



# OFFICE GYNECOLOGY

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# Preface

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Practitioners involved in the health care of women spend the largest portion of their working hours in an office or clinic. Despite this, the focus of most journal articles and textbooks in gynecology is on hospital practice. Up to date information on office practice must be obtained in a fragmented fashion from throw-away journals or medical newspapers. The aim of this book is to present, in one volume, current information on a variety of issues vital to the office practice of gynecology. No attempt is made to be encyclopedic, but rather there is a conscious effort to concentrate on common problems.

The authors are all clinicians who have special areas of expertise. They consistently have met the editor's goal to provide complete, concise, and practical information. Even the most experienced gynecologist will find material here that will be useful to him or her in clinical practice, and the book provides a standard against which all practitioners can measure their information and their response to women. The book should be helpful not only to the gynecologist but also to all others involved in the health care of women—family practitioners, internists, residents, interns, medical students, nurse practitioners, and nurse midwives.

I am indebted to the contributors who have given of their time, interest, and knowledge.

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# PELVIC INFECTION AND VENEREAL DISEASE

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WILLIAM J. LEDGER, M.D.

## INTRODUCTION

Pelvic infection from sexually transmitted microorganisms represents the most important infectious disease problem facing the gynecologist in his office practice in the 1970's. This eminence is based partly on the large numbers of women involved. For example, although the reporting of *Neisseria gonorrhea* infections represents only a minority of such organism infections, and although these specific organism infections include only a portion of all sexually acquired pelvic infections, there were 874,161 reported cases of *N. gonorrhea* in the United States in 1974, indicating the epidemic proportions of this problem.<sup>1</sup> The fact that a minority of these cases, 350,863, were in women probably reflects under-reporting of asymptomatic women. The reported rate of gonorrhea increased each year from 1971 (624,371) to 1974 (874,161), an increase of 40%, with the greatest increase seen in the number of infected women (Table 1.1). In addition to the large numbers of women involved, pelvic infection is an important problem because there is good medical evidence that early detection and treatment of infections in females can achieve a clinical cure without the unacceptable residuals of infertility and pelvic pain. The seriousness of pelvic infection should not be downgraded. A recent study demonstrated tubal occlusion by laparoscopy in 12.8% of women after one clinical episode of salpingo-oophoritis.<sup>2</sup> With this serious outcome in mind, our goal as physicians should be appropriate employment of all diagnostic and therapeutic techniques so that the full female potential for reproduction and normal adult living can be assured. This is a major responsibility for the practicing physician.

## PATHOPHYSIOLOGY OF SEXUALLY ACQUIRED PELVIC INFECTIONS

There is substantial evidence that the gram negative aerobe *N. gonorrhea* plays a significant role in the early manifestations of sexually acquired pelvic infections in women. In the pre-antibiotic era, Curtis performed a number of detailed microbiologic studies (including grinding up tubal material for culture) on pelvic tissue removed at operation.<sup>3</sup> His descriptions of the relationship between the microbiologic recovery of *N. gonorrhea* and clinical observations in the operating room were interesting. This organism was isolated from minced fallopian tubes removed at operation only when there was visual evidence of acute inflammation.

TABLE 1.1  
*Reported Cases of Gonorrhea*

Fiscal year	Male	Female	Total	Percentage increase over previous year		
				Male	Female	Total
1971	448,731	175,640	624,371			
1972	494,652	223,749	718,401	10.2	27.4	15.1
1973	504,706	304,975	809,681	2.0	36.3	12.7
1974	523,298	350,863	874,161	3.7	15.0	8.0

In fact, in no cases were gonococci isolated from non-inflamed fallopian tubes in this pre-antibiotic era study. This circumscribed time interval of microbiologic recovery has been confirmed in modern studies based upon surface recovery of the gonococcus. Eschenbach and Holmes<sup>4</sup> and Chow et al.<sup>5</sup> recovered this organism from cervix and cul de sac aspirations in patients with clinical evidence of acute salpingitis. These investigators noted the gonococcus was recovered more frequently from the endocervix than from the peritoneal fluid. The common microbiologic isolation of this organism from the endocervix, minced fallopian tubes, and cul de sac aspirations in women with clinical evidence of acute salpingitis, and the absence of peritoneal or tubal recovery when there is no inflammation, strongly indicate the importance of this organism in acute salpingitis. An unfortunate additional observation is that although prior exposure to this potential pathogen elicits an immunologic response that can be measured in the serum, no absolute protection against future infection is established.

