Multi-resistant Infections: A Global Concern

Associate Professor Geoff Sussman

International Wound Infection Institute

What is antimicrobial resistance?

- Antimicrobial resistance (AMR) is resistance of a microorganism to an antimicrobial drug that was originally effective for treatment of infections caused by it.

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What is antimicrobial resistance?

- Resistant microorganisms (including bacteria, fungi, viruses and parasites) are able to withstand attack by antimicrobial drugs, such as antibacterial drugs (e.g., antibiotics), antifungals, antivirals, and antimalarials, so that standard treatments become ineffective and infections persist, increasing the risk of spread to others.

What is antimicrobial resistance?

The evolution of resistant strains is a natural phenomenon that occurs when microorganisms replicate themselves erroneously or when resistant traits are exchanged between them. The use and misuse of antimicrobial drugs accelerates the emergence of drug-resistant strains. Poor infection control practices, inadequate sanitary conditions and inappropriate food-handling encourages the further spread of Antimicrobial resistance .

What is the difference between antibiotic and antimicrobial resistance?

Antibiotic resistance refers specifically to the resistance to antibiotics that occurs in common bacteria that cause infections.

Antimicrobial resistance is a broader term, encompassing resistance to drugs to treat infections caused by other microbes as well, such as parasites (e.g. malaria), viruses (e.g. tuberculosis and HIV) and fungi (e.g. *Candida*).

Why is antimicrobial resistance a global concern?

- New resistance mechanisms emerge and spread globally threatening our ability to treat common infectious diseases, resulting in death and disability of individuals who until recently could continue a normal course of life.
- Without effective anti-infective treatment, many standard medical treatments will fail or turn into very high risk procedures.

Antimicrobial resistance: a global view from the 2013 World Healthcare-Associated Infections Forum

Antimicrobial resistance is now a global threat. Its emergence rests on antimicrobial overuse in humans and food-producing animals; globalization and suboptimal infection control facilitate its spread. While aggressive measures in some countries have led to the containment of some resistant gram-positive organisms, extensively resistant gram-negative organisms such as carbapenem-resistant enterobacteriaceae and pan-resistant Acinetobacter spp. continue their rapid spread.

Huttner et al. Antimicrobial Resistance and Infection Control 2013, 2:31

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Antimicrobial resistance: a global view from the 2013 World Healthcare-Associated Infections Forum

Antimicrobial conservation/stewardship programs have seen some measure of success in reducing antimicrobial overuse in humans, but their reach is limited to acute-care settings in high-income countries. There is scant or no oversight of antimicrobial administration to food-producing animals, while evidence mounts that this administration leads directly to resistant human infections.

Huttner et al. Antimicrobial Resistance and Infection Control 2013, 2:31

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Antimicrobial resistance: a global view from the 2013 World Healthcare-Associated Infections Forum

Novel antimicrobials are urgently needed; in recent decades pharmaceutical companies have largely abandoned antimicrobial discovery and development given their high costs and low yield.

Huttner et al. Antimicrobial Resistance and Infection Control 2013, 2:31

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Antimicrobial resistance: a global view from the 2013 World Healthcare-Associated Infections Forum

Educational programs targeting both antimicrobial prescribers and consumers must be further developed and supported. The general public must continue to be made aware of the current scale of AMR's threat, and must perceive antimicrobials as they are: a non-renewable and endangered resource.

Huttner et al. Antimicrobial Resistance and Infection Control 2013, 2:31

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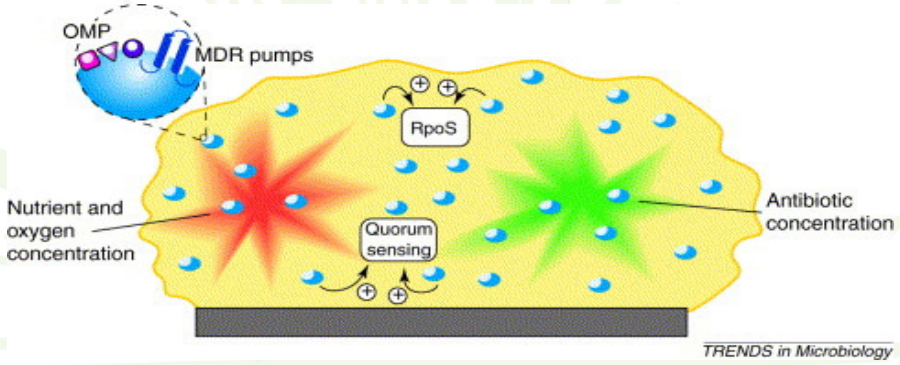
Antibiotic Resistance

Microbial resistance is emerging faster than we are replacing our armamentarium of antimicrobial agents. Resistance to penicillin developed soon after it was introduced into clinical practice in 1940s. Now resistance developed to every major class of antibiotics. In healthcare facilities around the world, bacterial pathogens that express multiple resistance mechanisms are becoming common.

Antibiotic Resistance

The origins of antibiotic resistance genes can be traced to the environmental microbiota. Mechanisms of antibiotic resistance include alterations in bacterial cell wall structure, growth in biofilms, efflux pump expression, modification of an antibiotic target or acquisition of a new target and enzymatic modification of the antibiotic itself.



Mechanisms of resistance in the biofilm include increased cell density and physical exclusion of the antibiotic. The individual bacteria in a biofilm can also undergo physiological changes that improve resistance to biocides.

