



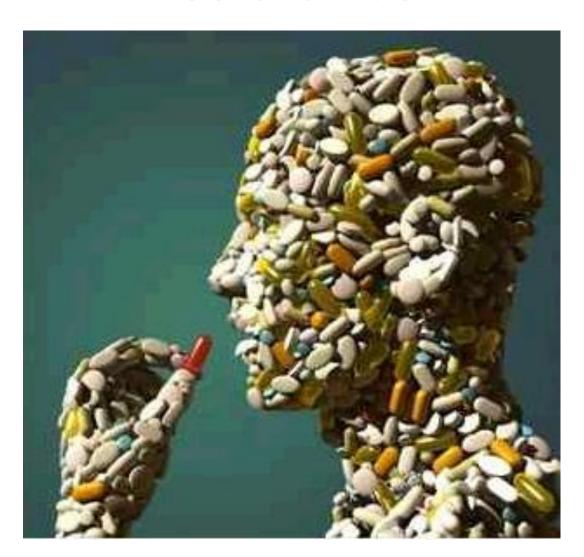
Antimicrobial Prescribing and Stewardship

John Ferguson, Microbiology & Infectious Diseases, John Hunter Hospital, University of Newcastle, NSW, Australia

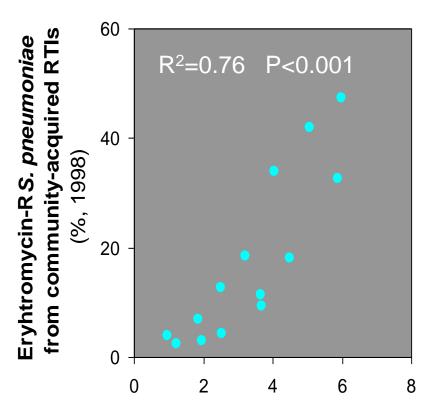
M Med Part 1 updates

UPNG 2017

Antibiotic usage drives resistance!



Correlation of resistance with Antimicrobial Use in Community-Acquired Infections in Europe, 1997-2000



Each dot represents a different European nation

A very tight relationship between overall community consumption and resistance (erythromycin is a macrolide)

Community consumption of macrolides and lincosamides (DDD per 1,000 inh-days, 1997)

Source: Alexander Proj., FINRES, STRAMA, DANMAP and Cars O, et al. Lancet 2001.

How are antibiotics used in PNG?

- PMGH (Steven Yennie, 2012)
 - Medical ward 72% of patients receiving an antiinfective (excluding TB and ARV treatment)
- Alotau Hospital (Nick Ferguson, Nov 2012)
 - Medical ward: 60% of patients on anti-infective
 - Obstetric ward: 34%

Common survey findings

- Very prolonged courses, prolonged IV courses
- Undocumented reasons for therapy
- Treatments not in accord with Standard Treatment Guidelines

PMGH non-urine antibiogram - 2016

PMGH Cumulative antibiogram 2016

Includes isolates from all samples except urine cultures

		Isolates	Ampicillin/ benzylpen	Amoxycillin + clavulanate	Cefazolin / cephalexin	Flucloxacillin/ dicloxacillin	Erythromycin/ clindamycin	Tetracycline	Trimethoprim+ S'methoxazole	Vancomycin	Gentamicin (aminoglycoside)	Ceftriaxone	Piperacillin + tazobactam	Ceftazidime	Meropenem (carbapenem)	Ciprofloxacin
	Staphylococcus aureus- ALL	33	-	52%	52%	52%	66%	100%	97%	100%	n/a					_
isolates																
	Methicillin-susc. S. aureus	17	n/a	S	S	100%	76%	100%	100%	100%	n/a	S	S	-	S	n/a
positive																
Gram	Methicillin-resistant S. aureus	16	R	R	R	R	56%	100%	94%	100%	n/a	R	R	R	R	n/a
9																

Tetracycline	Potential first line antibiotic for treatment of S.aureus infections.
Vancomycin	Vancomycin is reserved for serious MRSA infections - e.g with bacteraemia.
n/a	not available - not routinely tested in this laboratory or no testing standard available
93%	> 90% of isolates susceptible
S	Susceptible by extrapolation or intrinsically susceptible.
75%	70-89% of isolates susceptible
45%	< 70% of isolates susceptible
R	Intrinsically resistant

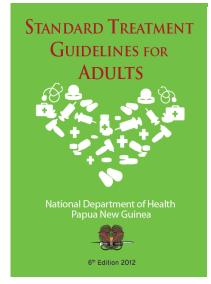
Insufficient numbers of Gram negative isolates to produce antibiogram; Pseudomonas aeruginosa – 24 isolates; gentamicin 54% susceptible, cipro 63%

Urines – species > 30 isolates

PMGH 2016 Urine antibiogram

Species	Isolates	Ampicillin	Amoxycillin+clavulanate	Cefazolin / cephalexin	Nitrofurantoin	Trimethoprim+ S'methoxazole	Gentamicin (aminoglycoside)	Ceftriaxone	Norfloxacin
Escherichia coli	52	8%	17%	n/a	96%	26%	79%	83%	79%
Klebsiella species	31	R	23%	n/a	50%	26%	47%	38%	78%

n/a	Not available - not routinely tested in this laboratory or no testing standard available
93%	> 90% of isolates susceptible
S	Susceptible by extrapolation or intrinsically susceptible
75%	70-89% of isolates susceptible
45%	< 70% of isolates susceptible
R	Intrinsically resistant



PNG therapeutic resources

Adult Medicine

- Adult medical standard treatment guide- 2012 <a>B.
- HIV Adult standard treatment guideline 2009 March . This is the current version in use in 2012.

