The drugs don't work!

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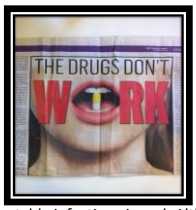


"The threat of untreatable infections is real. Although previously unthinkable, the day when antibiotics don't work is upon us. We are already seeing germs that are stronger than any antibiotics we have to treat them. **"**

- Arjun Srinivasan, MD, Associate Director for Healthcare Associated Infection Prevention Programs, Division of Healthcare Quality Promotion, US Centres for Disease Control and Prevention

Introduction

- Antibiotic use and resistance
- Consequences of antibiotic resistance-post antibiotic era?
- What can we do about it

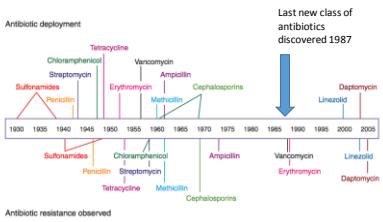
Antibiotics

- Alexander Fleming's accidental discovery of penicillin
- Average life span USA extended by 10 years
- Common yet frequently deadly illnesses such as pneumonia and tuberculosis (TB) could be treated effectively
- A small cut no longer had the potential to be fatal if it became infected, and the dangers of routine surgery and childbirth were vastly reduced.

"Penicillin should only be used if there is a properly diagnosed reason and, if it needs to be used, use the highest possible dose for the shortest time necessary. Otherwise antibiotic resistance will develop"

Alexander Fleming, 1945

Antibiotic discovery and resistance timeline



Scale of antibiotic use

- 100,000 million kg antibiotics produced since 1941
- 50% human use

-80% community
-20% hospitals

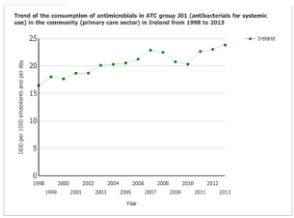
35-50% of hospital patients are prescribed an antibiotic of which 50% could be classed as inappropriate

- 50% agricultural use

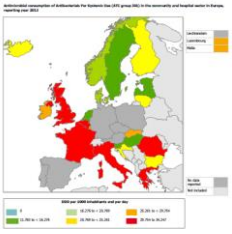
-20% therapeutic
-80% prophylactic/growth promotion

Harrison and Lederberg, *Antimicrobial Resistance* 1998

Trend of antimicrobial consumption of Antibacterials For Systemic Use (ATC group J01) in the community (primary care sector) in Ireland from 1998 to 2013



Geographical distribution of antimicrobial consumption of Antibacterials For Systemic Use (ATC group J01) in the community and hospital sector in Europe, reporting year 2013



Consumption of antimicrobials of Antibacterials For Systemic Use (ATC group J01) in the community and hospital sector in Europe, reporting year 2013

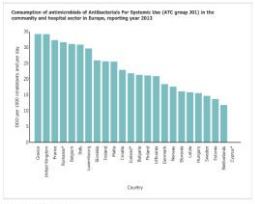


Table 1. Breakdown by pharmacological drug groups for outpatient antibiotic use in Ireland for 2012 and 2013.

	2012	Percent of 2012	2013	Percent of 2013	Percent Change 2012 to 2013
Penicillins	12.5	54.6%	13.1	55.1%	5.0%
Narrow spectrum penicillins	1.0	4.4%	1.1	4.5%	7.2%
Beta-lactamase resistant penicillins	1.0	4.6%	1.2	5.0%	13.6%
Broad spectrum penicillins	3.7	15.9%	3.9	16.4%	6.8%
Penicillin with beta-lactamase inhibitor	6.8	29.7%	7.0	29.2%	2.4%
Macrolides and related drugs	4.2	18.2%	4.4	18.5%	5.7%
Tetracylines	2.9	12.8%	3.0	12.5%	1.6%
Cephalosporins and other beta-lactam drugs	1.2	5.2%	1.4	5.7%	14.6%
First-generation cephalosporins	0.2	0.8%	0.2	0.8%	10.9%
Second-generation cephalosporins	0.9	4.0%	1.1	4.5%	17.9%
Third-generation cephalosporins	0.1	0.4%	0.1	0.4%	-8.5%
Quinolones	0.9	3.8%	0.9	3.7%	0.3%
Sulfonamides and Trimethoprim	1.2	5.0%	1.0	4.1%	-14.5%
Other antibiotics	0.1	0.5%	0.1	0.4%	-8.1%
TOTAL	**22.9**	**100.0%**	**23.8**	**100.0%**	**4.0%**

HPSC

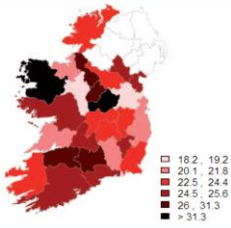


Figure 2. Outpatient antibiotic consumption in Ireland by county, in DDD per 1000 inhabitants per day for 2013.

