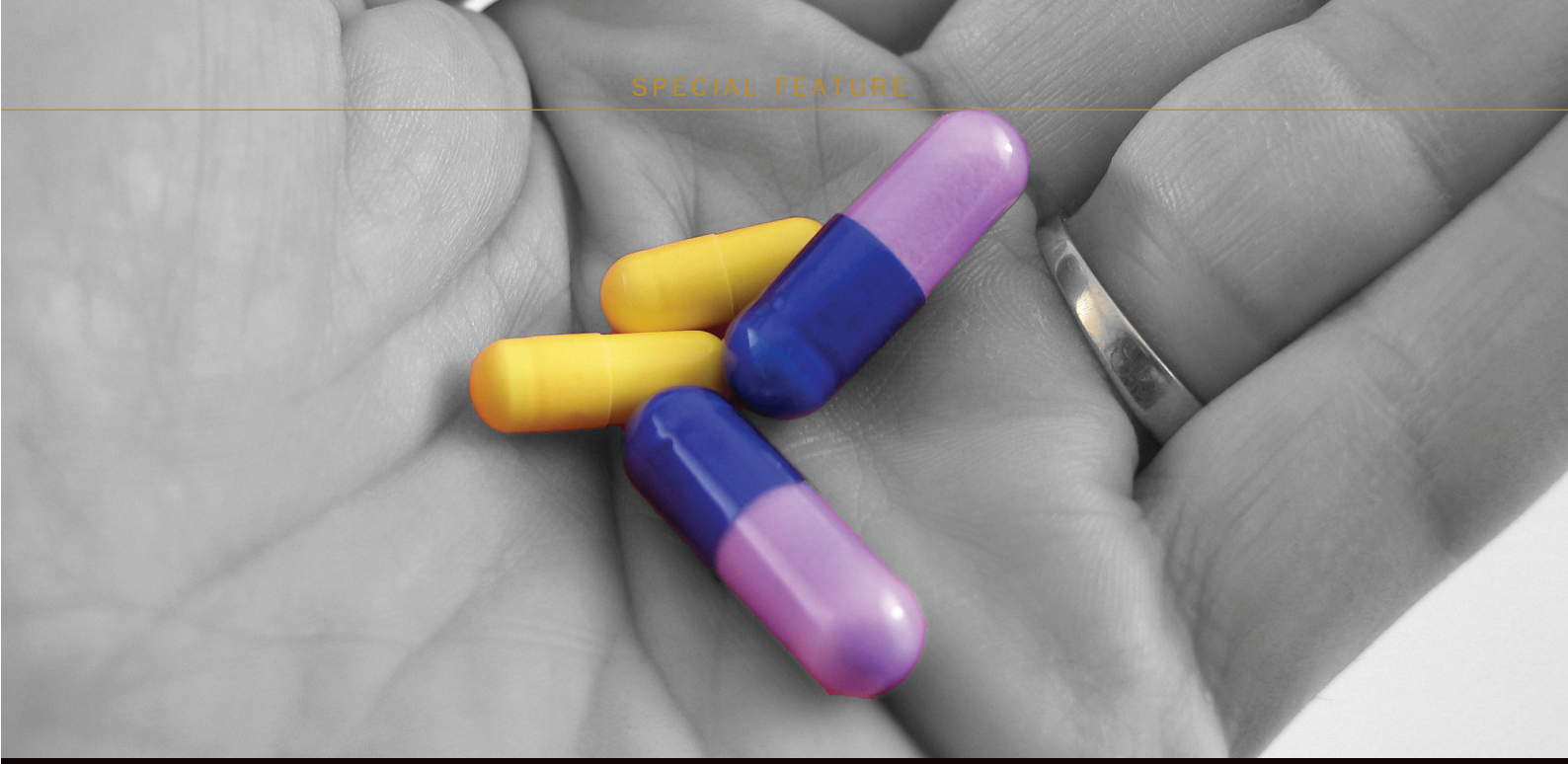


The path of least resistance

Antibiotic resistance is one of the greatest global health challenges to be addressed in the 21st Century. Many scientists now believe that the common good of antibiotics has been mismanaged for decades, directly affecting health indicators the world over, and across countries with high and low socioeconomic status alike.