Paediatrics

- PNG Paediatric standard treatment guides
 Main resource site
- WHO Integrated Management of Childhood Illness resources Page-4
- Recommendations for management of common childhood conditions 2012

 Excellent evidence-based extensive review.
- International Child Health Review Collaboration
- Royal Childrens Hospital Melbourne Paediatric Handbook 8th Edition &
- WHO Treatment of Children living with HIV
- Manual on paediatric HIV care and treatment for district hospitals WHO 2011 &

Obstetrics and Gynaecology

■ Current Standard PNG Treatment Book for O&G 6th Edition, 2010

Surgery

- Standard Treatment book awaited
- WHO Guidelines for Safer Surgery 2009 ₽.

See also Safer surgery: resource poor countries

PNG Medical Journal

Full index to all issues with text links are available from here . The PNGMJ is indexed by Medline and so the easiest way to sear See this quick start guide to PUBMED . For more instructions. It is essential for practitioners in PNG to be aware of the local literal PNG which have been well researched in the past.

http://idmic.net

Q1. What is the primary aim(s) of antimicrobial stewardship?

Reduce antibiotic resistance generally by reducing antibiotic selective pressure on bacteria

Improve the effectiveness of antibiotic treatment of individual patients with infection

Improve patient safety by reducing unintended consequences of antibiotic treatment

Correct response	Results (n=30)
All three is the correct answer	90%

Purpose of antimicrobial stewardship

- Optimise outcome for patient with infection - right diagnosis, right antibiotic, timing, dose, duration etc
- 2. Reduce antimicrobial resistance
- Minimise individual and community unintended consequences of antimicrobials- adverse events, added (super)infection

Unintended consequence: antibiotic mortality

Antibiotic class	Mechanism	Mortality risk
Chloramphenicol	Aplastic anaemia	1 in 20-60,000 courses
Betalactams	Anaphylaxis	1 in 50-66,000 courses
Trimethoprim	Hyperkalaemia from reduced distal renal tubular tubular K secretion	In a population of patients > 65 years on ACE inhibitors, excess mortality of 1 in 350 courses
Macrolides (azithromycin)	Prolonged QT – sudden death	1 in 26,000 courses (33 studies involving 20,779,963 participants)
Quinolones (ciprofloxacin and others)	Prolonged QT – sudden death	Similar level of risk for ciprofloxacin death in the trimethoprim study above Risk remains higher for 2 weeks following rx

Clinicians as stewards

"Stewardship is an ethic that embodies the responsible planning and management of [scarce] resources." Wikipedia

<u>Leadership</u>, advocacy and collaboration amongst prescribers required to reduce AMR.

We have the agency and scope to change patient management in ways that will reduce the impact of AMR on our patients and the community

