

Researchers treating benign infections with old antibiotics to fight resistance

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Doctors are beginning to prescribe antibiotic treatments from the 1950s for benign infections to fight antibiotic resistance and preserve the effectiveness of newer antibiotics. But these "old" antibiotics were not tested in the same way as their modern counterparts before being put on the market, particularly in terms of their treatment effectiveness and side effects. Doctors from the University of Geneva (UNIGE) and the University Hospitals of Geneva (HUG), Switzerland, recently analysed two antibiotics frequently used against uncomplicated urinary tract infections. They discovered that the most-widely prescribed antibiotic today does not meet the expected success rate, while the second most commonly prescribed antibiotic seems as effective as the newer drugs used for this kind of infection. The study published in the journal JAMA shows the importance of evaluating old antibiotics against today's standards so that patient well-being can be ensured at the same time as restricting the use of newer antibiotics to more serious diseases.

Antibiotic resistance: the scourge of infectious diseases

Current [antibiotics](#) perform well against serious infections but are also used against benign infections such as cystitis (an [infection](#) of the bladder). But in response, the bacteria found in our digestive tracts are now developing a resistance to these agents. What is more, they are spreading among the general population, especially via the food chain and wastewater, which means that more and more bacteria are becoming

resistant to treatment. With the increasing overuse of these [new antibiotics](#), doctors are losing a valuable resource for combating certain serious diseases. "We currently estimate that up to 20% of the bacterial population causing urinary tract infections is resistant to ciprofloxacin, a highly effective broad-spectrum antibiotic," warns Angela Huttner, a researcher in UNIGE's Department of Internal Medicine Specialties and HUG's Infectious Diseases Division. "It follows that it is essential to reserve the use of this antibiotic for serious cases!"

A return to treatments from the 1950s—but with what side effects?

Since 2011, doctors have been urged to avoid treating cystitis with the newer classes of antibiotics, which date from the late 1980s to the present day – for uncomplicated [urinary tract infections](#). The aim is to preserve ciprofloxacin and other newer antibiotics as a way of restricting the emergence of resistant bacteria. When cystitis is diagnosed, doctors can then either prescribe a drug such as nitrofurantoin, which was approved in 1953, or a drug called fosfomycin, which was released in 1971.

"The use of these drugs nowadays has increased five-fold with our knowing neither how effective they really are nor their true safety profile," says Huttner, because the evaluation and commercialisation of pharmaceuticals was not as strict when these medications were developed. "And since these products were already on the market, the large pharmaceutical companies don't want to invest money to carry out in-depth trials on them. That means it's the job of researchers to give the general public the information they need on the antibiotics they use," adds Stephan Harbarth, professor in the Department of Internal Medicine Specialties in UNIGE's Faculty of Medicine and professor at HUG Infection Prevention and Control Division.

Two old antibiotics tested on 513 women

The most commonly-prescribed drug for cystitis today is fosfomycin since it only requires one single-dose sachet. Nitrofurantoin, on the other hand, is supplied in the form of tablets to be taken three times a day for five days. At present, fosfomycin is prescribed nearly three times more often than nitrofurantoin in Switzerland.

513 women from Geneva (Switzerland), Tel Aviv (Israel) and Lodz (Poland) aged between 18 and 101 years were selected at random to follow either a fosfomycin or nitrofurantoin treatment. "We performed bacterial checks before the women took the drug at 14 days and 28 days after the treatment in order to observe the elimination of the infectious bacteria," says Huttner. The outcomes were clear: 70% of the women responded positively to the nitrofurantoin, with complete resolution of their symptoms, and 74% had elimination of the bacteria in their urine, while only 58% of women receiving fosfomycin had full symptom resolution and only 63% had elimination of bacteria. "Given that a woman already has a 33% chance of recovering from cystitis without taking an antibiotic, the results show that fosfomycin has little effect, even though it is the treatment that is the most commonly prescribed by the medical community," says Huttner.

Conversely, the success rate for nitrofurantoin is comparable to other classes of antibiotics, which makes it a suitable substitute. The rate of side effects (diarrhoea, headache and abdominal cramps) for fosfomycin, nitrofurantoin and ciprofloxacin is similar: there is a 7% risk of developing them when taking all three treatments. "The new antibiotics get better results from the point of view of eliminating harmful bacteria, which is why they replaced the old drugs," says Harbarth. "But it is now essential that we preserve ciprofloxacin's effectiveness by only using it for serious infections. If we don't, we will soon be helpless against certain infections."

Returning to the use of the old antibiotics is for the time being one of the strategies on offer for beating [antibiotic resistance](#). "But we need to test their effectiveness and the real influence they have on bacteria so that we avoid creating other [bacteria](#) that are also resistant to these antibiotics," points out Huttner. This requires an in-depth analysis of the arsenal available to infectious disease specialists, including the medications already on the market, so that they prescribe only drugs that are genuinely effective and well targeted to the infection that they will best combat. "Our study, which was funded by the European Commission, demonstrates that single-dose fosfomycin is not the optimal solution against cystitis. But if it is administered in an optimised manner, it may be effective for something else," says Huttner in conclusion. The best way to administer [fosfomycin](#) – and thereby preserve its antibacterial effect – will be the subject of future studies.

More information: Angela Huttner et al. Effect of 5-Day Nitrofurantoin vs Single-Dose Fosfomycin on Clinical Resolution of Uncomplicated Lower Urinary Tract Infection in Women, *JAMA* (2018). [DOI: 10.1001/jama.2018.3627](https://doi.org/10.1001/jama.2018.3627)

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