It was on a short-cut through the hospital kitchens that Albert was first approached by a member of the Antibiotic Resistance.

Antimicrobial resistance kills

Infections caused by resistant microorganisms often fail to respond to the standard treatment, resulting in prolonged illness, higher health care expenditures, and a greater risk of death.As an example, the death rate for patients with serious infections caused by common bacteria treated in hospitals can be about twice that of patients with infections caused by the same non-resistant bacteria. For example, people with MRSA (methicillin-resistant *Staphylococcus aureus*, another common source of severe infections in the community and in hospitals) are estimated to be 64% more likely to die than people with a non-resistant form of the infection.

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AMR hampers the control of infectious diseases

- Antimicrobial resistance reduces the effectiveness of treatment; thus patients remain infectious for a longer time, increasing the risk of spreading resistant microorganisms to others. For example, the emergence of *Plasmodium alciparum* resistance in the Greater Mekong subregion is an urgent public health concern that is threatening global efforts to reduce the burden of malaria.

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AMR increases the costs of health care

When infections become resistant to first-line drugs, more expensive therapies must be used. A longer duration of illness and treatment, often in hospitals, increases health care costs as well as the economic burden on families and societies.

AMR increases the costs of health care

The achievements of modern medicine are put at risk by Antimicrobial resistance. Without effective antimicrobials for prevention and treatment of infections, the success of organ transplantation, cancer chemotherapy and major surgery would be compromised.

Present situation Resistance in bacteria

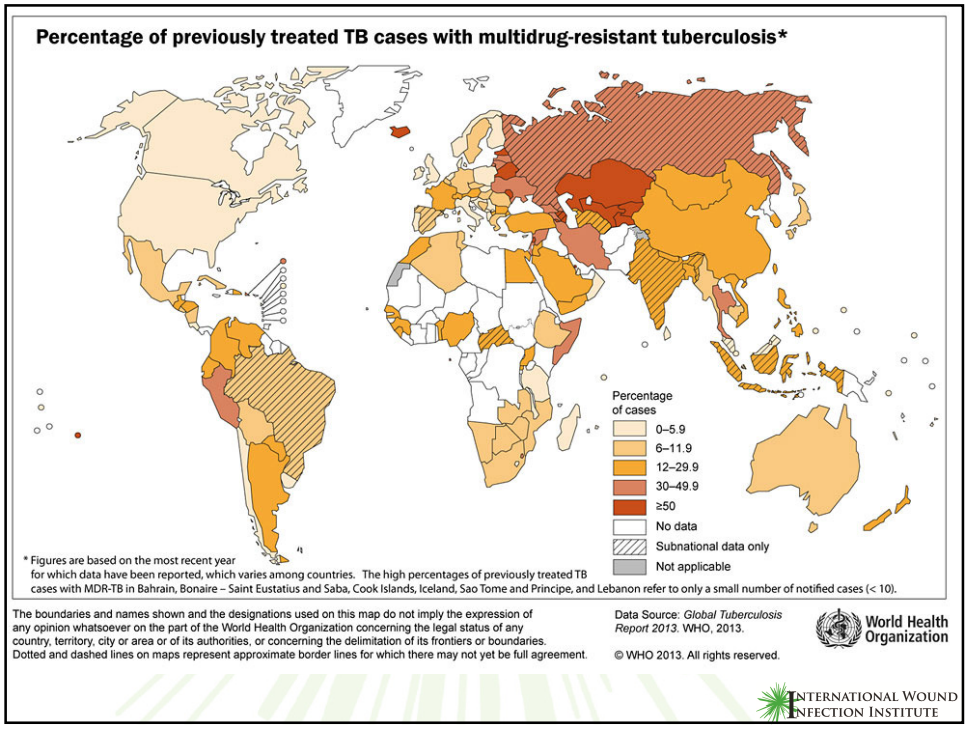
WHO's 2014 report on global surveillance of antimicrobial resistance reveals that antibiotic resistance is no longer a prediction for the future; it is happening right now, across the world, and is putting at risk the ability to treat common infections in the community and hospitals. Without urgent, coordinated action, the world is heading towards a post-antibiotic era, in which common infections and minor injuries, which have been treatable for decades, can once again kill.

- Treatment failure to the drug of last resort for gonorrhoea – third-generation cephalosporins – has been confirmed in several countries. Untreatable gonococcal infections result in increased rates of illness and complications, such as infertility, adverse pregnancy outcomes and neonatal blindness, and has the potential to reverse the gains made in the control of this sexually transmitted infection.
- Resistance to one of the most widely used antibacterial drugs for the oral treatment of urinary tract infections caused by *E. coli* – fluoroquinolones – is very widespread.

- Resistance to first-line drugs to treat infections caused by *Staphlylococcus aureus* – a common cause of severe infections acquired both in health-care facilities and in the community – is also widespread.
- Resistance to the treatment of last resort for life-threatening infections caused by common intestinal bacteria – carbapenem antibiotics – has spread to all regions of the world. Key tools to tackle antibiotic resistance – such as basic systems to track and monitor the problem – reveal considerable gaps. In many countries, they do not even seem to exist.

