

Antibiotic Resistance is becoming a Mainstream Challenge to Public Health

Abstract:

The Saturday Financial Times ¹ 16th March 2013 carried a full-page article on antimicrobial resistance. The article was in response to the annual Report of Dame Sally Davies, the UK's Chief Medical Officer ². Her Report emphasised the growing global problem of antibiotic resistant 'superbugs'. Seven per cent of all deaths are due to infection. She warned British politicians of an 'apocalyptic scenario' of insufficient antibiotics. She also referred to it as a 'ticking time bomb'. She wants the issue discussed at the next G8 Summit in London. She said that antimicrobial resistance represents a threat that may be as important as climate change for the world. Her US counterpart Thomas Frieden at the Centre for Disease Control has recently spoken about the 'nightmare bacteria', the Carbapenem-resistant Enterobacteria. One of Sally Davies' concerns is the under-provision of new antibiotics. She pointed out that there hasn't been a new class of antibiotics developed since the late 1980s. She has held meetings with industry in order to stimulate new antibiotic productions. The obstacles to pharmaceutical companies developing new antibiotics are the high costs in their generation, their short term use compared with drugs for chronic conditions and the limited sales market secondary to the policy of 'saving' new antibiotics for serious infections. Andrew Witty at GlaxoSmithKline said that there is a need for greater rewards for those companies involved in the production of new antibiotics.

The banner statistics are alarming. It is estimated that 25,000 patients die annually in the EU from drug-resistant bacteria. These serious infections are costing billions of Euros in terms of additional healthcare. The rise in international travel has facilitated the spread of resistant organisms. It would appear that concerns about antibiotic resistant infections have spread beyond the academic corridors of microbiology and have now reached everyday clinical practice and the public consciousness. There are multiple reasons for the development of resistance. There is an excessive and ill-controlled use of antibiotics particularly for viral infections. In many EU countries medications can be obtained without a doctor's prescription. The use of antibiotics in animal husbandry is also a concern in the development of cross-resistance.

Resistant microorganisms are those that are not inhibited by antibiotics. The resistance to treatment starts as a random mutation in the bacteria's genetic code. Antibiotic resistance has steadily increased since systemic antibiotics were introduced in the 1930s and 1940s. The new concern, however, is the breath of resistance and the shortage of new antibiotics being produced. Increased numbers of critically ill susceptible patients are being nursed in close proximity in our intensive care units. The real danger is the gram-negative Enterobacteriaceae such as E. Coli and Klebsiella. E. Coli alone accounts for 36% of bacteraemias. Multi-resistant E. Coli septicaemia has a 30% mortality while the mortality is 15% in those with a susceptible E. Coli. Extended Spectrum Beta Lactamase (ESBL) producing organisms are causing increased concern. These organisms produce a lactamase capable of breaking the beta lactam ring of the antibiotic when deactivates its efficacy. An ESBL-producing E. Coli strain, which is more difficult to treat than MRSA, affects 30,000 patients annually in the UK. The first case of ESBL presented 4 years ago. ESBL producing antimicrobials are resistant to cephalosporin antibiotics.

A typical large 1,000 bed acute hospital will have 500 bacteraemias involving Gram-negative bacteria, 15% being multiple antibiotic resistant. In addition there will be 60 cases of C. difficile and 3 cases of MRSA.

The concept of antimicrobial stewardship is being widely promoted. Its goals are the optimal use of antibiotics for the individual patients, the prevention of overuse and to minimise resistance at patient and community levels. The problem is how to balance between the appropriate early use of antibiotics in the face of potentially severe infections and the inappropriate use of antibiotics for minor illnesses. The first step is the institution of antibiotic guidelines in all hospitals which should avoid broad-spectrum antibiotics where possible. Try to avoid antibiotics that lead to multi-resistant bacteria or C. difficile. The justification for the commencement of the antibiotics should be entered in the case notes. Blood culture and all other appropriate swabs should be taken before commencing therapy. Prescribe the shortest, effective course. One of the limitations that diagnostics other than the blood culture such as C-reactive protein and white cell counts lack specificity. During the period awaiting the blood culture the treatment is a 'best guess'.

There have been a number of gains and successes in the area of infection prevention. There has been a welcome reduction in the number of MRSA bacteraemias. In England in 2011 there was an 84.7% reduction in MRSA septicaemias compared with 2004, 1,185 cases compared with 7,700 cases. Since 2008 the C. difficile cases have reduced by 53%. This has been achieved by a number of measures. There has been a concerted effort to improve hand washing. The 5 moments of hand washing developed by the WHO are: before touching the patient, before a clean or aseptic technique, after body fluid exposure risk, after touching a patient, after touching the patient's surroundings. There has also been a major drive to prevent medical device infections. The prevention of catheter-related bloodstream infection has been spearheaded by Peter Pronovost and his team at Michigan. He demonstrated that meticulous line care can reduce line infection by 60%. The bundle of interventions now considered a standard of care are hand washing, use of chlorhexidine for skin antisepsis, use of maximum sterile precautions for catheter insertion and dressing changes, avoidance of the femoral vein and prompt removal of unnecessary catheters.

Vaccines have played an important role for children. The Streptococcal pneumonia vaccine has been effective in reducing invasive infections including pneumonia, meningitis.

In Ireland the Strategy for the Control of Antimicrobial Resistance in Ireland (SARI) was established in 2001. For over a decade it promoted the prudent use of antibiotics, surveillance and infection control. The HIQA infection control standards were launched in 2009. In 2011 SARI handed over its functions to the National Health Care Associated Infection (NHAi) Clinical Programme. The primary aim is the prevention and control of antimicrobial resistance and healthcare associated infection. It measures compliance with standards. The Programme's workstreams include hand hygiene, hospital antimicrobial stewardship, medical device infection prevention and avoidance of surgical site infection. There is an emphasis on guidelines for the large scale usage of antibiotics conditions such as urinary tract infection. The use of antibiotics in long term facilities is also being addressed. There are public education activities such as 'antibiotics don't cure colds or the flu', European antibiotic day, WHO hand hygiene day.

It is clear that concerns about antibiotic resistant bacteria are increasing. It is now a public health issue. The relative paucity of new antibiotics means that the emphasis must be on infection control and prevention. In children a comprehensive, effective vaccination is of paramount importance. The Report of Sally Davies has added a new stimulus for all those involved in the process. One of the final comments in her Report is that in the last 50 years we had a wide array of agents to fight infection but the next 50 years may be very different with the emergence of highly resistant bacteria.
JFA Murphy
Editor

1. Jack J. Chief medic to launch superbug campaign. Financial Times 16th March 2013 page 3.
2. Annual Report of Chief Medical Officer. Infections and the rise of antimicrobial resistance. Volume 2. 2013
3. Pronovost P, Needham D, Berenholtz S, Sinopoli D, Chu H, Cosgrove S, Sexton B, Hyzy R, Welsh R, Roth G, Bander J, Kepros J, Goeschel C. An intervention to decrease catheter-related blood stream infections in the ICU. N Engl J Med 2006;355:2725-2732.

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