Antibiotic prescribing and Resistance

Angharad Davies
Clinical Associate Professor/Hon. Consultant Microbiologist

Overview

1. The importance of antimicrobial resistance
2. What to prescribe?–antibiotic spectra
3. Overview of some important resistant pathogens
   - what do all the acronyms mean?
4. Antimicrobial stewardship

World Health Organization

Pandemic influenza

Vaccine Hesitancy

Dengue

Antimicrobial Resistance

Ebola & other high threat pathogens

HIV

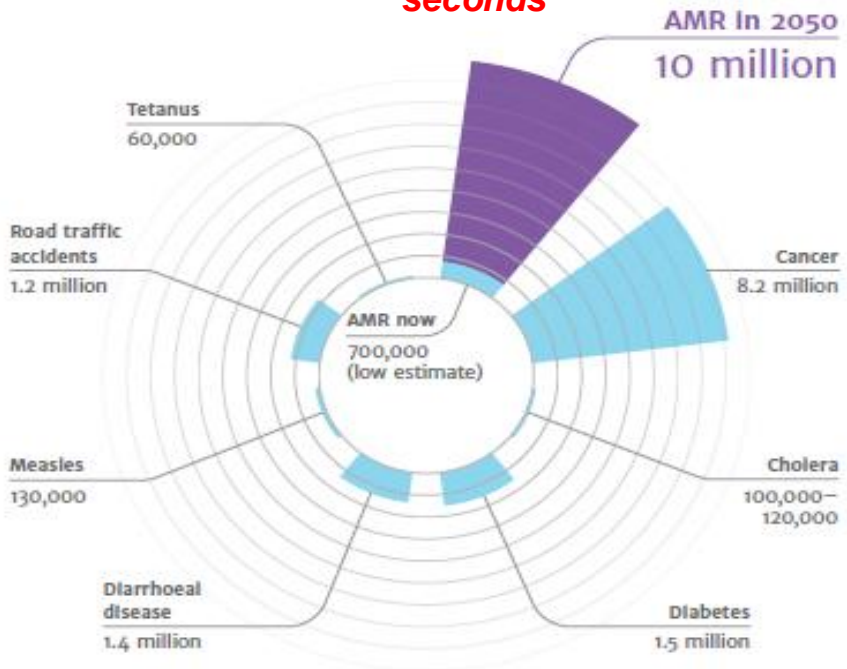
Antimicrobial Resistance – a slow-moving pandemic

‘COVID is the lobster dropped into boiling water where it makes a lot of noise and everyone notices, and it’s dead. AMR is the lobster put in cold water slowly heating up so it doesn’t make noise and people aren’t noticing’

Professor Dame Sally Davies, UK Special Envoy on Antimicrobial Resistance

DEATHS ATTRIBUTABLE TO AMR EVERY YEAR

"The death toll could be a staggering one person every three seconds"



O'Neil Review 2014

Antibiotic resistance as big a threat as climate change – chief medic

Dame Sally Davies calls for Extinction Rebellion-style campaign to raise awareness

Fiona Harvey
Environment correspondent

Mon 29 Apr 2019
13.17 BST

Antibiotics

Antibiotic resistance could spell end of modern medicine, says chief medic

Prof Dame Sally Davies says action is needed around the world to tackle 'hidden' problem that is already claiming lives

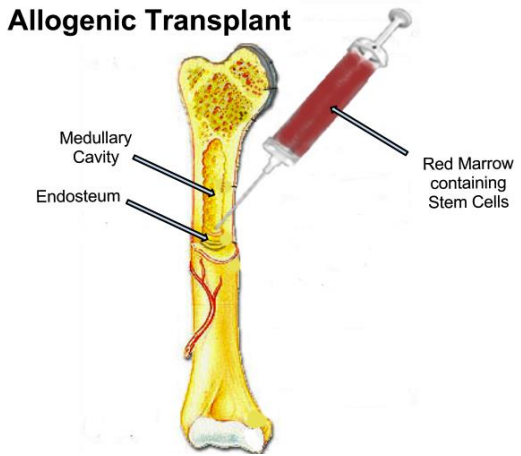
4,232

Press Association

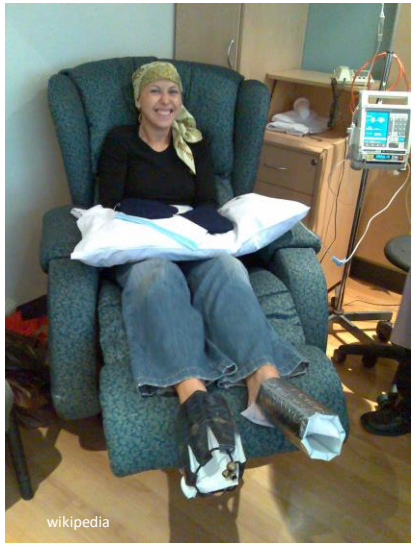
Friday 13 October 2017 08.41 BST

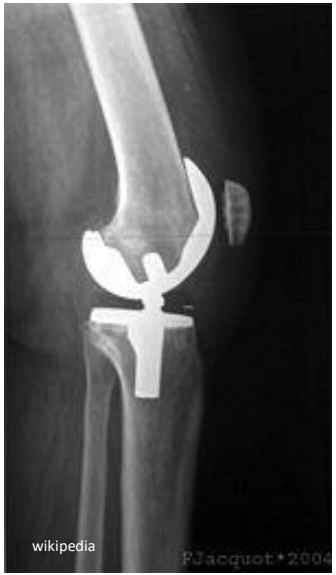
The end of modern medicine?

