MICROBIOLOGY

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Number

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Subject

Urinary Tract Infection & GONORRHEA

Doctor

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Genito-Urinary System

Urinary Tract Infection & GONORRHEA

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Urinary Tract Infection

- Bacterial colonization of the urine within this tract (**bacteriuria**) is common and can, at times, result in microbial invasion of the tissues responsible for the manufacture, transport, and storage of urine.
  "Kidneys" "Ureters" "Urinary bladder"
- Infection of the upper urinary tract (kidney and its pelvis), is known as **pyelonephritis**. المريض: "دكتور خاصرتي بتوجعني"
- Infection of the lower tract may involve the bladder (**cystitis**), urethra (**urethritis**), or prostate (**prostatitis**), the genital organ that surrounds and communicates with the first segment of the male urethra.

Bartholinitis: is inflammation of one or both of the two Barotholin's glands. "Located on either sides of the opening of the vagina".

Colonization of normal flora "microbiota" in the openings of our body (nose, mouth, urethra, anus ..)

If the the normal flora moved from one place to another it'll become pathogenic.

For example: staph aureus is a normal flora founded on the skin but if you cut your finger and the bacteria gets inside it'll produce infection.

EPIDEMIOLOGY

- Urinary tract infection (UTI) is among the most common of diseases particularly among women. Shorter and wider urethra.
- Prevalence is age and sex dependent. Approximately 1% of children, many of whom demonstrate functional or anatomic abnormalities of the urinary tract, develop infection during the neonatal period. First 28 days of life "4weeks".
- It is estimated that 20% or more of the female population suffers some form of UTI in their lifetime.

They are prone for recurrent infections.
Failure to thrive, and even later in their lives.
"ما بينمو نمو مزبوط"
That's why the pediatricians always order investigations of the urinary system.

- Infection in the male population remains uncommon through the fifth decade of life (<50 years.), when enlargement of the prostate begins to interfere with emptying of the bladder. Senile prostatic hyperplasia
- In the elderly of both sexes, gynecologic or prostatic surgery, incontinence, instrumentation, and chronic urethral catheterization push UTI rates to 30 to 40%.
- A single bladder catheterization carries an infectious risk of 1%, and at least 10% of individuals with indwelling catheters become infected.

Foley's catheter

"موضوعة لمدة طويلة"

Any obstruction or anything that could result in stagnation of urine will eventually cause infections.
Diabetics, prostate patients and even in females "chronic debilitating patients" are more prone to urinary tract infections.

PATHOGENESIS

- The urine produced in the kidney and delivered through the renal pelvis and ureters to the urinary bladder is sterile in health. Here even one single organism is significant.
- Infection results when bacteria gain access to this environment and are able to persist. Access primarily follows an ascending route for bacteria that are resident or transient members of the perineal flora. These organisms are derived from the large intestinal flora, which is uncomfortably nearby.

Ecoli... Most common

Through the voiding urine "urine that gets out" we should have 100,000 of one microorganism/ml of urine to diagnosed not infection "remember we have normal flora"

- Conditions that create access are varied, as relatively minor trauma, but the most important is the mechanical effect of sexual intercourse, which has been shown to transiently displace bacteria into the bladder. This puts the female partner is at risk because of the short urethral distance. And wider
- Factors that violate bladder integrity and other manipulations of the urethra carry risk as well, particularly medical ones such as catheterization, or that obstruct urine outflow (enlarged prostate).

- Bacteria may also reach the urinary tract from the bloodstream. This is obviously much less common, because it requires an uncontrolled infection at another site. Sinusitis, pneumonia... The organism then goes to the blood >> Bacteremia >> UTI.
- Persistence of bacteria is favored by host factors that interrupt or retard the urinary flow such as instrumentation, obstruction, or structural abnormalities.
- In youth, factors are congenital malformations, and with age these include changes that alter the mechanics of outflow, such as prostatic hypertrophy.

