YOUR FRIENDS IN THE LAB:
HOW MICROBIOLOGY CAN HELP IN THE FIGHT AGAINST ANTIMICROBIAL RESISTANCE

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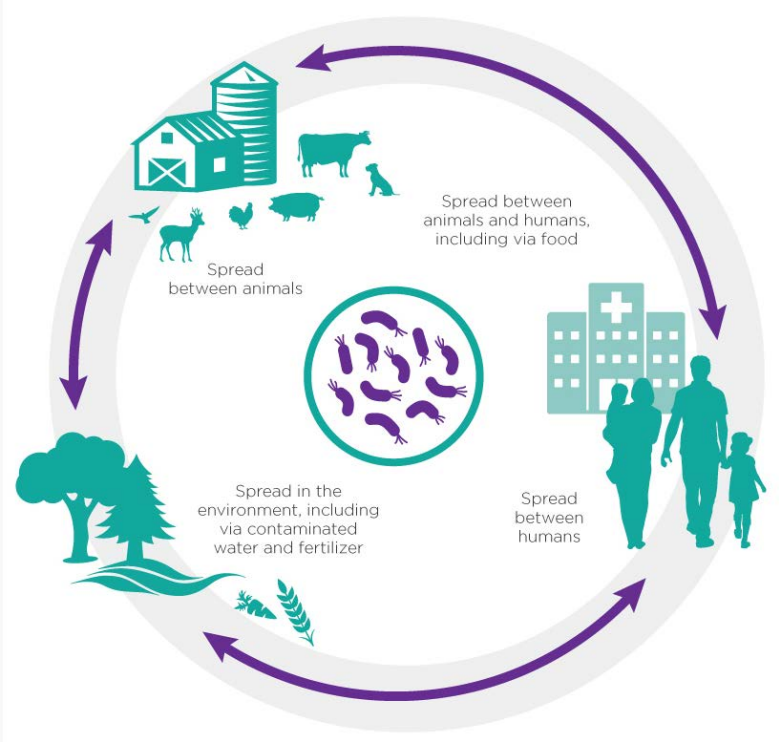
OBJECTIVES

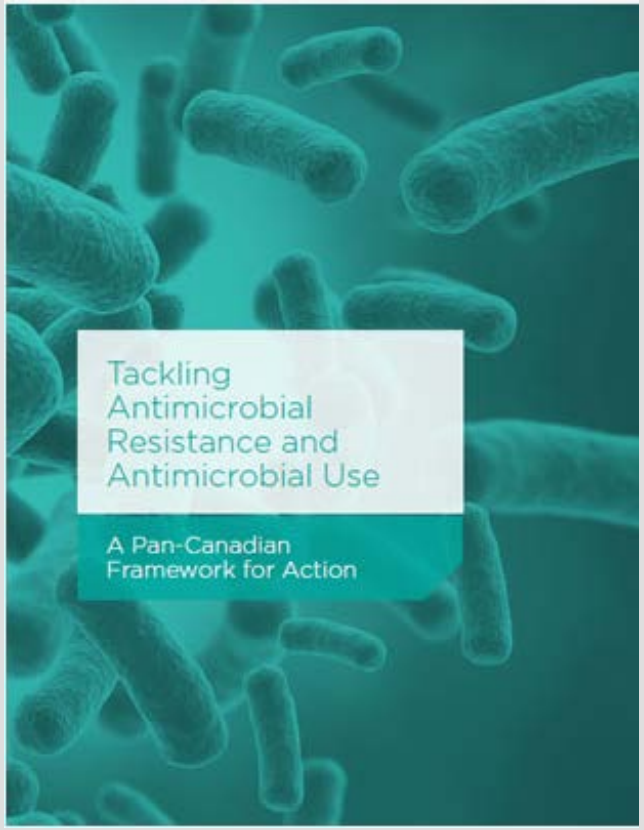
- Beyond Screening: what is the role of microbiology in the fight against antimicrobial resistance?
- Antibiograms & Resistance
- Interventions based in the Lab

DECLARATION OF CONFLICTS OF INTEREST

- none

PAN-CANADIAN FRAMEWORK ON AMR





PAN-CANADIAN FRAMEWORK ON AMR

	Surveillance	Stewardship	Infection Prevention & Control	Innovation
MICROBIOLOGY	Antibiograms Defining Resistance	Communication Selective Reporting New Diagnostics	Detection Outbreaks Transmission	POCT CRISPR Metagenomics

KEY FEATURES OF ANTIBIOGRAMS

- Cumulative Susceptibility Report, for a given population over a specific period of time.
- Report of prior laboratory results, often used to predict future results
- Used for:
  - Empiric treatment decisions
  - Monitoring trends in resistance
  - Targeting antimicrobial stewardship initiatives & monitoring the effectiveness of interventions whose goal is to reduce antimicrobial resistance
  - Analysis of subgroups to determine drivers of resistance in your community

WHAT GOES INTO AN ANTIBIOGRAM?

Last Word	Include only final, verified test results
Trustworthy	Include only species with testing data for at least 30 isolates overall
Relevance	Include only diagnostic (not surveillance) isolates
Duplicity	Eliminate duplicates by including only the first isolate of a species per patient per analysis period irrespective of body site or antimicrobial profile
Include	Include only antimicrobial agents routinely tested, not supplemental agents selectively tested on resistant isolates only
Combine	Reports %S; Intermediate and Resistant interpretations are combined

WHAT CAN INFLUENCE YOUR ANTIBIOGRAM RESULTS?

- Antibiograms will be affected by:
  - Patient population served
  - Lab utilization patterns
  - Lab protocols and policies
  - Temporal outbreaks

PRACTICAL EXAMPLES

MS. D

- 70 yr old woman, living in long term care in Regina
- Diagnosed with lower UTI, urine specimen sent to lab
- Started on Ciprofloxacin

- Next day, lab reports culture + 10^8 *E.coli*
- Susceptibility to follow

- Treatment OK?

Regina Qu'Appelle Health Region ANTIBIOGRAM
All Patients
January 1, 2016 - December 31, 2016

Gram Negative Bacilli in Urine Only – % Susceptible

GRAM-NEGATIVE BACTERIA	# Isolates tested	Penicillin PO	Penicillin IV M	Penicillin IV NM	Ampicillin/Amoxicillin	Amoxicillin-Clavulanic acid	Piperacillin-Tazobactam	Cephalexin[3]	Cefazolin	Cloxacillin	Ceftriaxone	Ceftriaxone IV M	Ceftriaxone IV NM	Ceftazidime	Ertapenem	Meropenem	Clindamycin	Erythromycin	Tetracycline/Doxycycline	Ciprofloxacin	Levofloxacin	Trimethoprim-Sulfamethoxazole	Nitrofurantoin (urine only)	Gentamicin	Tobramycin	Vancomycin
Escherichia coli[1]	4787				56	85	97	55			94				100	100				83		76	96	91	91	
Klebsiella pneumoniae[1]	711				R	96	96	92			97				100	100				98		96	42	99	99	
Proteus mirabilis[1]	309				81	99	100	89			98				100	100				93		85	R	93	94	
Klebsiella oxytoca	121				R	92	93	84			95				100	100				96		97	95	98	98	
Enterobacter cloacae complex[2]	136														97	99				99		92	38	100	99	
Citrobacter freundii complex[2]	99														99	100				89		81	97	92	93	
Morganella morganii[2]	60														100	100				83		71	R	75	86	
Citrobacter koseri	72					99	99	97			99				100	100				99		99	93	100	100	
Enterobacter aerogenes[2]	61														100	100				100		98	15	100	100	
Serratia marcescens[2]	*19														100	100				95		100	R	100	94	
Pseudomonas aeruginosa	237				R	R	93	R	R		R			96	R	93				89		R	R	96	100	
Stenotrophomonas maltophilia																										
Haemophilus influenzae																										

- Other options?
- Nitrofurantoin
  - Overall: 97%
  - Urine Specimens: 96%
  - LTC residents: 93%

- *E.coli* cumulative susceptibility to Cipro in RQHR:
  - Overall: 82% (n=5024)
  - Urine Specimens: 83% (n=4787)
  - LTC residents: 55% (n=350)

Regina Qu'Appelle Health Region ANTIBIOGRAM
Long Term Care†
January 1, 2016 - December 31, 2016

All Specimens – % Susceptible

GRAM-NEGATIVE BACTERIA	# Isolates tested	Penicillin PO	Penicillin IV M	Penicillin IV NM	Ampicillin/Amoxicillin	Amoxicillin-Clavulanic acid	Piperacillin-Tazobactam	Cephalexin[3]	Cefazolin	Cloxacillin	Ceftriaxone	Ceftriaxone IV M	Ceftriaxone IV NM	Ceftazidime	Ertapenem	Meropenem	Clindamycin	Erythromycin	Tetracycline/Doxycycline	Ciprofloxacin	Levofloxacin	Trimethoprim-Sulfamethoxazole	Nitrofurantoin (urine only)	Gentamicin[4]	Tobramycin	Vancomycin
Escherichia coli[1]	350				43	79	95	35			86				100	100				55		62	93	86	85	
Klebsiella pneumoniae[1]	65				R	97	98	94			97				100	100				98		94	53	97	98	
Proteus mirabilis	92				67	98	100	78			100				100	100				86		80	R	96	98	
Klebsiella oxytoca					R																					
Enterobacter cloacae complex	*11														100	100				100		82	36	100	100	
Citrobacter freundii complex	*13														100	100				92		77	85	92	92	
Morganella morganii																										
Citrobacter koseri																										
Enterobacter aerogenes																										
Serratia marcescens																										
Pseudomonas aeruginosa	50				R	R	88	R	R		R			92	R	96				82		R	R	100	100	
Stenotrophomonas maltophilia																										
Haemophilus influenzae																										

MR. J

- 48 yr old man on chemotherapy for ALL
- Diagnosed with sepsis, blood cultures sent to lab
- Started on PipTazo

- Next day lab reports culture + GPC clusters, 2 hours later presumptive ID = *Staphylococcus epidermidis*
- Susceptibility to follow

- Treatment OK?