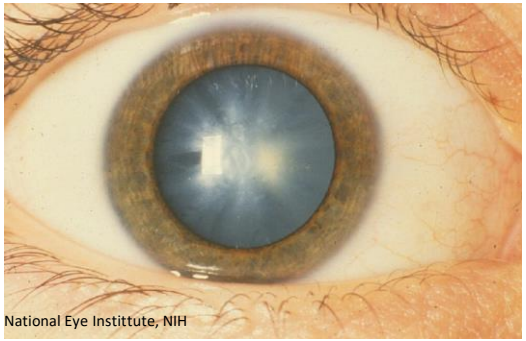
Professor Dame Sally Davies, ex UK CMO



Wikimedia commons

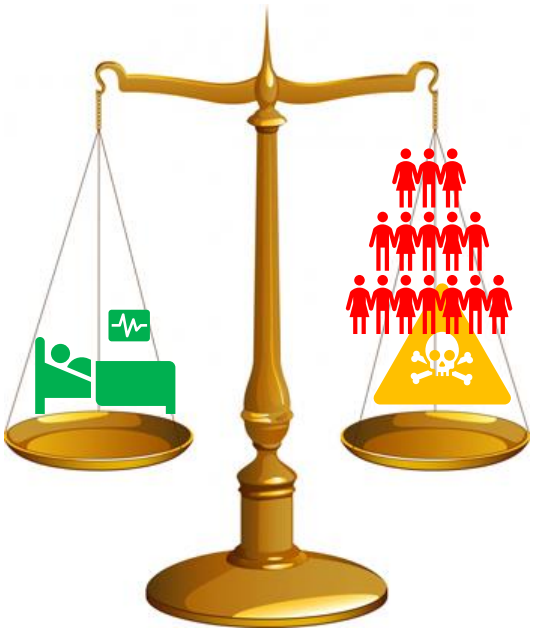






National Eye Institute, NIH

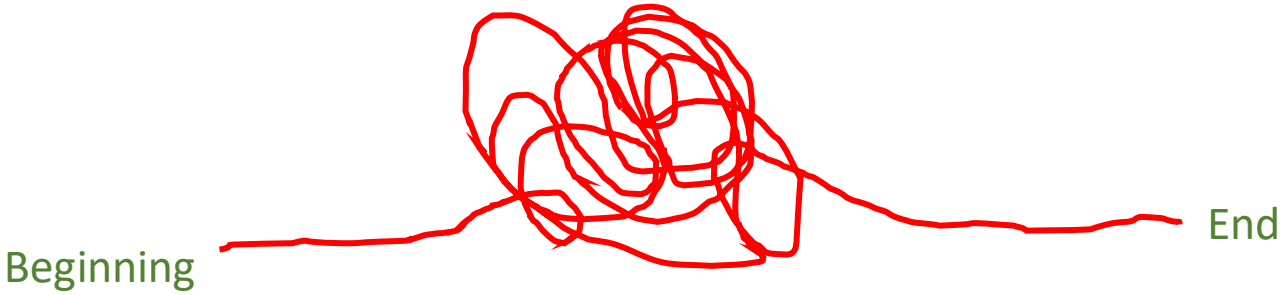
2. What to prescribe and antibiotic spectra



1/3 hospital in-patients receive antibiotics

Every single medical and surgical specialty

Every day


Beginning
End
Muddle

Choosing an antibiotic

- 1. What is the likely source of infection?
  (clinical assessment)

- 2. What organisms are likely to cause infection in that source?

KNOW YOUR ENEMY (basic knowledge of microbiology)

- 3. What antimicrobials are needed for those organisms? -in general choose narrow spectrum agent where possible.

KNOW YOUR ARMOURY (understand antibiotic spectra)

https://www.antibioticaware.com

Not sync

AWARE Home | AWARE project | Medical Students | Post-16 Page | Blog | Cymraeg | Contact

Follow

Infection & Antibiotics for Medical Students

This webpage has been set up to provide a virtual learning resource about infection and antibiotics for medical and physician associate students. Scroll down or click here to find a variety of useful resources, guidelines, games and lecture slides.

BUGS: Clinical Microbiology made Simple (or, All you Need to Know on 3 sides of A4)

NB This crib-sheet only deals with bacteria and not other pathogens like viruses and fungi.

There are three sections:

1. **GRAM STAINING**
2. **CLINICALLY IMPORTANT BACTERIA**
3. **WHICH BACTERIA CAUSE WHICH INFECTIONS?**

1. GRAM STAINING

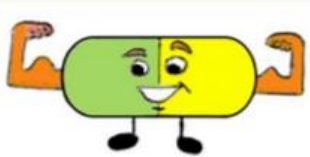
Bacteria can be seen under the microscope by performing a Gram stain.

The Gram stain appearance depends on the cell wall structure. Since this is also relevant to antibiotic sensitivity, Gram stain appearance is incredibly helpful in deciding on an antibiotic even before you know the full identity of the organism.

Gram **P**ositives look **Purple** under the microscope.

Gram n**E**gatives look r**E**d under the microscope

The *shape* of the organism is described as cocci (round) or bacilli/rods (rod-shaped)



DRUGS – a crib-sheet about commonly used antibiotics

The pathogens referred to will all be ones mentioned in the BUGS crib-sheet. It's advisable to be familiar with that first.

