

Antimicrobial Stewardship and Antibiotic Management of Respiratory Tract Infections.

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Antimicrobial Resistance



Overview of Presentation

- ▶ Establish Antibiotic Resistance as problem
- ▶ Global perspective
- ▶ Antibiotic Stewardship
- ▶ Role of the Pharmacist
- ▶ Principles of Antibiotic Prescribing
- ▶ Application to the treatment of RTI's

Background

- ▶ Antibiotic resistance: major public health problem: **US \$55b!!**
- ▶ CDC: >2m affected; 23,000 deaths/yr
- ▶ 200-300 million antibiotics are prescribed annually
- ▶ 45% for outpatient use; 50-80% is inappropriate
- ▶ 25-40% of hospitalized patients receive antibiotics
 - ▶ At least 30% are unnecessary or sub-optimal

Antibiotic Stewardship

- ▶ No wonder we need to steward our antibiotics!
- ▶ Systems to monitor & provide feedback: Pharmacist
- ▶ Maximizes antibacterial action; optimizes clinical outcomes; minimizes emergence of resistance
- ▶ Reduces costs: Inappropriate or unnecessary therapy
- ▶ Provides the infrastructure to preserve antibiotics

Roadside One Stop Pharmacy?



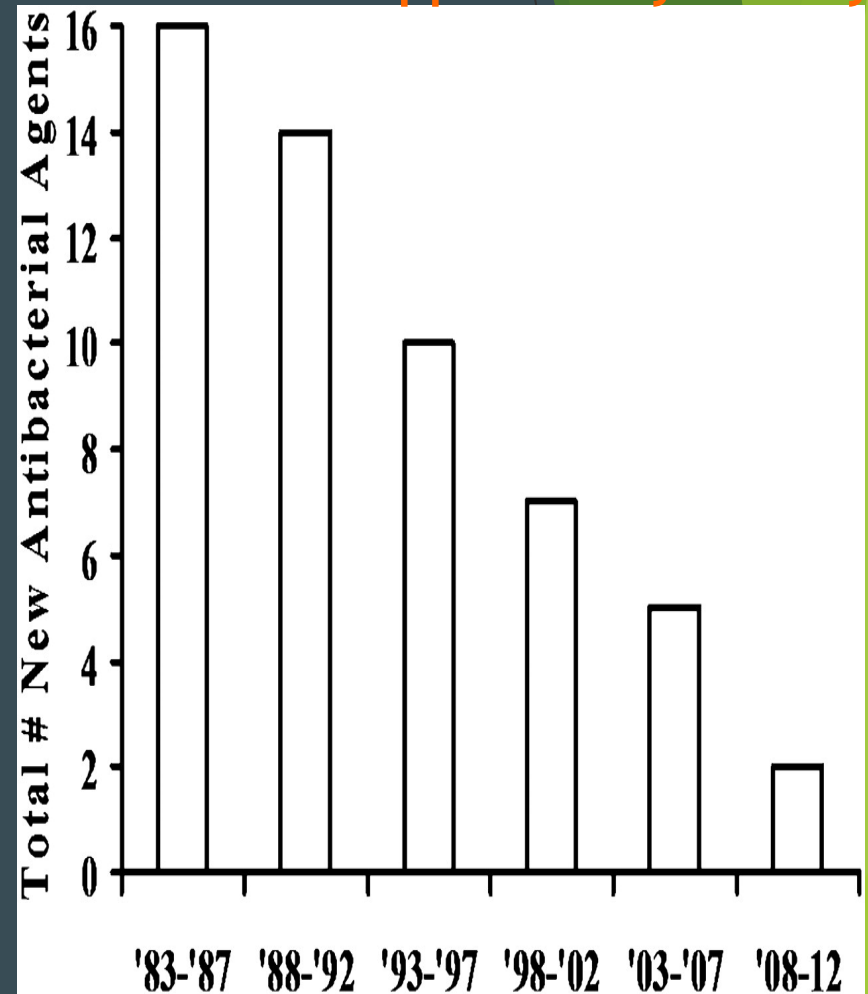
Various types of antibiotics for sale on the streets of Port-au-Prince, Haiti.

Stewardship



New Antibiotics Approved by FDA/5yrs

- ▶ Increased resistance; decreased production
- ▶ ?Post antibiotic era: Srinivasan (CDC)
- ▶ Success of many of the advances in medicine is predicated on availability of AB's. Loss of antibiotics would therefore wipe out many of these
- ▶ Challenge of practicing medicine without antibiotics



As it was in the beginning.....

1940's

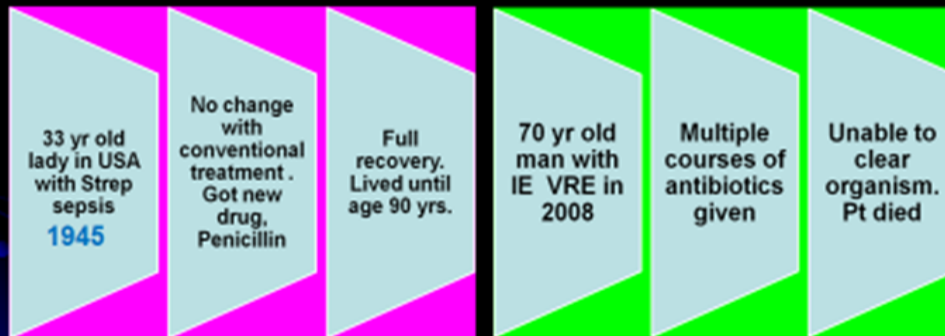


After 14 dys penicillin

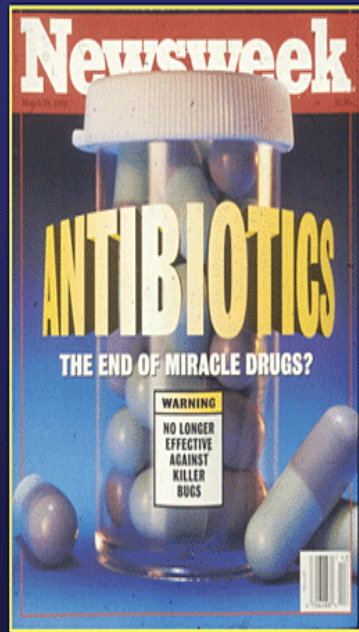


So is it again.....

A Tale of Two Bugs!



Antibiotic Resistance: Global Crisis!



JAMAICA ANTIBIOTIC RESISTANCE
CAMPAIGN??



WHO World Health Day: April 7, 2011

Antimicrobial Resistance & Its Global
Spread

Dear Mr President

President Obama's Executive Order

President Obama's Executive Order

The White House

Office of the Press Secretary

For Immediate Release

September 18, 2014

Executive Order -- Combating Antibiotic-Resistant Bacteria

By the authority vested in me as President by the Constitution and the laws of the United States of America, I hereby order as follows:

.....
Combating antibiotic-resistant bacteria is a national security priority.