Regina Qu'Appelle Health Region ANTIBIOGRAM
All Patients
January 1, 2016 - December 31, 2016

All Specimens – % Susceptible

	# Isolates tested	Penicillin PO	Penicillin IV M	Penicillin IV NM	Ampicillin/Amoxicillin	Amoxicillin-Clavulanic acid	Piperacillin-Tazobactam	Cephalexin[4]	Cefazolin	Cloxacillin	Ceftriaxone	Ceftriaxone IV M	Ceftriaxone IV NM	Ceftazidime	Ertapenem	Meropenem	Clindamycin	Erythromycin	Tetracycline/Doxycycline	Ciprofloxacin	Levofloxacin	Trimethoprim-Sulfamethoxazole	Nitrofurantoin (urine only)	Gentamicin[5]	Tobramycin	Vancomycin
GRAM-POSITIVE BACTERIA																										
Staphyloccocus aureus, all	1881							72	72	72							82	67	98			96	100			100
- methicillin-susceptible	1379							100	100	100							84	80	98			95	100			100
- methicillin-resistant (MRSA)	546				R	R	R	R	R	R	R			R	R	R	78	36	98			96	100			100
Staphylococcus epidermidis	153							30	30	30							65	39	88			56	100			100
Viridans group streptococci	35	69									97						76	38								100
Enterococcus species (urine)[2]	555				91			R	R	R	R			R	R	R	R		23	78		R	95			100
Enterococcus faecalis[2]	160				86			R	R	R	R			R	R	R	R		20	81		R	100	76		100
Enterococcus faecium[2]	141				11			R	R	R	R			R	R	R	R		69	9		R	34	86		45
Streptococcus pneumoniae	162	83	83	100								97	100					75	94		98	85				100
Group B Streptococcus	54	100						100	100		100						70	61								100
Group A Streptococcus	46	100						100	100		100						91	89								100
Streptococcus anginosus group	94	98									99						75	75								100

- Other options?
  - Vancomycin 100%

But PipTazo isn't on the Antibiogram!?

- *Staphylococcus epidermidis* cumulative susceptibility to beta-lactams in RQHR:
  - Overall: 30% (n=153)
  - Blood: 25% (n=45)

Regina Qu'Appelle Health Region ANTIBIOGRAM
All Patients
January 1, 2016 - December 31, 2016

Blood Culture Isolates – % Susceptible

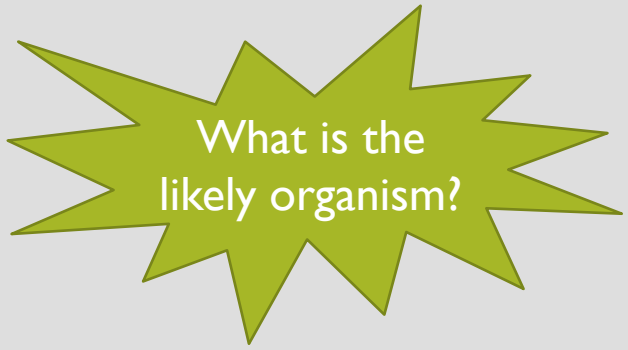
	# Isolates tested	Penicillin PO	Penicillin IV M	Penicillin IV NM	Ampicillin/Amoxicillin	Amoxicillin-Clavulanic acid	Piperacillin-Tazobactam	Cephalexin[4]	Cefazolin	Cloxacillin	Ceftriaxone	Ceftriaxone IV M	Ceftriaxone IV NM	Ceftazidime	Ertapenem	Meropenem	Clindamycin	Erythromycin	Tetracycline/Doxycycline	Ciprofloxacin	Levofloxacin	Trimethoprim-Sulfamethoxazole	Nitrofurantoin (urine only)	Gentamicin[5]	Tobramycin	Vancomycin
GRAM-POSITIVE BACTERIA																										
Staphyloccocus aureus, all	161								65	65																100
- methicillin-susceptible																										
- methicillin-resistant (MRSA)																										
Staphylococcus epidermidis	45								25	25																100
Viridans group streptococci																										
Enterococcus species (urine)																										
Enterococcus faecalis[2]	*29				82				R		R			R	R	R						R		78		100
Enterococcus faecium[2]	*15				20				R		R			R	R	R						R		73		67
Streptococcus pneumoniae	35		82	100								97	100								100					100
Group B Streptococcus																										
Group A Streptococcus																										
Streptococcus anginosus group																										

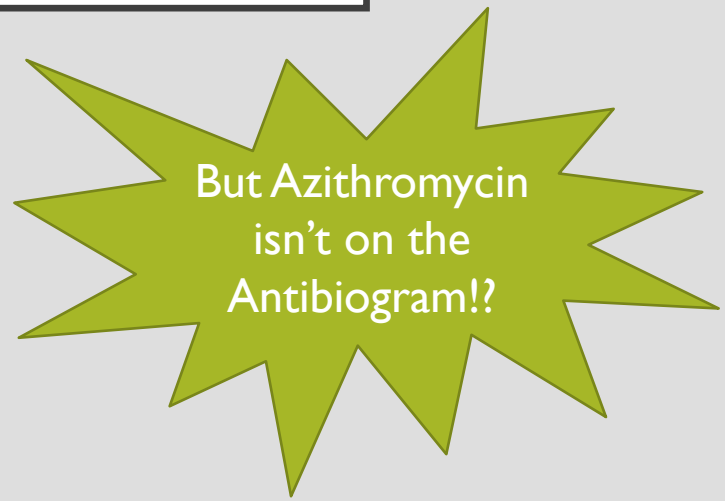
BABY G

- 3 month old female
- Diagnosed with pneumonia, respiratory specimen sent to lab
- Started on azithromycin

- Lab reports Gram:
  - 4+ Polymorphonuclear cells
  - 2+ Squamous epithelial cells
  - 4+ Gram positive diplococci
  - 1+ mixed morphotypes

- Treatment OK? Need to change?





Regina Qu'Appelle Health Region ANTIBIOGRAM
All Patients
January 1, 2016 - December 31, 2016

All Specimens – % Susceptible

	# Isolates tested	Penicillin PO	Penicillin IV M	Penicillin IV NM	Ampicillin/Amoxicillin	Amoxicillin-Clavulanic acid	Piperacillin-Tazobactam	Cephalexin[4]	Cefazolin	Cloxacillin	Ceftriaxone	Ceftriaxone IV M	Ceftriaxone IV NM	Ceftazidime	Ertapenem	Meropenem	Clindamycin	Erythromycin	Tetracycline/Doxycycline	Ciprofloxacin	Levofloxacin	Trimethoprim-Sulfamethoxazole	Nitrofurantoin (urine only)	Gentamicin[5]	Tobramycin	Vancomycin
GRAM-POSITIVE BACTERIA																										
Staphyloccocus aureus, all	1881							72	72	72							82	67	98			96	100			100
- methicillin-susceptible	1379							100	100	100							84	80	98			95	100			100
- methicillin-resistant (MRSA)	546				R	R	R	R	R	R	R			R	R	R	78	36	98			96	100			100
Staphylococcus epidermidis	153							30	30	30							65	39	88			56	100			100
Viridans group streptococci	35	69									97						76	38								100
Enterococcus species (urine)[2]	555				91			R	R	R	R			R	R	R	R		23	78		R	95			100
Enterococcus faecalis[2]	160				86			R	R	R	R			R	R	R	R		20	81		R	100	76		100
Enterococcus faecium[2]	141				11			R	R	R	R			R	R	R	R		69	9		R	34	86		45
Streptococcus pneumoniae	162	83	83	100								97	100					75	94		98	85				100
Group B Streptococcus	54	100						100	100		100						70	61								100
Group A Streptococcus	46	100						100	100		100						91	89								100
Streptococcus anginosus group	94	98									99						75	75								100

- Other options?
  - Septra 85-90%
  - Beta-lactams?

	# Isolates tested	Penicillin PO	Penicillin IV M	Penicillin IV NM	Ceftriaxone IV M	Ceftriaxone IV NM
Streptococcus pneumoniae	114	80	80	100	93	100

- *Streptococcus pneumoniae* cumulative susceptibility to macrolides in RQHR:
  - Overall: 75% (n=162)
  - Pediatrics: 70% (n=114)

Regina Qu'Appelle Health Region ANTIBIOGRAM
Pediatrics (≤17 years)
January 1, 2014 - December 31, 2016

All Specimens – % Susceptible

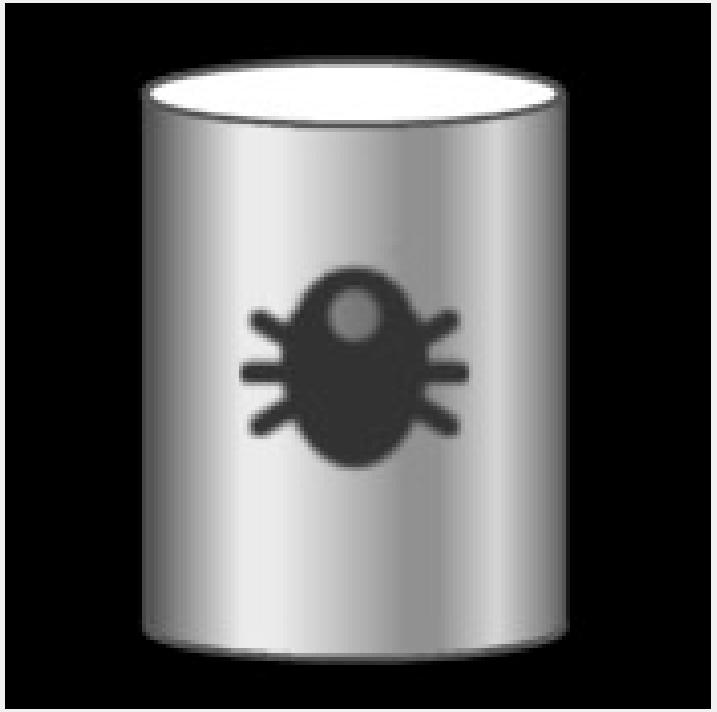
	# Isolates tested	Penicillin PO	Penicillin IV M	Penicillin IV NM	Ampicillin/Amoxicillin	Amoxicillin-Clavulanic acid	Piperacillin-Tazobactam	Cephalexin[4]	Cefazolin	Cloxacillin	Ceftriaxone	Ceftriaxone IV M	Ceftriaxone IV NM	Ceftazidime	Ertapenem	Meropenem	Clindamycin	Erythromycin	Tetracycline/Doxycycline	Ciprofloxacin	Levofloxacin	Trimethoprim-Sulfamethoxazole	Nitrofurantoin (urine only)	Gentamicin[5]	Tobramycin	Vancomycin
GRAM-POSITIVE BACTERIA																										
Staphyloccocus aureus, all	857							78	78	78							86	76	97			94	99	99		100
- methicillin-susceptible	681							100	100	100							85	83	97			94	99	100		100
- methicillin-resistant (MRSA)	194				R	R	R	R	R	R	R			R	R	R	88	52	100			93	100	96		100
Staphylococcus epidermidis	37							46	46	46							57	35	95			73	100	87		100
Viridans group streptococci																										
Enterococcus species (urine)[2]	116				99			R	R	R	R			R	R	R	R		18	97		R	99	88		100
Enterococcus faecalis[2]	*19				90			R	R	R	R			R	R	R	R		16	100		R	100	74		100
Enterococcus faecium								R	R	R	R			R	R	R	R					R				
Streptococcus pneumoniae	114	80	80	100								93	100					70	89		99	90				100
Group B Streptococcus																										
Group A Streptococcus	*24	100									100						92	84								100
Streptococcus anginosus group	*14	93									93						86	93								100

