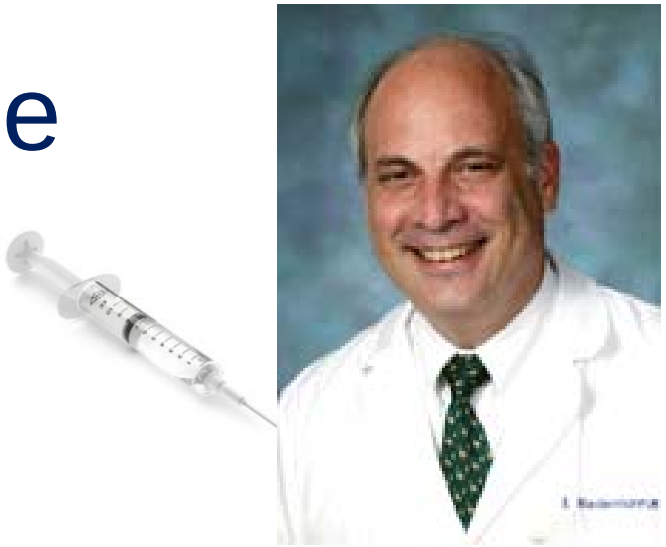
Antibiotic Roulette



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Attending in Infectious Diseases
Professor of Pediatrics

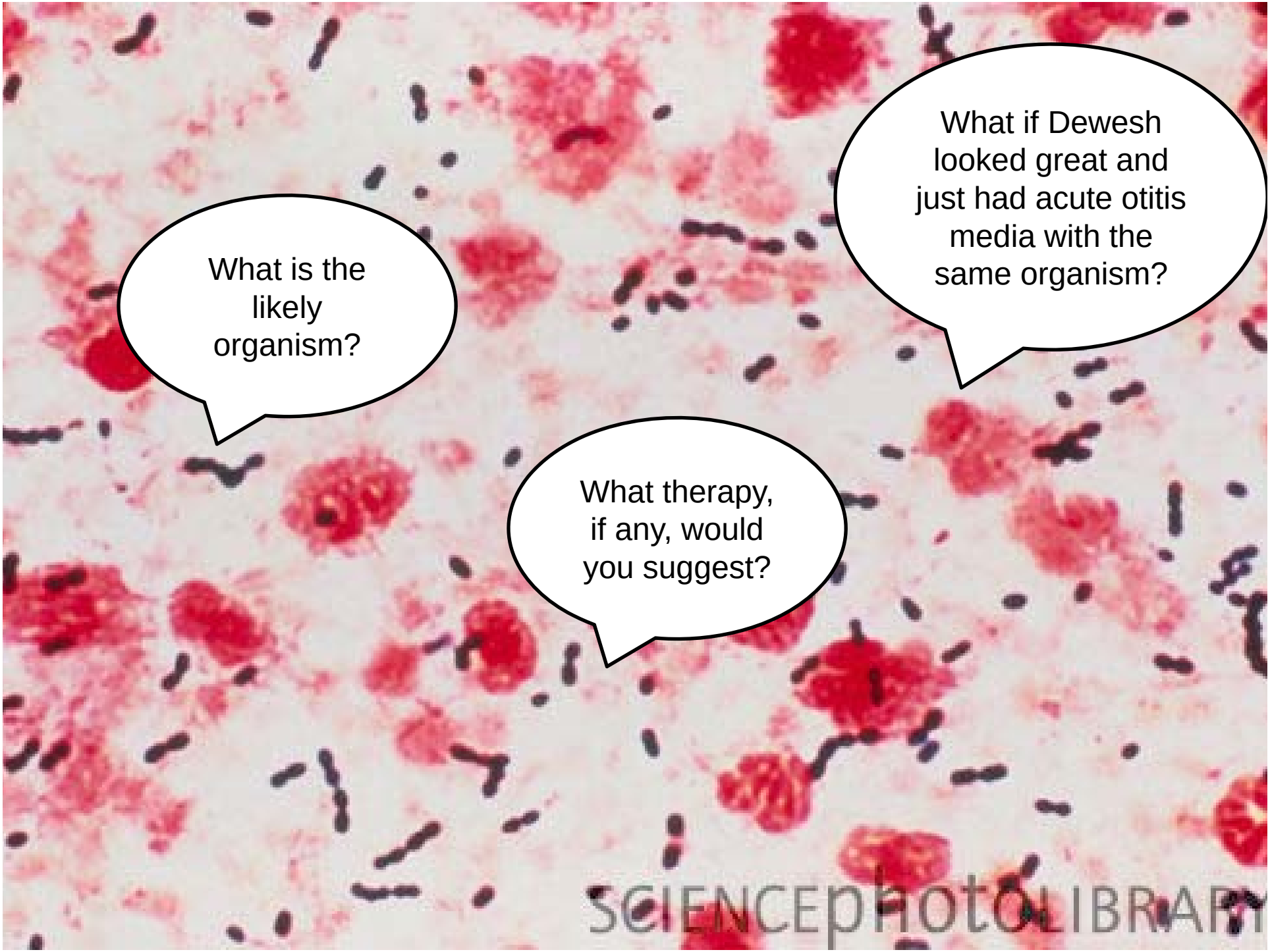
Pediatric Resident Noon Conference
July 20, 2015

