# ANTIBIOTICS RESISTANCE: A CONSEQUENCE OF DRUG MISUSE

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# OUTLINE OF LECTURE

### Bacteria

- What are they?
- Why do they cause disease?

### Antibiotics

- What are they?
- How do they kill bacteria?
- What do antibiotics treat?
- Misuse/Overuse of Antibiotics

### Antibiotics Resistance

- What is Antibiotic Resistance?
- Why does it occur?
- What are the consequences of its occurrence?
- Antibiotic use in agriculture and spread of antibiotic resistance
- How does antibiotic resistance spread?
- WHO guidelines on the use of antimicrobials/antibiotics in agriculture

# OUTLINE OF LECTURE

- Decline in the development of new antibiotics
- Prevention and Control of Antibiotics Resistance
  - Role of Individuals
  - Role of Healthcare Professionals (doctors, pharmacists, nurses, etc.)
  - Role of Healthcare Facilities (hospitals, clinics, etc.)
  - Role of the Agriculture Sector
  - Role of Policy Makers/Government
  - Role of WHO: Global Action Plan
  - Role of NAFDAC: Recommendations and Action Plan
- Summary and Conclusions
- Acknowledgements

### Bibliography



- Single cell microorganisms.
- First life forms on earth.
- Simple organisms with cell walls but lack organelles and an organized nucleus.
- Exist in soil, water, air
- Live in symbiotic and parasitic relationships with plants and animals.
- Size:
  - 0.5-5 micrometers long (microscopic)
  - Different shapes (spherical, spirals, rods)
- I gram of soil contains 40 million bacterial cells.
- 1 milliliter of fresh water contains 1 million bacterial cells.

### Shapes of Bacteria



### H. influenzae



E. coli



S. pneumoniae





# **• BENEFICIAL ROLES OF BACTERIA**

- Food industry: preparation of fermented foods such as cheese, yoghurt and wine.
- Waste Management: used to clean up oil spills.
- Mining: used for the recovery of gold, palladium and copper.
- Agriculture: used in place of pesticides in pest control.



# **• BENEFICIAL ROLES OF BACTERIA**

- Biotechnology: used in the manufacture of antibiotics.
- Research: in fields of molecular biology and genetics, bacteria is used to study the function of genes and metabolic pathways.
- Gut: aids in food digestion and synthesis of vitamins
   B and K in humans.



# **•HARMFUL ROLES OF BACTERIA**

Can cause diseases in animals.

 Cholera, typhoid, pneumonia, tuberculosis and tetanus are common human diseases.

- Can cause diseases in plants.
  - Bacterial wilt of tomato and brown rot of potato are common plant diseases.

 Can cause spoilage of unprotected foodstuffs such as fruits and bread.



# Overview of Bacterial infections

#### **Bacterial meningitis**

- Streptococcus pneumoniae
- Neisseria meningitidis
- Haemophilus influenzae
- Streptococcus agalactiae
- Listeria monocytogenes

#### Otitis media

- Streptococcus pneumoniae

#### Pneumonia -

Community-acquired:

- Streptococcus pneumoniae
- Haemophilus influenzae
- Staphylococcus aureus Atypical:
- Mycoplasma pneumoniae
- Chlamydia pneumoniae
- Legionella pneumophila Tuberculosis
- Mycobacterium tuberculosis

#### Skin infections

- Staphylococcus aureus
- Streptococcus pyogenes
- Pseudomonas aeruginosa

### Sexually transmitted diseases

- Chlamydia trachomatis
- Neisseria gonorrhoeae
- Treponema pallidum
- Ureaplasma urealyticum
- Haemophilus ducreyi

#### Eye infections

- Staphylococcus aureus
- Neisseria gonorrhoeae
- Chlamydia trachomatis

#### Sinusitis

- Streptococcus pneumoniae
- Haemophilus influenzae

### Upper respiratory tract infection

- Streptococcus pyogenes
- Haemophilus influenzae

#### Gastritis

- Helicobacter pylori

#### - Food poisoning

- Campylobacter jejuni
- Salmonella
- Shigella
- Clostridium
- Staphylococcus aureus
- Escherichia coli

