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Corneal ulceration at an urban African hospital

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SUMMARY During a one-year survey 283 corneal ulcers from 274 patients were seen at St John's Eye Unit of Baragwanath Hospital. Central bacterial ulcers constituted the largest problem, and the commonest isolate in this group was *Streptococcus pneumoniae*. Mycotic and dendritic keratitis were relatively uncommon, while marginal catarrhal ulceration secondary to chronic staphylococcal lid disease was frequently seen. The microbiology of the various ulcers is described, and the placing of organisms into classes is stressed in determining significance of isolates. Many of the patients were male Africans who were either manual labourers or unemployed. Half the patients had used topical antibiotics before presentation.

The spectrum of micro-organisms responsible for corneal ulceration varies according to geographical location. Reports from the northern parts of the United States of America show predominantly Gram-positive organisms[1,2] while the southern parts show a striking number of fungal and Gram-negative isolates.[3] A recent study from Britain[4] also showed predominantly Gram-positive isolates. Variations such as these are probably worldwide, but studies of them have not been forthcoming from many areas. Relatively little is known about the situation in Africa. A report from Nigeria in 1976[5] concentrated on cases of mycotic keratitis selected from the 'large number of patients with corneal ulcers' treated at that hospital.

Baragwanath Hospital serves the population of Soweto, a sprawling city near Johannesburg, South Africa, whose inhabitants number about one million. In addition Baragwanath Hospital is a referral centre for medical problems from many parts of the country and occasionally further afield. The St John's Eye Unit is an integral part of the hospital and is adjacent to it. Cases of corneal ulceration constitute about 5% of admissions to St John's Eye Unit. The present survey was intended to establish the numbers of the various types of corneal ulcers seen at the hospital, the spectrum of micro-organisms isolated, and to collect data relating to local and general predisposing factors with a view to prophylactic intervention should this be possible.

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Material and methods

PATIENTS

Patients with corneal ulcers were divided into mild, moderate, and severe groups. The mild group contained patients with corneal ulcers considered suitable for outpatient treatment. Patients with moderate and severe corneal ulcers were admitted for intensive investigation and treatment. The severe cases had features of severity as defined by Jones.[6] Ulceration due to chemical burns and simple traumatic ulcers without secondary infection were excluded from the study group.

From the beginning of July 1982 to the end of June 1983 113 cases of mild corneal ulceration (116 eyes) and 161 moderate and severe cases (167 eyes) were treated. The mild group was treated in the outpatient department by a number of different doctors, and treatment methods varied.

Recording sheets were used to detail relevant history and examination, and a drawing of the cornea was made along the lines suggested by Bron[7] and Harrison.[8] Anterior segment photography recorded the appearance of the ulcer on admission, discharge, and when otherwise indicated.

CULTURE TECHNIQUES

All cultures except two were taken prior to admission by the doctor supervising the cases, and the other two were cultured under direct supervision by the same technique.

The culture technique was as advocated by Jones.[9] Conjunctival specimens were taken with calcium alginate swabs (Calgiswab, Inolex) moistened in

serum broth. One was swabbed over the lower fornix, avoiding the lid margins, plated on to blood agar, and inoculated into serum broth. A second swab was moistened in chopped meat broth and a conjunctival swab taken in the same way and placed in the chopped meat broth. The cornea was then anaesthetised with oxybuprocaine or proparacaine hydrochloride. Multiple corneal scrapings were then taken with platinum spatulae and inoculated on to blood agar in several rows, and serum broth and brain-heart infusion broth were also inoculated. From corneal scrapings two smears were made, one of which was stained the same day with Gram's staining technique, while the other was examined microscopically the following day by the Mycology Department. A swab moistened in chopped meat broth was rubbed over the base and edges of the ulcer and inserted into the chopped meat broth. The chopped meat broth replaced a brain-heart infusion broth under oil which was used for the first four months of the study (80 cases) and during which time no anaerobic bacteria were grown. In 54 cases a dry cotton swab was used to take a specimen for viral culture, and this was placed in bovine plasma albumin for transport to the laboratory. In 30 cases corneal scrapings were plated on to Lowenstein and Jensen media to check specifically for mycobacteria, as tuberculosis is not uncommonly treated at Baragwanath Hospital. The viral cultures were kept at 4°C and the rest of the specimens were incubated overnight. The serum broths were incubated in 10% CO_2 to enhance the growth of more fastidious organisms. Swabs moistened in serum broth were used to take lid margin cultures from the same eye in cases of marginal corneal ulcer, and these were plated on to blood agar.

