Drug War: The Growing Threat from Antimicrobial Resistance

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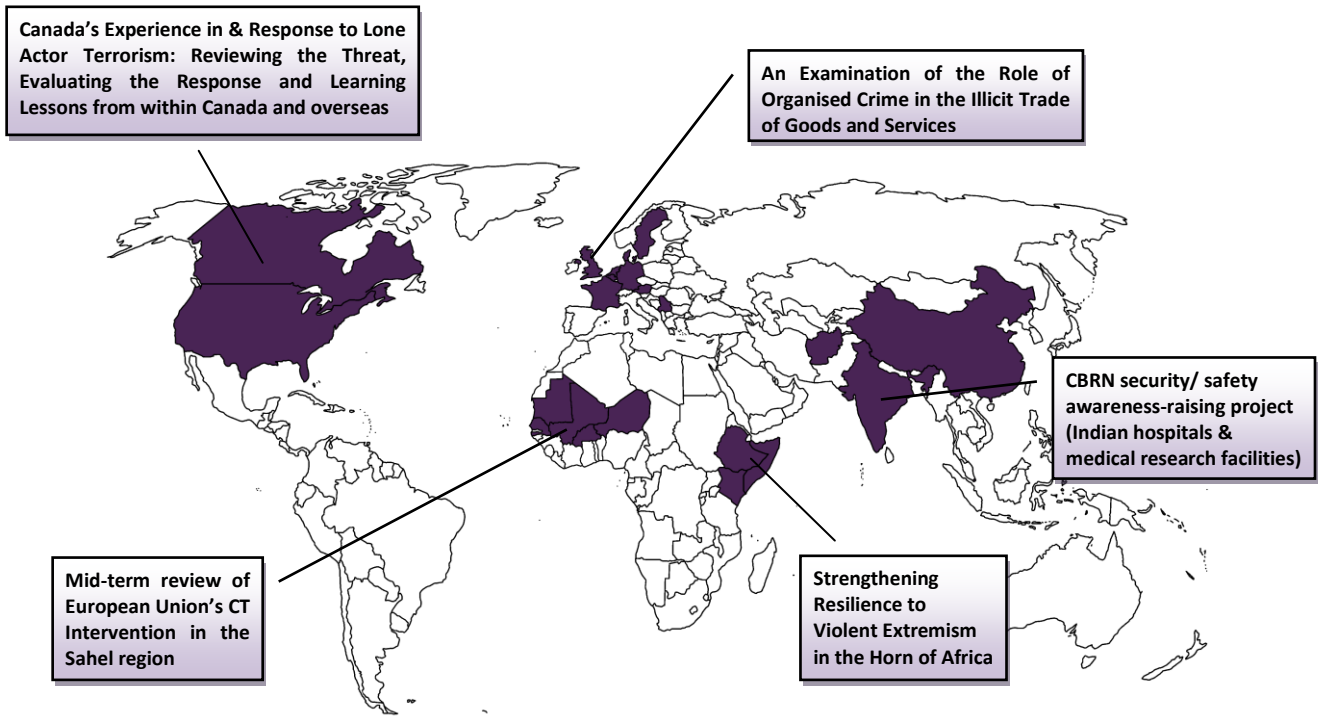

Drug War: The Growing Threat from Antimicrobial Resistance

The risk from antimicrobial resistance (AMR) has evolved beyond its impact on the healthcare sector alone. It is a serious risk to security and resilience that is now being considered in the National Security Risk Assessment for possible inclusion on the UK's National Risk Register alongside pandemic flu and serious infection disease. Group Captain Andy Green and Jennifer Cole explain the growing threat and its particular impact on military operations.

Antimicrobial resistance (AMR) – the resistance of microorganisms including bacteria and viruses to medicines that have previously been used to treat them – is a growing concern not only for the healthcare sector[1] but, increasingly, for defence, security and resilience more widely. The emergence of drug-resistant bacteria, viruses and other microorganisms is forcing governments into greater collaboration and influencing both domestic and international policy but there is still a huge amount to be done to raise awareness of the issue and to take the steps needed to tackle the challenge it presents. This paper will set out the risk posed by AMR, highlight particular issues it raises for military operations, and will outline some of the steps that are being taken to address current concerns.

