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Health: Both a prerequisite and an outcome of sustainable development.

[BRIEF]
Antimicrobial Resistance

Antimicrobial resistance (AMR) has become a global security threat with potential devastating effects on human beings, livestock, and the global economy. Considering its ominous impact, The World Economic Forum identified AMR as one of the greater risks to human health in 2013. AMR threatens to undermine gains made through the Millennium Development Goals (MDGs) and major advances of modern medicine. This brief provides an overview of the problem framing AMR from the development and aid perspective and outlines opportunities for dialogue and increased awareness.

The discovery and availability of medicines to treat infectious diseases changed the world by saving and improving countless lives while paving the way for many health achievements of the 20th century. Regrettably, these health accomplishments are at risk because of a rapidly growing number of infections caused by microbes (such as bacteria, viruses, parasites and fungi) that no longer respond to the medicines used to combat them. This phenomenon is known as **antimicrobial resistance (AMR)**, and in the specific case of bacterial infections, **antibiotic resistance (ABR)**.

AMR moves from one country to another, without notice, and has been documented in all regions of the world. It exists across different conditions – from TB, pneumonia, HIV and malaria to respiratory and urinary tract infections, blood-stream infections and wound infections. Today we cannot safely treat multi-drug resistant (MDR) strains of typhoid fever, neonatal sepsis and pneumonia. MDR bacteria are causing hospital outbreaks and killing patients around the world. Likewise, for malaria just one new drug class- artemisinins- stand between success and failure.

AMR is not a new phenomenon but it has reached a crisis point caused by two fundamental processes: ***first***, massive use and misuse of antibiotics in human and veterinary medicine and agriculture/aquaculture have led bacteria to successfully exploit and share adaptive mechanisms to resist antibiotics; ***second*****,** the spread of ABR-bacteria facilitated by poor sanitation, hygiene and infection control practices, unreliable water supplies, poor housing, and has been fuelled by increased human mobility, food trade and civil conflicts. The threat is compounded by a distressing decline in the antimicrobial research and development pipeline.

Antibiotics are used to cure and prevent bacterial infections in humans and animals. They are also used for growth promotion and disease prevention in agriculture, aquaculture, and horticulture, these activities account for approximately 70 % of antibiotic use globally. Environments polluted by antibiotics used in aquaculture and agriculture practices and by wastewater from municipalities, hospitals and pharmaceutical manufacturing play a role in AMR development and dissemination. Resistant microbes and resistant genes thus can spread and circulate from animals to humans through food, water and the environment. Addressing AMR requires an *ecosystem approach* and a *One Health* vision due to the interconnectedness and environmental impact of antibiotic use in humans, animals and food production. As a transnational and multi-sectorial issue AMR requires global collective action since states cannot address this individually.

IMPACT AND COST OF AMR

AMR makes it difficult and sometimes impossible to treat even common bacterial infections. It results in prolonged recovery, higher mortality and time of infectiousness, lengthy hospital care, and increased costs. In both rich and poor nations, resistant bacteria cause the most frequent, costly, and deadly infections in hospitals and intensive care units. The impact extends beyond health risks; reduced productivity caused by sickness (of both humans and animals) is a drain to the global economy.

AMR currently claims an estimated 700.000 deaths annually and – without effective action – is predicted to cause 10 million deaths annually by 2050 with a cost of 100 trillion USD. Across USA and Europe AMR causes at least 50,000 deaths each year with an annual economic impact of more than 55 USD billion. In LMICs where the burden of infectious diseases is higher, AMR consequences are devastating. Studies have shown that approximately 70% of neonatal infections are resistant to first line antibiotics, and resistant malaria, HIV and TB infections are leading to increased mortality and high societal costs. In South Africa drug resistant TB represent 3 % of all cases but consumes more than one third of the total national budget for TB.

Definitions

Antimicrobials Medicines that kill or inhibit the growth of microorganisms and include antibiotics, antivirals, antiparasitics and antifungals.

Antibiotics Attack and destroy bacteria (e.g. causing tuberculosis, gonorrhoea, pneumonia). If bacteria acquire resistance to more than one antimicrobial, they are called multi-drug resistant (MDR). Bacteria, for example, can develop resistance to antibiotics by inactivating the antibiotic, decreasing the entry of the antibiotic or removing it, modifying the target of the antibiotic, or circumventing the pathways of antibiotic action. Bacteria can do so either by mutating existing genes or by acquiring/sharing new genes from other bacteria.