#### - Urinary tract infections

- Escherichia coli
- Other Enterobacteriaceae
- Staphylococcus saprophyticus
- Pseudomonas aeruginosa

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# ANTIBIOTICS

- Antibiotics (also named Antibacterial drugs)
  - Drugs used in the prevention and treatment of infections caused by bacteria.
  - Antibiotics are one of the most frequently prescribed drugs in modern medicine.
  - Antibiotics are chemicals produced naturally from living organisms such as fungi, mold and certain soil bacteria

#### HOW DID THEY MAKE PENICILLIN?



FOR MANY YEARS, scientists knew that certain molds killed some bacteria. However, researchers needed to understand how to harness this antibacterial microbe and to manufacture enough of the substance before they could make a useful medicine.





#### www.nlm.nih.gov

# How do antibiotics work?

 Antibacterials exploit the difference between the prokaryotic bacterial cell and the host's eukaryotic cell.

They work by being either:

- bacteriostatic, preventing cells from multiplying so that the bacterial population remains static, allowing the host's defence mechanism to fight the infection.
- bactericidal, by killing the bacteria.

Antibiotics acting on bacteria causing them to expand and burst.



#### www.slideshare.net

# WHAT DO ANTIBIOTICS TREAT?

- Antibiotics are only needed to treat certain infections caused by bacteria such as:
  - Pneumonia
  - Sepsis
- Antibiotics do not work on viruses such as:
   Colds and flu
- Antibiotics may not work on some common bacterial infections such as:
  - Most cases of bronchitis
  - Many sinus infections
  - Some ear infections

# **MISUSE/OVERUSE OF ANTIBIOTICS**

- Examples include:
  - Self prescription
  - Prescription of antibiotics to treat symptoms or diseases that do not respond to these drugs (e.g., viral infections).
  - Incorrect or suboptimal doses of antibiotics are prescribed for some bacterial infections.
  - Excessive use of antibiotics as prophylactics for travelers.
  - Failure to take the entire prescribed course of antibiotics

### **SUMMARY OF KEY FINDINGS**

#### PROFESSIONALS

28% of clinicians say

patient request is one of the reasons they prescribe an antibiotic when they are not certain that it is necessary

### 11% OF CLINICIANS REPORT

that they prescribe an antibiotic if the patient demands it

### 11% OF CLINICIANS STATE

that, in the absence of certainty that an infection is not bacterial, "antibiotics cannot hurt"

### 21.5% OF THE TIME CLINICIANS PRESCRIBE ANTIBIOTICS

when they are not sure that they are absolutely necessary

#### CONSUMERS

### 23% OF CONSUMERS

they have asked a clinician to prescribe an antibiotic

### 97% OF CONSUMERS

that it is more difficult to cure some bacterial infections or diseases today because some bacteria have become resistant to one or more of the antibiotics used to treat them

#### 12% OF CONSUMERS REPORT

that they or a close family member/friend have already experienced an infection caused by antibiotic-resistant bacteria



### PATIENT RESPONSES WHEN ANTIBIOTIC NOT NEEDED

# What is the consumer experience after being told an antibiotic is not needed?

Of our 1,174 respondents,

they have **never asked** their clinician to prescribe an antibiotic.

#### Of the

23% WHO HAVE ASKED

their clinician to prescribe an antibiotic for themselves, their children, or someone else for whom they provide care (respondents could choose more than one answer)

# 35%<sup>SAY</sup>

they have **never been told** that the requested antibiotic was not necessary.

#### Of the

65% WHO HAVE BEEN TOLD

on at least one occasion that the requested antibiotic is not necessary,

# 11.5% WERE ASKED

at the end of that discussion whether they still wanted the antibiotic and

ACCEPTED THIS OFFER FOR ANTIBIOTICS.