.....
By February 15, 2015, the Task Force shall submit a 5-year National Action Plan (Action Plan) to the President that outlines specific actions to be taken to implement the Strategy.

UK Pledge

- ▶ November 18th is European Antibiotic Awareness Day. Everyone in the UK to become **Antibiotic Guardians.**
- ▶ Call to action: Choose one simple pledge about how you'll make better use of antibiotics and help save this vital medicine from becoming obsolete.
- ▶ UK 5 yr Antimicrobial Resistance Strategy: 2013-2018

Lives Devastated/Lost Due to Antibiotic-Resistant Organisms



If you or your loved ones have been devastated by an antibiotic resistant bacterial infection and you would like to share your story, please contact.....

Role of the Pharmacist: Antibiotic Police?

- ▶ Today's Pharmacist must be vigilant
- ▶ Monitor usage; intercept abuse; antibiotic police
- ▶ Must work as part of a team



**Effective
Antimicrobial
Stewardship
needs teamwork:**

**Microbiologist
Physician
Pharmacist
Nurse
ICP
Housekeeping
Other**

**We need all
hands on
deck!**



Summary: Collateral Damage

	3 rd Generation Cephalosporins	Quinolones	Carbapenems
Vancomycin-resistant <i>E. faecium</i> (VRE)	x		
MDR <i>Enterobacter</i> (Sermor Proven F)	x		
Methicillin-resistant <i>S. aureus</i> (MRSA)	x	x	
<i>Clostridium difficile</i> infection (CDI)	x	x	x
Multidrug-resistant (MDR) <i>Klebsiella</i>	x	x	
MDR <i>Acinetobacter</i>	x	x	x
MDR <i>Pseudomonas aeruginosa</i>		x	x
<i>Klebsiella pneumoniae</i> carbapenemases (KPC) β -lactamases, NDM			x

Today's Pharmacist: Know The Bugs That Come From The Drugs

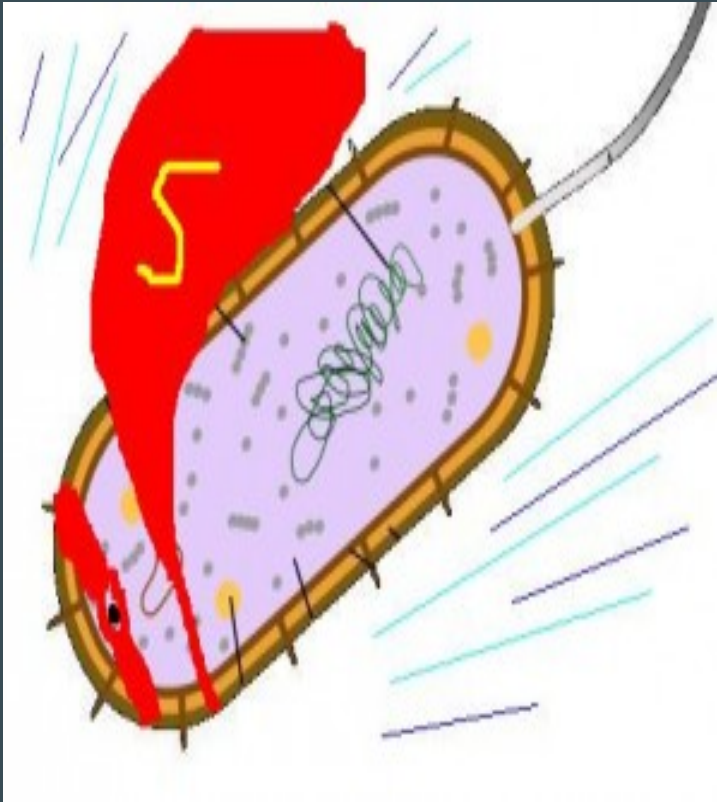


ESKAPE PATHOGENS:

Enterococcus: VRE

- *Staph aureus*: MRSA, VRSA, VISA
- *Klebsiella pneum.* ESBL's
- *Acinetobacter* -cb MDRGNB
- *Pseudomonas aeruginosa* MDRGNB
- *Enterobacter* spp/ E coli ESBL

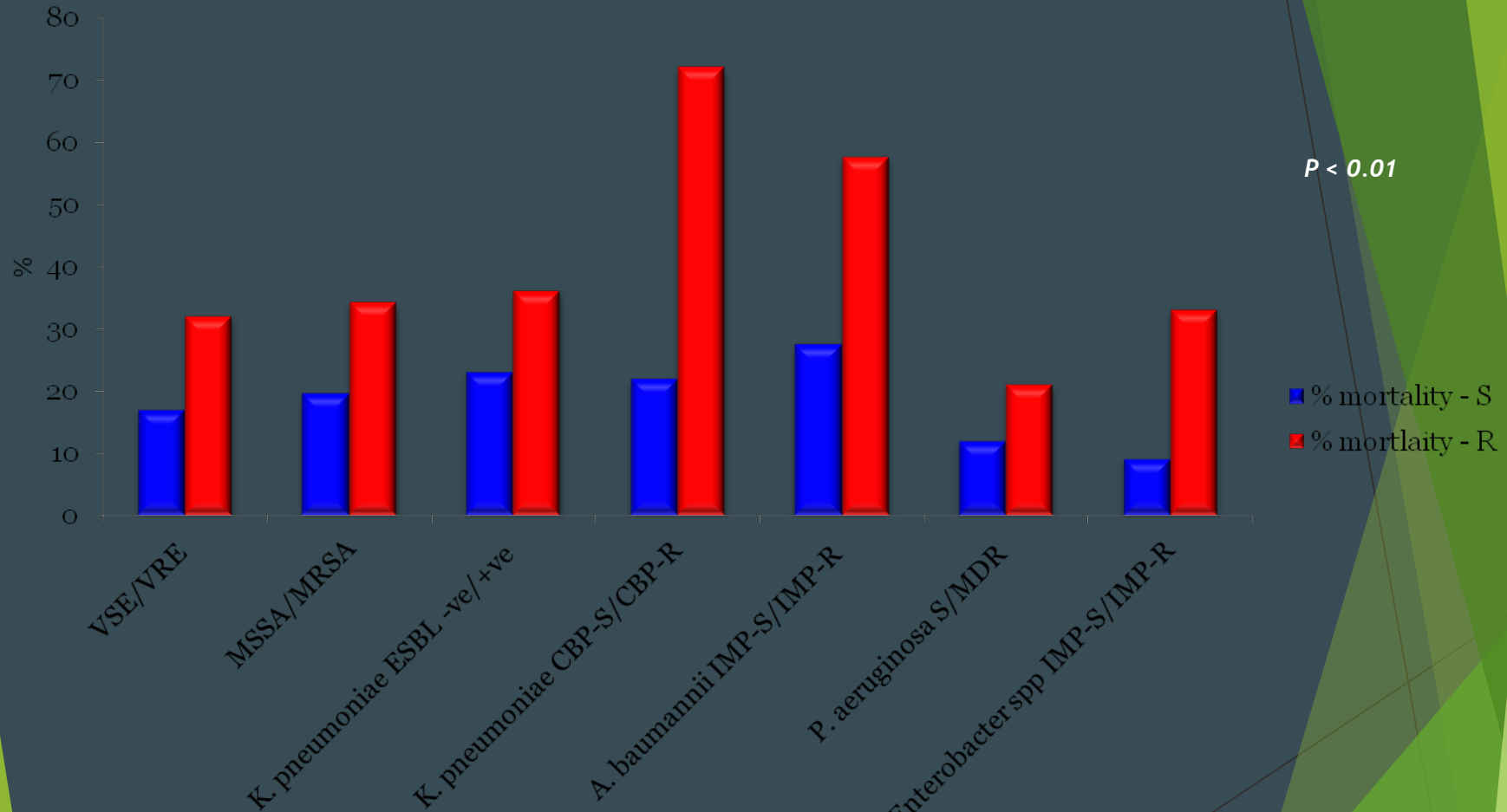
Super Bugs: New Bugs, Old Bugs with new Resistance