AMR FROM A SUSTAINABLE DEVELOPMENT PESPECTIVE

Tackling AMR has been a Swedish priority for more than ten years. In relation to development cooperation, the Swedish government's results strategy for global action on socially and sustainable development 2014–2017 includes, as a key expected result, improved basic health where access to rapid diagnostics, vaccines and drugs, as well as the rational use of antibiotics is considered central to long term work on improved survival and healthy lives.

Agenda 2030 should address the fact that AMR jeopardizes positive global health outcomes that has been achieved so far. The Lancet Commission in the Investing in Health report from 2013 identifies AMR as one of the areas for collective action.

Although AMR is a challenge for all countries, the burden of resistant infection is disproportionately borne by the poor. Infection thrives in poor settings with limited access to water and sanitation, medicines and health care. Furthermore, interventions designed to contain AMR, or to improve health, are not necessarily accessible to the people who most need them. Emergence and spread of resistance is strongly influenced by socioeconomic factors at the individual and national levels.

Access to effective antibiotics is crucial to address reproductive, maternal, newborn and child health. Every year, bacterial infections kill more than 2 million children and one out of four of neonatal deaths are caused by infections. Less than 50% of mothers with pre-term rupture of membranes and only 8% of children with neonatal infections receive antibiotics. From a SRHR perspective, resistant gonorrhoea represents the highest risk with 106 million new cases per year and may become untreatable unless new drugs become available.

HOW TO TACKLE THE PROBLEM

Addressing the causes and consequences of AMR at different levels is possible. AMR is driven by both excessive and irrational use of antibiotics on one hand and by lack of access to them on the other one. While in many parts of the world antibiotics are available without any prescription and are inappropriately used, most of the yearly 0.8 million under-five child deaths due to pneumonia result from poor access to antibiotics rather than from AMR. Understandably, antibiotics figure twice in the UN list of the 13 identified "Life-Saving Commodities for Women and Children" which complement the UN Secretary-General's Global Strategy for Women's and children'.

A global concern

- AMR impedes the control of infectious diseases: it prolongs the time of infectiousness and increases spreading risk
- AMR kills: death rate is about twice in patients with AMR infections
- AMR increases health care costs: resistant infections extend duration of illness and treatment and require more expensive drugs
- AMR reverses health gains and risk modern medicine procedures like organ transplantation, cancer chemotherapy and major surgery

In resource-constrained settings, blind and irrational therapy is aggravated by the lack of diagnostic tests, fewer antimicrobials available, absence of surveillance system for AMR and poor drug quality. Markets in LMICs with weak regulatory oversight are highly infiltrated with counterfeit drugs, antibiotics account for one fourth of global counterfeit medicines. To combat substandard falsified medicines Rwanda has since 2011 formed pharmacovigilance sub-committees at all health centers that are overseen by the country's district hospitals. Around 2,400 health workers have been trained in the implementation of the guidelines.

The large-scale international commitment to specific diseases – diarrhea, pneumonia, HIV, malaria, and TB, for all of which resistance is a major concern – provides important tie-ins for securing effective treatment building and sustaining efforts at reducing AMR for many other common bacterial infections. As a global good and global priority health product, radical changes in how we access and use antimicrobials as well as to embed surveillance should be part of these agendas. Sweden as a major funder of global health against the 'big three' has a major stake in ensuring that these investments are not wasted because of drug resistance.

As a global public good, the effectiveness of antimicrobials requires robust, collective international action to conserve their use. Sweden's successful work on containment of AMR in human medicine, with a focus on the rational use of antibiotics and resistance monitoring can be used as a tool and inspiration. Promoting rational prescribing and use is possible through stewardship programs that could be a component of the support to health systems. Successful interventions consider local contexts and engage relevant stakeholders throughout the design, testing, implementation and monitoring. Encouraging examples include a web-based intervention to reduce antibiotic prescribing for acute cough in European countries, and the Antibiotic Smart Use Program in Thailand.

Strengthening health systems with focus on building capacity of regulatory authorities, capacity for enhanced infection control, training of health personnel, and supporting efforts directed at educating and empowering health consumers will lead to better containment of AMR. This will provide a practical focus contributing to the implementation of national medicines polices and their integration into health systems.

The case of MDR-tuberculosis

Worldwide TB kills 1.5 million people every year, mostly the poor and vulnerable.

The WHO strategy to end the global TB epidemic by 2035 approved in 2014 noted its alarm at "the grave individual and public health risks" posed by MDR-TB. Globally, an estimated half a million people developed MDR-TB and an estimated 210 000 died from it.

