SPECIFIC AND NON-SPECIFIC INFLAMMATORY DISEASES OF THE FEMALE REPRODUCTIVE ORGANS

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Assotiated professor
Pelvic inflammatory disease (PID) refers to acute infection of the upper genital tract structures in women, involving any or all of the uterus, fallopian tubes, and ovaries.

Early diagnosis and treatment are believed to be key elements in the prevention of long-term sequelae, such as infertility and ectopic pregnancy.

PID is primarily a disease of sexually active women.
Epidemiology

- **Russian Federation**: Incidence of inflammatory diseases of the female genitalia is 60-70% of the total number of visitors in outpatient clinic and 30% of hospitalized patients in a gynecological departments.

- **USA**: Pelvic inflammatory diseases are diagnosed in about 1,000,000 women annually: 250,000 of them have been hospitalized and 115 undergo surgery for this.
Classification

Localization:

- **Lower genital tract**
  - Bartholinitis
  - Vulvitis
  - Vaginitis
  - Cervicitis

- **Upper genital tract**
  - Endometritis
  - Salpingitis
  - Oophoritis
  - Parametritis
  - Pelvioperitonitis
Classification

Clinical course:
• Acute – up to 6 weeks
• Subacute – from 6 weeks to 6 months
• Chronic – more than 6 months
**Ethiology:** PID is a polymicrobial infection.

- **Non-specific** – conditionally pathogenic microflora
- **Specific**
  - *T. vaginalis*
  - *N. gonorrhoeae*
  - *C. trachomatis*
  - *U. urealyticum*
  - *M. hominis*
  - *M. tuberculosis*
  - *C. albicans*
  - *Herpes simplex virus*
  - *Cytomegalovirus*
  - *Human papilloma virus*

+ Bacterial Vaginosis
+ Anaerobic infection
1. STD-causing bacteria may enter vagina with semen

2. Bacteria may pass through cervix and enter uterus

3. Bacteria enter fallopian tubes and ovaries, which can become infected

4. Infection can leave fallopian tubes and spread to other parts of body
XIV (N) Diseases of the genitourinary system

I (A, B) Certain infectious and parasitic diseases
## Clinical course

<table>
<thead>
<tr>
<th>Pain syndrome</th>
<th>Lower abdominal pain, often following the menstruation, irradiating to perineum, lumbar and sacral region. It could be itch, bloating, hot in the perineal region.</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Menstrual dysfunction</strong></td>
<td>Algodyssmenorea, oligoopsomenorea, menometrorrhagia, premenstrual and postmenstrual spotting.</td>
</tr>
<tr>
<td><strong>Sexual dysfunction</strong></td>
<td>Dyspareunia, anorgasmia, vaginismus. Infertility.</td>
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<tr>
<td><strong>Vaginal discharge</strong></td>
<td>Purulent, mucopurulent, mucous. Odor of vaginal discharge.</td>
</tr>
<tr>
<td><strong>Disuria</strong></td>
<td>Frequent urination with a feeling of tingling, cramping.</td>
</tr>
<tr>
<td><strong>Common symptoms</strong></td>
<td>Fever, weakness, general fatigue, psycho-emotional disorders.</td>
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NON-SPECIFIC INFLAMMATION OF FEMALE REPRODUCTIVE ORGANS
Bartholinitis

N75.0 Cyst of Bartholin’s gland
N75.1 Abscess of Bartholin’s gland
N75.8 Other diseases of Bartholin’s gland
N75.9 Disease of Bartholin’s gland, unspecified
Treatment of bartholinitis

- **Conservative:**
  - antibiotic therapy
  - physiotherapy

- **Surgical:**
  - emergency (incision and drainage) – abscess of Bartholin’s gland, festering cyst of Bartholin’s gland
  - elective (cystectomy, marsupialization) – cyst of Bartholin’s gland
Vulvovaginitis