Bacteria were classified according to Bergey's *Manual*.[10] Conventional microbiological techniques were used for the isolation and identification of bacteria, fungi, and viruses isolated. All specimens were processed by the Central SAIMR (South African Institute for Medical Research), Johannesburg, except for virology specimens, which were forwarded to the National Institute for Virology.

CLASSIFICATION OF ISOLATES

The following classification to determine the significance of bacterial isolates, suggested by Jones,[6] was used:

Class 1. Growth of any organism(s) in two or more corneal media.

Class 2. Growth (more than one colony) in one solid medium of *Staphylococcus aureus*, *Streptococcus pneumoniae*, or *Pseudomonas aeruginosa*.

Class 3. Growth in one medium of an organism identified in the direct smear.

In addition to these three classes it was found useful to consider two other situations for clinical purposes, though these may not be acceptable in terms of a case definition:

Class 4. Growth of any organism(s) in a corneal medium plus conjunctival media.

Class 5. Growth of a pathogen on conjunctival media only.

As anaerobic bacteria were cultured from a single corneal and conjunctival medium these were not placed in the above mentioned classes.

A simple classification of the ulcers was used according to a method similar to that described by Kumura.[11]

Results

The number of ulcers in each category is shown in Table 1. There was a slight seasonal variance in the presentation of the ulcers to the hospital with a peak late in winter and into spring. There were 79 right and 76 left eyes with unilateral ulcers, and these together with the six bilateral cases gave 161 patients with 167 ulcers. Three of the bilateral cases were marginal catarrhal. There was no significant difference in mean age between the two largest groups. The central bacterial group had a mean age of 42·5 years and the marginal catarrhal group a mean age of 44·9 years. Within the group of admitted patients 30

Table 1 *Types of corneal ulcers*

Type of ulcer	*Number of eyes*	
	Mild (outpatients)	*Moderate and severe (admitted cases)*
Central:		
Bacterial	30	91
Fungal	0	6
Viral	24	13
Other	0	0
Marginal:		
Catarrhal	30	30
Ring/melting	4	12
Mooren's	0	4
Primary infection	0	6
Other	28	5
Total	116	167

Table 2 *Occupation of adult corneal ulcer patients*

Type of work	*Number*	*Percentage*
Manual labourer (non-farm)	61	47
Manual labourer (farm)	8	6
Unemployed	33	25
Domestic worker	16	12
Pensioner	11	8
Clerical	2	2
Total	131	100

Table 3 *Comparison of numbers of central bacterial and marginal catarrhal corneal ulcers in the various ethnic groups*

Ethnic group	*Central bacterial*	*Marginal catarrhal*
Zulu	26	11
Sotho	22	9
Xhosa	8	4
Tswana	7	2
Ndebele	6	1
Swazi	6	1
Shangaan	5	0
Coloured	3	0
Venda	1	0
Indian	1	0
Not known/other	6	2
Total	91	30

Table 4 *Comparison of numbers of central bacterial and marginal catarrhal corneal ulcers for males and females*

Sex	*Central bacterial*	*Marginal catarrhal*
Male	79	21
Female	12	9
Total	91	30

ulcers occurred in children (16 years of age and younger). Of the adults half were manual labourers and a quarter were unemployed (Table 2).

Of the cases which were admitted to hospital, 39% originated from Soweto, 48% from other urban areas within the Transvaal province, and 13% from rural areas within the Transvaal Province. Tables 3 and 4 show the ethnic and sex distribution of patients with corneal ulcers in the two largest ulcer groups.

