ASPECTS OF SEXUALLY TRANSMITTED DISEASES

AT KING EDWARD VIII HOSPITAL

BY

ANWAR AHMED HOOSEN

A research project report submitted in partial fulfilment of the requirements for the degree of

MASTER OF MEDICINE

in the
Department of Medical Microbiology
University of Natal
DURBAN

1988

ABSTRACT

This study was undertaken to determine the prevalence of sexually transmitted pathogens in the genital tract of women with acute pelvic inflammatory disease (PID) and in males with acute urethritis. Two groups of women (50 with a clinical diagnosis of acute PID and 50 asymptomatic women attending the family planning clinic (FPC)) and two groups of men (230 unselected males with acute urethritis and 75 males previously treated with procaine penicillin for gonococcal urethritis and returning with persistent urethral discharge) were investigated.

Specimens were collected by non-invasive, lower genital tract sampling and processed initially in the clinic for microscopy, culture and other investigations.

Endocervical Neisseria gonorrhoeae was present in 62% of the PID group and 10% of the FPC group. Of these isolates, 33% were penicillinase-producing. The carriage of Mycoplasma hominis and Trichomonas vaginalis in vaginal specimens was significantly higher in the acute PID group; whereas the prevalence of Chlamydia trachomatis and Ureaplasma urealyticum was equally high in both groups. Furthermore, syphilis serology was positive in 34% of the PID group as compared to 10% of the FPC group.

Gonococcal infection is the most common cause of urethritis in males, being detected in 95,9% of untreated patients and 77,3% of previously treated

patients, with penicillinase-producing strains accounting for 26,2% and 58,6% of isolates respectively. C. trachomatis was detected in 17% of untreated and 10,7% of treated males. U. urealyticum was cultured from 64,1% of untreated and 33,3% of treated patients, occurring almost always in association with N. gonorrhoeae. T. vaginalis was detected in 14,7% of patients with persistent urethral discharge.

The high prevalence of recognised sexually transmitted pathogens in these groups of patients underlines the need for appropriate antimicrobial therapy for the management of these patients and the control of the spread of resistant pathogens.

PREFACE

This study represents original work by the author and has not been submitted in any form to another University. Where use was made of the work of others, it has been duly acknowledged in the text.

The research described in this project was carried out in the Department of Medical Microbiology, University of Natal, under the supervision of Professor Jan van den Ende.

27 October, 1988
.....
DATE

.....
SIGNATURE

ACKNOWLEDGEMENTS

I wish to express my sincere gratitude to the following:

Professor Jan van den Ende, Head of the Department of Medical Microbiology, University of Natal, for his expert guidance, encouragement and constructive criticism.

Professor J Moodley of the Department of Obstetrics and Gynaecology, University of Natal and Dr L E D F Joubert, Head of Special Clinic, King Edward VIII Hospital, for allowing access to patients.

Miss H G Fehler of the Emergent Pathogen Research Unit of the of the South African Institute for Medical Research (SAIMR) Johannesburg, for assistance with chlamydia cultures.

Mrs Kay George for typing the manuscript.

CONTENTS

1 INTRODUCTION

Sexually transmitted diseases (STDs) constitute a group of infectious diseases that have in common the feature of being transmitted predominantly by sexual contact.

With recent advances in laboratory technology, knowledge of this group of diseases has increased tremendously. More than 20 different infectious agents are now recognised as being responsible for STDs (Holmes et al, 1984). The diseases caused by these agents include the five classical diseases - syphilis, gonorrhoea, chancroid, lymphogranuloma venereum and granuloma inguinale - as well as a number of newly recognised protozoal, bacterial, fungal and viral diseases including the much dreaded acquired immunodeficiency syndrome (AIDS). The epidemiological considerations of the AIDS epidemic in South Africa have recently been elucidated (Schoub et al, 1988).

STDs have become a major health problem in most developing countries because of their increasing prevalences, their impact on maternal and infant health, social consequences and subsequent drain on economic resources (Antal, 1987).

In South Africa, a wide spectrum of STDs is encountered (Ballard and Duncan, 1983). In developed communities, the classical STDs such as gonorrhoea and syphilis, though still encountered, have been largely replaced by chlamydia and herpes genitalis, as the commonest cause of acute urethritis and genital ulcer disease respectively; whereas in

developing communities, the classical infections remain endemic and often epidemic in their prevalences.

In order to determine rational and effective guidelines for the management and control of this group of infectious diseases, it is imperative to obtain data on the relative prevalences of the various aetiological agents and their antimicrobial susceptibility patterns.

Clinical syndromes - prevalent at King Edward VIII Hospital - in which sexually transmitted pathogens are considered to play an important aetiological role and which are prevalent locally, include acute pelvic inflammatory disease in patients attending the gynaecology clinic, and acute urethritis amongst male patients attending the STD clinic. However, since little data have been available regarding the sexually transmitted pathogens involved, their respective prevalences and antimicrobial susceptibility patterns, it is vitally important that studies on these common conditions be undertaken locally.

ACUTE PELVIC INFLAMMATORY DISEASE

Pelvic inflammatory disease is defined as an inflammatory process involving the female genital structures above the level of the internal os of the cervix or any structure within the pelvic brim (White, 1981). The term 'pelvic inflammatory disease' is commonly abbreviated to PID and is usually used synonymously with salpingitis (Holmes et al, 1980), because attempts to subdivide this syndrome on anatomical grounds into entities such as endometritis, salpingitis, pelvic peritonitis, are not clinically practical.

PID is a serious infection resulting in hospitalization of more than 250 000 women in the United States of America annually, (Thomason et al, 1986). In South Africa, it has been estimated that approximately one third of all admissions to gynaecology wards at any large Black hospital are on account of PID (Lithgow and Rubin, 1972).

After a single episode of salpingitis 10-25% of all patients develop subsequent episodes of PID and due to tubal damage which is a common sequela, patients are at risk of developing complications such as infertility, ectopic pregnancy and chronic pelvic pain (Thomason et al, 1986). Clearly, PID ought to be accurately diagnosed in all patients and treated appropriately.

The large majority of cases of acute salpingitis are the result of canalicular spread of micro-organisms from the cervix over the surface epithelium to the fallopian tubes. Only about one percent of cases are caused by contiguous spread of infection from other organs of the pelvic cavity (Westrom and Mardh, 1984).

An accurate clinical diagnosis of PID is not easy because the intraperitoneal organs which are involved are not readily accessible for examination. Ideally, the management of patients with acute PID should be based on visual confirmation of the clinical diagnosis and the isolation, identification and determination of antimicrobial susceptibilities of pathogens from the site(s) of infection.

If exclusively, clinical criteria are to be used for diagnosing salpingitis, consideration ought to be given to those (criteria) standardised by the

Infectious Diseases Society of Obstetrics and Gynaecology in the USA (Hager et al, 1983). These compose the presence of all of the following:

1 lower abdominal pain and tenderness

2 cervical motion tenderness

3 adnexal tenderness

4 and in addition, a minimum of one of the following:

a temperature greater than 38°C

b peripheral leucocyte count greater than 10 000/uℓ

c increased ESR

d inflammatory mass visualised by sonography

e purulent material obtained from culdocentesis

Published South African data on the aetiology of acute PID are scarce. Allen and Schoon (1984) in a study on women attending the out-patient department at Ngwelezana Hospital, northern KwaZulu, confirmed acute salpingitis by laparoscopy in only 52% (53 of 103) of patients clinically diagnosed as suffering from acute PID. Neisseria gonorrhoeae was isolated from the cervix of 57% (30) patients and in 73% (22 of 30) patients, the organism was also isolated from tubal or cul de sac exudates. Other aetiological agents were not sought for in this study.

In Bloemfontein, at the Pelonomi Hospital, Burchell and Schoon (1987) confirmed the clinical diagnosis of acute PID by laparoscopy in 55% (22 of 40) patients. Microbiological findings reported in another publication (Burchell et al, 1987) from the same centre, indicated Chlamydia trachomatis (73,3%) to be the most commonly associated pathogen, others being N. gonorrhoeae (40%), anaerobic bacteria (46,6%) and aerobic

bacteria (26,6%). Specimens in this study were collected both from the lower genital tract (vaginally) and from the tubal end (laparoscopically).