Rational antibiotic use: essential principles – AIMED

<u>A</u> ntimicrobial selection and dosage compliant with guidelines

Indication for treatment documented

M icrobiology before treatment

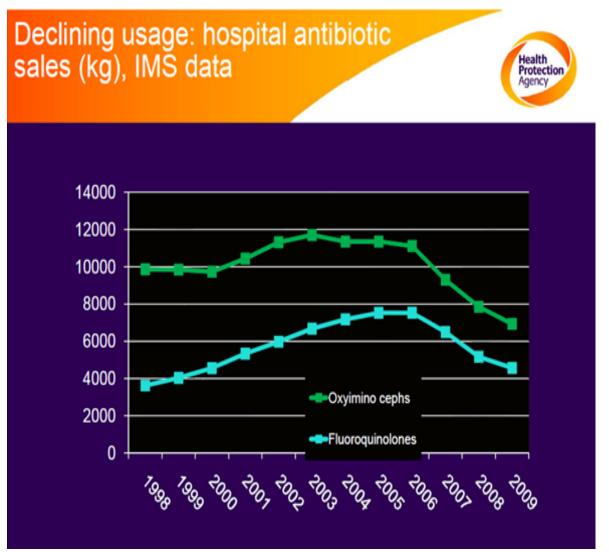
Evaluate at 48-72hrs

<u>D</u>uration or review date explicit



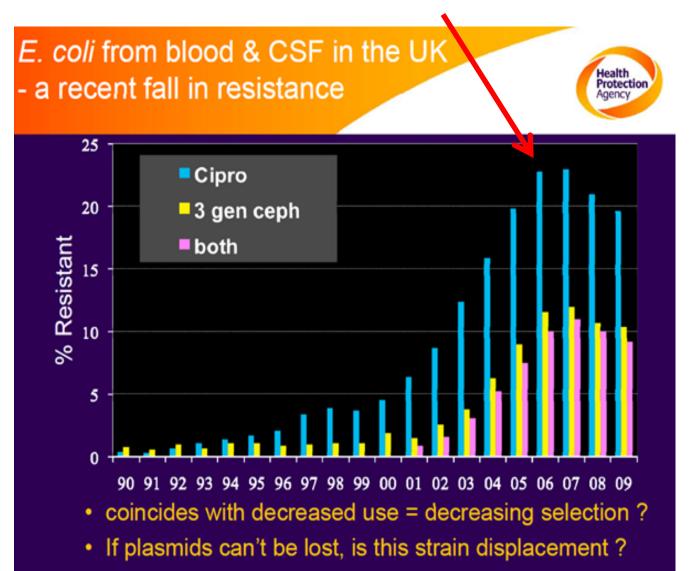
http://aimed.net.au

UK: country-wide experiment – restrictions on cephalosporin and quinolone use implemented



Slides courtesy of Neil Woodford, HPA 2012

AMR is dynamic- reducing use will usually reduce resistance



Q1: What class of antibiotic is vancomycin?

Correct response	Results (n=30)
Glycopeptide	17%

- Why understand the class? Differences in:
 - Pharmacodynamics and dosing
 - Toxicity potential
 - Antibacterial spectrum
 - Mechanisms of resistance

DIFFERENT CLASSES OF ANTIBIOTICS - AN OVERVIEW

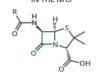
COMMONLY ACT AS BACTERIOSTATIC AGENTS, RESTRICTING GROWTH & REPRODUCTION



COMMONLY ACT AS BACTERICIDAL AGENTS, CAUSING BACTERIAL CELL DEATH

B-LACTAMS

MOST WIDELY USED ANTIBIOTICS IN THE NHS



All contain a beta-lactam ring

EXAMPLES

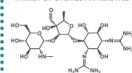
Penicillins (shown) such as amoxicillin and flucloxacillin: Cephalosporins such as cefalexin.

MODE OF ACTION

nhibit bacteria cell wall biosynthesis.

AMINOGLYCOSIDES

FAMILY OF OVER 20 ANTIBIOTICS



All contain aminosugar substructures

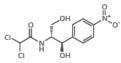
EXAMPLES

Streptomycin (shown), neomycin, kanamycin, paromomycin.

Inhibit the synthesis of proteins by bacteria, leading to cell death.

CHLORAMPHENICOL

COMMONLY USED IN LOW INCOME COUNTRIES



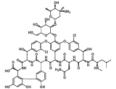
Distinct individual compound

MODE OF ACTION

Inhibits synthesis of proteins. preventing growth.

No longer a first line drug in any developed nation (except for conjunctivitis) due to increased resistance and worries about safety.

GLYCOPEPTIDES



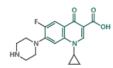
Consist of carbohydrate linked to a peptide formed of amino acids

EXAMPLES Vancomycin (shown), teicoplanin.

MODE OF ACTION Inhibit bacteria cell wall biosynthesis.

OUINOLONES

RESISTANCE EVOLVES RAPIDLY



contain fused aromatic rings with a carboxylic acid group attached

EXAMPLES

Ciprofloxacin (shown), levofloxacin, trovafloxacin

MODE OF ACTION

Interfere with bacteria DNA replication and transcription.

OXAZOLIDINONES

POTENT ANTIBIOTICS COMMONLY USED AS 'DRUGS OF LAST RESORT'

All contain 2-oxazolidone somewhere in their structure

EXAMPLES

Linezolid (shown), posizolid, tedizolid, cycloserine.

Inhibit synthesis of proteins by bacteria, preventing growth.

DISCOVERY

1930

1940

1950

1960

1970

1980

SULFONAMIDES

FIRST COMMERCIAL ANTIBIOTICS WERE SULFONAMIDES

$$H_2N$$

All contain the sulfonamide group

EXAMPLES

Prontosil, sulfanilamide (shown), sulfadiazine, sulfisoxazole.

MODE OF ACTION

Do not kill bacteria but prevent their growth and multiplication. Cause allergic reactions in some patients.

TETRACYCLINES

BECOMING LESS POPULAR DUE TO DEVELOPMENT OF RESISTANCE

All contain 4 adjacent cyclic hydrocarbon rings

EXAMPLES

Tetracycline (shown), doxycycline, limecycline, oxytetracycline.

MODE OF ACTION

Inhibit synthesis of proteins by bacteria, preventing growth.

MACROLIDES

SECOND MOST PRESCRIBED ANTIBIOTICS IN THE NHS

All contain a 14- 15- or 16-membered macrolide ring

EXAMPLES

Erythromycin (shown), clarithromycin, azithromycin.