In 154 cases the mean delay between the onset of symptoms and presentation to St John's for treatment was 16 days, but there was marked variation depending on the type of ulcer (Table 5). There was a significantly longer ($p<0.05$, Student's t test) delay before referral for the marginal catarrhal group than with the central bacterial group. About half the patients had been previously treated with topical antibiotics, and the antibiotic varied according to the type of ulcer being treated (Table 6). In 11 cases oral antibiotics had certainly been given in addition to local treatment. In a further five cases the description of the tablets suggested that they were antibiotics. Only one patient was on systemic steroid therapy, and this was a case of systemic lupus erythematosus with keratitis sicca which developed a pseudomonas corneal ulcer.

Table 5 *Delay before presentation for treatment*

Type of ulcer	*Mean (days)*	*Number in group*
Central:		
Bacterial	11	82
Fungal	26	6
Viral	10	13
Marginal:		
Catarrhal	19	29
Ring	34	12
Mooren's	43	3
Primary infection	27	5
Other	9	4
Total		154

Table 6 *Local treatment of corneal ulcers before admission*

Central group (110 ulcers)

	Bacterial	*Fungal*	*Viral*	*Total*	
Antibiotic:					
Definite	16	3	2	21	51
Probable	22	0	5	27	(46% of
plus Steroid	2	0	1	3	central ulcers)
Steroid only	3	0	1	4	
Antiviral	0	1	0	1	
Other	19	0	2	21	
Total	62	4	11	77	(70% of central ulcers)

Marginal Group (57 ulcers)

	Catarrhal	*Ring*	*Mooren's*	*Primary infect.*	*Other*	*Total*	
Antibiotic:							
Definite	7	4	1	3	1	16	31
Probable	8	2	1	0	1	12	(54% of
plus Steroid	1	1	0	0	1	3	marginal ulcers)
Other	4	2	0	0	1	7	
Total	20	9	2	3	4	38	(67% of marginal ulcers)

Antibiotic: 'Definite'—the patient could produce the antibiotic or knew the name; 'probable'—the patient was using ointment, or drops and ointment, which had been obtained from a medical source such as a doctor, clinic or chemist; 'other'—the patient was using drops only, which may or may not have contained antibiotic.

MICROBIOLOGY OF CENTRAL CORNEAL ULCERS

Corneal isolates were obtained in 62 of the 91 eyes in the central bacterial group (Table 7). By far the commonest isolate was *Str. pneumoniae*, which was cultured from 26 eyes. Other streptococcus species were isolated from a further four eyes. Of the pneumococci which were isolated from the central

bacterial ulcers four were isolated from children, three of whom were under 5 years old. From all types of ulcers there were 29 pneumococcal isolates, of which 24 were typed. Type 6 was the commonest (six isolates), followed by type 10 (four isolates). These and the eight other types reflected the usual upper respiratory tract pneumococci in the area. Minimal inhibitory concentrations (MICs) of drugs against 12 pneumococcal isolates were determined and they were all susceptible to penicillin-G MIC levels at <0·01 μg/ml except one which had an MIC of 0·25 μg/ml.

Staph. aureus was not found to be a common cause of central corneal ulceration in this survey. Isolates of Gram-negative bacteria were obtained from 18 eyes, with *Pseudomonas aeruginosa* (nine isolates) being the most common, followed by *Moraxella* species (four significant isolates).

In class 5 (conjunctival pathogens) there were three isolates of *Staph. aureus*, two of *Proteus mirabilis*, and one each of *Ps. aeruginosa* and *Str. pneumoniae*.

The anaerobes cultured were all obtained from chopped meat broth and consisted of nine isolates from eight cases. Four were conjunctival isolates only, and, of the remaining five, two were isolated in conjunction with class 1 pneumococci and were not considered significant in their own right. The remaining three were possibly significant. The case shown in Table 7 suffered from severe bullous keratopathy, and there were no aerobic bacteria cultured from the ulcer. The *Peptococcus prevotii* was cultured from the cornea and a *Peptococcus asaccharolyticus* was isolated from the conjunctiva. Scanty Gram-positive cocci were seen on the direct smear from the cornea. The other two isolates, a *Peptococcus micros* and a *Propionibacterium acnes* were not confirmed on direct smear and are thus probably not significant.