Resistance in tuberculosis

In 2012, there were an estimated 450 000 new cases of MDR-TB in the world. Globally, 6% of new TB cases and 20% of previously treated TB cases are estimated to have MDR-TB, with substantial differences in the frequency of MDR-TB among countries. Extensively drug-resistant TB (XDR-TB, defined as MDR-TB plus resistance to any fluoroquinolone and any second-line injectable drug) has been identified in 92 countries, in all regions of the world.


Percentage of previously treated TB cases with multidrug-resistant tuberculosis*
Percentage of cases
0–5.9
6–11.9
12–29.9
30–49.9
≥50
No data
Subnational data only
Not applicable
* Figures are based on the most recent year for which data have been reported, which varies among countries. The high percentages of previously treated TB cases with MDR-TB in Bahrain, Bonaire – Saint Eustatius and Saba, Cook Islands, Iceland, Sao Tome and Principe, and Lebanon refer to only a small number of notified cases (< 10).
The boundaries and names shown and the designations used on this map do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted and dashed lines on maps represent approximate border lines for which there may not yet be full agreement.
Data Source: Global Tuberculosis Report 2013. WHO, 2013.
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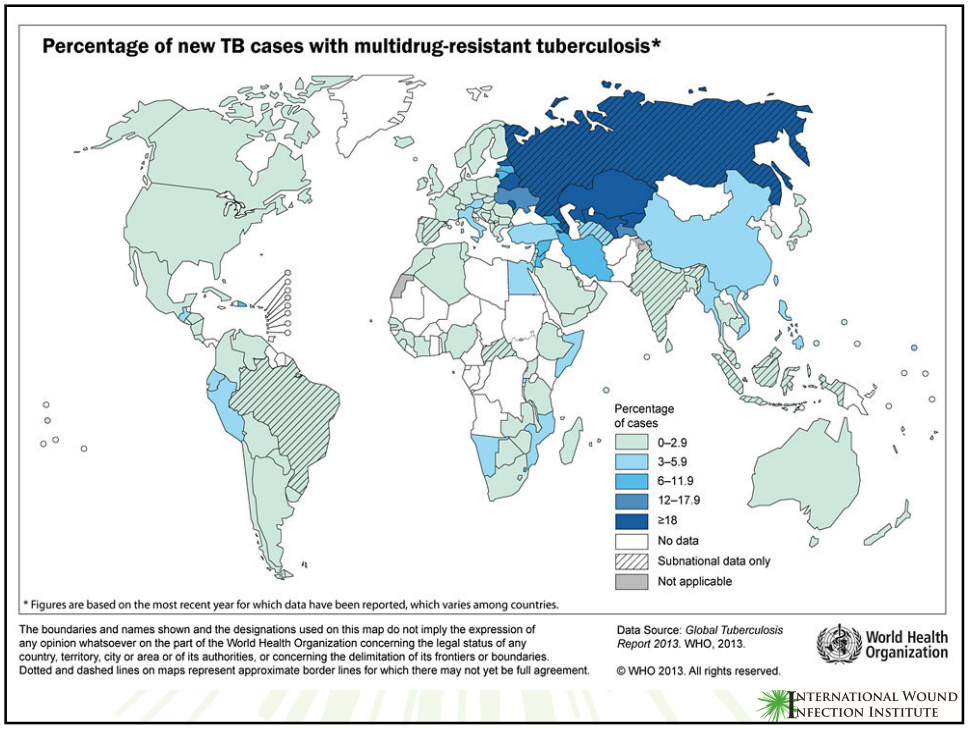
Percentage of new TB cases with multidrug-resistant tuberculosis*
Percentage of cases
0–2.9
3–5.9
6–11.9
12–17.9
≥18
No data
Subnational data only
Not applicable
* Figures are based on the most recent year for which data have been reported, which varies among countries.
The boundaries and names shown and the designations used on this map do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted and dashed lines on maps represent approximate border lines for which there may not yet be full agreement.
Data Source: Global Tuberculosis Report 2013. WHO, 2013.
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A multidisciplinary initiative to save antibiotics: the world alliance against antibiotic resistance (WAAR)

In 2011 an international network, named the World Alliance Against Antibiotic resistance (WAAR). It gathers health professionals, veterinarians, environment specialists, economists, politicians and delegates of the public. This association is Supported by 51 professional societies and counts 470 members, from 45 different countries.

Carlet and Pulcini: A multidisciplinary initiative to save antibiotics: the world alliance against antibiotic resistance (WAAR). Antimicrobial Resistance and Infection Control 2013 2(Suppl 1):O8.

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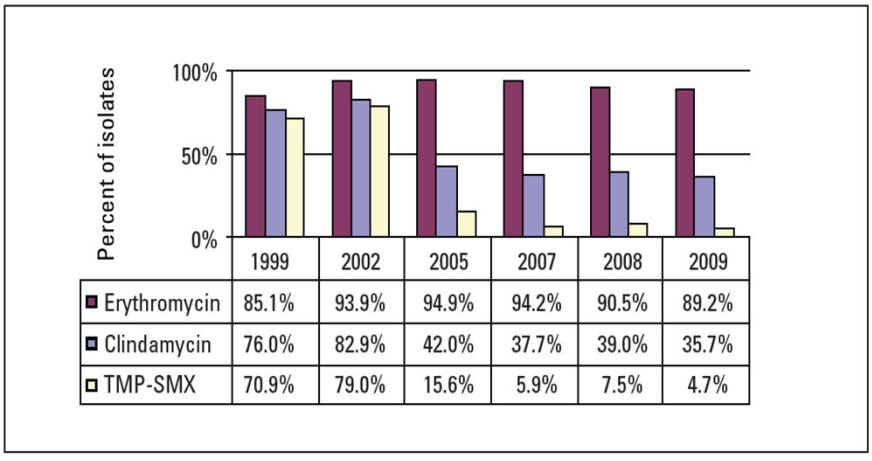

	1999	2002	2005	2007	2008	2009
Erythromycin	85.1%	93.9%	94.9%	94.2%	90.5%	89.2%
Clindamycin	76.0%	82.9%	42.0%	37.7%	39.0%	35.7%
TMP-SMX	70.9%	79.0%	15.6%	5.9%	7.5%	4.7%

Figure 1. Percent of MRSA non-susceptible to clindamycin, erythromycin, and TMP-SMX.