Inhibit protein synthesis by bacteria, occasionally leading to cell death.

ANSAMYCINS

CAN ALSO DEMONSTRATE

All contain an aromatic ring bridged by an aliphatic chain.

EXAMPLES

Geldanamycin (shown), rifamycin, naphthomycin.

MODE OF ACTION Inhibit the synthesis of RNA by

STREPTOGRAMINS

TWO GROUPS OF ANTIBIOTICS THAT ACT SYNERGISTICALLY

Combination of two structurally differing compounds, from groups denoted A & B

EXAMPLES

Pristinamycin IIA (shown), Pristinamycin IA.

MODE OF ACTION

Inhibit the synthesis of proteins by

LIPOPEPTIDES

All contain a lipid bonded to a peptide EXAMPLES

Daptomycin (shown), surfactin.

MODE OF ACTION

Disrupt multiple cell membrane functions, leading to cell death.



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https://aimed.net.au/2017/02/01/antibiotic-classes-why-soimportant-to-know-about-them/

PK and PD

- <u>Pharmacokinetics</u> describes the time course of drug levels in body fluids as a result of absorption, distribution, and elimination of a drug after administration. Parameters include:
 - Bioavailability and influence of food on absorption
 - Peak level
 - Vd- Volume of distribution (lipo versus hydrophilic drugs)
 - T1/2 Half life
 - AUC area under the concentration-time curve
- <u>Pharmacodynamics</u> describes the rate and extent of bactericidal action and postantibiotic effects – used to provide a rational basis for determination of optimal dosing regimens in terms of the dose and the dosing interval

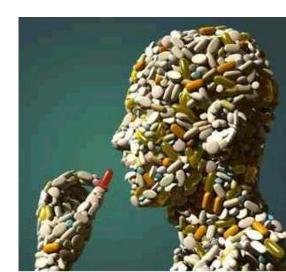
Maximising therapeutic effect

Dose in accord with PK/PD understanding:

- Time-dependent kill betalactams, vancomycin ensure drug concentration above organism MIC for > 50% of the time; i.e. more frequent dosing gives better efficacy than higher doses
- Concentration-dependent kill aminoglycosides, quinolones, metronidazole - ensure drug dose high enough to achieve adequate kill – target area under the curve – AUC/MIC parameter used. Concentration dependent Post antibiotic effect (PAE)
- 3. <u>Bacteriostatic agents</u> that produce moderate to prolonged PAEs (e.g., macrolides, clindamycin, tetracyclines). Because of their prolonged PAE, their efficacy is determined less by time and more by the AUC that is greater than the MIC.

Therapeutic factors promoting antibiotic resistance

- 1. Antibiotic selective pressure
 - Number of patients exposed (volume of use)
 - Breadth of spectrum
 - Duration of use
- 2. Inadequate dosing



Eliminate unnecessary use

- Patients may receive antibiotics for extended post operative prophylaxis or for 'just in case' situations where there is little actual evidence of infection
- These exposures put patients at great risk of acquiring resistant organisms and should be avoided

(Post operative prophylaxis doesn't protect patients from poor hygiene or hospital acquired infection)

Unnecessary use – trusting in scalpel-mycin

- Appendectomy
 - Post operative dosing largely unnecessary for unperforated cases; 4 days for others
- Cholecystectomy cease antibiotics post op
- Diverticular disease
 - Antibiotics unnecessary for non-surgical patients (2 RCTs)
- Perforated viscus with source control achieved
 : 4 days (or less) sufficient; 2015 NEJM trial

Rational empirical antibiotic use

- Evaluate likelihood of sepsis by presence of SIRS, other organ system dysfunction
- Withhold antibiotics if there is not a strong case and severe sepsis is absent
- Do pre-antibiotic microbiology tests
- Select empirical antibiotic(s) based on local guidelines and AMR incidence
- Document the reason for antibiotics in the patient record

Narrow spectrum empirical treatment

- Skin/soft tissue infection without sepsis: surgical management; MRSA cover
- Community acquired pneumonia
- Early (< 5 days from admission) Hospital acquired pneumonia

	Isolates	Ampicillin/ benzylpen	Amoxydllin + clavulanate	Cefazolin / cephalexin	Flucioxacillin/ dicloxacillin	Erythromydin/ clindamydin	Tetracycline	Trimethoprim+ S'methoxazole	Vancomycin
Staphylococcus aureus- ALL	33		52%	52%	52%	66%	100%	97%	100%
Methicillin-susc. S. aureus	17	n/a	s	s	100%	76%	100%	100%	100%
Methicillin-resistant S. aureus	16	R	R	R	R	56%	100%	94%	100%

Post empiric evaluation at 48-72 hours

Assess:

- Response to treatment
- Source control
- WCC, biochem and microbiology results can treatment be directed against proven pathogen(s)?
- Is there a non-infective cause?
- Is antibiotic treatment still indicated (patient has rapidly improved)?
- If ongoing treatment indicated consider early switch to oral (most agents are bioavailable)
- Define duration of treatment required

Limit durations of treatment

A very effective way to reduce selective pressure!