A short history of AMR

Over the last seventy years, the efficacy, ready availability and relatively low cost of antimicrobial drugs – medicines that kill microorganisms such as bacteria and viruses or inhibit their multiplication, growth and pathogenic action – has led to their considerable overuse. It is estimated that nearly 50 per cent of all antimicrobial use in hospitals is unnecessary or inappropriate[2] while in neonatal care, the figure is even higher, with infection confirmed in less than ten per cent of neonates treated with antibiotics[3]. The more antimicrobials are used, the faster the microorganisms they target evolve into new, resistant strains, a natural process of evolution that threatens to undermine the tremendous life-saving potential of these drugs. Put into context, before the introduction of antibiotics, 40 per cent of deaths in the UK were caused by infection: today, the figure is closer to 7 per cent but is in danger of increasing if the efficacy of antibiotics is lost[4]. Without effective antibiotics, medical procedures we take for granted today, such as routine surgery and chemotherapy for cancer treatments will become much more risky for the patient. Organ transplants will become virtually impossible and the likelihood of surviving childhood diseases that are easily treatable today will be greatly reduced.

AMR is a natural progression of evolution. When pressure is put on living organisms, they adapt to survive: this is as true of pathogenic bacteria as it is for any other lifeform and, therefore, the more frequently, and the greater the quantities in which antimicrobials are used, the faster the microorganisms they target will evolve into new, resistant strains. This is not a new issue. In a lecture given at RUSI to mark European Anitbiotics Awareness Day 2012, Professor Neil Woodford of the

[1] See World Health Organization Fact sheet No194, *Antimicrobial resistance,* Reviewed March 2012, http://www.who.int/mediacentre/factsheets/fs194/en/, last accessed 6 August 2012

[2] See *Combating* Antimicrobial Resistance: Policy Recommendations to Save Lives, *Clinical Infectious Diseases*, IDSA, 2011 <http://ecdc.europa.eu/en/activities/diseaseprogrammes/TATFAR/Documents/210911_TATFAR_Report.pdf>, accessed on 6 August 2012.

[3] See *Antibiotics for early-onset neonatal infection: antibiotics for the prevention and treatment of early-onset neonatal infection*, National Institute for Health and Clinical Excellence.

[4] Figure given by Chief Medical Officer in presentation to The Parliamentary and Scientific Committee on 11 June 2013 at the House of Parliament, London, UK.

(then) Health Protection Agency[5], presented evidence of microorganisms displaying resistance found within the carcasses of animals from the ice age[6]. Alexander Fleming, who discovered penicillin, made reference to the dangers of antibiotic resistance in his 1945 Nobel Prize acceptance speech[7]. Streptomycin, the first antibiotic to fight tuberculosis (TB), was introduced in the mid-1940s[8] but TB resistant to one drug (monotherapy) developed within months and was observed even during the clinical trials for Streptomycin's introduction[9].

The medical use of antimicrobials has, since their introduction, involved a constant battle to stay ahead of the mutation curve caused by the selective pressure of fighting the pathogenic strains, and over the past two decades medical science has been losing. Drug-resistance in gonhorroea, for example, is close to reaching a stage where the disease will no longer be treatable, and while efforts to eradicate tuberculosis worldwide nearly succeeded during the twentieth century, the number of cases began to increase again during the 1980s. In 1993, the situation was declared a global health emergency by the World Health Organization (WHO). Extremely Drug Resistant TB (XDR-TB), defined as TB resistant to 'quadruple therapy' of four common frontline drug – rifampicin, isoniazid plus at least one quinolone and at least one injectable antibiotic – was first identified in 2006 and by the turn of the last decade,[10] cases had been reported in fifty-eight countries. In recent years, new drug-resistant strains of *E. coli, Salmonella* and *Streptococci* (responsible for pneumonia) have emerged.

The international burden of AMR

AMR places a significant burden on international governments, both in terms of patient morbidity and financial cost. For example, more than 450,000 new cases of multidrug-resistant tuberculosis (MDR-TB) and Extensively Drug-Resistant Tuberculosis (XDR-TB) emerge worldwide each year, causing approximately 150,000 deaths. Resistance to previously effective anti-malarial drugs such as chloroquine is growing in most malaria-endemic countries[11]. A high percentage of Hospital Acquired Infections (HAIs), which lead to 37,000 deaths in the EU each year (a number comparable with the numbers that die in road traffic accidents[12]), are caused by bacteria such as meticillin-resistant *Staphylococcus aureus* (MRSA) and *Clostridium difficile (C.dif)*. An even more tangiable illustration of the problem is the fact that at the time of the 11 September 2001 attacks on the World Trade Center in New York in which just under 3,000 people lost their lives, more than 14,000 Americans died every year from drug-resistant diseases caught in hospitals, yet the issue received little interest outside of specialist medical circles.

