is estimated that 7% to 29% of pregnant women in developing countries have chlamydial infection. Approximately one in three infants exposed to C. trachomatis gets an eye infection if no prophylaxis is given [27].

A prospective study of ophthalmia neonatorum in Nairobi in 1986 revealed a high prevalence of sexually transmitted diseases among women in labour and a subsequent high prevalence of gonococcal and chlamydial ophthalmia neonatorum (rates of 3.6% and 8.1% respectively) [27].

Seventy-eight percent of mother's in this study reported having a vaginal discharge. This may explain why 12 of the 95 neonates (12.4%) were positive for C. trachomatis eye infection; similar to a Kenyan study done in 1986 where 20 of the 199 babies (13%), were positive for C. trachomatis among the conjunctivitis cases studied. [11].

Table 5.4 shows the relative frequency of chlamydia among all cases ophthalmia neonatorum from differe .t parts of the world. It is apparent that Chlamydia contributes in similar proportion to the overall numbers of conjunctivitis as in other countries.

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TABLE 5.4: RELATIVE PREVALENCE OF CHLAMYDIA FROM VARIOUS STUDIES

Country	Year	Relative Prevalence	Prophylaxis used
Kenya (6)	1986	13 %	None
Thailand (5)	1993	29 %	Silver nitrate
Japan (33)	1988	22 %	Unknown
India (9)	1994	0	Unknown
Spain (23)	1995	8 %	Unknown
England (34)	1986	51 %	Unknown
Belgium (35)	1987	5 %	Argyrol
Sweden (36)	1986	21 %	Unknown
Denmark (31)	1984	0.6 %	Unknown
USA (20)	1989	8 %	Silver nitrate, erythromycin and tetracycline
Sebokeng	1996	12.4%	Sulphacetamide

Based on the fact that our chlamydial ophthalmia neonatorum rates are similar to the Kenyan neonates and on the high rate of vaginal discharge reported; it is probably acceptable to extrapolate the 8.9% intrapartum chlamydial infection rate seen among Kenyan mothers to Sebokeng women. Thus, approximately 42 mothers among the average of 480 mothers who delivers at Sebokeng Hospital each month will be infected with Chlamydia.

Interventions to curb this dangerous situation need to be considered. Preece, et al in 1989 at Birmingham Children's Hospital, screened 3309 pregnant women for C. trachomatis infection [37]. The prevalence of C. trachomatis infection was highest in women under 20 years (14.5%), in single women (14.2%) and in black women (16.8%). Binomial regression of this data revealed a relative risk of 2.9 for women under 20 years compared with women aged 25 years and above. Infants of 174 antigen-positive mothers were followed up. Cultures for C. trachomatis were positive in 24% of infants.

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Pearson et al, reported similar findings where younger women less than 25 years were shown to be more susceptible to C. trachomatis infection [38]. They also suggested some sort of screening programme for this group of younger and single women to be instituted at antenatal clinics.

Introduction of any type of intervention may impinge on the already strained budget. However, focussing on this group of younger women (< 25 years) and screening them specifically for chlamydia may prevent eye infection and other complications among their neonates and may be cost-effective [39]. Taking an endocervical swab for tissue culture and treating them with erythromycin in the antenatal clinic may be one way of doing it.

5.3.5 Gonococcus

In our study 12 of the 105 cases (11.4%) were infected with gonococcal conjunctivitis. In several African studies N. gonorrhoeae was isolated from 24-44% of cases of ophthalmia neonatorium [6,40 42]. The higher incidences were reported in areas where no prophylaxis was being used.

A summary of the relative frequency of gonococcal conjunctivitis is given in table 5.5 below: It appears that the importance of gonococcal conjunctivitis is diminishing in both developed and developing countries. However, it remains an important contributor to the development of conjunctivitis in this study.

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TABLE 5.5: GONOCOCCAL CONJUNCTIVITIS
(Relative prevalence in various studies)

Country	Year	Relative Prevalence	Prophylaxis
Kenya (6)	1986	43%	None
Zaire (17)	1988	0%	Tetracycline
USA (20)	1989	0.06%	Erythromycin
India (9)	1994	0%	None
Spain (23)	1995	0.02%	None
Sebokeng	1996	11.4%	Sulphacetamide

The significantly greater contribution of gonococcus in Sebokeng can be explained in two ways:

a) Suphacetamide is ineffective as prophylaxis for gonococcus

b) The incidence of gonorrhoea is much higher in pregnant women in Sebokeng than elsewhere.