Shorter duration treatments are feasible with:

- community pneumonia (3-5d)- extensive studies
- Intensive care unit pneumonia (7d)
- Localised UTI (3 days), UTI with sepsis (7-10d)
- Intra-abdominal sepsis with source controlled (1-4d)

Local guidelines need to specify recommended durations

Limiting durations of treatment

Effective way to reduce selective pressure

Few situations require prolonged treatment:

- Endocarditis
- Prosthetic infections etc

Short, sharp and directed best idea Single dose surgical prophylaxis!

Paterson-D et al . Strategies for Reduction in Duration of Antibiotic Use in Hospitalized Patients Clinical Infectious Diseases 2011: 52: 1232

Sawyer RG et al. **Trial of short-course antimicrobial therapy for intra-abdominal infection.** N Engl J Med. 2015 May 21;372(21):1996-2005.

Randomized clinical trial to compare a single dose with 3 doses of prophylactic antibiotic in open reduction and internal fixation of the fractures of long bones

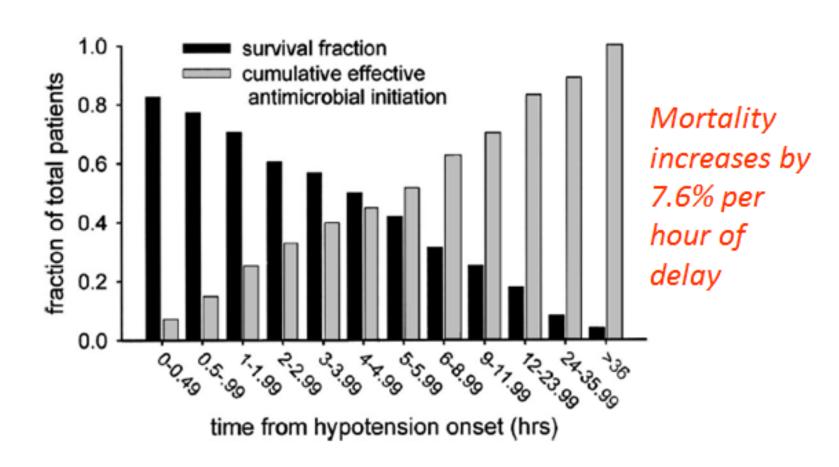
IKAU KEVAU1 AND JERZY KUZMA2

School of Medicine and Health Sciences, University of Papua New Guinea, Port Moresby and Faculty of Medicine and Health Sciences, Divine Word University and Modilon General Hospital, Madang, Papua New Guinea

SUMMARY

To reduce the incidence of surgical site infection (SSI), perioperative antimicrobial prophylaxis has long been advocated for joint replacement and open reduction with internal fixation of long bones. Increasing health care costs have focused hospital interest on more cost-effective procedures. Although current literature indicates that single-dose antibiotic prophylaxis is comparable to a 3-dose regimen, there are no reports from lowincome countries. The primary aim of this study was to compare the infection rate following open reduction and internal fixation of long-bone fractures in groups with a single dose and 3 doses of prophylactic antibiotic. The secondary aim was to compare the costeffectiveness of both antibiotic regimens. This is a prospective randomized clinical trial (RCT) to compare the incidence of surgical site infection between the patients allocated randomly into two groups with different antibiotic prophylactic regimens: single dose or 3 doses 8 hourly of 1g ceftriaxone administered intravenously. 200 consecutive patients who underwent open reduction and internal fixation (ORIF) for closed long-bone fractures were enrolled in this study. The rate of postoperative SSI was 4.1% in the single-dose group and 2.2% in the 3-dose group; the overall SSI rate was 3.2%. The primary endpoint of this study, which is the incidence of SSI, showed no significant difference between the single-dose and 3-dose prophylactic antibiotic groups. Furthermore, there was no

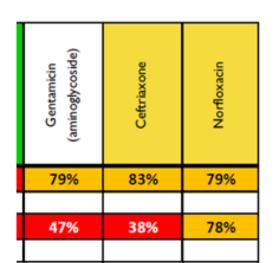
Consequence: delay effective rx in severe sepsis



Kumar: Crit Care Med 2006; 34:1589–1596)

Aminoglycosides- choice for potential Gram negative sepsis

- Most rapidly bactericidal agent still (concentration-dependent kill)
- Best coverage of Gram negative pathogens based on local patterns of susceptibility
- Australia: safe dosing regimens maximum 48hrs (3 doses)





Gentamicin questions!

Q8 What weight is used for calculation of gentamicin dosing?

Correct response	Results (n=30)
Ideal body weight	27%

Q4 What initial dose of gentamicin is recommended on PNG adult STG?