Session Objectives

- Recognize that only 2 common bacteria drive empiric antibiotic choices for pediatric CNS, respiratory, and skin and skin structure infections.
- List pediatric-specific issues that impact on antibiotic choices.
- Recognize opportunities to avoid spread of bacterial resistance

Case #1

Dewesh A. is a 6 month old boy with fever and irritability for 1 day. On physical exam, he has a temperature of 39.5, is very irritable, and has nuchal rigidity. CSF exam shows WBC 2200 with 95% segs, glucose 24, protein 109, and Gram stain as shown.


What if Dewesh looked great and just had acute otitis media with the same organism?
What is the likely organism?
What therapy, if any, would you suggest?
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Drug Resistant *Streptococcus pneumoniae* CNMC 2012 (n=50)

	Penicillin (non/CSF)	**Cefotaxime (non/CSF)**
Susceptible	86%/53%	88%/80%
Intermediate	12%/0%	12%/8%
Resistant	2%/47%	0%/12%

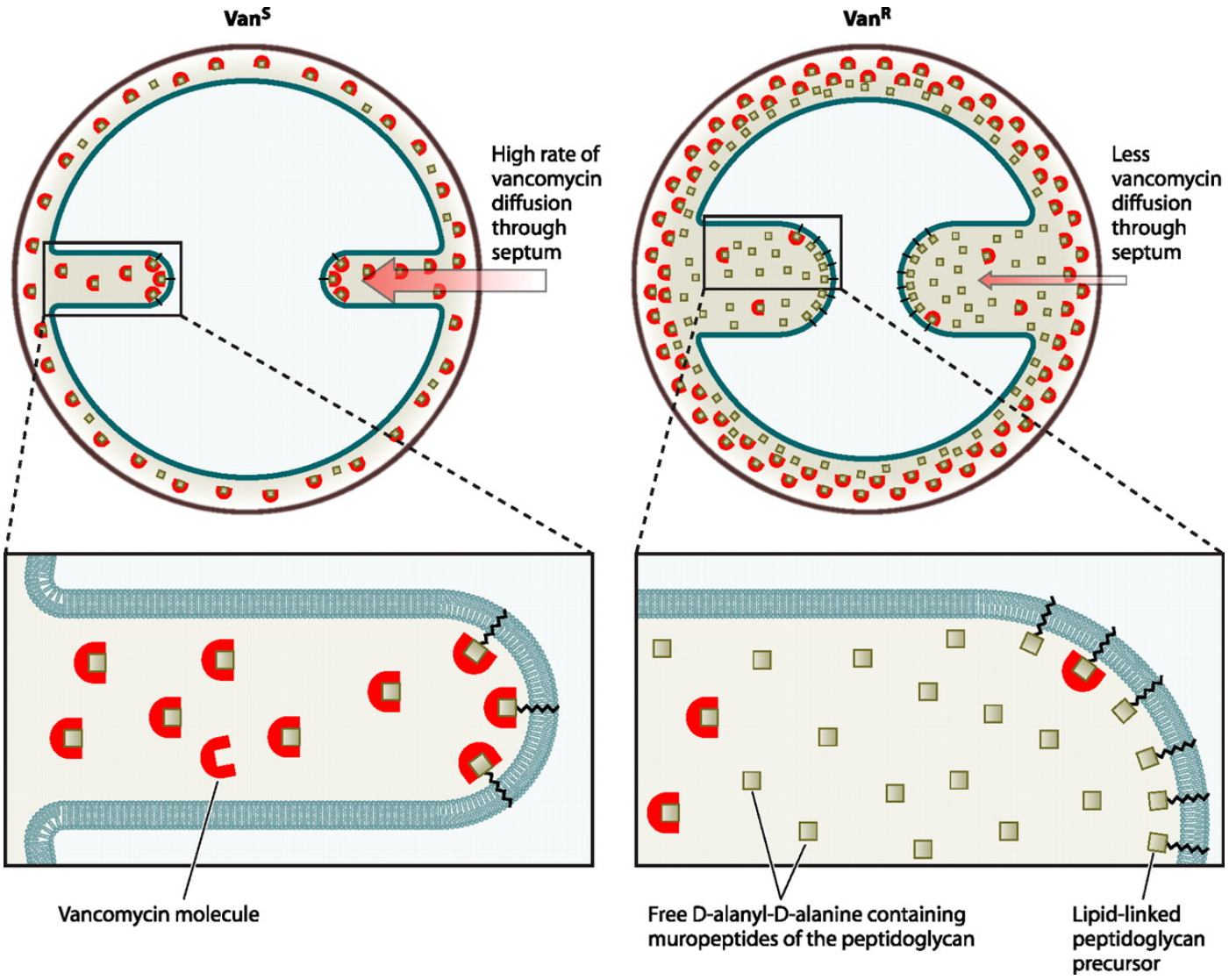
Case #2

Janet B. is a 7 year old girl who complains of fever and a painful red rash on her leg, surrounding an area she scraped on a tennis court 2 days ago. Her temperature is 38.7 C, and the right lower leg shows a 5X7 cm area that is red, warm, mildly raised, and tender to palpation. What would you do?

Drug Resistant *Staphylococcus aureus* CNMC 2014 (% susceptible)

	MSSA (n=428)	MRSA (n=282)
Penicillin	17	0
Amox/clav	100	0
Cefazolin	100	0
Oxacillin	100	0
Clindamycin	76	79
Vancomycin	100	100
Linezolid	99	100
TMP/SXT	99	99

What Do You Know About Vancomycin Creep?