Easy, very easy 😎😎

- Bacterial factors include the ability to adhere to the perineal and uroepithelial mucosa and to produce other classical virulence factors like exotoxins.
- *Escherichia coli* is by far the most common and potent UTI pathogen. The ability of uropathic *E. coli* (UPEC) to produce UTI is related to general virulence factors such as α-hemolysin, together with pili-mediated adherence to uroepithelial cells.
- The percentage of *E. coli* with P pili increases from 20% in the fecal flora to 70% in pyelonephritis isolates. ☆

- P pili adhere to digalactoside receptor present on uroepithelial cells, to which the bacteria bind avidly, particularly in the upper urinary tract (involved in pyelonephritis). By aiding in periurethral colonization as the prelude to bladder access, type 1 pili are important as well. In addition, type 1 pili are essential for attachment to urinary epithelium in the urinary bladder.

- Urease-producing members of the genus *Proteus* are associated with urinary stones, which themselves are predisposing factors for infection.

Stones; related to the PH, alkaline secretions that will precipitate certain type of renal calculi "calcium oxalate appears on X-Rey's while in urease stones will not appear so we do IVP or ultrasound"

The proteus will produce swarming growth on blood agar "أمواج"

ETIOLOGIC AGENTS

- Over 95% of UTIs are caused by a single bacterial species and 90% of these are *E. coli*. So more than 80% of UTIs are EColi
- Other Enterobacteriaceae, *Pseudomonas*, and Gram-positive bacteria (enterococci) become increasingly frequent with chronic, complicated, and hospitalized patients. *Staph. saprophyticus*, is significant in young, sexually active women.
  - Part of group D streptococci.
  - (+ klebsiella)
  - Coagulase negative
  - 👉 Pseudomonas; Mostly in immuno compromised patients or those with catheter "colonization and ascending infection".
- Yeasts, particularly species of *Candida,* may be isolated from catheterized patients receiving antibacterial therapy and from diabetic individuals, but they seldom produce symptomatic disease. "chronic debilitating patients"

MANIFESTATIONS

- The clinical manifestations of UTI are variable. Approximately 50% of infections do not produce recognizable illness and are discovered incidentally during a general medical examination.
- Infections in infants produce symptoms of a nonspecific nature, including fever, vomiting, and failure to thrive.
- Manifestations in older children and adults, when present, often suggest the diagnosis and sometimes the localization of the infection within the urinary tract.

Cystitis التهاب المثانة

Burning sensation.

- The symptoms of cystitis are dysuria (painful urination), frequency (frequent voiding), and urgency (an imperative "call to toilet").
- It is clinically distinguished from pure urethritis by a more acute onset, more severe symptoms, the presence of bacteriuria, and in approximately 50% of cases, hematuria. The urine is often cloudy and malodorous and occasionally frankly bloody, and pain and tenderness in the suprapubic area. Fever and systemic manifestations are usually absent unless infection spreads to involve the kidney.

Pyelonephritis

- The typical presentation of upper urinary infection consists of **flank pain** and **fever** that exceeds 38.3°C. These findings may be preceded or accompanied by manifestations of cystitis. Rigors, vomiting, diarrhea, and tachycardia are present in more severely ill patients.
- Physical examination reveals tenderness over the costovertebral areas of the back and, occasionally, evidence of septic shock. In case of severe infection.

- In the absence of obstruction, the clinical manifestations usually abate within a few days, leaving the kidneys functionally intact.
- It has been estimated, however, that 20 to 50% of pregnant women with acute pyelonephritis give birth to premature infants.
- In the presence of obstruction, a neurogenic bladder, or vesicoureteral reflux, clinical manifestations are more persistent, occasionally leading to necrosis of the renal papillae and progressive impairment of kidney function with chronic bacteriuria.

- If a renal calculus or necrotic renal papilla impacts in the ureter, severe flank pain with radiation to the groin occurs. to the testicles or labia in females
- ~~The term chronic pyelonephritis is used to describe inflamed, scarred, contracted kidneys often in association with compromised renal function.~~
- ~~There is no known connection between UTI and chronic pyelonephritis.~~

Prostatitis

- Infection of the prostate is typically manifested as pain in the lower back, perirectal area, and testicles. In acute infection, the pain may be severe and accompanied by high fever, chills, and the signs and symptoms of cystitis. Inflammatory swelling can lead to obstruction of the neighboring urethra and urinary retention. On rectal palpation, the prostate is boggy and exquisitely tender. PR
- Response to antibiotic therapy is good, but occasionally develop abscess, epididymitis, and seminal vesiculitis or chronic infection.