Obviously, not every pelvic infection is directly related to the gonococcus. A whole series of recent evaluations have confirmed the importance of other bacteria, particularly anaerobic microorganisms, in pelvic infections. Eschenbach and Holmes,<sup>4</sup> Chow et al.,<sup>5</sup> Thadepalli et al.,<sup>6</sup> Swenson et al.,<sup>7</sup> and our own anaerobic laboratory at the Los Angeles County-University of Southern California (LAC-USC) Medical Center<sup>8</sup> have frequently isolated anaerobic organisms from infection sites in women with sexually acquired pelvic infections. All these investigators have found anaerobic organisms in the majority of these serious soft tissue pelvic infections.

In fact, these investigations suggest that a number of classical beliefs about the mechanisms of bacterial soft tissue pelvic infections may not be correct. Emerging from these studies is a pattern of infection that will require re-orientation of gynecologic thinking about both the mechanisms and the treatment of pelvic infections. These new facts include the observations that anaerobes can be recovered from over 70% of soft tissue pelvic infections. These infections are a mixed microbiologic bag, i.e. more than one microorganism is frequently recovered. This is in contrast to the single-pathogen concept that applies so well to such infections as pyelonephritis. The antibacterial therapy of these mixed infections has not been established by prospective study. Some of the preliminary studies suggest that less than complete antibiotic coverage of the recovered organism may still yield a clinical cure.<sup>9</sup> Finally, we have been impressed at the LAC-USC Medical Center that operative drainage or removal of a pelvic abscess

may be necessary for cure. What has been most significant to us has been the observation that the organisms recovered from the infected site have not been resistant in the laboratory to the antibiotics given to the patient prior to operation. Unlike observations by Gorbach that anaerobes were not recovered after 24 hours of clindamycin therapy, we have been able to recover anaerobes from previously undrained soft tissue infection sites despite prior clindamycin therapy.<sup>8</sup> If confirmed by other investigators, this will be a significant observation. In the past, physicians have generally equated therapeutic failure of response by the patient to the presence of resistant organisms at the site of infection. The physician's automatic response was to switch the patient to more powerful and potentially more toxic antibiotics. In view of these findings, our concern should be directed toward the discovery of a pelvic abscess with the appropriate operative intervention or the use of anticoagulants for the treatment of septic pelvic thrombophlebitis. This decision will be dealt with in detail in the section on therapeutics.

Besides the anaerobes, the other components in these mixed bacterial soft tissue pelvic infections are the aerobes. Recently, most of our attention has been directed toward the gram-negative aerobes, particularly *Escherichia coli*, which is one of the most common microorganisms recovered from these patients. In addition, there is new awareness of gram-positive cocci in such infections. Unlike the late 1950's when the predominant organism of concern was the coagulase-positive staphylococcus, more frequent pathogens recovered in the 1970's are the streptococci. The Group A beta-hemolytic streptococcus is not a frequent isolate, but can be associated with serious, life-threatening pelvic infections. A more frequent isolate on our service is the enterococcus. Although doubts have been expressed about the pathogenicity of this organism, it has been associated with serious infections in our patients.

The role of mycoplasma in pelvic infections has not been established as yet. Members of this group of organisms have been isolated in pure culture from a Bartholin's abscess<sup>10</sup> and, in combination with other organisms, from patients with a tubo-ovarian abscess. The clinical significance of these observations is not known.

No discussion would be complete without some comments on the influence of changes in social mores and medical practice upon the incidence of pelvic infection. There has been a worldwide revolution in sexual mores, reflected in an increasing rate of gonorrhea among an ever younger population. One factor influencing this more permissive sexual attitude has been the development of such methods of contraception as the oral contraceptives and the intrauterine device. These contraceptives are more effective than those previously available, and their employment is not related to the act of intercourse, as was the case with such mechanical methods as the condom, diaphragm, or jelly. Physicians have emphasized the lack of complete protection with mechanical methods. Fiumara quotes a description of a condom-like penile sheath of the 17th century as an "armor against enjoyment and a spider web against danger."<sup>11</sup> Despite this, it is likely that an asymptomatic male with gonorrhea using a condom would be less of a risk to a female sexual contact than the same male not using a condom. In addition, Bolch and Warren<sup>12</sup> noted an antigonococcal effect of one of the vaginal

foams used as a spermicidal agent. This obviously would have some protective action for the women.