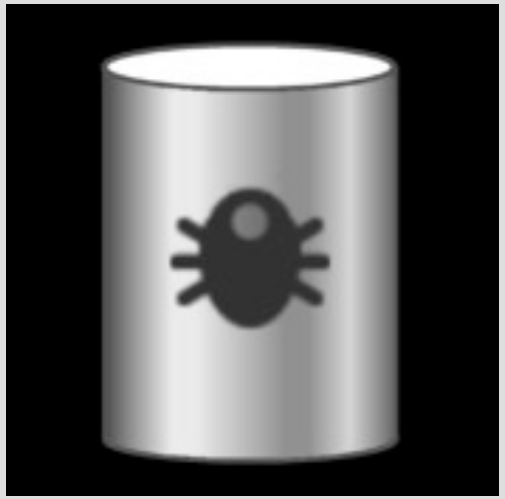
CAN I USE SOMEONE ELSE'S ANTIBIOGRAM?

- Can you walk in your friend's shoes?
- You *CAN* … but you shouldn't if you don't have to
- Variability in microbial populations can be significant in different geographic locations
- Just like any infectious disease!
- Added variability in ordering practices, transmission dynamics, lab protocols
- Consider patient characteristics/demographics

INFORMATION AT THE POINT OF CARE

- Antibiograms app – available FREE for iPhone and Android devices
- Search app store for "Antibiograms" and download onto mobile device
- Open database file (.db) from email/website
  - 'What program do you want to open this with?'
- Requires your lab to create a .db file
  - LABS! Call me if you need help creating your database file





iPad 7:39 AM 35%

(Select a Bacterium)

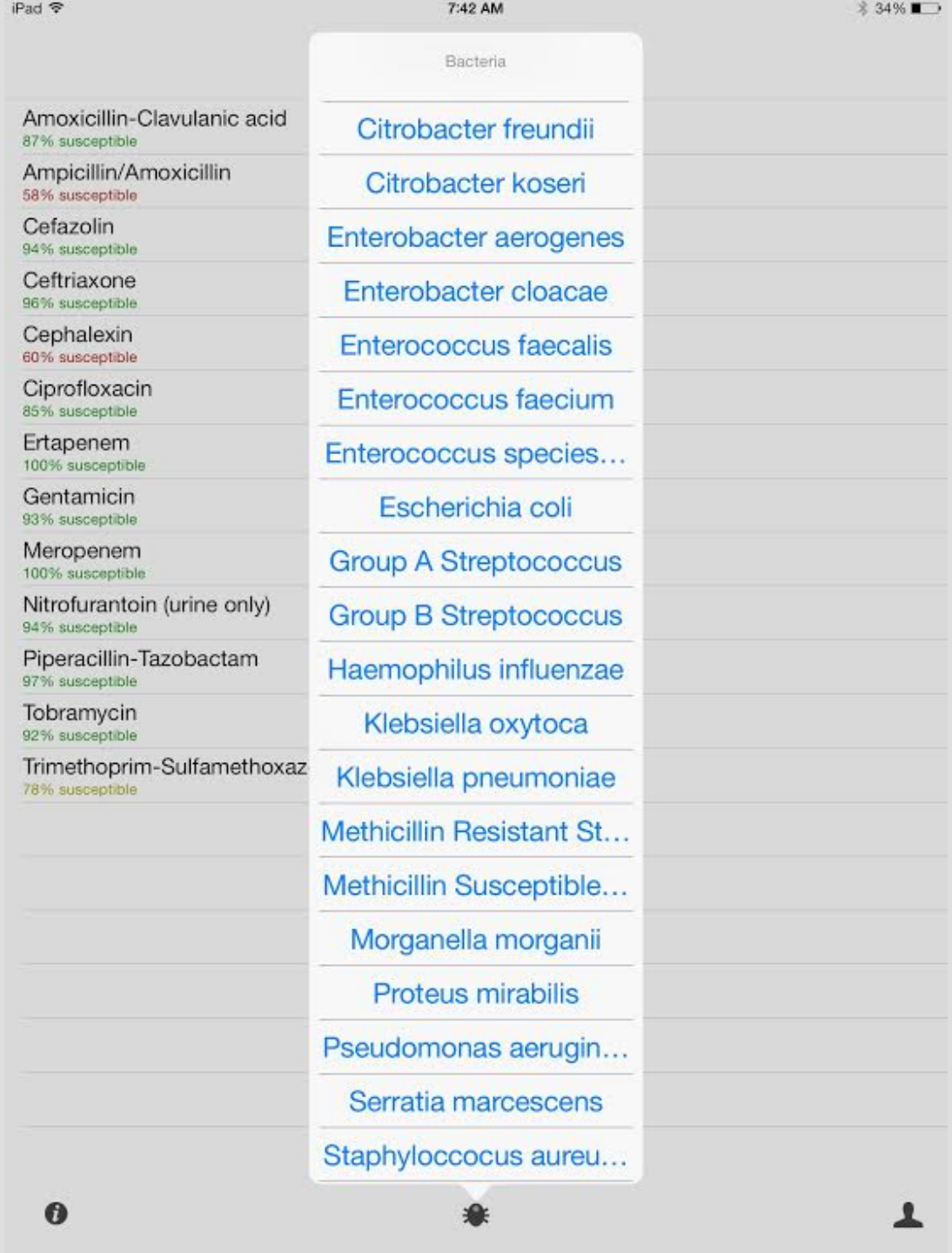
Antibiograms

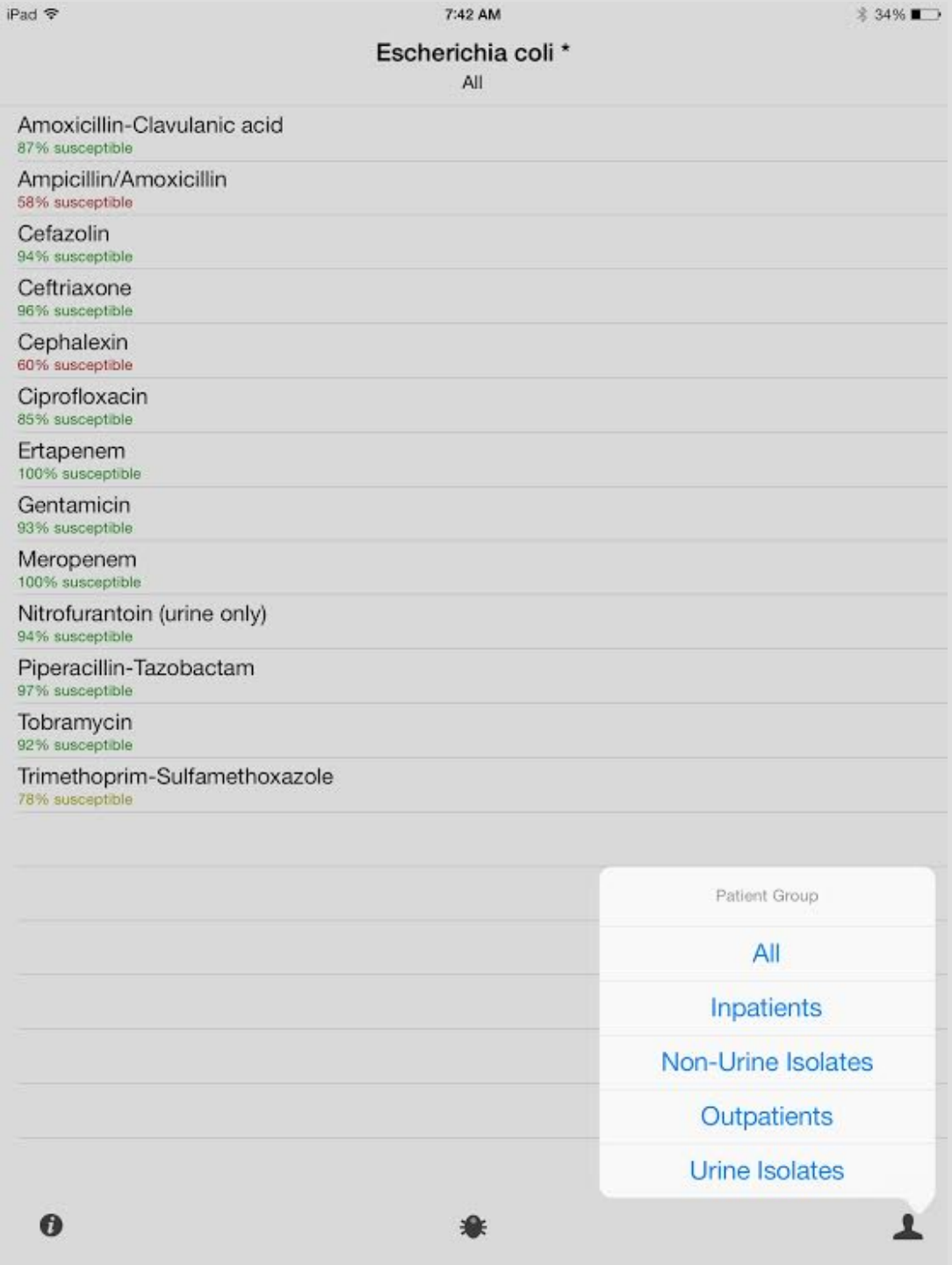
Download

(Pre-loaded database)
Oct 20, 2013, 9:22:36 PM

RQHR Antibiogram 2012 - ap...
Nov 20, 2013, 7:37:47 AM

About | Help | Databases


iPad
7:42 AM
34%
Amoxicillin-Clavulanic acid
87% susceptible
Ampicillin/Amoxicillin
58% susceptible
Cefazolin
94% susceptible
Ceftriaxone
96% susceptible
Cephalexin
60% susceptible
Ciprofloxacin
85% susceptible
Ertapenem
100% susceptible
Gentamicin
93% susceptible
Meropenem
100% susceptible
Nitrofurantoin (urine only)
94% susceptible
Piperacillin-Tazobactam
97% susceptible
Tobramycin
92% susceptible
Trimethoprim-Sulfamethoxaz
78% susceptible
Bacteria
Citrobacter freundii
Citrobacter koseri
Enterobacter aerogenes
Enterobacter cloacae
Enterococcus faecalis
Enterococcus faecium
Enterococcus species…
Escherichia coli
Group A Streptococcus
Group B Streptococcus
Haemophilus influenzae
Klebsiella oxytoca
Klebsiella pneumoniae
Methicillin Resistant St…
Methicillin Susceptible…
Morganella morganii
Proteus mirabilis
Pseudomonas aerugin…
Serratia marcescens
Staphyloccocus aureu…