N76.0 Acute vaginitis
N76.1 Subacute and chronic vaginitis
N76.2 Acute vulvitis
N76.3 Subacute and chronic vulvitis
N76.4 Abscess of vulva
N76.5 Ulceration of vagina
N76.6 Ulceration of vulva
N76.8 Other specified inflammation of vagina and vulva
### Species of the normal microflora of the vulva, vagina and cervix in women of the reproductive age

<table>
<thead>
<tr>
<th>Gram stain</th>
<th>Facultative bacteria</th>
<th>Anaerobes</th>
</tr>
</thead>
</table>
| **Gram-positive cocci** | Staphylococcus epidermidis  
Staphylococcus aureus  
Group D Streptococcus  
B–Hemolytic Streptococcus | Peptococcus species  
Peptococcus anaerobius  
Peptococcus asaccharolyticus  
Peptococcus prevotii  
Peptococcus variabilis  
Peptostreptococcus species  
Peptostreptococcus anaerobius |
| **Gram-negative cocci** |                                          | Veillonella species  
Acidominococcus fermentas                                                 |
| **Gram-positive rods** | Lactobacillus species  
Corinebacterium species | Bifidobacterium species  
Clostridium species  
Eubacterium species  
Propionibacterium species |
| **Gram-negative rods** | Echerichia coli  
Klebsiella species  
Другие виды семейства Enterobacteriaceae  
Gardnerella vaginalis | Bacteroides melaninogenicus  
Bacteroides vulgatus  
Bacteroides species  
Fusobacterium nucleatum  
Fusobacterium species  
Leptotrichia species  
Campylobacter species «anaerobic vibrios» |
Bacterial vaginosis (BV)

Polymicrobial disease with characteristic and prolonged vaginal discharge **WITHOUT** inflammation of the mucous membrane of the vagina

Bacterial vaginosis results in complex alterations of the normal vaginal flora, which may alter host defense mechanisms in the cervicovaginal environment

**Amsel's Diagnostic Criteria**
- homogeneous creamy discharge with a special “fishy odor”;
- presence of “clue cells”
- positive amine test (fishy odor when 10% potassium hydroxide solution is added to vaginal secretions);
- vaginal pH greater than 4.5.
Differential diagnosis of vaginitis and vaginosis

• Complaints
• Clinical examination
• Microscopy of vaginal discharge
• Vaginal culture

**NB!!!** Exclusion of specific infections
## Microscopy of vaginal swabs

<table>
<thead>
<tr>
<th>State (type) of biocenosis</th>
<th>Characteristic signs</th>
<th>Nosological forms</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal biocenosis</td>
<td>Predominantly lactobacilli, single epithelial cells. Absence of Gram-negative microflora, spores, mycelium, pseudohyphae, leukocytes.</td>
<td>The typical state of the normal vaginal biotope</td>
</tr>
<tr>
<td>Intermediate type</td>
<td>Moderate or reduced amount of lactobacilli. Presence of Gram-positive cocci, Gram-negative rods. WBC, monocytes, macrophages and epithelial cells are found.</td>
<td>Frequently observed in healthy women with no complaints and clinical manifestation</td>
</tr>
<tr>
<td>Dysbiosis</td>
<td>A small amount or complete absence of lactobacilli. Abundant polymorphic Gram-positive and Gram-negative rod and coccal flora. Presence of “clue cells”. WBC count is variable, missing or incomplete phagocytosis.</td>
<td>Bacterial vaginosis</td>
</tr>
<tr>
<td>Inflammatory type</td>
<td>A large number of WBC, macrophages, epithelial cells, complete phagocytosis. Detection of gonococci, trichomonas, mycelium, pseudohyphae, spores.</td>
<td>Nonspecific vaginitis</td>
</tr>
</tbody>
</table>

Gonorrhea, trichomoniasis, mycotic infection
Treatment of vaginitis and vaginosis

- **1 stage**
  
  **Antibiotic therapy:** Hexicon, Betadine, Tergynan, Polygynax, Klion-D, Gynoflor, Dalacin

- **2 stage**
  
  **Restoration of the vaginal flora:** Acilact, Lactobacterinum, Bifidumbacterinum, Linex, Vaginorm-C
Endometritis

N71.0 Acute inflammatory disease of uterus

N71.1 Chronic inflammatory disease of uterus

N71.9 Inflammatory disease of uterus, unspecified
Endometritis: features

Often occurs as a result of pregnancy complications (spontaneous abortion, missed abortion) or after intrauterine manipulations (criminal abortion, artificial abortion, curettage of the uterus, insertion of the IUCD, HSG, etc.)