BCMJ 52(4) Perce

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WATER AS A DISSEMINATION ROUTE FOR RESISTANCE

Bacteria do not live in isolation, but are readily Dispersed through the world by humans, animals, plants, soil, water, and air. An underappreciated exposure route for the dissemination of antibiotic resistance is water, and multidrug-resistant bacteria have been detected from various water sources, Including drinking water.

Environment and Resistant Infections • CID 2013:57 (1 September) 2013

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WATER AS A DISSEMINATION ROUTE FOR RESISTANCE

Current water quality guidelines tend to focus only on specific bacteria, but do not have appropriate guidance for the presence of antibiotics introduced by manufacturers,domestic disposal, agriculture, and/or the medical sector.

Environment and Resistant Infections • CID 2013:57 (1 September) 2013

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Antibiotic Resistance in Gram(+)'s

- 65% nosocomial blood stream infections are Gram(+)
- Increasing resistant Gram(+) - MRSA/E, PRSP, VRE
- VREF hospital acquired infections increased 20x between January 1989 and March 1993 (Centers for Disease Control)
- Mortality of VRE bacteremia is 50%
- Reports of Intermediate glycopeptide resistance in Staphylococcus spp. (GISA, GISE, GRSE)

" We face the prospect of untreatable bacterial infections, a situation not encountered since the pre-antibiotic era with a critical need for new agents"

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Science & Society

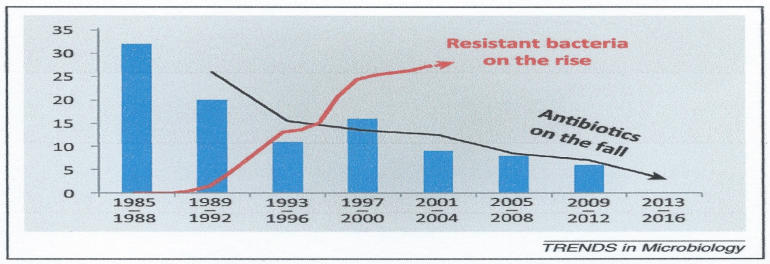

Figure 1. Reverse development of new antibiotics versus resistant bacteria. The abscissa shows a time bar. The ordinate shows blue bars that indicate the number of antibiotics launched in the depicted period; the red line shows the percentage of bacteria resistant against the last resort antibiotic vancomycin in US hospital intensive care units; the black line shows a moving average trend line of antibiotics launched in the depicted period [5,6]. The number of antibiotic-resistant bacteria infections is increasing whereas the development of new antibiotics is constantly decreasing.

Trends in Microbiology April 2014, Vol. 22, No. 4

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The CDC describes an infectious disease landscape in which 2 million people in the United States are sickened annually with antibiotic-resistant infections. The report estimates that at least 23,000 people a year die from antibiotic-resistant infections. It is emphasized that these numbers are very conservative estimates.

In addition, the report quantifies the effects of antibiotic use on the number of illnesses and deaths resulting from *Clostridium difficile* infections. The report estimates that at a minimum, 250,000 illnesses and 14,000 deaths from *C difficile* are directly related to antibiotic use and resistance

The true cost of antimicrobial resistance

They took the study that found the highest cost of antimicrobial resistance, of $55bn per year overall to the US, and compared it with economic burden figures for other health problems in the US. These burden figures are taken from a variety of studies, and the dates range considerably, but it is clear that resistance rates fairly low down. However, the costs of resistance could be much higher than these estimates suggest.

BMJ 2013;346:f1493 doi: 10.1136/bmj.f1493 (Published 11 March 2013)

The true cost of antimicrobial resistance

To calculate the true economic burden of resistance we have to consider the burden associated with not having any effective antimicrobial drugs. And,as witnessed when there are outbreaks of hospital acquired infection, the system can very quickly come to a Standstill. In the future we may need to rethink how the health system is developed if effective antibiotic treatments are no longer available.

BMJ 2013;346:f1493 doi: 10.1136/bmj.f1493 (Published 11 March 2013)

Inappropriate use of medicines leads to drug resistance.

Inappropriate use of antimicrobials drives the development of drug resistance. Both overuse, underuse and misuse of medicines contribute to the problem. Many infectious diseases may one day become uncontrollable. With the growth of global trade and travel, resistant microorganisms can Spread promptly to any part of the world.

Inappropriate use of medicines leads to drug resistance.

Ensuring that patients are informed about the need to take the right dosage of the right antimicrobial requires action from prescribers, pharmacists and dispensers, pharmaceutical industry, nurses, the public and patients, as well as policy makers.

