Sequelae of infection of the upper genital tract are the major cause of infertility in the female and most probably also of extra-uterine pregnancy (Walters et al., 1988; Westrom & Mårdh 1990). At present there is a 'boom' of extra-uterine pregnancy cases which to a great extent seems to be the result of the epidemic of sexually-transmitted disease (STD) that occurred at the beginning of the 1980s (and which is still on-going). Also the pattern of contraceptive usage has had an impact on the epidemiology of extra-uterine pregnancy as certain contraceptives influence the inflammatory response in pelvic inflammatory disease (PID) and the likelihood of ascending genital infection (see further below).

In many European countries there has recently been a decrease in the number of hospitalized cases of acute salpingitis (Weström, 1988). This trend may partly be due to a true decrease in PID cases, related to a reduction of the annual number of cases of gonorrhoea in many regions, for example, but also to a change in the aetiology of the condition with a relatively greater proportion of cases of chlamydial as against gonococcal salpingitis. This may have meant a switch to clinically milder cases, cases that are treated without hospital admission, if at all (cf. Mårdh, Paavonen & Puolakkainen, 1981). In primary PID, anaerobic bacterial infections are uncommon. Earlier there was a discrepancy in the assumed importance of both chlamydial and anaerobic infections in PID, between the USA and Europe. The view expressed in the USA of the aetiological spectrum of PID, however, has by this time become more and more similar to that of European research workers (Welner-Hanssen et al., 1986; Washington, Browner & Korenbrof, 1988).

An aetiological diagnosis of PID is difficult to obtain, even when sampling is made from the upper genital tract. As diagnostic laparoscopy is comparatively easy to perform and can be carried out in ambulant patients; in most PID cases it provides the best type of sample material for aetiological studies (Mårdh et al., 1981). However, to obtain an answer about aetiology, or histological examinations, generally takes too long to be useful for therapeutic decision-making in assumed PID cases. Therefore an epidemiological approach to the choice of therapeutic agents in PID must be considered. Antibiotic therapy in PID should be active against most strains of the most common aetiological agents, at least covering *Chlamydia trachomatis* and *Neisseria gonorrhoeae*. In the case that cervical gonorrhoea is diagnosed by direct microscopy, 'standard' therapy for gonorrhoea (which now varies widely among different countries) is given, followed by 'standard' therapy covering *C. trachomatis*.

In all cases of assumed PID, a gonococcal culture should be made (even if phagocytosed diplococci have been found in genital secretions) because of the highly varied susceptibility pattern of the presently circulating strains of *N. gonorrhoeae*. Diagnostic tests should always be performed for *C. trachomatis*, even if no development of antibiotic resistance has yet been observed in strains of this species, because a positive test forms the basis for contact tracing. In most instances of PID a tetracycline or a macrolide has so far been the drug of choice. The treatment of PID may be with a tetracycline analogue, e.g., 200 mg doxycycline daily for 10 days, or 300 mg lymecycline twice daily for 10 days, or 500 mg erythromycin twice daily, as recommended in the WHO's recently published 'Guidelines for Prevention of Chlamydial Infections' (Guidelines, 1989). The value of several new macrolides for the treatment of chlamydial infections in women, e.g., azithromycin, to be taken as one single dose, remains to be established, as does the role of certain quinolones, e.g., ofloxacin, which has been shown to be particularly active against chlamydiae (Liebowitz et al., 1986).

The occurrence of *N. gonorrhoeae*, *Mycoplasma hominis* and of many anaerobic
bacterial species, e.g., of Bacteroides and Mobiluncus spp. (common vaginal isolates in women with bacterial vaginosis which have recently been detected in mixed cultures of tubal secretions in PID cases) and of gonococcal strains with chromosomal resistance to tetracycline, implies a threat to successful treatment of PID by the conventional regimen. Further spread of highly tetracycline-resistant (MIC, 4 mg/l) gonococcal strains (resistance mediated by the newly discovered plasmid coding exclusively for tetracycline-resistance as well as by other mechanisms) may in the future further restrict the value of tetracycline treatment in PID (Morse et al., 1986; Gascoyne, Heritage & Hawkey, 1990). Erythromycin and other macrolides are not first-line treatment for gonococcal infections and they are not active against Myco. hominis. Myco. hominis is often tetracycline-resistant (Christiansson & Mardh, 1983; Koutsky et al., 1983).