Correct response	Results (n=30)
5mg/kg	27% (60% incl 5-7
	response)

Gentamicin: unintended consequences

- Nephrotoxicity cumulative effect
- Ototoxicity vestibular function
 - Cumulative dose effect
 - Rare idiosyncratic effect
 - Salicylate may attenuate toxicity
- Cumulative dose effects minimised by:
 - single daily dosing saturates uptake into sites of potential toxicity
 - Short courses

Gentamicin: safety in practice

ANTIMICROBIAL AGENTS AND CHEMOTHERAPY, Mar. 1995, p. 650–655 0066-4804/95/\$04.00+0 Copyright © 1995, American Society for Microbiology

Vol. 39, No. 3

Experience with a Once-Daily Aminoglycoside Program Administered to 2,184 Adult Patients

DAVID P. NICOLAU, 1,2,3* COLLIN D. FREEMAN, $^{1,3}\dagger$ PAUL P. BELLIVEAU, $^{1,3}\ddagger$ CHARLES H. NIGHTINGALE, 3,4 JACK W. ROSS, 2 and RICHARD QUINTILIANI 2,5

- 7mg/kg / day; dose interval adjusted in presence of preexisting renal failure
 - median dose 450mg (R 200 925)
 - median length of therapy 3 days (R 1-26)
 - median age 46 years (R 13 97)
- Clinically apparent ototoxicity :
 - 3 patients (durations of rx before sx : 5 d, 5 weeks!, and third patient had a single dose)
 - Symptoms resolved in patients 1 and 3; patient 2 had some residual changes
- 1.2% developed nephrotoxicity

Q2. What is main mechanism by which Staphylococcus aureus becomes resistant to penicillin?

Correct response	Results (n=30)
Betalactamase production	50%

- 90% + of methicillin-susceptible strains are resistant to penicillin due to blactamase
- Clavulanate in Augmentin inhibits this
- Flucloxaxillin is betalactamase stable

Q5. What is the drug of choice for a methicillin-susceptible Staphylococcus aureus bloodstream infection (SAB)?

Correct response	Results (n=30)
Flucloxacillin	50%

- Benpen NO
- Vancomycin NO less rapidly acting inferior outcomes
- Ceftriaxone NO technically will work but is too broad spectrum – selects for more resistance
- Eyrthomycin NO not suitable for systemic infection bacteriostatic

Staphylococcus aureus bloodstream infections

- PMGH 2016: 8 of 11 (78%) events were due to MRSA
- Community and healthcare-associated events occur; risk of undisclosed endocarditis
- Minimum 2 weeks IV therapy required for "uncomplicated" cases- dosing as appropriate for endocarditis
- Vancomycin IV required in PNG!

SAB management

High mortality infection; best practice treatment reduces same: 10 essential steps to consider

See HNELHD_CG_14_20_Management_of_Staphylococcus_aureus_bacteraemia for detailed advice.

What to do if your patient has Staphylococcus aureus grown in

1.3 Complicated SAB

Complicated SAB is defined as the presence of ANY of the following features [5]:

- Persistent bacteraemia at 48-72 hours following initiation of appropriate antibiotics.
- Persistent fever for >72 hours following initiation of appropriate antibiotics.
- Bacteraemia where no removable focus of infection is identified ("removable" foci include intravascular lines, drained skin and soft tissue abscesses and simple skin lesions).
- Metastatic focus (e.g. endocarditis, vertebral osteomyelitis, visceral abscesses).
- Intravascular prosthetic material (e.g. prosthetic cardiac valve, pacing wires, pacemaker, implanted defibrillator, prosthetic fistula).

10. **Provide verbal & written advice to your patient and their family** about the symptoms of relapse and the need for early review if problems occur. The guideline has a patient information card within.

https://aimed.net.au/2015/10/15/essential-clinical-care-of-staphylococcus-aureus-bloodstream-infection-sab/

Vancomycin: how to use

- Slow onset of action
- Australian Guidelines Ed 15 give loading dose of 25-30mg/kg (based on actual body weight)
- Then give 1.5g 12-hrly for GFR>90, lower dosing for patients with renal failure



The clinical spectrum of staphylococcal bacteraemia: a review of 101 Melanesian patients from Papua New Guinea.

John R, Naraqi S, McDonnell G.

- 101 patients with Staphylococcus aureus bacteraemia observed during two 2-year periods (1977-1979 and 1985-1987) at PMGH
- 12 to 70 years; 69% male
- Diabetes mellitus (15%) most common predisposing factor.
- 87% had community-acquired infection.
- Sites of infection: soft-tissue infection, pneumonia, arthritis, osteomyelitis, intravenous-site thrombophlebitis, cerebral abscess, endocarditis and cavernous sinus thrombosis
- Soft tissues and lungs most common sites of primary and secondary foci of infection, respectively.
- Penicillin 1% susceptible; no MRSA detected
- The overall case fatality rate 24%.

Q7: According to the STG, what is the recommended treatment for moderate severity community acquired pneumonia?