- *Neisseria gonorrhoeae* MDR
- *Stenotrophomonas maltophilia*
- *Clostridium difficile*
- CRE, PRSP, MDRSP
- URGENT/ SERIOUS/ CONCERNING

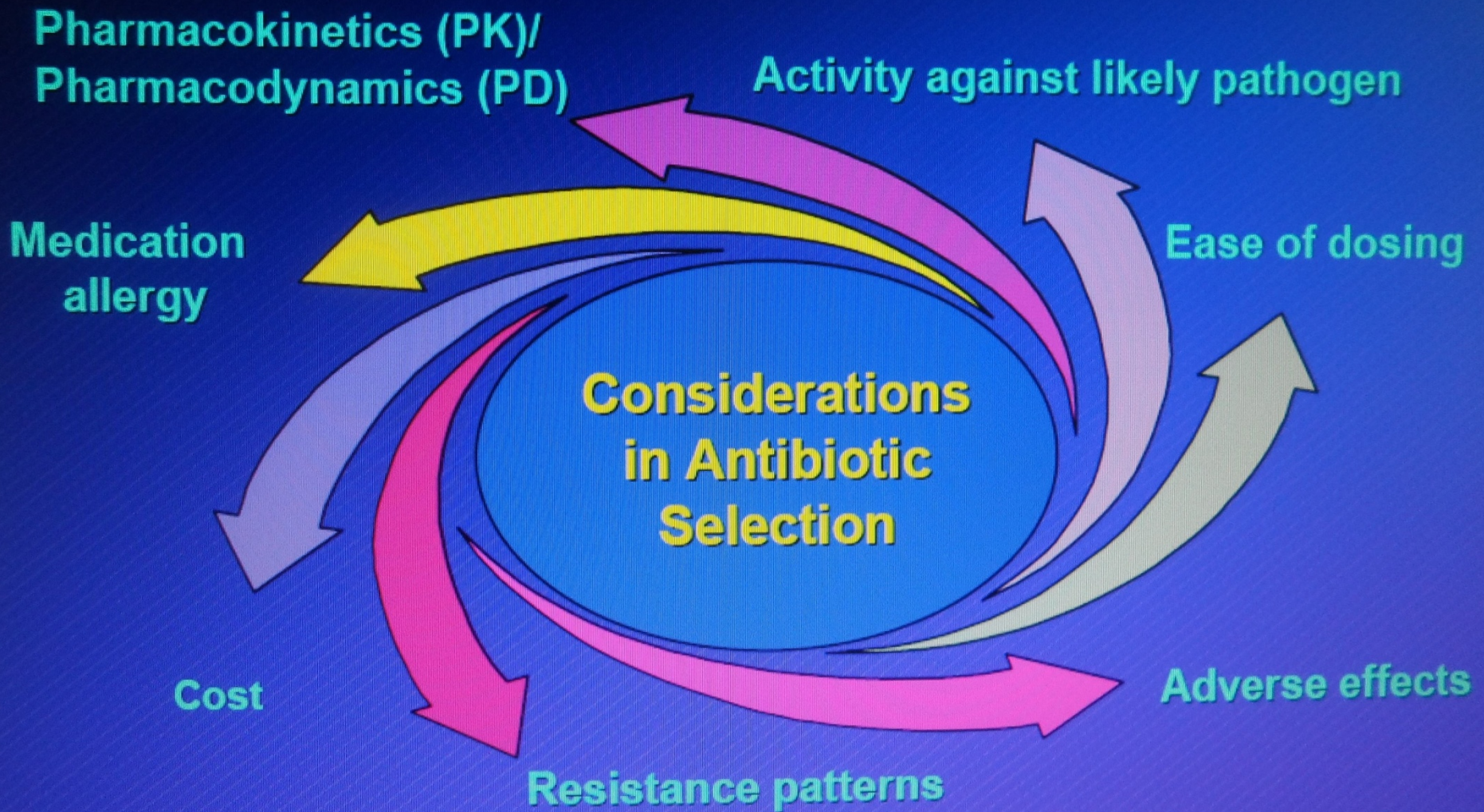
ESKAPE Pathogens

Poor Clinical Outcomes & Increased Mortality



1. Butler et al. *Infect Control Hosp Epidemiol.* 2010; 31:28–35.
2. Shurland et al. *Infect Control Hosp Epidemiol.* 2007;28:273–79.
3. Szilágyi et al. *Acta Microbiol Immunol Hung.* 2009;56:251–62.
4. Borer A, et al. *Infect Control Hosp Epidemiol.* 2009;30:972–6.
5. Kwon K. et al. *J Antimicrob Chemother.* 2007;59:525–530.
6. Aloush V. et al. *Antimicrob Agents Chemother.* 2006;50: 43–48.
7. Marchaim D. et al. *Antimicrob Agents Chemother.* 2008; 52:1413–1418.

Considerations in Antibiotic Selection



Gwaltney et al. *Ann Otol Rhinol Laryngol Suppl* 1995;167:22.
Sinus and Allergy Health Partnership. *Otolaryngol Head Neck Surg* 2000;123:S1.

