

# Med Pulse



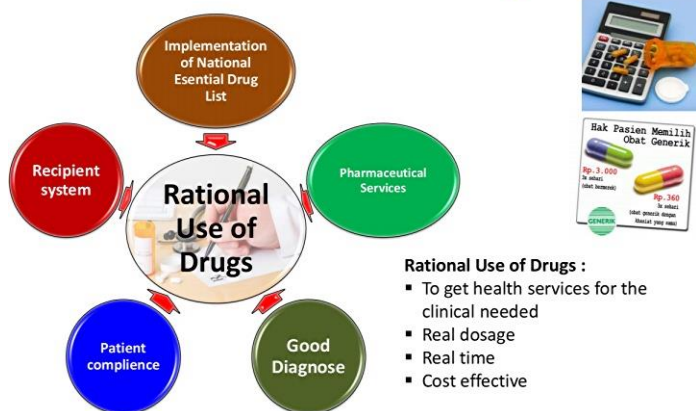
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## RATIONAL USE OF DRUGS

Essential medicines, as defined by the World Health Organization are "those drugs that satisfy the health care needs of the majority of the population. They should therefore be available at all times in adequate amounts and in appropriate dosage forms, at a price the community can afford."

### - Rational Use of Drugs -



This definition focuses on four important aspects of the rational use of medicines:

- correct medication,
- correct dose,
- correct duration of treatment and
- Correct cost.

Access to essential drugs is an important pre-requisite in health care. Available, affordable, good quality and properly used drugs can offer a simple and cost-effective answer to many health problems.

Lack of access to medicines or inappropriate doses result in serious morbidity and mortality. This is seen particularly in childhood infections and chronic diseases

such as hypertension, diabetes, epilepsy and mental disorders. Inappropriate use and over-use of medicines wastes resources. This also causes often out-of-pocket payments by patients. The result is significant patient harm in terms of poor patient outcomes and adverse drug reactions.

Efforts to promote rational drug use have been mainly targeted at the formal health care services. This started back in the 1970s, when WHO introduced the concept of essential drugs. The principle of the concept is that a limited number of drugs would lead to a better supply of drugs, better prescribing and lower costs for health care.

### Anti- microbial resistance

#### Key facts

- Antimicrobial resistance (AMR) threatens the effective prevention and treatment of an ever-increasing range of infections caused by bacteria, parasites, viruses and fungi.
- It is an increasingly serious threat to global public health that requires action across all government sectors and society.
- AMR is present in all parts of the world. New resistance mechanisms emerge and spread globally.
- In 2012, there were about 450 000 new cases of multidrug-resistant tuberculosis (MDR-TB). Extensively drug-resistant tuberculosis (XDR-TB) has been identified in 92 countries. MDR-TB requires treatment courses that are much longer and less effective than those for non-resistant TB.
- Resistance to earlier generation anti-malarial drugs is widespread in most malaria-endemic countries. Further spread or emergence in other regions, of artemisinin-resistant strains of malaria could jeopardize important recent gains in control of the disease.

- There are high proportions of antibiotic resistance (ABR) in bacteria that cause common infections (e.g. urinary tract infections, pneumonia, bloodstream infections) in all regions of the world. A high percentage of hospital-acquired infections are caused by highly resistant bacteria such as methicillin-resistant *Staphylococcus aureus* (MRSA) or multidrug-resistant Gram-negative bacteria.
- Treatment failures due to resistance to treatments of last resort for gonorrhoea (third-generation cephalosporins) have now been reported from 10 countries. Gonorrhoea may soon become untreatable as no vaccines or new drugs are in development.
- Patients with infections caused by drug-resistant bacteria are generally at increased risk of worse clinical outcomes and death, and consume more healthcare resources than patients infected with the same bacteria that are not resistant.

## What is antimicrobial resistance?

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

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.

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 encourage the further spread of AMR.

