

Seroepidemiological study of gonorrhoea in Ethiopian women

1. Prevalence and clinical significance

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Abstract

Objective—To measure the prevalence of gonorrhoea in Ethiopian women attending gynaecologic, obstetric and family planning clinics: to determine the reliability of patient self history of sexually transmitted disease (STD); to correlate the serological diagnosis of gonorrhoea with clinical evidence of pelvic infection in order to define a reliable clinical diagnosis of gonorrhoea in a country where pelvic inflammatory disease is very common but where routine laboratory culture and serological tests for gonorrhoea are unavailable.

Subjects—1851 Ethiopian women: 50% symptomatic, 50% asymptomatic.

Setting—Gynaecological outpatient department, antenatal, postnatal and family planning clinics (Ethiopian Family Guidance Association (EFGA)), in two teaching hospitals and a mother and child health centre in Addis Ababa, Ethiopia.

Methods—The indirect haemagglutination test with gonococcal pilus antigen as an epidemiological tool was used in a cross-

section study to screen 1851 sera for evidence of past or current gonococcal infection. The gonococcal antibody test (GAT) seropositivity was correlated with patient's history of STD, age, clinic attended and the clinical evidence of infection in "gonococcal target organs" urethra, salpinges or Bartholin glands.

Results—Fifty nine per cent of the study group were seropositive for the gonococcal antibody test, 22% with titres $\geq 1/320$, indicative of current, recent or recurrent infection. Seropositivity indicating past or present gonococcal infection was highest in those who gave a history of having had treated syphilis (85%), in women aged 40-49 (72%), and family planning attenders (EFGA) (66%) of whom 31% had titres $\geq 1/320$. Fifty per cent had clinical evidence of past or present infection in the urethra, salpinges or Bartholin glands. Gonococcal antibodies were present in 54% of women with no evidence of clinical infection, compared with 91% of those with pyosalpinx and 86% of those with triple infection of urethra, salpinges and Bartholin glands.

Conclusion—The high prevalence of gonococcal antibodies in Ethiopian women, especially in asymptomatic clinic attenders must be of concern for all health workers especially those in gynaecology and obstetrics and the related disciplines of family planning and neonatal paediatrics. While seropositivity was highest in those giving a past history of syphilis, the patient's history of STD was unreliable, as of those who denied having any history of STD, fifty per cent were GAT seropositive.

Despite a high correlation between GAT seropositivity with pyosalpinx and clinical evidence of infection in urethra, salpinges and Bartholin glands, gonococcal antibodies were present in 54% of women with no clinical evidence of infection. Thus we were unable to define a diagnostic clinical picture of gonorrhoea in Ethiopian women.

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Introduction

Gonorrhoea is highly prevalent in much of sub-Saharan Africa. Prevalence rates are comparable with those for Europe at the beginning of the 20th century.¹ For the few African countries where detailed data are available, the incidence of gonorrhoea has been rising steadily since 1960 particularly amongst men,² as it has in the industrialised nations.³ Contrary to earlier thinking that the prevalence of gonorrhoea is an indictment of the community, it is now being recognised that a candid honest appraisal of the problem is a prerequisite for a realistic approach to effective action.²

A major obstacle in the control of gonorrhoea is the asymptomatic nature of the infection particularly in women: up to 90% of infected women may be asymptomatic.^{4,5}

The symptoms of gonorrhoea and pelvic inflammatory disease (PID) may be so non specific that there is no statistical difference in the symptomatology of two groups of prostitutes, one with gonorrhoea and the other without.⁶ The symptoms of PID (fever, abdominal pain) may be confused with or ascribed to some other condition prevalent in the tropics such as typhoid, dysentery or amoebiasis.⁷ Furthermore inadequate treatment and self medication have caused the development of drug resistant strains of *N gonorrhoeae*, and as a result inadequately treated acute infections rapidly become sub-acute and chronic.⁸ Gonorrhoea is chiefly associated with pelvic inflammatory disease: "the high incidence of pelvic inflammatory disease in tropical Africa is due primarily to the appalling high prevalence of gonorrhoea".⁷

Pelvic inflammatory disease accounts for 25–40% of admissions to acute gynaecological beds in Africa.^{9,10} The extent to which the gonococcus can be identified as the pathogen for causing this PID depends on many factors, laboratory expertise, prior antibiotic therapy and the presence of polymicrobial infection. In Rhodesia (Zimbabwe) only 4% of PID was attributed to gonorrhoea,¹¹ compared with 28% in Ethiopia,¹⁰ 38% in Uganda,¹¹ 43% in Kenya,¹¹ and 46% in Lusaka in Zambia.⁹ Some of these very high figures may be due to the selection of patients, for example, the Zambian figures are for women attending an STD clinic.