iPad
7:42 AM
34%
Escherichia coli *
All
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87% susceptible
Ampicillin/Amoxicillin
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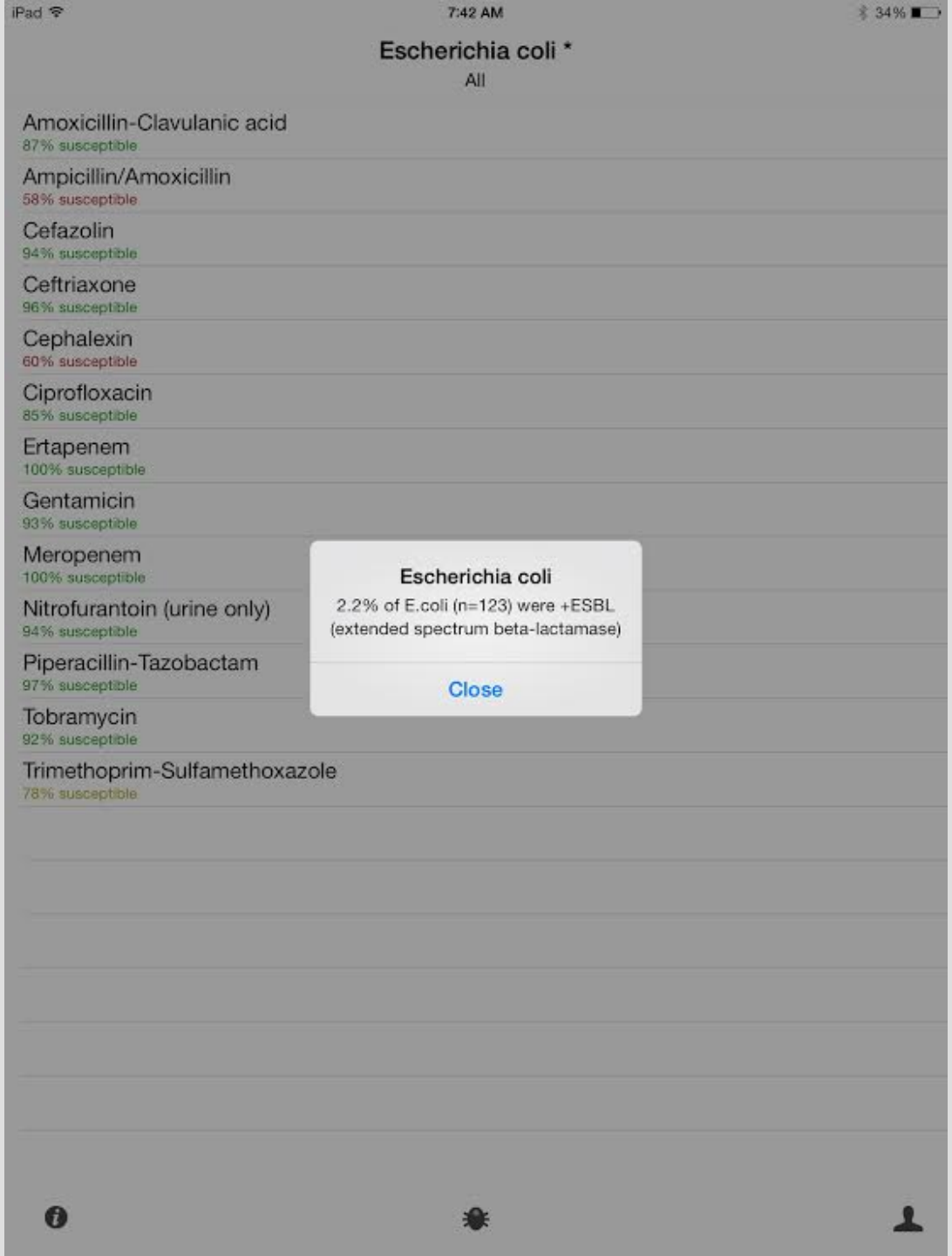
Cefazolin
94% susceptible
Ceftriaxone
96% susceptible
Cephalexin
60% susceptible
Ciprofloxacin
85% susceptible
Ertapenem
100% susceptible
Gentamicin
93% susceptible
Meropenem
100% susceptible
Nitrofurantoin (urine only)
94% susceptible
Piperacillin-Tazobactam
97% susceptible
Tobramycin
92% susceptible
Trimethoprim-Sulfamethoxazole
78% susceptible
Patient Group
All
Inpatients
Non-Urine Isolates
Outpatients
Urine Isolates


iPad
7:42 AM
34%
Escherichia coli *
All
Amoxicillin-Clavulanic acid
87% susceptible
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58% susceptible
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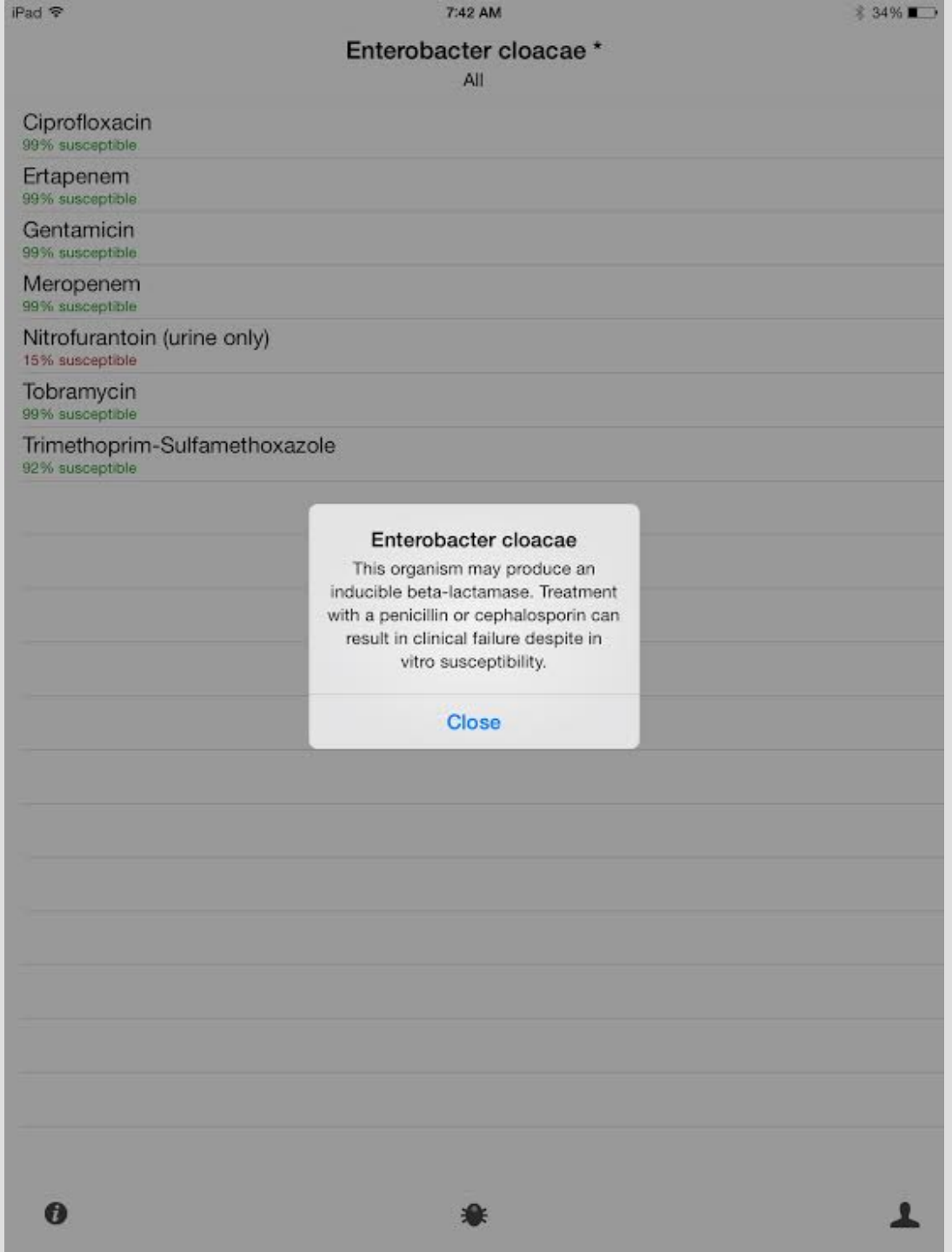
Ceftriaxone
96% susceptible
Cephalexin
60% susceptible
Ciprofloxacin
85% susceptible
Ertapenem
100% susceptible
Gentamicin
93% susceptible
Meropenem
100% susceptible
Nitrofurantoin (urine only)
94% susceptible
Piperacillin-Tazobactam
97% susceptible
Tobramycin
92% susceptible
Trimethoprim-Sulfamethoxazole
78% susceptible
Escherichia coli
2.2% of E.coli (n=123) were +ESBL (extended spectrum beta-lactamase)
Close


iPad
7:42 AM
34%
Enterobacter cloacae *
All
Ciprofloxacin
99% susceptible
Ertapenem
99% susceptible
Gentamicin
99% susceptible
Meropenem
99% susceptible
Nitrofurantoin (urine only)
15% susceptible
Tobramycin
99% susceptible
Trimethoprim-Sulfamethoxazole
92% susceptible
Enterobacter cloacae
This organism may produce an inducible beta-lactamase. Treatment with a penicillin or cephalosporin can result in clinical failure despite in vitro susceptibility.
Close

SUBGROUPS

- Patient Type Subgroups
  - Inpatient
  - Outpatient
  - LTC
  - Emergency
  - ICU
  - Pediatric, Adult, Senior
  - Length of Stay?
- Specimen Type Subgroups
  - Blood
  - Urine
  - Excluding Urine
- Specialty Organisms
  - Anaerobes
  - Yeast

CONTINGENT ANTIBIOGRAMS

- The likelihood of at least one antibiotic being susceptible when given in combinations

- E.g. Hypothetical Pseudomonas aeruginosa susceptibility:
  - PipTazo 85%
  - Ceftazidime 80%
  - Cipro 75%

- What 2 drug regimen will yield the highest coverage rates?
  - Given PipTazo=R, what is ceftaz %S?
  - Given Ceftaz=R, what is Cipro %S?
  - etc

WEIGHTED INCIDENCE SYNDROMIC CONTINGENT ANTIBIOGRAM (WISCA)

- Takes into account the site of isolation and provides a weighted susceptibility of all organisms causing a specific infectious syndrome

- E.g. Hypothetical Urinary Tract Infections
  - 80% caused by E.coli
  - 10% caused by Enterococcus
  - 7% caused by other GNB
  - 3% caused by other GPC

Ampicillin Susceptibility
- E.coli 50% S
- Enterococcus 90% S
- Other GNB 85% S
- Other GPC 95% S

Weighted Susceptibility
- 0.8 * 50 = 40
- 0.1 * 90 = 9
- 0.07 * 85 = 5.95
- 0.03 * 95 = 2.85

Sum = 57.8%

DEFINING RESISTANCE

NO LACK OF DEFINITIONS

INTRINSIC vs. ACQUIRED?