## 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. 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.

### **AMR 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 (*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.

### **AMR hampers the control of infectious diseases**

AMR reduces the effectiveness of treatment; thus patients remain infectious for a longer time, increasing the risk of spreading resistant microorganisms to others.

### **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 jeopardizes health care gains to society**

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

## **AMR has the potential to threaten health security, and damage trade and economies**

The growth of global trade and travel allows resistant microorganisms to be spread rapidly to distant countries and continents through humans and food. Estimates show that AMR may give rise to losses in Gross Domestic Product of more than 1% and that the indirect costs affecting society may be more than 3 times the direct health care expenditures. It affects developing economies proportionally more than developed ones.

### **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 have 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 *Staphylococcus 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**

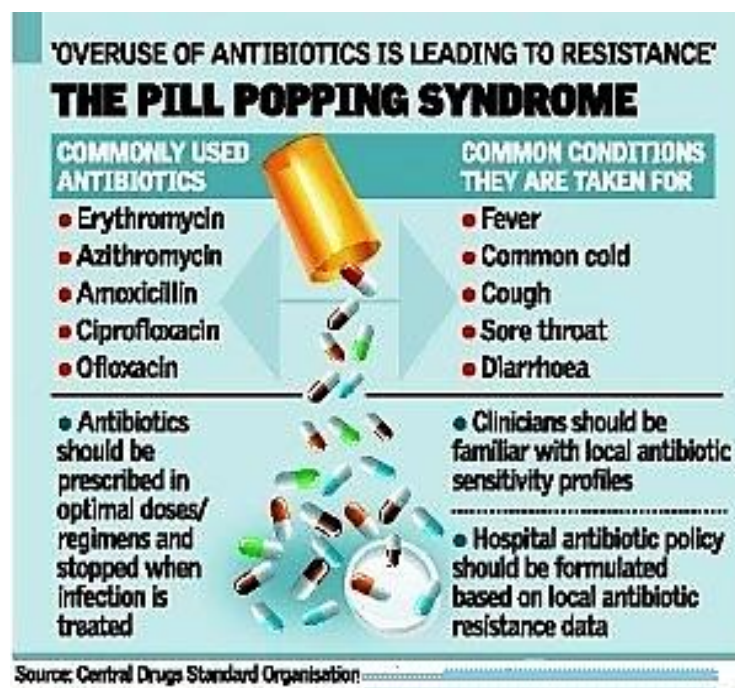
In 2012, there were an estimated 450 000 new cases of MDR-TB in the world. Globally, 6% of new TB cases and 20% of previously treated TB cases are estimated to have MDR-TB, with substantial differences in the frequency of MDR-TB among countries. Extensively drug-resistant TB (XDR-TB, defined as MDR-TB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

#### **Resistance in HIV**

Resistance is an emerging concern for treatment of HIV infection, after the rapid expansion in access to antiretroviral drugs in recent years; national surveys are underway to detect and monitor resistance.

At the end of 2011, more than 8 million people were receiving antiretroviral therapy in low- and middle-income countries to treat HIV. Although it can be minimized through good programme practices, some amount of resistance to the medications used to treat HIV is expected to emerge.

Analysis of data from WHO surveys that target people who have been recently infected with HIV indicates increasing levels of resistance to the non-nucleoside reverse transcriptase (NNRTI) class of drug used to treat HIV. This increase is particularly noticeable in Africa, where the prevalence of resistance to NNRTI reached 3.4% in 2009.



There is no clear evidence of increasing levels of resistance to other classes of HIV drugs. Of 72 surveys of transmitted HIV drug resistance conducted between 2004 and 2010, 20 (28%) were classified as having moderate (between 5% and 15%) prevalence of resistance.

Available data suggest that there is an association between higher levels of coverage of antiretroviral therapy and increased levels of HIV drug resistance.

### ***What accelerates the emergence and spread of antimicrobial resistance?***

The development of AMR is a natural phenomenon. However, certain human actions accelerate the emergence and spread of AMR. The inappropriate use of antimicrobial drugs, including in animal husbandry, favours the emergence and selection of resistant strains, and poor infection prevention and control practices contribute to further emergence and spread of AMR.

