CHI Health

Infectious Disease Update

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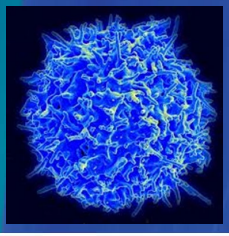
I have no relevant financial relationships to disclose

Objectives

- Update on CMV resistance and treatment
- Review BK virus
- Discuss infections, antibiotics, and antibiotic resistance
- Describe specific superbugs and treatment

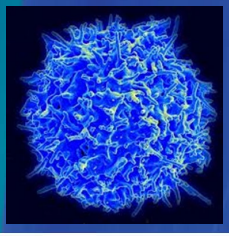
VIRAL INFECTIONS

CMV: Mechanism of infection



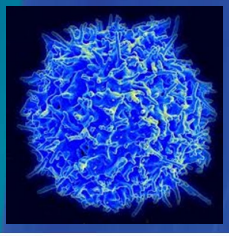
- Primary infection
  - CMV naïve recipient
  - CMV D+/R-
- Secondary (reactivation) infection
  - CMV seropositive recipient
- Serology is important to determine risk factors
  - CMV D+/R- highest risk
  - CMV D+/R+, D-/R+ intermediate risk
  - CMV D-/R- low risk

Risk Factors for CMV



- Type of organ transplanted
  - Lung, small bowel, and pancreas have highest risk
  - Liver, kidney have lowest risk
- Increased net state of immunosuppression
  - Mycophenolic acid and/or steroids
- Thymoglobulin or Campath induction
- Allograft rejection
  - Bidirectional relationship between CMV and rejection
  - Immunomodulatory effect
- Concurrent viral infections
- Serologic status

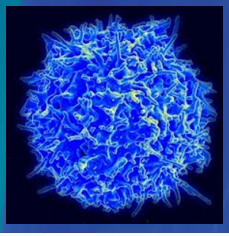
Prevention



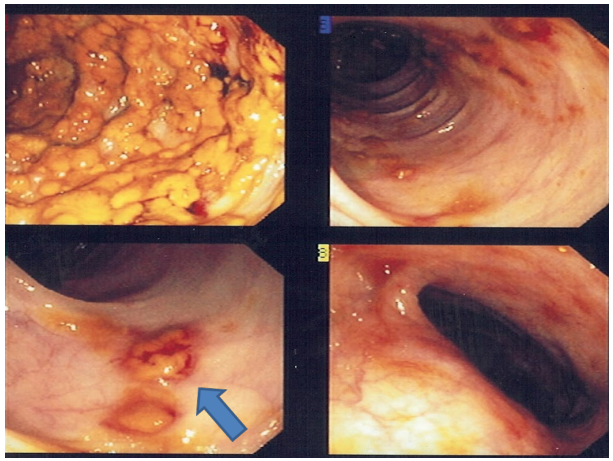
- Preemptive therapy
  - CMV DNA monitored at regular intervals
  - Patients are treated when early replication noted to prevent symptomatic disease
  - Advantage: Decreases drug cost and toxicity
  - Disadvantage: Logistic coordination and lack of standardized testing
- Universal prophylaxis
  - Antiviral therapy to all at-risk patients
  - Theoretical advantage of preventing reactivation of other viruses
  - High rates of neutropenia
  - Delayed-onset of post-prophylaxis disease
  - Based on serologies:
    - High risk (D+/R-) Valgancyclovir 450mg po qday x 3-6months
    - Intermediate risk (D+/R+,D-/R+) Acyclovir 800mg qid (OR) Valacyclovir 1gm tid x 3-6months
    - Low risk (-/-) Acyclovir 400mg bid x 3months
    - Letermovir 480mg po/IV qday (not inferior to Valgancyclovir in kidney transplant)
      - Only covers CMV so need Acyclovir in addition
      - Much more expensive
- Hybrid approach
  - Prophylaxis followed by surveillance

Raglow Z, Kaul DR. A New Antiviral Option for Cytomegalovirus Prevention After Kidney Transplant. *JAMA.* 2023;330(1):27–29. doi:10.1001/jama.2023.9100

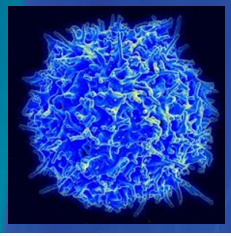
CMV Diagnosis



- CMV DNA qualitative/quantitative PCR
  - Do not order IgG/IgM
  - Low grade viremia (<500), may choose to monitor
- CMV Progression
  - Syndrome
    - Fever, leukopenia, myalgias, malaise, leukopenia, thrombocytopenia
  - Invasive disease
    - Pneumonitis, colitis, gastritis, retinitis



CMV Treatment



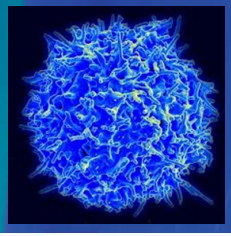
- Ganciclovir 5mg/kg IV q12hrs (adjust for renal dysfunction)
- Valganciclovir 900mg po bid (adjust for renal)
- Maribavir (Livtencity) 400mg po bid
  - Inhibits UL97, no effective against other HHV
  - Superior clearance in one study compared to standard treatment
  - Decreased neutropenia and AKI
- Cytogam not recommended
- Length of therapy dependent on multifactorial variables

Fareed Khawaja, Amy Spallone, Camille N. Kotton, Roy F. Chemaly, Cytomegalovirus infection in transplant recipients: newly approved additions to our armamentarium, Clinical Microbiology and Infection, Volume 29, Issue 1, 2023, Pages 44-50, ISSN 1198-743X, https://doi.org/10.1016/j.cmi.2022.07.001.