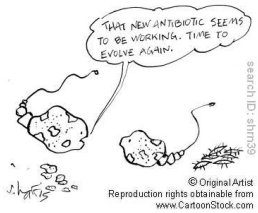
HPSC

Antibiotic use in nursing home patients

- Crude national antimicrobial prevalence of 9.8%
- Indications-Treatment and prophylaxis of infection
- Relevant microbiology specimen obtained for 27% of antibiotic prescriptions with the following isolated
- E.coli 33% (of which 29% were classed as ESBL)
- Staph aureus 22% (of which 44% were MRSA)
- No CRE isolated

PPS of HCAI & antimicrobial use in long term care facilities (HALT) 2013. hpsc

Meanwhile in the bacterial world



Lots of resistant bugs around!!

MRSA

VRE

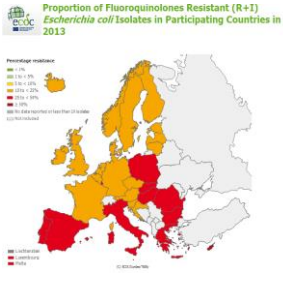
MRSA

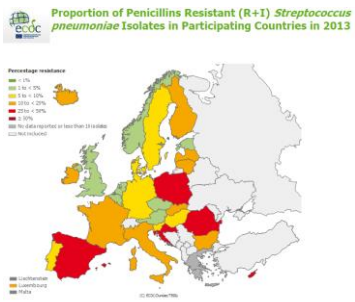
Clostridium difficile

MDR-TB

Penicillin Resistant Strep pneumonias

Klebsiella Enterobacteraceae Serratia Pseudomonas



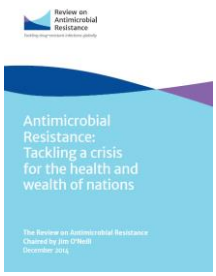


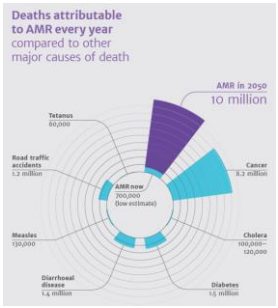
Consequences of antimicrobial resistance

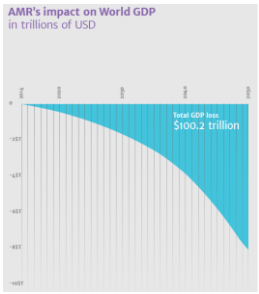
- Treatment failures with empiric antibiotics
  - Increased morbidity/duration of illness
  - Increased mortality
  - Increased healthcare costs
- Empiric use of broader spectrum antibiotics
  - Further selection of resistance
- Return to pre-antibiotic era?
  - High mortality from primary infectious diseases
  - Loss of high-tech medicine

MRSA in Ireland report

- Prolonged hospital stays increase the chances of acquiring a HAI
- Patients who acquire a HAI will spend on average an extra 11 days in hospital and these patients are 7 times more likely to die than uninfected patients
- Cost of treating HAI annually in Ireland is estimated at €230 million







Medical consequence of no action

- Previously treatable infections will no longer be so
- Surgical procedures e.g. hip and knee replacement will become too risky to carry out
- Innovations in cancer treatments and radical surgical procedures will no longer be possible due to the risk of untreatable infections in immunocompromised patients

Post antibiotic era?

So what can we do about it

- New antibiotics-20 by 2020
- Antimicrobial stewardship-We all need to make better use of the antibiotic resources we already have

Why has the pipeline of new drugs run dry?