The Lowenstein-Jensen media were all negative for mycobacteria. The isolates from the cases of fungal keratitis are listed in Table 8 together with some of their relevant clinical details. None of the cases gave a history of trauma and none was wearing a contact lens. The nodular form of climatic droplet keratopathy which flakes off, leaving an area denuded of epithelium, was seen in two of these cases (it was also a local predisposing factor in eight of the central bacterial ulcers). As might be expected, half the group came from rural areas. There was only one significant bacterial isolate in this group and that was a class 1 *Staph. epidermidis* from case 5.

The group of central viral ulcers consisted largely of cases of indolent corneal ulceration with loss of corneal sensation. In some cases a clinical diagnosis could be made of stromal herpes keratitis with ulceration, and in one of these cases *Herpes simplex* was isolated. There was only one dendritic ulcer in this group.

Table 7 *Corneal isolates from central bacterial ulcers*

	Organism	*Number of isolates*
Single isolates		
Class 1:	*Streptococcus pneumoniae*	20
	Pseudomonas aeruginosa	9
	Staphylococcus aureus	3
	Corynebacterium species	2
	Staph. epidermidis	2
	Str. sanguis	2
	Proteus mirabilis	2
	Moraxella lacunata	1
	Klebsiella pneumoniae	1
Class 2:	*Str. pneumoniae*	1
Class 3:	*Moraxella lacunata*	3
	Str. pneumoniae	1
	Corynebacterium species	1
Class 4:	*Staph. epidermidis*	2
	Corynebacterium species	1
	Moraxella species	1
Anaerobe:	*Peptococcus prevotii*	1
Total		53 isolates from 53 eyes
Mixed isolates (class of isolates in brackets)*		
Str. pneumoniae (2) + *Staph. aureus* (1)		
Str. pneumoniae (2) + *Staph. epidermidis* (4)		
Str. pneumoniae (1) + *Propionibacterium acnes*		
Str. pneumoniae (1) + *Pasterurella* species (4)		
M. lacunata (3) + *Corynebacterium* species (1)		
M. lacunata (1) + *Staph. epidermidis* (1)		
Staph. epidermidis (4) + *Corynebacterium* species (4)		
Str. pyogenes (1) + *Staph. epidermidis* (1): this combination was isolated from both eyes of a case of bilateral corneal ulceration		
Total		18 isolates from 9 eyes

*For description of classes of isolates see 'Materials and methods'.

Table 8 *Corneal isolates from central fungal ulcers*

Isolate	*Class of isolate*	*Rural*	*Predisposing factor*
Aspergillus flavus	1	Yes	Diabetic
*Phoma eupyrena**	1†	No	Climatic droplet
Candida guilliermondii	BHI	No	Diabetic
*Fusarium moniliforme**	1†	Yes	Nil
*Curvularia lunata**	BHI	No	Diabetic, renal
*Curvularia lunata**	1†	Yes	Climatic droplet

*Identification confirmed at the Identification Services, Commonwealth Mycological Institute, Surrey, England.
†Confirmation of fungus on direct smear.
BHI = Fungus cultured from brain heart infusion broth only after repeated corneal scraping in clinically suggestive cases.
Climatic droplet means climatic droplet keratopathy.

MICROBIOLOGY OF MARGINAL CORNEAL ULCERS

The organisms isolated from the marginal catarrhal group are shown in Table 9.

Direct smears were helpful in 85 of the 128 instances (66%), in which one was done (see Table 10).

