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REVIEW ARTICLE

Updated French guidelines for diagnosis and management of pelvic inflammatory disease

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ABSTRACT

Background: Pelvic inflammatory disease (PID) is commonly encountered in clinical practice. *Objectives:* To provide up-to-date guidelines on management of PID. *Search strategy:* An initial search of the Cochrane database, PubMed, and Embase was performed using keywords related to PID to identify reports in any language published between January 1990 and January 2012, with an update in May 2015. *Selection criteria:* All identified reports relevant to the areas of focus were included. *Data collection and analysis:* A level of evidence based on the quality of the data available was applied for each area of focus and used for the guidelines. *Main results:* PID must be suspected when spontaneous pelvic pain is associated with induced adnexal or uterine pain (grade C). Pelvic ultrasonography is necessary to exclude tubo-ovarian abscess (grade B). Microbiological diagnosis requires vaginal and endocervical sampling for molecular and bacteriological analysis (grade B). First-line treatment for uncomplicated PID combines ofloxacin and metronidazole for 14 days (grade B). Treatment of tubo-ovarian abscess is based on drainage if the collection measures more than 3 cm (grade B), with combined ceftriaxone, metronidazole, and doxycycline for 14–21 days. *Conclusions:* Current management of PID requires easily reproducible investigations and treatment, and thus can be applied worldwide.
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1. Introduction

Pelvic inflammatory disease (PID) is commonly seen in clinical practice. PID includes different forms of complicated and uncomplicated uterine-adnexal infections: endometritis, salpingitis, tubo-ovarian abscess, and pelvic peritonitis of genital origin [1]. Isolated endocervicitis is excluded from the definition of PID [1].

The present report summarizes up-to-date guidelines from the French College of Gynecologists and Obstetricians (CNGOF) that are designed for clinicians working in women's health, whether gynecologists, obstetricians, surgeons, radiologists, infectious disease specialists, or general practitioners.

2. Materials and methods

The CNGOF appointed a committee to select experts, compile a list of questions to answer, and summarize recommendations. The experts selected were specialists in obstetrics/gynecology, microbiology, or infectious disease, and were all working in French university hospitals and involved in the specialty of PID. The experts searched the Cochrane Central Register of Controlled Trials, PubMed, and Embase for reports published between January 1990 and January 2012, using the search terms "PID," "diagnosis," "treatment," "follow-up," "sequelae," "fertility," and "contraception." Some additional keywords were also used: "post-abortum," "post-partum," "puerperal infection," "thrombophlebitis," "prophylactic antibiotics," "hysterography," "hysteroscopy," "intra-uterine device," and "placenta removal." No language restrictions were applied. An additional search was subsequently performed in May 2015.

All studies relevant to the questions to be answered were assessed, whether prospective or retrospective. They were first selected by

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looking at the abstract, followed by full-text review. Meta-analyses were preferred when available.

For each question, the valid scientific data from identified studies were analyzed by the experts and given a level of evidence (LE), which was based on the quality of the data available. LE was defined according to the rating scheme developed by the French National Authority for Health: LE1 indicates the evidence comes from a high-power randomized comparative trial or meta-analysis of randomized comparative trials; LE2 indicates the evidence comes from low-power randomized trials, well-conducted non-randomized comparative studies, and cohort studies; LE3 indicates the evidence is from case–control studies; and LE4 indicates the evidence is from non-randomized comparative studies with substantial bias, retrospective studies, cross-sectional studies, and case series [2].

On the basis of the available scientific data, practice guidelines were formulated and given a grade. Grade A indicates that the guidelines are based on established scientific evidence, grade B indicates a basis of scientific presumption, and grade C indicates a basis of a low level of evidence. Guidelines established on the basis of professional consensus (PC; no conclusive scientific evidence) were reduced to a strict minimum.

The CNGOF committee selected a separate group of external readers and physicians from the various specialties involved (gynecologists, obstetricians, surgeons, infectious disease specialists, radiologists, and general practitioners) and diverse practice settings (private and public) to assess the answers to the list of posed questions and the formulated guidelines. The original full guidelines were published in French in 2012 [2–10] and were subsequently reviewed [11–16].

3. Results

3.1. Diagnosis

3.1.1. Clinical and paraclinical criteria

Major and additive criteria must be used for the diagnosis of PID (Box 1) [3]. The presence of major criteria (in the absence of another diagnosis) is sufficient to justify initiation of treatment (grade C). A complete blood count is required, with a C-reactive protein assay, but the absence of abnormalities does not rule out a diagnosis of uncomplicated PID (grade B). Routine pelvic ultrasonography must be systematically performed both to identify specific signs of PID and to rule out a form of complicated PID (tubo-ovarian abscess) or another disease (grade B).