#### www.medscape.com

### Misusing and overusing ANTIBIOTICS puts us all at risk



Taking antibiotics when they are not needed accelerates emergence of antibiotic resistance, one of the biggest threats to global health

#### You can help reduce antibiotic resistance



Always follow the advice of a qualified health care professional when taking antibiotics



When bacteria become resistant to antibiotics, common infections will no longer be treatable



Overuse of antibiotics can cause bacteria to become resistant, meaning current treatments will no longer work



It is the bacteria itself not the person or the animal – that becomes resistant to antibiotics





Antibiotic resistant infections can lead to longer hospital stays, higher medical costs and more deaths



Antibiotic resistant infections can affect anyone, of any age, in any country



# WHAT IS ANTIBIOTIC RESISTANCE?

• Antibiotic Resistance (AR) refers to the ability of the bacteria to resist the effects of drugs designed to kill or incapacitate them.

Other microorganisms such as fungi, viruses and parasites also develop resistance to drugs designed to kill them (referred to as Antimicrobial Resistance).

 Bacteria, but not humans or animals become resistant to antibiotics

#### Susceptible bacteria

#### **Resistant bacteria**



Antibiotic resistance tests; the bacteria in the culture on the left are sensitive to the antibiotics contained in the white paper discs. The bacteria on the right are resistant to most of the antibiotics.

Dr. Graham Beards @en.wikipedia

# WHY DOES ANTIBIOTIC RESISTANCE OCCUR?

## **CAUSES OF** ANTIBIOTIC RESISTANCE



Antibiotic resistance happens when bacteria change and become resistant to the antibiotics used to treat the infections they cause.



www.who.int/drugresistance #AntibioticResistance







www.cdc.gov

# MECHANISMS OF DEVELOPMENT OF RESISTANCE BY BACTERIA

Inhibition of uptake of drugs into bacteria.

 Activation of efflux pumps to remove drugs from bacteria.

Inactivation of drugs by bacterial enzymes.

• Alteration of drug target by bacteria.



CONSEQUENCES OF DEVELOPMENT OF ANTIBIOTIC RESISTANCE

• According to WHO, Antibiotic Resistance is one of the biggest threats to global health and food security that requires action across government sectors and the society.

 Antibiotics Resistance can affect anyone, of any age, in any country.

• Antibiotic Resistance threatens the effective prevention and treatment of an increasing range of infections caused by bacteria (such as pneumonia, gonorrhea and tuberculosis). CONSEQUENCES OF DEVELOPMENT OF ANTIBIOTIC RESISTANCE

 Without effective antibiotics, the success of major surgery and cancer chemotherapy would be compromised.

• Antibiotics Resistance leads to longer hospital stays, higher medical costs and increased mortality.

• Antibiotics Resistance occurs naturally, but misuse of antibiotics in humans and animals is accelerating the process. ANTIBIOTIC USE IN AGRICULTURE AND SPREAD OF ANTIBIOTICS RESISTANCE

- ADVANTAGES IN FOOD-PRODUCING ANIMALS
   ADVANTAGES
   ADVANTAGES
  - Animals receiving antibiotics in their feed tend to gain more weight than their untreated counterparts.
  - Antibiotics are used for the prevention or treatment of diseases in animals.
  - Livestock treated with antibiotics tend to live longer than their untreated counterparts.

 Overall shell-life is increased for poultry, meat, eggs and diary products when animals are treated with antibiotics.

Hao et al. Benefits and risks of antimicrobial use in food-producing animals. Front Microbiol. 5:28, 2014 ANTIBIOTIC USE IN AGRICULTURE AND SPREAD OF ANTIBIOTICS RESISTANCE

OISADVANTAGE IN FOOD-PRODUCING ANIMALS

- Widespread use of antibiotics in food-producing animals has led to drug-resistant bacteria!
- Recent Observations:
  - According to US FDA: in 2016, 70% of antibiotics used in the US were administered to animals (especially cows)!
  - On October 17, 2018, the US Public Interest Research Group published a study which found that out of 25 hamburger restaurant chains (including McDonald's), only two passed its test of using antibiotics-free beef on their menu!