In a report on a limited study conducted in Johannesburg, (Ballard et al, 1981), N. gonorrhoeae was isolated from the cervix of 6 of 24 patients. These patients also had higher serum anti-chlamydial antibody titres than did a group of ante-natal patients. In addition, antichlamydial antibodies were also detected in cervical secretions of 7 of 23 patients - suggesting a chlamydial aetiology.

At King Edward VIII Hospital (KEH) Durban, acute PID is one of the most common clinical problems seen amongst women attending the gynaecology out-patient department. With the exception of a study to determine the prevalence of gonorrhoea in women attending the gynaecology clinic (Vink and Moodley, 1980), no studies on the prevalence of sexually transmitted pathogens in PID have been conducted locally. Moreover, the treatment for PID at KEH is empirical and directed against pathogens thought to be common. Therefore, most therapeutic regimens utilised include an agent active against penicillin-sensitive N. gonorrhoeae, facultative Gram-negative bacteria and anaerobic bacteria. This antimicrobial strategy is based on the premise that the polymicrobial aetiology of acute PID is now firmly established, the most common initiating micro-organisms being N. gonorrhoeae, C. trachomatis and Mycoplasma hominis (Thomason et al, 1986).

As mentioned above the clinical diagnosis of acute PID is not totally reliable and when pelvic viscera are visualised, the diagnosis is confirmed in only 55-70% cases (Allen and Schoon, 1983; Burchell and Schoon, 1987;

Wasserheit et al, 1986; Jacobson and Westrom, 1969). At KEH, the performance of diagnostic laparoscopy for all patients with clinical diagnosis of acute PID would be logistically and economically impractical, especially in view of the large patient numbers and limited facilities. Lower genital tract sampling cannot establish the aetiology of tubal infection with certainty, especially in respect of secondary bacterial invaders (Westrom and Mardh, 1984). The yield of recognised sexually transmitted pathogens from cervical specimens is higher than that from tubal or peritoneal specimens (Westrom, 1983; Sweet et al, 1979). Furthermore, since lower genital tract sampling is non-invasive, more rapid and less costly; it is therefore considered adequate for the functioning of the overstressed facilities at KEH.

ACUTE URETHRITIS

Acute urethritis is the response of the urethra to inflammation of any aetiology. In adult males, it usually manifests as a urethral discharge with an accompanying complaint of burning on micturition. The characteristic physical finding is urethral discharge. The presence of urethritis can be confirmed by the demonstration of increased numbers of inflammatory cells in gram-stained endourethral smears (Bowie, 1984).

Urethritis is termed gonococcal if N. gonorrhoeae is detected in endo-urethral specimens; or non-gonococcal urethritis (NGU) when this organism is not detected. Other micro-organisms commonly implicated as causative agents of acute urethritis include C. trachomatis and Ureaplasma urealyticum, whilst Trichomonas vaginalis, Gardnerella vaginalis and the human herpes virus constitute rare or unusual causes (Rein, 1985).

The role of N. gonorrhoeae in the aetiology of male urethritis is well established. However, recent work has highlighted two areas of concern; these being, the presence of asymptomatic urethral infection amongst males and the increasing resistance of the gonococcus to penicillin (Bowie, 1984).

Antimicrobial resistance to N. gonorrhoeae was first observed against the sulphonamides and by the late 1940s, the majority of clinical isolates were resistant to this group of antibiotics (Dunlop, 1949). With the subsequent extensive use of penicillin for therapy, chromosomal mutations led to progressive increases in resistance and while initially 150 000 units of penicillin cured gonorrhoea, the dose necessary for therapeutic success increased to 4,8 million units plus the requirement of oral probenecid to delay renal excretion. The chromosomal-mediated resistance increased further and now non-penicillinase producing N. gonorrhoeae (non-PPNG) completely resistant to penicillin have been described (Centers for Disease Control, 1983).

Penicillinase-producing strains of N. gonorrhoeae (PPNG) emerged in the Far East and West Africa in 1975. The first cases of imported PPNG in South Africa were detected in 1977 when isolated cases were reported from Johannesburg (Robins-Brown et al, 1977) and Durban (Hallet et al, 1977). Subsequent published studies from different South African centres have focussed on the prevalence of PPNG in male urethritis.

Studies from Cape Town (Simpson and Oliver, 1987) have shown that whilst in 1980, no strains of PPNG were isolated from males with acute urethritis, in 1984, 1,9% of N. gonorrhoeae isolates were found to be penicillinase-producing. This figure increased to 8,6% by July 1985. Until

the middle of 1984, despite routine screening in Bloemfontein of N. gonorrhoeae isolates for penicillinase production, no such strains were detected. Subsequently a study undertaken at a municipal clinic on patients with acute urethritis, revealed a 2,2% PPNG prevalence (Dove et al, 1987).

A 4% prevalence of PPNG was first reported from Pretoria in 1984 (Crewe-Brown et al, 1985), from a study on male urethritis in patients attending a general practice. The following year, a prevalence of 10% PPNG was reported from the same city (Dangor, 1985). The first report of PPNG from Port Elizabeth was in 1985 (Jennings et al, 1986).

After their initial detection in 1977 (Hallet et al, 1977) penicillinase-producing N. gonorrhoeae were not encountered again in Durban until 1983 (Coovadia et al, 1984a). Since then, their prevalence has been investigated at intervals. The last local prevalence study was undertaken in 1984 (Ballard, 1984).

Whilst most South African studies have focussed predominantly on the prevalence of PPNG in acute urethritis, published data on the prevalence of the various other microorganisms implicated in the aetiology of acute urethritis have been scarce. Ballard et al (1986) in a study from Johannesburg, reported that C. trachomatis was isolated from significantly fewer black males than white males with NGU; whilst a significantly higher proportion of black males with gonococcal urethritis harboured U. urealyticum.

Despite the high prevalence of PPNG in Durban, the standard antibiotic therapy employed locally (at the Sexually Transmitted Diseases Clinic) for

patients presenting with untreated acute gonococcal urethritis - diagnosed by a Gram-stained smear - remains intramuscular procaine penicillin in a dose of 4,8 million units plus 1 gram oral probenecid. For penicillin allergic patients, oral minocycline (100mg BD for 7 days) is provided as alternative therapy.

On occasion patients do return complaining of persistent urethral discharge. Because of the high local prevalence of PPNG and the relatively low prevalence of associated chlamydial infection in similar patients, (12% reported from Johannesburg, Ballard et al, 1986), it has been assumed that persistent infections are most probably due to PPNG.

Until recently, it has been the practice at the STD clinic to treat such patients who have 'failed' penicillin therapy with intramuscular spectinomycin. However, no systematic study had previously been performed to ascertain the aetiology of urethritis in such patients.

OBJECTIVES

The aims of the studies performed in this project are the following:

1 to determine the prevalence of sexually transmitted pathogens in women with acute PID. A control group consisting of asymptomatic women attending a family planning clinic is included for purposes of comparison.

2 to investigate the aetiology of acute urethritis in males attending the local sexually transmitted diseases clinic and determine the prevalence of PPNG and the susceptibility to penicillin of non-PPNG strains.

3 to determine the aetiology of persistent urethral discharge in patients treated with penicillin for gonococcal urethritis.

2 PATIENTS AND METHODS

2.1 PATIENT SELECTION

2.1.1 Acute pelvic inflammatory disease

This study was conducted between June 1986 and July 1987 on 100 women attending KEH. Two groups of women were studied:

50 patients with clinical diagnoses of acute PID attending the gynaecology clinic and

50 asymptomatic women attending the family planning clinic (FPC).

Only women between the ages of 16-35 years were included in the study. The diagnosis of acute PID was made on the basis of a history of lower abdominal pain and the clinical findings of cervical motion tenderness and adnexal tenderness. Additional criteria for inclusion were peripheral blood leucocyte count greater than 10 500 x 10^9/L and/or temperature equal to or greater than 37,5°C.

Patients were excluded from the study if they had received antibiotics in the preceeding 30 days, were using an intrauterine contraceptive device, were less than 3 months post-delivery or had undergone any recent procedure involving cervical manipulation (eg hysterosalpingography, cone biopsy or curretage). Furthermore, as other workers have shown that acute PID is rarely associated with normal vaginal wet smear findings, patients with this finding on microscopic screening were also excluded (Westrom, 1983).