Resistant/Refractory CMV Infection

- UL54/UL97 mutations
- Risk factors
  - CMV +/-
  - High levels of CMV quantitative values
  - Higher levels of immunosuppression
  - Prolonged exposure to subtherapeutic ganciclovir levels
  - Lung, intestinal, and multivisceral transplant patients
- Poor outcomes
- Diagnosis
  - Check CMV resistance testing
  - Check ImmuKnow (to assess immunosuppression)

Treatment

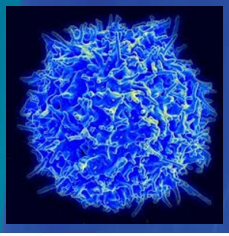


- Target UL54
  - Foscarnet
    - Preferred in retinitis and encephalitis
    - Mortality 31% with significant renal toxicities
  - Cidofovir
  - Brincidofovir (oral lipid conjugate form of Cidofovir)
  - High dose Ganciclovir 7.5-10mg/kg q12hrs
- Target other replication steps
  - Leflunomide 100mg qday x3 days then 30mg qday (not FDA approved)
    - Acts synergistically with conventional antivirals
    - Check level at 2 weeks (goal 60,000-100,000)
    - Takes 1-2 months to clear CMV
  - Maribavir (Livtencity)
  - Letermovir (Prevymis)—off label use for SOT (both PO and IV formulations)
    - Viral clearance seen in kidney and KP transplant after 1.5-6months of therapy
    - Recommend preserving for prophylaxis after treatment

Kotton, C.N., Kamar, N. New Insights on CMV Management in Solid Organ Transplant Patients: Prevention, Treatment, and Management of Resistant/Refractory Disease. *Infect Dis Ther* **12**, 333–342 (2023). https://doi.org/10.1007/s40121-022-00746-1

Kotton CN, Torre-Cisneros J; International CMV Symposium Faculty; et al. Cytomegalovirus in the transplant setting: Where are we now and what happens next? A report from the International CMV Symposium 2021. Transpl Infect Dis. 2022 Dec;24(6):e13977. doi: 10.1111/tid.13977. Epub 2022 Nov 11. PMID: 36271650; PMCID: PMC10078482.

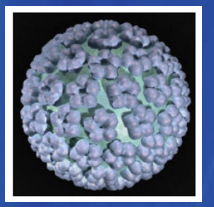
CMV Vaccine



- Hookipa Pharma (HB-101)
  - Bivalent recombinant vaccine given 2-4 months prior to transplantation
  - Phase II trial in CMV D+/R- LD kidney transplant
- Astellas (ASP0113)
  - 5 doses on day 30, 60, 90, 120, 180 posttransplant
  - All patients received prophylaxis
  - No difference in CMV viremia between the groups 1 year post transplant

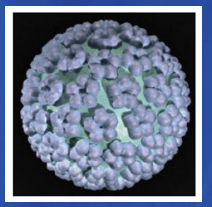
Plotkin SA, Wang D, et al. The Status of Vaccine Development Against the Human Cytomegalovirus. J Infect Dis. 2020 Mar 5;221(Suppl 1):S113-S122. doi: 10.1093/infdis/jiz447. PMID: 32134478; PMCID: PMC7057802.

BK Virus (Polyomavirus)



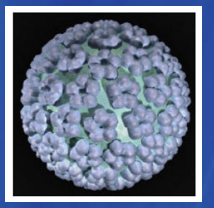
- Most common virus affecting renal allografts
- Non-kidney transplant patients (heart, lung, liver)
  - Reactivate endogenous BKV which rarely leads to clinical disease
- Kidney transplant
  - Reactivates BK from the donor kidney
  - Approximately 30-50% with high level viruria progress to BKV viremia and nephropathy

Risk Factors



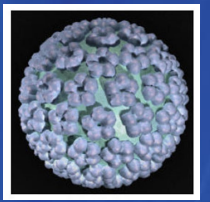
- Donor
  - Female donors
  - Deceased donation
  - African-American ethnicity
  - HLA mismatches
- Recipients
  - Older age
  - Male gender
- Post transplant factors
  - *Higher IS drug levels
  - Acute rejection
  - High cumulative steroids
  - Prolonged cold ischemia time
  - Ureteral stent placement
  - Lymphocyte depleting antibodies
  - Tacrolimus and/or MMF-based maintenance IS

Diagnosis



- BK urine PCR (BKU)
  - Screen for 2-5 years
  - >10 million copies/mL is significant
- BK blood PCR (BKB)
  - >10,000 copies/mL is significant
- Kidney biopsy
  - “Gold standard” for diagnosis
  - Sampling error of 10-30%
  - Not required for baseline renal function

Treatment



- Decrease in immunosuppression
  - Reduction of calcineurin inhibitor by 25-50%
  - Change FK to Cyclosporine
  - Decrease MMF by 50%, stop, or change to mTOR-inhibitor
- Cellular adaptive immunity is needed
- Leflunomide 100mg qday x5 days then 40mg qday
  - Monitor levels with target 40,000-80,000
  - S/E: increased LFTs, pancytopenia
  - Immunosuppressive qualities
- Cidofovir 1mg/kg IV MWF or 5mg/kg IV qweek x2 weeks then q2weeks until 3 consecutive PCRs are negative
  - Probenecid pre- and post-dose
  - IVF