Both these arguments need to be examined:

The rate of gonococcal eye infection was apparently higher in home born infants (30 %) as compared to the 11 % in the hospital born infants who had received prophylaxis with 10% Spersamide. However, this finding was not statistically significant ($\chi^2 = 2.776$ and $p = 0.957$). This may be due to the small number of home born babies.

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One single application of sulphacetamide eye drops is unlikely to impact against N. gonorrhoeae because it is bacteriostatic and the duration of application is too short. Sulphonamides are usually not effective against gonococci even if used in the correct dose for a longer duration. [43]

It therefore appears valid to argue that the greater contribution of gonococci to ophthalmia neonatorium is due to the ineffectiveness of sulphacetamide.

Assuming a transmission rate of at least 50% from mother to child (personal communication – R Ballard) approximately 23% of mothers in the study group may have had gonorrhoea. The estimated range of maternal gonococcal infection in Africa is 3 to 22% [4; 25]. This contradicts the suggestion that more mothers in Sebokeng have gonorrhoea. The overall incidence of gonococcal ophthalmia in this study is also no higher than elsewhere (table 5.4)

5.4 SUSCEPTIBILITY TO DRUGS

5.4.1 Sulphacetamide

The role of sulphacetamide as a prophylactic agent for neonatal conjunctivitis must be questioned, for the following reasons:-

- It appears to be ineffective in preventing gonococcal ophthalmia neonatorum. The use of sulphonamide resulted in a decrease in the rate of gonococcal infection (from 30% to 11%) and that of S. aureus infection (from 30% to 23%); when home born babies were compared to hospital born babies. However, this was not statistically significant.

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- Sulphonamide alone is inadequate for prevention of infection due to Gram negative bacilli.
- Spersamide is not recommended by the manufacturers for use in new-borns in the USA because of the possibility of icterus (Spersamide package insert).
- Lack of effectivity of Spersamide eye drops in preventing eye infection among hospital born babies at Sebokeng Hospital is quite evident from the incidence calculations given under results (1 in 27). It translates to the fact that, since ± 16 deliveries take place at Sebokeng per day, on average one new-born gets eye infection every 40 hours. Though no prophylaxis is 100% effective, this is still unacceptable.

Although C. trachomatis is susceptible to sulphonamide, a single dose is inadequate to treat chlamydial infection of the eyes. [43]. Sulphonamides are not optimal antimicrobial agents for treatment of chlamydial genital infections.

A South African study by Dangor et al [44] examined the changing patterns of antimicrobial susceptibilities of Neisseria gonorrhoeae isolated in Johannesburg in 1991. Unfortunately, it does not contain specific information about the susceptibility of Neisseria gonorrhoeae to sulphonamides alone. This study found that 19% of penicillinase-producing N. gonorrhoeae (PPNG) and 6% of non-PPNG were resistant to cotrimoxazole.

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A consolation is that our rates of chlamydial and gonococcal infection are lower than those in neonates from Nairobi who did not receive any prophylaxis. Chlamydial infection occurred in 8 per 100 live births in the Kenyan study whereas in our study the incidence was 0.45 per 100 live births. It was reported that they had 3.6 cases per 100 live births at Nairobi for gonococci compared to 0.41 cases per 100 live births in Sobokeng area [11].

It should also be noted that spersamide is not recommended by the manufacturer for use in new borns in the USA because of the possibility of icterus (Spersamide package insert).

A study published by Heggie, et al in 1985 (USA) used sulphacetamide as a topical agent to treat chlamydia conjunctivitis. They concluded that sulphacetamide is totally ineffective as a topical agent and its use resulted in persistent conjunctival infection [45].

5.4.2 Povidone iodine

Among the various pharmacological agents used around the world, some studies have focussed on a solution of povidone iodine.[18] A controlled trial conducted by Isenberg et al in 1995 in Kenya showed that povidone iodine (2.5% solution) is a promising drug in preventing both bacterial and viral eye infection in babies, is safe compared to silver nitrate and is cheap.