Diagnosis

Acute endometritis
- Bimanual examination
- Microscopy and culture of cervical discharge
- USG
- Blood test, CRP

Chronic endometritis
- Hysteroscopy
- Dilatation, curettage and histopathological examination of endometrium, endometrial biopsy
Salpingitis and oophoritis

N70.0 Acute salpingitis and oophoritis
N70.1 Chronic salpingitis and oophoritis
N70.9 Salpingitis and oophoritis, unspecified
Complicated salpingitis and oophoritis

- Hydrosalpinx
- Saktosalpinx
- Pyosalpinx
- Pyosaktosalpinx
- Pyovarum
- Tubo-ovarian complex

Pelvic inflammatory disease (PID)

- Endometritis
- Salpingitis and oophoritis and complications
- Pelvioooperitonitis
Pathogenesis of PID

- Infectious agents
  - Vaginitis, cervicitis
- Related factors
- PID
- Infertility
- Pelvic pain
- Pathology of pregnancy
  - Ectopic pregnancy
  - Miscarriage
  - Puerperal endometritis
- Pathology of pregnancy
  - Tubo-ovarian abscess
  - Pelviperitonitis
- Adhesive disease
  - Sepsis
  - Death
• Fitz Hugh Curtis Syndrome – Inflammation of the liver capsule can occur with chlamydia and gonococcal infection.

• Patient has right upper quadrant pain & liver tenderness.
## PID diagnostic criteria

<table>
<thead>
<tr>
<th>Minimum</th>
<th>Additional</th>
<th>Most specific</th>
</tr>
</thead>
<tbody>
<tr>
<td>Uterine tenderness</td>
<td>Oral temperature &gt; 38,3°C</td>
<td>Endometrial biopsy with histopathologic evidence of endometritis</td>
</tr>
<tr>
<td>Adnexal tenderness</td>
<td>Abnormal cervical or vaginal mucopurulent discharge</td>
<td>Transvaginal sonography or magnetic resonance imaging techniques showing thickened, fluid-filled tubes with or without free pelvic fluid or tubo-ovarian complex, or Doppler studies suggesting pelvic infection (e.g. tubal hyperemia)</td>
</tr>
<tr>
<td>Cervical motion tenderness</td>
<td>Presence of abundant numbers of WBC on saline microscopy of vaginal fluid</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Elevated erythrocyte sedimentation rate</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Elevated CRP</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Laboratory documentation of cervical infection with N. gonorrhoeae or C. trachomatis</td>
<td></td>
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<td></td>
<td></td>
<td>Laparoscopic abnormalities consistent with PID</td>
</tr>
</tbody>
</table>
Principles of PID treatment

• Antibiotic therapy:
  cephalosporins III + metronidazole,
  lincosamides + aminoglycosides III,
  quinolones + metronidazole,
  doxycycline + macrolides,
  inhibitor protected aminopenicillins
• Fluid treatment for detoxification
• Nonsteroidal anti-inflammatory drugs
• Immunomodulating drugs
• Physiotherapy

NB!!! Surgery – in tubo-ovarian abscess, pyoperitonitis, ineffectiveness of conservative treatment
CDC guideline for acute PID – inpatient therapy

Cefoxitin (2 g intravenously every 6 hours) or cefotetan (2 g IV every 12 hours)
plus
Doxycycline (100 mg orally every 12 hours).
IV therapy is discontinued 24 hrs after patient is fever free..
Continue oral doxy for 14 days.
Regimen B

Clindamycin (900 mg intravenously every 8 hours) plus gentamicin loading dose (2 mg/kg of body weight) followed by a maintenance dose (1.5 mg/kg) every 8 hours. Single daily intravenous dosing of gentamicin may be substituted for three times daily dosing.
Indications for surgical intervention