Moving AMR up the political agenda

In recent years, however, increasing concerns over AMR have driven a number of international co-operation and national initiatives. Since 2008, European Antibiotics Awareness Day has been held

[5] Now Public Health England.
[6] Barrett, R., et al, *Emerging and Re-emerging Infectious Diseases: The Third Epidemiologic Transition*, Annual Review of Anthropology, Vol 27, 1998, pp 247-71.
[7] Presentation by the Chief Medical Officer to The Parliamentary and Scientific Committee at a discussion meeting on antibiotics held on 11 June 2013 at the Houses of Parliament, London, UK.
[8] See www.umdnj.edu/ntbcweb/tbhistory.htm, last accessed 6 September 2012.
[9] Gillespie, S. H., 'Evolution of Drug Resistance in *Mycobacterium tuberculosis*: Clinical and Molecular Perspective', *Antimicrobial Agents and Chemotherapy*, Vol. 46, No 2, pp267-274, http://aac.asm.org/content/46/2/267, last accessed 7 September 2012.
[10] See www.who.int/mediacentre/news/releases/2010/drug_resistant_tb_20100318/en/index.html, last accessed 22 August 2012.
[11] Ben Amor Y, Nemser B, Sing A, Sankin A, Schluger N. Underreported threat of multidrug-resistant tuberculosis in Africa. Emerg Infect Dis [serial on the Internet]. 2008 Sept. Available from http://wwwnc.cdc.gov/eid/article/14/9/06-1524.htm, last accessed 28 September 2012.
[12] *English National Point Prevalence Survey on Healthcare-associated Infections and Antimicrobial Use, 2011*, Health Protection Agency, July 2011.

annually on 18 November. In 2011, the WHO World Health Day was dedicated to the issue. Another example is the review of Hospital Acquired Infections and Antimicrobial Use across seventeen EU countries by the European Centre for Disease Control (ECDC) undertaken in 2008,[13] which aims to standardise the way data is collected so that it can be more easily analysed, while the US National Institute of Allergy and Infectious Diseases, National Institutes of Health[14] has teamed up with the European Centre for Disease Control to form the Transatlantic Taskforce on Antimicrobial Resistance (TATFAR), which published its first major report, *Recommendations for future collaboration between the US and EU*, in 2011[15]. The purpose of the taskforce is to intensify co-operation in three key areas it has identified: appropriate therapeutic use of antimicrobial drugs in the medical and veterinary communities; prevention of healthcare and community associated drug-resistant infections; and strategies for improving the supply of new antimicrobial drugs. These key findings are mirrored in the key actions of the EU Action Plan against the rising threat of antimicrobial resistance[16] released in November 2011 and the revised UK Five Year Antimicrobial Resistance Strategy and Action Plan 2013-2018 published in September 2013[17]. The latter contains seven strategic aims including responsible prescribing to preserve existing therapies, raising awareness of the problem and strengthening international collaboration. Implementing these strategies and action plans will involve not only public sector healthcare practitioners and the pharmaceutical industry, but also veterinarians, the agricultural sector, medical retailers, the travel industry, food standards and the leisure sector as well as emergency planners more generally. Raising awareness of the issue, and the emerging threat, will ensure that mitigation strategies can be embedded early.

The impact of AMR on defence and security is also gaining increasing attention. Academics such as Rambhia and Gronvall (2009)[18] have linked it directly to national security concerns, and the European Commission's Seventh Framework Programme of Research and Development (FP7) invested €147 million in AMR research between 2007 and 2013, stating, "Antimicrobial resistance is reaching alarming levels and is a very significant health threat to all Europeans"[19]. The US National Center for Biotechnology Information, the World Health Organization[20], the EU and national government departments responsible for human and animal health have all pushed it further up their security agendas in recent months. A major NIHR call to fund AMR-related research is currently open[21].