The risk of widespread antibiotic resistance threatens to mitigate the positive changes made in modernising healthcare systems, therefore fresh approaches are essential, as well as new and effective antibacterial drugs.

Solutions in the research and development pipeline have been somewhat limited in recent decades, but the last few years have offered positive developments that indicate that the world is now ready to take concerted action, as this special feature explores...

In treatment we trust

Before the introduction of antibiotics, bacterial infections – such as blood stream infection, pneumonia, meningitis, syphilis and wound infections – were major killers. Thanks to antibiotics, these scourges were transformed into manageable health problems. Antibiotics are indispensable in virtually all of today's modern medicine: major surgery, organ transplantation and cancer chemotherapy would not be possible without effective treatment and prevention of bacterial infections.

Today, antibiotic resistance is threatening the health and safety of patients all over the world. A recent report from the European Antimicrobial Resistance Surveillance Network reveals disquieting new figures: the example of *Klebsiella pneumoniae (K. pneumoniae)*, a common cause of infection amongst hospital patients where the proportion of resistance to powerful last-line antibiotics, such as carbapenems, is mounting. In the worst off European country, over 25% of patients infected with *K. pneumoniae* do not respond to treatment with last-line antibiotics, leaving doctors with virtually no treatment options left. Corresponding comprehensive surveillance data for low income countries are unavailable, but several smaller studies indicate that multi-resistance is a widespread problem causing significant mortality, especially in young children.

The issue of bacterial resistance to antibiotics is comparable to that of climate change in the sense that

both phenomena involve non-renewable global resources, both are caused by human activity and are intrinsically linked to our behaviour. Another similarity is that if we fail to turn the tide, all countries will be affected, but the poorest countries will suffer earliest and most. On the other hand, when it comes to global community response the difference could not be greater. While climate change is at the very top of political agendas throughout the world, antibiotic resistance has been conspicuously absent. The ongoing pandemic spread of resistant bacteria illustrates that the problem can only be addressed through international cooperation.

A spectrum of different interventions and health technologies must be employed to contain antibiotic resistance. Finding ways of accelerating the development of new drugs is one strategy. Drugs have served as the mainstay of tackling resistant infections, but their very use also engenders further problems of resistance. Complementing this strategy, other technologies can help reduce the unnecessary use of antibiotics, eg. through the use of existing and novel diagnostics. Finally, vaccines might prevent the need for antibiotic treatment occurring in the first place.

The complex issue of antibiotic resistance necessitates a systems view. Several sectors in society, including healthcare, veterinary medicine, drug regulation and infection control, need to be engaged. In the 2005 World Health Assembly resolution WHA58.27, member states were urged to take action at national, regional and global levels and to ensure the development of a coherent, comprehensive and integrated national approach to formulate and implement a strategy for the containment of antibiotic resistance. The difficulties of enforcing these recommendations on a global level are evident. Presently, the links between the well-formulated strategies at the level of global society and their acceptance by national policy-makers are weak. Building strong public awareness is vital in order to translate recommendations into action.

Earlier this autumn, a three day conference at Uppsala University, Sweden, marked what might be seen as a new beginning. The conference, entitled 'The Global Need for Effective Antibiotics – Moving towards Concerted Action', was attended by 190 delegates representing 45 countries and many leading stakeholders – civil society, academia, industry, governments, authorities, and supranational organisations.