Table 9 *Corneal isolates from marginal catarrhal ulcers*

Organism	*Number of isolates*	*Class of isolate**
Single isolates		
Staphylococcus aureus	6	1, 1, 1, 3, 4, 4
Corynebacterium species	3	1, 4, 4
Staph. epidermidis	2	1, 4
Corynebacterium hofmanii	1	4
Streptococcus pneumoniae	1	1
Propionibacterium acnes	1	
Total	14 isolates from 14 eyes	
Mixed isolates (classes in brackets)		
Proteus mirabilis (4), *Str. pneumoniae* (4)		
Staph. aureus (1), *Str. pyogenes* (1)		
Staph. aureus (1), *Str. pyogenes* (1)		
Str. anginosus (1), *Neisseria flava* (4)		
Str. anginosus (1), *N. flava* (1), *Proteus vulgaris* (1)		
Total	11 isolates from 5 eyes (the last 2 eyes were from a bilateral case)	

*For description of classes of isolates see 'Material and methods'.

Table 10 *Results of microscopy of smears*

Result	*Ulcer group (numbers)*		*Total*	
	Central	*Marginal*	*Number*	*Percentage*
Organism identified	40	7	47	37
Slide negative, Culture negative	23	15	38 (85)	29 (66)
Slide negative, Culture positive	21	20	41	32
Slide positive, Culture negative	2	0	2	2
Total	86	42	128	100

A hypopyon was present in 69 eyes, two-thirds of these being central bacterial ulcers. More than 80% of the hypopyons were 2 mm or less at the time of presentation. A significant corneal isolate was obtained in 45 of the 69 eyes, 17 of which were pneumococci. Ten of the 30 ulcers in the marginal catarrhal group were associated with hypopyon.

All aerobic bacterial isolations were tested for antibiotic susceptibility with a modified Kirby-Bauer disc diffusion technique on blood agar plates. All isolates were sensitive to either cefazolin or gentamicin, which were the two antibiotics used in treating the bacterial infections.

Discussion

Patients with many different types of corneal ulcers present for treatment at St John's Eye Hospital every year. As a general rule, owing to a shortage of beds (110 beds), only fairly severe cases will receive inpatient treatment, and this group of patients included 69 with hypopyon and 34 with perforated corneal ulcer. Most of the patients were male Africans, half of whom were manual labourers. This group might be expected to be exposed to corneal trauma, and indeed corneal foreign bodies and other corneal injuries such as corneal abrasions were the commonest local predisposing factors, followed by nodular climatic droplet keratopathy. The differences in the numbers of patients from various ethnic groups probably reflect differences in population size. The marked male predominance has commonly been reported and was as high as 80% in a retrospective study of 677 cases.[2]

The class system for the isolates is intended to assess relevance of isolates and exclude contaminant bacteria. From class 1 to class 5 presents a decreasing likelihood of significance. Florid growth of an organism in several media (class 1) would be highly significant, whereas recovery of a pathogen only from the conjunctiva would be of questionable significance. The latter isolate may be considered when pretreatment is suspected of having sterilised the cornea. Classes 4 and 5 are included in an attempt to use conjunctival isolates in a meaningful way rather than relying only on corneal specimens. A class 4 isolate may reflect a tear film contaminant such as *Staph. epidermidis* or a more fastidious organism that will grow only on a certain type of medium, such as *Moraxella* species in serum broth of cornea and conjunctiva. Conjunctival isolates obtained which did not occur as class 4 or 5 isolates are not reported in this paper.

Bacterial corneal ulcers constituted the largest group of ulcers seen, and pneumococci were prominently isolated within the group. *Staph. aureus* is usually the commonest Gram-positive bacterium reported as a cause of central bacterial keratitis,[1-4 6] though an early series reported by Thygeson[12] showed pneumococci to be causative in 70% of 50 central corneal ulcers. The difference in the range of organisms is at least partly due to a worldwide difference in the conjunctival sac carrier rates of various organisms.[1] In a large series Locatcher-Khorazo and Seegal[1] showed a high (13%) carrier rate of pneumococci in the normal conjunctival sac in the children under 5 but only 2–3% thereafter. In the same series the carrier rate of *Staph. aureus* was 25% in the children under 5, but this remained constant in all age groups thereafter. In this study five children had pneumococcal ulcers, four of whom were under 5 years old (three were central bacterial ulcers). The other pneumococcal ulcers were evenly spread through the age groups over 20 years.