- USG guided pus aspiration - Pelvic abscess, subhepatic abscess
- Posterior colpotomy - Pelvic abscess
- Laparoscopic aspiration of pus or drainage or adhesiolysis
- Laparotomy for to abscess/ or rupture of same or multiple collection in abdomen
- Salpingoophorectomy.
Management of Sexual partners

• Contact partners within 6 months of onset of disease.
• Screen for gonococcal/chlamydial infection
• If screening not possible, start empirical therapy.
• Avoid intercourse till the partner completes treatment.
Counseling

• Early treatment reduces the risk of sequelae but does not eliminate it.
• Barrier contraception reduces risk
• Recurrence of infection increases the risk of infertility.
• Sexual partner must be treated.
Chronic PID

Women who are inadequately treated, untreated or have recurrent infections, chronic PID ensues.
Chronic PID- Pathology

- Tubo ovarian mass
- Pyosalpinx pus
- Hydrosalpinx
- Frozen pelvis
Risk Factors for PID

• Young age
• Low socioeconomic status
• Multiple sex partners
• Unmarried/ widowed women
• Past h/o STI
• Vaginal douching
• IUCD for 3 weeks after insertion
• Smoking/ substance abuse.
SPECIFIC INFLAMMATORY DISEASES OF FEMALE GENITAL ORGANS: METHODS OF DIAGNOSIS
Methods with the lowest diagnostic value

**Complaints, medical history, examination**
- Nonspecific
- There are some characteristic features: "fishy" odor of discharge, "cottage-cheese" discharge, blisters, etc.
- Multiple sexual partners

**Microscopy**
- Information content of 30-40%
- Determined by the resolution of the microscope and the size of the microorganism
- More useful to extracellular bacteria
Serological methods

**EIA – enzyme multiplied immunoassay**
- Information content of 70-80%
- Performed with serum
- Reveals not the causative agent but the response of the organism to its implementation: Ig M, Ig G, Ig A
- The method is not effective for microorganisms with low immunogenicity

**ELISA – enzyme-linked immunosorbent assay**
- Information content of 70-90%
- Conducted with cervical, vaginal and urethral swab
- Detects antigens of microorganisms
The most informative methods

Culture

- «Gold» standard of diagnosis – 100%
- Requires different culture media
- Needs time
- The most expensive method of diagnosis

PCR – polymerase chain reaction

- Information content of 99%
- It’s possible to diagnose multiple infections simultaneously
- Allows to determine the number of agents

NASBA – nucleic acid sequence based amplification
INFECTIONS WITH A PREDOMINANTLY SEXUAL MODE OF TRANSMISSION (STD)
STD

Classic venereal diseases
- Syphilis
- Gonorrhea
- Chancroid
- Lymphogranuloma venereum
- Donovanosis

Infections with a predominantly sexual mode of transmission
- Trichomoniasis
- Chlamydial infection
- Genital herpes
- HPV infection

Infection with a possible sexual mode of transmission
- Cytomegalovirus infection
- Mycoplasma infection
- Candidiasis
- HIV infection
- Tuberculosis
Urogenital trichomoniasis

*Trichomonas vaginalis*

A59.0 Urogenital trichomoniasis
Trichomoniasis: features

Diagnosis:
- Examination
- Native smear microscopy
- Microscopy of stained smears
- PCR

Treatment:
- **Imidazoles**: Metronidazole, Tinidazole, Ornidazole
- **Vaccine**: Solcotrichovac
- **Combined drugs for vaginal use**: Neo-Penotran, Tergynan, Klion-D
Urogenital chlamydial infection (UCI)

Chlamydia trachomatis

A56.0 Chlamydial infection of lower genitourinary tract
A56.1 Chlamydial infection of pelvioperitoneum and other genitourinary organs
A56.2 Chlamydial infection of genitourinary tract, unspecifed
A56.3 Chlamydial infection of anus and rectum
UCI: outcome
## UCI: features