In cases of diagnostic doubt or in minor forms, endometrial biopsy sampling is necessary; this histologic examination is both sensitive and specific for a diagnosis of PID (grade B). The relevant criteria are: 1) neutrophil polymorphonuclear leukocyte infiltrate with at least five polymorphonuclears per field (×400) of superficial endometrial epithelium, and 2) at least one plasmacyte per field (×120) of endometrial tissue [17].

If diagnostic doubt remains after clinical and ultrasonographic examination, abdominopelvic computed tomography (CT) should be performed to specify the abnormalities and to make some differential diagnoses (grade C). Second-line magnetic resonance imaging (MRI) can be considered.

For uncomplicated PID, diagnostic laparoscopy is not recommended as first-line treatment (grade B), but it is the reference examination when diagnostic doubt remains after imaging (grade B) [11]. The following criteria must be used to document the laparoscopic diagnosis (grade C): tubal edema, tubal erythema, and fimbrial exudate at the level of the infundibulum (LE2). Concomitant histologic, endometrial, or fimbrial biopsy sampling is recommended when the laparoscopy is macroscopically normal and PID is clinically suspected (grade C).

Box 1
Major and additive criteria for the diagnosis of PID.

Major criteria
Absence of these criteria tends to rule out a PID diagnosis.

- Spontaneous pelvic pain (in the absence of another disorder) AND
- Induced adnexal pain AND/OR
- Pain on uterine mobilization

Additive criteria
Each of these criteria increases the probability of PID.

- History: sexually transmitted infection; postpartum or post-abortion; recent endouterine maneuvers; rectal syndrome (tenesmus, other anal spasms); vaginal bleeding
- Clinical examination: temperature > 38 °C; purulent leukorrhea
- Laboratory tests: elevated C-reactive protein; presence of *Chlamydia trachomatis*, *Neisseria gonorrhoeae*, or *Mycoplasma genitalium* on bacteriological examination; endometritis on endometrial biopsy sample; salpingitis on fimbrial biopsy sample
- Ultrasonography: thickening of the tubal wall (>5 mm); cogwheel sign (thickened tubal fringes resembling incomplete septa); heterogeneous latero-uterine mass potentially septated with fine echoes

Abbreviation: PID, pelvic inflammatory disease.

3.1.2. Microbiological diagnosis

When PID is suspected, two steps are required [4,12]. First, a vaginal sample needs to be obtained for direct examination to look for altered leukocytes (count) and other abnormalities (trichomoniasis, bacterial vaginosis), and for molecular tests and nucleic acid amplification testing to identify *Chlamydia trachomatis*, *Neisseria gonorrhoeae*, or *Mycoplasma genitalium* (grade B). Second, an endocervical sample needs to be obtained after disinfection of the exocervix, with bacteriological analysis (aerobic and anaerobic bacteria, including capnophilic species) (grade A).

If a laparoscopy or laparotomy is performed, tuboperitoneal samples must be taken (grade B). These samples do not alone justify these surgical procedures because their performance is not better than those of vaginal and endocervical samples (LE2).

Serology for *C. trachomatis* is not useful for diagnosis of PID in the acute phase or for monitoring disease course (grade B). If PID is associated with a sexually transmitted infection (STI), a supplementary serologic workup for other STIs should be performed (grade C).

3.2. Management

3.2.1. Uncomplicated PID

Data from the literature cannot differentiate between the treatment of uncomplicated endometritis and that of uncomplicated salpingitis [5].

In cases of suspected PID, probabilistic broad-spectrum antibiotic therapy must begin early, without awaiting bacteriological results, to optimize fertility preservation (grade B).

In cases of uncomplicated PID, neither inpatient nor intravenous treatment provides any advantages compared with outpatient treatment (LE1) and does not affect subsequent prognosis (LE2). Therefore, the use of the oral (and/or intramuscular) route in an outpatient setting is recommended whenever possible (grade B).

The combination of 400 mg ofloxacin twice a day and 500 mg metronidazole twice a day for 14 days must be initiated as first-line treatment, in the absence of contraindications, because it has been evaluated against a reference treatment and is in line with current bacteriological constraints (grade B). An intramuscular injection of 500 mg ceftriaxone must be given immediately if there is a high risk of multiple sexually transmitted infections, there are risk factors, or

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