Animal husbandry is a source of drug resistance.

Sub-therapeutic doses of antibiotics are used in animal-rearing for promoting growth or Preventing diseases. This can result in resistant microorganisms, which can spread to humans.

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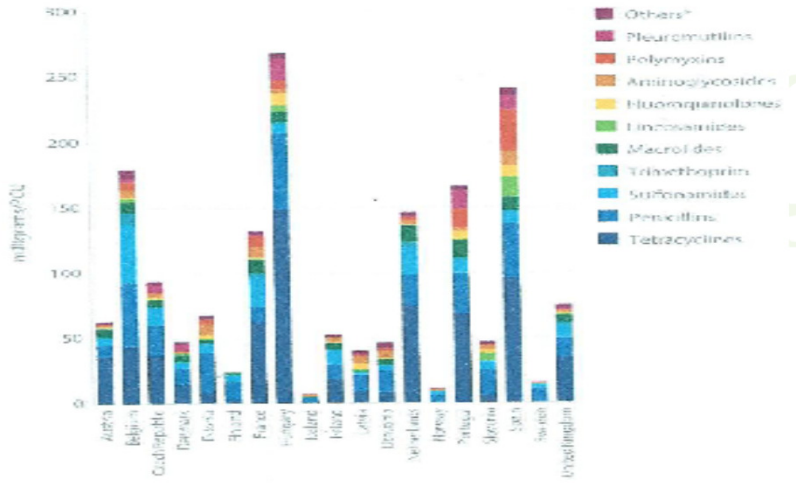
Animal husbandry is a source of drug resistance.

Figure 19: Sales of Antibiotics for Food-Producing Animals[48]

Sales of antibiotics for food-producing animals, including horses, in milligrams of antibiotics per population correction unit (PCU, i.e. 1 kilogram of animal), 2010



Source: Adapted from Sales of Veterinary Antimicrobial Agents in 19 EU/EEA Countries in 2010, 2012, European Medicines Agency

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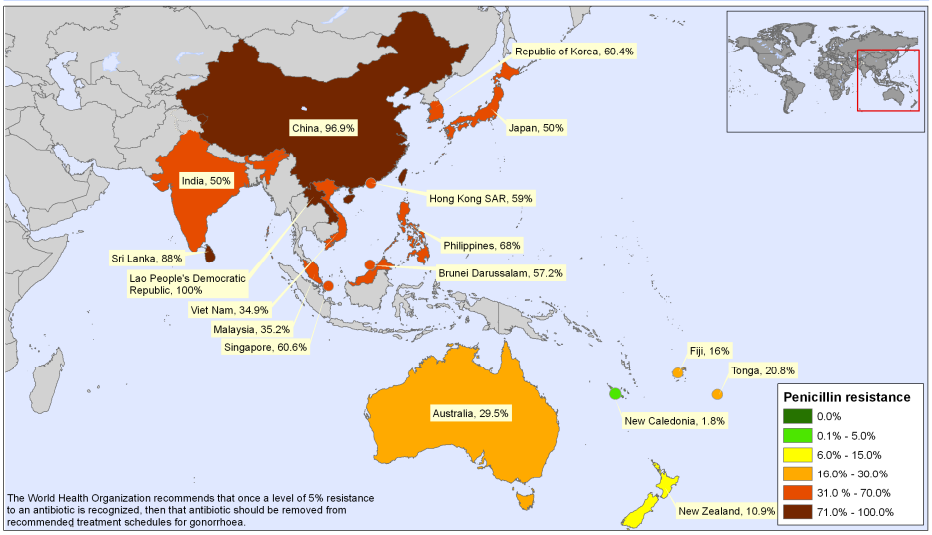
Penicillin resistance of strains of Neisseria gonorrhoeae isolated in countries, areas and territories of WHO South-East Asia and Western Pacific Regions (2005), shown as the % of resistant isolates



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CHANGING RESISTANCE TO SOME PATHOGENS

Escherichia coli

amoxy/clav	10%
ampicillin	46%
cotrimoxazole	17%
trimethoprim	18%

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CHANGING RESISTANCE TO SOME PATHOGENS

Haemophilus influenzae

ampicillin	21%
cotrimoxazole	11%

CHANGING RESISTANCE TO SOME PATHOGENS

Klebsiella pneumoniae

amoxy/clav	7%
cephalexin	13%
ciprofloxacin	4%
cotrimoxazole	12%
trimethoprim	16%

CHANGING RESISTANCE TO SOME PATHOGENS

Streptococcus pneumoniae

cotrimoxazole	33%
macrolides	16%
penicillin	24%
tetracyclines	15.7
trimethoprim	48%

Penicillin resistance in 10 629 strains of *Neisseria gonorrhoeae*

Country	Tested (N)	Resistant or less susceptible (%)
Australia	3 772	17
China	1 254	92.5
Hong Kong	3 378	63.3
Japan	200	77.8
Korea	212	77.8
Singapore	200	51.5

Quinolone resistance in 10 629 strains of *Neisseria gonorrhoeae*

Country	Tested (N)	Resistant or less susceptible (%)
Australia	3 772	14
China	1 254	93.4
Hong Kong	3 378	88.6
Japan	200	85.5
Korea	212	96.7
Singapore	200	56

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Tetracycline resistance in 10 629 strains of *Neisseria gonorrhoeae*

