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Emergence of multi-drug resistant *Neisseria gonorrhoeae* – Threat of global rise in untreatable sexually transmitted infections

Emergence of multi-drug resistant *Neisseria gonorrhoeae* – Threat of global rise in untreatable sexually transmitted infections

Key facts

- Resistance of *Neisseria gonorrhoeae* (*N. gonorrhoeae*) to antibiotics, including quinolones, has increased rapidly in recent years and has reduced the options for treatment.
- High rates of penicillin, tetracycline, and quinolone resistance have long been detected and these medicines are currently not recommended for the treatment of gonorrhoea in the majority of countries in the world.
- Gonococcal resistance to third-generation cephalosporins given orally has emerged in Japan, Norway and elsewhere, with even wider spread of gonococci that have determinants for cephalosporin resistance!

Situation today:

Gonorrhoea is a sexually transmitted infection (STI) that remains a major public health concern. It represents 106 million of the estimated 498 million new cases of curable STIs – that also includes syphilis, chlamydia and trichomoniasis – which occur globally every year.

Antimicrobial resistance (AMR) in *N. gonorrhoeae* became apparent shortly after the introduction of antimicrobials into clinical practice. This has continued to increase and instances of AMR to tetracyclines, macrolides (including azithromycin), sulfonamide and trimethoprim combinations and, more recently, quinolones. Reports are now emerging of decreasing gonococcal susceptibility to extended-spectrum cephalosporins. There are verified treatment failures to cefixime (oral cephalosporin) treatment in Australia, Japan, Norway and Sweden as well as reports from China (Hong Kong SAR) and the United Kingdom. This emergence of decreased susceptibility of *N. gonorrhoeae* to the “last line” treatment option of cephalosporins together with AMR already shown to penicillins, sulphonamides, tetracyclines, quinolones and macrolides (including azithromycin) make *N. gonorrhoeae* a multidrug-resistant organism.

Unrestricted access to antimicrobials, inappropriate selection and overuse of antibiotics, and suboptimal quality of antibiotics, as well as inherent genetic mutations within the organism have contributed to the development of this pattern of resistance in *N. gonorrhoeae*. Extra genital infections – anorectal and pharyngeal – particularly affect key populations such as men who have sex with men. This may also play an important role in the development of resistant strains as *N. gonorrhoeae* interact and exchange genetic material with other co-infections in these anatomical sites.

Implications:

Gonococcal infections have critical implications to reproductive, maternal and newborn health including:

- a fivefold increase of HIV transmission;
- infertility, with its cultural and social implications;
- inflammation, leading to acute and chronic lower abdominal pain in women;
- ectopic pregnancy and maternal death;
- first trimester abortion;
- severe neonatal eye infections that may lead to blindness.

The financial costs of these complications as well as the disability-adjusted life years are very high and add to the global health burden resulting from unsafe sex.

The emergence of different forms of resistance in *N. gonorrhoea* is often followed by a rapid spread of the disease. This is not a problem only of the poor as shown by recent treatment failures emerging from more developed countries. It can be justifiably assumed that these data represent only the tip of the global health burden as surveillance data from resource-constrained settings are scarce and a silent epidemic of antimicrobial resistance may be occurring.

Interventions that can make a difference

To make a sustained difference in the continuing problem of multidrug-resistant *N. gonorrhoeae* infection, two overlapping goals must be met: broad-based control of drug resistance, and control of gonorrhoea. Both should be approached in the wider contexts of global control of antimicrobial resistance. For gonococcal infections, the public health approach must build upon lessons learnt and put the following into action:

- effective prevention and control of gonococcal infections, using prevention messages and interventions and appropriate treatment regimens;
- effective drug regulations put in place;
- antimicrobial resistance surveillance strengthened, especially in countries with a high burden of gonococcal infections;
- capacity building to establish regional networks of laboratories to perform gonococcal culture, with good quality control mechanisms;
- systematic monitoring of treatment failures by developing a standard case definition of treatment failure and protocols for monitoring;
- support of research into newer molecular methods for monitoring and detecting antimicrobial resistance;
- identification of, and research into, alternative effective treatment regimens for gonococcal infections.

The WHO gonococcal antimicrobial surveillance programme (GASP)

GASP seeks to ensure a successful implementation of an evidence-based response plan that includes:

1. In collaboration with Member States, supporting countries to strengthen laboratory capacities to isolate and culture the pathogens and perform antimicrobial susceptibility tests through re-training of health-care providers and laboratory technicians.
2. Working with WHO Collaborating Centres and other international and national reference centres to maintain and distribute standardized WHO reference strains of *N. gonorrhoeae* to ensure comparability and validity of antimicrobial resistance data.
3. Producing and disseminating standards for performing antimicrobial susceptibility testing.
4. Facilitating an exchange of information and technologies, including mapping of drug resistance patterns to highlight the situation.
5. Given the threat of untreatable gonococcal infections, WHO will collaborate with partners to ensure that the issue is highlighted within key initiatives such as the Global Health Initiative and the United Nations Secretary-General's *Global Strategy for Women's and Children's Health* to stress the consequences of untreatable gonococcal infection on the sexual and reproductive health of women and men, newborns and people living with HIV, and underscore the need for research and production of new treatments.

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