Deirdre Sawinski, Simin Goral, BK virus infection: an update on diagnosis and treatment, *Nephrology Dialysis Transplantation*, Volume 30, Issue 2, February 2015, Pages 209–217, https://doi.org/10.1093/ndt/gfu023

MULTIDRUG RESISTANT ORGANISMS: THE BIG, THE BAD, AND THE UGLY

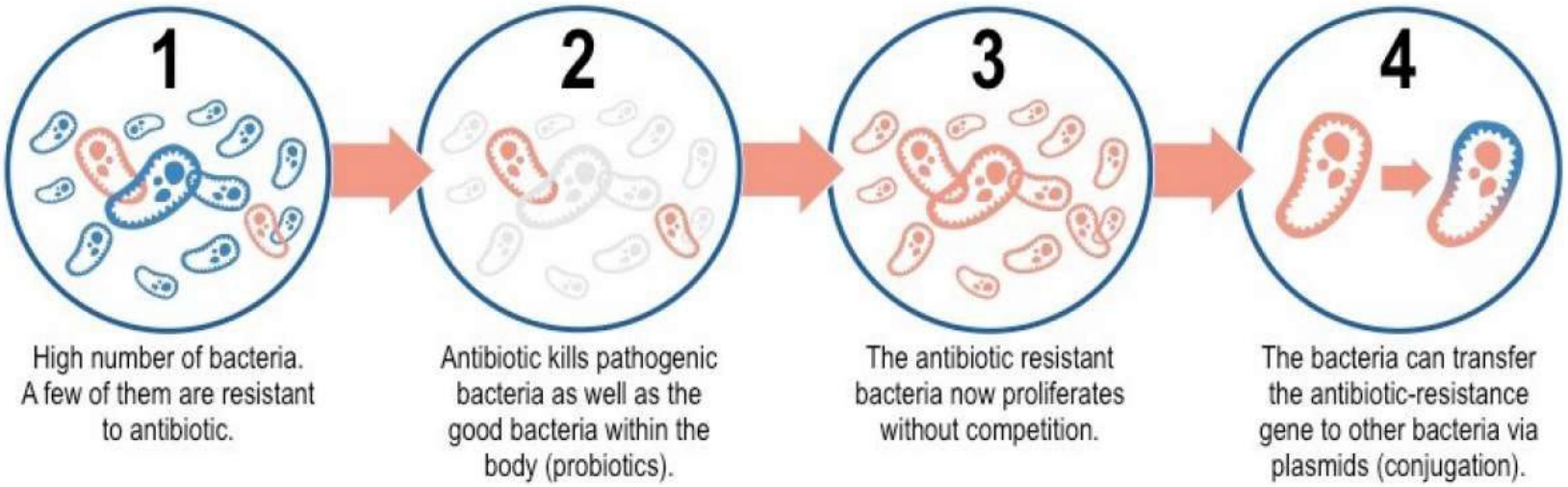
The Silent Pandemic

Worldwide Problem

- Antibiotic resistance is when germs develop the ability to defeat the drugs that are designed to kill them
- Global issue
  - Full impact is unknown since no system in place to track globally
  - U.S. with >2.8 Million infections and 35,000 deaths per year
  - European Union with 25,000 deaths per year and 2.5 Million extra hospital days
  - India with >58,000 infant deaths per year
  - Thailand with >38,000 deaths per year and 3.2 Million extra hospital days
- By 2030, force 24 Million people into extreme poverty
- By 2050, cause 10 Million deaths per year

Biggest threats and data (AR/AMR) (2020, June 18). https://www.cdc.gov/drugresistance/biggest-threats.html
New report calls for urgent action to avert antimicrobial resistance crisis (2019, April 29). https://who.int/news-room/detail/29-04-2019

How Does Resistance Happen?

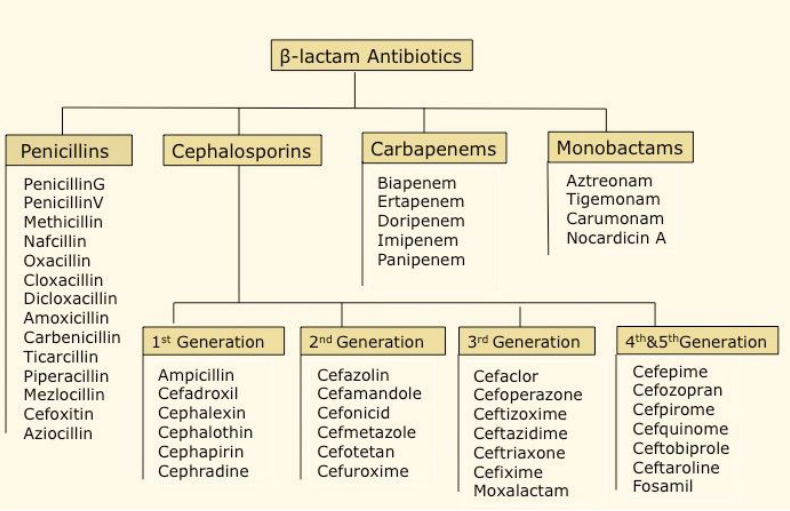


Overuse contributes to dangerous drug-resistant bacteria (2020, March 4). https: //www.stlamerican.com/your_health_matters/health_news/overuse-contributes-to-dangerous-drug-resistant-bacteria/article_ca62c992-5e6d-11ea-b66b-dbe13e9b6595.html