The control group (women attending the FPC) were asymptomatic and had no past histories of acute PID. The same exclusion criteria were applied, with the exception that vaginal smear findings were not considered.

2.1.2 Acute urethritis

230 unselected adult male patients presenting to the STD Clinic at KEH with acute urethritis were investigated. Information regarding recent antimicrobial chemotherapy was elicited by questioning and from referral notes. The study period extended from 18 November to 2 December, 1985.

2.1.3 Persistent urethritis

A total of 75 adult males were investigated during the period July to September 1987. All patients returned to the STD Clinic at KEH complaining of persistent urethral discharge, within 30 days of having been treated with a standard intramuscular dose of 4,8 million units procaine penicillin plus 1 gram oral probenecid. On specific questioning, all patients denied having had any sexual contact subsequent to treatment.

2.2 MICROBIOLOGICAL METHODS

2.2.1 Acute pelvic inflammatory disease

All specimens were collected before the commencement of any antimicrobial therapy. After a general examination, each patient was placed in the lithotomy position and a sterile unlubricated Cusco's speculum passed into the vagina.

Vaginal secretions from the posterior fornix were collected on 2 sterile cotton-tipped swabs. One was used for the preparation of a saline wet smear, which was examined microscopically for the presence of bacteria, inflammatory and epithelial cells, yeasts and motile trichomonads. This was done at the bedside within 10 minutes of collection.

Vaginal wet smears were regarded as normal if rod-shaped bacteria, resembling lactobacilli, were the predominant organisms and epithelial cells outnumbered inflammatory cells, provided no clue cells, yeasts or trichomonads were present (Westrom, 1983). The second vaginal swab was inoculated onto Shepards A-7 agar for the isolation of genital mycoplasmas (Shepard and Lunceford, 1976). The A-7 agar plates were inoculated anaerobically at 36°C for 48 hours and then examined microscopically (100x magnification) for the presence of characteristic colonies of M. hominis and U. urealyticum.

Endocervical specimens were collected after wiping the ectocervix with one or two large sterile swabs to clear vaginal secretions. Sterile cotton-tipped swabs were then carefully inserted into the cervical canal and rotated firmly to obtain cervical cells and any exudate. Swab specimens were also taken from the urethra and rectum.

For each patient, one endocervical and the rectal and urethral swabs were inoculated onto modified New York City Medium (MNYC) (Young, 1978) for the culture of N. gonorrhoeae and placed immediately in a candle extinction jar.

These agar plates were transported to the laboratory within 30 minutes of collection and incubated at 36°C in an atmosphere of 10% CO_2 in air for 48-72 hours. Colonies of N. gonorrhoeae were provisionally identified by colonial morphology, gram staining, positive oxidase test and identity confirmed by carbohydrate tests (Young and Pyrula, 1978). All isolates were tested for penicillinase production using chromogenic cephalosporin as substrate (O'Callaghan, 1972).

An endocervical swab was also inoculated onto an A-7 agar plate which was processed as described above. The third endocervical swab was used to prepare a smear for subsequent direct immunofluorescence staining for detection of C. trachomatis (Microtrak, Syva, USA).

Venous blood was collected from each patient for the following serological tests: (i) syphilis, Rapid Plasma Reagin-RPR (BBL Microbiology Systems, Maryland, USA). All RPR reactive sera were

titred and subjected to confirmatory tests: Treponema pallidium haemagglutination test-TPHA (Fujirebio, Tokyo, Japan) and the fluorescent treponemal absorption test-FTA-Abs (Wellcome Diagnostics, UK); (ii) Hepatitis B surface antigen (HBsAg) - radio-immunoassay (Abbott, Austria); and (iii) antibodies to Human Immunodeficiency Virus (HIV) - Abbott recombinant HIV ELISA kit (Abbott Diagnostics, West Germany).

2.2.2 Acute urethritis

Endo-urethral specimens were obtained using calcium alginate-tipped swabs (Calgiswab type 1, Inolex, USA). Smears were prepared on 2 glass slides, one for Gram-staining and the other for subsequent direct immunofluorescence staining for C. trachomatis (Microtrak, Syva, USA).

Swabs for the isolation of N. gonorrhoeae were inoculated directly onto modified MNYC medium (Young, 1978) and immediately placed in a candle extinction jar. These were transported to the laboratory within 2 hours of collection and incubated at 36°C in an atmosphere of 10% CO_2 in air for 48-72 hours. Colonies of N. gonorrhoeae were identified as described above (2.2.1).

One swab from each patients was expressed into 2mℓ of chlamydial transport medium which was kept at 4°C until transported to the laboratory and, if not processed immediately, was stored at -70°C. The cell culture method used for isolation of C. trachomatis was that

of Ripa and Märdh (1977), using McCoy cells treated with cycloheximide immediately after inoculation.

For the isolation of U. urealyticum and M. hominis swabs were inoculated into Shepard's U-9 broth (Shepard and Lunceford, 1970) and A-7 agar plates (Shepard and Lunceford, 1976). These were then incubated at 36°C anaerobically. The U-9 cultures were observed twice daily for colour change (due to alkalinity resulting from urea hydrolysis) (Shepard, 1973) in the absence of turbidity, whereupon they were immediately sub-cultured onto Shepard's A-7 agar.

The A-7 agar plates were incubated anaerobically for 48 hours and then examined under 100x magnification for the presence of characteristic colonies of U. urealyticum and M. hominis.

Gram-stained smears were examined microscopically for the presence of inflammatory cells. Smears showing more than 4 cells per field (1000x magnification) were considered confirmatory of urethritis. Immunofluorescence staining and microscopy for detection of C. trachomatis was performed according to the kit manufacturer's instructions.

Antibiotic susceptibility testing:

All isolates of N. gonorrhoeae were tested for penicillinase production using chromogenic cephalosporin as substrate (O'Callaghan, 1972). Minimal inhibitory concentrations (MICs) for penicillin G against N.

gonorrhoeae were determined by the agar dilution method using Diagnostic Sensitivity Test Agar (DST, Oxoid) supplemented with 6% lysed horse blood.

Inocula of approximately 10^4 organisms were applied by means of a multipoint inoculator (Denleys Instruments, UK). Controls included Staphylococcus aureus (NCTC 6571) and plates containing no antibiotics. The penicillin G concentrations tested ranged from 0,0017-32mg/ℓ.

Inoculated plates were read after overnight incubation at 36°C in an atmosphere of 10% CO_2 in air and the MIC was recorded as the lowest concentration of antibiotic which completely inhibited growth of the isolate.

For tetracycline, spectinomycin, rosoxacin, chloramphenicol, sulphamethoxazole-trimethoprim (19:1 ratio) and kanamycin breakpoint MICs were determined using a single concentration for each antimicrobial agent (breakpoint MICs).

2.2.3 Persistent urethritis

Endo-urethral specimens were obtained from each patient using sterile calcium alginate-tipped swabs (Calgiswab type 1 Inolex, USA). These swabs were processed as follows:

i a smear for Gram-staining

ii a wet-mount and

iii a smear for direct immunofluorescence staining for C. trachomatis (Microtrak, Syva, USA).

Gram-stained urethral smears were examined microscopically for the presence of inflammatory cells and bacteria. Urethritis was regarded as being present if more than 4 inflammatory cells per high-power oil immersion field (1000x magnification) were observed. Immunofluorescence staining and microscopy for detection of C. trachomatis was performed according to the manufacturer's instructions. Wet-mounts were examined microscopically for inflammatory cells, yeasts and motile trichomonads.

The following culture media were inoculated in the clinic:

i modified New York City medium (MNYC) (Young, 1978) for the isolation of N. gonorrhoeae.

ii human blood agar for Gardnerella vaginalis

iii modified Diamond's medium for T. vaginalis (Philip et al, 1987) and

iv Shepard's U-9 broth (Shepard, 1970) for genital mycoplasmas.