Hao et al. Benefits and risks of antimicrobial use in food-producing animals. Front Microbiol. 5:28, 2014

### ANTIBIOTIC USE IN AGRICULTURE AND SPREAD OF ANTIBIOTICS RESISTANCE

### ADVANTAGES IN FOOD-PRODUCING PLANTS ADVANTAGES ADV

- Antibiotics are used for control of bacterial diseases of plants.
- In the US, springtime antibiotic sprays suppress pathogen growth on flowers and leaf surfaces before infection.
- Antibiotics are active on plants for less than a week and significant residues have not been found on harvested fruit.
- Antibiotics have been indispensable for crop protection in the US for more than 50 years without reports of adverse effects on human health.
  - Stockwell and Duffy. Use of antibiotics in plant agriculture. Rev Sci Tech. 31:199-210, 2012



# HOW DOES RESISTANT BACTERIA SPREAD ?

### • Facilitated by:

- Poor hygiene
- Poor sanitation
- Poor infection control
- Occurs through:
  - Person to person transmission
  - Animals to humans and vice versa
  - Food
  - Water
  - Traveling
- Occurs at:
  - Health care facilities
  - Community
  - Animal production facilities



### **Examples of How Antibiotic Resistance Spreads**



Simply using antibiotics creates resistance. These drugs should only be used to treat infections.

#### www.uws.edu

WHO GUIDELINES ON USE OF MEDICALLY IMPORTANT ANTIMICROBIALS IN FOOD-PRODUCING ANIMALS (2017)

### RECOMMENDATIONS:

- An overall reduction in use of all classes of medically important antimicrobials in food-producing animals.
- Complete restriction of use of all classes of medically important antimicrobials in food-producing animals for growth promotion.
- Complete restriction of use of all classes of medically important antimicrobials in food-producing animals for prevention of infectious diseases that have not yet been clinically diagnosed.

WHO GUIDELINES ON USE OF MEDICALLY IMPORTANT ANTIMICROBIALS IN FOOD-PRODUCING ANIMALS (2017)

### RECOMMENDATIONS:

- We suggest that antimicrobials classified as critically important for human medicine should not be used for control of the dissemination of a clinically diagnosed infectious disease identified within a group of food-producing animals.
- We suggest that antimicrobials classified as highest priority critically important for human medicine should not be used for treatment of food-producing animals with clinically diagnosed infectious disease.

WHO GUIDELINES ON USE OF MEDICALLY IMPORTANT ANTIMICROBIALS IN FOOD-PRODUCING ANIMALS (2017)

### • BEST PRACTICE STATEMENTS:

- Any new class of antimicrobials or new antimicrobial combination developed for use in humans will be considered critically important for human medicine unless categorized otherwise by WHO.
- Medically important antimicrobials that are not currently used in food production should not be used in the future in food production including in food-producing animals or plants.

DECLINE IN THE DEVELOPMENT OF NEW ANTIBIOTICS

Major pharmaceutical companies have abandoned research into the discovery of new antibiotics!

 Decline in financial reward: Big pharma can make greater profits on drugs that can be used regularly without losing effectiveness (such as antidepressants and anti-inflammatory medications).

New pharma are not interested in this market.
#### Decline in the Number of New Antibacterial Agents Approved in the USA, 1983-2012<sup>1</sup>



#### Percent Decline in Approved Antibiotics Compared With 1983-1987 (n=16 new agents)

YEAR	NUMBER OF ANTIBIOTICS APPROVED BY US FDA
2013	0
2014	1 NEW DRUG*; 4 new drug formulations
2015	4 new drug formulations
2016	1 NEW DRUG*
2017	2 NEW DRUGS*; 1 new formulation
2018 (up to Sept)	1 NEW DRUG*; 2 new formulations

(Ohia, 2018; unpublished data)

• According to WHO, Antibiotics Resistance is facilitated by:

- Misuse and overuse of antibiotics
- Poor infection prevention and control

#### ROLE OF INDIVIDUALS

- Only use antibiotics when prescribed by a certified/qualified health professional
- Never demand antibiotics if your health professional says you don't need them
- Always follow your health professional's advice when using antibiotics (e.g., never skip doses)

#### ROLE OF INDIVIDUALS

- Never share or use leftover antibiotics.
- Never take an antibiotics for a viral infection such as cold or flu.
- Prevent infections by:
  - Regularly washing hands.
  - Preparing food hygienically.
  - Avoiding contact with sick people.
  - Utilizing methods for safe sex.
  - Keeping vaccinations up to date.