The significance of gonorrhoea is that it not only causes gynaecological problems for women, but as it is a marker for sexual activity, it is also used as an index of potential infection for any STD newly introduced into a community. This is of particular significance when projections are made regarding the introduction into and potential spread of HIV within a community not previously affected by it.¹²

The development of an indirect haemagglutination test using gonococcal pilus antigen has shown that (1) non-specific gonococcal antibody test results

occur only rarely; (2) at least half the people who have had gonorrhoea remain sero-positive, thus a positive gonococcal antibody test (GAT) cannot always be considered as being diagnostic of active present gonorrhoea; (3) for the diagnosis of current infection a positive test result is more significant the younger the patient and the higher the titre.¹³

Patients and methods

Serum from 1851 Ethiopian women was tested by the indirect haemagglutination test (Gonococcal antibody test—GAT) using gonococcal pilus as antigen.¹³

The following groups of women were studied: 961 patients attending gynaecological outpatient departments (GOPD), 481 attenders at family planning clinics (EFGA: Ethiopian family guidance association), 308 routine antenatal clinic attenders (ANC), 99 routine post natal clinic attenders (PNC), two women attending gynaecology outpatient departments (GOPD) who had been mis-directed there as they had no obstetric or gynaecological complaint but had some other medical condition.

The 1851 women from a larger study of the aetiology of cervical cancer and STD in Ethiopia took part after giving informed consent. The women studied were the first to register at the various clinics on the study days, thus allowing time for completion of the questionnaires before examination began. Gynaecological patients were first attenders at the hospital, those attending EFGA, ANC or PNC were routine attenders, some of them being first attenders. The data collected from them included: (1) a detailed medico-socio-economic history on a questionnaire completed by a female Ethiopian assistant; (2) history of previous STD, in particular syphilis and gonorrhoea, and details of treatment (in Ethiopia both syphilis and gonorrhoea are widely recognised without social stigma—the information was obtained by direct question and not from any patient records); (3) details of a full gynaecological examination—particular attention was paid to the condition of the cervix and to "gonococcal target organs" namely the urethra, salpinges and Bartholin glands (USB) which were inspected (UB) and palpated (USB); (4) cytological examination of a Papanicolaou stained cancer smear preparation; (5) the results of serological testing for evidence of previous or present STD: gonorrhoea, syphilis, infections with chlamydiae, HSV2, HBV and HIV.¹⁴ The collection of data, cytology slides, and sera was done in 1975 and 1976 while ethnic, religious and other factors could still be assessed independently of population migration (as occurred during the Ethiopian revolution). It was not until 1977 and 1978 that the data and specimens could be despatched from the country, although full permission had been given by the

Table Concentrations of antibodies to gonococcal pilus antigen (GAT titres) in sera from Ethiopian and Danish women

Gat titre	Ethiopian women		Danish women*		healthy from the general population n = 419	
	n = 1851		at STD clinic n = 477			
≤ 1/20	762	41%	271	57%	391	93%
1/40	126	23%	51	24%	11	5%
1/80	302		63		10	
1/160	248	14%	41	8%	4	1%
1/320	188	22%	25	11%	1	1%
1/640	131		12		2	
1/1280	61		10		0	
1/2560	27		3		0	
1/5120	5		1		0	
1/10240	1		0		0	

*Results of Danish women GAT serology from Reimann *et al*¹³

Ethiopian Ministry of Health. Sera were kept frozen until serological testing became available.

Gonococcal antibody test (GAT)

The test was performed as described previously^{13,14} using pili purified according to the method of Hermodsen *et al*¹⁵ with a few modifications.¹³ Serum was diluted twofold from a dilution of 1/20. Titres of ≥ 1/40 were considered to show positive test results.