Provided one is dealing with a susceptible (non-β-lactamase-producing) strain of N. gonorrhoeae in a case of gonococcal PID, a β-lactam antibiotic is still the drug of choice. β-Lactam antibiotics seem also to be active against C. trachomatis. Theoretically, however, there is not yet an explanation of why such drugs should be effective. Nevertheless, there is clinical evidence that β-lactam antibiotics can be therapeutic alternatives in chlamydial infections, at least in male cases of nongonococcal urethritis (NGU) (Ibsen et al., 1989).

In cases of PID where there are reasons to assume that anaerobic bacteria might be involved (e.g., secondary PID and in cases with pelvic abscess formation), a nitromidazole should be instituted in combination with a tetracycline (Heinonen et al., 1986). Approximately 40% of all cases of chlamydial cervicitis, i.e., the most common cause of this condition, have concomitant endometritis (Paavonen et al., 1985). In complicated upper genital chlamydial infections a longer course of antibiotic therapy than in cervicitis is generally recommended. Without invasive techniques it is, however, generally not possible to distinguish uncomplicated (cervicitis) from complicated (PID) genital chlamydial infections. Therefore the dose regimen recommended in any case of genital chlamydial infection in the female should logically follow that recommended for complicated (PID) chlamydial infections (Guidelines, 1989). It seems advisable therefore to use at least ten days or probably even 14 days of antibiotic therapy. Undertreatment with, for example, too small doses of tetracyclines (e.g., 200 mg doxycycline as a start dose followed by 100 mg per day for seven to ten days), resulting in too low concentrations of the drugs, must be avoided (Danielsson, Forslin & Kjellander, 1986). Therapy resulting in chronic 'latent' tubal, endometrial and cervical infections with chlamydiae may be due to undertreatment. This may lead to tubal damage resulting in extrauterine pregnancy, occlusion causing infertility, or to further spread to the abdominal cavity with adhesion causing chronic abdominal pain.

There are other factors than effective antibiotic therapy that may be of importance for a good fertility prognosis after salpingitis. To maintain fertility is the ultimate goal for any treatment and behavioural advice to patients with this condition is necessary. The choice of contraceptive method is important, as, for example, certain oral contraceptives may protect against reinfection of the fallopian tubes (Svensson, Weström & Mardh, 1984), while an intrauterine device involves a future increased risk of ascending infections (Weström, Bengtsson & Mardh, 1976). There have been some observations that the use of anti-inflammatory drugs in therapy of PID might result in a better fertility prognosis. A renewed interest in the role of such drugs has recently emerged but their true value has not yet been established.

To sum up, a number of questions have to be addressed in the treatment of PID. Is the antibiotic regimen prescribed likely to be effective (treatment on epidemiological grounds or from knowledge of the antibiotic susceptibility pattern of isolated aetiological agents)? Is the drug regimen used adequate (daily dose and length of therapy)? Has contact tracing been performed (treatment of all partners in ongoing relationships, independently of the outcome of aetiological studies, and of casual partner(s) when STD-agents have been isolated)? Should additional (non-antibiotic) therapy be given (antifungal or anti-inflammatory drugs)? Has contraceptive advice for the future been given? Has the patient been told about the character of her disease (likely mode of transmission of causative agent and risk of sequelae)? Has the patient been informed about means of protection for herself in the future from genital infections, in order to reduce the increased risk of tubal reinfection seen after a primary episode of PID? Has the patient, if concerned about her future fertility, been given the chance to discuss this matter thoroughly with her physician? This consul-
tation is probably best conducted at a return visit.

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References


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