### ***Need for concerted actions***

AMR is a complex problem driven by many interconnected factors. As such, single, isolated interventions have little impact. Coordinated action is required to minimize emergence and spread of AMR.

### **People can help tackle resistance by:**

- using antibiotics only when they are prescribed by a certified health professional;
- completing the full treatment course, even if they feel better;
- Never sharing antibiotics with others or using leftover prescriptions.

### **Health workers and pharmacists can help tackle resistance by:**

- enhancing infection prevention and control;
- prescribing and dispensing antibiotics only when they are truly needed;
- Prescribing and dispensing the right antibiotic(s) to treat the illness.

### **Policymakers can help tackle resistance by:**

- strengthening resistance tracking and laboratory capacity;

- strengthening infection control and prevention;
- regulating and promoting appropriate use of medicines;
- Promoting cooperation and information sharing among all stakeholders.

### **Policymakers, scientists and industry can help tackle resistance by:**

- Fostering innovation and research and development of new vaccines, diagnostics, infection treatment options and other tools.

### **WHO's response**

WHO is working in collaboration with partners across many sectors to identify strategies and actions to mitigate AMR. WHO is already working closely with the World Organisation for Animal Health (OIE) and the Food and Agriculture Organization of the United Nations (FAO) to promote best practices to avoid the emergence and spread of antibacterial resistance, including optimal use of antibiotics in both humans and animals.

In 2011, the theme of World Health Day was “Antimicrobial resistance: no action today, no cure tomorrow”, and a six-point policy package was published to assist countries with tools to combat antimicrobial resistance.

In 2014, WHO published its first global report on surveillance of antimicrobial resistance, with data provided by 114 countries.

### **WHO is guiding the response to AMR by:**

- bringing all stakeholders together to agree on and work towards a coordinated response;
- strengthening national stewardship and plans to tackle AMR;
- generating policy guidance and providing technical support for Member States;
- Actively encouraging innovation, research and development.

### **References:**

- Rational use of drugs policy- FPA India
- WHO guidelines for rational use of drugs