We have interpreted the results of the indirect haemagglutination test as follows: Test results at a titre of ≤ 1/20 are regarded as negative; titres of 1/40 or 1/80 are regarded as weakly positive; titre 1/160 is regarded as intermediate positive; titres ≥ 1/320 are considered as strongly positive.

Titres 1/40–1/160 may either indicate current infection or be due to residual antibodies following previous infection. Titres ≥ 1/320, for Danish patients, are suggestive of current or recent infection.

The validity of this test has been established on populations from Denmark and Greenland.^{13,16} In Denmark 10–25% of individuals born between 1900 and 1960 have had gonorrhoea. The finding that 7–12% of healthy people (blood donors) are seropositive is consistent with the assumption that about 50% of patients with gonorrhoea become seropositive and remain so for many years, probably for life. In a community where repeated infections are common, the average level of persisting antibodies will be higher than in Denmark, where the majority of patients (95%) only contract gonorrhoea once. In addition, the percentage of patients in whom seroconversion can be demonstrated will increase to more than 90% in women, if early diagnosis and treatment is the exception and not the rule. The serological test is not considered a diagnostic test but a screening test with confirmation being carried out by culture of appropriate specimens.

Statistical methods

Statistical analysis was made using the chi square test

to determine the significance level of any kind of association found between GAT seropositivity and other recorded data for the various groups of patients.

Results

Sero-positivity of the population tested

The number of Ethiopian women who were GAT positive was 1089 (59%). The seropositivity according to titre is shown in the table: 428 (23%) were positive with titres 1/40 to 1/80, 248 (14%) were positive with a titre of 1/160 and 413 (22%) were positive in titres of 1/320 or more. For comparison the seropositivity of Danish women is shown in the same table.

The sero-positivity amongst Ethiopian women tested was higher (59%) than amongst the Danish women: 33% (206/477) attending STD clinic and 7% (28/419) of the general population. Titres of ≥ 1/320 were found more frequently (22%) in Ethiopian women compared with 11% (51/477) at an STD clinic and 1% (3/419) of healthy women in Denmark.

Sero-positivity and history of STD

Replies to questioning were received from 1549 patients; a history of STD, either gonorrhoea or syphilis or both, was given by 395 patients (25%); 1154 (75%) denied having had any STD (fig 1). There was a significant increase ($p < 0.001$) in GAT positivity (particularly in antibody titre ≥ 1/320) in those who had had either syphilis or gonorrhoea or both (fig 1). The highest correlation is for the group who gave a history of having had treated syphilis: 85% (155/183) of those had a positive GAT. However, of those who denied having had any STD, 53% (610/1154) were GAT seropositive.