- Catheterization or suprapubic aspiration from the distended bladder may be necessary when the laboratory examination produces equivocal results or the patient cannot comply with the requirements of the clean-voided technique.
- For the diagnosis of prostatitis, urine is collected in three segments by interrupting a single bladder excavation. The first voiding is considered a urethral washout. The MSU specimen that follows is used to assess cystitis.
- Prostate is then massaged, and the final urine is a prostatic secretions washout. Quantitative culture results are then compared.

- Typically, acute prostatitis develops in young adults; however, it can also follow placement of an indwelling catheter in an older man.
- Patients with chronic prostatitis seldom give a history of an acute episode. Many are totally without symptoms; others experience low grade pain and dysuria.
- Periodic spread of prostatic organisms to the urine in the bladder produces recurrent bouts of cystitis. In fact, chronic prostatitis is probably the major cause of recurrent bacteriuria in men. The etiologic agents are the same as in cystitis and pyelonephritis. "EColi ..."

Microscopic Examination

- Approximately 90% of patients with acute symptomatic UTI have pyuria (that is, 10 white cells/mm3 of urine) but is not specific.

  We use counting chamber.
  Pyuria; pus in urine.

- More specific is the presence of white cell casts, which occur primarily in pyelonephritis.
- A more sensitive and specific procedure is a Gram-stained smear of uncentrifuged urine.
- The presence of at least one organism per oil-immersion field is almost always indicative of bacterial infection.
- Absence of WBCs and bacteria makes the diagnosis unlikely, but does not rule it out.

Some other bacteria that cause UTI and pyuria (chlamydia, ureaplasma, TB...) in which the bacteria is present but it won't appear on routine culture.

Chemical Screening Tests

- A number of nonmicroscopic urinary screening tests have been commercially marketed. The most successful detects leukocyte esterase from inflammatory cells and nitrite produced from urinary nitrates by bacterial metabolism.
- Although technically simpler, the sensitivity and specificity of these products are similar to that of microscopic examination. Like microscopic examination, they do not reliably detect bacteriuria below the level of 10^5 organisms/mL.

Urine Culture

- Quantitative bacteriology has been the gold diagnostic standard for UTI. Bacterial count above 10^5 /mL is UTI, below it is contamination.
- It is possible to void more than 10^5 of contaminants and to have a genuine UTI with less than 10^5 bacteria.
- ~~In women voided contaminants are most often mixtures of vaginal flora not associated with UTI such as lactobacilli, diphtheroids, and streptococci, but can include urinary pathogens.~~

- Bacterial counts in UTI represent a spectrum from 10^2 to more than 10^6 bacteria/mL. The lower counts are typical for simple cystitis and the high counts for pyelonephritis.
- Fully one third of women with UTI limited to the bladder demonstrate counts less than 10^5 bacteria/mL.
- Presence of both pathogens and symptoms in females is diagnostic. Asymptomatic positives should be repeated.
- Catheterized and suprapubic specimens may be accepted at face value, because they come directly from the bladder.

TREATMENT

- The treatment of UTI is best guided by the results of cultures and antimicrobial susceptibility tests. In simple isolated instances of cystitis in a young woman, the etiology is often assumed to be *E. coli* and the antimicrobic selected empirically based on knowledge of the susceptibility of local strains.
- Sulfonamides and trimethoprim alone or in combination with sulfamethoxazole, a fluoroquinolone, and nitrofurantoin are the agents most commonly used.

Urine sample needs to stay in the incubator for only 24hours, if it was positive then we need another 24hours for the antibiotic sensitivity test.

الدكتور ذكر اسماء الأدوية بعدين حكا وأقتبس:
"الأدوية مش مشكلة" 🖐🖐

- ~~In most areas, the use of ampicillin is precluded by resistance rates exceeding 25%.~~
- ~~For children and patients with risk factors or recurrent infections, empiric therapy should always be confirmed by culture and susceptibility testing.~~
- Likewise, the duration of therapy depends on the severity of the infection and the risk status of the patient.
- Success of treatment may be tested by a follow-up urine culture 1 to 2 weeks after therapy is completed.