AMR and the Military

Embedding awareness of AMR within the military is essential as Armed Forces operations overseas often carry particular risks for the acquisition of infectious diseases. Military personnel operate in areas of the world where the incidence of drug resistant strains is high, and in addition, the British

[13] See *English National Point Prevalence Survey on Healthcare-associated Infections and Antimicrobial Use, 2011*, Health Protection Agency, May 2012 <http://www.hpa.org.uk/Publications/InfectiousDiseases/AntimicrobialAndHealthcareAssociatedInfections/1205HCAIEnglishPPSforhcaiandamu2011prelim/>, accessed 8 August 2012.
[14] See <http://www.niaid.nih.gov/topics/antimicrobialresistance/Pages/default.aspx>, accessed 6 August 2012
[15] See *Combating* Antimicrobial Resistance: Policy Recommendations to Save Lives, *Clinical Infectious Diseases*, IDSA, 2011 <http://ecdc.europa.eu/en/activities/diseaseprogrammes/TATFAR/Documents/210911_TATFAR_Report.pdf>, last accessed on 6 August 2012.
[16] Communication from the Commission to the European Parliament and the Council: Action plan against the rising threats from Antimicrobial resistance, Directorate-General for Health & Consumers, European Commission COM (2011) 748, Brussells, 2011. See <http://europa.eu/rapid/press-release_IP-11-1359_en.htm>, last accessed 2 November 2012.
[17] See: < https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/244058/20130902_UK_5_year_AMR_strategy.pdf>, last accessed 18 November 2013
[18] Rambia, K. J., and Gronvall, G.K. 'Antimicrobial Resistance', *Biosecur Bioterror,* Vol. 7 No. 4, pp. 371-377, December 2009.
[19] FP7 Final Call Factsheets on Strategic Priorities - Antimicrobial Resistance, see <http://ec.europa.eu/research/fp7/pdf/antimicrobial_resistance_fact_sheet.pdf>, last accessed 31 October 2012.
[20] *Ibid.*
[21] See < http://www.themedcalls.nihr.ac.uk/amr/meet-the-programmes>, last accessed 18 November 2013

Armed Forces have recruited extensively from overseas for many years. Gurkhas from Nepal and the Irish Regiments are perhaps the best known examples but in fact, any individual from a Commonwealth country may join the Services, and at any one time up to five percent of recruits may be from overseas. On occasions, the proportion has been even greater than this: in 2011, 7.9 percent of the British Army were foreign nationals[22].

Military activities overseas include operational deployments up to and including warfare, which may be in conjunction with a variety of coalition or Allied Forces and in association with host nation personnel. These may be as part of a formal international intervention such as the United Nations or NATO, or as bilateral agreements with individual countries. Missions to support civilian populations range from evacuation of non-combatants from war zones to humanitarian work and disaster relief operations. The Royal Navy maintains a maritime presence worldwide, with port visits forming an integral part of their role. A key element of any Force preparation is training, and there are well established overseas training locations in a number of hot and cold climates, as well as regular exercises held overseas.

In addition to formed units in operational and training missions, there are also large numbers of military personnel who travel as a part of small groups or alone. These include diplomatic staff, individuals seconded to foreign Armed Forces, specialist military groups such as Special Forces and Weapons Inspectors, and expeditions including Adventurous Training.

In every situation, safe food and water supplies may be compromised, personnel may be exposed to arthropod and animal vectors of disease, have limited access to medical care and be in close contact with local populations during times of heightened disease transmission. Each of these activities involves exposure to a different level of risk to that of a civilian holidaymaker or businessman, and leads to the term “sentinel soldier” reflecting the possibility of a novel disease appearing for the first time in this group. As a result, the military has often been at the forefront of medical research on the understanding and treatment of infectious diseases.

Medical issues

Military personnel are as dependent on antibiotics to ensure continued good health as anyone else. While the public perception of the people who make up the military is that they are young, fit and healthy, this is not necessarily true. Recruits may be fit on entry but go on to develop illness or injury during their service, so that many serving personnel have impaired immunity that makes them susceptible to infectious diseases. In addition, an increasing proportion of deployed personnel are drawn from Reserve Forces, some of whom will have increased risk factors for disease and will return to their civilian place of work after duty overseas.

Bullets and bombs are often considered to be the greatest health threat to deployed military forces but personnel are in fact far more likely to be incapacitated by infectious disease. Recent advances in medical care mean that death from these causes is far less likely today than it has been in the past, but the numbers of casualties overall still out-number trauma cases by a factor of 5 to 10[23].