Country	Tested (N)	Resistant or less susceptible (%)
Australia	3 772	11
China	1 254	32.1
Hong Kong	3 378	not tested
Japan	200	3.8
Korea	212	1.9
Singapore	200	58.5

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Development of antibiotic resistance in Gram negative bacilli

To determine the distribution of bacterial pathogens causing nosocomial Infections and their antibiogram, a surveillance data from January to December 2011. A total of 1800 samples from different sources were included in the study like pus, blood, urine, sputum, etc., which were taken from patients admitted in the hospital for more than a week. Gram negative bacilli were isolated, identified, and subjected to antibiotic sensitivity test

Ravinder Pal Singh, Sonali Jain, Parduman Singh, Nikunj Gupta Medical Journal of Dr. D.Y. Patil University | May-June 2014 | Vol 7 | Issue 3

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Development of antibiotic resistance in Gram negative bacilli

Out of the total 1800 samples included, maximum positivity was found in the pus samples (70%). Extended-spectrum beta-lactamase (ESBL) positivity was also maximum in the pus samples (90%). These ESBL positive organisms were further subjected to antibiotic sensitivity tests and huge amounts of resistance was noted to the conventional drugs including the higher end agents like Carbapenems.

Ravinder Pal Singh, Sonali Jain, Parduman Singh, Nikunj Gupta Medical Journal of Dr. D.Y. Patil University | May-June 2014 | Vol 7 | Issue 3

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Results

Table 1: Sample Distribution

Specimen	Total No.	Positive sample	Percentage positivity
Urine	766	276	37
Blood	428	50	11
Pus	216	152	70
Sputum, throat swab	106	40	37
Stool	44	10	22
Fluid	40	4	1

Ravinder Pal Singh, Sonali Jain, Parduman Singh, Nikunj Gupta Medical Journal of Dr. D.Y. Patil University | May-June 2014 | Vol 7 | Issue 3

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Lack of New Antibiotics

In 2012, antibiotic development continues to stagnate. Two systemic antibacterial agents have been approved for use in humans by the U.S. FDA from 2008 through the current year. Compare that to sixteen that were approved from 1983-1987. In particular, we have had no new classes of antibiotics to treat Gram-negative bacilli for more than 40 years – amazingly, the fluoroquinolones were the last new class of antibiotics to treat Gram-negative bacilli Meanwhile, antibiotic resistance continues to spread like wildfire, particularly among the Gram-negative bacilli

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Antibiotic class; example	Year of discovery	Year of introduction	Year resistance observed	Mechanism of action	Activity or target species
Sulfadrugs; prontosil	1932	1936	1942	Inhibition of dihydropteroate synthetase	Gram-positive bacteria
β-lactams; penicillin	1928	1938	1945	Inhibition of cell wall biosynthesis	Broad-spectrum activity
Aminoglycosides; streptomycin	1943	1946	1946	Binding of 30S ribosomal subunit	Broad-spectrum activity
Chloramphenicols; chloramphenicol	1946	1948	1950	Binding of 50S ribosomal subunit	Broad-spectrum activity
Macrolides; erythromycin	1948	1951	1955	Binding of 50S ribosomal subunit	Broad-spectrum activity
Tetracyclines; chlortetracycline	1944	1952	1950	Binding of 30S ribosomal subunit	Broad-spectrum activity
Rifamycins; rifampicin	1957	1958	1962	Binding of RNA polymerase β-subunit	Gram-positive bacteria
Glycopeptides; vancomycin	1953	1958	1960	Inhibition of cell wall biosynthesis	Gram-positive bacteria
Quinolones; ciprofloxacin	1961	1968	1968	Inhibition of DNA synthesis	Broad-spectrum activity
Streptogramins; streptogramin B	1963	1998	1964	Binding of 50S ribosomal subunit	Gram-positive bacteria
Oxazolidinones; linezolid	1955	2000	2001	Binding of 50S ribosomal subunit	Gram-positive bacteria
Lipopetides; daptomycin	1986	2003	1987	Depolarization of cell membrane	Gram-positive bacteria
Fidaxomicin (targeting *Clostridium difficile*)	1948	2011	1977	Inhibition of RNA polymerase	Gram-positive bacteria
Diarylquinolines; bedaquiline	1997	2012	2006	Inhibition of F_1F_O-ATPase	Narrow-spectrum activity (*Mycobacterium tuberculosis*)

Nature Reviews Drug Discovery Volume: 12, Pages: 371–387 Year published: (2013)

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In the context of increasing resistance to antibiotics and the dramatic fall in the number of antibiotics in development, restriction of other potentially useful antimicrobial treatments such as silver dressings is particularly unfortunate. Topical antiseptics, such as silver, differ from antibiotics: they have multiple sites of antimicrobial action on target cells and therefore a low risk of bacterial resistance. As a result, antiseptics have the potential to play an important part in controlling bioburden in wounds while limiting exposure to antibiotics and reducing the risk of development of further antibiotic resistance

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Topical Wound Management

Antibacterials may be used topically with care
They include:

- Antibiotics
- Antiseptics

Topical Antibiotics

Topical antibiotics should only be used in infected wounds under very specific circumstances by experienced clinicians

Topical metronidazole gel might be used for the treatment of malodour in fungating wounds

Silver Sulphadiazine in burns and in wounds

Mupiricin a specific topical antibiotic with no similar Compounds used systemically or orally

Topical Antibiotics

- Don't penetrate tissue
- Decompose in contact with tissue
- Diluted by exudate and decomposition
- Inhibition of contraction
- Delay re-epithelialisation
- Can cause sensitization
- Induce Resistance
- Mostly formulated to be applied to skin (or elsewhere) and act locally, not for exposed tissue

The overall evidence on the efficacy of topical antimicrobials in the management of wounds is confusing.
Most use is based on laboratory studies and not on clinical research.