Other Factors Influencing the Doctor

Many RTI's caused by viruses or bacteria: hard to differentiate

(Non) Availability of Drugs

Unaware of impact on resistance



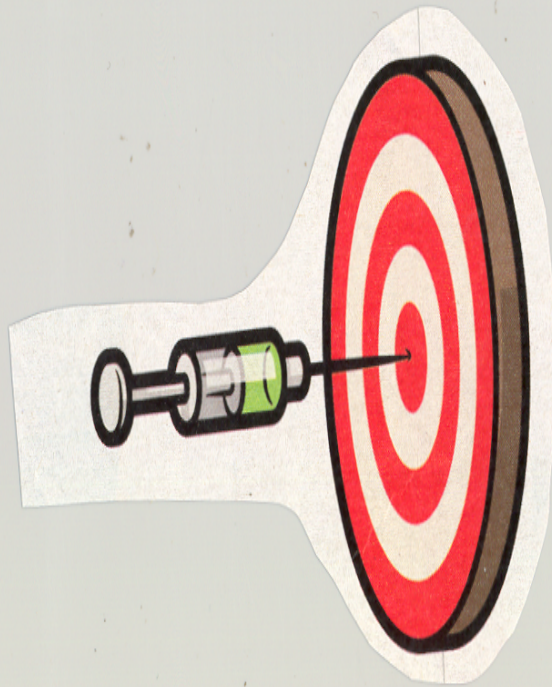
Pts. & parents' demands

Habit

No local guidelines

Pharmaceutical reps: (35% of profits on marketing)

Basic Considerations For Prescribing Antibiotics



- 1) Know the likely pathogens
- 2) Treat bacterial infections only!
- 3) Know LOCAL resistance patterns
- 4) Simplest, most effective AB that will work
- 5) Correct dose
- 6) Duration
- 7) Best route: po switch 3hr
IV: Mem; GM: od
- 8) Side effects

Role of Pharmacist:

- ▶ Note unusual prescriptions: dose, choice, duration etc
- ▶ Monitor prescribing practices where unusual
- ▶ Monitor (surveillance) & Feedback
- ▶ Formulary restrictions
- ▶ De-escalation
- ▶ IV-PO switch
- ▶ Cost of antibiotics
- ▶ Give instructions eg before or after meal, no alcohol, do not share, discontinue etc??
- ▶ Delayed prescription
- ▶ Viral treatment pad
- ▶ Other

Viral Treatment Pad

Name: _____

Date: _____ / _____ / _____

Diagnosis:

Cold Middle ear fluid (Otitis Media with Effusion, OME)

Cough Viral sore throat

Flu Other: _____

You have been diagnosed with an illness caused by a virus. Antibiotics do not cure viral infections. If given when not needed, antibiotics can be harmful. The treatments prescribed below will help you feel better while your body's own defences are fighting the virus.

General instructions:

Drink extra water and juice.

Use a cool mist vaporizer or saline nasal spray to relieve congestion.

For sore throats, use ice chips or sore throat spray; lozenges for older children and adults.

Specific medicines:

Fever or aches:

Ear pain:

Use medicines according to the package instructions or as directed by your healthcare provider. Stop the medication when the symptoms get better.

Follow up:

If not improved in _____ days, if new symptoms occur, or if you have other concerns, please call or return to the office for a recheck.

Other: _____

Signed: _____

For More Information call 1-800-CDC-INFO or visit www.cdc

Respiratory Tract Infections

- ▶ Not enough POC tests.
- ▶ RTI's acct for 10% of w/w burden of mortality & morbidity
- ▶ Acct for 75% of antibiotic usage though most are viral

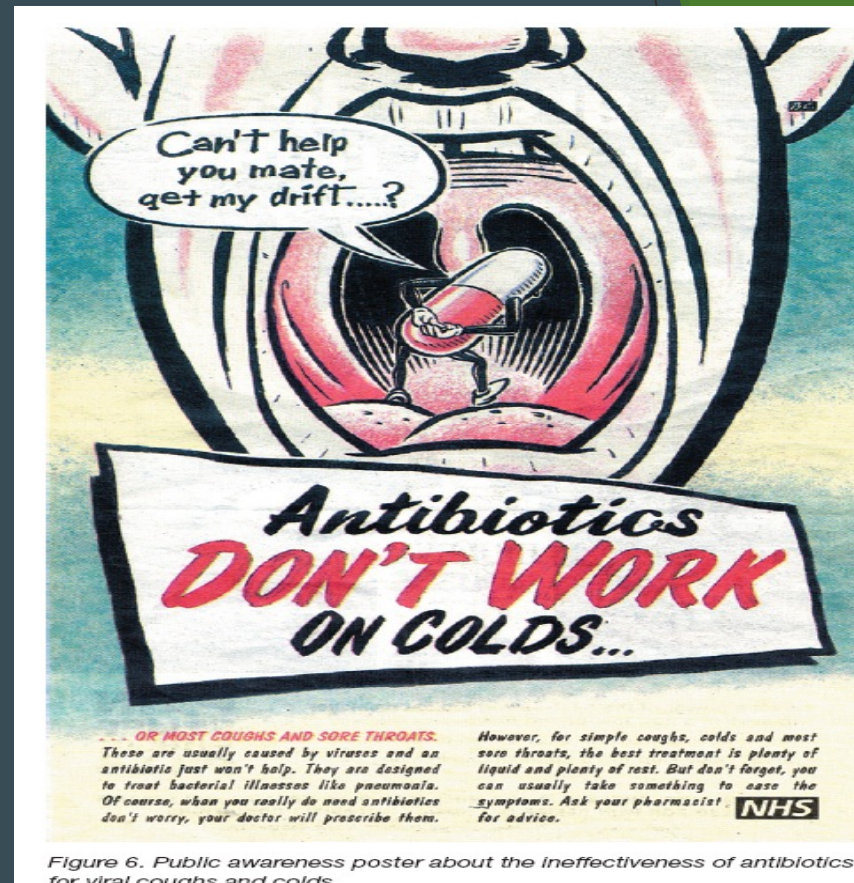


Figure 6. Public awareness poster about the ineffectiveness of antibiotics for viral coughs and colds.

Common Bacteria: R/Tract

- ◆ *Group A Streptococcus*: Sens to Pen
- ◆ *Streptococcus pneumoniae*: PRSP: 3.2% ↑
- ◆ *Haemophilus influenzae*: ↑ing B/L production
- ◆ *Moraxella catarrhalis*: ↑ing B/L production
- ◆ *Staph aureus*: 3.2% MRSA
- ◆ *Enterobacteriaceae*: *E coli*, *K pneumo*
- ◆ Others

Know the organisms implicated in specific infections



Fig. 78 Acute follicular tonsillitis.