#### ROLE OF INDIVIDUALS

#### Utilizing WHO Recommendations for Safer Food:

- Keep food preparation environment clean.
- Separate raw food from cooked ones.
- Cook food thoroughly.
- Store food at safe temperatures.
- Use safe water.
- Use safe raw materials for cooking.
- Choose foods that have been produced without the use of antibiotics for growth promotion or disease prevention in health animals.

### ANTIBIOTIC RESISTANCE



Antibiotic resistance happens when bacteria change and become resistant to the antibiotics used to treat the infections they cause. This is compromising our ability to treat infectious diseases and undermining many advances in medicine.

We must handle antibiotics with care so they remain effective for as long as possible.



www.who.int/drugresistance



#AntibioticResistance

#### ROLE OF HEALTHCARE PROFESSIONALS

- To prevent and control the spread of Antibiotics Resistance, healthcare professionals can:
  - Prevent infections by ensuring your hands, instruments and practice environment are clean.
  - Only prescribe and dispense antibiotics when they are needed using established guidelines.
  - Report antibiotic-resistant infection to appropriate monitoring agencies.
  - Talk to your patients about how to take antibiotics correctly, antibiotic resistance and the dangers of misuse.
  - Talk to your patients about preventing infections (e.g., covering mouth and nose when sneezing, safer sex).

#### • <u>ROLE OF HEALTHCARE FACILITIES</u>

- To prevent and control the spread of Antibiotics Resistance, health care facilities (hospitals, clinics) can:
  - Know what types of drug-resistant infections are present in your facility and patients.
  - Request immediate alert when the lab identifies drugresistant infections in your patients.
  - Alert receiving facility when you transfer a patient with a drug-resistant.
  - Protect patients from drug-resistant infections.
  - Prescribe antibiotics wisely.
  - Remove temporary medical devices such as catheters and ventilators when no longer needed.
  - Follow relevant guidelines and precautions at every patient encounter.

#### ROLE OF AGRICULTURE SECTOR

- To prevent and control the spread of Antibiotics Resistance, the agriculture sector can:
  - Only give antibiotics to animals under veterinary supervision.
  - Not use antibiotics for growth promotion or to prevent diseases in health animals.
  - Vaccinate animals to reduce the need for antibiotics.
  - Promote and apply good practices at all steps of production and processing of foods from animal and plant sources.
  - Prevent infections through improved hygiene and animal welfare.

### ANTIBIOTIC RESISTANCE WHAT THE AGRICULTURE SECTOR CAN DO



Antibiotic resistance happens when bacteria change and become resistant to the antibiotics used to treat the infections they cause.



- Ensure that antibiotics given to animals—including food-producing and companion animals—are **only used to control or treat** infectious diseases and under veterinary supervision
- 2 Vaccinate animals to reduce the need for antibiotics and develop alternatives to the use of antibiotics in plants
- 3 Promote and apply **good practices** at all steps of production and processing of foods from animal and plant sources
- Adopt **sustainable systems** with improved hygiene, biosecurity and stress-free handling of animals
- <sup>5</sup> Implement **international standards** for the responsible use of antibiotics and guidelines, set out by OIE, FAO and WHO

www.who.int/drugresistance www.oie.int/antimicrobial-resistance www.fao.org/antimicrobial-resistance

#### #AntibioticResistance



Food and Agriculture Organization of the United Nations WORLD ORGANISATION FOR ANIMAL HEALTH



#### ROLE OF POLICY MAKERS/GOVERNMENT

- To prevent and control the spread of Antibiotics Resistance, policy makers/Government can:
  - Ensure a robust national action plan to tackle antibiotic resistance is the law of the land.
  - Establish infrastructure to improve surveillance of antibiotic-resistant infections.
  - Strengthen policies, programs and implementation of infection prevention and control measures.
  - Make information available on the impact of antibiotic resistance through public health education.
  - Regulate and promote the appropriate use and safe disposal of medications.

#### **STOP OVERUSE AND MISUSE OF ANTIBIOTICS COMBAT RESISTANCE**

Antimicrobial resistance happens when bacteria and other microorganisms change after being exposed to antimicrobial drugs. Antibiotics are among the most common antimicrobial drugs used in humans and animals. The overuse and misuse of antibiotics is speeding up the development of resistance and putting us all at risk.