Besides the loss of the protective roles of the barrier forms of contraception, there has been concern about the direct influence of contraceptive methods upon the incidence of pelvic infection. Clinical data seem to support the concept that the minority of untreated women exposed to the gonococcus develop salpingitis. Fiumara has stated that women who use oral contraceptives are at greater risk of developing gonococcal salpingitis.<sup>18</sup> If this is true, it would identify a high risk population that should have more frequent screening examinations for lower genital tract gonorrhea. A possible relationship between the intrauterine contraceptive device and pelvic infection has been suspected by many physicians. Although early studies did not confirm an increased incidence of pelvic infections with these intrauterine foreign bodies, there have been a number of isolated observations that suggest that such a relationship in fact does exist. Eschenbach and Holmes have found a statistically significant increase in the number of patients with serious pelvic infections among intrauterine device wearers.<sup>4</sup> In addition, I have been aware of occasional serious and life-threatening pelvic infection due to the Group A beta hemolytic streptococcus in intrauterine device users. Besides this, some unilateral tubo-ovarian abscesses have been seen in intrauterine device patients. This unilateral disease seems more common among intrauterine device users. The mechanism is not known, but the relationship seems real. These potential factors must be weighed in the evaluation of office patients with the symptomatology of fever, pelvic or abdominal pain, or an adnexal mass. Some of these masses may be inflammatory in origin.

#### **MICROBIOLOGY OF THE LOWER GENITAL TRACT IN ASYMPTOMATIC SEXUALLY ACTIVE WOMEN**

A common example of clinician confusion is the search through the clinical microbiology report of endocervical or vaginal cultures for the presence of pathogens to confirm the diagnosis of salpingo-oophoritis. It has been thought that the presence of such gram negative aerobes as *E. coli* can be equated with infection. There is no good modern basis for this supposition, and evaluation of the vaginal bacterial flora of asymptomatic women, prior to the insertion of an intrauterine device<sup>14</sup> or at the time of uterine removal with vaginal hysterectomy<sup>15, 16</sup> revealed many potential pathogens (Table 1.2). A striking observation of all of these studies was the large number of anaerobes recovered, over 70% of the specimens in a recent study.<sup>16</sup> In fact, one recent study of the endocervical anaerobic bacterial flora of "normal" women found many anaerobes, and no differences in the types of isolates from these women could be found when compared to the endocervical cultures of patients with symptomatic pelvic infection.<sup>17</sup> This indicates that the recovery of anaerobic organisms or other "pathogens" from endocervical cultures is not a discriminating laboratory test for the presence of a pelvic infection. Does the recovery of any bacterial species have clinical significance? I believe there can be an affirmative answer when either of two species is recovered. The isolation of the aerobic group A beta hemolytic streptococcus from the lower genital tract is not always associated with clinical disease. However, since this organism has been

TABLE 1.2

*Bacteria Recovered from the Endocervix or Vagina of Asymptomatic, Sexually Active Women*

	Gram positive	Gram negative
Aerobes	<i>Streptococcus viridans</i> Enterococci Beta streptococcus, not A or D Coagulase positive staphylococcus Coagulase negative staphylococcus Diphtheroids Lactobacilli <i>Bacillus subtilis</i>	<i>Escherichia coli</i> <i>Proteus</i> <i>Aerobacter aerogenes</i> <i>Klebsiella</i> <i>Pseudomonas</i> <i>Mima polymorpha</i>
Anaerobes	<i>Peptostreptococcus</i> <i>Peptococcus</i> <i>Clostridium</i> , not perfringens <i>Clostridium perfringens</i> <i>Propionibacterium acnes</i>	<i>Bacteroides</i> species <i>Bacteroides fragilis</i> Fusobacteria

related to severe pelvic infections, particularly in women utilizing an intrauterine contraceptive device, the discovery of this streptococcus on culture is an indication to me for systemic antibiotic therapy. In addition to this aerobe, *N. gonorrhea* isolation has significance for the clinician. Its presence is not always associated with clinical evidence of upper genital tract disease, even in the absence of systemic antibiotic therapy, but aggressive treatment is indicated so that the possible complications of acute salpingitis can be avoided.

### PROPER MICROBIOLOGIC TECHNIQUES FOR THE ISOLATION OF *N. GONORRHEA*

The microbiologic isolation of *N. gonorrhea* requires knowledge of both the host environment and the specific growth requirements of this organism. In a clinical setting, the most frequent site of sampling for this organism is the endocervix, a location that is rich in other bacteria. Any microbiologic sample from this site will contain a multiplicity of organisms. This is an important fact to keep in mind, because organisms competing for the nutrients of the culture media may successfully implant and overgrow, so that *N. gonorrhea* present at the culture site will not survive in the laboratory. This has required two major modifications in culture techniques. First, specific media are utilized, rich in glutamine and carboxylase. Next, the samples are placed in a carbon dioxide-rich environment, so that the most favorable setting is available for the growth of *N. gonorrhea*. To reduce the problem of competing organisms, the antibacterial agents vancomycin and colistimethate, plus the antifungal agent nystatin have been added. As a result, few species other than *N. gonorrhea* can survive on these media. To be certain that colony growth is due to *N. gonorrhea*, oxidase and sugar fermentation tests can be applied to the colonies, as well as microscopic evaluation of the morphology of a gram stain from the bacterial colonies.