Some of the research use animal models and there is debate as to how relevant these studies are to chronic wounds.

Topical Antiseptics

There have been many substances used topically over thousands of year including Hypochlorites, Peroxides, Acetic Acid, Honey etc.
Over the past ten years the evidence supports the used in particular of the following:

- Iodine
- Silver
- PHMB

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Iodine

Iodine in its various forms has been used as a topical antiseptic since 1840. The newer forms of iodophores have been used since the 1950's. Most of these new forms combine Iodine in a complex with a polymer eg. Povidone, Cadexomer these slowly release the iodine. Iodine is active against bacteria, mycobacteia,fungi, Protozoas, spores and viruses. There is no evidence of resistance to Iodine.

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What is Silver ?

Silver is a metalic element that in solution, exhibits Three Forms Ag+, Ag++ and Ag+++ each capable of forming inorganic and organic compounds and chemical complexes.
Compounds involving Ag++ or Ag+++ are unstable or insoluble in water.
Silver ions attack multiple microbial cells sites compared with antibiotics that mostly attack only one

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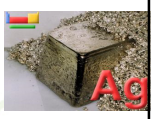

Silver is effective against a broad range of aerobic, anaerobic, gram-negative and gram-Positive bacteria, yeast, filamentous fungi and Viruses. The experience of many clinicians, and more Recent systematic reviews and meta-analyses, Have confirmed positive effects of silver dressings when used appropriately

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Should Silver dressings be used in children ?

Silver dressings should be used in the treatment of children with caution and the dressings should not be used for more than two weeks without good clinical reasons

Silver dressings are toxic to wounds and delay healing

Silver dressings should not be used on wounds where bioburden is not a problem, ie they should be reserved for use in wounds with or at risk of high bioburden or local Infection

Bacteria become resistant to silver

An apparent lack of response to silver does not relate to resistance, rather to inappropriate treatment of the underlying infection and/or wound aetiology

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What do we mean by the two-week challenge?

THE TWO WEEK 'CHALLENGE'

It has been recommended that antimicrobial dressings should be used for two weeks initially and then the wound, the patient and the management approach should be re-evaluated. The consensus group has suggested that this initial two week period can be seen as a two week 'challenge' period during which the efficacy of the silver dressing can be assessed.

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What do we mean by the two-week challenge?

If after two weeks:

- there is improvement in the wound, but continuing signs of infection it may be clinically justifiable to continue the silver dressing with further regular reviews

- the wound has improved and the signs and symptoms of wound infection are no longer present – the silver dressing should be discontinued

- there is no improvement – the silver dressing should be discontinued and consideration given to changing the dressing to one that contains a different antimicrobial agent and if the patient is unwell using a systemic antibiotic and re-evaluating possibly untreated comorbidities.

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When not to use silver dressings

- In the absence of signs of localised (overt or covert), spreading or systemic infection
- Clean surgical wounds at low risk of infection,
- eg donor sites, closed surgical wounds
- Chronic wounds healing as expected according to comorbidities and age
- Small acute wounds at low risk of infection
- Patients who are sensitive to silver or any of the dressing components
- Wounds being treated with enzymatic debridement

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When not to use silver dressings

- During pregnancy or lactation
- When contraindicated by the manufacturer, for example, some manufacturers recommend that their silver dressings are not used during magnetic resonance imaging (MRI), or on/near body sites undergoing radiotherapy

Silver dressings should be used in the context of accepted standard wound care which involves a holistic assessment of the patient and the wound, management of underlying comorbidities, and wound bed preparation

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The major roles for antimicrobial dressings such as silver dressings in the management of wounds are to:

- reduce bioburden in acute or chronic wounds that are infected or are being prevented from healing by microorganisms

- act as an antimicrobial barrier for acute or chronic wounds at high risk of infection or re-infection

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PHMB

Polyhexanide a Biguanid antiseptic related to Chlorhexidine. PHMB was recognised as possessing superior antimicrobial effect to other cationic biocides. PHMB is marketed as a broad-spectrum antimicrobial agent in a number of diverse applications.
PHMB was shown to bind rapidly to the envelope of both Gram-positive and Gram-negative bacteria The toxicity profile of polymeric biguanides is excellent it is not a primary skin irritant nor a hypersensitising agent.

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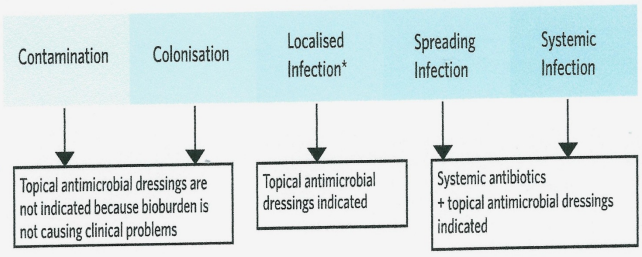
Recommendations

Figure 1 | When to implement antimicrobial dressings (adapted from[14,15,64])



*Including critical colonisation (also known as 'covert' or 'silent' infection or 'pre-infection'). Patients with chronic wounds often have comorbidities that suppress the signs of inflammation and make identification of infection difficult.
NB: Treatment for wound infection should take place in the context of standard care for the wound type, eg debridement, offloading and correction of underlying factors such as malnutrition, ischaemia and hyperglycaemia to enhance the patient's healing potential and ability to fight infection.