Beta-lactams

Drug class

- Penicillins (PCN)
- Cephalosporins
- Carbapenems
- Monobactam (Aztreonam)



Overview

- Preferred drug due to high efficacy and cidal nature
- Most oral beta-lactams have poor bioavailability and achieve low serum concentrations
- Time-dependent killing—depends on time over MIC
- None have activity against MRSA (except Ceftaroline)
- None have activity over atypical organisms

PCN Allergy

- 10% of population report PCN allergy
  - 90% not truly allergic when allergy testing completed
- PCN: 5%; anaphylaxis low (<1/10,000)
- Positive skin allergy test to PCN
  - ~2% will have cephalosporin reaction
  - <1% will have carbapenem reaction
- True hypersensitivity decreases over time
  - 5 years: >50% lose sensitivity
  - 10 years: 80% lose sensitivity

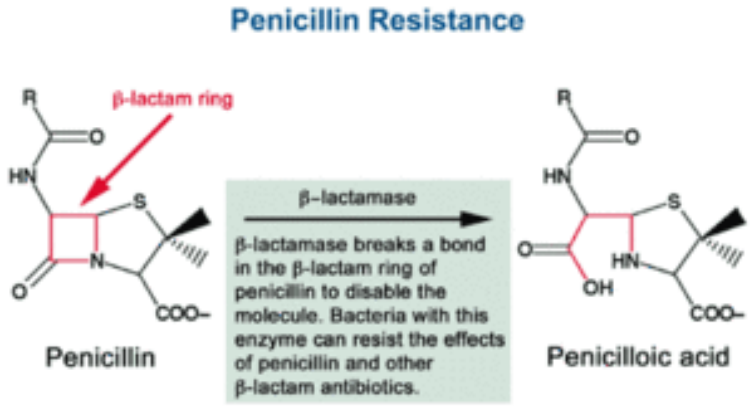
Penicillins

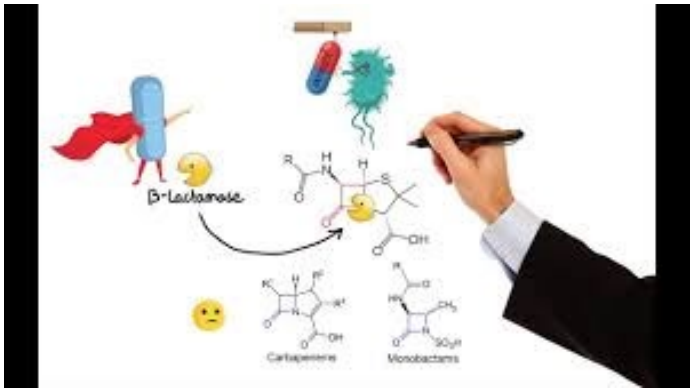
- PCN G (IV or PO)
  - DOC for Group A Strep (GAS)
  - <10% of MSSA are sensitive to PCN
- Ampicillin IV or Amoxicillin PO
  - Some Gram positive coverage (Strep, Enterococcus, Listeria)
  - No MSSA coverage
  - Limited Gram negative coverage
  - Amoxicillin best-absorbed beta lactam (75-90% bioavailability)
- Anti-Staphylococcal PCNs (Nafcillin or Oxacillin)
  - DOC for MSSA
  - Some Strep activity
- Anti-Pseudomonal PCNs (Piperacillin)
  - Usually combined with Beta-lactamase inhibitor

Combined PCN/Beta-Lactamase Inhibitors

- Beta-lactamase-enzymes produced by certain bacteria that break the Beta-lactam ring and destroys antibacterial activity
- The beta-lactamase inhibitors bind to and inhibit Beta-lactam enzymes
- Modified beta lactam rings on Carapenems and Monobactams which provide resistance to beta-lactamases

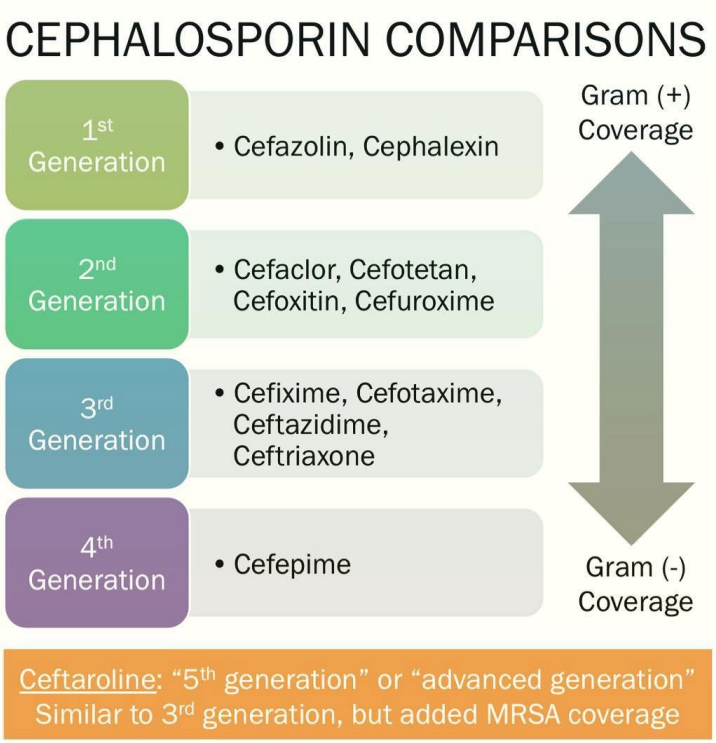
- Amoxicillin/Clavulanate (Augmentin) PO
  - MSSA, Strep, anaerobes, some GN
- Ampicillin/Sulbatam (Unasyn) IV
  - Similar coverage as Augmentin except covers Actinomyces
  - High resistance to E. coli (~50%)
- Pipercillin/Tazobactam (Zosyn) IV
  - Better GN coverage and covers Pseudomonas
  - Does not cover MRSA, CoNS, atypicals