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5.4.3 Erythromycin

Usage of erythromycin as a topical ointment is widely recommended by experts from the USA, including the Centre for Disease Control, where C. trachomatis is commonly responsible for conjunctivitis [19;46]. Hammerschlag found that none of the 24 infants of Chlamydia-positive mother who were given erythromycin prophylaxis developed chlamydial conjunctivitis. However, Chen (Taiwan) found that there was no significant effect of erythromycin in preventing chlamydial conjunctivitis as compared to no prophylaxis (13).

Erythromycin may have been a suitable prophylactic in our patient population, since most of the common organisms in our study i.e. C. trachomatis, S. aureus, etc were susceptible to erythromycin. Unfortunately, a similar preparation is not available at Provincial hospitals in South Africa.

5.4.4 Tetracycline

The use of tetracycline eye ointment for prophylaxis against ophthalmia neonatorum, is in practice in many parts of the world particularly in many African countries e.g. Kenya and Zaire. It is recommended by the WHO [17].

In one study conducted in Kenya, the efficacy of tetracycline was compared with silver nitrate. Tetracycline reduced the transmission of gonococcal infection to a greater extent than silver nitrate (93% vs 83%) and it also fared better than silver nitrate in preventing chlamydial infection (77% vs 68%) [47].

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In a publication from Zaire, Fisher et al reported a study in which they included 450 neonates. Tetracycline was prescribed for each of these neonates as prophylaxis against eye infection, but nurses believed it to be too messy an ointment and did not apply it to every neonate's eye. As a result, only 236 newborns received tetracycline. None from them developed conjunctivitis [17]

In many hospitals in South Africa, tetracycline is considered as a popular prophylactic drug against eye infection.

We avoided the drug for the treatment of conjunctivitis for two reasons :

1. It is very messy and the author and his consultant felt that sometimes it is confused with a purulent discharge and at times would mask such discharge since both have a similar yellow colour.

2. The report by Dangor et al showed that 34% of non-PPNG isolates and 56% of PPNG were resistant to tetracycline in the Johannesburg area, reducing its potential value as a prophylactic or therapeutic agent in any population where gonococci feature as prominent pathogenic organisms. [44]

When tetracycline first appeared on the market, it was considered as an effective antimicrobial agent with a broad spectrum of activity against both Gram positive and Gram negative bacteria. With time the susceptibility has diminished. Resistance to tetracycline has resulted from alteration of ribosomal binding sites

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in the various organisms. Failure of any antibiotic to bind to its target sites on the ribosomes disrupts its ability to inhibit protein synthesis and cell growth in the bacteria.

The "TetM" resistance gene protects the ribosome from tetracycline. The precise mechanism of action of this resistance gene is not clear at present but it has been established that this "TetM" determinant is widely dispersed in Gram positive organisms in addition to other organisms e.g. Neisseria spp [48]

The first isolates of Neisseria gonorrhoeae shown to carry the 25.2 MDa tetracycline resistance conjugative plasmids (TetM genes) in Southern Africa were isolated in 1993 from Botswana and Namibia [49] In a study in the Free State carried out in 1994 and 1995 the TetM-encoding conjugative plasmids were shown to increase from 2% to 18.5% and were associated with high level tetracycline resistance [49] Tetracycline resistant N. gonorrhoeae isolates have also increased in other specific population groups e.g. miners at Carltonville where resistance rose to 51% in 1997.

Because of increasing resistance, particularly the potential for spread of resistance plasmids, it is advisable for susceptibility tests on N. gonorrhoeae isolates to be monitored in future.

Similar alteration of ribosomal binding sites, is a mechanism used by S. aureus also to develop resistance against a wide variety of antimicrobials including tetracycline [48]

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5.4.5 Chloramphenicol

There are a number of other publications where chloramphenicol has been used as a prophylactic or therapeutic agent against eye infection in neonates. The advantages of chloramphenicol are that it has a broad spectrum of activity and rarely causes local irritation or hypersensitivity. It is also considered to be valuable in treating eye infections because of its high liquid solubility, excellent corneal penetration and low ocular toxicity.

Concerns about its ability to cause aplastic anaemia after prolonged topical use has precluded its routine use[50]. Such incidents are much less frequent when it is applied topically than when it is used orally or parenterally. The use of ocular chloramphenicol is restricted in the USA for the above reason but such restriction is probably unjustifiable in a developing country for cost reasons. Moreover, there is no need to use chloramphenicol for a prolonged period either for prophylaxis or as a therapeutic agent. For prophylaxis it is used only once and for treatment it is used for a period of 5 to 7 days.