Sero-positivity and age of patients

The association between age of the patients and level

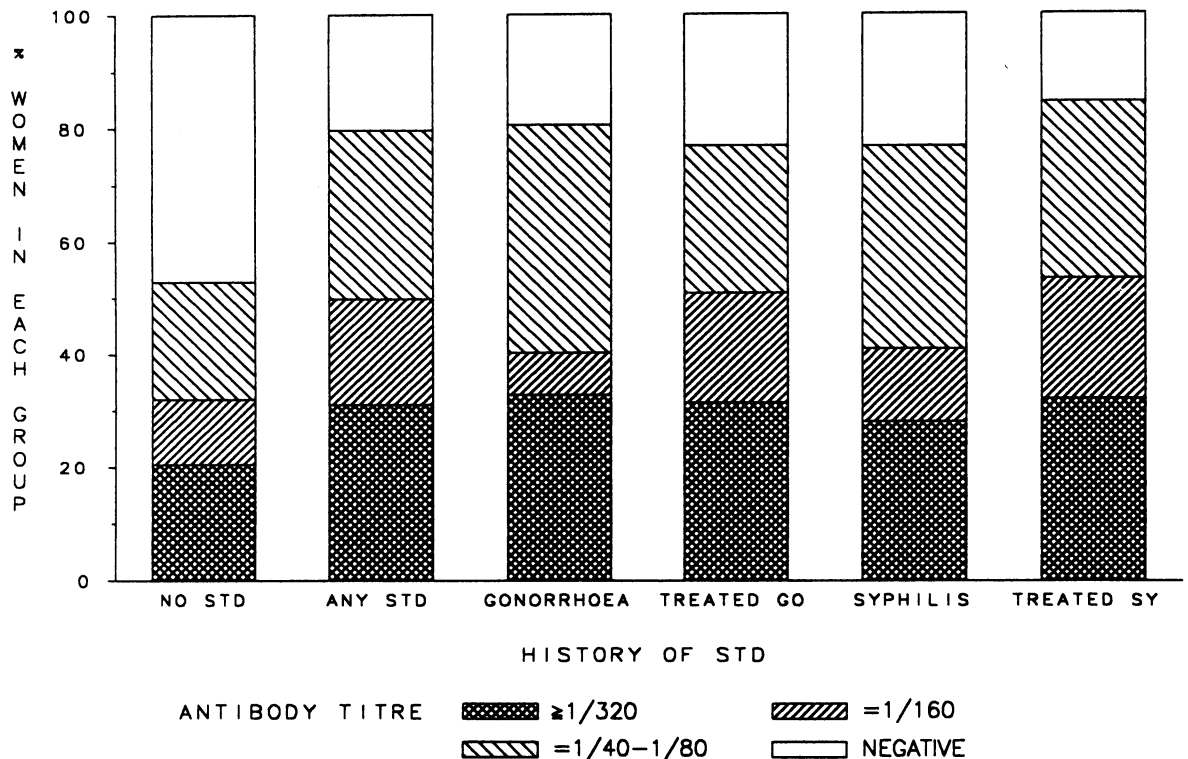


Figure 1 Gonococcal antibody tests seropositivity and past history of sexually transmitted disease (STD): Syphilis (SY) and Gonorrhoea (GO) with and without treatment.

of antibodies is shown in fig 2 ($p < 0.001$). Of those aged less than 20 41% (65/157) were found to have a positive GAT, 28 (18%) with antibody titres $\geq 1/320$, thereafter the level of GAT sero-positivity rose to 72% (111/155) in those aged 40-49: this rise was due to an increase in levels of antibodies 1/40-1/160, antibody levels $\geq 1/320$ remained at about 23% (379/1635) for women aged 20-49. Fewer women (57%: 26/46) over the age of 50 were seropositive due to a smaller percentage (7%) with higher titres of antibodies.

Sero-positivity in patients attending various clinics

The mean level of antibody titres in women differed significantly ($p < 0.001$) from one clinic to another (fig 3). Fifty seven per cent (177/308) of women attending antenatal and 53% (52/99) attending post-natal clinics had no evidence of current or previous gonococcal infection compared with 39% (371/963) of those attending GOPD and 34% (162/481) attending Ethiopian Family Guidance Association Clinic (EFGA). The chief difference between the patients attending the different clinics was the percentage with titres $\geq 1/320$. Ten per cent (32/308) and 15% (15/99) of sera obtained from antenatal (ANC) and post natal clinic (PNC) attenders respectively had titres of

antibodies $\geq 1/320$ while 31% (147/481) of sera from EFGA attenders and 23% (219/963) of sera from GOPD attenders had titres of antibodies $\geq 1/320$

Association of levels of gonococcal antibodies with clinical evidence of past/present infection of gonococcal target organs

Percentage of seropositives among women with or without evidence of past/present infection of gonococcal target organs: urethra, salpinges, Bartholin glands (USB), is shown in fig 4. Fifty per cent (921/1851) of the patients had palpable thickening/enlargement of USB without/with tenderness on palpation: clinical evidence suggestive of past or present infection of gonococcal target organs. In the patients who showed no clinical evidence suggestive of infection it is significant that 54% (503/930) had serological evidence of gonococcal infection: 18% (170/930) had titres $\geq 1/320$. Of those who had evidence of infection in one or more of the gonococcal target organs (USB) 64% (586/921) were GAT positive, 26% (243/921) with high titres. The association between the level of antibody titres and the infection of gonococcal target organ was lowest for the urethra and highest for the Bartholin glands: Bartholin abscess was most frequently caused by