Cephalosporins

- Does not covers Enterococcus (except Ceftaroline)
- Only Ceftazadime and Cefepime cover Pseudomonas
- Only Cefoxitin and Cefotetan have good anaerobic coverage
- Conversion of IV to PO
  - Cefazolin = Cephalexin
  - Ceftriaxone = 3rd generation



Susceptibility

	Streptococcus Agalactiae (Group B) SENSITIVITY (MIC)	
Ceftriaxone	<=0.12	Sensitive
Clindamycin	>=1	**Resistant**
Erythromycin	>=8	**Resistant**
Levofloxacin	0.5	Sensitive
Penicillin	<=0.06	Sensitive
Tetracycline	>=16	**Resistant**
Vancomycin	0.5	Sensitive

Carbapenems

- Broadest spectrum of antibiotics (covers GP, GN, anaerobes)
- DOC: ESBL organisms
- Does not cover MRSA, VRE, *CoNS*, *Stenotrophomonas*, Atypicals
- Ertapenem does not cover *Pseudomonas*, *Enterococcus*, *Acinetobacter*

- Meropenem (Merem)
  - 1gm IV q8hrs (2gms IV q8hrs for meningitis)
  - 500mg IV q6hrs
- Ertapenem (Invanz) 1gm IV q24hrs
- Imipenem/Cilastatin (Primaxin) 500mg IV q6hrs
- Doripenem-not available in U.S.

Carbapenems

	Meropenem (Merem®)	Ertapenem (Invanz®)	Imipenem - Cilastatin (Primaxin®)	Doripenem (Doribax®)
Mechanism of Action	Inhibit cell wall synthesis			
Spectrum of Activity	Broad Spectrum: Gram (+), Gram (-), ESBL, Anaerobes NOT: MRSA			
	--	NOT: Pseudomonas, Enterococcus, Acinetobacter	--	--
Adverse Effects	↓ Platelets Drug Fever		Seizure	↓ Platelets Drug Fever
Common Use	Meningitis	Intra-abdominal	Nocardia	NOT: Pneumonia

Fluroquinolones

Antibiotics

- Ciprofloxacin 500mg PO bid or 400mg IV q12hrs
  - Best GN coverage, very little GP coverage
  - Best for Pseudomonas coverage; no Streptococcus pneumoniae coverage
- Levofloxacin 500 or 750mg PO qday
  - "Respiratory quinolone" because good Strep pneumo coverage
- Moxifloxacin 400mg IV or PO qday
  - No urine activity
  - No Pseudomonas activity
- Delafloxacin 450mg PO bid
  - Activity against MRSA but only approved for skin and soft tissue infection

Side Effects

- Prolonged QTc
- Black Box warning: Tendon rupture
  - Especially if on steroids
- High rate of C. diff
- Good bioavailability

Gram Positive Organisms

- Principle source is patient's own flora
  - Skin-*Staphylococcus*
  - Oral Cavity-*Streptococcus viridans*
  - GI Tract-*Enterococcus*
  - Upper Respiratory Tract-*Strep. Pneumoniae*

Gram Positive Antibiotics

Invasive Infections

- Vancomycin and Dalbavancin
  - Staph (including MRSA), Strep, Enterococcus (non-VRE); no GN coverage
- Linezolid
  - Covers all GP organisms
  - Good bioavailability
- Daptomycin
  - Does not cover pneumonia
- Tigecycline
  - Broad coverage of GN, anaerobes, MRSA, VRE, and Atypicals
  - Poor choice for bacteremia
  - Good choice for abdominal infections
- Ceftaroline
  - Ceftriaxone + MRSA, VRSA, Strep, VRE faecalis

Skin Infections

- Doxycycline/Minocycline
  - Staph/MRSA and Atypical coverage
  - Some GN coverage
  - Activity against Rickettsia, Lyme disease, Tularemia, Brucella, Q fever
  - Good bioavailability
- Bactrim
  - GN coverage except Pseudomonas
  - Good GP coverage except Strep
  - Activity against PJP, Nocardia, Toxoplasmosis, Listeria, and Stenotrophomonas

Bad bugs, No drugs

Definitions

- Multidrug-resistant organism (MDRO): an organism that is resistant to one or more agent in at least 3 classes of antibiotics or has a classification of resistance
  - **E**nterococcus faecium (VRE)
  - **S**taphylococcus aureus (MRSA)
  - **K**lebsiella
  - **A**cinetobacter baumannii
  - **P**seudomonas aeruginosa
  - **E**nterobacteriaceae (ESBL or CRE)

