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A Call to Arms: The International Effort to Combat Antimicrobial Resistance

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Author's Note: Last Fall in the Destination HealthEU blog series I warned of the growing global public health crisis of antimicrobial resistance (AMR). I emphasized that without new antimicrobials, certain bacterial infections may become untreatable, returning us to the dark days of the pre-antibiotic era pre-1938 (Figure 1) for many infections; for the purposes of this blog, the words antimicrobials and antibiotics are used interchangeably.

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To quantify the problem of anti-microbial resistance, in the United States alone each year approximately 2 million people develop infections by AMR bacteria and 23,000 people die. The numbers worldwide are even more terrifying: currently 700,000 deaths per year and an estimated 10 million deaths per year will be the result of AMR by 2050 unless new antimicrobials are developed. It is important to emphasize that the 2050 projection of deaths due to AMR bacteria will surpass worldwide deaths due to cancer (Figure 1). The reader is directed to an outstanding recent opinion article [1] that highlights these statistics, economic costs of AMR and drug development, and international action plans.

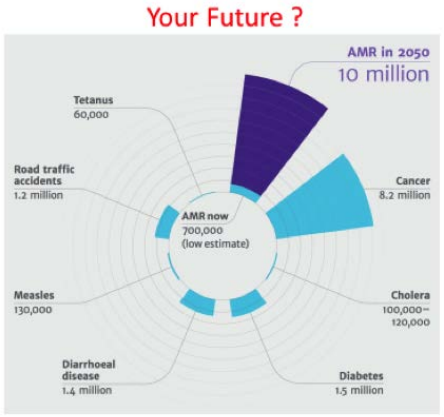

Figure 1

Clearly, we are at a point in time where action is needed to prevent a global catastrophe. It is gratifying that international awareness of the 'clear and present danger' of AMR has heightened in the past year. Critical action plans are being developed at the national and international levels. In the United States, for instance, on September 18th, 2014 the White House announced plans for a $1.2 billion investment in AMR for the fiscal 2016 budget that will provide funds across government agencies (Figure 1). The National Institutes of Health (NIH; mostly the National Institute of Allergy and Infectious Disease; NIAID) will receive over $100 million in new funding to combat AMR. Additionally, the Centers for Disease Control and Prevention (CDC) will realize an increase level of support to provide funds for their initiatives to combat AMR. If these funds do

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August 2012
July 2012
June 2012
February 2012
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indeed become available, important research in areas of public health policy, antibiotic stewardship, surveillance of AMR, new drug development, improved diagnostics and basic AMR research can be initiated and continued. Of special note is a $20 million prize to be awarded to the creative person who develops a point-of-care diagnostic that will rapidly inform clinicians of an AMR bacterial infection. In March of this year, the White House announced an "Antibiotic Action Plan for Combating Antibiotic Resistant Bacteria" (please visit http://1.usa.gov/1Bub1Je for details), which embraces a whole government approach. My sense is that people 'get' that AMR is a real threat not only to the health of the population but also the economy given the increased healthcare and other costs to the global economy that currently result from AMR, which will only worsen if new antimicrobial drugs are not developed.[1]

Figure 2

On the international level, the World Health Organization (WHO) and the European Union have taken leadership positions and announced important steps in combating AMR. In late May members of the European Union of Parliament adopted a new resolution that significantly regulates antibiotic usage and to encourage new antibiotic development. Also in May, member states of the United Nations overwhelmingly agreed to an action plan developed by the World Health Organization that emphasizes the need to combat AMR on several fronts: surveillance of resistance, prevention of AMR infections, better stewardship of antibiotic use and development of financial support for new

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drug development.

All of the above mentioned action plans, resolutions, and active voices regarding AMR are important. Everyone agrees what we really need to stave-off the impending disaster of AMR bacteria are new antimicrobials that are safe and effective. The National Action Plan for Combating Antibiotic-Resistant Bacteria has a stated goal to "intensify research and development of new therapeutics and vaccines, first-in-class drugs and new combination therapies for treatment of bacterial infections". This action plan calls for the development by 2020 of at least two new antibiotic drug candidates as well as 3 drug candidates or probiotics that could be used as alternatives to classical antibiotics. Overall, this plan is consistent, but not as aggressive, with an earlier recommendation from the Infectious Diseases Society of America (IDSA), which called for ten new antibacterial drugs by 2020.[2] The boldness of the "10 X 20 Initiative" proposed by IDSA in 2010 with its associated challenges was compared to the pronouncement of President Kennedy in 1961 that within 10 years man would walk on the moon

A major breakthrough for the search for a new antibacterial treatment recently made by Kim Lewis Ph.D. (Northeastern University) and colleagues [3] gives reason for optimism. This new antibiotic, teixobactin, was isolated from an unculturable bacteria during a hunt for novel antibiotics. Teixobactin inhibits bacterial cell wall biosynthesis by a novel process heretofore not exploited. It has proven safe and effective in curing experimental infections in mice and bacteria have difficulty developing resistance; the latter point deserves a cautionary note since bacteria are notorious for their capacity to resist antibiotics. All of these properties point towards a new therapeutic option for treating AMR bacterial infections and hopefully teixiobactin will ultimately move into clinical trials. Regardless of the future of teixobactin, similar academic basic research enterprises must be encouraged and nurtured with funding and industrial partners for important clinical trials. Towards this end, it is important to note that the aforementioned National Action Plan calls for a consortium between academia and industry to facilitate antibiotic development.

Despite the gloom and doom of predictions regarding AMR and how this will impact the future of global public health, I have to remain optimistic that with political and financial

support that science will meet the challenges of AMR. Otherwise, it would be difficult to sleep at night as I worryingly contemplate a return to the pre-antibiotic era.

References:

1. Hampton T. 2015. Novel programs and discovers aim to combat antibiotic resistance. JAMA. Published on-line June 3, 2015.

2. Infectious Diseases Society of America. 2010. The 10 X 20 Initiative: Pursuing a global commitment to develop 10 new antibacterial drugs by 2020. Clinical Infectious Disease. 50: 1081-1083.

3. Ling LL, Schneider T, Peoples AJ, Spoering AL, Engels I, Conlon BP, Mueller A, Schäberle TF, Hughes DE, Epstein S, Jones M, Lazarides L, Steadman VA, Cohen DR, Felix CR, Fetterman KA, Millett WP, Nitti AG, Zullo AM, Chen C, Lewis K. 2015. A new antibiotic kills pathogens without detectable resistance. Nature 517: 455-59.

Additional websites of interest:

www.antibiotic-action.com: This site is from my colleague Laura Piddock Ph.D. of the University of Birmingham in the UK. Laura has been a leading investigator in antibiotic resistance research and public information regarding dangers of AMR.

www.cdc.gov.drugresistance/threat-report-2013/: You can download a pdf of 114 pages (!) to get the important statistics regarding AMR bacteria and threat levels.

www.idsociety.org/AR_Policy/: This site from the IDSA has many useful sub-sites regarding multiple aspects of AMR, including one on "Antibiotics in Agriculture"

www.niaid.nih.gov/topics/antimicrobial resistance/pages/default.aspx: Provides important information from the NIH regarding intra- and extra-mural efforts on AMR. The current and future efforts on AMR can be downloaded as a pdf.

http://www.eurosurveillance.org: A nice website to keep informed regarding AMR matters in Europe

In addition to these websites, one might also wish to view the movie "Resistance" which can be downloaded from Netflix. I also highly recommend the PBS "Frontline" special: "Hunting the Nightmare Bacteria"

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