MUTATIONS vs. HORIZONTAL GENE TRANSFER?

PHENOTYPIC vs. GENOTYPIC?

MECHANISM OF ACTIVITY?
Target modification vs.
Antibiotic alteration vs.
Restricted target access vs.
Global adaptive processes

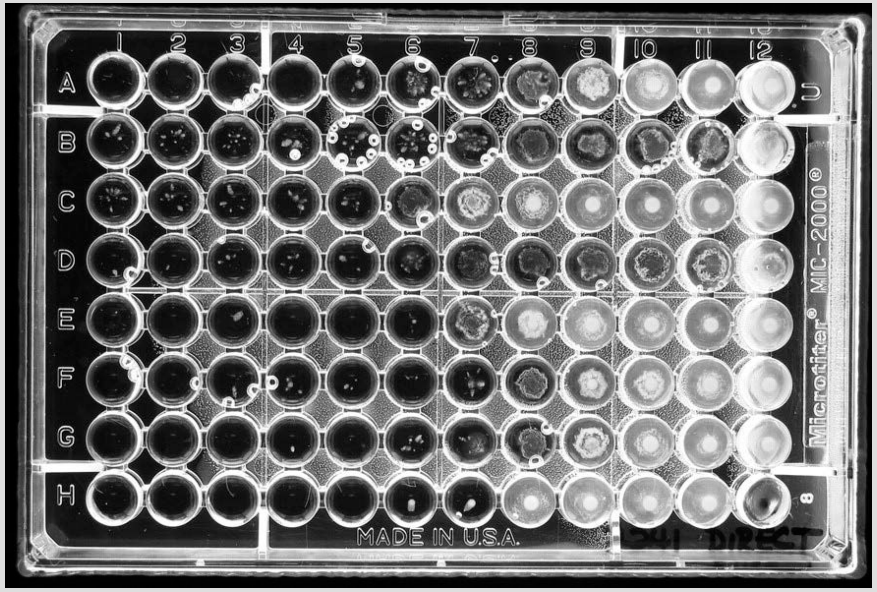
DETERMINING SUSCEPTIBILITY

PHENOTYPIC

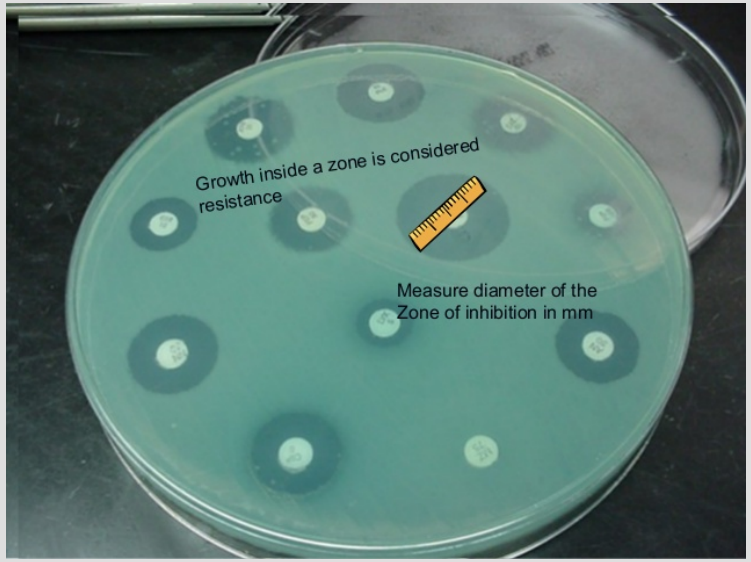
- How well does bug grow in presence of drug in vitro
- Yields MIC – "the lowest concentration of antimicrobial that will inhibit the visible growth of a microorganism after overnight incubation"
- Requires minimum 24 hrs
- Interpretation requires breakpoints
- E.g. microdilution, E-tests, Kirby-Bauer, automated methods

GENOTYPIC

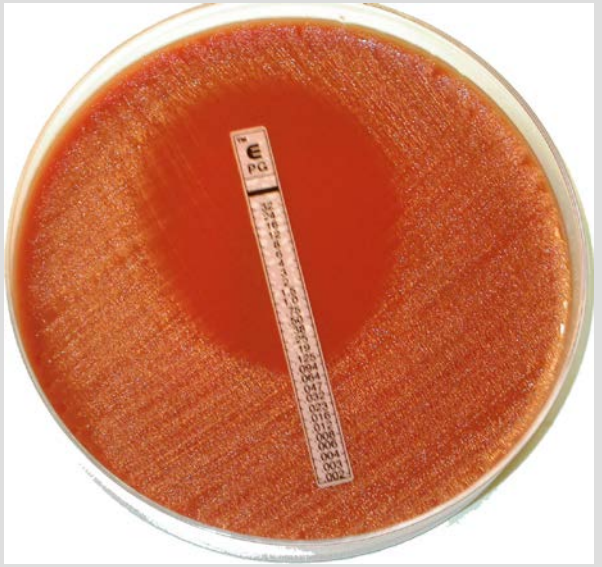
- Detect presence of genes associated with mechanism of resistance
- Needs robust association with phenotype for interpretation
- Rapid
- Interpretation = present/absent
- E.g. PCR, genetic sequencing



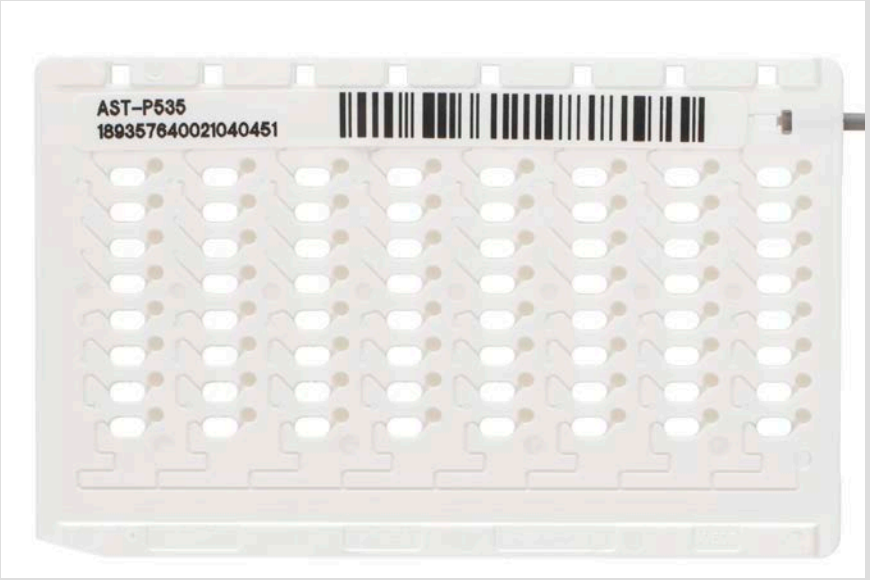
Broth Microdilution



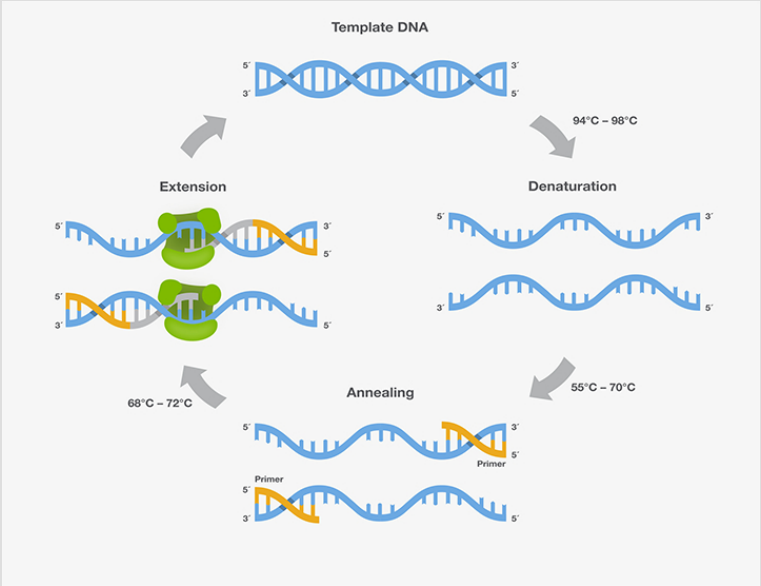
Kirby-Bauer



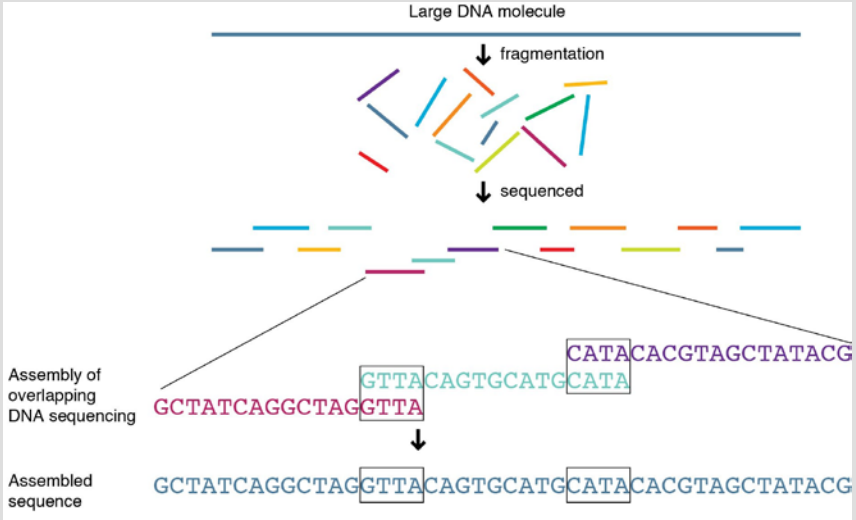
E-tests®



Automated (Vitek® Microscan®)