Prudent Use to ↓ Resistance

- Use antibiotics only when necessary
- Select agent with narrow spectrum
- Reserve broad spectrum agents for more resistant bacteria
- Continue for an “appropriate” duration
- Avoid chronic prophylaxis if possible
- Policy (guidelines, formulary, restrictions)
- Monitor trends in microbial sensitivity
- Pharmacokinetic/Pharmacodynamic Optimisation
- Cycling of antibiotics

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Box 1. Measures to counter the threat of antibiotic resistance

- Limit antibiotic use in general.
- Increase public awareness of the antibiotic resistance problem. Several campaigns can be considered good practice: Australia – Antibiotic Awareness Week; Canada – AntibioticAwareness.ca; Europe – Antimicrobial Resistance; United States – Get Smart: Know When Antibiotics Work. In India, clinicians are calling for a national policy to ban the sale of antibiotics over the counter, a practice currently leading to the excessive use of antibiotics [7].
- Put basic research on a broad basis.
- Increase cooperation between industry and academia.
- Accelerate the antibiotic development process and facilitate clinical studies.
- Lower too high regulatory hurdles.
- Distribute the burden of financing onto different players.
- Create long-lasting financing mechanisms.

International Wound Infection Institute

The Future of Antibiotics and Resistance

In its recent annual report on global risks, the World Economic Forum concluded that "arguably the greatest risk . . . to human health comes in the form of antibiotic-resistant bacteria. We live in a bacterial world where we will never be Able to stay ahead of the mutation curve.

n engl j med 368;4 nejm.300 org january 24, 2013

The Future of Antibiotics and Resistance

World Economic Forum report underscores the facts that antibiotic resistance and the collapse of the antibiotic research and- development pipeline continue to worsen despite our ongoing efforts on all these fronts.

n engl j med 368;4 nejm.300 org january 24, 2013

New Interventions to Address the Antibiotic-Resistance Crisis.*

Preventing infection and resistance

"Self-cleaning" hospital rooms; automated disinfectant application through misting, vapor, radiation, etc.

Novel drug-delivery systems to replace IV catheters; regenerative-tissue technology to replace prosthetics; superior, noninvasive ventilation strategies

Improvement of population health and health care systems to reduce admissions to hospitals and skilled nursing facilities

Niche vaccines to prevent resistant bacterial infections

n engl j med 368;4 nejm.300 org january 24, 2013

INTERNATIONAL WOUND INFECTION INSTITUTE

New Interventions to Address the Antibiotic-Resistance Crisis.*

Refilling antibiotic pipeline by aligning economic and regulatory approaches

Government or nonprofit grants and contracts to defray up-front R&D costs and establish nonprofits to develop Antibiotics

Institution of novel approval pathways (e.g., Limited Population Antibiotic Drug proposal)

n engl j med 368;4 nejm.300 org january 24, 2013

INTERNATIONAL WOUND INFECTION INSTITUTE

New Interventions to Address the Antibiotic-Resistance Crisis.*

Preserving available antibiotics, slowing resistance

Public reporting of antibiotic-use data as a basis for benchmarking and reimbursement

Development of and reimbursement for rapid diagnostic and biomarker tests to enable appropriate use of Antibiotics

Elimination of use of antibiotics to promote livestock growth

New waste-treatment strategies; targeted chemical or biologic degradation of antibiotics in waste

Studies to define shortest effective courses of antibiotics for infections

n engl j med 368;4 nejm.300 org january 24, 2013

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New Interventions to Address the Antibiotic-Resistance Crisis.*

Developing microbe-attacking treatments with Diminished potential to drive resistance

Immune-based therapies, such as infusion of monoclonal antibodies and white cells that kill microbes

Antibiotics or biologic agents that don't kill bacteria but alter their ability to trigger inflammation or cause disease

n engl j med 368;4 nejm.300 org january 24, 2013

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New Interventions to Address the Antibiotic-Resistance Crisis.*

Developing treatments attacking host targets rather than Microbial targets to avoid selective pressure driving Resistance

Direct moderation of host inflammation in response to infection (e.g., cytokine agonists or antagonists, PAMP receptor agonists)

Sequestration of host nutrients to prevent microbial access to nutrients

Probiotics that compete with microbial growth

n engl j med 368;4 nejm.300 org january 24, 2013

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Conclusions:

The situation is quite dangerous. The time is not far when we will be back in the dark ages of the preantibiotic era.

The need of the hour is to be alert of the gravity of this situation and take necessary measures to halt its progress.

Ravinder Pal Singh, Sonali Jain, Parduman Singh, Nikunj Gupta Medical Journal of Dr. D.Y. Patil University | May-June 2014 | Vol 7 | Issue 3

International Wound Infection Institute

Conclusion

Infection will continue to be a problem with wounds
Complicating the issue is the increased resistance
to Antibiotics and the lack of development of new
Antibiotics. Antiseptics play an important role in
Reducing bioburden and as an antimicrobial barrier.
It is essential to understand when they are
appropriate and how best and how long to use them.