With this theoretical knowledge, many practical problems remain for the clinician. He must determine the microbiologic technique that works best for him

in his own office environment. Most of the patients who need to be tested for the presence of this organism will be seen in clinics and private offices, far removed from the hospital microbiology laboratory. Transportation may be a critical item in the successful isolation of this organism, for it does not survive in an unfavorable environment for long periods. Nearly all of the studies with transport media demonstrate fewer recoveries of *N. gonorrhea* with increasing time intervals. The most popular and rational microbiologic strategy has been the use of direct specimen plating and incubation by the clinician prior to transport to the laboratory. A number of commercial systems, including Trans-grow, are available for this purpose. Many of the systems have a short shelf life which is increased by refrigeration storage. It is important for the physician and office staff to allow these culture tubes to warm to room temperature before use. The gonococcus, which survives so well in the human host, may not tolerate the chill of the cold medium plate. The crucial ingredient for success still seems to be to minimize the time between specimen collection and the laboratory receipt of the sample. Although the endocervical smear has been downgraded as a diagnostic technique in asymptomatic women, the presence of gram negative intracellular diplococci should have significance for the clinician and result in treatment before the culture report returns in patients with symptoms. However, the absence of gram negative intracellular diplococci does not eliminate the possibility of gonorrhea.

When the clinician has decided upon the appropriate microbiologic system, the next decision is the site for specimen collection to isolate the gonococcus. A number of large scale clinical trials have been performed to provide a basis for choice in this area. These studies indicate that the endocervix is the best single site for culture collection, and that a combination of an endocervical sample and rectal sample provided the highest yield of positive cultures.<sup>18</sup> These results have to be viewed within the framework of clinical practicality for the physician. On our own service at the LAC-USC Medical Center, the added yield of positive cultures by rectal sampling has not been high enough to make us routinely utilize this site in our diagnostic screening maneuvers. Every physician must be aware of the finding by Schroeter and Lucas that one-third of the gonococcal treatment failures were discovered only by rectal culture.<sup>18</sup> For this reason, the rectum, as well as the endocervix, is always sampled as a test of cure 7 to 14 days after the completion of therapy. It is important for the physician to obtain a complete history of the patient's sexual practices. If the woman is practicing rectal intercourse, then rectal cultures are indicated. If she is practicing fellatio, oral pharyngeal cultures should be done. There is one final practical note for specimen collection. The commonly used vaginal lubricants contain preservatives that can be bactericidal to the gonococcus. It is important to avoid their use prior to the obtaining of a specimen.

#### WHAT POPULATION SHOULD BE SAMPLED?

The physician's decision about the population of women to be sampled must acknowledge the current state of flux that still exists in this area. There was a major drive in the 1960's, with considerable government support, for universal screening of women of child-bearing age. This was based upon the presumptions that the male who had gonorrhea was symptomatic while the woman usually was not. The

goal was the discovery and treatment of this large reservoir of asymptomatic females. Recently, a number of clinical observations have opened this observation to doubt. Contemporary studies indicate that infective males may be asymptomatic<sup>19</sup> and, more important, that infected females may have symptomatology.<sup>20</sup> These observations may have some implications for future outpatient gynecologic practice. Rather than the random screening of the entire office patient population, the physician may be able to selectively culture all females of child bearing age with the symptomatology of a vaginal discharge, abnormal uterine bleeding, or urinary tract symptomatology suggestive of a cystitis. One recent study indicated a high yield of positive gonococcal cultures in that population group.<sup>20</sup> I still believe that universal microbiologic screening for this pathogen in sexually active women is the best medical goal, but decisions on the cost-yield ratio of such a screening survey still have to be made. Even if the costs of universal screening are prohibitive, certainly symptomatic patients need to be screened.

The most important impact of these new observations is the significance of the asymptomatic male. As a specialty, Obstetrics-Gynecology has directed all of its efforts towards the improvement of health care for women, and has tried to implement this by restricting the practice of individual specialists to women. In the area of pelvic infection control, this is clearly not an acceptable policy. Our goals should be to prevent re-infection of the treated female by the asymptomatic male, and we must implement in some way the discovery and treatment of such contacts.