In the study published by Dangor et al in 1991 in Johannesburg, they reported that for the same minimal inhibitory concentration (MIC), chloramphenicol was more effective compared to tetracycline against gonococci. Chloramphenicol resistance was recorded in 7% of PPNG strains, whereas tetracycline resistance was recorded in 56%. For non PPNG strains choramphenicol resistance was found in only 3% compared to 34% resistance sh[illegible]tracycline. Other advantages are that chlorampenicol is cheap, [illegible]d presented in a

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drop form, aplicap form and eye ointment form. It is also white in colour and is unlikely to be confused with purulent discharge. However, the researcher's view is that any ointment is messy and prevents proper drainage from the eyes by the way of sticking eyelids together.

For this reason the researcher prefers drops, though they have the disadvantage of having a shorter period of action compared to ointment.

Chloramphenicol is not usually recommended for chlamydial infection, but a study done by Hobson et al in 1982 in England showed that usage of chloramphenicol as prophylaxis delayed onset of chlamydial eye infection in neonates [51]. Since in our study chlamydia featured as the second most common organism, this could have helped a few neonates to some extent. But Sandstrom in his study reported that chloramphenicol failed both clinically and microbiologically in treating chlamydia [29].

As shown in table IV, chloramphenicol showed an overall rate of 96% effectiveness in treating all the important bacteria among Sebokeng neonates with conjunctivitis.

5.4.6 The Ideal Prophylactic?

Various studies to establish the most effective prophylactic agent against eye infection have yielded controversial result. In some part of the world certain antimicrobials are found effective where as in other parts prophylaxis versus no

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prophylaxis has shown no significant differences. The following table (table 5.6), shows various studies using different prophylaxis done over many years all around the world.

TABLE 5.6: VARIOUS PROPHYLACTIC AGENTS USED AND THE CONTROVERSY ABOUT THEIR EFFICACY

Country	Year	Prophylactic agents compared	Results	Conclusion
U.S.A (19)	1980	*ERY and *SN	A)None of the infants who received *ERY developed chlamydial conjunctivitis B)33% of infants who received SN developed conjunctivitis	ERY is very effective in preventing chlamydial conjunctivitis
U.S.A (16)	1981	*TET and SN	A)Poor response of gonococcal conjunctivitis to TET B)100% increase in overall conjunctivitis rate	Both agents are inadequate in preventing neonatal conjunctivitis
Kenya (27)	1988	SN and TET	TET effective in 93% and SN in 83%	Both agents are almost equally effective
Zaire (17)	1988	SN and TET	None of the infants who received SN or TET developed conjunctivitis	Both agents equally effective

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Country	Year	Prophylactic agents compared	Results	Conclusion
U.S.A. (20)	1989	SN,ERY and TET	The incidents of chlamydial conjunctivitis as follows: SN 20%;ERY 14%; TET 11%	Prophylaxis with either of the agent doesn't reduce incidence of conjunctivitis among off springs of mothers with chlamydial genital infection
Taiwan (13)	1992	TET,ERY,SN, no prophylaxis and ERY twice	The overall incidence of conjunctivitis were as follows: TET 1.3%;ERY 1.5%;SN 1.7%;no prophylaxis 1.6% and ERY twice 1.4%	No significant difference in the rates of conjunctivitis with either agent or no prophylaxis
Japan(32)	1993	Norfloxacin, and Gentamycin	One case out of 70 for Norfloxacin and four out of hundred in the Gentamycin group developed conjunctivitis	Both agents are equally effective
Kenya (18)	1995	*PI, SN and ERY	Incidence of infection in the various groups were as follows: PI 13.1%; SN 17.5%; ERY 15.2%	PI 2.5% solution is effective as a prophylactic agent

***ERY- Erythromycin, *SN- Silver Nitrate, *TET- Tetracycline, *PI- Povidone Iodine**

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5.5 TREATMENT

The recent protocol booklet published by the Directorate of HIV/AIDS and STD's in South Africa recommends spectinomycin 25 mg/kg as a single intramuscular injection combined with erythromycin orally for the treatment of neonatal conjunctivitis. It also recommends irrigation of eyes and treatment of parents [52]. This may be effective but the availability of spectinomycin in State Hospitals and clinics must be assured and may prove to be too expensive for general use. During the period of this research spectinomycin was not available at Sebokeng Hospital pharmacy.