Pneumococcal typing is not particularly useful in that the organisms usually reflect upper respiratory tract pneumococci.[1] This was found to be true in this

study, though the types of pneumococci predominantly found differed from those previously reported. As multiply resistant pneumococci have been reported from South Africa,[13 14] a careful watch was kept for these organisms, but none was found. *Ps. aeruginosa* and *Moraxella* species were the two commonest Gram-negative isolates in the population studied. Moraxella corneal ulcers have been described as occurring in derelict populations, who have a high carrier rate of these organisms in their noses and conjunctival sacs.[15] The carrier rate in our area is not known.

Direct smears were found to be significantly more helpful in central as opposed to marginal ulcers ($p<0.05$, normal deviate test). This difference was largely due to the fact that an organism could be identified from many of the central ulcers. The results confirm the fact that, if an organism is seen on the smear, it is very likely to be the causative organism, but if no organism is seen there is still a 50% chance that an organism will be cultured.

Only 24 cases of dendritic keratitis were seen during the year (two admitted and 22 treated at outpatients). This might represent a racial difference in susceptibility, and in support of this seven of the 24 were coloured and one Asian. This was the only group of ulcers with such a large proportion of race groups other than African. There are many clinics throughout Soweto and the surrounding areas, and certainly many corneal ulcers are prevented or treated at an early stage by these primary health care workers. To some extent, therefore, the patients presenting to St John's for treatment represented a 'screened' population, but many 'mild' cases were seen, as well as referral problem cases, and it is unlikely that the dendritic ulcer patients were being selectively screened out.

The 60 catarrhal corneal ulcers treated during the year (half at outpatients and half admitted) testify that chronic staphylococcal blepharitis/meibomianitis and its sequelae were commonly seen, often with a secondary bacterial infection.

When dealing with large numbers of corneal ulcers the culture technique used must be accurate and yet reasonably quick to perform. The multiple scrape technique, described by Jones,[9] was largely successful in view of the fact that half the cases had been pretreated with antibiotics. The use of multiple media is essential if significance is to be determined and contaminants recognised. The serum broth was supplied in Bijou bottles and the brain-heart infusion and chopped meat in McCartney bottles, which made transport easier than with media in tubes.

Reliable isolation of anaerobic bacteria is more time-consuming than of aerobic bacteria, and indications are that these organisms should not be ignored. Corneal ulceration caused by anaerobic bacteria was considered uncommon enough to warrant single case reporting from the 1950s into the 1970s.[16–19] In 1977 Jones and Robinson reviewed the subject[20] and included details of five cases of anaerobic keratitis. They also proposed guide lines for defining a significant isolate. Perry *et al.*[21] reported 11 cases of anaerobic corneal ulcer, using very stringent criteria for case definition, from a series of 162 bacterial corneal ulcers. All these cases[20 21] had some predisposing factor(s). Anaerobic bacteria may be pathogenic alone or acting synergistically with aerobic bacteria as has been suggested.[22 23] The practical implications of this group of organisms with respect to treatment is uncertain, as they are usually susceptible to the same antibiotics as have been used for aerobic bacterial keratitis. A change to chloramphenicol is recommended[21] once an anaerobe is isolated, but this information may not be available in time to be useful.

If bacteriology is to play an active role in the management of acute keratitis, provisional results must be available within 24 hours, as these cases can deteriorate rapidly. It was pleasing to note during the study period that in nine cases of uncontrolled infection (six pneumonococcal and three pseudomonas) the organism was identified in eight cases on the day of admission on direct smear and provisionally confirmed on culture the following day. This places the clinician in the best possible position to make decisions on antibiotic choices in spite of having to wait a further day for antibiotic sensitivity results. It is usually sufficient to be able to make a distinction between Gram-positive cocci and Gram-negative bacilli for the purpose of choosing an antibiotic. Mixed infections are common enough to keep one humble, and a broad spectrum of antibiotic cover is used initially, with a change to more specific treatment made with positive confirmation of the causative organism.

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