PCR

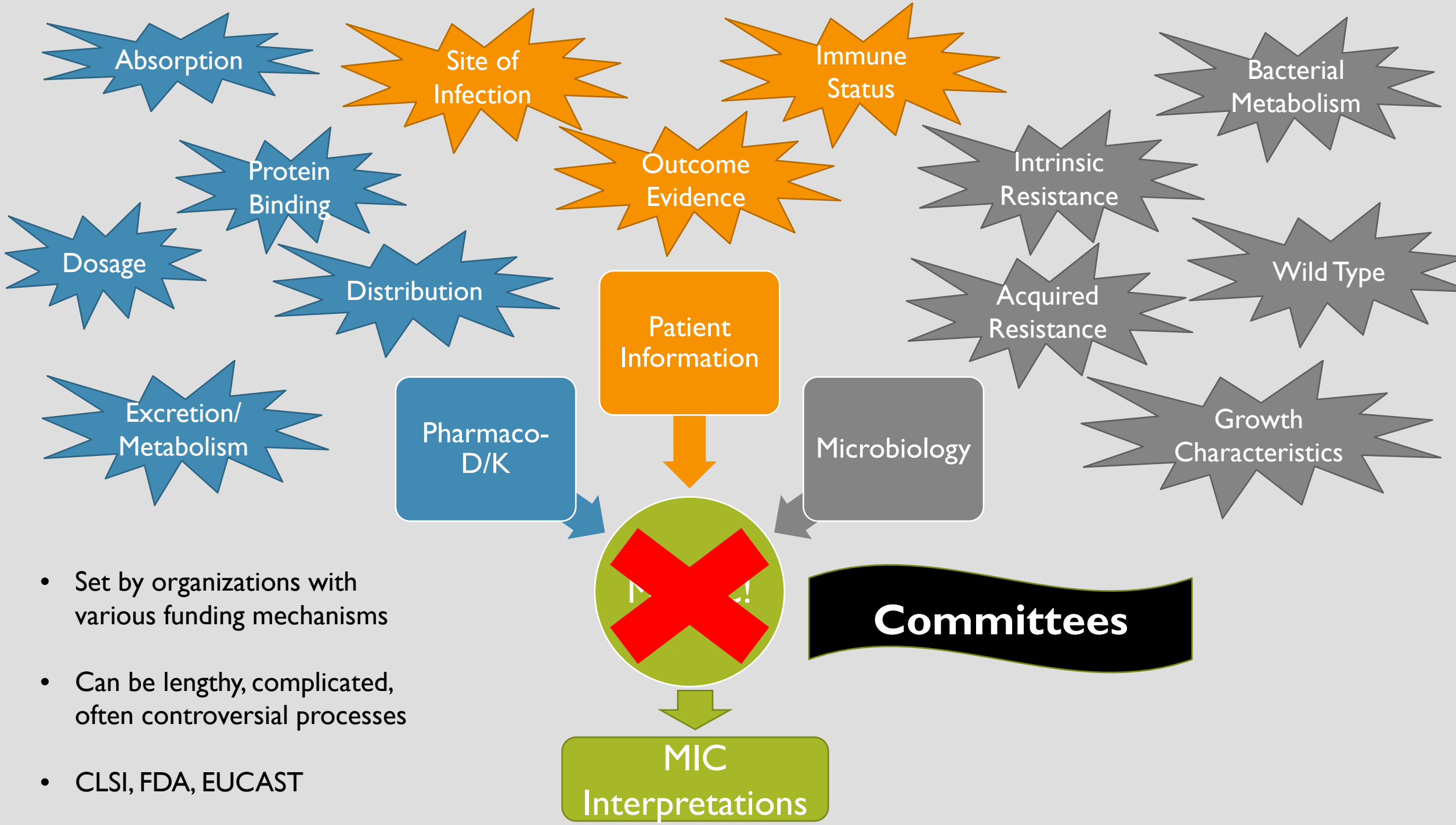


Sequencing

DETERMINING SUSCEPTIBILITY

- What you want to know: "Is my patient's infection likely to respond to treatment with this antibiotic?"
- What an MIC tells you: "This concentration of antibiotic inhibits visible growth on a plate after 24 hours."

Breakpoints



- Set by organizations with various funding mechanisms
- Can be lengthy, complicated, often controversial processes
- CLSI, FDA, EUCAST

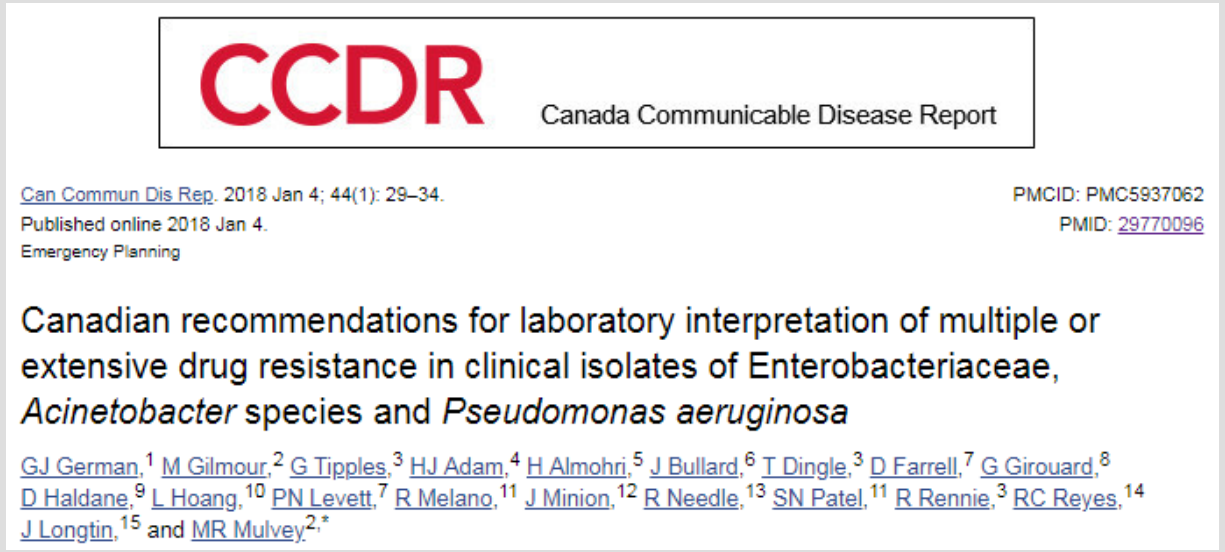
MULTI-DRUG RESISTANCE / EXTENSIVE DRUG RESISTANCE

Considers resistance to categories of antimicrobials

More patient-oriented

Resistance vs. Non-susceptibility

Phenotypic definitions



CCDR Canada Communicable Disease Report

Can Commun Dis Rep. 2018 Jan 4; 44(1): 29–34.
Published online 2018 Jan 4.
Emergency Planning

PMCID: PMC5937062
PMID: 29770096

Canadian recommendations for laboratory interpretation of multiple or extensive drug resistance in clinical isolates of Enterobacteriaceae, *Acinetobacter* species and *Pseudomonas aeruginosa*

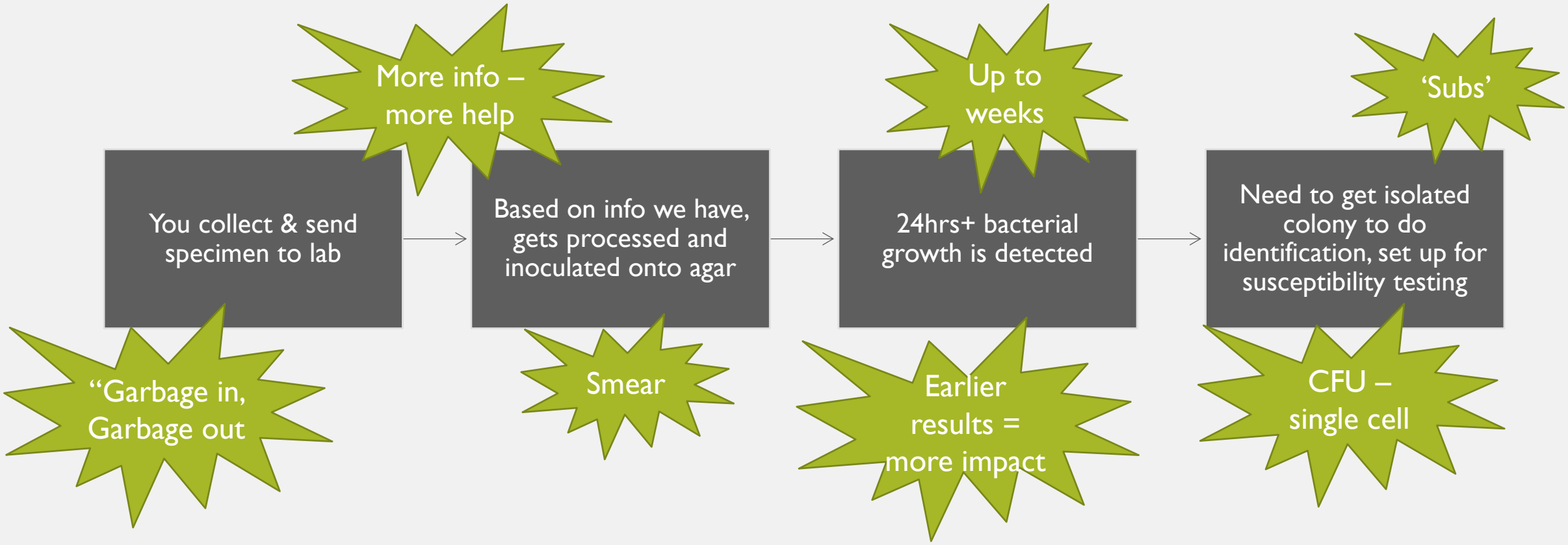
GJ German,[1] M Gilmour,[2] G Tipples,[3] HJ Adam,[4] H Almohri,[5] J Bullard,[6] T Dingle,[3] D Farrell,[7] G Girouard,[8] D Haldane,[9] L Hoang,[10] PN Levett,[7] R Melano,[11] J Minion,[12] R Needle,[13] SN Patel,[11] R Rennie,[3] RC Reyes,[14] J Longtin,[15] and MR Mulvey[2,*]

CCDR (2018) Volume 44(1): 29-34, Jan 4, 2018

4 PILLARS OF ANTIMICROBIAL STEWARDSHIP

	Surveillance	Stewardship	Infection Prevention & Control	Innovation
MICROBIOLOGY	Antibiograms Defining Resistance	Communication Selective Reporting Improved Diagnostics	Detection Outbreaks Transmission	POCT CRISPR Metagenomics

WHAT'S INSIDE THE BLACK BOX



DIAGNOSTICS & STEWARDSHIP

BETTER TURNAROUND TIME

- ID & Susceptibility

BETTER DIAGNOSTICS

- Biomarkers of Infection

SPEED IT UP!