Better diagnostic tests, and new drugs and regimens are needed. Despite improvements in diagnosis of MDR-TB, many cases still go undetected, and many diagnosed await access to treatment, the gap between diagnosis and treatment has widened in several countries. The treatment of MDR-TB remains long, costly and toxic. Out of the 100 000 patients who started MDR-TB treatment in 2013 only half are successfully treated.

Since 1994, WHO has monitored the global and country burden and trends of MDR-TB. This is the oldest and largest project on AMR surveillance worldwide. By 2014, data on drug resistance were available for 144 countries, which collectively have 95% of the world's population and TB cases. Eastern European and Central Asian countries have the highest levels of MDR-TB, reaching up to 50% of all tuberculosis cases. MDR-TB also is a severe threat in parts of Asia and in some of the countries in Southern Africa with heavy TB-HIV burdens.

Extensively drug-resistant TB (XDR-TB) has been reported by 100 countries. On average, an estimated 9% of people with MDR-TB have XDR-TB.

In keeping with the global AMR strategy, and as part of the End TB Strategy, WHO recommends a five-point response: (i) Preventing drug resistance through high-quality treatment; (ii) Rapid testing; (iii) Immediate access to treatment and care; (iv) Infection control; and, (v) Increased political commitment and financing.

The case of India: A 5 year pragmatic plan

- To combat AMR Indian medical societies developed a pragmatic roadmap, the Chennai Declaration, which considers options ranging from imposing restrictions on certain classes of antibiotics to accepting over the counter sales (OTC). The important role of NGOs and media is also considered.
- Keeping with its pragmatic "Practical not Perfect" approach participants prepared realistic, achievable targets for 1st, 2nd and 5 year marks.
- The plan encompasses activities including antibiotic stewardship, infection control, OTC sale of antibiotics for humans and animals, private-public partnership to develop new molecules, medical education and improving laboratory capabilities.

The "Chennai Declaration" 2013.

OPPORTUNITIES /ENTRY POINTS FOR DIALOGUE

- In May 2015 the World Health Assembly endorsed a Global Action Plan (GAP) and resolution to tackle AMR, which include strengthening surveillance and research, develop bettermedicines, and alert those at the highest level of government about the problem. Member States were urged to have national action plans in place by May 2017. In countries where Sida supports the health sector, the status of AMR and plans that are aligned with the GAP should be brought up. Ask about the main challenges and constraints to develop and implement such plan.
- WHO and UN design awareness days for health, use these opportunities to raise awareness about AMR and need to address it. Support public campaigns to raise awareness and understanding.
- Universal Health Care reforms: availability and access to antimicrobials. How is procurement of medicines at health system operating? Do national drug procurement programs and policies ensure the availability, quality and adequate distribution of antimicrobials and promote their rational use?
- Get information about successful approaches in achieving responsible use of antibiotics in the region. Civil society and others need to share. In countries receiving or planning to apply for support from Global Fund and/or other international initiatives that provide medicines, make questions about the inclusion of surveillance and mapping of resistance in order to ensure and monitor that the antimicrobials provided are effective.
- When discussing sexually transmitted infections (STIs) and/ or other SHRH related issues ask about what is known in terms of the incidence of gonorrhoea. Inform about the fact that gonorrhoea is a major public health challenge today due to the high incidence of infections accompanied by a dwindling number of treatment options. WHO has developed special guidelines to give guidance on ways to contain the spread of AMR. gonorrhoea designed to be implemented in conjunction with broader national and international strategies for the prevention and control of STIs.
- Get information about existing regulations on prescribing of antimicrobials in human, veterinary and agriculture.

KEY READING

1) ReAct, Action on Antibiotic Resistance, which receives support from Sida, has developed a Toolbox to provide inspiration and guidance on what can be done to address the pressing issue.
http://www.reactgroup.org/toolbox/

2) Antimicrobial resistance: tackling a crisis for the health and wealth of nations. Jim O'Neill et al. Dec 2014.
http://goo.gl/aX6U2b

3) Draft global action plan on antimicrobial resistance. WHO March 2015
http://goo.gl/2WiW3o

4) The World's Collective Responsibility to Conserve Antibiotic Effectiveness. ReAct 2014
http://goo.gl/hHK3Ia

5) The Chennai Declaration: a roadmap to tackle the challenge of antimicrobial resistance. Indian J Cancer. 2013.
http://goo.gl/zvNrWT

6) Global action plan to control the spread and impact of antimicrobial resistance in Neisseria gonorrhoeae. WHO 2012. http://goo.gl/BHD0tb

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