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The global need for effective antibiotics—Moving towards concerted action

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ABSTRACT

Antibiotic resistance has emerged as one of the greatest global health challenges to be addressed in the 21st Century. The risk of widespread antibiotic resistance threatens to mitigate the positive changes made in modernizing healthcare systems; therefore, fresh approaches are essential, as well as new and effective antibacterial drugs. In a globalized world, a spectrum of different interventions and health technologies must be employed to contain antibiotic resistance. Finding ways of accelerating the development of new drugs and diagnostic tools is one strategy, as is better surveillance of antibiotic resistance and ways of improving use of existing antibiotics. Moreover, a framework to regulate use is called for to avoid that potential new antibiotics are squandered. Finally, the ongoing pandemic spread of resistant bacteria illustrates that the problem can only be addressed through international cooperation and thus that any new strategy to manage antibiotic resistance must take into consideration issues of global access and affordability.

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Antibiotics are among the most important medical discoveries and their introduction represents a remarkable success story. However, the extensive use and misuse of antibiotics have resulted in selection and worldwide spread of antibiotic resistant bacteria and we now face an immediate risk of entering a post-antibiotic era where our medical advances are lost. Within just a few years, we may very well be faced with unimaginable setbacks, medically, socially, and economically, unless we react now. Antibiotics are indispensable in virtually all modern medicine; for example major surgery, organ transplantation, treatment of preterm babies and cancer chemotherapy would not be possible without effective treatment and prevention of bacterial infections.

The emergence of antibiotic resistance is further complicated by the fact that bacteria and their resistance genes are travelling faster and further. Resistant and multiresistant bacteria pose a risk to people everywhere. A study from Tanzania showed a 43.5% mortality from bloodstream infections caused by Gram-negative bacteria and antibiotic resistance was a predictor of fatal outcome (Blomberg et al., 2007). Antibiotic resistance is not only costly in terms of human suffering but also in monetary terms. Presently, at least 25,000 patients in Europe die per year because their bacterial infections are not treatable with available antibiotics at the estimated cost of more than 1.5 billion EUR annually (ECDC/EMEA, 2009). The overall positive trend of economic development in low and middle-income countries also brings about increased availability

and demand of antibiotics, which exacerbate the already excessive consumption around the world. Simultaneously, with the increasing level of resistance to first line drugs, antibiotic resistance leads to the need for more costly second and third line drugs which often are unaffordable to many in low-income countries. In the dual problem of access and excess, the challenges lie in reducing irrational use and improving access without ruining the antibiotic effectiveness – a global public good.

Reducing the spread of bacterial infections, using existing antibiotics correctly and developing new antibiotics are literally a matter of life and death, and should be regarded as a collective responsibility. As stated by Elinor Ostrom, 2009 Nobel Laureate in Economic Sciences and Tercentenary Linnaeus Honorary Doctor of Uppsala University, Sweden, “the issue 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 behavior. The problem can only be addressed through international cooperation”. Another similarity with the issue of climate change is that if we fail to turn the tide, all countries will be affected, but the poorest countries will suffer the earliest and the 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.

To promote international collaboration, several resolutions concerning antibiotic resistance have been adopted by the World Health Assembly (WHA). In 2000 the WHO presented a global strat-

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egy for the containment of antimicrobial resistance, calling for a multidisciplinary and coordinated approach. However, sufficient financial and human resources to implement the strategy were never provided. In 2005, the WHO member states requested the director general to strengthen the leadership role of the WHO in containing antimicrobial resistance and to provide technical support. Moreover, the same resolution urges the member states to ensure the development of a coherent, comprehensive and integrated national approach. Still to this date, little has been done to implement the global strategy. The links between well-meant strategies at the global level and the uptake by national governments and agencies are unfortunately very weak. Stronger leadership and coordination by the WHO is urgently needed, coupled with the building of strong public awareness in order to translate recommendations into action.

A wide range of measures is needed to ensure that currently available antibiotics remain effective as long as possible. This can be achieved primarily by means of greater awareness among the public, health care professionals and the food- and agriculture sector regarding the importance of rational use of these medicines as well as ways to prevent infections and spread of antibiotic resistant bacteria. However, in parallel with these measures we urgently need to address the serious lack of new antibiotics in the drug pipeline (Freire-Moran et al., 2011) as well as investigate novel drugs as alternatives to traditional antibiotics (Fernebro, 2011).

In order to kick-start the discussions for how to incentivize the research and development of new antibiotics, Sweden initiated an expert conference during its Presidency of the European Union in 2009. The results of conference entitled “Innovative Incentives for Effective Antibacterials” led to a set of conclusions by the European Health Minister which included a call to the EU Commission to develop an EU Action Plan on Antibiotic Resistance. This plan will include among a number of other important issues, concrete proposals concerning incentives to develop new effective antibiotics. The plan is to be presented in November 2011. Moreover, during the Swedish EU Presidency, a transatlantic taskforce (EU and US) on antimicrobial resistance (TATFAR) was established which also will address the need to reinvigorate the research and development pipeline for novel antibiotics.

To keep the momentum of these discussions and developments and to further deepen the dialogue on the need for new antibiotics, ReAct—Action on Antibiotic Resistance (www.reactgroup.org) arranged a global conference in Uppsala, Sweden in September 2010 on “The global need for effective antibiotics—Moving towards concerted action”. The conference gathered 200 participants from around the world, representing 45 countries and many leading stakeholders—civil society, academia, pharmaceutical industry, governments, and supranational organizations. Among many important contributions at the conference the European Federation of Pharmaceutical Industries and Associations (EFPIA) gave a clear signal that return of investment on research and development of new antibiotics will have to be delinked from market sales in order to boost necessary innovation while yet limiting the use of antibiotics. This will require a new business model where private and public sectors cooperate (So et al., 2011). Moreover, there is a clear understanding and commitment from EFPIA to make any future new antibiotics globally accessible and affordable (Bergström, 2011).

While developing a new model for the development of novel classes of antibiotics, several other tracks need to be explored in

parallel as we must ensure that potential new antibiotics are not squandered in the future. It is also necessary to make better use of the antibiotics that are available today by looking more closely at dosage, treatment duration and drug combinations (Mouton et al., 2011). In addition, diagnostic tests are under-used as tools for resistance containment and need to be developed to provide rapid and reliable results (Okeke et al., 2011). Lastly, all these measures require improved global surveillance of resistance to generate the data on which to base priorities and ensure a needs-driven research and development process (Grundmann et al., 2011).

A fundamentally changed view of antibiotics is urgently needed. Antibiotics must be viewed as a global public good. ReAct strongly believes that for current and future generations to have access to effective prevention and treatment of bacterial infections as part of their right to health, all of us need to act now. The window of opportunity is rapidly closing. Managing the resistance problem requires political action and awareness of decision makers to promote research and implementation of global strategies for action.

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