- Scientific difficulties in developing new antibiotics
- Financial and regulatory hurdles
- Lack of incentive
- Patients will only receive short courses
- Once developed specialists will restrict use
- Resistance will eventually develop
- Patent will run out

ARTICLE

doi:10.1038/nature14098

A new antibiotic kills pathogens without detectable resistance

Losee L. Ling[1]*, Tanja Schneider[2,3]*, Aaron J. Peoples[1], Amy L. Spoering[1], Ina Engels[2,3], Brian P. Conlon[4], Anna Mueller[2,3], Till F. Schäberle[2,3], Dallas E. Hughes[1], Slava Epstein[5], Michael Jones[1], Linos Lazarides[1], Victoria A. Steadman[1], Douglas R. Cohen[1], Cintia R. Felix[1], K. Ashley Fetterman[1], William P. Millett[1], Anthony G. Nitti[1], Ashley M. Zullo[1], Chao Chen[4] & Kim Lewis[4]

Antibiotic resistance is spreading faster than the introduction of new compounds into clinical practice, causing a public health crisis. Most antibiotics were produced by screening soil microorganisms, but this limited resource of cultivable bacteria was overmined by the 1960s. Synthetic approaches to produce antibiotics have been unable to replace this platform. Uncultured bacteria make up approximately 99% of all species in external environments, and are an untapped source of new antibiotics. We developed several methods to grow uncultured organisms by cultivation in situ or by using specific growth factors. Here we report a new antibiotic that we term teixobactin, discovered in a screen of uncultured bacteria. Teixobactin inhibits cell wall synthesis by binding to a highly conserved motif of lipid II (precursor of peptidoglycan) and lipid III (precursor of cell wall teichoic acid). We did not obtain any mutants of Staphylococcus aureus or Mycobacterium tuberculosis resistant to teixobactin. The properties of this compound suggest a path towards developing antibiotics that are likely to avoid development of resistance.

Ling et al., Nature

Antimicrobial stewardship

Patient related factors –major drivers of inappropriate antimicrobial use

- Self medication
- Prescribers perceptions regarding patients expectations
- Patient compliance
- Hospital use of antibiotics

Inappropriate use and prescribing of antibiotics is causing the development of resistance

Inappropriate use includes:

- not taking your antibiotics as prescribed
- skipping doses of antibiotics
- not taking antibiotics at regular intervals
- saving some for later

Inappropriate prescribing

Inappropriate prescribing includes:

- unnecessary prescription of antibiotics
- unsuitable use of broad-spectrum antibiotics
- wrong selection of antibiotics and inappropriate duration or dose of antibiotics

Prudent Antimicrobial Use

- Develop policies and guidelines on the management of infection
- Support continued professional development
- Reduce inappropriate antimicrobial prescribing
- Use clinical governance arrangements to support improved antimicrobial prescribing
- Identify good prescribing practice
- Put strategies in place to help optimise concordance
- Monitor antimicrobial prescribing

3 things to remember if you are prescribed an antibiotic

1. Take them exactly as prescribed.
2. Make sure you finish the full course, *even if you begin to feel better,* to get rid of the bacteria completely.
3. Do not 'save' left over antibiotics for the next time you, your child, or any other family member is sick.

   Medication prescribed for you now may not be the right medicine for you again or for another person.

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Basic AMS programme

- Implement and assess compliance with local prescribing guidelines
- Review of indications and durations
- Review of consumption data
- Review of antimicrobial resistance data

- Education and resources

Community Acquired Pneumonia

Treatment in the Community (Adults)

Treatment	Dose	TX Duration
amoxicillin	500 mg - 1g TDS	Up to 10 days
clarithromycin	500 mg BD	Up to 10 days
OR doxycycline	200 mg stat/100 mg OD	Up to 10 days

HALT study

Table 7.4.2 Antimicrobials prescribed for the respiratory tract in GN>12m.

Antimicrobial name	Number of prescriptions (%)	Antimicrobial name	Number of prescriptions (%)
Treatment for RTI		**Prophylaxis against RTI**	
Amoxicillin and enzyme inhibitor	57 (43.5)	Amoxicillin and enzyme inhibitor	4 (28.6)
Amoxicillin	23 (17.6)	Azithromycin	3 (21.4)
Clarithromycin	18 (13.7)	Clarithromycin	2 (14.3)
Ciprofloxacin	5 (3.8)	Other	5 (35.7)
Doxycycline	3 (2.3)		
Cefaclor	2 (1.5)		
Cefuroxime	2 (1.5)		
Piperacillin and enzyme inhibitor	2 (1.5)		
Cefixime	2 (1.5)		
Erythromycin	2 (1.5)		
Levofloxacin	2 (1.5)		
Other	13 (9.9)		

What to prescribe?

Conclusion

- Antimicrobial resistance is a significant problem facing the world with the very real prospect of a situation where 'the drugs don't work'
- Antimicrobial stewardship is a key element in preserving the effectiveness of the antibiotic resources we already have
- Antimicrobial stewardship is everybody's responsibility

Thank you for your time

"Don't forget to take a handful of our complementary antibiotics on your way out."