  👉For simple cystitis a five days treatment is enough.

PREVENTION

- Those with several symptomatic episodes annually may be helped with long-term, low-dose chemoprophylaxis. In women whose recurrences are related to sexual activity, administration of the chemoprophylactic agent may be limited to immediately after intercourse.
- Infected children, men, and those who experience UTI relapse should be investigated with intravenous pyelography to allow detection and correction of any factor causing predisposition to infection.

NEISSERIA GONORRHOEAE Glucose fermentation

- *N. gonorrhoeae* are Gram-negative cocci that typically appear in pairs (diplococci) with the opposing sides flattened, imparting a "kidney bean" appearance. They are nonmotile, non-spore forming, and non- acid fast.
- *N. gonorrhoeae* grow well only on chocolate agar and on specialized medium enriched to ensure its growth. It requires carbon dioxide supplementation.

- Small, smooth, non-pigmented colonies appear after 18 to 24 hours and are well developed (2 to 4 mm) after 48 hours. They are oxidase positive.
- Gonococci possess numerous pili that extend through and beyond the outer membrane. In general, only fresh virulent isolates have pili.

GONORRHEA

- It is primarily localized to mucosal surfaces with relatively infrequent spread to the blood stream or deep tissues. Infection is sexually acquired, the primary manifestation is pain and purulent discharge at the infected site.

"Endocervix"

- In men, this is typically the urethra, and in women, the uterine cervix. Direct extension up the fallopian tubes produces fever and lower abdominal pain, a syndrome called pelvic inflammatory disease (PID). For women, sterility or ectopic pregnancy can be long-term consequences of gonorrhoea.

Fallopian tube >> ovaries >> peritoneum >>> pelvic inflammatory disease.

☆ PID is caused by:
1) Chlamydia.
2) Gonorrhea.
3) Anaerobes.

With recurrence; fibroses of the Fallopian tube.

EPIDEMIOLOGY

- The overall incidence is now 130 cases per 100,000 population, but the rates for adolescents are alarmingly high and increasing by 10% a year. The highest rates are in women between the ages of 15 and 19 years and men between the ages of 20 and 24 years.
- The major reservoir for continued spread of gonorrhea is the asymptomatic patient.
- Almost 50% of infected women are asymptomatic and most men (95%) have acute symptoms with infection.

PATHOGENESIS

Attachment and Invasion

- Gonococci are not normal inhabitants of the respiratory or genital flora. When introduced onto a mucosal surface, adherence ligands such as pili and Opa proteins, allow initial attachment of the bacteria to receptors (CD46, CD66) on non-ciliated epithelial cells (urethral and vaginal epithelium). Following attachment, gonococci invade epithelial cells.
- Once inside, the bacteria transcytose the cell and exit through the basal membrane to enter the submucosa.

Survival in the Submucosa

- Once in the submucosa, the bacteria must survive and resist innate host defenses as well as defenses that may have been acquired from previous infection.
- Receptors on the gonococcal surface enable the organisms to scavenge iron needed for growth from the human iron transport proteins transferrin and lactoferrin.
- Some antibodies to OMPs have blocking effect on bactericidal activity.
- Phagocytosed gonococci resist killing.

Spread and Dissemination

- *N. gonorrhoeae* bacteria tend to remain localized to genital structures, causing inflammation and local injury.
  Huge amounts of secretions...
  لذلك نسميه السيلان باللغة العربية.
- Local spread is to epididymis and fallopian tubes. Peptidoglycan shedding causes local injury.
- Reflux during menses may facilitate spread (disseminated gonococcal infection and salpingitis).

One of the components of the cell wall structure of the bacteria.

IMMUNITY

- The apparent lack of immunity to gonococcal infection has long been a mystery.
- Both serum and secretory antibodies are generated during natural infection but the levels are generally low, even after repeated infections.
- Gonococcus varies multiple structures to avoid immune surveillance.