Of our gonococcal conjunctivitis isolates, the majority were Beta lactamase negative (93%). So, as recommended by Framsen et al, systemic penicillin can still be used in the treatment of gonococcal (Beta lactamase negative) conjunctivitis in Sebokeng neonates, in confirmed cases [53]. However, a single dose of ceftriaxone is as effective and does not require admission of these neonates and hence is also cost effective [24]. Moreover, since S. aureus and C. trachomatis are also very common causes of conjunctivitis among Sebokeng neonates; empirical treatment with penicillin will also result in failure of therapy in many cases. For confirmed cases of gonococcal ophthalmia neonatorum, a single dose of Ceftriaxone injection intramuscularity at a dose of 50mg/kg has been recommended by many authors, which also adequately takes care of the systemic gonococcal infection (24, 54).

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Seega et al from Japan used Gentamycin and Norfloxacin in two different groups of neonates with conjunctivitis in 1993 and reported excellent outcome in both the groups. Erythromycin, both as an ophthalmic preparation and oral syrup form is recommended by the Centre for Disease Control in Atlanta for confirmed cases of chlamydial conjunctivitis at a dose of 25 to 50mg 12 hourly for 14 days.
Lockie, et al from Australia recommends the topical application of chloramphenicol and a single dose intramuscular injection of spectinomycin (25 to 40mg /kg per 24hrs) to be the most effective combination. [55].

In this study the researcher instituted an emperical treatment protocol using chloramphenicol eyedrops and erythromycin syrup orally as mentioned earlier, to treat all cases of neonatal conjunctivitis irrespective of the week of presentation. Although the clinical response to this treatment seemed to be effective in the majority of cases (± 87%); this data may not be viable scientifically due to the following reasons.

(i) No attempt was made to call the patients back after 10 days of treatment to take another swab from the eyes of those neonates who received the above treatment. This would have proved or disproved the efficacy of the above treatment regime.

(ii) The claim that only 15 cases came back reporting of persisting conjunctivitis does not prove anything. The mothers could have taken their babies elsewhere when they have noticed no improvement.

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5.6 QUESTIONNAIRE

Analysis of the questionnaire revealed that among the mothers who were included in the study, only 25 (22%) were married, most of whom had one partner. The rest of them were unmarried mothers mostly with single boyfriends in non-permanent relationships. So in the course of a few years, exposure to multiple partners could not be ruled out, predisposing them to infection.

Since the majority of Sebokeng mothers are unmarried as seen from the study, and have had vaginal discharges, prophylaxis has to be stepped up at antenatal clinics and in the new-born nursery.

Analyses also revealed that only 3 out of 10 home born babies' mothers did not attend antenatal clinic. All others attended the antenatal clinic. Of the 3 mothers who did not attend, only one baby developed gonococcal eye infection..

Of 115 mothers, 90 (78%) had a history of having a vaginal discharge during the antenatal period. Eleven of 115 (10%) who attended the antenatal clinic did not complain about it to antenatal clinic sisters and were not given any therapy. Even among the mothers who complained about the vaginal discharge and received treatment, it is likely that some did not receive appropriate treatment as seen by the infection being passed onto the offspring. In the majority of cases, partners were not treated which may have resulted in re-infection of mothers.

However, the fact that the majority of expectant mothers utilised the free antenatal clinic services, is very encouraging.

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5.7 RECOMMENDATION

5.7.1 Prevention

Primary health care clinics should aim to be adolescent friendly and offer comprehensive services where youth also receive education and counselling on various aspects of their sexuality, including knowledge of sexually transmitted diseases (STD) and healthy sexual behaviour. This would eventually result in reductions in the incidence of neonatal conjunctivitis.

More effort needs to be directed at diagnosing and treating sexually transmitted diseases at antenatal clinics. Pregnant women who complain of a vaginal discharge need to be examined to confirm the presence and nature of the discharge, i.e. is the discharge physiological or pathological. Both digital and speculum examinations needs to be done.

If the discharge appears pathological, vaginal swabs needs to be collected and send for microscopy, culture and susceptibility. Budgetary constraints prevent the widespread collection of separate swabs for chlamydia culture at present. Their introduction could have a significant impact in preventing transmission of this infection to their offspring. Focusing only on women who are below 25 years old would be potentially cost-saving and a reasonable interim strategy.