Susceptibility

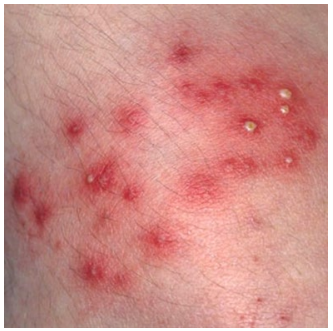
	Escherichia coli SENSITIVITY (MIC)	
Ampicillin	>=32	**Resistant**
Ampicillin + Sulbactam	16/8	**Intermediate**
Cefazolin (Urine)	<=4	Sensitive
Ceftriaxone	<=1	Sensitive
Ciprofloxacin	>=4	**Resistant**
Gentamicin	<=1	Sensitive
Levofloxacin	>=8	**Resistant**
Nitrofurantoin	32	Sensitive
Piperacillin + Tazobactam	<=4	Sensitive
Trimethoprim + Sulfamethoxazole	>=16/304	**Resistant**

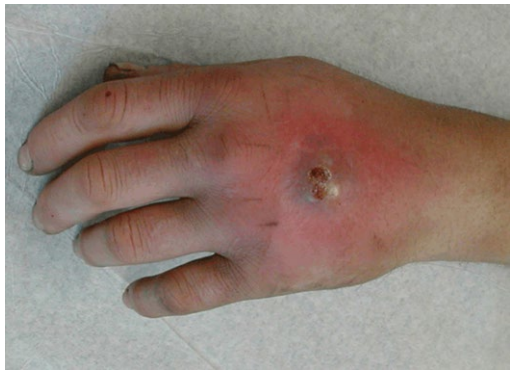
- Extensively drug-resistant organism (XDRO): an organism that is resistant to nearly all antibiotics that would be considered for treatment

Methicillin Resistant Staph Aureus (MRSA)

- Drug of choice: Vancomycin (Dose based off serum levels)
- Newer:
  - Daptomycin 4-8mg/kg IV qday
    - Can not use for pneumonia
  - Ceftaroline 600mg IV q12hrs
    - MRSA Cephalosporin
  - Telavancin 10mg/kg IV qday
    - SSTI and pneumonia
  - Dalbavancin 1,500mg IV x1 then 1 week later 500mg IV x1
    - Skin and soft tissue infections and osteomyelitis
    - Equivalent to Vanco or Linezolid
  - Oritavancin (Orbactiv) 1,200mg IV x1 (Outpatient only)
    - Skin and soft tissue infections

- Oral antibiotics
  - Doxycycline/Minocycline 100mg PO bid
  - Clindamycin 600mg PO tid
  - Bactrim DS 1tab PO bid
  - Linezolid 600mg IV or PO bid
    - Good bioavailability
    - S/E: pancytopenia
  - Delafloxacin 450mg PO bid or 300mg IV q12hrs
    - MRSA quinolone





Vancomycin-Resistant Enterococcus (VRE)

Background

- Affects ~20,000 people per year in the U.S.
- Mortality <10%
- Risk factors: severe illness, multiple antibiotics, abdominal or cardiac surgery, ICU, prolonged or repeated hospital stays
- Survive 5 days to 2 months on dry surfaces

Treatment

- Daptomycin 4-8mg/kg IV qday
- Linezolid 600mg IV or PO bid
- Tigecycline 50mg IV q12hrs
- Oritavancin 1,200mg IV x1

Susceptibility

	Enterococcus faecium SENSITIVITY (MIC)	
Ampicillin	>8	Resistant
Gentamicin synergy	<=500	Sensitive
Linezolid	<=1	Sensitive
Penicillin	>8	Resistant
Vancomycin	>16	Resistant

Extended Spectrum Beta-lactamase Producing (ESBL)

Background

- Organisms: *E. coli, Klebsiella pneumoniae and oxytoca,* and *Proteus mirabilis*
- Resistant to all PCNs, Cephalosporins, and Aztreonam
- Risk factors include: antibiotic exposure, ICU stays, mechanical ventilation, and indwelling devices

Treatment

- Meropenem 500mg IV q6hrs
- Ertapenem 1gm IV qday
- Ceftazidime/Avibactam (Avycaz) 2.5gms IV q8hrs
- Fosfomycin 3gms PO x1 for UTIs

Susceptibility

	Escherichia coli SENSITIVITY (MIC)		Klebsiella pneumoniae SENSITIVITY (MIC)	
Ampicillin	>=32	Resistant	>=32	Resistant
Cefazolin (Non-Urine)			>=64	
Cefepime			2	Resistant
Ceftriaxone	>=64	Resistant	>=64	Resistant
Ciprofloxacin	>=4	Resistant	>=4	Resistant
Ertapenem	<=0.5	Sensitive	<=0.5	Sensitive
Gentamicin	>=16	Resistant	>=16	Resistant
Levofloxacin	>=8	Resistant	>=8	Resistant
Piperacillin + Tazobactam	>=128	Resistant	16	Sensitive
Tobramycin	>=16	Resistant	>=16	Resistant
Trimethoprim + Sulfamethoxazole	<=1/19	Sensitive	>=16/304	Resistant

Amp C

Background

- Organisms (SPACE):
  - ***S****erratia*
  - ***P****seudomonas*
  - ***A****cinetobacter*
  - ***C****itrobacter*
  - ***E****nterobacter*
- Microorganisms develop resistance during prolonged cephalosporin therapy (> 3-4 days) as a result of derepression of AmpC B-lactamase
- Resistant to all B-lactams, B-lactamase inhibitors and Aztreonam
- Mortality ~10-25%