Antibiotic resistance can affect anyone, of any age, in any country. It is a threat to human health, food security and sustainable development.

#### WHAT GOVERNMENT CAN DO

Including policymakers, heads of ministries, regulatory authorities

#### Stop overuse and misuse of antibiotics by:

- Supporting a multi-sectoral national action plan on antimicrobial resistance
- > Developing and enforcing regulations to stop overuse and misuse of antibiotics in humans and animals
- > Making information on how to stop overuse and misuse of antibiotics available to citizens



#### Develop and enforce regulations to prevent the spread of infection through:

- > Monitoring hospitals' and clinics' compliance with infection prevention and control standards
- > Enforcing good agriculture and food production practices
- > Ensuring communities have access to safe water and sanitation





ANDLA

ANTIBIOTICS

ROLE OF WHO: GLOBAL ACTION PLAN

- To improve awareness and understanding of antimicrobial resistance through effective communication, education and training.
- To strengthen knowledge and evidence base through surveillance and research.
- To reduce incidence of infection through effective sanitation, hygiene and infection prevention measures.
- To optimize the use of antimicrobial medicines in human and animal health.
- To ensure a sustainable economic investment in countering antimicrobial resistance by all countries.
- To increase investment in new medicines, diagnostic tools, vaccines and other interventions.

#### ROLE OF NAFDAC: RECOMMENDATIONS

- Reduce availability and ease of access to antimicrobials from pharmacies and unauthorized sources with or without prescription (hawkers, vendor shops, buses).
- Stop the sale of antimicrobial prescription medicines as Over The Counter drugs in Nigeria and increase monitoring.
- Use antimicrobials only as directed by the physician/veterinarian on humans and animals, respectively.
  - Always completing the dose prescribed
  - Prescription should be based on appropriate diagnostic and sensitivity testing.

#### ROLE OF NAFDAC: RECOMMENDATIONS

- Buy antimicrobials only from registered pharmacies/veterinary outlets and insist on collecting a receipt.
- Do not use antibiotics as feed additives except when prescribed by a veterinarian:
  - Because we ingest antibiotics through meat, fish and poultry that we eat.
- Antibiotics sold in Nigeria must bear Mobile Authentication Scheme (MAS) hologram for tracking genuine product.

ROLE OF NAFDAC: ACTION PLAN

- Creation of awareness on the danger of antimicrobial resistance through:
  - Mass education on antimicrobial resistance.
  - Public enlightenment by the use of jingles.
  - Use of Information, Education and Communication (IEC) materials.
- Securing our borders from influx of fake drugs.
- Applying the full weight of the law by ensuring compliance with the Mobile Authentication Scheme.

NAFDAC ACTION PLAN:

- Educating farmers about the importance of biosecurity and Good Agricultural Practice.
- NAFDAC is reviewing the technical requirements for the registration of antibiotics.
- NAFDAC, in collaboration with the Ministry of Agriculture and Natural resources has prohibited the use of some antibiotics in food-producing animals.
- NAFDAC seeks the cooperation of all health professionals, farmers and the general public to ensure that the menace of antimicrobial resistance is stopped.

# SUMMARY AND CONCLUSIONS

- While exposure to most bacteria can be harmful to human health, there are some bacteria that have beneficial effects to life.
- If not properly prevented and controlled, the incidence of antibiotics (antimicrobial) resistance will continue to be a major threat to our existence on earth.
- Individuals, healthcare professionals, healthcare facilities, the agriculture sector, policy makers/government have a significant role to play in preventing and controlling the spread of antibiotic (antimicrobial) resistance.

## SUMMARY AND CONCLUSIONS

- Since antibiotic resistance has to be acknowledged as an integral part of our healthcare delivery process, the decline in research and discovery of new antibiotics by the pharmaceutical industry portends to be one of the greatest threats to the containment of bacterial infections in humans and animals.
- Some of common bacterial infections is not feasible due to the lack of active and potent antibiotics may lead to the demise of man on earth!

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QUESTIONS?