Correct response	Results (n=30)
Benzylpenicillin	62%

- Streptococcus pneumoniae remains the most important childhood and adult cause of bacterial pneumonia
- Remains susceptible to penicillin in almost all cases

12.4.2 Moderate Pneumonia

Symptoms and signs

- Fever, cough, pleuritic chest pain
- Respiratory distress (in-drawing of muscles between ribs, using neck muscles for breathing) OR
- Respiration rate 30-40/min.
- AND no complications



Treatment

Treat as an inpatient. If getting worse after 2 days treatment, treat for severe pneumonia.

- Give
 - benzyl-penicillin IV 2 MU (1.2g) every 4-6 hours
- When improved change to:
 - amoxycillin 500mg t.d.s for 5-10 days
- · Analgesia for chest pain (on page 16)
- Test for malaria (blood slide or RI

Treatment

- Chest physiotherapy/encourage t
- · Give:

chloramphenicol IM or IV 1g (1 whole vial with 4ml sterile water) q.i.d OR benzyl-penicillin IV 2 MU (1.2g) every 4-6 hours AND gentamicin IV 5mg/kg daily OR ceftriaxone IV 1g daily

 When the patient improves, has no fever and looks better (usually after 3-5 days) change to:

chloramphenicol 750mg (3 caps) orally q.i.d for 10 days

Community acquired pneumonia

- Range of viral, bacterial pathogens
- Non-severe pneumonia focus on supportive care + penicillin / amoxycillin
 - Non pneumococcal pathogens unlikely to require directed therapy – self limited course
 - Beware possible pertussis in infant
- Severe pneumonia requires broader spectrum cover for Gram negative pathogens (Klebsiella etc) – penicillin+ gentamicin (short course for gent)

Acute exacerbations of COPD

- Comprehensive viral detection studies indicate that around 70% have had an antecedent viral infection (with one or more of 15 different viruses)
- Most patients are chronically colonised with a range of Haemophilus, Moraxella or Strep. pneumoniae
- Varying degrees of bronchiectasis as well if sensitive CT scanning used

Acute exacerbations of COPD (2)

- A minority have obvious pneumonia beware of overdiagnosis – if pneumonia then exclude TB and treat as pneumonia
- Those without pneumonia need supportive care –
 oxygen, nebulisers. Antibiotics play a minor role at
 most, give 3 days of amoxycillin or doxycycline
- Treat chest infection if sputum increases in amount or becomes more green or yellow.
 Use:
 - amoxycillin 500mg (2x250mg or 1x500mg) t.d.s for 7 days
- · If no improvement, give:
 - doxycycline 100mg (1 tab) b.d for 7 days OR cotrimoxazole (Septrin) 960mg (2 tabs) b.d. for 7 days



Upper respiratory infections

Adults

- Overwhelmingly viral causes avoid antibiotics and manage symptoms (influenza vaccination)
- Pharyngitis appearance of throat and tonsils does NOT predict bacterial infection
- If antibiotics used at all, short course max 3 days and narrow spectrum. Do not repeat courses

Children

- Peak age incidence for Streptococcus pyogenes infection is 5-14 years. Penicillin-V for overt pharyngitis esp in association with cervical LNs.
- Otitis media guideline driven prone to over-diagnosis antibiotics for infants, those with severe or non-responsive disease
- Beware pertussis

The in vivo susceptibility test

- Scenario 1: patient treated with antibiotic appears to be improving – what are the possible explanations?
 - The antibiotic did it! Take credit...
 - The patient had a self limited illness
- Scenario 2: patient is failing to respond to antibiotic treatment.
 - They have a non-bacterial infection
 - They don't have an infection!
 - The antibiotic is inactive or the wrong one
 - The infection is due to a multi-resistant organism that is not susceptible to the treatment
 - The illness does not get better that quickly! E.g. typhoid takes a median of 4 days of treatment before temp falls

Q 6: First line treatment for non-severe Clostridium difficile diarrhoea

Correct response	Results (n=30)
Oral/IV metronidazole	50%

- PNG hospital and community incidence of *C. difficile* infection unknown- Needs to be studied!
- IV vancomycin does not enter the bowel no use!
- Oral vancomycin is second line not absorbed and effective
- Treatment is for 7-10 days; relapse not infrequent
- Cross infection risk

Osteomyelitis

- Acute osteomyelitis: symptoms present for < 14 days correlate with acute osteomyelitis histopathologically (i.e. lack of bone necrosis and sequestra). Symptoms > 48 hrs, generally surgery required.
- Chronic osteomyelitis: relapsed or long-standing bone infection that may involve a sinus or a compromised soft-tissue envelope. Pathologylow-grade inflammation, sequestra +/involucrum (new bone formation adjacent to a sequestrum). Antibiotics AND surgery.

2.2 Osteomyelitis and pyomyositis

2.2.1 Acute Osteomyelitis

Consider acute osteomyelitis in all patients with a painful limb and fever. If the pain is in the joint, treat for septic arthritis).