CLINICAL ASPECTS

MANIFESTATIONS

- Genital Gonorrhea

- In men, the primary site of infection is the urethra. Symptoms begin 2 to 7 days after infection and consist primarily of purulent urethral discharge and dysuria. Although uncommon, local extension can lead to epididymitis or prostatitis.

- The endocervix is the primary site in women. Symptoms include increased vaginal discharge, urinary frequency, dysuria, abdominal pain, and menstrual abnormalities.

Other Local Infections

- Rectal and pharyngeal infections relate to sexual practices. These conditions are generally asymptomatic.
- Infection of other structures near primary infection sites, such as Bartholin's glands in women, may lead to abscess formation.
- Severe, acute, purulent conjunctivitis. It may occur at any age, the most serious form is gonococcal ophthalmia neonatorum, acquired by a newborn from an infected mother. It can be prevented by the use of prophylactic topical (silver nitrate, erythromycin., tetracycl.) at birth.

AgNO3

It also protects the fetus from chlamydia "that causes trachoma"

Pelvic Inflammatory Disease (PID)

- The clinical syndrome develops in 10% to 20% of women with gonorrhea. The findings include fever, lower abdominal pain, adnexal tenderness, and leukocytosis with or without signs of local infection.
- Organisms causing PID include anaerobes and *Chlamydia trachomatis,* which may appear alone or mixed with gonococci. + NEISSERIA GONORRHOEAE
- Salpingitis and pelvic peritonitis cause scaring and infertility.
- The most serious complications of PID are infertility and ectopic pregnancy.

Disseminated Gonococcal Infection (DGI)

- Any of the local forms of gonorrhea or PID may lead to bacteremia.
- In the bacteremic phase, primary features are fever; migratory polyarthralgia; and a petechial, maculopapular, or pustular rash.
- The bacteremia may lead to metastatic infections such as endocarditis and meningitis, but the most common is purulent arthritis which involves large joints such as elbows and knees.
- Gonococci are readily cultured from the pus.

Also caused by NEISSERIA GONORRHOEAE. "Dissemination"