To see what to use for specific clinical conditions, check your Health Board policies on the Rx Guidelines app – these may vary but they are all based on the principles below

1. **Table of some antibiotic classes**
2. **Key facts about some important classes of antibiotics**
3. **Quick list of some important pathogens and what to use**

Considerations in antimicrobial prescribing

- **Guidelines/local policies – often on an app**
- Spectrum of cover
- Penetration into site of infection
  - eg brain/bone
- Side-effects eg antibiotic–associated diarrhoea/ *C. difficile*
- allergies
- Interactions
- intravenous vs oral route
  - Some achieve blood/tissue concentrations orally equivalent to intravenous eg quinolones, metronidazole
- Pregnancy/lactation
- Cost

Antibiotic spectra

- Broad vs narrow

- Gram-positive organisms
- Gram-negative organisms
- Anaerobes
- Resistant organisms, e.g:
  - Meticillin Resistant *S. aureus* (MRSA)
  - Vancomycin Resistant Enterococci (VRE)
  - Extended Spectrum Beta Lactamase (ESBL) carriers
  - Carbapenemase producing organisms (CPOs)

Gram staining

https://www.youtube.com/watch?v=OCJ6LxdOOvw&t=1s

Some important antibiotic classes

Class	Examples
Beta-lactams	Penicillin, flucloxacillin, cephalosporins, carbapenems
Tetracyclines	Tetracycline, doxycycline
Glycopeptides	Vancomycin
Macrolides	Erythromycin, clarithromycin
Quinolones	ciprofloxacin
Aminoglycosides	gentamicin

A closer look at beta-lactams

- **Penicillins**
- **Cephalosporins**
- Mono-bactams
- **Carbapenems**

Penicillins

Penicillin

—Narrow spectrum - streptococci

Flucloxacillin

—Narrow spectrum - *Staphylococcus aureus*

Ampicillin/amoxycillin

—Broader spectrum penicillin, tds dosing

Penicillins with beta-lactamase inhibitors

- **Amoxycillin +/- clavulanate***
  - **'Co-amoxiclav' (Augmentin®)**
  - Gram +, Gram – and anaerobes
- **Piperacillin +/- tazobactam***
  - **'Piptazo-bactam' (Tazocin®)**
  - Similar co-amoxiclav but broader cover and also *Pseudomonas aeruginosa* (PSA)
  - Neither active against MRSA/VRE/ESBL

*clavulanate and tazobactam are beta-lactamase inhibitors

Cephalosporins

Broad spectrum, G + and G- but not anaerobes
5 generations – mainly use generations 1-3

1st generation eg cephalexin
2nd generation eg cefuroxime
3rd generation eg cefotaxime, ceftazidime

Reputation for causing *C. difficile* disease

Carbapenems

- Imipenem, meropenem, ertapenem
- **Very broad spectrum** – G+ and G-, anaerobes
- Critical care
- ICUs/bone marrow transplant/chemotherapy units now very reliant on them