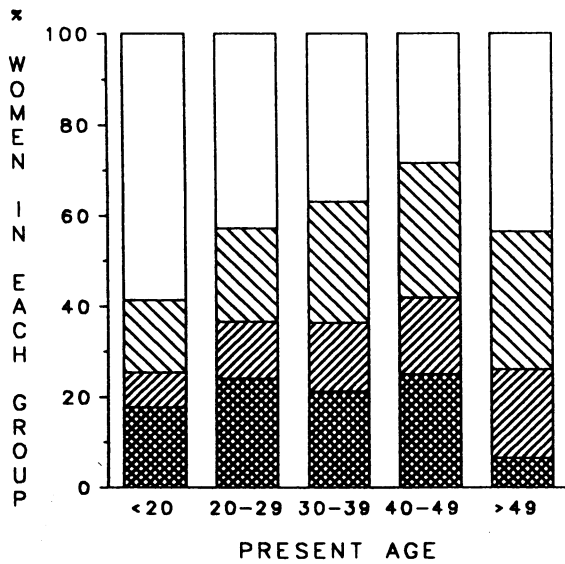


Figure 2 Gonococcal antibody test seropositivity according to age of the patients tested.

Escherichia coli (Duncan: unpublished observation). Detailed analysis of pathological conditions of the fallopian tubes showed significant association between high titres of gonococcal antibodies and a diagnosis of pyosalpinx.

Discussion

This study showed that the presence of antibodies to gonococcal pilus antigen amongst Ethiopian women was more common (59%) and the mean titres higher than amongst Danish women.¹³ Based on notified cases of gonorrhoea it can be calculated that 10-25% of people born in Denmark between 1900 and 1960 have had gonorrhoea resulting in 7-12% seropositive individuals. This shows that in a country where prompt diagnosis and treatment have been available for 50 years, about half of those contracting gonorrhoea have demonstrable antibodies persistently. In Ethiopia as in other developing countries there has in the pre-AIDS-era been apparently little interest in sexually transmitted diseases, largely owing to the lack of laboratory facilities. The size of the problem was not appreciated, thus only a small budget was allocated to deal with STD. Lack of diagnosis and treatment of gonorrhoea may imply that more than half of the individuals having had gonorrhoea will be

seropositive. In this study 59% of the women were seropositive indicating an extremely high prevalence of present or past gonorrhoea.

In Denmark titres $\geq 1/320$ were found in 1% (12/1384) of sera from the general population and 11% (51/477) of sera from women attending an STD clinic, whereas in Ethiopia these high titres were found in sera from 22% (413/1851) of the women studied. This can be due either to more current gonorrhoea or more episodes of gonorrhoea in the same woman; thus, an elevated titre $\geq 1/320$ may be found even though current infection is not present.

We have demonstrated a significant association between positive history of any STD and positive GAT. Nevertheless, it must be of concern that 53% of those who denied having had any STD were GAT positive. Initially *N gonorrhoeae* was very sensitive to penicillin treatment. During the 1960s and early 1970s it was common practice in Ethiopia to treat syphilis with a long acting depot penicillin which was also effective for gonorrhoea. Many patients were

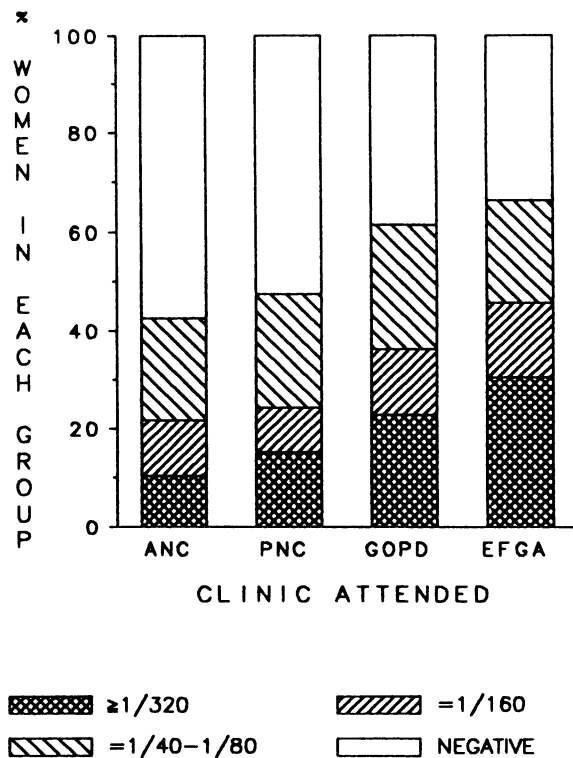


Figure 3 Gonococcal antibody test seropositivity according to clinic attendance. ANC = Antenatal clinic. PNC = Postnatal clinic. GOPD = Gynaecological Outpatient Department. EFGA = Family Planning Clinic of the Ethiopian Family Guidance Association.