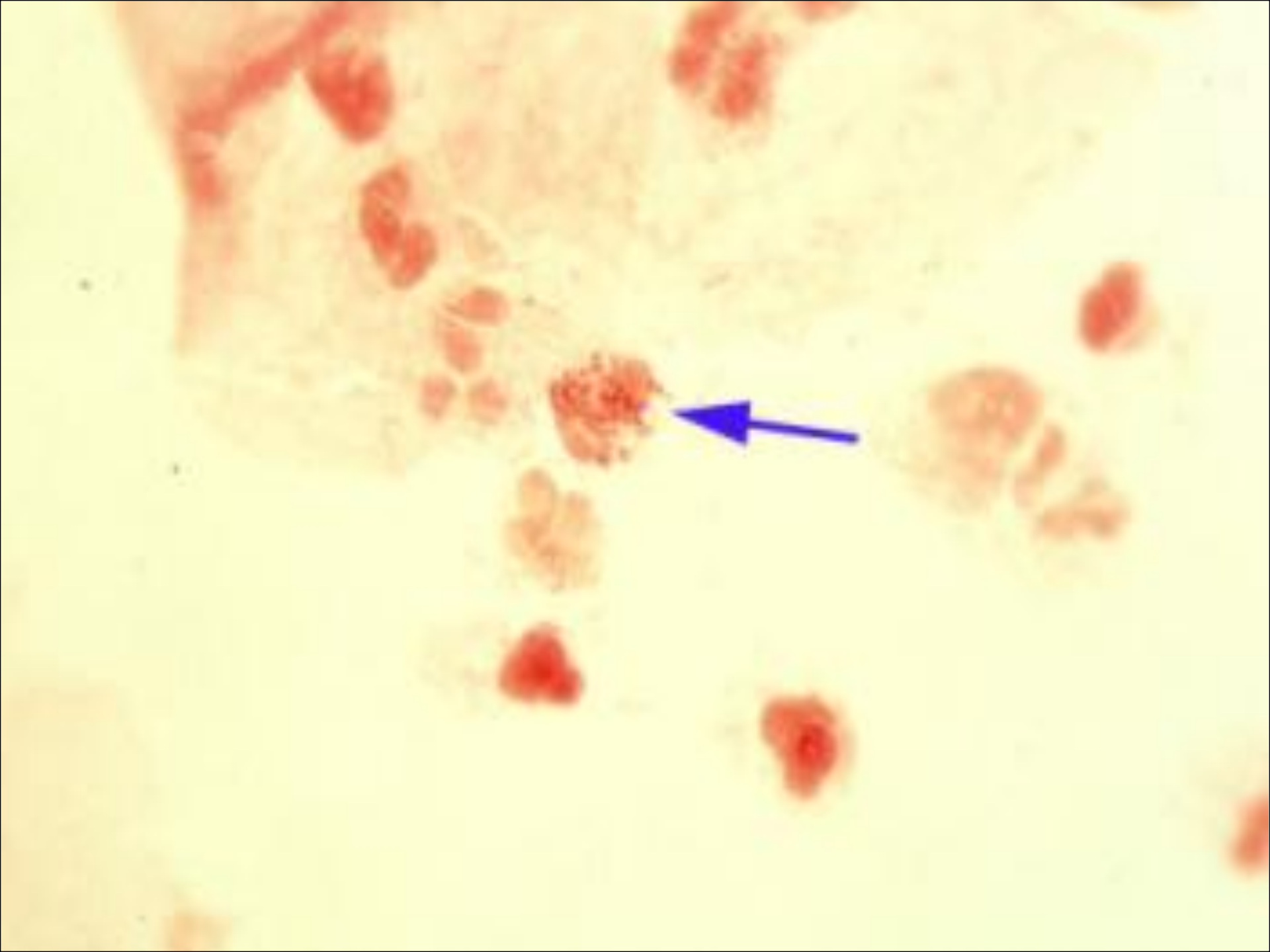
DIAGNOSIS

Gram Smear

Urethral discharge, endocervical swap, urethral swap ...

- The presence of multiple pairs of bean-shaped, Gram-negative diplococci within a neutrophil is highly characteristic of gonorrhea when the smear is from a genital site. The direct Gram smear is more than 95% sensitive and specific in symptomatic men. It is only 50 to 70% sensitive in women. Gram smear should not be used as the sole source for diagnosis when the findings are unexpected or have social (divorce) or legal (rape, child abuse) implications.

"Inside pus cells"



Culture

- In men, the best specimen is urethral exudate or urethral scrapings (obtained with a loop or special swab).
- In women, cervical swabs are preferred over urethral or vaginal specimens.
- Transport media required unless plating is immediate.
- The most common medium is Martin–Lewis agar, an enriched selective chocolate agar.
- Isolates are identified by fermentation or immunoassay.

NEISSERIA GONORRHOEAE ferments only glucose while
NEISSERIA meningitidis ferments both glucose and maltose.

Direct Detection

Molecular technology

- Immunoassay and nucleic acid hybridization methods that detect gonococci in clinical specimens without culture. Such methods could have particular importance for screening populations where culture is impractical. Of these only the DNA amplification methods have the sensitivity to substitute for culture.

Serology 😶 ... ما منعتمد عليها

- Attempts to develop a serologic test for gonorrhea have not yet achieved the needed sensitivity and specificity.

TREATMENT

- Penicillin is no longer used, because of the development of resistance.
- Because of their resistance to β-lactamases, shift in treatment of genital gonorrhea to third-generation cephalosporins has been used as single dose treatment either intramuscularly (ceftriaxone) or orally (cefixime).

Trade name: Rocephin.

- Other agents recommended for primary treatment include fluoroquinolones (ciprofloxacin or ofloxacin) and azithromycin. Doxycycline is also effective but must be given orally for 7 days.

PREVENTION

- Methods to block direct mucosal contact (condoms) or inhibit the gonococcus (vaginal foams, douches) provide protection.
- The classic public health methods of case –contact tracing and treatment are important but difficult due to the size of the infected population.
- The availability of a good serologic test would greatly aid control, as it has for syphilis.
- The development of a gonococcal vaccine awaits further understanding of immunity and its relationship to the shifting target.