Flucloxacillin/penicillin

Ceftriaxone

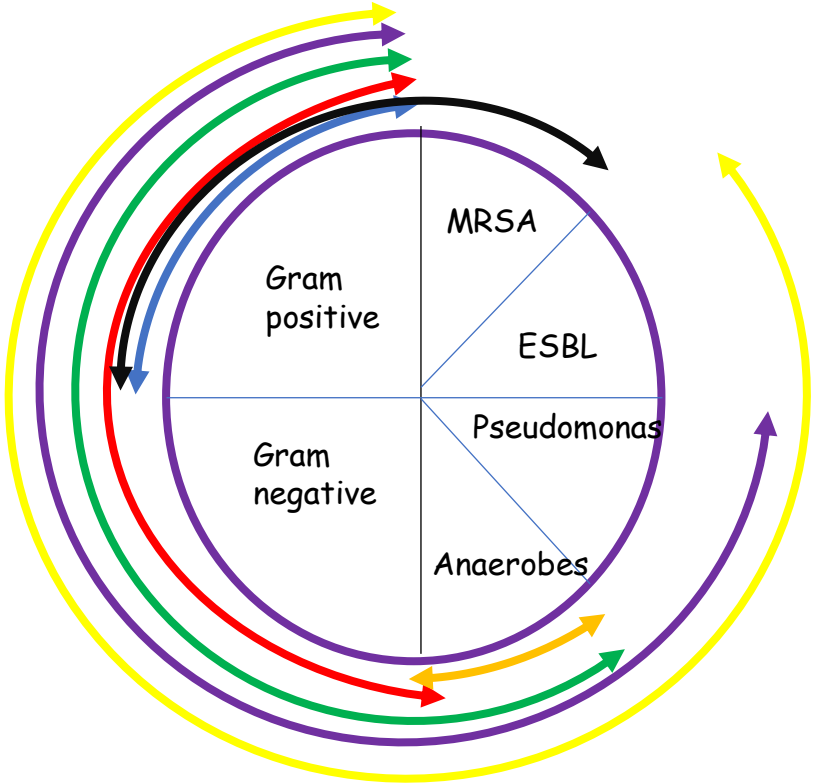
Metronidazole

Co-amoxiclav

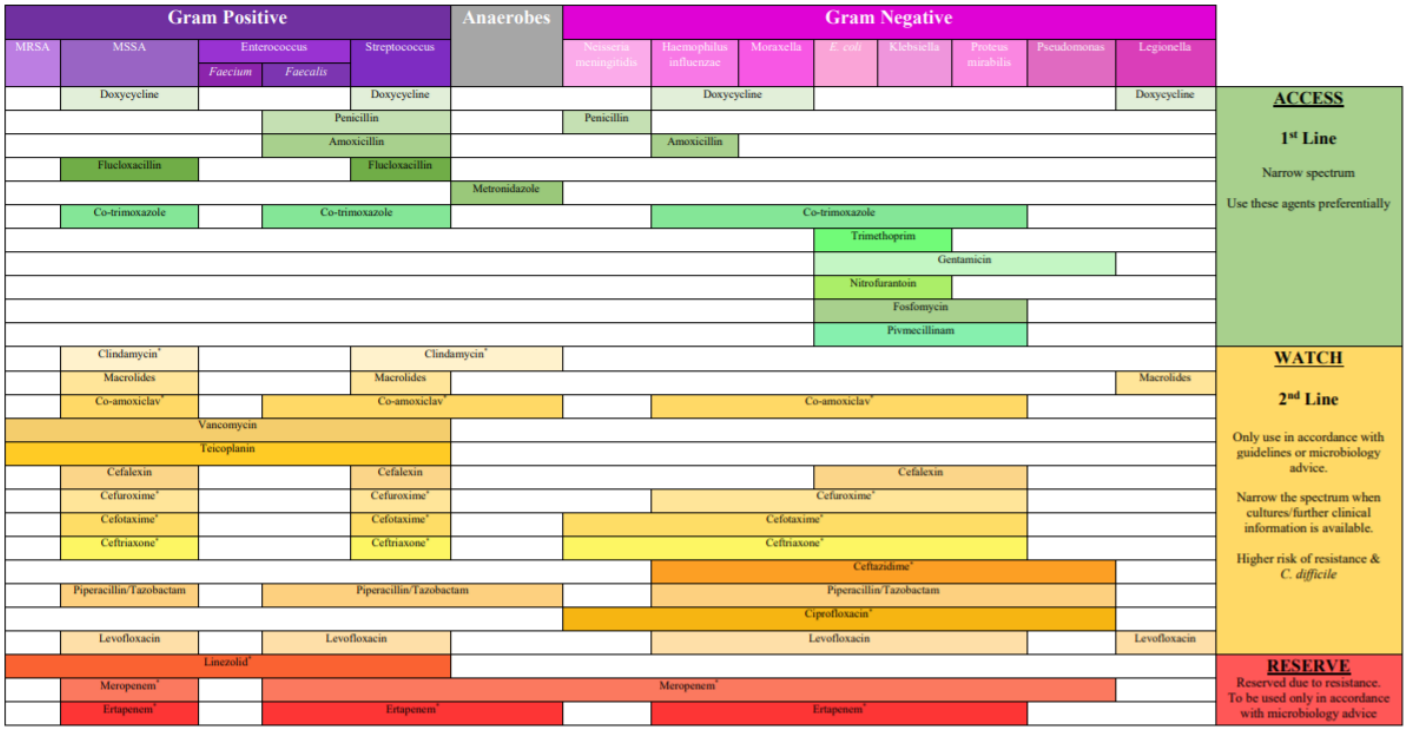
Tazocin

Meropenem

Vancomycin/Teicoplanin



A Pragmatic Guide to Antibiotic Spectrum



Disclaimer: This chart is intended for use as a guide only, pending identification, sensitivities and microbiology advice. It **does not** replace expert advice. Local guidelines and preferences will vary.
For simplicity, atypical organisms (except Legionella) are not included above. For *C. difficile* treatment, please consult local guidelines.
(*): Requires microbiology approval, unless in line with antimicrobial guidelines.

Consequences of antimicrobial resistance

- Delay in appropriate antibiotic therapy
  - Worse patient outcomes
  - Death
- Increased hospital length of stay
- Alternative antibiotics need to be used
  - Increased likelihood of adverse effects
  - Cost implications
  - Oral antibiotics may not be available

The great principle of antimicrobial resistance is

‘***Survival of the Fittest***’

https://vimeo.com/180908160

3. Overview of some important resistant pathogens - what do all the acronyms mean?

Important examples of resistant Gram positive organisms

MRSA – methicillin resistant *Staphylococcus aureus*

- Resistant to flucloxacillin
- Serious infections can be treated with glycopeptides (e.g. vancomycin)

GRE/VRE – glycopeptide resistant enterococci/vancomycin resistant enterococci

- Glycopeptides are ineffective
- Can use e.g. linezolid if treatment required

Newspaper of the Year

THE INDEPENDENT

No 5,660 TUESDAY 7 DECEMBER 2004 www.independent.co.uk

EXCLUSIVE: JANET OF THE JUNGLE

'I've given up salt, sugar and caffeine. My blood pressure is much better. And I'm more tolerant' Janet Street-Porter, in her own words » PAGES 24-25

MRSA

Each year, 100,000 people catch an infection in hospital. Of these, 5,000 die – more than are killed on the roads. It's one of the worst rates in the world. So is there a cure?

Today's story is Gram negative

Priority 1
Acinetobacter baumanni
Pseudomonas aeruginosa
Enterobacterales

Priority 2
Enterococcus faecium
Staphyloccus aureus
Helicobacter pylori
Campylobacter spp
Salmonellae
Neisseria gonorrheae

Priority 3
Streptococcus pneumoniae
Haemophilus influenzae
Shigella spp

Important examples: Gram negative resistant organisms

ESBL producers

‘Extended spectrum beta-lactamase’ producers

Often *E. coli* and *Klebsiella*

CPOs

‘Carbapenemase-producing organisms’