Inoculated media were immediately placed in a candle extinction jar and transported to the laboratory within 2 hours of collection. In the laboratory, MNYC and human blood agar plates were incubated at 36°C in an atmosphere of 10% CO_2 for 48-72 hours. Colonies of N. gonorrhoeae were identified as described under section 2.2.1.

For the isolation of genital mycoplasmas the U-9 broths were processed as described under section 2.2.2.

The modified Diamond's media were incubated anaerobically at 36°C. Wet-mounts were prepared daily for up to 7 days, and examined microscopically for the presence of T. vaginalis, which were identified by their characteristic motility and morphology.

3 RESULTS AND SPECIFIC DISCUSSION - ACUTE PELVIC INFLAMMATORY DISEASE

The results and a brief discussion on the findings of sexually transmitted pathogens in the two groups of women studied are presented.

3.1 RESULTS

Satisfactory specimens were obtained from all patients. Four patients with initial clinical diagnosis of acute PID were excluded, as they had normal vaginal wet smears. Two of these patients underwent laparotomy, one had appendicitis and the other torsion of an ovarian cyst.

3.1.1 Clinical data:

Patient data for age, parity, contraception usage, temperature and peripheral leucocyte count are shown in Table 3.1. The mean age of patients in both groups was similar. There were 34 parous patients in the PID group and 44 in the FPC group. Differences in respect of contraceptive usage are evident.

From the symptomatic group 35 (70%) were hospitalised for treatment and the rest (15) treated as out-patients. The majority in the PID group (44) had fever greater than 37,5°C and 30 had peripheral leucocyte counts of greater than $10,500 \times 10^9$/L.

3.1.2 Microbiological data:

An abnormal vaginal wet smear (inclusion criterion for symptomatic PID patients) was observed in 42% of FPC patients (Table 3.2). The prevalence of T. vaginalis (56%) and M. hominis (84%) in the vagina was significantly higher in PID patients as compared to the FPC patients (20% and 50% respectively). However, vaginal colonisation with U. urealyticum was similar in both groups (44% and 48%).

N. gonorrhoeae was isolated from the endocervix of 31 (62%) of PID patients as compared to 5 (10%) of FPC patients, a significant difference (Table 3.3), but in no patient was this organism isolated from the urethra or rectum and not from the endocervix. A third of the total isolates (12 of 36) were penicillinase-producing strains.

The prevalence of C. trachomatis in the endocervix was similar in both groups of patients (Table 3.3). Whereas cervical colonisation with M. hominis was significantly higher in the PID patients (72% vs 42%). There was no significant difference in cervical colonisation with U. urealyticum in both groups of patients (22% and 36%).

3.1.3 Serological tests:

The results of all serological tests conducted on the patients are shown in Table 3.4. A significantly higher prevalence of reactive syphilis serology (confirmed by specific treponemal tests) was detected in patients with acute pelvic inflammatory disease as compared to 8% in the FPC group (p=0,0026). Four PID patients were HBsAg positive, none of the FPC controls were positive. In none of the 100 women was antibody to HIV detected.

TABLE 3.1

CHARACTERISTICS OF THE TWO GROUPS STUDIED

	ACUTE PID (n=50)	FAMILY PLANNING (FPC) (n=50)
Mean age in years (range)	25(16-35)	24(16-35)
Parous (n)	34	44
Contraception used:		
Progesterone (depot)	6	40
Combined pill	3	5
None	37	2
Unknown	4	3
Temperature ($\geqslant$37,5°C)	44	-
Peripheral leucocyte count		
$>10,500 \times 10^{9}/L$	30	-
Admitted for treatment	35	-

TABLE 3.2

RESULTS OF MICROSCOPIC AND MICROBIOLOGICAL INVESTIGATIONS PERFORMED ON VAGINAL SPECIMENS FROM PATIENTS WITH ACUTE PID AND FPC CONTROLS

	Number and percentage positive:			
	Acute PID (n=50)	FPC (n=50)	p-Value	
Abnormal wet smear	*50(100%)	21(42%)		
Trichomonas vaginalis	28(56%)	10(20%)	0,0004	S
Mycoplasma hominis	42(84%)	25(50%)	0,0006	S
Ureaplasma urealyticum	22(44%)	24(48%)	0,8410	NS

S = Significant

NS = Not Significant

* Inclusion criterion for PID group

TABLE 3.3

RESULTS OF MICROSCOPIC AND MICROBIOLOGICAL INVESTIGATIONS PERFORMED ON CERVICAL SPECIMENS FROM PATIENTS WITH ACUTE PID AND FPC CONTROLS

	Number and percentage positive:			
	Acute PID (n=50)	FPC (n=50)	p-Value	
Neisseria gonorrhoeae	31(62%)	5(10%)	0,000	S
Penicillinase-producing strains	10/31	2/5	0,0277	TS
Chlamydia trachomatis	15(30%)	13(26%)	0,8240	NS
Mycoplasma hominis	36(72%)	21(42%)	0,0047	S
Ureaplasma urealyticum	11(22%)	18(36%)	0,1856	NS

S = Significant

NS = Not significant

TS = Trend towards significant

TABLE 3.4

RESULTS OF SEROLOGICAL TESTS IN BOTH GROUPS STUDIED

	Number and percentage positive:			
	Acute PID (n=50)	FPC (n=50)	p-Value	
Syphilis	17(34%)	4(8%)	0,0026	S
Hepatitis B surface antigen	4(8%)	0	0,1175	NS
HIV antibody	0	0		

S = Significant

NS = Not significant

HIV = Human Immunodeficiency Virus

3.2 DISCUSSION

The clinical syndrome of acute PID is largely due to the ascending spread of micro-organisms from the lower genital tract to the endometrium and fallopian tubes. Therefore, it is an important and common complication of sexually transmitted disease (Sweet, 1986). Although N. gonorrhoeae is known to be a common sexually transmitted pathogen at KEH (Vink and Moodley, 1980), no study on the prevalence of sexually transmitted pathogens in patients with acute PID has previously been undertaken locally.

N. gonorrhoeae is obviously an important pathogen and was found in 62% of the PID group, a figure which was significantly higher than the 10% in FPC control group. The latter prevalence is similar to previously reported prevalences of N. gonorrhoeae in gynaecology outpatients (Vink and Moodley, 1980) and in antenatal clinic patients locally (Hoosen et al, 1981) and elsewhere in South Africa (Welgemoed et al, 1986). It is important to note that 12 out of the 36 (33%) of N. gonorrhoeae isolates in this study were penicillinase producing strains (PPNG). Rates for PPNG in males presenting with acute gonococcal urethritis in Durban of up to 26,2% have been recorded (Section 4.1).

The isolation of C. trachomatis from the endocervices of both groups was remarkably similar (30% and 26%). Mardh (1977), in his study showed 36% (19/53) Scandinavian women with acute salpingitis to have C. trachomatis infection of their cervices. However, local studies amongst males with acute gonococcal urethritis have shown an

associated chlamydial infection in only up to 12% of patients (Ballard et al, 1981). The trend evidenced from these and other studies is that in developing countries, N. gonorrhoeae is a more common cause of urethritis than C. trachomatis, a direct contrast to the situation in developed countries. Further, the lower isolation rate of C. trachomatis as compared to N. gonorrhoeae from the cervices of patients with acute PID, reflects a relatively less prominent role of C trachomatis as an initiator of PID in developing countries.

The prevalence of M. hominis in the vagina and endocervix in both groups was extremely high; 84% and 72% in the PID group and 50% and 42% in the FPC group respectively. In Scandinavia, M. hominis was isolated from the endocervix in approximately half of patients with acute salpingitis (Mardh and Westrom, 1977). It has also been isolated from tubal specimens in patients with salpingitis (Mardh, 1980). However, the organism has not been isolated from macroscopically normal tubes.

There was also a high prevalence of U. urealyticum in both groups studied. This organism is generally considered to be of minor significance in the aetiology of PID and sexually acquired urethritis (Westrom and Mardh, 1984). In studies of acute urethritis in males, ureaplasmas were isolated in 64,1% of patients, being coexistent with N. gonorrhoeae in the majority and rarely being the sole potential pathogen isolated (Section 4.1). Collectively, these findings support the view that U. urealyticum, although a commonly encountered genital organism in sexually active persons is rarely of aetiological significance.