All aspects of STD management, including counseling for safer sex, condom promotion (even for pregnant women) and contact tracing and treatment are also critical.

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5.7.2 Treatment of mothers

In case of pregnant women in whom gonococcal infection is suspected Spectinomycin 2 gm intramuscularly as a single dose injection can be used. However, for any infective vaginal discharge among younger women (<25 years) erythromycin 500 mg four times daily for 7 days can be added to curb chlamydia infection. This can also be used safely in pregnant women. Cautious use of metronidazole for vaginitis needs to be made in pregnant women and it should only be used after the first trimester.

5.7.3 Prophylaxis for ophthalmia neonatorum

It is recommended that chlorampenicol eye drops/ointment be used for ocular prophylaxis in neonates. This is based on the 96% sensitivity of the common organisms to this agent in this study. Eye drops are preferred to eye ointment by the researcher as they do not interfere with the drainage from the eyes.

Though spersamide has shown acceptable level of efficacy in preventing conjunctivitis among neonates born in Sebokeng hospital, its inadequacy in treating gonococcal, chlamydial and S. aureus infection necessitates its replacement.

It is also recommended to first clean the neonate's eyes with a sterile cloth soaked in normal saline, followed by the instillation of 4–5 drops of chloramphenicol in both eyes only once.

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5.7.4 Treatment of neonates with conjunctivitis

Ideally, when a neonate presents with conjunctivitis, swabs should be collected from both the eyes for microscopy, culture and susceptibility testing, including chlamydia studies. In practice this will be impossible to implement at all primary and secondary care centres in this country.

As a minimum all infants with conjunctivitis should have, at least, a Gram stain done to exclude N. gonorrhoeae. Again, it is unlikely that many primary care centres will have even this facility.

In this situation, the suggestion would be to treat all clinically suspected conjunctivitis (ie. a purulent discharge or sticky eyelids with conjunctival injection) as pathogenic. However, specific treatment for gonococcus would be reserved for those confirmed to be positive on gram stain. This would mean that every infant with a **markedly purulent** discharge would have to have an eye smear sent to a centre with microscopy facilities. Unfortunately, this may result in some cases of gonococcus being missed early on and often re-presenting with more severe disease. However, it is unlikely that using this approach any infant with gonococcal ophthalmitis will go completely undiagnosed or untreated. There is little data in the literature to either support or refute this argument.

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If gonococci are identified a single intramuscular injection of ceftriaxone at a dose of 50 mg per kilogram body weight should be given. This recommendation is made despite the 93% sensitivity of the isolated N. gonorrhoeae to penicillin and is based largely on the cost saving of a single dose therapy.

Cleansing of the eyes with a sterile cloth soaked in normal saline should be followed with the instillation of chloramphenicol eye drops four times per day in both eyes for a period of 5 – 7 days. Mother should be educated on eye hygiene, cleaning of eyes and the proper instillation of eye drops. She should also be instructed to bring the baby back in a week's time if the condition does not improve.

If gonococci are not detected on the Gram stain study and the time of presentation of conjunctivitis is within first week of life, treatment would comprise only of cleaning the eyes with cloth soaked in normal saline followed by the regular instillation of chloramphenicol eye drops as described above.

From the second week onwards any neonate who presents with a conjunctivitis should be prescribed chloramphenicol together with erythromycin syrup orally at a dose of 25 – 50 mg per kilogram body weight per day in 3 – 4 divided doses for a period of 10-14 days. This treatment is aimed mainly at covering possible chlamydial infection. This approach may appear aggressive when considering that chlamydia are