e.g. strains of *Klebsiella, Acinetobacter, Pseudomonas*

ESBL producers

E. coli, Klebsiella sp

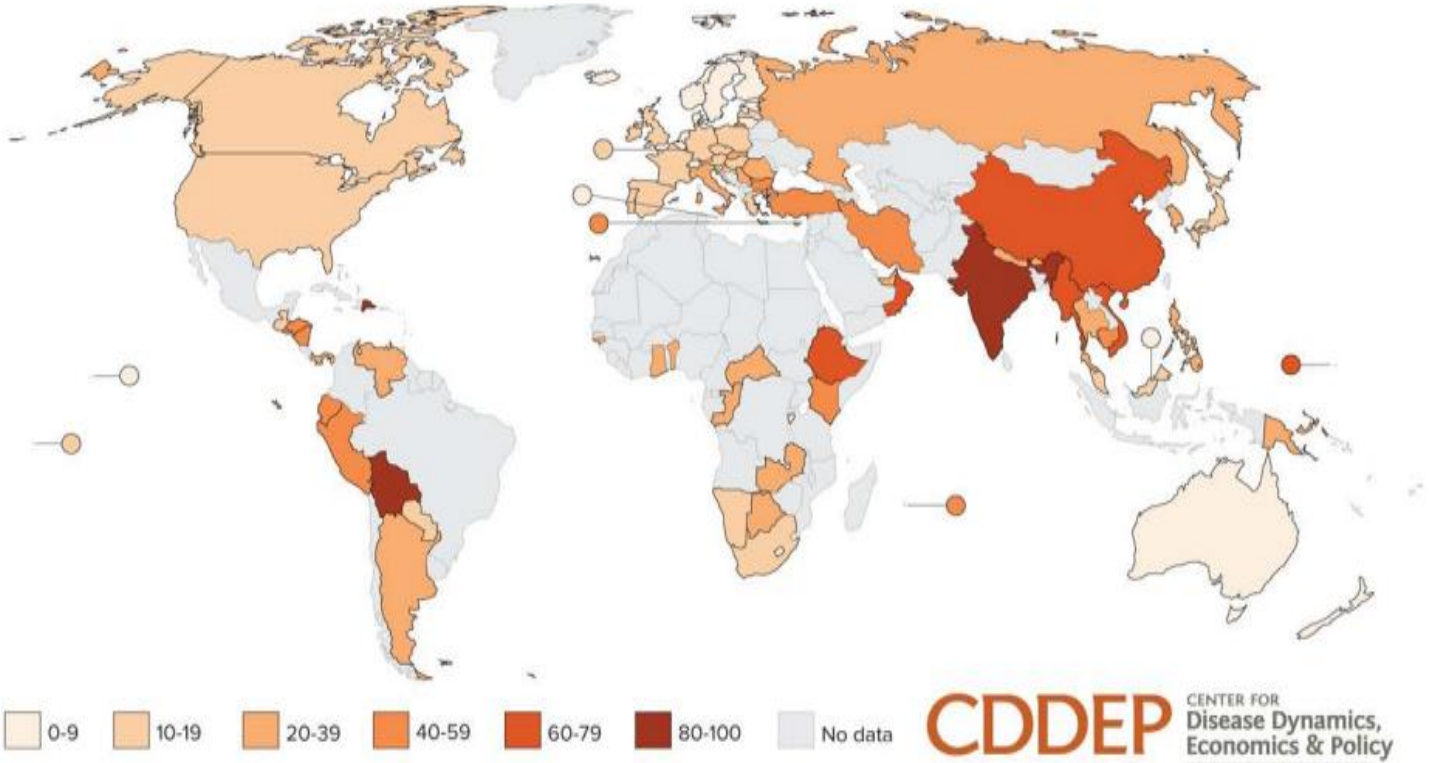
Resist penicillins and cephalosporins…

…often also carry resistance genes for other antibiotics

Common possible treatments:

- Nitrofurantoin (UTI)
- Aminoglycosides (Gram negative sepsis)
- Carbapenems (Gram negative sepsis)

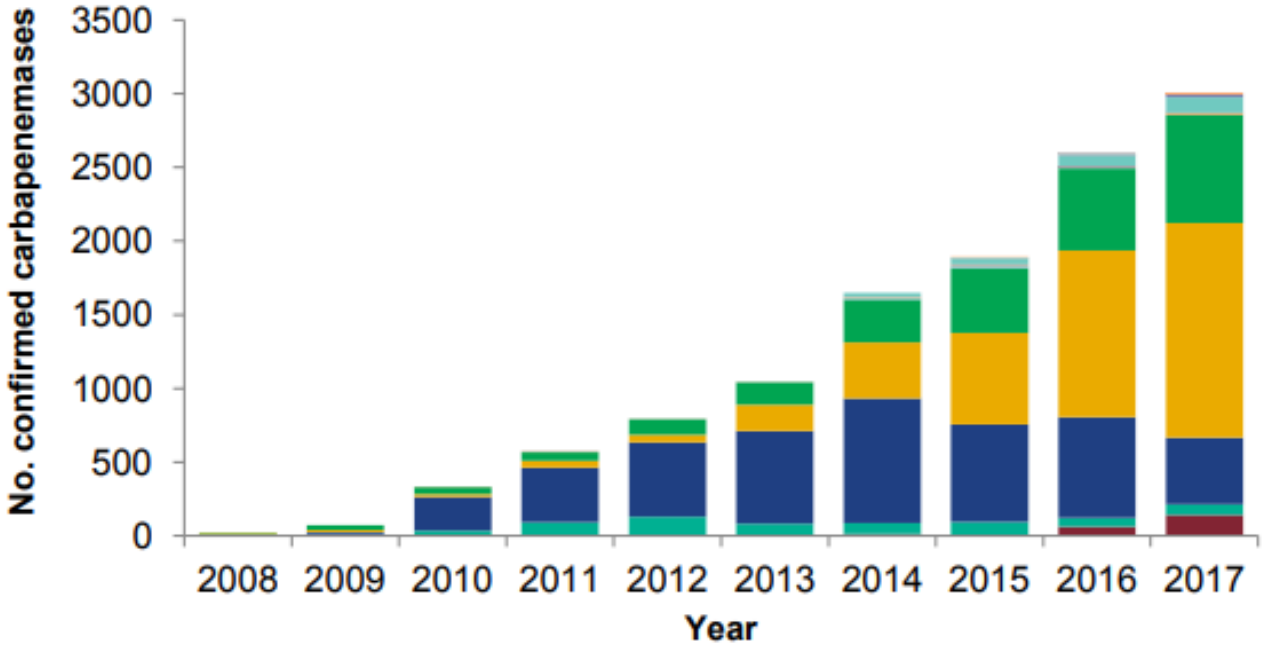
Percentage of extended-spectrum beta-lactamase producing *Escherichia coli**, by country (most recent year, 2011-2014)