- Decreasing TAT in micro lab can result in:
  - decreased antibiotic use
  - decreased inappropriate antibiotic use
  - decreased time to initiating appropriate antibiotic therapy
  - decreased length of stay
  - decreased ICU stay
  - fewer days of antimicrobial therapy,
  - decreased drug costs
  - decreased hospital costs
  - mortality

Rapid Gram stain communication alone decreases mortality due to blood stream infections!

<1hr (ave 0.1 hr) – 10.1% mortality
>1hr (ave 3.3 hr) – 19.2% mortality

Barenfanger J, Graham DR, Kolluri L, Sangwan G, Lawhorn J, Drake CA, Verhulst SJ, Peterson R, Moja LB, Ertmoed MM, Moja AB, Shevlin DW, Vautrain R, Callahan CD. 2008. Decreased mortality associated with prompt Gram staining of blood cultures. Am J Clin Pathol 130:870–876.

MANY STUDIES NOW…

Goff DA, Jankowski C, Tenover FC. Using rapid diagnostic tests to optimize antimicrobial selection in antimicrobial stewardship programs. Pharmacotherapy 2012;32:677–87.

Forrest GN, Mehta S, Weekes E, et al. [illegible] hybridization testing on coagulase-negative staphyloc[illegible]

Forrest NG, Mar[illegible] hybridization-bas[illegible] therapy costs. J C[illegible]

Forrest GN, Rog[illegible] hybridization for [illegible] antimicrobial the[illegible]

Carver PL, Lin S, DePestel DD, et al. Impact of mecA gene testing and intervention by infectious disease clinical pharmacists on time to optimal antimicrobial therapy for Staphylococcus aureus bacteremia at a university hospital. J Clin Microbiol 2008;46:2381–3.

Bauer KA, West JE, Balada-Llasat JM, et al. An antimicrobial stewardship program's impact with rapid polymerase chain reaction methicillin-resistant Staphylococcus aureus/S. aureus blood culture test in patients with S. aureus bacteremia. Clin Infect Dis 2010;51:1076–80.

Clerc O, Prod'hom G, Senn L, et al. Matrix-assisted laser desorption ionization time-of-flight mass spectrometry and PCR-based rapid diagnosis of Staphylococcus aureus bacteraemia. Clin Microbiol Infect 2013.

Heil EL, Daniels LM, Long DM, et al. Impact of a rapid peptide nucleic acid fluorescence in situ hybridization assay on treatment of Candida infections. Am J Health Syst Pharm 2012;69(21):1910–4.

Tan KE, Ellis BC, Lee R, et al. Prospective evaluation of a matrix-assisted laser desorption ionization-time of flight mass spectrometry system in a hospital clinical m[illegible]robiology [illegible]tification of bacteria and yeasts: a bench[illegible] for assessing the [illegible]2;50:3301–8.

[illegible]ption ionization [illegible]th gram-negative [illegible]–7.

[illegible]ation via matrix-[illegible]ial stewardship team int[illegible]. Clin Infect Dis 2013;57:1237–45.

Perez KK, Olsen RJ, Musick WL, et al. Integrating rapid pathogen identification and antimicrobial stewardship significantly decreases hospital costs. Arch Pathol Lab Med 2013;137(9):1247–54.

Tamma PD, Tan K, Nussenblatt VR, et al. Can matrix-assisted laser desorption ionization time-of-flight mass spectrometry (MALDI-TOF) enhance antimicrobial stewardship efforts in the acute care setting? Infect Control Hosp Epidemiol 2013;34(9):990–5

Not Comprehensive!
I stopped collecting evidence in 2013…

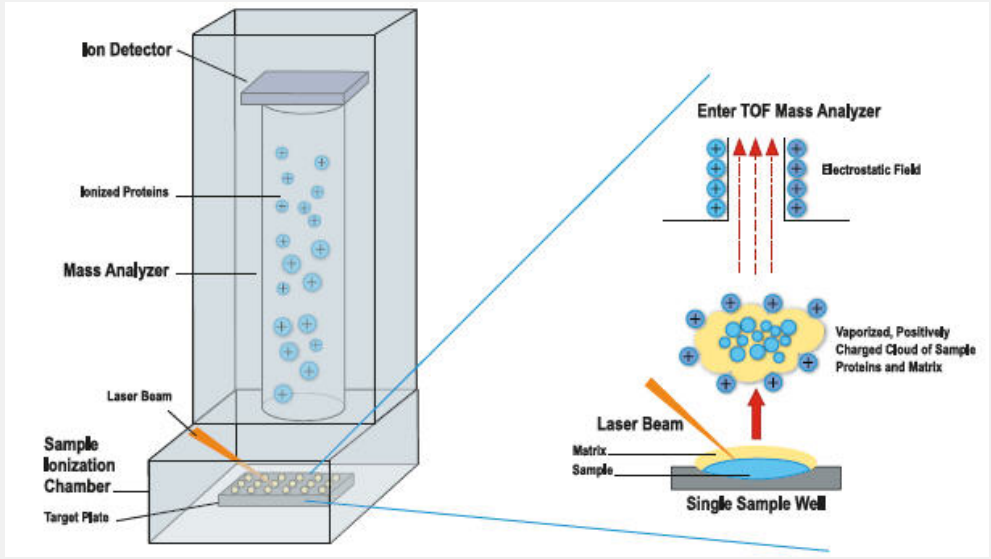
BETTER TURNAROUND TIME

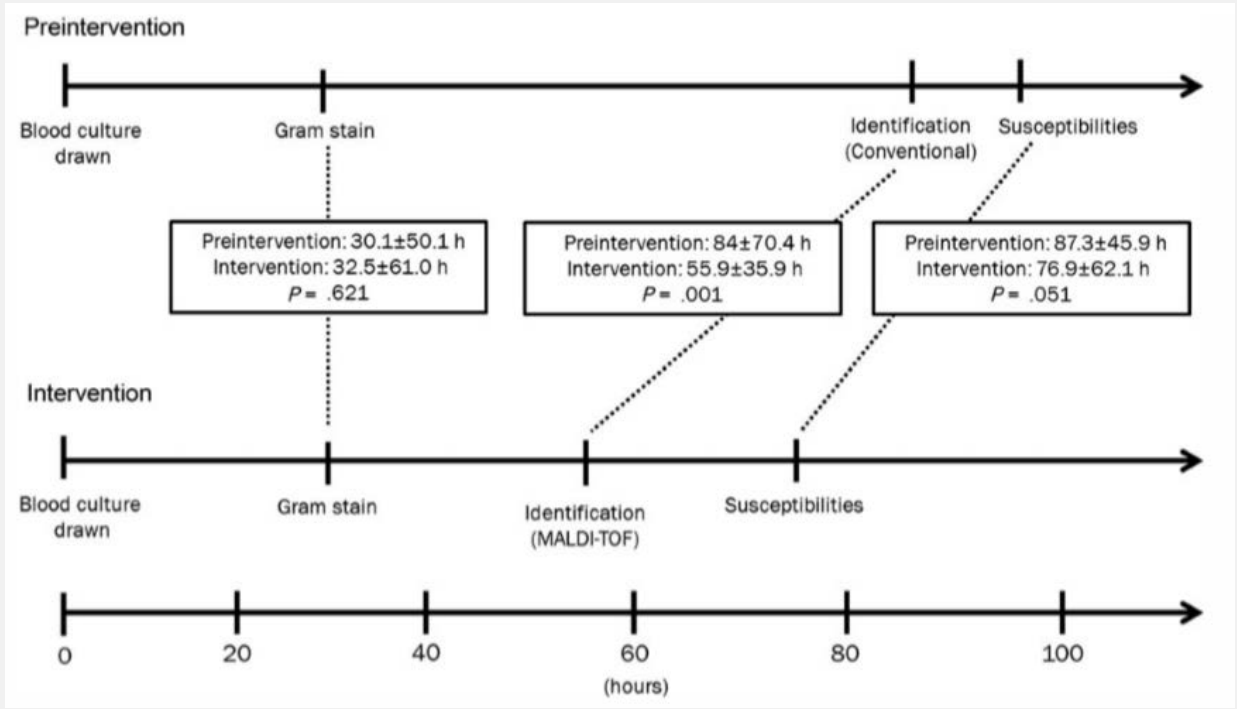
- Can be achieved through process improvement, staffing changes, laboratory policies

- New testing technology:
  - Peptide Nucleic Acid-Fluoresence In Situ Hybridization (FISH)
  - Real-time Polymerase Chain Reaction Assays (RT-PCR)
  - Matrix-assisted Laser Desorption Ionization Time-of-Flight Mass Spectrometry (MALDI-TOF)
  - Broad-based Multiplexed Nucleic Acid Assays for Blood Cultures (Arrays, Panels)

- New laboratory automation

MALDI-TOF





- Decreased time to identification 84.0 vs 55.9 hrs
- Improved time to effective Abx therapy 30.1 vs. 20.4 hrs
- Time to optimal antibiotic therapy 90.3 vs. 47.3 hrs
- Mortality 20.3% vs. 14.5%
- Length of ICU stay 14.9 vs. 8.3 days
- Recurrent bacteremia 5.9% vs. 2.0%

Huang AM, Newton D, Kunapuli A, et al. Clin Infect Dis 2013;57:1237–45.