T. vaginalis was demonstrated in 20% of asymptomatic non-pregnant women at our hospital as shown in 10 of 50 of the control (FPC) patients and in 20 of 100 women attending the diabetic out-patient clinic (Hoosen et al, 1988). The prevalence of trichomoniasis was significantly higher in the acute PID group (56%) which is in keeping with a similar high prevalence of 42% demonstrated in patients complaining of a vaginal discharge attending the STD clinic at the same hospital (Hoosen et al, 1987).

Screening for syphilis is essential in all sexually active women attending KEH (Manning and Moodley, 1985) and women with acute PID are a particularly high risk group (prevalence of 34%). A prevalence of 8% for HBsAg in the PID group is almost double that recorded for nurses screened at KEH (4,7%) (Windsor et al, 1984). Although no patients were positive for antibody to the HIV, the sample was too small to draw any reassuring conclusions.

with N. gonorrhoeae in all except one patient. This patient had U. urealyticum alone.

M. hominis was cultured from 21 patients. In none was it the sole organism detected; always occurring in association with U. urealyticum, N. gonorrhoeae and/or C. trachomatis.

4.1.2 Antimicrobial susceptibility of N. gonorrhoeae isolates:

Of the 206 isolates from untreated patients, 54 (26,2%) produced beta-lactamase. One hundred and eighty-six of the 206 isolates were available for MIC determinations; of these, 51 (27,4%) were penicillinase-producing N. gonorrhoeae (PPNG). Of the 135 non-PPNG strains, 40,9% were fully sensitive to penicillin G, 30,6% showed reduced susceptibility (intermediate resistance) and 1,1% were fully resistant to penicillin G. These data and MIC criteria appear in Table 4.3.

The results of breakpoint susceptibility testing for the 186 isolates showed all to be sensitive to the following agents (breakpoint MIC in brackets) : tetracycline ($<$ 1mg/ℓ), rosoxacin ($<$ 0,5mg/ℓ), chloramphenicol ($<$ 4mg/ℓ), sulphamethoxazole:trimethoprim in 19:1 ratio ($<$ 16mg/ℓ), kanamycin ($<$ 16mg/ℓ) and spectinomycin ($<$16mg/ℓ).

Investigation of the 11 strains from patients admitting to treatment, revealed 9 to be PPNG. Eight of these patients had received penicillin (6 intramuscular procaine penicillin G and 2 an injection presumed to be penicillin), and one had received metronidazole orally. The two

non-PPNG were isolated from patients who had received oral metronidazole, one of these was fully sensitive and the other of reduced susceptibility to penicillin G. All were sensitive to the other 6 antimicrobial agents tested.

TABLE 4.1 :

MICROBIOLOGY OF URETHRAL SPECIMENS FROM 217 ADULT MEN WITH UNTREATED ACUTE URETHRITIS

Micro-organisms	Patients positive	
	No	%
Neisseria gonorrhoeae	208	95,9
Chlamydia trachomatis	37	17,0
Ureaplasma urealyticum	139	64,1
None of the above	3	1,4

TABLE 4.2 :

SINGLE AND MIXED INFECTIONS IN 217 ADULT MEN WITH UNTREATED ACUTE URETHRITIS

Micro-organism(s)	Patients	
	Number	Percentage
N. gonorrhoeae	60	27,6
N. gonorrhoeae + C. trachomatis	14	6,5
N. gonorrhoeae + U. urealyticum	113	52,1
N. gonorrhoeae + C. trachomatis + U. urealyticum	21	9,7
C. trachomatis*	1	0,5
C. trachomatis* + U. urealyticum	1	0,5
U. urealyticum	4	1,8
None of the above detected	3	1,4

*Detected by immunofluorescence only

TABLE 4.3

BETA-LACTAMASE PRODUCTION AND PENICILLIN G SUSCEPTIBILITY OF 186 N. gonorrhoeae ISOLATES FROM UNTREATED MEN WITH ACUTE URETHRITIS

B-lactamase	Desig-nation	MIC for penicillin G (mg/ℓ)	No of isolates	%
+	PPNG	2- 32	51	27,4
-	non-PPNG			
	fully sensitive	0,06	76	40,9
	reduced susceptibility	0,12-0,5	57	30,6
	resistant	1,0	2	1,1

4.2 DISCUSSION

Previous South African studies on the aetiology of acute urethritis in untreated Black males, have shown a high prevalence of N. gonorrhoeae infection. The figure of 95,9% in this study is consistent with high prevalence rates reported previously from this and other centres (Coovadia et al, 1984; Meheus et al, 1980; Dove et al, 1987; Simpson and Oliver, 1986).

Non-gonococcal urethritis (NGU) appears to be an uncommon presentation in these patients; C. trachomatis being detected in the absence of N. gonorrhoeae in only 0,5%. This finding is consistent with those of Meheus et al (1980). In Johannesburg, Ballard et al (1981) noted C. trachomatis to be present in 12% of Black men with gonococcal urethritis, a figure similar to the 17% recorded in this study. Of the 7 patients in whom neither N. gonorrhoeae nor C. trachomatis were isolated, U. urealyticum was the sole organism detected in 4. It was, however, isolated in 64,1% of patients with N. gonorrhoeae infection.

Of the 37 C. trachomatis infections, 22 were detected by immunofluorescence only, 8 by culture only and 7 by both methods. The difference between the results of immunofluorescence and culture for the detection of C. trachomatis is somewhat surprising in view of the high specificity and sensitivity reported for these techniques in high risk patient groups (Thomas et al, 1984). Six cultures were contaminated. A single culture was performed for each patient and it

is possible that unrecognised technical problems, especially any related to transport and storage of specimens, may have adversely affected the yield of positive cultures.

The striking findings in this study relate to the penicillin susceptibility of local N. gonorrhoeae isolates. A 26,2% prevalence of PPNG far exceeds prevalences previously recorded in Durban. These were 5% in 1983, and 12% in 1984 (Coovadia et al, 1984a; Ballard, 1984). In early 1985, a small unpublished study performed in Durban and surrounding areas revealed PPNG prevalences of between 13% and 16%. This rapid and disturbing increase in the prevalence of PPNG is similar to that documented in Zimbabwe (Latif et al, 1983) in recent years and in other developing countries, especially in Africa and the Far East. The finding of PPNG in all 8 patients admitting to recent penicillin therapy serves to underline the inadequacy of penicillin G for the therapy of infections caused by these strains.

The occurrence of non-PPNG strains exhibiting decreased susceptibility to penicillin G has been recorded previously in South Africa. Although higher prevalences and even outbreaks of penicillin-resistant non-PPNG (MICs equal to or greater than 1,0, mg/ℓ) have been reported in other parts of the world (Faruki et al, 1985), such strains have so far been rare in South Africa (Dove et al, 1987; Robins-Browne et al, 1978; Robins-Browne et al , 1979), as in this study where they comprise only 1% of N. gonorrhoeae isolates. Strains exhibiting intermediate resistance (MICs for penicillin G 0,12-0,5mg/ℓ), otherwise referred to as showing reduced susceptibility are more common, and prevalences between 15% and 23%

have been recorded in various South African centres (Dove et al, 1987; Robins-Browne et al, 1978; Liebowitz et al, 1982).

The prevalence of such strains was 14% in Durban in 1984 (Coovadia et al, 1984b); thus the current figure of 30,6% also reflects a worrying trend towards increasing resistance. The implication of this increase for the therapy of N. gonorrhoeae infections locally is less clear than the more obvious problem posed by the high prevalence of PPNG. Resistance to spectinomycin and the other antimicrobial agents tested, was not detected.

The frequency of PPNG is now so high as to compel the use of antimicrobials other than penicillin G or ampicillin for the first-line therapy of gonococcal urethritis in Durban. In addition, ongoing local surveillance of N. gonorrhoeae susceptibility patterns should be regarded as essential.

5 RESULTS AND SPECIFIC DISCUSSION - PERSISTENT URETHRITIS

5.1 RESULTS

On average, patients returned to the clinic with a complaint of persistent urethral discharge 11,5 days after initial penicillin therapy (range 3-30 days). The mean age of the patients was 27 years (range 16-51 years).