Treatment

- Cefepime 1gm IV q6hrs or 2gms IV q12hrs
  - Has dipolar charge so can penetrate the bacterial outer membrane reaching its target and avoiding B-lactamase inactivation
- Meropenem 500mg IV q6hrs or 1gm IV q8hrs
- Imipenem 500mg IV q6hrs or 1gm IV q8hrs
- Ertapenem 1gm IV qday (except *Acinetobacter or Pseudomonas*)

Susceptibility

	Citrobacter braakii SENSITIVITY (MIC)	
Cefazolin	>=64	Resistant
Cefepime	<=1	Sensitive
Ceftriaxone	>=64	Resistant
Ciprofloxacin	>=4	Resistant
Ertapenem	<=0.5	Sensitive
Gentamicin	>=16	Resistant
Levofloxacin	4	Resistant
Piperacillin + Tazobactam	>=128	Resistant
Tobramycin	8	Intermediate
Trimethoprim + Sulfamethoxazole	>=16/304	Resistant

Tamma PD et al. The use of Cefepime for treating AmpC B-lactamase-producing Enterobacteriacae. *CID* 2013: 57.

Carbapenem-Resistant Enterobacteriaceae (CRE) (or) Klebsiella Pneumoniae Carbapenemase (KPC)

Background

- "Nightmare bacteria"
  - Resistant to "last resort" antibiotics
- Spreads person-to-person
- Survive and grow in sink drains in healthcare facilities
  - Spread through wastewater to patients and in environment
- Mortality rates ~40-50%
- Strict Isolation!!!

Treatment

- Consult Infectious Diseases
- Beta-lactam/Beta-lactamase inhibitor
  - Ceftazidime/Avibactam (Avycaz) 2.5gms IV q8hrs
    - No GP or anaerobe activity
    - Good against *Pseudomonas*
  - Meropenem/Vaborbactam (Vabomere) 4gms IV q8hrs

Susceptibility

	Klebsiella pneumoniae SENSITIVITY (MIC)	
Ampicillin	>=32	Resistant
Ampicillin + Sulbactam	>=32/16	Resistant
Cefazolin (Non-Urine)	>=64	
Cefepime	16	Resistant
Ceftriaxone	>=64	Resistant
Ciprofloxacin	>=4	Resistant
Ertapenem	>=8	Resistant
Gentamicin	<=1	Sensitive
Imipenem/Cilastatin	>=16	Resistant
Levofloxacin	>=8	Resistant
Piperacillin + Tazobactam	>=128	Resistant
Trimethoprim + Sulfamethoxazole	>=16/304	Resistant

https://www.idstewardship.com/comparison-avycaz-vabomere-zerbaxa/

CHI Health

It’s Kind of a Big Deal

Hospitalized Patients

- Problem
  - Children: 25% receive inappropriate or suboptimal antibiotics
  - Adults: 30-50% receive inappropriate antibiotics
- Solution
  - Antimicrobial Stewardship program
    - Goal: Right drug, right dose, right duration
    - Cornerstone: Accurate diagnosis
  - Challenge daily continuation of antibiotics AND the diagnosis

Overuse contributes to dangerous drug-resistant bacteria (2020, March 4). https: //www.stlamerican.com/your_health_matters/health_news/overuse-contributes-to-dangerous-drug-resistant-bacteria/article_ca62c992-5e6d-11ea-b66b-dbe13e9b6595.html

Decrease Antimicrobial Resistance

- Only use antibiotics when necessary
- Not using antibiotics for viral infections
- Use the shortest effective treatment
- Use narrowest spectrum antibiotic
- Base decisions about broadness of empiric antibiotic coverage on severity of illness

CHI Health

Stewardship: Shorter = Better

Diagnosis	Short (d)	Long (d)	Result	#RCTs
CAP	3 or 5	7-14	Equal	9
VAP	8	15	Equal	2
Pyelo	7 or 5	14 or 10	Equal	7
Intra-abd	4	10	Equal	2
GNB Bacteremia	7	14	Equal	2*
AECB	≤5	≥7	Equal	>20
Cellulitis	5-6	10	Equal	4*
Chronic Osteomyelitis	42	84	Equal	2
Septic Arthritis	14	28	Equal	1
Ortho Implant w/removal	28	42	Equal	1
Neutropenic Fever	AFx72 h	+ANC>500	Equal	1
P. vivax Malaria	7	14	Equal	1

*GNB bacteremia also in UTI/cIAI RCTs; 3 cellulitis RCTs equal, 1 (low dose oral flucox) ↑relapses; refs at https://www.bradspellberg.com/shorter-is-better