Military personnel who become ill or are injured overseas will receive immediate medical care, but how and where this is delivered will be dependent on their circumstances. Large operational

[22] Defence Analytical and Statistics Agency. UK Defence Statistics 2011, Chapter 2, Table 2.14. www.dasa.mod.uk/modintranet/UKDS/UKDS2011/c2/table214.php

[23] Smallman-Raynor MR, Cliff AD. Cliff. War Epidemics: An Historical Geography of Infectious Diseases in Military Conflict and Civil Strife, 1850-2000. Oxford University Press 2004. ISBN: 0-19-823364-7

deployments will have full medical support, including immediate First Aid if required, Primary Care, Hospital Care and Aeromedical Evacuation if required. Individuals on isolated detachments on the other hand may be entirely dependent on local health care facilities and/or will be repatriated to the UK by Aeromedical Evacuation if necessary.

In 2010, there were just under 5000 patients repatriated to the UK, of which more than 100 were intensive care patients requiring Critical Care Air Support Team (CCAST) deployment and dedicated aircraft. Most but not all of these were trauma patients from the current conflict in Afghanistan[24].

Severely injured battle trauma patients are likely to be colonised or infected with organisms. This results from the heavy inoculation of environmental material at time of injury, either as a result of gunshot wounds or improvised explosive devices, auto-inoculation by microflora from their own gut or other organs, or healthcare associated infection (HAI). Without aggressive surgical management to remove dead and dying tissues and foreign material, the organisms present may become invasive and cause severe disease. Historically, the leading cause of death from trauma after the initial resuscitation was sepsis, and even with modern management techniques it remains a significant cause of late morbidity and mortality[25].

Trauma patients injured in Afghanistan are repatriated to the UK as soon as they have had immediate life-saving surgery and have been stabilised, which is usually within 24-48 hours. Patients repatriated from other locations such as civilian hospitals elsewhere in the world may have been in-patients for many days or sometime weeks. Both scenarios raise the possibility of transfer of individuals with multi-drug resistant organisms, acquired from primary environmental exposure or HAI related to hospital stays.

MDR bacteria imported by the military

Within days of the start of the Iraq War in 2003, there were reports of MDR bacteria from US military medical facilities that were treating local civilian casualties. These were predominantly related to *Acinetobacter baumannii*, which is an organism commonly isolated from hospitals worldwide and often noted to be resistant to a wide range of antimicrobial agents. Over the following months and years this organism in particular became widely reported as being problematic in military personnel, primarily in the US[26]. It has also been observed in injured personnel from other nations, though not to the same degree. The organism is regarded as being a low-grade pathogen, as it is commonly found colonising patients (i.e. it is present, but not causing disease) and only rarely progressing to infection in individuals with other pre-disposing factors for invasive disease (such as IV lines or ventilatory support)[27]. In common with other related bacteria, it has become important because on those occasions when therapy is indicated there are few available antimicrobial agents available. As such, it means that individuals who are identified as being colonised or infected are managed using infection control measures to prevent spread in the hospital environment to other, more susceptible patients.

In the UK there have been regular admissions of military trauma patients colonised with *A. baumannii* which have generally been identified at an early stage. The spread to other patients has been

[24] Op Herrick casualty and fatality tables up to 30 April 2013. Ministry of Defence. https://www.gov.uk/government/publications/op-herrick-casualty-and-fatality-tables

[25] Hutley EJ, Green AD. Infection in wounds of conflict - old lessons and new challenges. J R Army Med Corps. 2009 Dec;155(4):315-9.

[26] Murray, CK (2008 Mar). "Epidemiology of infections associated with combat-related injuries in Iraq and Afghanistan.". The Journal of trauma 64 (3 Suppl): S232–8. PMID 18316967.

[27] Stuart TL, Mulvey M, Simor AE, Tien HC, Battad A, Taylor G, Vayalumkal JV, Weir C, Ofner M, Gravel D, Paton S. *Acinetobacter baumannii* in casualties returning from Afghanistan. Can J Infect Control. 2007 Fall;22(3):152-4.

prevented by good infection control practices. There have been some outbreaks related to the breakdown of these practices, however, with spread from military personnel to civilian patients[28].