Urethritis was present in all patients as determined by the presence of more than 4 inflammatory cells per high power field in Gram-stained smears. N. gonorrhoeae was detected in 58 (77,3%) patients by culture. In 57 of these, typical Gram-negative intracellular diplococci were seen. Of the 58 N. gonorrhoeae isolates, 34 (58,6%) produced penicillinase.

The micro-organisms detected in endourethral specimens are summarized in Table 5.1. T. vaginalis was detected in 11 (14,7%) patients; in 7 by culture in Diamond's medium and in 8 by positive wet smears. C. trachomatis was detected in 8 (10,7%) patients. Of the genital mycoplasmas, U. urealyticum was cultured from the urethra of 25 (33,3%) patients and M. hominis from 7 (9,3%). These micro-organisms were the sole isolates in only 5 patients (M. hominis in 3 and U. urealyticum in 2).

A single aetiological agent was identified in 44 patients. N. gonorrhoeae was the most common, being present in 31 (41,3%). T.

vaginalis was the sole agent detected in 5 (6,7%) whilst in only one patient was C. trachomatis the sole organism detected.

In two patients, beta-haemolytic streptococci were the only organisms isolated - one patient had a group A strain and the other a group F strain. Gram-positive cocci were not detected microscopically in Gram-stained smears from these patients. G. vaginalis was not isolated from any patient. There were only 3 patients in whom none of the micro-organisms sought were detected.

Mixed infections were detected in 28 patients. These data are presented in Table 5.2. In 17 (22,7%) of these, U. urealyticum was present in association with N. gonorrhoeae. Of the other 11 mixed infections, 5 (6,7%) were N. gonorrhoeae plus C. trachomatis and 4 (5,3%) were N. gonorrhoeae plus T. vaginalis.

TABLE 5.1

SUMMARY OF MICRO-ORGANISMS ISOLATED FROM ENDOURETHRAL SPECIMENS OF 75 PREVIOUSLY TREATED PATIENTS

Micro-organism	Total No of patient isolates(%)	No of patients in whom micro-organism was sole isolate	No of patients in whom micro-organism was associated with other micro-organisms
N. gonorrhoeae	58(77,3)	31	27
T. vaginalis	11(14,7)	5	6
C. trachomatis	8(10,7)	1	7
U. urealyticum	25(33,3)	2	23
M. hominis	7(9,3)	3	4
Beta-haemolytic strep	2(2,7)	2	0
G. vaginalis	0(0,0)	-	-

Number of patients in whom 1 or more micro-organisms detected	72 (96%)	Number of patients with mixed infections	28 (37%)
No micro-organisms detected	3(4%)	Number of patients with single infection	44 (59%)

TABLE 5.2

MIXED URETHRAL INFECTIONS IN 28 OF 75 PREVIOUSLY TREATED PATIENTS

Micro-organism	Number Positive (%)
N. gonorrhoeae + *U. urealyticum*	17(22,7)
N. gonorrhoeae + *C. trachomatis*	5(6,7)
N. gonorrhoeae + *T. vaginalis*	4(5,3)
C. trachomatis + *T. vaginalis*	1(1,3)
N. gonorrhoeae + *T. vaginalis* + *C. trachomatis*	1(1,3)

5.2 DISCUSSION

Urethral inflammation or discharge which persists in patients successfully treated for gonococcal urethritis is generally regarded as post-gonococcal urethritis (PGU). The micro-organisms commonly implicated in the aetiology of PGU include C. trachmatis and U. urealyticum, whilst T. vaginalis and G. vaginalis are regarded as unusual or rare causes (Bowie, 1984).

In this study of patients previously treated with penicillin for gonococcal urethritis and who denied re-infection, the single major cause of persistent urethral discharge was N. gonorrhoeae. Furthermore, in only 11 (14,7%) of the patients was a recognised mixed infection detected. This high prevalence of N. gonorrhoeae is in keeping with its high prevalence in patients with untreated acute urethritis reported from this centre (87% and 96%) (Coovadia et al, 1984) (Section 4.1). The fact that nearly 60% isolates were PPNG was not surprising in view of the high prevalences (up to 26,2%) of PPNG recorded in studies on patients with untreated gonococcal urethritis at the same clinic (Section 4.1).

The importance of C. trachomatis in the aetiology of acute urethritis appears to differ significantly in different communities in South Africa. In a Johannesburg study of acute urethritis (Ballard et al, 1981), C. trachomatis was isolated from significantly fewer black male than white male patients. Moreover, the majority of chlamydial infections in Black males were found to be associated with N. gonorrhoeae. In a local study, we detected C. trachomatis in 17% of

Black males presenting with urethral discharge and these were predominantly associated with gonococcal infection (refer Section 4.1). The finding of 10,7% C. trachomatis in this study group gives support to a less important role for this agent in acute urethritis amongst lower socio-economic groups. Alternatively, as suggested by Ballard et al (1981), high titres of antibodies to C. trachomatis present in this population group may result in failure to isolate the organism.

T. vaginalis is generally considered to cause self-limiting, asymptomatic infections in men. In the USA, it has been shown to infect up to 4% of men attending STD clinics (Wright and Jackson, 1978). A recent report from Zimbabwe recorded a 5,5% prevalence amongst males attending a STD clinic in Harare (Latif et al, 1987). However, in females, T vaginalis is a frequent cause of vaginitis and a prevalence of over 40% has been shown for women attending the STD clinic in which this study was performed (Hoosen et al, 1987). The relatively high prevalence of 15% in this study suggests an important aetiological role for T. vaginalis in patients that have persistent urethritis after penicillin treatment. It is our opinion that such patients should be appropriately investigated for infection with this protozoan and treated accordingly.

G. vaginalis was not isolated from any of the patients investigated. U. urealyticum was the sole isolate in only 2 patients whilst it was isolated from 17 patients with N. gonorrhoeae infection, indicating a less important aetiological role. This view is supported by other workers and the results of previous studies performed locally.

The high prevalence of PPNG isolates which did not respond to therapy with penicillin and the relatively high prevalence of T. vaginalis amongst the study group, raises important diagnostic and therapeutic considerations. The present study also confirms previous findings that the recommended antibiotic therapy for gonococcal infections is ineffective in the eradication of C. trachomatis and T. vaginalis. Some workers have suggested that first-line antibiotic therapy against N. gonorrhoeae be changed from penicillin to an agent active against both PPNG and non-PPNG when PPNG levels reach 3% or greater (Centers for Disease Control, 1987).

6 GENERAL DISCUSSION

The findings of this study highlight the high prevalence of various sexually transmitted pathogens in different patient groups presenting to King Edward VIII Hospital. With regard to PID, most investigators agree that it is a polymicrobial disease involving both sexually transmitted pathogens and endogenous micro-organisms (Thomason et al, 1986). However, this study was directed towards the detection of common sexually transmitted pathogens such as N. gonorrhoeae, C. trachomatis and genital mycoplasmas in patients with clinically diagnosed salpingitis, by means of non-invasive lower genital tract sampling.

Since lower genital tract infection is considered a pre-requisite for sexually transmitted acute PID, and the exclusion of patients with a normal wet smear has been shown to increase the accuracy of clinical diagnosis (Westrom, 1983). This criterion was included in the selection of patients for this study. However, the value of such screening has not been evaluated locally.

The microbiology of PID shows marked geographical variability in respect of the prevalence of sexually transmitted initiating pathogens. In Europe and the USA, C. trachomatis is the commonest agent occurring in 25-60% cases, N. gonorrhoeae occurring in 15-30% and M. hominis being responsible in 10-12% (Westrom and Mardh, 1984). In this study, N. gonorrhoeae (62%) and M. hominis (72%) were the most common cervical isolates. Findings of other South African studies have been reviewed in the introduction.

When considering appropriate antimicrobial therapy for acute PID, knowledge of the relative prevalences of sexually transmitted pathogens, as well as that of secondary bacterial invaders from the lower genital tract is required. Different treatment regimens are recommended by the Centers for Disease Control, based on clinical severity of disease (Centers for Disease Control, 1985). Clinically mild or moderately severe infections are felt to be exclusively associated with sexually transmitted pathogens and accordingly treatment is directed towards the eradication of such micro-organisms. Clinically severe infections are shown to be associated with anaerobic bacteria or mixed anaerobic-facultative organisms and in such cases intravenous therapy directed against these organisms is suggested (Westrom and Mardh, 1984).