Cicely W. is a 12 yo girl with a 4 day history of fever, nausea, emesis, and abdominal pain that begin around the umbilicus and now is in her right lower quadrant. Last night she felt better briefly, but now has return of pain and higher fever. On exam, temperature is 39.8 C and she has moderate tenderness in the right lower quadrant with rebound tenderness. Abdominal sonogram shows a likely periappendiceal abscess. How would you manage her?

Anaerobic Antibiotics

Good	Better	Best
Penicillin	Clindamycin	Meropenem (Ertapenem)
Ampicillin	Cefoxitin	Ampicillin/ sulbactam
	Metronidazole	Ticarcillin/ clavulanate
		Amoxicillin/ clavulanate

Antibiotic Pitfalls in Peds

- Tetracyclines
- Fluoroquinolones
- Ceftriaxone
- Erythromycin

Azithromycin Has a Long Half-Life

Antibiotic	Pharmacokinetic Parameter Estimate			
	Dose (mg/kg)	C_{max} (mg/l)	T_{max} (h)	$t_{½}$ (h)
Macrolides/azilides				
Erythromycin				
Estolate	10	1.6	2.7	4.1
Ethylsuccinate	10	1.1	1.8	2.3
Azithromycin	12	0.34	2.4	50
Clarithromycin	7.5	3.6	3.1	~2.6†
Amoxicillin/clavulanate	6.6/1.7	2.8/0.8	1/1	1.3/1.1
	13.3/3.3	4.9/1.5	1/1	1.5/1.2
	20/5	7.2/2	1/1.5	1.4/1
Cephalosporins				
Cefaclor	10	13.1	0.5	1
Cefixime	3	1.6	3.7	3.3
Ceftibuten	9	16.2	2.2	2.4
Cefprozil	15	11.2	1.2	1.8

* All studies performed in infants/children using a suspension formulation. Adapted from References 59 and 60.

† Estimated from concentration-time data presented in text.

C_{max}, maximal drug concentration in serum/plasma at time T_{max}; $t_{½}$, elimination half-life; AUC, area under the serum/plasma drug concentration time

Pediatr Infect Dis J 1997; 16:1069

Cephalosporins

The Cephalosporin Generations

1st Gen	2nd Gen	3rd Gen	4th Gen	5th Gen
Cefazolin	Cefuroxime	Cefotaxime	Cefepime	Ceftaroline
Cephalexin	Cefoxitin	Ceftriaxone		
	Cefuroxime axetil	Ceftazidime		
	Cefprozil	*Cefixime*		
		Cefdinir		

Italicized drugs are oral preparations.