MDR bacteria and current Operations: a multi-national melting pot

The current NATO mission in Afghanistan comprises fifty nations contributing personnel, which provides an opportunity for sharing of micro-organisms from many different parts of the world, particularly when operating in a harsh environment and sharing healthcare facilities. South Asia is also well recognised as being a reservoir for many MDR infectious diseases in local populations for reasons that are not entirely clear, but may reflect both the unregulated use of antimicrobial agents for therapy and environmental selective pressure from saprophytic organisms[29].

Examples of endemic microorganisms with inherent multi-drug resistance include common gastrointestinal pathogens such as *Salmonella species* and *Shigella flexneri* [30], *Mycobacterium tuberculosis* [31], extended spectrum β-lactamase-producing *Escherichia coli* (ESBL) and meticillin-resistant *Staphylococcus aureus* (MRSA). Whilst NATO personnel have regularly acquired gastrointestinal infections, infections with the other organisms have been rare to date, which may reflect limited close contact with local populations that would facilitate transmission.

NATO partner nations often adopt different disease prevention strategies, and this may inadvertently lead to selection of MDR strains of bacteria. For example, the US Armed Forces in Afghanistan are issued with field treatment packs which include broad-spectrum antimicrobial agents to be taken if they are injured[32]. Such regimens are generally ineffective at reducing the incidence of infection and deliver low concentrations of antimicrobial agents to devitalised and heavily contaminated tissues, which in turn provide ideal conditions for the generation of resistance. A particular concern is the use at forward locations of injectable carbapenem agents, in a region where the appearance of novel MDR resistance in some bacteria poses a global threat[33].

Military forces can pose a threat to the host environment as well as being at risk themselves. The increasing use of multinational forces across the world for disaster relief and peace-keeping operations means that fragile ecosystems may be exposed to novel infective agents. In 2010 in Haiti, an outbreak of cholera affected large numbers of internally displaced civilians following a major earthquake, with more than 7,600 dying. The subsequent investigation indicated that the likely source was a Nepalese military unit deployed to assist the Haitian population as part of a UN mission[34]. The organism involved was not highly drug resistant, but the case serves as an example of how easily infections that may have profound consequences can spread around the globe.

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[28] Jones, A; Morgan, D; Walsh, A; Turton, J; Livermore, D; Pitt, T; Green, A; Gill, M; Mortiboy, D (2006 Jun). "Importation of multi drug-resistant Acinetobacter spp infections with casualties from Iraq.". The Lancet infectious diseases 6 (6): 317–8. PMID 16728314.

[29] Wellington EM, Boxall AB, Cross P, Feil EJ, Gaze WH, Hawkey PM, Johnson-Rollings AS, Jones DL, Lee NM, Otten W, Thomas CM, Williams AP.The role of the natural environment in the emergence of antibiotic resistance in Gram-negative bacteria. Lancet Infect Dis. 2013 Feb;13(2):155-65. doi: 10.1016/S1473-3099(12)70317-1.

[30] Threlfall EJ. Antimicrobial drug resistance in Salmonella: problems and perspectives in food- and water-borne infections. FEMS Microbiology Reviews Volume 26, Issue 2, pages 141–148, June 2002

[31] World Health Organization. Global Tuberculosis Report 2012. www.who.int/tb/publications/global_report/gtbr12_main.pdf

[32] Hospenthal DR, Murray CK, Andersen RC, et al. Guidelines for the prevention of infections associated with combat-related injuries. J Trauma. 2011 Aug;71(2 Suppl 2):S210-34. doi: 10.1097/TA.0b013e318227ac4b.

[33] McGann P, Millo M, Clifford R, elt al. Detection of New Delhi Metallo-β-Lactamase (blaNDM-1) in *Acinetobacter schindleri* during routine surveillance. Published ahead of print 3 April 2013, doi: 10.1128/JCM.00281-13. http://jcm.asm.org/content/early/2013/03/29/JCM.00281-13.abstract#aff-1

[34] Cravioto A, Lanata CF, Lantagne DS, Nair GB. Final report of the independent panel of experts on the cholera outbreak in Haiti. United Nations, 4 May 2011. Available at: http://www.un.org/News/dh/infocus/haiti/UN-cholera-report-final.pdf

Infection control

The threat posed by MDR organisms during medical care of casualties on operational deployments means that infection control is critically important in all military medical facilities, including care at point of injury, medical evacuation from the battlefield, Role 3 care (Field Hospital), and strategic Aeromedical Evacuation to the UK. All British Field Hospitals such as that at Camp Bastion include a trained Infection Control Practitioner as part of their permanent manning, and clinical practices follow UK civilian best practice whenever possible within operational constraints. The hospital is inspected at intervals by the UK Care Quality Commission, which has found the standards of infection control practice to be "exceptionally high"[35]. A recent review of Infection Control at NATO medical facilities in Afghanistan found the practices at Camp Bastion to be significantly better than at any other location[36].