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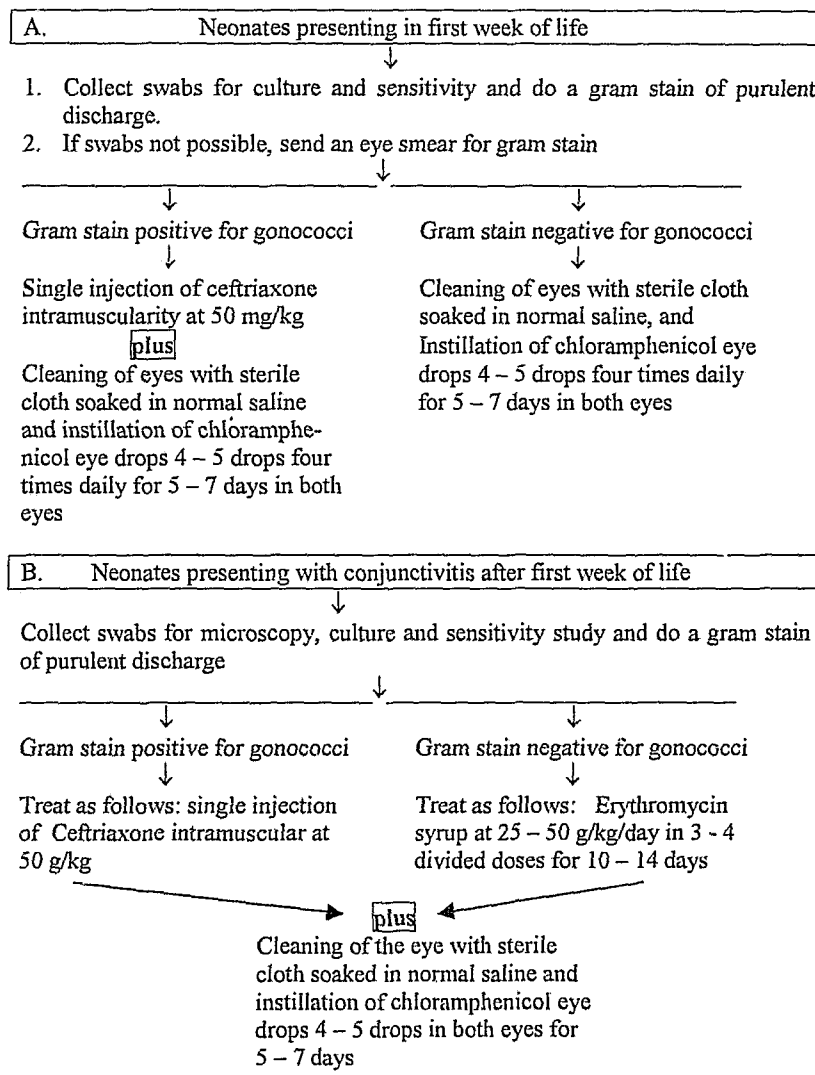
only responsible for 1 in 4 cases of conjunctivitis during the 2nd to the 4th week of life. However, the risk of not treating chlamydia is that about 20% of all infants who are colonised with chlamydia will later develop pneumonia.

The following flow chart (Figure III) can be used as a guideline for treatment of neonatal conjunctivitis at Sebokeng Hospital.



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5.8 CONCLUSION

1. Comparison of incidence rate of conjunctivitis in neonates born in Sebokeng to those from studies done in other parts of the world showed comparable rates generally.

2. Three-quarter of cases of neonatal conjunctivitis presented in the first week of life.

3. S. aureus (23.8%) was the commonest pathogenic organism isolated in this study followed by C. trachomatis (17.9%) and N. gonorrhoeae (11.4%).

4. Though Spersamide (10% sulphacetamide) eye drops appeared to function adequately as a prophylactic agent, its efficacy in treating N. gonorrhoeae, S. aureus and C. trachomatis were inadequate.

5. An overall 96% sensitivity rate to chloramphenicol was shown by the commonest pathogenic organisms.

6. Home-born babies who did not receive any prophylaxis showed a higher rate of gonococcal and S. aureus infection rate (30% each) than hospital born babies. However, this was not statistically significant owing to the small number of neonates in this subset (10 neonates).

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APPENDIX

UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG

Division of the Deputy Registrar (Research)

COMMITTEE FOR RESEARCH ON HUMAN SUBJECTS (MEDICAL)
Ref: R14/49 Thomas

CLEARANCE CERTIFICATE PROTOCOL NUMBER M 960241

PROJECT	Etiology of conjunctivitis in Sebokeng Hospital Neonates who received routine prophylaxis at birth against eye infection
INVESTIGATORS	Dr C Thomas
DEPARTMENT	Community Paediatrics, Sebokeng Hospital
DATE CONSIDERED	960301

DECISION OF THE COMMITTEE *

Approved unconditionally

DATE 960322

CHAIRMAN. .....Russano.....pp (Professor P E Cleaton-Jones)

c c Supervisor: Professor Crewe-Brown
Dept of Microbiology, Baragwanath Hospital

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DECLARATION OF INVESTIGATOR(S)

To be completed in duplicate and ONE COPY returned to the Secretary at Room 10001, 10th Floor, Senate House, University.

