ISSN 0125-7447

รายงานการเฝ้าระวังโรคประจำสัปดาห์

WEEKLY EPIDEMIOLOGICAL SURVEILLANCE REPORT

VOLUME 17 NUMBER 25
JUNE 27, 1986

Neisseria Gonorrhoea: Resistance to Multiple Antibiotics 293

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สถานการณ์โรค 304

บทความ

Neisseria Gonorrhoeae: Resistance to Multiple Antibiotics

The constant use and abuse of chemotherapeutic agents in human medicine, in animal breeding, and in agriculture have led to the selection and spread of bacteria that are highly resistant to today's antibiotics. The loss of efficacy of penicillin G against staphylococci in the early 1950s was followed ten years later by the multiple antibiotic resistance of *Proteus, Pseudomonas aeruginosa,* and later of *Shigella* and *Salmonella*. Multiple antibiotic resistance is a worldwide problem that demands international attention. This paper provides general guidelines, based on WHO recommendations,[1] for the appropriate use of antibiotics in the treatment of gonococcal infections to maintain their optimal effectiveness under current conditions.

General Misuse of Antibiotics in Humans

Antibiotic resistance is widely attributed to the overuse and other misuse of antibiotics for unnecessary treatment of illness and unjustified prophylaxis. Social pressures such as the anxiety of the patient and his family and the sometimes unrealistic eagerness of the physician to do the best for his patient favor the excessive use of antibiotics, particularly in primary health

care. Considerable overuse of tetracycline, penicillin, and chloramphenicol has led to the development and spread of resistant bacterial strains, particularly through the mechanism of transmissible plasmid-mediated resistance. Damage by antibiotics to the physiological bacterial flora may eliminate germs that biologically suppress other organisms, thereby favoring the proliferation of potentially pathogenic germs, as examples, *Candida* after application of tetracyclines or *Chlamydia* and *Mycoplasma* after the use of beta-lactam antibiotics.

As a general principle, antibiotic treatment is inappropriate under the following conditions:

- When the agent used is unsuitable or given in incorrect dosage.
- When the disease can be controlled by other, simpler, equally effective measures.
- When there is no clear evidence that serious clinical infection would occur in the absence of prophylactic use of antibiotics.

Use of Antibiotics in Treating Sexually Transmitted Diseases

The following criteria influence the choice of an antibiotic regimen for the treatment of sexually transmitted diseases (STD):

Efficacy

Efficacy is the single most important criterion in choosing among available regimens. Cure rates lower than 95% may be responsible for the development of resistant strains and thus rapidly limit the usefulness of the respective drug. Regimens with cure rates lower than 90% are unacceptable in the therapy of STD. Practitioners are cautioned not to use less that the recommended doses.

Toxicity

Patients with STD caused by resistant bacteria sometimes require higher doses than those with other infections and the schedules employed are often at the limits

of human tolerance. Toxicity also has to be taken into account in reinfected patients exposed to repeated courses of antimicrobial agents. Pregnant women should be given special attention.

Cost

Although cost is a major limiting factor in developing areas, the use of cheap but inappropriate antibiotics or regimens may result in expensive consequences, such as inefficacy, drug resistance, or secondary diseases.

Compliance

Noncompliance usually decreases the success of treatment and contributes to the risk of resistance. Multidose regimens, such as those used for tetracyclines, may limit effectiveness, and therefore single-dose or very-short-course regimens should be used.

Hazard for Other Uses

Single-dose regimens used in STD treatment reduce the exposure of human flora to antimicrobials and thus the risk of the development of resistance among these organisms. Therefore, drugs that have no uses beyond the treatment of STD should be employed preferentially.

Comments on Individual Drugs Used for Treating Gonorrhea

Aqueous procaine penicillin G (APPG) is administered in well-tolerated doses in most instances. The increased occurrence of penicillinase-producing strains of *N. gonorrhoeae* limits the value of penicillin in some countries. However, its usefulness in aborting coincident syphilis is important and has been supported by observations from Singapore, where, when treatment for gonorrhea was shifted from penicillin to aminoglycosides, the incidence of syphilis increased.

Ceftriaxone is a third-generation cephalosporin and has the highest antigonococcal activity in vitro. It is highly effective against penicillinase-producing strains

and can be administered intramuscularly in small doses. It appears to have very low toxicity and can be used in pregnancy. However, its cost reduces its applicability in many countries, and it thus remains a drug of second or third choice.

Cefotaxime and *cefoxitin* are quite similar, but neither drug reliably cures pharyngeal gonococcal infection.

Spectinomycin and the *aminoglycosides* are highly effective and widely used against penicillinase-producing gonococci. However, reports of the isolation of spectinomycin-resistant, penicillinase- and non-penicillinase-producing gonococcal strains have recently increased. Spectinomycin resistance may develop as a result of one single-dose treatment. Infections with resistant strains may be treated with cephalosporins as mentioned above. Spectinomycin should be reserved for treatment of patients who are infected with penicillinase-producing strains.

Kanamycin (aminoglycoside) has been used in some areas instead of spectinomycin because of its lower price. Kanamycin A is preferred to kanamycin B, but toxicity limits the application of both drugs. Neither spectinomycin nor kanamycin aborts coincident incubating syphilis.

Thiamphenicol is an effective drug. Potential bone marrow depression should be considered, particularly in patients who receive repeated courses.

Tetracycline resistance of gonococcal infections has reached unacceptably high levels in many areas, for example, in East Asia. Tetracyclines, however, are still highly active against infections by chlamydia and mycoplasmas. Nevertheless, tetracycline-resistant isolates of *Ureaplasma urealyticum* were recently identified in the United States of America. Tetracyclines are not recommended for pregnant women because of the risks of maternal hepatic toxicity and fetal (skeletal) deposition.

Rosoxacin is only 70 to 93% efficacious in infection by *N. gonorrhoeae*. Its value is further limited by bacterial resistance, which might develop during therapy, and by the fact that 30 to 40% of the patients so treated develop side reactions in the central nervous system.

(อ่านต่อฉบับหน้า : Vol. 17 No. 26)