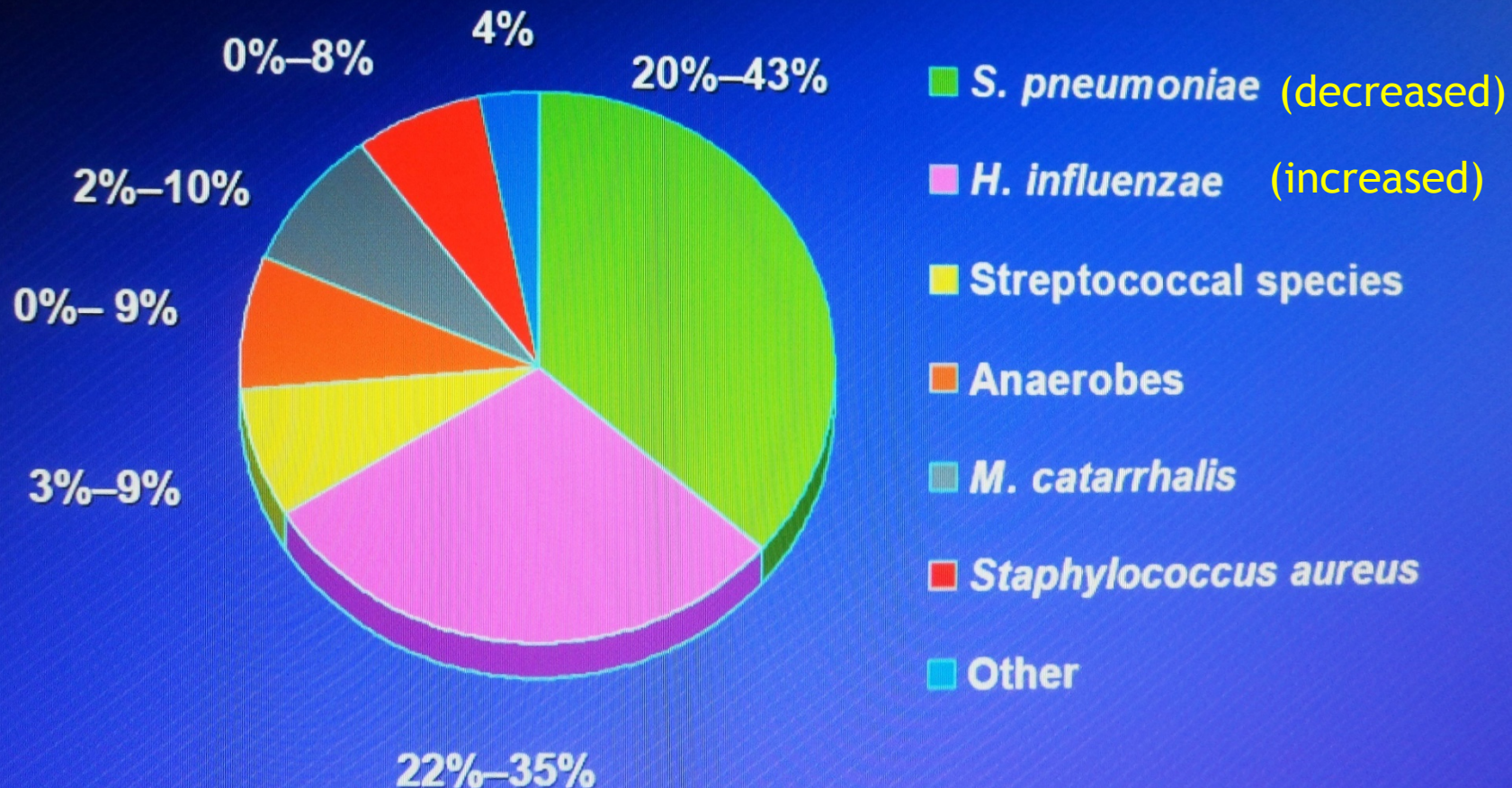
Tonsillo-pharyngitis : Organisms

- ▶ Most common cause is viral: 50-80%!!
- ▶ Most important cause: Gp A Strep: uniformly sens to pen!
- ▶ Accounts for 5-15% of acute pharyngitis in adults
- ▶ 50% pts improve by day 3; 85% day 5: without antibiotics
- ▶ Caution in areas with high GABHS & complications ARF eg Jamaica

Acute Bacterial Rhinosinusitis

- ▶ Bacteria implicated in 2-10%; virus in 90-98%!
- ▶ 70% pts improve without antibiotics
- ▶ 81% adults will get AB's
- ▶ 5th leading indication of antibiotic prescription by primary care physician
- ▶ Annual cost of sinusitis in USA: \$5.8b

Microbiology of ABRS (Adults)



Sinus and Allergy Health Partnership. *Otolaryngol Head Neck Surg* 2000;123:S1.

Acute Bacterial Rhinosinusitis

IDSA 2013 guidelines:

- ▶ Acute URI with either nasal discharge &/or daytime cough for > 10 dys or
- ▶ Severe onset of fever (>39C), purulent nasal discharge and other R/T symptoms for > 3 dys or
- ▶ URI with worsening symptoms after initial improvement
- ▶ **Clinicians may observe children with persistent infection lasting >10 dys for another 3 dys before AB's but give Ab's to pts with worsening symptoms**

ABRS: Antibiotics contd

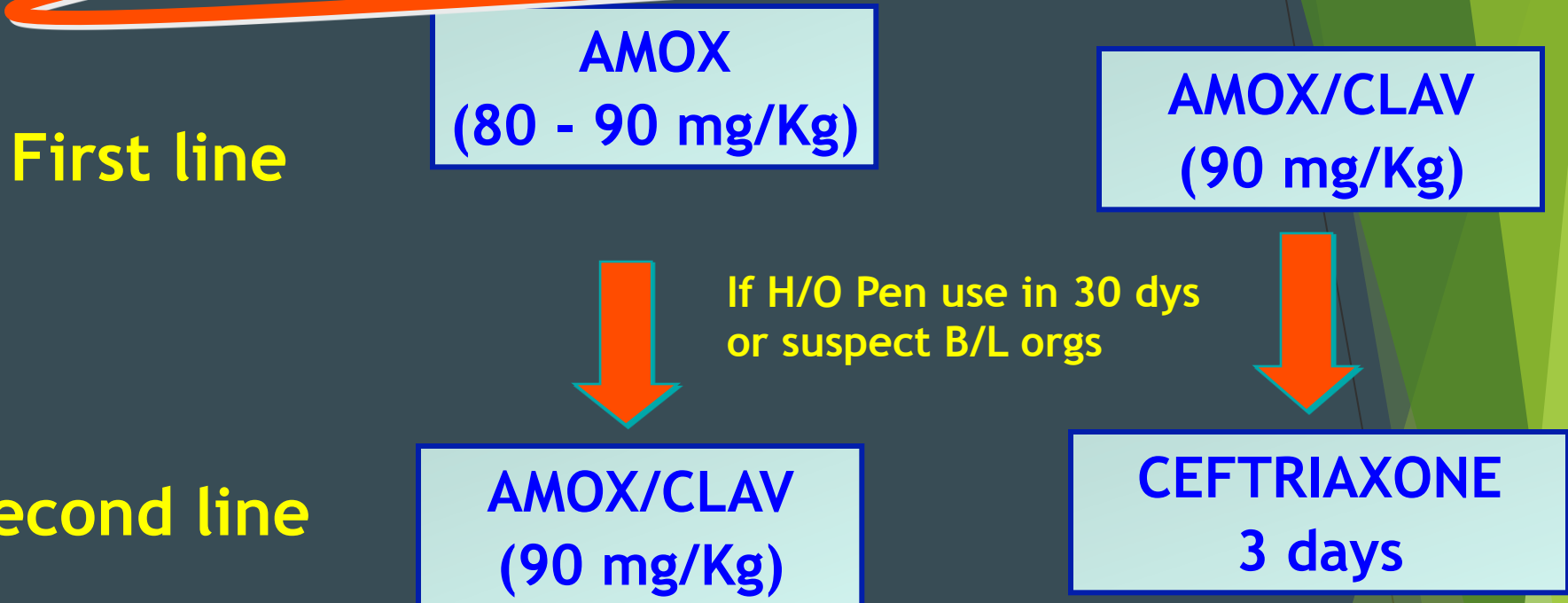
- ▶ Betalactam eg Amox-clav
- ▶ Macrolides not recommended empirically: PRSP
- ▶ SXT: not recommended emp: both PRSP & H. infl
- ▶ Doxy may be alternative to AMC in adults
- ▶ Do not use 2nd & 3rd gen oral ceph alone: ?CRSP
- ▶ Reserve FQ's for : no response to 1st line
H/O pen allergy; Risk of PRSP