CDDEP CENTER FOR Disease Dynamics, Economics & Policy
WASHINGTON DC • NEW DELHI

Source: CDDEP 2015, WHO 2014 and PAHO, forthcoming

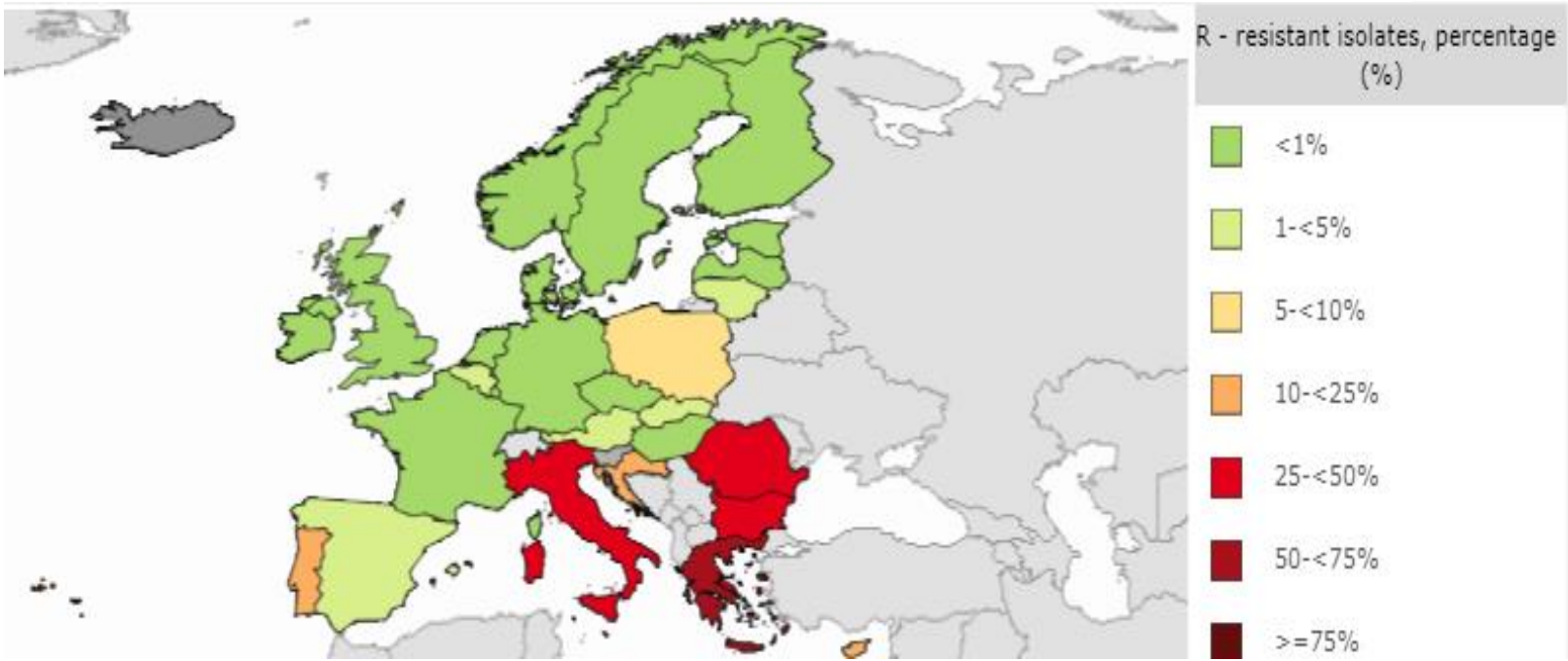
CPEs sent to AMRHAI (PHE) from UK clinical laboratories, 2008- 2017



https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/759975/ESPAUR_2018_report.pdf

CP *Klebsiella* sp, Europe (EARS-Net) 2019

Treatment options very limited. D/w microbiology



GIG CYMRU NHS WALES
Bwrdd Iechyd Prifysgol Abertawe Bro Morgannwg University Health Board

Infection Prevention & Control Standard Operating Protocol

Preventing the Spread of Carbapenem Resistant Gram negative Bacteria

Public Health England

Acute trust toolkit for the early detection, management and control of carbapenemase-producing Ente

Factors contributing to antimicrobial resistance

Misuse of antibiotics in medicine
Lack of control of use of antibiotics
Lack of effective infection control procedures
Use of antibiotics in animal husbandry and agriculture – 40% of UK antibiotic use has been in animals
Over the counter medicines
Lack of laboratory capacity and tests too slow
Low quality pharmaceuticals
International travel
‘Medical tourism’

What is misuse of antibiotics?

Prescribing antibiotics unnecessarily
Delaying antibiotic treatment unnecessarily in critically ill patients
Using broad spectrum antibiotics too generously or narrow-spectrum antibiotics incorrectly
Inappropriately high or low doses in a specific patient
Too long or short courses
Not streamlining treatment after the culture results received
Omitting or delaying doses of antibiotics