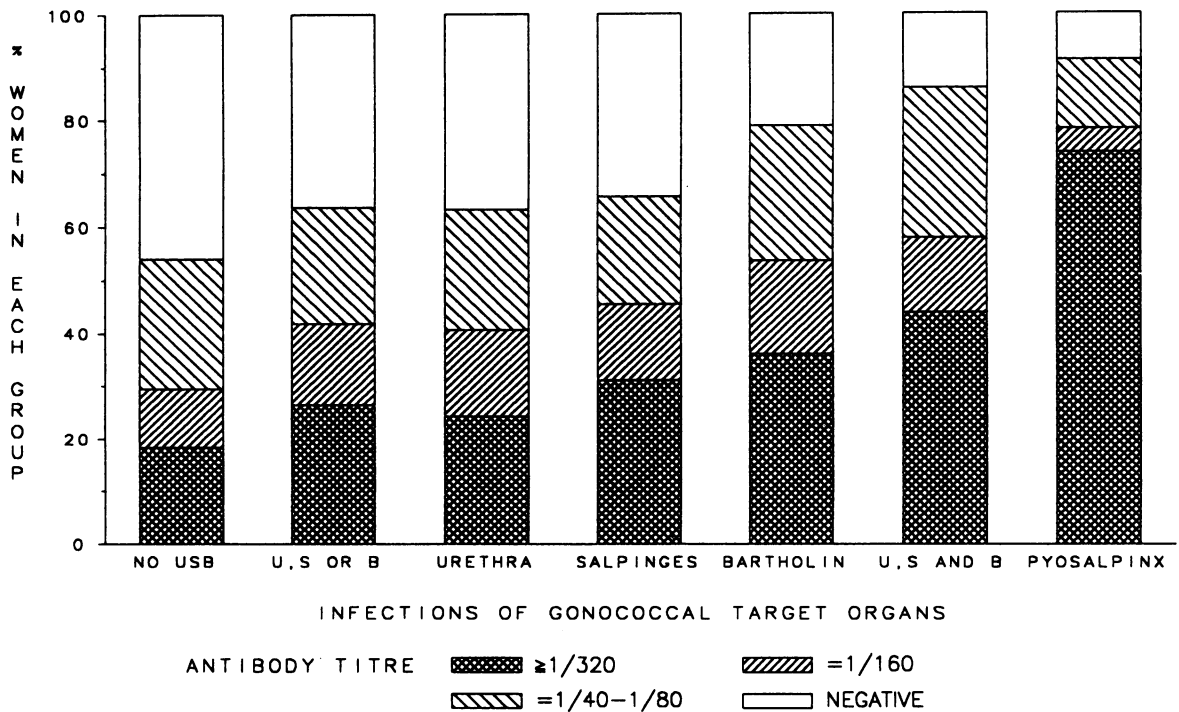


Figure 4 Gonococcal antibody test seropositivity and clinical evidence of infection in urethra, salpinges and Bartholin glands. U = Urethra. S = Salpinges. B = Bartholin glands.

likely to have had both infections. It may well be that our results reflect that, but because syphilis could be confirmed with a reasonably reliable serological test, the patients were more likely to be told that they had syphilis than gonorrhoea. Alternatively, patients may have been confused about which infection was actually treated: our results show a very similar correlation between gonococcal antibodies and history of either syphilis or gonorrhoea or both.

Gonococcal antibodies in women attending different clinics is of interest. Ten per cent of women attending antenatal clinics had high titres of antibodies $\geq 1/320$. This percentage corresponds to 9% of parturient women who were found to be culture positive for *N gonorrhoeae*.¹⁰

A slightly higher (15%) number with high titres of antibodies found at the postnatal clinic could reflect the fact that women who were asymptomatic tended to default a routine postnatal clinic while those with symptomatology would be more likely to attend.