Acute Otitis Media

Pathogens:

- ▶ *Streptococcus pneumoniae*
- ▶ *Haemophilus influenzae*
- ▶ *Moraxella catarrhalis* (100% B/lact +ve)
- ▶ Group A *Streptococcus* (<5%)

2004 AAP Guidelines for the Rx of AOM:



Amox-clav: Best bact. eradication rate cf all other licensed oral drugs

Ceftriaxone: if po not possible or if no response, 3 days preferred

▪ **SXT + E combination:** not good : R

If treatment failure: use CC +/- AB for H infl & M cat eg Cefuroxime (CXM)

MDRSP: Levofloxacin or Linezolid

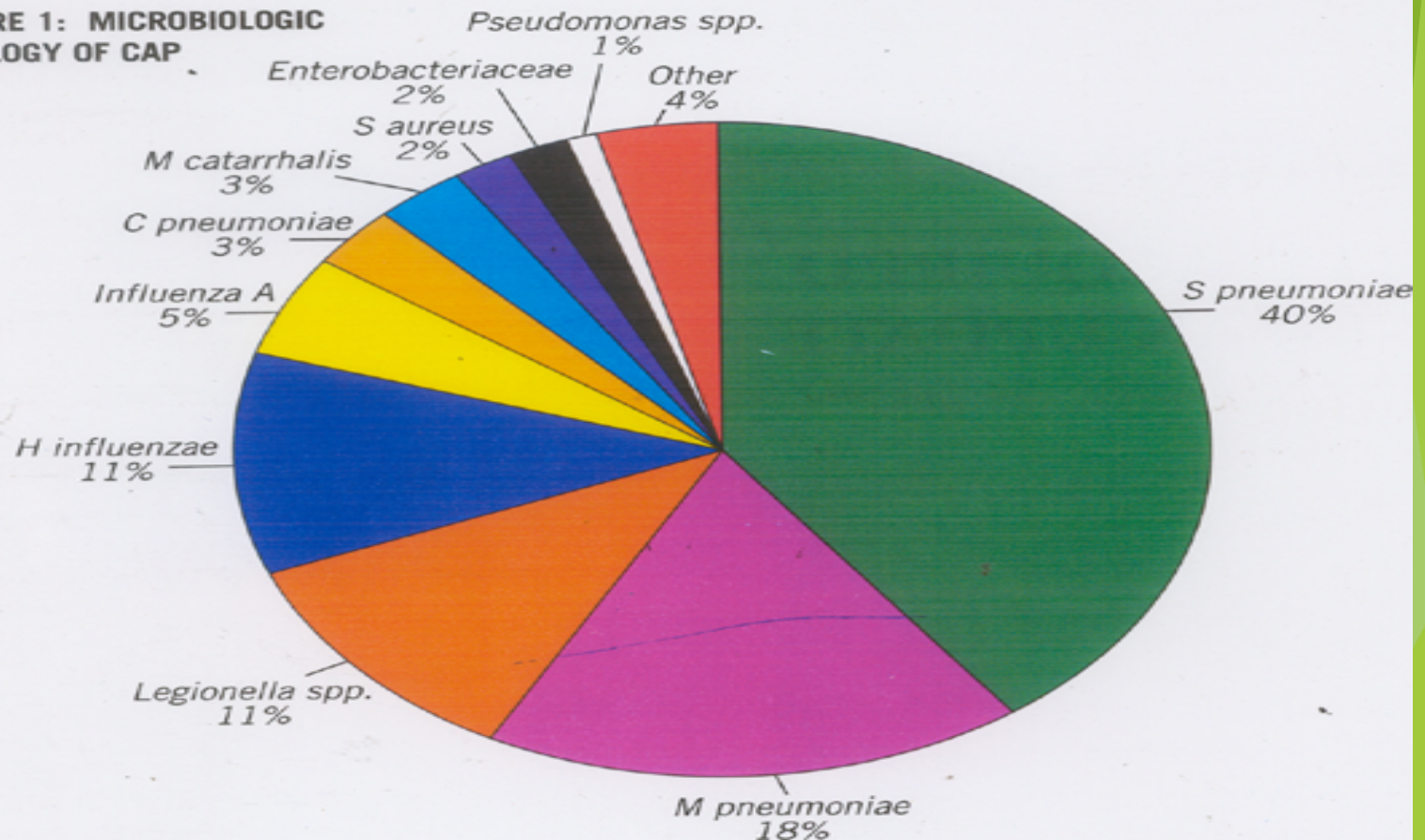
Not approved by FDA yet

Community Acquired Pneumonia

ETIOLOGY OF COMMUNITY-ACQUIRED PNEUMONIA

The etiology of CAP based on microbiologic diagnosis is shown in Figure 1. These data were based on the 71% of cases in the study with an etiology documented by sputum culture.⁴

FIGURE 1: MICROBIOLOGIC ETIOLOGY OF CAP



Treatment of CAP

- ▶ Treat with B/L + macrolide / doxy
- ▶ If on Wd: B/L + macrolide. May change type B/L
- ▶ IV or PO depending on severity
- ▶ Risk factors for MDRSP: B/L + Resp FQ's
- ▶ ICU: Resp FQ +/- Betalactam
- ▶ Refine treatment after C/S report

Antimicrobial Stewardship Strategies

- ▶ Cycling
- ▶ Restriction of antibiotic use: counter signature
- ▶ De-escalate
- ▶ Prolonged IV admin over 3 hrs of MEM, TZP
- ▶ Reduce use of combination?
- ▶ Amino: od vs tid IV
- ▶ IV to PO Switch

Switch Therapy

- Useful in treating: RTI, UTI, SSI, Bone & joint...
- ▶ Oral agents less expensive (hidden costs: lines, nurses)
- ▶ Earlier discharge possible
- ▶ Increased pt mobility
- ▶ **Exclude:** Infective endo, meningitis, line sepsis, *S.aureus* or *Enterococcus* bacteremia
- Unreliable oral response eg continuous NG suction, ileus, protracted vomiting, diarrhea
- The oral agent does NOT have to be from the same class as the IV drug but should be culture directed.