4. Antimicrobial Stewardship

Principles of Antimicrobial Stewardship

Right Drug, Right Dose, Right Time,
Right Duration
..... Every Time

Public Health England

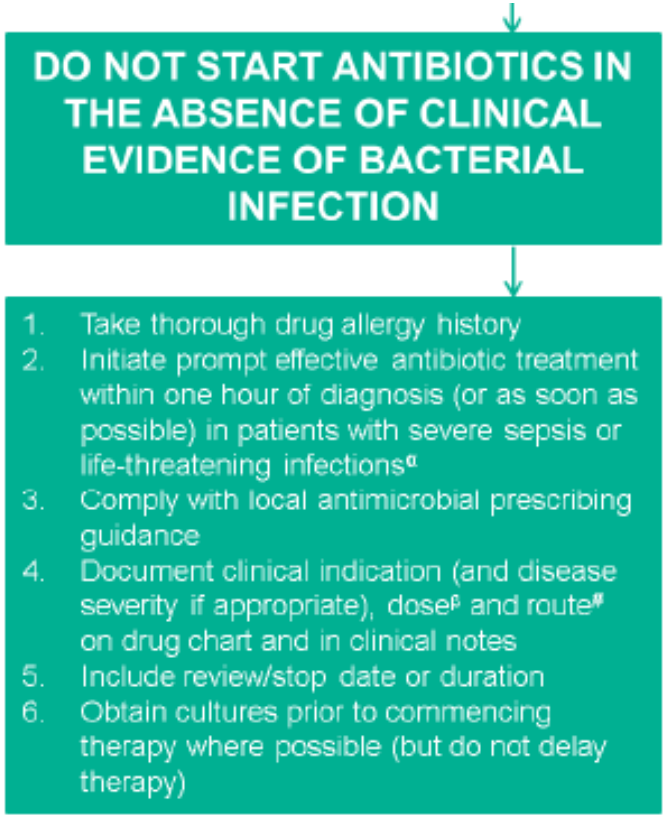
Protecting and improving the nation's health

Start Smart - Then Focus

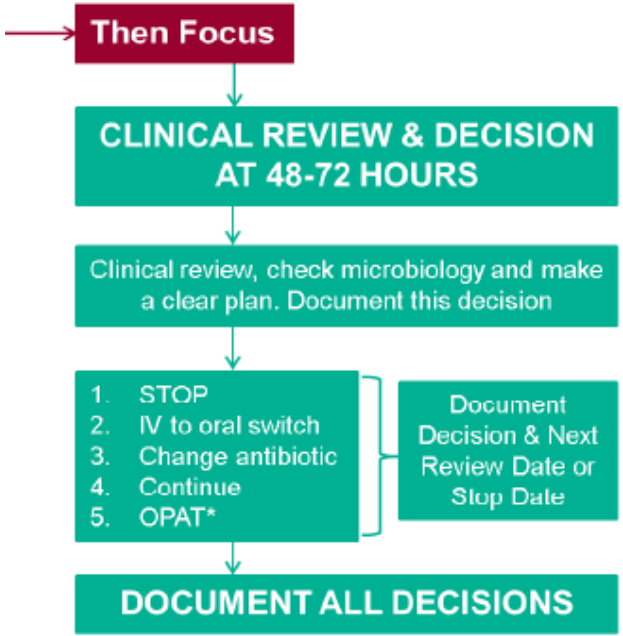
Antimicrobial Stewardship Toolkit for English Hospitals

Updated March 2015

“Start Smart……”


DO NOT START ANTIBIOTICS IN THE ABSENCE OF CLINICAL EVIDENCE OF BACTERIAL INFECTION
1. Take thorough drug allergy history
2. Initiate prompt effective antibiotic treatment within one hour of diagnosis (or as soon as possible) in patients with severe sepsis or life-threatening infections[α]
3. Comply with local antimicrobial prescribing guidance
4. Document clinical indication (and disease severity if appropriate), dose[β] and route[#] on drug chart and in clinical notes
5. Include review/stop date or duration
6. Obtain cultures prior to commencing therapy where possible (but do not delay therapy)

….then focus”


Then Focus
CLINICAL REVIEW & DECISION AT 48-72 HOURS
Clinical review, check microbiology and make a clear plan. Document this decision
1. STOP
2. IV to oral switch
3. Change antibiotic
4. Continue
5. OPAT*
Document Decision & Next Review Date or Stop Date
DOCUMENT ALL DECISIONS

Prudent use of antibiotics can prevent the emergence and selection of antibiotic-resistant bacteria.

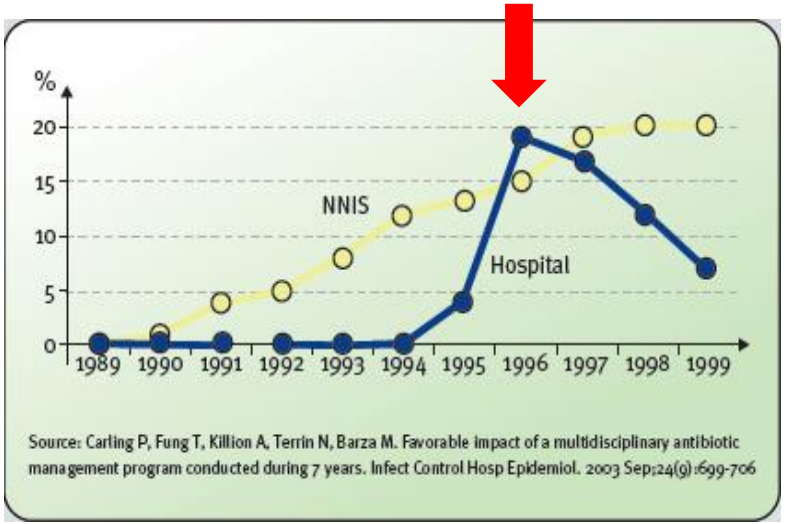


Figure 6: Rates of Vancomycin-resistant *Enterococci* in hospital before and after implementation of the antibiotic management program compared with rates in National Nosocomial Infections Surveillance (NNIS) System* hospitals of similar size. *NNIS is now the National Healthcare Safety Network (NHSN).

Carling P, et. Al. Infect Control Hosp Epidemiol. 2003 Sep;24(9):699-706.