Adult males presenting at KEH with acute urethritis are mainly infected with N. gonorrhoeae, the organism being isolated in up to 95,9% of untreated and 77,3% of patients who had received penicillin for gonococcal urethritis.

A major problem in the treatment of gonococcal infections is the continued evolution of strains of N. gonorrhoeae with decreased susceptibility to various antimicrobial agents. Resistance occurs through two genetic mechanisms. Chromosomal mutations resulting in reduced affinity of penicillin for penicillin binding proteins (PBP) as well as permeability changes in the outer membrane of the organism. Secondly, through the acquisition of plasmids which code for beta-lactamase production, conferring absolute resistance to penicillin and some cephalosporins (Easmon, 1985).

Local isolates of N. gonorrhoeae are becoming increasingly resistant to penicillin; as evidenced by the extremely high prevalence of PPNG strains; 26,2% in patients with untreated acute urethritis and 58,6% in patients treated with penicillin for gonococcal urethritis. Furthermore, there has been a considerable increase in strains exhibiting intermediate resistance to penicillin (MICs 0,12 to 0,5mg/ℓ); from 14% detected in 1984 (Coovadia et al, 1984b) to the present 30,6%. The therapeutic implications of this are not clear. However, breakpoint MICs showed all strains tested to be sensitive to tetracycline, rosoxacin, cotrimoxazole, kanamycin, chloramphenicol and spectinomycin.

It has been suggested that when the prevalence of PPNG in endemic areas reaches levels greater than 3%, first line therapy be changed to include an antimicrobial agent active against both PPNG and non-PPNG strains (Centers for Disease Control, 1987).

The question of adequate treatment of concurrent sexually transmitted infections raises considerable problems. In developed countries it has been shown that when heterosexual males are treated for gonorrhoea with regimens ineffective against C. trachomatis, there is a 20-30% risk of post-gonococcal urethritis (Stamm, 1984). In this study, C. trachomatis was isolated from 17% males with untreated urethritis and the infection was largely in association with gonococcal urethritis. In males previously treated with penicillin for acute urethritis, C. trachomatis was detected in 10,7% patients. The outcome of such concurrent infections and their sequelae have not been investigated in local studies. However, the problems of controlling the spread of such infections are obvious. Other problems in the management of chlamydial infections include the lack of

effective single dose regimens, the limited therapeutic options and problems of toxicity (Handsfield, 1986).

7 CONCLUSIONS AND RECOMMENDATIONS

7.1 CONCLUSIONS

Conclusions based on the findings of this study are:

7.1.1 There is a high prevalence of recognised sexually transmitted pathogens in patients with acute PID. The prevalence of N. gonorrhoeae, M. hominis, T. vaginalis and reactive syphilis serology was significantly higher in patients with acute PID as compared to asymptomatic women attending the family planning clinic. Up to a third of N. gonorrhoeae isolates were penicillinase-producing. The prevalence of C. trachomatis and U. urealyticum was equally high in both groups of women studied.

7.1.2 In untreated adult males with acute urethritis, N. gonorrhoeae was the most common isolate, being detected in 95,9% patients, with 26,2% of strains being penicillinase-producing. C. trachomatis was identified in 17% patients. U. urealyticum was cultured from 64,1% patients, occurring almost always in association with N. gonorrhoeae.

7.1.3 In adult males presenting with persistent urethritis after receiving penicillin therapy for gonococcal urethritis, N. gonorrhoeae was detected in 77,3% patients, with 58,6% strains being penicillinase-producing. T. vaginalis was demonstrated in 14,7% and C. trachomatis in 10,7% patients.

7.2 RECOMMENDATIONS

Recommendations based on the findings of this study:

7.2.1 In view of the high prevalence of recognised sexually transmitted pathogens in the lower genital tract of women with acute PID, empirical treatment ought to include an agent or agents active against N. gonorrhoeae, C. trachomatis and M. hominis. Furthermore, because of the high prevalence of PPNG (33%) amongst these patients, routine use of an agent(s) active against such strains is indicated.

7.2.2 In view of the extremely high prevalence of PPNG strains in males with acute urethritis - both in untreated patients and those treated empirically with procaine penicillin - the routine use of penicillin as first line agent should be discontinued locally. Instead, single dose antimicrobial agents, such as spectinomycin or ceftriaxone, which are active against both PPNG and non-PPNG strains, should be employed as first line therapy.

7.2.3 Investigations in patients presenting with persistent urethral discharge after receiving therapy for gonococcal urethritis should include those for C. trachomatis and T. vaginalis.

Finally, the need for appropriate and early treatment of sexual partners must be borne in mind in order to reduce the possibility of reinfection.

8 REFERENCES

Allen LA, Schoon MG. Laparoscopic diagnosis of acute pelvic inflammatory disease. Br J Obstet Gynecol 1983; 90: 966-968.

Allen LA, Schoon MG. Diagnostic laparoscopy and management of patients with confirmed acute pelvic inflammatory disease. S Afr Med J 1984; 65: 201-202.

Antal GM. Epidemiology of sexually transmitted diseases in the tropics. In : Balliers Clinical Tropical Medicine and Communicable Diseases, April 1987; Vol 2, No 1; 1-16.

Ballard RC. Editorial. S Afr J Sex Transm Dis 1984; 4:21.

Ballard RC, Duncan MO. Problems in the management of sexually transmitted diseases in South Africa. S Afr Med J 1983; 64: 1083-1086.

Ballard RC, Fehler HG, Duncan MO, van der Wat IJ. Urethritis and associated infections in Johannesburg - the role of Chlamydia trachomatis. S Afr J Sex Transm Dis 1981; 1: 24-26.

Ballard RC, Fehler HG, Bilgeri YL, Duncan MO, Koornhof HJ. A clinical and microbiological evaluation of the treatment of urethritis with minocycline. South Afr J Epidemiol Infect 1986; 1: 19-24.

Bowie WR. Urethritis in males. In : Holmes KK, Mardh PA, Sparling P F, Weisner PJ. (eds). Sexually Transmitted Diseases. McGraw Hill, New York 1984; 638-650.

Burchell HJ, Cronje HS, de Wet JI. Efficacy of different antibiotics in the treatment of pelvic inflammatory disease. S Afr Med J 1987; 72: 248-249.

Burchell HJ, Schoon MG. The value of laparoscopy in the diagnosis of acute pelvic inflammatory disease. S Afr Med J 1987; 67: 197-198.

Centers for Disease Control. Chromosomally mediated resistant Neisseria gonorrhoeae in the United States. MMWR 1983; 33: 408-410.

Centers for Disease Control. STD treatment guidelines MMWR. 1985; 34: 75S-108S.

Centers for Disease Control. Antibiotic resistant strains of Neisseria gonorrhoeae. Policy guidelines for detection management and control MMWR. 1987; 36: 1S-18S.

Coovadia YM, Dada MA, Kharsany A, Ramsaroop U, Bhamjee A. The emergence of penicillinase-producing strains of Neisseria gonorrhoeae in Durban. S Afr Med J 1984a; 65: 835-837.

Coovadia YM, Kharsany A, Ramsaroop U. Antimicrobial susceptibility of Neisseria gonorrhoeae isolated in Durban, South Africa. Brit J Vener Dis 1984b; 60: 306-308.

Crewe-Brown HH, Mahomed MF, Pochee E, Shewan KA. Penicillinase-producing strains of Neisseria gonorrhoeae in Pretoria. S Afr Med J 1985; 67: 159.

Dangor Y, Mdlovu M, Duncan MO, Exposto F, Fehler HG, Ballard RC. The emergence of penicillinase-producing strains of Neisseria gonorrhoeae in Southern Africa. Paper presented at the Second International Congress of Sexually Transmitted Diseases in Southern Africa, Cape Town 7-8 October, 1985.

Dove MG, Wende LM, Anthony M, van den Ende J. Gonococcal urethritis in Bloemfontein : Emergence of penicillinase-producing strains of Neisseria gonorrhoeae. South Afr J Epidemiol Infect 1987; 2: 33-38.