UNIVERSITY HOSPITAL OF THE WEST INDIES

Antibiotic Switch Therapy: IV to PO Conversion Order Form

DRAFT

Timely conversion from intravenous to oral therapy ('switch therapy') may be used for some infections. The Drug and Therapeutics Committee has approved that patients who meet the required criteria should be considered for oral therapy.

Patients eligible if:

- Infection resolving
- Tolerating food or drugs orally or via NG tube
- Functioning gastrointestinal tract
- None of the exclusion criteria below

Exclusion Criteria: Patients who should NOT be considered for 'switch therapy':

- Specific diagnoses such as: line sepsis, endocarditis, meningitis and bacteremia caused by *Staphylococcus aureus* or *Enterococcus spp.*
 - B) Uncertain response to oral medication as seen with : Persistent nausea /vomiting/ diarrhoea/ Ileus / Active GI bleed / Loss of consciousness / Malabsorption / Continuous NG suctioning

Restart intravenous therapy if patient does not continue to improve on oral therapy

Name of patient: _____ Reg. Number: _____

DOB: _____ Weight: _____ Ward: _____

Diagnosis: _____

Current antibiotic therapy: _____

Pharmacist recommends: _____

Start date: _____ End Date: _____

Approved by: _____

Doctor's Signature: _____

Bioavailability

DRUG	Oral Absorption	Dosage
Amoxicillin	89%	250/500mg po
Cloxacillin	50-75%	500mg po
Ciprofloxacin	70-80%	500mg po/ 400mg IV
Levofloxacin	98%	500mg po/IV
Azithromycin	37%	250/500mg po, 500mg IV
Tetracycline	60-80%	250/500 PO, 500mg IV
Linezolid	100%	600mg od/bd po/bd IV
Co-trimoxazole	85-90%	160/800 po/IV
Metronidazole	80-90%	250-500 po/500IV
Clindamycin	90%	150mg po, tid IV
Cefuroxime	37-50%	250/500 mg
Penicillin V	60-73%	500mg po

Antimicrobial Cost Awareness

Antibiotic	Route	Bioavail	Adult dose	Cost/day (oral) \$JA	Cost/day (parenteral) \$JA
Gentamycin	I.M./I.V.		80 mg TID /240 mg od	N/A	\$238.50
Amikacin	I.M./I.V.		500 mg TID	N/A	\$3,628.10
Ciprofloxacin	P.O./I.V.	70-80%	500 mg BID /400mg BID	\$115.20	\$11,340.00
Levofloxacin	P.O./I.V.	98%	500 mg q24h	\$376.90	\$4,421.25
Moxifloxacin	P.O./I.V.		400 mg q24h	\$355.55	\$3510.00
Amoxi-clav	P.O./I.V.		1gm q12h/1.2 gm q8h	\$96.45	\$1,188.00
Amoxicillin	P.O./I.V.	89%	500 MG TID	\$67.95	\$351.00
Cloxacillin	P.O./I.V.	50-75%	500 MG QID	\$69.94	\$318.00
Pip/Tazobactam	I.V.		4.5 GM Q6H	N/A	\$11,340.00
Ertapenem					\$4,000.00
Cefazolin	PROPHYLAXIS?		1gm tid		J\$300.00
Cefuroxime	P.O./I.V.	37-50%	500MG BID/1.5 MG Q8H	\$292.5	\$1,944.00
Cetrixone	I.M./I.V.		1GM Q12H	N/A	\$2,280.00
Ceftazidime	I.M./I.V.		1 GM Q8H	N/A	\$2,936.25
Imipenem	I.M./I.V.		500 MG Q8H	N/A	\$3347.04
Meronem	I.V.		1GM Q8H	N/A	\$1,1776.50
Linezolid	I.V.	100%	600MG Q12H	\$11,769.44	\$12,887.90
Vancomycin	I.V.		1GM Q8H	N/A	\$4,500.00
Azithromycin	P.O.	37%	500 MG OD	\$71.50	N/A
Clarithromycin	P.O.		500 MG Q12H	\$291.50	N/A
Clindamycin	P.O./I.V.	90%	300 MG Q6H	\$218.40	\$1,836.00
Co-trimoxazole	P.O./I.V.	85-90%	960 MG BID	\$45.50	\$1,051.92
Nitrofurantoin	P.O.		100 MG BID	\$10.50	N/A

Post Antibiotic Era?

MSU: October 2013 Kingston, Jamaica

- ▶ Female patient: 40's
- ▶ Significant growth of *Burkholderia cepacia*
- ▶ Sensitive to: ?? Colistin
- ▶ Resistant to: Ampicillin, Amoxicillin-clavulanic acid, gentamicin, amikacin, tobramycin, cotrimoxazole, furadantin, piperacillin-tazobactam, meropenem, nalidixic acid, norfloxacin, ciprofloxacin, levofloxacin, cefuroxime, ceftazidime, ceftriaxone, cefepime, ceftriaxone-sulbactam, tigecycline, rifampicin, minocycline.

So..... we are in trouble.....

- ▶ There currently exists a significant and growing problem of antibiotic resistance
- ▶ The antibiotic pipeline is drying up and is unable to deal with this problem
- ▶ Resistance from the community is also increasing!
- ▶ We need all hands on deck, **especially YOU**, the Pharmacists, to help roll back the tide of antibiotic resistance

The development of new antibiotics without having mechanisms to ensure their appropriate use is much like supplying your alcoholic patients with a finer brandy.”