The next year holds hope for a sustained, global effort:

- The 2011 World Health Day will be devoted to antimicrobial resistance;
- A final report from the Transatlantic Task Force on Antibiotic Resistance (TATFAR);
- A policy meeting on antibiotic resistance in Delhi, India;
- A WHO Action Plan on Antibiotic Resistance;
- A number of regional initiatives, including in Southeast Asia, Africa and the Middle East.

The signals from the Uppsala meeting included:

- A shared conviction that antibiotic resistance is a universal problem. Like global warming, it requires joint action, not least by governmental alliances;
- A clear signal from the pharmaceutical industry that return of investment on research and development of new antibiotics and diagnostic tools will have to be unlinked from market sales in order to boost necessary innovation while yet limiting the use of antibiotics. This requires a new business model where private and public sectors cooperate;
- A strong recommendation to all stakeholders to speed up the efforts to limit unnecessary use of antibiotics, while at the same time making the medicines affordable and accessible in low income countries;
- A commitment to improve the monitoring of antibiotic resistance across the world, through shared data and increased efforts. A global network of surveillance will require common methods, and is crucial for both prudent use and needs driven development of new agents.

Considering the combined power of the aforementioned factors, there is more reason to be optimistic now than there has been for many years.

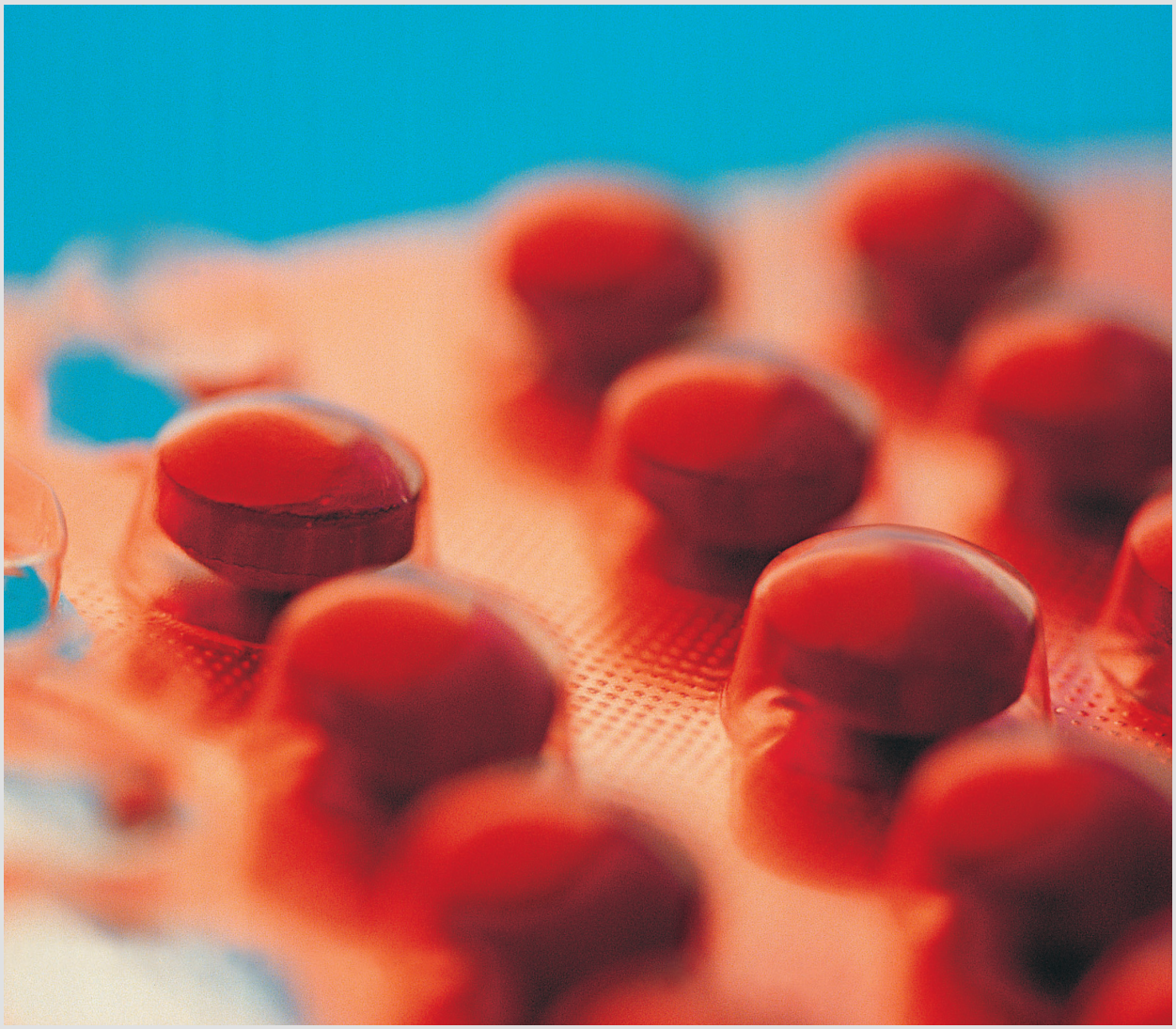
Andreas Heddini
Executive Director
ReAct – Action on Antibiotic Resistance