I/~~we~~ fully understand the conditions under which I am/~~we are~~ authorized to carry out the abovementioned research and I/~~we~~ guarantee to ensure compliance with these conditions. Should any departure to be contemplated from the research procedure as approved I/~~we~~ undertake to resubmit the protocol to the Committee.

DATE.....8/5/96....SIGNATURE ...Emp.....

PLEASE QUOTE THE PROTOCOL NUMBER IN ALL ENQUIRIES

Faculty of Health Sciences
UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG
7 York Road, Parktown, 2193 South Africa • Telegrams Witsmed • Telephone (011) 647-1111 • Fax: (011) 643-4318

14 November 1996

Dr C Thomas
Private Bag X058
Sebokeng Hospital
Vanderbijlpark
1900

Dear Dr Thomas,

APPROVAL OF PROTOCOL ENTITLED "AETIOLOGY OF CONJUNCTIVITIS IN SEBOKENG HOSPITAL NEONATES WHO RECEIVED ROUTINE PROPHYLAXIS AT BIRTH AGAINST EYE INFECTION"

I should like to advise you that the protocol that you have submitted for the degree of MSc(Med) (Paediatrics and Child Health)(Community Paediatrics Option) has been approved by the Postgraduate Committee for continuation of candidature. It is noted that ethics clearance has been obtained.

Professor H Crewe-Brown of the Department of Medical Micrbiology has been appointed as your supervisor. You are asked to maintain regular contact with your supervisor who must be kept advised of your progress.

Please note that all candidates for higher degrees must make reference in their research reports to the clearance number of the relevant ethics committee. The final title, when submitting the research, should comply with the above approved title, and a signed declaration, noting that the work has been your own and not submitted to any other University, must also be included.

Please also note that Postgraduate students are required to register with the Faculty Office every year until they graduate from the University.

Yours sincerely

MRS G GABRIEL
FACULTY OFFICER (POSTGRADUATE)
FACULTY OF HEALTH SCIENCES

cc: Professor H Pettifor
Professor H Crewe Brown

QUESTIONNAIRE FOR RESEARCH ON CONJUNCTIVITIS IN NEONATES

1. NAME : .....

2. DATE OF BIRTH : .....

3. HOS REG NO : .....

4. DAY ON WHICH DISCHARGE FROM EYES DEVELOPED : .....

5. PLACE OF BIRTH : HOSPITAL ☐ HOME ☐

6. RECEIVED EYE DROPS AS PROPHYLAXIS : YES ☐ NO ☐

7. MARITAL STATUS OF MOTHER : MARRIED ☐ UNMARRIED ☐

8. PV DISCHARGE DURING PREGNANCY : YES ☐ NO ☐

9. ATTENDED ANTENATAL CLINIC : YES ☐ NO ☐

10. TREATMENT RECEIVED FOR VAGINAL DISCHARGE FROM CLINIC : YES ☐ NO ☐

.....
DATE

.....
PLACE

.....
DR C. THOMAS

RESEARCH REPORT FOR MSc (Med) IN CHILD HEALTH

PAED 805

CANDIDATE	:	Dr Cherian Thomas
STUDENT NUMBER	:	9411311G
DEPARTMENT	:	Paediatrics & Child Health
DEGREE	:	MSc (Med) in the field of Child Health option Community Paediatrics
SUPERVISOR	:	Prof H. Crewe-Brown
TITLE	:	"Aetiology of conjunctivitis in Sebokeng Hospital neonates who received routine prophylaxis at birth against eye infection"
POSTAL ADDRESS	:	P.O. Box 901 Kiashapark 1829
TELEPHONE NO (H) AND CODE (W) CELL	:	(011) 855-5343 (011) 489-1011 0832845526
ETHICS COMMITTEE APPROVAL	:	Received Ethics Committee approval on 22.03.96 (Copy attached)
POST-GRADUATE COMMITTEE APPROVAL	:	Received post-graduate committee approval on 14.11.96 (Copy attached)

Research done as part fulfillment of MSc (Med) Child Health with the University of Witwatersrand.