Dennis Maki, 1998



THE END

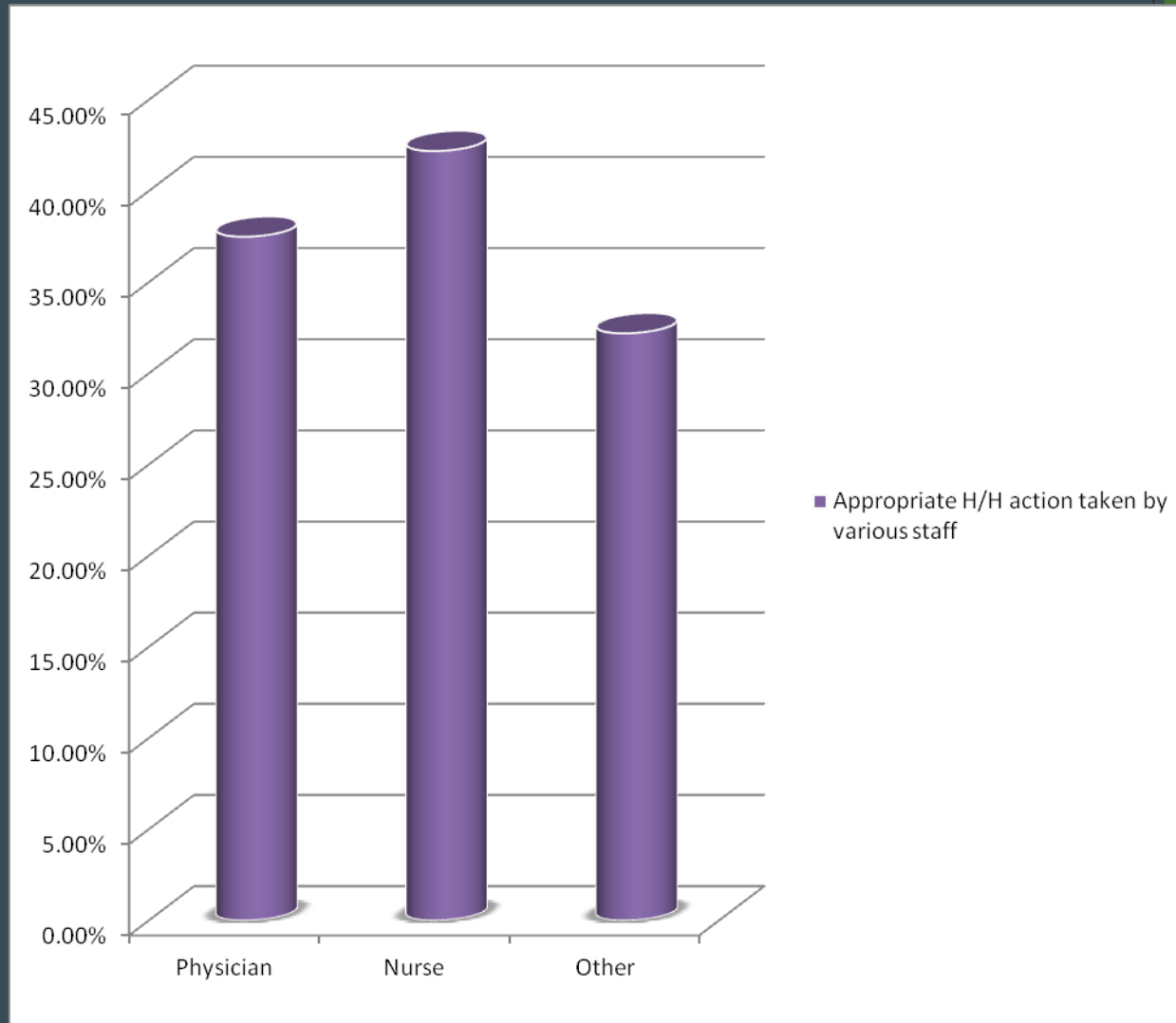
Mechanics of Antibiotic Stewardship

- 1) Establish a Multidisciplinary team : Physician, pharmacist, microbiologist, ICP
- 2) Establish necessary infrastructure to implement antimicrobial stewardship program (ASP)
- 3) Establish and implement computer-based surveillance
- 4) Identify both process measures and outcome measures to track to determine impact of interventions
- 5) Identify antimicrobial intervention strategies and prioritize implementation of strategies : i) audit & feedback ii) de-escalation iii) IV-PO switch iv) formulary restriction v) cycling vi) Amino:od vii) prolonged infusion
- 6) Educate staff:

Newer Antibiotics

- ▶ **Streptogramins** eg quinopristin/ dalfopristin (Synercid) (**Gm pos** vs VRE & MRSA)
- **Oxazolidinones** eg **Linezolid (Zyvox)** (**Gm pos** vs VRE, MRSA, GISA)
- **Lipopeptide** eg Daptomycin: **Gm pos** vs MRSA, VRE, PRSP, GISA
- **Antimetabolite**: Iclaprim (**Gm pos** & neg)
- ▶ **New Glycopeptides** eg Dalbavancin, Oritavancin, Televancin (**Gm pos**)
- ▶ **Glycylcycline** eg **Tigecycline: conditions apply**: MRSA, PRSP, VRE, (ESBL, **Gm pos** & Neg MRGNB}
- ▶ **5th gen Cephalosporins** eg Ceftobiprole, ceftaroline (**Gm pos** & neg)
- ▶ **New Quinolones**: Garenoxacin, sitafloxacin (**Gm pos** & neg)
- ▶ **New carbapenems**

Hand Hygiene at the UHWI (2010)



• If senior staff members set an example, it will be much more difficult for juniors not to follow!!

Antibiotic Treatment (AAP; AAFP)

OM 1st line treatment:

- ▶ High dose Amoxicillin: good vs common paths.

Gives middle ear fluid levels > MIC even for pen intermed. Good taste/cost/ safe.

BUT

If H/O Amoxicillin in 30 dys or suspect B/lactamase producing H infl. or Morax catarrh., use high dose AMC bd

- ▶ Alternatives to Amoxicillin:

Cefuroxime bd: Active vs 70-80% *S pneumo* vs 80-90% c Am.

Ceftriaxone: Active vs 98% H infl vs 58% with Amox

OM: More AB's contd.

- ▶ Macrolides not good vs Strep pneum or H infl. (R)
- ▶ CC not active vs Haem infl. Good vs PRSP but not MDRSP. Taste enhanced
- ▶ Duration: 5-10 dys depending on age & severity

Treatment of CAP

- ▶ CURB 65: Decide to treat at home or refer
- ▶ Treat with B/L + macrolide /doxy
- ▶ Macrolide: Azithro: 500mg bd x3/7 or 500mg stat then 250mg bd x4/7
- ▶ Curb 65 : Decide admit or home; Wd or ICU
- ▶ If on Wd: B/L + macrolide. May change type B/L
- ▶ IV or PO depending on severity
- ▶ Check risk factors for MDRSP: B/L + Resp FQ's
- ▶ ICU: Resp FQ +/-Refine treatment with C/S report

Outpatient Treatment

Previously well (no co-morbid factors)	Comorbid +/- antibiotic use	Macrolide resist S pneumo
Amoxicillin Amox-claualanic +/- macrolide OR Doxycycline	Newer macrolide OR Doxycycline OR	Resp fluoroquin OR <u>Newer drugs</u>
OR Macrolide (if no H/O DRSP) Clarithro 500mg bd	Beta-lactam (amox 3g, Aug 2g bd, cefurox, ceftri 2gm od) + macrolide / doxy	
	OR Fluorquinolone	

CDC Guidelines: Centor Criteria/ Strep Score

Screen pts for:

- 1) History of fever 2) Tonsillar exudates
- 3) Cervical LN 4) Absence of cough

- a) Do **NOT** treat pts. with none or only one
- b) Test pts with 2 or more criteria using RAT. Treat only positives OR
- c) Test pts with 2 or 3 criteria. Treat RAT +ve and treat pts with 4 criteria OR
- d) No RAT. Treat pts with 3 or 4 criteria