Duration of IV Antibiotic Therapy in Bacterial Meningitis (days)

Bug	IDSA	NICE	Minimum Effective in Recent RCTs
GBS	14-21	14	No studies
N. meningitidis	7	7	1-5
H. influenzae b	7	10	4-5
S. pneumoniae	10-14	14	4-5

Try a Patient-Centered Approach to Treatment Duration and IV versus PO

- Cheapest and safest
- Avoid encouraging resistance
- Initial severity
- Response to therapy
- Compliance
- Family preferences
- Harms of alternatives
- Guidelines

J Hosp Med 2014; 9:604

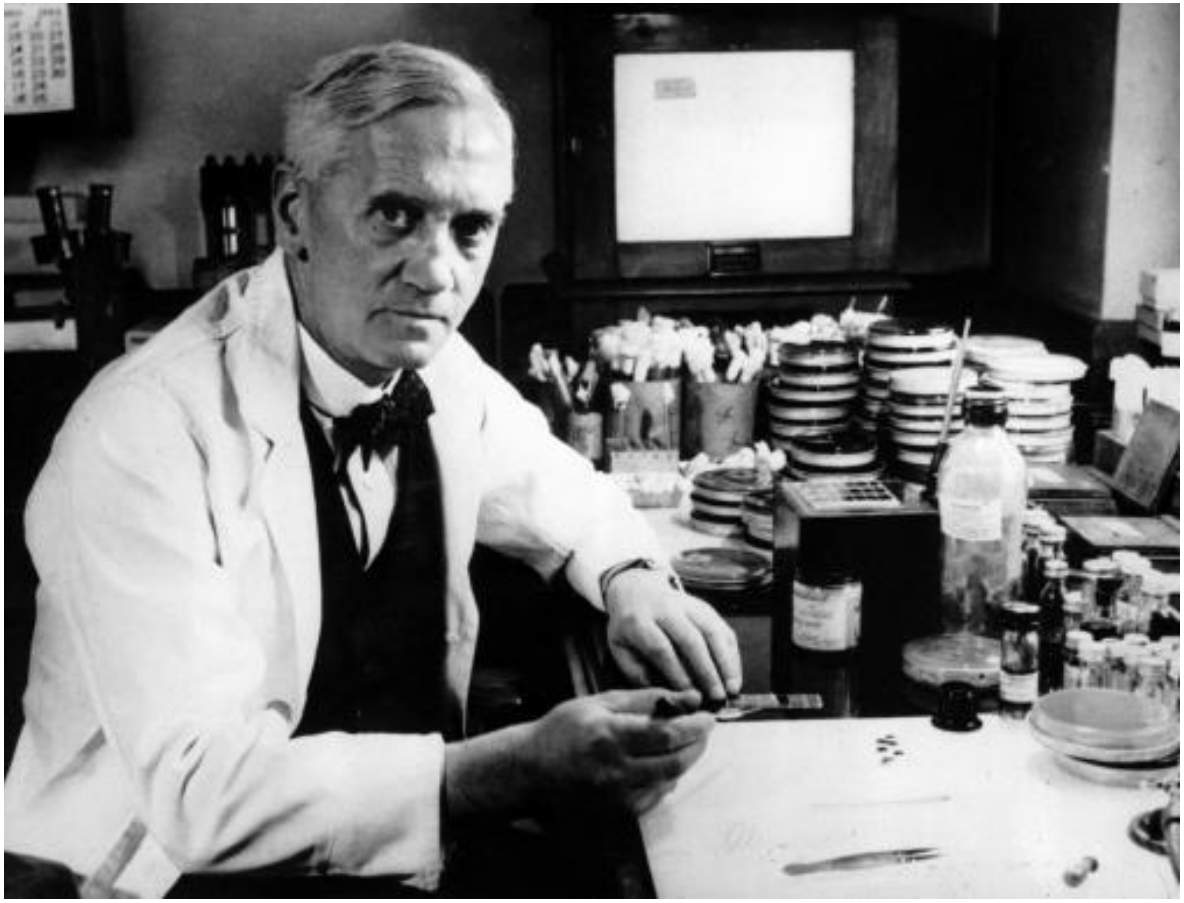
IDSA Guidelines for Pediatrics* http://www.idsociety.org

- Bacterial meningitis (2004)
- Community acquired pneumonia in infants and children (2011)
- Rhinosinusitis (2012)
- Lyme disease (2006)
- MRSA (2011)
- Group A streptococcal pharyngitis (2012)

*These specifically include children, but many more guidelines for adults are on this site.

Bud's (sort of) Laws

1. The bugs don't know.
2. Look it up, don't make it up.
3. Public nose picking is impolite.
4. 2 antibiotics + 1 patient = pimping time.
5. 10 fingers, 10 days.
6. Evidence is a 4-letter word.
7. Avoid the PICU paradox.
8. E + R = O.
9. Remember Eleanor.
10. Remember Aretha.



"... the public will demand [the drug] ...then will begin an era ... of abuses....the thoughtless person playing with penicillin treatment is morally responsible for the death of a man who succumbs to infection with the penicillin-resistant organism."

NY Times 10/26/45, p. 21.