**GOOD PRESCRIBING IS NOT SIMPLY MATCHING THE DISEASE AND THE DRUG.....!**

## Current and Emerging Resistant Bacteria

Current and Emerging Resistant Bacteria	Type	Representative Clinical Infections	Antibiotics Associated with Resistance	Treatment Options (as determined based on culture & sensitivity, local guidelines, clinical presentation)
Methicillin-resistant Staphylococcus aureus (MRSA) <sup>[2]</sup>	gram (+) cocci	skin/soft tissue infections, UTI, bacteremia, toxic shock syndrome, pneumonia, osteomyelitis, endocarditis, meningitis; assoc. with IV catheters	beta-lactam antibiotics (e.g., oxacillin, penicillin, amoxicillin, and most cephalosporins) erythromycin	vancomycin  alternatives: linezolid; clindamycin (confirm with D-test); daptomycin; TMP-SMX; quinupristine-dalfopristin
Vancomycin intermediate and resistant Staphylococcus aureus (VISA/hVISA/VRSA)	gram (+) cocci	skin/soft tissue infections, UTI, bacteremia, toxic shock syndrome, pneumonia, osteomyelitis, endocarditis, meningitis	vancomycin; beta-lactam antibiotics (e.g., oxacillin, penicillin, nafcillin, amoxicillin, and most cephalosporins) erythromycin	linezolid; clindamycin; daptomycin; TMP-SMX; quinupristine-dalfopristin
Community-acquired methicillin-resistant Staphylococcus aureus (cMRSA)	gram (+) cocci	necrotizing pneumonia; skin infections, boils, abscesses (seen in IV drug abusers, athletes who share equipment, day care centers, military personnel; prisons); drainage of abscess is primary treatment; treat with antibiotic only if needed	beta-lactam antibiotics (e.g., oxacillin, penicillin, amoxicillin, and most cephalosporins, erythromycin)	Doxycycline or minocycline; clindamycin (confirm with D-test); linezolid; TMP-SMX
Streptococcus pneumoniae (multi-drug resistant)	gram (+) diplococcus	pneumonia, otitis media, sinusitis, bronchitis, bacteremia, peritonitis, cellulitis, meningitis, arthritis	multi-drug resistance; penicillin G, cephalosporins, TMP-SMX, erythromycin, Doxycycline	for multi-drug resistance consider: vancomycin +/- rifampin; fluoroquinolone (gemifloxacin, moxifloxacin, levofloxacin)  alternatives: linezolid; clindamycin; imipenem/cilastatin
Escherichia coli (E. Coli) - CTX-M extended spectrum beta-lactamases (ESBL)	gram (-) rod	UTIs	Oral cephalosporins, TMP/SMX, fluoroquinolones	Fosfomycin, nitrofurantoin, ertapenem, doripenem, imipenem/cilastatin
Enterococcus faecium (E. faecium) vancomycin resistant enterococci (VRE)	gram (+) cocci	meningitis, UTI, bacteremia (central venous catheter-related), endocarditis	vancomycin; streptomycin; gentamicin; penicillin; Ampicillin	linezolid; quinupristine-dalfopristin; daptomycin, Fosfomycin (for UTI)
Pseudomonas aeruginosa (multidrug resistant strains)	gram (-) rod	UTIs, pneumonias, skin and soft-tissue infections, endocarditis, meningitis	imipenem/cilastatin, meropenem, non-antipseudomonal penicillin, oral cephalosporins	colistin, polymyxin B (for multidrug resistant strains)

<b>Current and Emerging Resistant Bacteria</b>	<b>Type</b>	<b>Representative Clinical Infections</b>	<b>Antibiotics Associated with Resistance</b>	<b>Treatment Options (as determined based on culture &amp; sensitivity, local guidelines, clinical presentation)</b>
Klebsiella pneumoniae -extended spectrum beta-lactamases (ESBL)	gram (-) rod	pneumonias, UTIs, upper respiratory tract infections, surgical wound infections	2nd, 3rd generation cephalosporins; aztreonam; carbapenem	imipenem; meropenem; colistin
multi-drug resistant Mycobacterium tuberculosis (MDR-TB)	acid-fast	tuberculosis (lung infection)	isoniazid; rifampin; possibly streptomycin	multiple agents required for treatment: aminoglycoside (amikacin or kanamycin) or polypeptide antibiotic (capreomycin) + antimycobacterials (pyrazinamide + ethambutol) + fluoroquinolone (moxifloxacin) + rifabutin; other agents may need to be substituted based on drug availability
Acinetobacter baumannii	gram (-) rod	immunocompromised patients: pneumonia (commonly ventilator-associated), UTI, septicemia, central venous catheter-related infections, traumatic wound infections	imipenem; meropenem; antipseudomonal agents, fluoroquinolones, carbapenem	ampicillin-sulbactam ; colistin
Staphylococcus epidermidis (methicillin resistant)	gram (+)	bacteremia, catheter, implant, and prostheses-related infection (biofilm formations), endocarditis	penicillin, amoxicillin	vancomycin  if infected implant, surgical removal or replacement may be required; vancomycin +/- (rifampin + gentamicin)  alternative regimens if vancomycin resistant: daptomycin, linezolid

\* Note: Table 1 is not a comprehensive listing of all resistant bacteria and treatments. Antibiotic resistance patterns are constantly evolving and bacteria may not always exhibit resistance to select antibiotics in every patient. In all cases, antibiotic selection should be based on site of infection and clinical presentation as evaluated by a health care professional, culture/sensitivity and other needed laboratory results, local resistance/susceptibility patterns, and patient-specific characteristics.. In many instances, the care of a team of healthcare providers, including an infectious disease specialist, may be required.