A recent development of some interest to the practicing gynecologist has been the finding that there is some immunologic response to exposure to the gonococcus, which might obviate the problem of obtaining a culture. A number of tests methods have been devised to measure serum immunoglobulin response to the gonococcus, utilizing a latex agglutination test. To date, there have been serious shortcomings with this method. Some patients, seen early, with a positive culture for *N. gonorrhea* have a negative test. A different problem is seen in women who have had gonorrhea in the past but who presently are culture negative. Many of these women will have a positive serologic test for gonorrhea. These false negative and false positive results severely restrict the practical application of these serologic tests for gonorrhea. Perhaps a more significant clinical observation is the realization that the presence of these antibodies is insufficient for protection against recurrent disease.<sup>21</sup>

#### MICROBIOLOGIC EVALUATION OF OTHER POTENTIAL PATHOGENS

In addition to the gonococcus, the presence of other "pathogens" will on occasion need to be evaluated by the clinician. Previously mentioned studies have shown no difference in bacterial flora of the endocervix between asymptomatic and symptomatic women, so that this site should not be used for microbiologic evaluation for organisms (other than the group A beta hemolytic streptococcus). The alternate site, the peritoneal cavity, sampled through the posterior cul de sac, has been shown to be free of bacteria in asymptomatic women.<sup>5</sup> This clearly defines our study population, i.e. those patients with clinical evidence of acute salpingitis. In these patients, in the absence of a cul de sac mass, the vagina should be prepped



with an iodine solution, and the peritoneal cavity entered through the posterior cul de sac with a long spinal needle for aspiration. Chow *et al.* have utilized only the needle and have added sterile saline without preservative to lavage the peritoneal cavity and permit the reaspiration and collection of a fluid sample.<sup>5</sup> Eschenbach and Holmes have used a large bore #14 needle and have inserted polyethylene tubing through this for peritoneal cavity aspiration.<sup>4</sup> In symptomatic women, cultures for the gonococcus, aerobes, and anaerobes, as well as a gram stain of the exudate should be performed. This requires some minimal microbiologic materials to be present and available in the office setting.

Minimal microbiologic equipment is needed to adequately equip a gynecology office. There should be a microscope with a satisfactory oil immersion lens, and fresh material should be available for the gram stain. Sterile tubes of a transport medium and sterile oxygen-free tubes should be present for the transport of appropriate specimens to the hospital laboratory for aerobic and anaerobic cultures. If possible, fresh media for the culture of *N. gonorrhea* should be present in the office. Specimens should be transported on a frequent basis, if necessary, during normal office hours.

The exact role of *Mycoplasma* organisms in pelvic infections remains confused and unclear at present. Mycoplasma can be a "pathogen," on occasion, for it has been recovered in pure culture from a Bartholin's abscess,<sup>10</sup> and has been isolated along with other organisms from tubo-ovarian abscesses.<sup>22</sup> In addition, the effectiveness of tetracyclines in the treatment of patients with salpingo-oophoritis suggests that these organisms may have clinical significance. Mycoplasma can frequently be isolated from the endocervix and vagina of sexually active women.<sup>23</sup> Indeed, the multiplicity of male sexual partners seems to increase the recovery rate of this organism from the lower genital tract of females. However, recovery from the lower genital tract does not have the same significance as recovery of the gonococcus. In addition, the complexity of the culture techniques makes it unlikely that either the clinician or the laboratory will employ these isolation techniques at present. If more convincing cause-and-effect evidence of pathogenicity is produced, then changes in future office practice modes will be required.

The incidence of herpes genitalis has reached epidemic proportions. In fact, in many office practices this is the most common venereal disease seen. The clinician usually can recognize the clustered outbreak of vesicles visually on examination. Laboratory confirmation is seldom needed, but can be provided by viral isolation, the presence of multinucleated giant cells on Pap smear, or increase of herpes titer in the blood. On practical grounds for the office gynecologist, evaluation of the Pap smear is the most frequently employed laboratory technique.

### SYPHILIS

Any review of sexually acquired pelvic infections in women would be incomplete without a discussion of syphilis. This disease, usually acquired during sexual intercourse, has a limited impact upon pelvic organs and may not be associated with any apparent symptomatology. However, if untreated, it can have disastrous effects in later years upon such vital organ systems as the cardiovascular or central nervous system. The detection of the early phases of this disease by physicians is an