Decreasing antibiotic use have also been shown to result in lower incidence of *Clostridium difficile* infections.

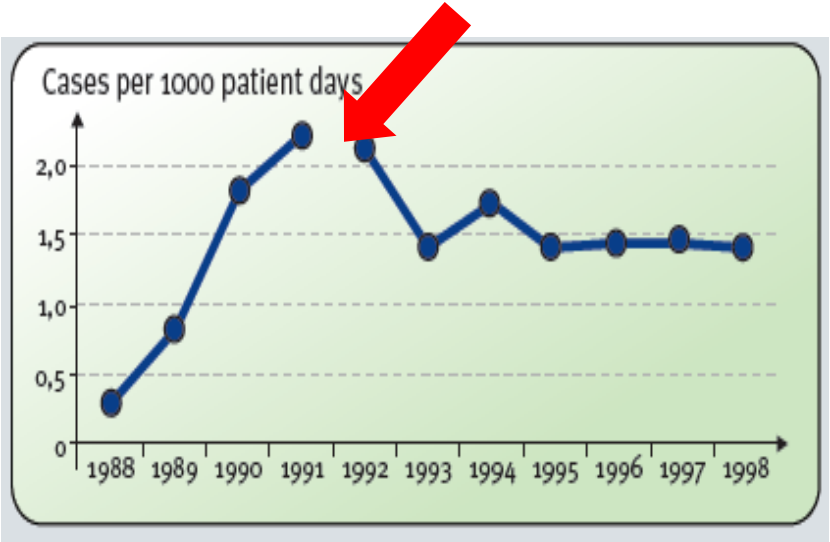


Figure 7: Rates of nosocomial *Clostridium difficile*, expressed per 1,000 patient-days, before and after implementation of the antibiotic management program.

Carling P, et. Al. Infect Control Hosp Epidemiol. 2003 Sep;24(9):699-706.

Good Antimicrobial Prescribing - 1

Start antibiotics promptly **when indicated**

Collect cultures **before** first dose of antibiotic wherever possible and **review the results**

NB: Do not treat colonisation e.g. skin flora in wound swabs

Consult the guidelines for empirical treatment

Consider previous resistant organisms e.g. MRSA, ESBL-producing organisms

Be aware of adverse effects related to specific antibiotics

Good Antimicrobial Prescribing - 2

Document indication and stop/review date

Seek advice from **Antimicrobial pharmacist** or Consultant Microbiologist if necessary

Good Antimicrobial prescribing - 3

Secondary care: **Review in 48 hours** (stop/IV→ oral switch, change antibiotic, continue)

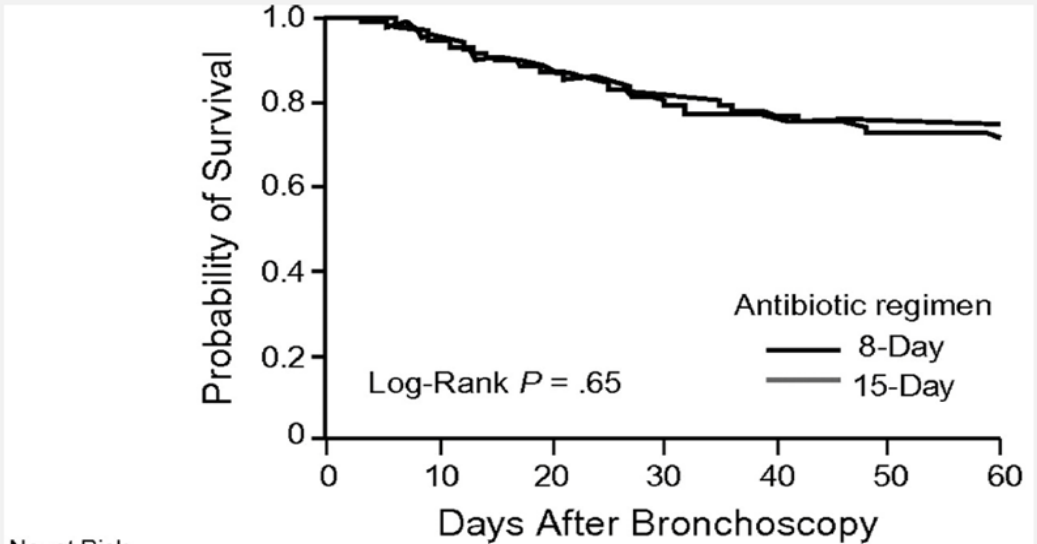
De-escalate if appropriate

- Narrower spectrum agents
- Lower *Clostridium difficile* risk

Stop antibiotics if the culture is negative unless clinically indicated – **antibiotics can be stopped at ANY TIME if not indicated**

Probability of survival for 8 vs 15 days of antibiotic therapy for ventilator-associated pneumonia

(Kaplan-Meier estimates)



No. at Risk							
8-Day Antibiotic Regimen	197	187	172	158	151	148	147
15-Day Antibiotic Regimen	204	194	179	167	157	151	147

Kollef M H et al. *Clin Infect Dis.* 2011;53:S33-S55

ANTIBIOTIC GUARDIAN

https://antibioticguardian.com/

Antibiotic resistance is one of the biggest threats facing us today.

Why it is relevant to you: without effective antibiotics many routine treatments will become increasingly dangerous. Setting broken bones, basic operations, even chemotherapy and animal health all rely on access to antibiotics that work.

What we want you to do: To slow resistance we need to cut the unnecessary use of antibiotics. We invite the public, students and educators, farmers, the veterinary and medical communities and professional organisations, to become Antibiotic Guardians.

Call to action: Choose one simple pledge about how you'll make better use of antibiotics and help save these vital medicines from becoming

CURRENT PLEDGES: 109900

http://www.catchshortfilm.com/