A task force for change

Antimicrobial resistance is a threat to people's health the world over because a dwindling stock of available drugs is being confronted with new resistant forms of disease. Even relatively new drugs, such as artemisinin-based combination therapy for treatment of malaria, do not remain efficacious for long in the face of the international mobility of people and the germs that accompany them, improper and overuse of drugs, and poor quality and counterfeit drugs flooding the markets of poor countries.

How can we measure the true cost in health and economic terms of antimicrobial resistance? Specifically, are there costs to the developed world of drug resistance that arises in the developing world? And if these costs are steep, what should be the developed country response?

First, drug resistant pathogens anywhere in the world pose health risks to people everywhere. Just as diseases travel – ever more briskly and efficiently thanks to modern transportation – so too do the mutations that lead to resistant disease forms. There is no better example than the recently identified NDM-1 mutation, found among Europeans coming from India and named after New Delhi, where they appear to have picked up the mutation. NDM-1 has now been found on multiple continents and in multiple kinds of *Enterobacteriaceae* bacteria. An enzyme from the microbe apparently destroys antibiotics. Because of the growing number of resistance mutations like NDM-1 altering the disease environment, even if a person living in a wealthy country doesn't travel, avoids hospitals where resistant bacteria



are likely to be present and uses all medicine carefully, they may still face a brutal surprise from a common *Staph* or *Strep* infection when the antibiotics they are given don't work.

Second, the economic costs of antimicrobial resistance can be measured directly through higher prices for second and third-line drugs, which we have documented in our report, 'The Race Against Drug Resistance'. In developed countries, however, even expensive antibiotics are within reach of most patients in need, whether through private insurance or government funded programmes that absorb the costs of the high-priced drugs and extended hospital or outpatient care needed to treat a resistant form of disease. However, when considering needs in developing countries, the high cost of drugs becomes a major burden. Part of the costs of drug treatment for high-burden diseases, such as HIV/AIDS, TB, and malaria, as well as many childhood diseases, are paid by donors. Drug resistance vastly increases the door costs of curing the diseases of poor people, as well as reducing the number of lives that can be saved because the scarce funds do not go as far when resistant forms of disease are prevalent.

People and governments in developed countries have a strong interest – for their own health and for improving the health of people in poor countries around the world – in tackling antimicrobial resistance in a serious manner. A good place to start is with the newly-created EU-US Task Force on Antimicrobial Resistance (TATFAR.) The TATFAR is a collaboration of health and health research agencies in the EU and US charged by their respective presidents with proposing effective actions to reduce the problem of drug resistance. The TATFAR mission could be explicitly oriented to find global solutions, with the EU and US providing assistance to poor regions to reduce this serious global problem.

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