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Culture</td>
<td>• <strong>Macrolids:</strong> Azithromycin,</td>
</tr>
<tr>
<td>• PCR</td>
<td>Josamycin</td>
</tr>
<tr>
<td>• NASBA</td>
<td>• <strong>Tetracyclines:</strong> Doxycyclin</td>
</tr>
<tr>
<td>• ELISA</td>
<td>• <strong>Quinolones:</strong> Ofloxacin</td>
</tr>
</tbody>
</table>
Urogenital mycoplasma infection (UMI)

Mycoplasma hominis
Mycoplasma genitalium
Ureaplasma urealyticum
Ureaplasma parvum

A49.3 Mycoplasma infection, unspecified
UMI: features

**Diagnosis**
- Culture – diagnostic titer $10^4$ CFU/ml
- PCR – real-time
- NASBA

**Treatment**

*Antibiotic therapy*

is indicated if M. genitalium or other myco-ureaplasma in titer $10^4$ CFU/ml or more are detected

**Macrolides:** Josamycin, Clarithromycin, Azithromycin

**Tetracyclines:** Doxycycline

**Quinolones:** Levofloxacin
Vulvovaginal candidiasis (VVC)

Candida albicans
Candida glabrata
Candida krusei
Torulopsis glabrata

B37.3 Candidiasis of vulva and vagina
B37.4 Candidiasis of other urogenital sites
VVK: clinical manifestation
VVC: features

**Diagnosis criteria:**
- Vaginal pH 4.0-4.5
- No odor
- Detection of yeasts or pseudohyphae in wet swabs (40-60%)
- detection of yeasts or pseudohyphae in a smear Gram (65%)
- culture on medium Sabouraud

**Treatment**
- **In vagina:** Butoconazole, Ketoconazole, Clotrimazole, Nystatin
- **Per os:** Fluconazole, Itraconazole
Genital herpesviral infection (GHI)

*Herpes simplex virus*

A60.0 Herpesviral infection of genitalia and urogenital tract
A60.1 Herpesviral infection of perianal skin and rectum
A60.9 Anogenital herpesviral infection, unspecified
GHI: clinical manifestation
## GHI: features

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Examination</td>
<td>Guanosine analogue: Aciclovir,</td>
</tr>
<tr>
<td></td>
<td>Famciclovir, Valaciclovir</td>
</tr>
<tr>
<td>• PCR</td>
<td>Interferons and interferon inducers: Kipferon,</td>
</tr>
<tr>
<td></td>
<td>Viferon</td>
</tr>
<tr>
<td>• Culture – in chicken embryos</td>
<td>Immunoglobulins:</td>
</tr>
<tr>
<td></td>
<td>Specific antiherpes</td>
</tr>
<tr>
<td></td>
<td>immunoglobulin,</td>
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<tr>
<td></td>
<td>Human normal</td>
</tr>
<tr>
<td></td>
<td>immunoglobulin</td>
</tr>
</tbody>
</table>
Cytomegaloviral infection (CMVI)

Cytomegalovirus

B25.8 Other cytomegaloviral diseases
CMVI: features

Clinical manifestation
- Asymptomatic indolent lesion of female reproductive organs
- Activated in pregnancy: spontaneous and missed abortion, congenital anomalies

Diagnosis
- Microscopy and fluorescent test with urine sediment
- PCR
- NASBA
- ELISA
Papillomaviral infection (PVI)

*Human Papillomavirus*

A63.0 Anogenital (venereal) warts

B97.7 Papillomavirus as a cause of diseases classified elsewhere
PVI: clinical manifestation
PVI: features

**Diagnosis**
- Clinical and visual method
- Colposcopy
- Pap smear
- PCR

**The goals of treatment:**
- Destruction of exophytic warts and atypical changes in the epithelium:
  - surgical
  - chemical: Solcoderm, Condyline, Fluorouracil
- Correction of immune homeostasis

**Prevention of HPV - vaccine Gardasil and Cervarix:**
for girls and women aged 9-25 years,
for boys and men 11-21 years
The end