Most patients arrive at the receiving centre in the UK, at Queen Elizabeth University Hospital Birmingham, within 48 hours of injury. This is before any microbiological results from initial assessment at Camp Bastion are available and therefore all patients are managed as potentially colonised with MDR bacteria. By careful isolation of these patients, the risk of transmission is minimised. Such policies have been refined over a decade of experience with such cases.

In 2011, the UK Government accepted more than 50 trauma casualties from the Libya conflict, who had been treated in a variety of hospitals in the Mediterranean region. These cases were widely distributed across NHS hospitals to share the workload but in common with casualties managed elsewhere in Europe, most were colonised with MDR bacteria, which in turn could potentially have led to widespread distribution of the organisms within UK hospitals[37].

Geopolitical issues and MDR bacteria

Infectious diseases have played a role in fashioning the development of societies throughout history, with effects ranging from a direct impact on civilian populations, such as the Black Death[38], to the limitation of human settlement by the geographical distribution of diseases such as malaria[39]. In addition, they have influenced the course of many military campaigns, and in some cases changed the outcome of a conflict[40]. Antimicrobial resistance may influence these effects. During the Rwandan Civil War in the 1990s, large numbers of refugees and internally displaced personnel were accommodated in temporary camps with limited water and sanitation. Outbreaks of bacillary dysentery were complicated by the appearance of a MDR strain of *Shigella dysenteriae* Type 1, which was resistant to all available therapies and associated with increased mortality in casualties[41]. Resistance is also becoming more common in other pathogens associated with significant morbidity and mortality in developing countries. Examples include lower respiratory tract infections due to *Streptococcus pneumoniae*[42] and severe sepsis due to *Neisseria meningitidis*[43].

[35] Care Quality Commission. Defence Medical Services: A review of compliance with the essential standards of quality and safety. June 2012. http://www.cqc.org.uk/public/reports-surveys-and-reviews/reviews-and-studies/defence-medical-services
[36] Murray, C.K., personal communication with the author
[37] Koole K, Ellerbroek PM, Lagendijk R et al. Colonization of Libyan civil war casualties with multidrug-resistant bacteria. Clin Microbiol Infect. 2013 Jan 13. doi: 10.1111/1469-0691.12135. [Epub ahead of print]
[38] Slack P. The black death past and present. 2. Some historical problems. Transactions of the Royal Society of Tropical Medicine and Hygiene 1989 July-August, Volume 83, Issue 4, Pages 461–463
[39] Carter R, Kamini N. Mendis K. Evolutionary and Historical Aspects of the Burden of Malaria. Clin. Microbiol. Rev. October 2002 vol. 15 no. 4 564-594
[40] Zapor MJ, Moran KA. Infectious diseases during wartime. Curr Opin Infect Dis 2005 Oct;18(5):395-9.
[41] Kernéis S, Guerin PJ, von Seidlein L, et al. A Look Back at an Ongoing Problem: Shigella dysenteriae Type 1 Epidemics in Refugee Settings in Central Africa (1993–1995). PLoS ONE 4(2): e4494. doi:10.1371/journal.pone.0004494
[42] Schrag SJ, Beall B, Dowell S. Resistant pneumococcal infections: the burden of disease and challenges in monitoring and controlling antimicrobial resistance. World Health Organization 2002.
[43] Oppenheim B. Antibiotic Resistance in Neisseria meningitidis. Clinical Infectious Diseases 1997;24(Suppl 1):S98-101

The consequences of widespread drug resistance amongst bacteria that cause common and severe infections are significant. Many of the diseases predominantly affect children and young adults, which may in turn lead to changes in population demographics if infections with high mortality become refractory to therapy. Similar effects have been seen in societies where HIV is common, with the loss of large numbers of economically active adults consequently having a destabilising effect on society.[44] The military, therefore, has the same interest as civilian health authorities in controlling the spread of antimicrobial drug resistance.