Dunlop EMC. Gonorrhoeae and the sulphonamides. Br J Vener Dis 1949; 25: 81-83.

Easmon CSF. Gonococcal resistance to antibiotics. J Antimicrob Chemoth 1985; 16: 409-412.

Faruki H, Kohmescher RN, McKinney WP, Sparling PF. A community based outbreak of infection with penicillin-resistant Neisseria gonorrhoeae not producing penicillinase (chromosomally mediated resistance). New Eng J of Med 1985; 313: 607-610.

Hager WD, Eschenbach DA, Spence MR, et al. Criteria for diagnosis and grading of salpingitis. Obstet Gynecol 1983; 61: 113-114.

Hallet AF, Appelbaum PC, Cooper R, et al. Penicillinase-producing Neisseria gonorrhoeae from South Africa. Lancet 1977; 1: 1205.

Holmes KK, Eschenbach DA, Knapp JS. Salpingitis : Overview of etiology and epidemiology. Amer J Obstet Gynecol 1980; 138: 893-901.

Holmes KK, Mardh P-A, Sparling PF, Weisner PJ. eds. Sexually Transmitted Diseases. McGraw Hill, New York, 1984.

Hoosen AA, Coetzee DK, van den Ende J. Microbiology of vaginal discharge in patients attending a sexually transmitted disease clinic in Durban. Infectious Diseases and Sexually Transmitted Diseases Congress, Durban, October 1987, Abstract, 040.

Hoosen AA, Peer AK, Seedat MA, Omar MAK, Roux L, Kharsany ABM, van den Ende J. Aetiology of vaginal infection in diabetic females. 24th SEMDSA Congress, March 1988.

Hoosen AA, Ross SM, Mulla MJ, Patel M. The incidence of selected vaginal infections among pregnant urban Blacks. S Afr Med J 1981; 59: 827-829.

Jennings DL, Meiring JA, Koornhof HJ. Penicillinase-producing Neisseria gonorrhoeae in Port Elizabeth. S Afr Med J 1986; 69: 344-345.

Jacobson L, Westrom L. Objectivized diagnosis and prognostic value of routine laparoscopy. Amer J Obstet 1969; 10S: 1088-1098.

Latif AS, Summers RS, Mason PR. Penicillinase- producing Neisseria gonorrhoeae in Harare, Zimbabwe. Centr Afr J Med 1983; 29: 121-122.

Latif AS, Mason PR, Marowa E. Urethral trichomoniasis in men. Sex Transm Dis 1987; 14: 9-11.

Liebowitz LD, Ballard RC, Koornhof HJ. In vitro susceptibility and cross-resistance of South African isolates of Neisseria gonorrhoeae to 14 antimicrobial agents. Antimicrob Agents Chemoth 1982; 22: 598-603.

Lithgow DM, Rubin A. In : Charlewood GP. Gynaecology in Southern Africa. Witwatersrand University Press, Johannesburg 1972; 177.

Manning B, Moodley J. Syphilis in pregnant black women. S Afr Med J 1985; 67: 966-967.

Mardh P-A. Role of Chlamydia trachomatis in acute salpingitis. N Eng J Med 1977; 196: 1377-1378.

Mardh P-A. An overview of infectious agents of salpingitis, their biology, and advances in methods of detection. Amer J Obstet Gynecol 1980; 933-939.

Mardh P-A, Westrom L. T-mycoplasmas in genitourinary tract of the female. Acta Path Microbiol Scand 1977; 78: 367-369.

Meheus A, Ballard R, Dlamini M, Ursi JP, van Dyck E, Piot P. Epidemiology and aetiology of urethritis in Swaziland. Int J Epid 1980; 9: 239-245.

O'Callaghan CH, Morris A, Kirby SM, Slinger AH. Novel method for detection of B-lacatamase by using chromogenic cephalosporin substrate. Antimicrob Agents Chemoth 1972; 1: 282-288.

Philip A, Carter-Scott P, Rogers C. An agar culture technique to quantitate Trichomonas vaginalis from women. J Infect Dis 1987; 155: 304-308.

Rein MF. Urethritis. In : Principles and Practice of Infectious Diseases. Mandell GL, Douglas RG, Bennett JE eds. John Wiley and Sons, New York 1985; 720-728.

Ripa KT, Mardh P-A. Cultivation of Chlamydia trachomatis in cycloheximide treated McCoy cells. J Clin Microbiol 1977; 6: 328-331.

Robins-Browne RM, Gaillard MC, Koornhof HJ. Penicillinase-producing Neisseria gonorrhoeae. S Afr Med J 1977; 51: 568.

Robins-Browne RM, Gaillard MC, Koornhof HJ, Schneider J. Antibiotic susceptibility of Neisseria gonorrhoeae isolated in Johannesburg. S Afr Med J 1978; 54: 601-603.

Robins-Browne RM, Gaillard MC, Koornhof HJ. Antibiotic susceptibility testing of Neisseria gonorrhoeae. J Antimicrob Chemother 1979; 5: 67-72.

Schoub BD, Smith AN, Lyons SF et al. Epidemiological considerations of the present status and future growth of the acquired immunodeficiency syndrome epidemic in South Africa. S Afr Med J 1988; 74: 153-156.

Shepard MC. Differential methods for identification of T-mycoplasmas based on demonstration of urease. J Infect Disc 1973; 127: 22.

Shepard MC, Lunceford CD. Urease color test medium U-9 for the detection and identification of T-mycoplasmas in clinical material. Applied Microbiol 1970; 20: 539-543.

Shepard MC, Lunceford CD. Differential agar medium (A-7) for identification of Ureaplasma urealyticum (human T-mycoplasmas) in primary cultures of clinical material. J Clin Microbiol 1976; 3: 613-625.

Simpson JA, Oliver SP. Beta-lactamase-producing isolates of Neisseria gonorrhoeae in Cape Town. S Afr Med J 1986; 69: 307-308.

Sweet RL, Mills J, Hadley KW et al. Use of laparoscopy to determine the microbiological aetiology of acute salpingitis. Amer J Obstet Gynecol 1979; 134: 68-71.

Sweet RL, Pelvic Inflammatory Disease. Sex Trans Dis 1986; 13: 192-198.

Thomas BJ, Evans RT, Hawkins DA, Taylor-Robinson D. Sensitivity of detecting Chlamydia trachomatis elementary bodies in smears by use of a fluorescein labelled monoclonal antibody : comparison with conventional chlamydial isolation. J Clin Pathol 1984; 37: 812-816.

Thomason JL, Wilcoski LM, Lee GM, Peterson AK, Hamilton PR. Pelvic Inflammatory Disease. Clinical Microbiology Newsletter 1986; 8-181-184.

Vink G, Moodley J. Gonorrhoea in Black woemn attending a gynaecological outpatient department. S Afr Med J 1980; 58: 901-902.

Wasserheit JN, Bell TA, Kiviat NB et al. Microbial causes of proven pelvic inflammatory disease and efficacy of clindamycin and tobramycin. Ann Intern Med 1986; 104: 187-193.

Welgemoed NC, Mahaffey A, van den Ende J. Prevalence of N. gonorhoeae infection in patients attending an ante-natal clinic. S Afr Med J 1986; 69: 32-35.

Westrom L. Clinical manifestations and diagnosis of pelvic inflammatory disease. J Reprod Med 1983; 10S: 703-708.

Westrom L, Mardh P-A. Salpingitits. In : Holmes KK, Mardh P-A, Sparling PF. Weisner PJ eds Sexually Transmitted Diseases.McGraw Hill, New York; 1984; 615-632.

White RG. Acute pelvic inflammatory disease - a review. S Afr J Sex Transm Dis 1982; 2: 24-26.

Windsor IM, Arbuckle DD, Spencer IWF et al. Markers of hepatitis B in nurses and domestic staff in an area of high endemicity. J Hosp Infect 1984; 5: 81-88.

Young H. Cultural diagnosis of gonorrhoea with modified New York City Medium (MNYC). Br J Vener Dis 1978; 54: 36-40.

Young DCT, Pyrula A. Rapid micro-carbohydrate test for confirmation of Neisseria gonorrhoeae. J Clin Microbiol 1978; 6: 643-647.