DIRECT PCR

GRAM POSITIVE COCCI IN CLUSTERS POSITIVE for S. aureus (SA) DNA by real time PCR. POSITIVE for METHICILLIN RESISTANT S. aureus (MRSA) DNA by real time PCR
GRAM POSITIVE COCCI IN CLUSTERS POSITIVE for S. aureus (SA) DNA by real time PCR. NEGATIVE for METHICILLIN RESISTANT S. aureus (MRSA) DNA by real time PCR
GRAM POSITIVE COCCI IN CLUSTERS NEGATIVE for S. aureus (SA) DNA by real time PCR. NEGATIVE for METHICILLIN RESISTANT S. aureus (MRSA) DNA by real time PCR

NOTE. The rapid PCR methicillin-resistant *Staphylococcus aureus*/*S. aureus* blood culture test is approved by the Food and Drug Administration for MRSA or SA identification.

- ID Pharmacist contacted with results
- Time to switch from empiric vancomycin to cefazolin in patients with MSSA 1.7 days shorter
- Length of stay 6.2 days shorter
- Mean hospital costs $21,387 less

Bauer KA, West JE, Balada-Llasat JM, et al. Clin Infect Dis 2010;51:1074–80.

TOTAL LAB AUTOMATION

- Robotics can now automate:
  - Culture plate inoculation and streaking
  - Gram smears and staining
  - "Smart Incubators" decrease time to result
  - Image Analysis of culture growth
  - Hands-free discard of negative cultures
  - Digital selection of isolates for work-up
  - Performance of ID and Susceptibility testing

Copan WASP™ Lab:
https://www.youtube.com/watch?v=AFQBPoQZZ9Y

CAUTION

- Benefits often are not realized if implemented by lab alone
  - Synergy when implemented in partnership with Antimicrobial Stewardship Programs, to ensure translation of decreased TAT of results to action

- We need your help!
  - Laboratory interventions and new diagnostics usually COST more money in the lab, while SAVING money outside the lab
  - We can achieve net savings for health system by investing in lab, if done properly.
  - Joint Business Cases which estimate/demonstrate return on investment in clinical area

- WARNING! Buyer beware! Diagnostics market is not well controlled…
  - Do not engage with sales reps who want to bypass your lab personnel
  - Ignore claims of performance made in product inserts
  - I've never met a distributor who doesn't sell "The Best" brand of test X
  - Lab personnel – be skeptical, check references and literature, verify verify verify! RFPs can be your friend.

Public Health Ontario | Santé publique Ontario

PARTNERS FOR HEALTH | PARTENAIRES POUR LA SANTÉ

Antimicrobial Stewardship Strategy:

Cascading microbiology susceptibility reporting

The selective suppression of an organism's susceptibility to broader-spectrum or more expensive secondary agents when it is susceptible to preferred primary agents.

- https://www.publichealthontario.ca/en/BrowseByTopic/InfectiousDiseases/AntimicrobialStewardshipProgram/Documents/ASP_Strategy_Cascading_Microbiology_Reporting.pdf

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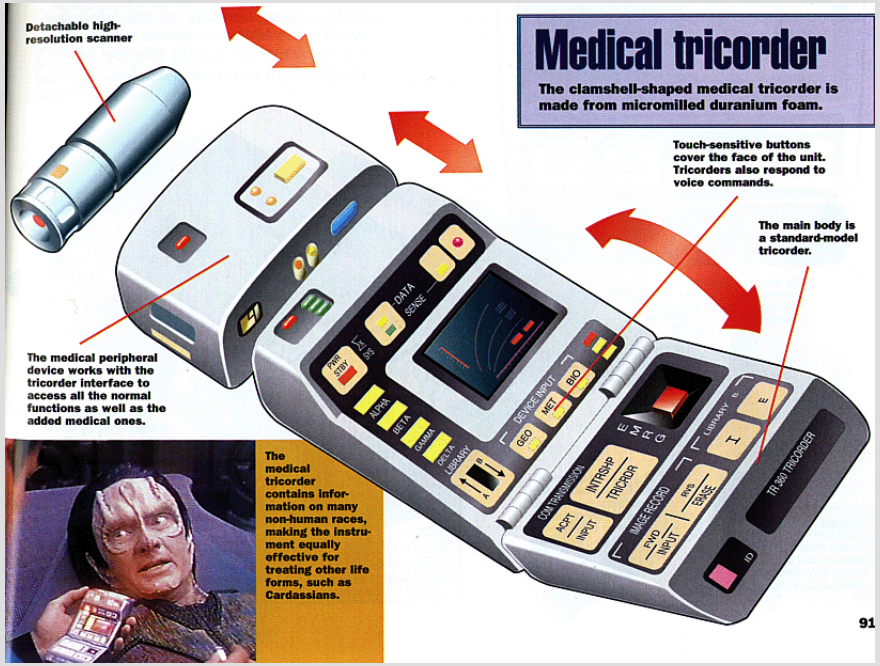
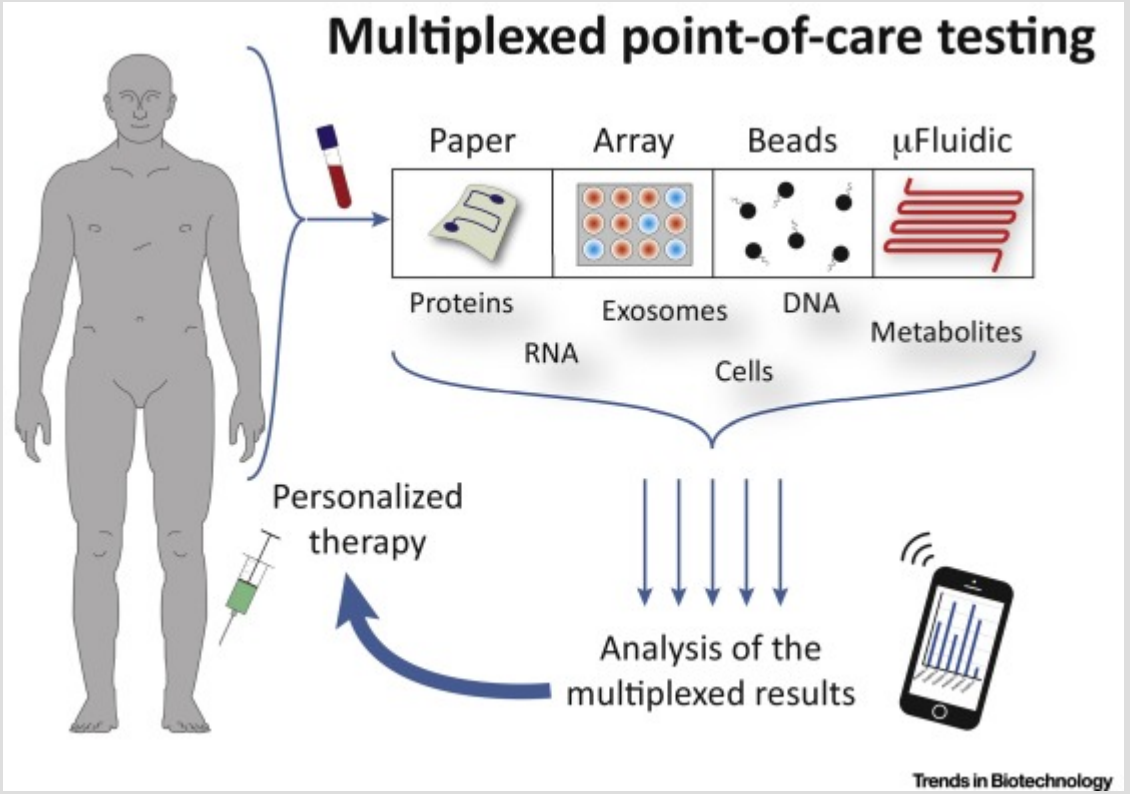
	Surveillance	Stewardship	Infection Prevention & Control	Innovation
MICROBIOLOGY	Antibiograms Defining Resistance	Communication Selective Reporting New Diagnostics	Detection Outbreaks Transmission	POCT CRISPR Metagenomics

POINT OF CARE TESTING





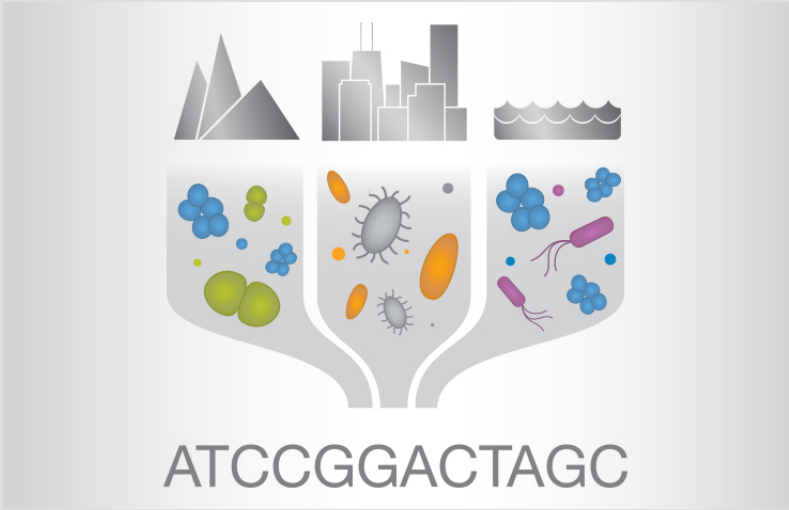
CRISPR TECHNOLOGY

"Clustered regularly interspaced short palindromic repeats"

- Programmable, sequence-specific genome modification using the RNA-guided nuclease Cas9, delivered by a bacteriophage
- Based on bacterial immune system enzymes – Cas9
  - Target virulence genes?
  - Target antimicrobial resistance genes?
  - Immunize avirulent strains against acquiring resistance genes or virulence factors?

METAGENOMICS

- Looks at all the genetic material in a sample
- More accurately reflects how microbes (and host cells) live and exist together
  - Bugs don't live in pure cultures, they live in complex communities
  - Genetic diversity exists within strains, yet we deal with clonal cultures
  - Recognizes the large pool of 'unculturable' organisms
- Characterization of the Microbiome
  - Which microbiome?
  - Disease associations
  - Cause ←→ Effect
  - Bug ←→ Drug




Thank
you!!