As AMR increases, treatment of infections on the battlefield will become more complex, both for trauma and infectious diseases; in addition military patients may return MDR organisms from overseas to their homeland. However, the increased use of multinational forces to provide humanitarian aid and disaster relief means that they in turn might export novel bacteria to receptive environments. There also remains the potential destabilising effect of MDR on fragile societies, which may have unpredictable consequences.

Increasing security concerns from AMR

Awareness of the likely impact of AMR on defence and security operations is growing and, over the past year, political interest in AMR has reached an important tipping point. The threat was covered extensively in the 2013 World Economic Forum Report which, in a chapter dedicated to the subject stated, *"We will never stay ahead of the [AMR] mutation curve. A test of our resilience is how far behind it we allow ourselves to fall."*[45] The Department of Health has considered how it affects existing National Risk Assessment emergency scenarios and has agreed to consider how it affects UK National security interests more widely for the next National Security Risk Assessment (NSRA) in 2014. The NSRA is summarised in the UK's National Security Strategy, which in turn informs the National Risk Register.

Policy and academia both tend to move slowly, however, while, at the grass roots level – whether this be military field hospitals and refugee camps overseas, or hospitals and GPs surgeries at home – frontline healthcare providers are facing a threat from AMR that is growing every day. It is essential that the issue is highlighted and addressed and that early adopters and champions of better antibiotic stewardship practicses are identified. The importance of antimicrobial resistance to all sectors of society, not just to health, needs to be communicated widely and effectively.

[44] Barnett T, Whiteside A, Desmond C. The social and economic impact of HIV/AIDS in poor countries: a review of studies and lessons. Progress in Development Studies April 2001 vol. 1 no. 2 151-170

[45] See< http://reports.weforum.org/global-risks-2013/view/risk-case-1/the-dangers-of-hubris-on-human-health/> last accessed 17 May 2013

Author biographies

Group Captain Andy Green trained at St George's Hospital Medical School, London and joined the Royal Air Force in 1983. He is part of the National Institute for Health Research Surgical Reconstruction and Microbiology Research Centre (NIHR SRMRC) at Birmingham, where a series of active research programmes are examining the microbiological aspects of wounds in returning military trauma patients. He advises the Surgeon General on all aspects of infectious diseases and their control and has published more than 90 scientific articles.

Jennifer Cole is Senior Research Fellow, Resilience and Emergency Management at the Royal United Services Institute, where her research portfolio includes planning for and responding to CBRN attacks, naturally occurring pandemics and cyber security. She read Biological Anthropology at Cambrigde University and is currently a Reid Scholar in Health, the Human Body and Behaviour at Royal Holloway, University of London, where she is studying for a PhD in Digital Epidemiology, and a Visiting Fellow at Symbiosis School of Biomedical Sciences in Pune, India. Her essay '*Antimicrobial resistance, infection control and planning for pandemics: The importance of knowledge transfer in healthcare resilience and emergency planning*', published in the Journal of Business Continuity and Emergency Planning, Vol 6, No 2, pp122-123, Autumn/Winter 2012-2013 is shortlisted for the Lloyds Science of Risk Prize 2013.

Further reading

Cole, J. , 'Antimicrobial resistance and healthcare resilience: a game changer for the 21st century?', RUSI website commentary, 23 August 2013, see http://www.rusi.org/analysis/commentary/ref:C5036107D33E1C/

Cole, J. 'Antimicrobial resistance, infection control and planning for pandemics: The importance of knowledge transfer in healthcare resilience and emergency planning', *Journal of Business Continuity and Emergency Planning*, Vol 6, No 2, pp122-123, Autumn/Winter 2012-2013, Henry Stewart Publications, London See http://www.henrystewartpublications.com/jbcep/v6

Drug War: The Growing Threat from Antimicrobial Resistance

The risk from antimicrobial resistance (AMR) has evolved beyond its impact on the healthcare sector alone. It is a serious risk to security and resilience that is now being considered in the National Security Risk Assessment for possible inclusion on the UK's National Risk Register alongside pandemic flu and serious infection disease. Jennifer Cole and Group Captain Andy Green explain the growing threat and its particular impact on military operations.