It has been reported that *N gonorrhoeae* were cultured from 28% of women with puerperal sepsis.¹⁰ In women attending the GOPD 23% had titres of $\geq 1/320$ indicative of present gonococcal infection or repeated episodes of gonorrhoea: this corresponds

well with the figures obtained from a study of aetiology of pelvic inflammatory disease in which we showed that when we eliminated those patients who received antibiotics, the frequency of isolates of *N gonorrhoeae* would increase from 20% to 32% of PID patients.¹⁰ It must be of great concern that 31% of women attending family planning clinics for routine family planning advice had titres $\geq 1/320$. This confirms the reports from other countries that a high percentage of women with gonococci are asymptomatic and hence form an important reservoir of infection.

It has been said that 10–15% of those with cervical gonorrhoea go on to develop gonococcal salpingitis.⁷ Our high figure for salpingitis, associated with high GAT titres, in contrast to the relatively low percentage (6%) diagnosed as having cervicitis may indicate that many women who had cervicitis and a vaginal discharge may have thought that they had gonorrhoea and therefore went to the STD clinic at an early stage of the infection. Those who then attended the GOPD on account of lower abdominal pain and abnormal bleeding, and were found to have salpingitis, did so at a later stage of the infection.

The detailed analysis of the association of gonococ-

cal antibodies with the clinical evidence of infection in the gonococcal target organs (USB) is of great interest (fig 4). The clinical finding of palpably thickened urethra,¹⁷ Bartholin glands and salpinges^{18,19} with/without tenderness on palpation is that of chronic gonorrhoea, as recorded in the pre- and early antibiotic era in Europe (E Rees, personal communication). It is not a feature of gonococcal infection in countries with a well developed health service. Amongst the population with no evidence of USB infection 46% were seronegative. Of the 54% who were seropositive, only 18% had high titres $\geq 1/320$. There was a statistically significant ($p < 0.001$) increase in percentage of seropositive women in those who had evidence of clinical infection of one or more gonococcal target organ, particularly the percentage with high titres. There was least increase in those with evidence of urethritis only and most in those who had bartholinitis. In the pre-antibiotic era bartholinitis was "practically pathognomonic for gonorrhoea", *N gonorrhoeae* being the primary pathogen.²⁰ Of those who had clinical evidence of infection of all three organs, only 15% were seronegative and of those who were seropositive, 42% had high titres $\geq 1/320$. The highest percentage of seropositive women was in the group who had clinical evidence of pyosalpinx: only 9% had no gonococcal antibody and 74% had high titres. This observation is of particular interest as it has been suggested that in pelvic inflammatory disease, particularly pyogenic infections resulting in pelvic abscess formation, the first pathogen is *N gonorrhoeae*, thereafter polymicrobial infections follow with anaerobic infections occurring last. This would suggest that for those with pyosalpinx more than 90% had had an initial gonococcal infection, which possibly predisposed the fallopian tubes to subsequent pyogenic infection, tubal obstruction and pyosalpinx formation.

Literature search revealed no record of previous study, in developing countries, using the haemagglutination tests for gonorrhoea. Comparison with results from previous studies is therefore difficult.

Prevalence for individual countries have been based on screening women attending particular clinics; thus the prevalence of gonorrhoea at family planning clinics varies between 2% for Swaziland to 19% in Nairobi.¹¹ The prevalence in healthy women attending antenatal clinics ranges from 3 to 22%, many African countries reporting 18% culture positive for gonorrhoea.¹ Nine per cent of parturient women and first attenders at a gynaecological outpatient department in Ethiopia were culture positive.¹⁰ The prevalence rate of gonorrhoea in women attending STD clinics ranges from 7% in Sudan,²¹ to 19% in Zambia⁹ and 19% in Zimbabwe,²² with far higher rates being reported for clinics allocated specifically for prostitutes, 51% in Rwanda⁶

and 35% in Kenya² with a lower number (18%) in those attending for routine checkup on a regular basis,² or those who regularly took antibiotics (16%).²³

Prevalence figures for gonococcal infection in other African countries are based on diagnosis of acute/present gonorrhoea by cultural techniques. The higher prevalence which we report is a measure of exposure to gonococcal infection past and present and as such is not in contradiction with the relatively lower prevalence rate reported from the above mentioned epidemiological studies. The prevalence of seropositivity at $\geq 1/320$ is comparable to the prevalence of present, active infection in other studies.^{1,10}

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