Aetiology - Children haematogenous:

Staphylococcus aureus, Streptococcus pyogenes Haemophilus influenzae type B (HIB), Streptococcus pneumoniae M. Tuberculosis

Adults haematogenous:

Staphylococcus aureus, Streptococcus, E. coli

Treatment

- Give empiric antibiotics:
 flucloxacillin 1q IV q.i.d for 2-6 weeks (see below)
- · Refer immediately to medical officer
- Intravenous therapy should continue for a minimum of 2 weeks. Thereafter, give: flucloxacillin 1g (2 tabs) q.i.d for 4 weeks
- If there is no improvement with flucloxacillin, consider the possibility of MRSA (methicillin-resistant Staphylococcus aureus) and give:

lincomycin 600mg IV t.d.s for 2 weeks followed by cotrimoxazole 960mg (2 tabs) b.d for 4 weeks



Management of childhood haematogenous osteomyelitis in a rural Papua New Guinean hospital.

Van Gurp G, Kila R, Hutchinson T.

Abstract

Haematogenous osteomyelitis, especially in its more common chronic stage, is an important cause of morbidity in children in the Southern Highlands Province. Hospital stays are lengthy and the incidence of fractures is high. While awaiting, or in the absence of, culture and sensitivity results, cloxacillin 200 mg/kg/day plus probenecid 40 mg/kg/day is an appropriate first choice antibiotic when it is available. Antibiotic therapy in chronic disease should be limited to the specific settings of associated soft tissue infection; preand post-sequestrectomy; and radiological signs of ongoing bone necrosis and systemic signs of active infection. Surgical drainage of subperiosteal pus and possibly the medullary canal is required in all but the very early (less than 48 hours) cases of acute osteomyelitis that sometimes respond to antibiotics alone. Sequestrectomy should be reserved for cases where a sequestrum and adequate involucrum can be seen on X-ray. Effective management of this disease is possible only if ongoing communication exists between hospital-based medical staff and the staff of health centres or subcentres. including the network of aid post orderlies and their supervisors. Since the majority of patients present to facilities other than hospitals, any campaign directed at improving management must involve co-workers in rural areas, namely the health extension officer, nurse and aid post orderly. Only in this way can we hope to achieve earlier appropriate treatment and more systematic long-term follow-up.

Osteomyelitis: durations of treatment

Suggested duration of therapy for long-bone or vertebral osteomyelitis (Table 2.12)

	Age	Duration of antibiotic therapy (modify according to clinical response)	
		Intravenous [NB1]	Total duration (can be completed with oral therapy)
Acute osteomyelitis [NB2]	neonate	4 weeks	4 weeks (all IV)
	child	3 days	minimum 3 weeks
	adult	4 weeks	minimum 6 weeks
Chronic osteomyelitis [NB2]	child	may not be necessary	minimum 6 weeks
	adult	2 weeks	many months

NB1: If the patient is improving, earlier conversion to oral therapy may be possible, as long as there is an appropriate oral antimicrobial available that is as effective as intravenous therapy (eg ciprofloxacin, clindamycin). Conversely, some patients will need a longer duration of intravenous therapy than recommended here. Seek expert advice.

2016-17 PNG NATIONAL ACTION PLAN ON ANTIMICROBIAL RESISTANCE

Recommendations drafted against the WHO policy package on AMR under these headings:

- 1. National coordination mechanisms (governance)
- 2. Access to, and quality of, essential medicines
- 3. Surveillance and laboratory capacity
- 4. Rational use of medicines in humans and animals
- 5. Infection prevention and control
- 6. Research and development

Potential M Med projects!

- Descriptive studies of blood culture isolates, clinical details and antibiograms (where available):
 - Staph aureus bloodstream infection (adults, children, neonates)
 - Gram negative bloodstream infections (ditto)
- Antimicrobial prescribing survey point prevalence- every patient on an a/m – National Antimicrobial Prescribing Survey methods (Oz)
 - Documented reason?
 - When started?
 - Dose and mode of administration
 - In line with STG?
 - In line with documented microbiology for the patient?
- Antimicrobial prescribing and resistance knowledge, attitudes and practice:
 - Surveys of prescribers, students
 - Surveys of community
- Culture surveys of community and hospital patients to document carriage of MROs – MRSA, MRGN

Projects: infection prevention

- Healthcare infection point prevalence survey- hospital wide or ward- WHO methodology
- Surgical wound infection studies- analysis of risk factors, microbiology, use of surgical prophylaxis and potential changes for prevention
- Hand hygiene practice knowledge, attitudes and practice of healthcare staff – doctors, nurses etc. What are the barriers to uptake/compliance amongst medicos?
- Aseptic practice audits IV device insertion and management, IV medication preparation, adverse outcomes (local and blood stream infections)
- Urinary catheter usage who gets catheterised? How long do catheters remain? Study patient acceptability of catheter fixation devices. Study outcomes (infection).
- Bubble humidifiers microbiological culture survey of the fluid from these devices!

References

- http://ldmic.net for access to PNG STG
- http://aimed.net.au for discussions on antibiotic stewardship
- WHO Information sheet on AMR excellent overview -

http://www.who.int/mediacentre/factsheets/fs194/en/index.html