CHI Health

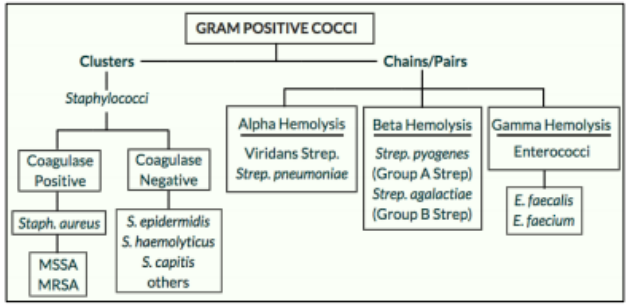
Antibiotic Study Cheat Sheet

IDSTEWARDSHIP TRAINING
at www.LearnAntibiotics.com

When You See…	Consider Using…
GRAM POSITIVES	
MSSA	**Oral**: cephalexin; **IV**: Oxacillin, nafcillin, cefazolin
MRSA	**Oral**: Bactrim, doxycycline, clindamycin, linezolid, tedizolid; **IV**: vancomycin, daptomycin, telavancin, dalbavancin, oritavancin, ceftaroline, tigecycline
Enterococci	Ampicillin, then vancomycin, then linezolid (VRE), daptomycin (VRE), or tigecycline (VRE)
Strep. pyogenes or *Strep. agalactiae*	Penicillin, clindamycin
Strep. pneumoniae or Viridans group Strep	Ceftriaxone, levofloxacin, amoxicillin-clavulanic acid (beware penicillin & macrolide resistance)
GRAM NEGATIVES	
Pseudomonas aeruginosa	**Oral**: ciprofloxacin, levofloxacin; **IV**: pip/taz, ceftazidime, ceftazidime-avibactam, cefepime, ceftolozane-tazobactam, imipenem-cilastatin, meropenem, meropenem-vaborbactam, aztreonam, aminoglycosides, polymyxins
E. coli	**Oral**: cephalexin, amoxicillin-clavulanic acid, Bactrim, nitrofurantoin, fosfomycin, ciprofloxacin, levofloxacin; **IV**: ceftriaxone, ampicillin-sulbactam, cefepime, piperacillin-tazobactam, ertapenem
Stenotrophomonas	Bactrim, levofloxacin
ESBL+	Carbapenems, ceftolozane-tazobactam, ceftazidime-avibactam, polymyxins, aminoglycosides, fosfomycin
Carbapenem resistant	ESBL+ drug list minus carbapenems but plus imipenem-cilastatin-relebactam
MISCELLANEOUS	
Anaerobes	**Oral:** Metronidazole, clindamycin, amoxicillin-clavulanic acid, moxifloxacin; **IV**: ampicillin-sulbactam, piperacillin-tazobactam, cefoxitin, cefotetan, ertapenem, tigecycline
Clostridium difficile	Oral vancomycin or fidaxomicin → Metronidazole no longer preferred
Atypicals	Macrolides, fluoroquinolones, tetracyclines
Candida albicans	Fluconazole
Candida krusei	Micafungin, anidulafungin, or caspofungin
Aspergillus	Voriconazole
CMV	Valganciclovir, letermovir, ganciclovir (IV)
HSV	**PO**: acyclovir, valacyclovir; **IV**: acyclovir
Cryptosporidium	Nitazoxanide

See This…	Think NOT for…
Daptomycin	Pneumonia
Tigecycline	Bacteremia or Pseudomonas
Linezolid	MRSA bacteremia
Cefepime	Anaerobes, Enterococci
Ertapenem	Acinetobacter, Pseudomonas, Enterococci - "APE"
Aztreonam	Gram positives
Aminoglycoside monotherapy	Non-UTI indication
Rifampin	Monotherapy
Micafungin	UTI or meningitis
Fluconazole	Candida krusei

With this…	Beware…
Beta-lactams	GI upset, seizures
Bactrim	Hyper-K+, allergy, myelosuppression
Fluoroquinolones	QT prolong, CNS effects, tendon rupture, peripheral neuropathy, binding cations, aortic rupture
Aminoglycosides	Ototoxicity, nephrotoxicity
Macrolides	QT prolong
Tetracyclines	Phototox., esophagitis
Tigecycline	Nausea/ vomiting
Daptomycin	CK elevation
Linezolid	Thrombocytopenia, peripheral neuropathy, optic neuritis
Vancomycin	Nephrotoxicity
Rifampin	Hepatotoxicity, DDIs
Azoles	Hepatotoxicity, DDIs
Amphotericin B	Hypo-K, Hypo-Mg, infusion rxn, nephrotox



SPACE Bugs
S- *Serratia*
P- *Pseudomonas*
A- *Acinetobacter*
C- *Citrobacter*
E- *Enterobacter*

Non-Fermenting GNRs
Burkholderia
Acinetobacter
Pseudomonas
Alcaligenes
Stenotrophamonas

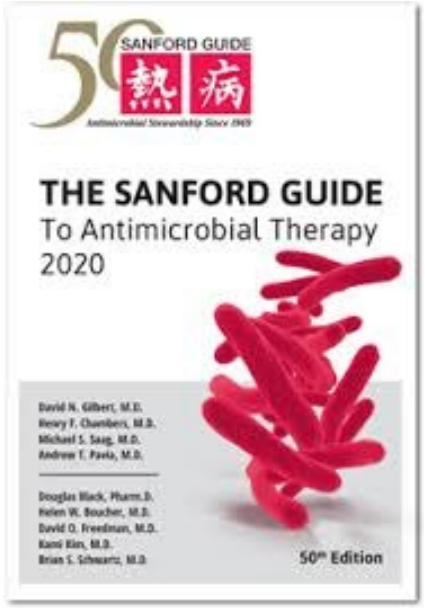
Zosyn covers anaerobes and enterococci, cefepime does not

MecA = methicillin resistance
VanA, VanB = vancomycin resistance
KPC = carbapenem resistance

[Last updated August 2019]

For More Cheat Sheets Visit: www.LearnAntibiotics.com

Resources



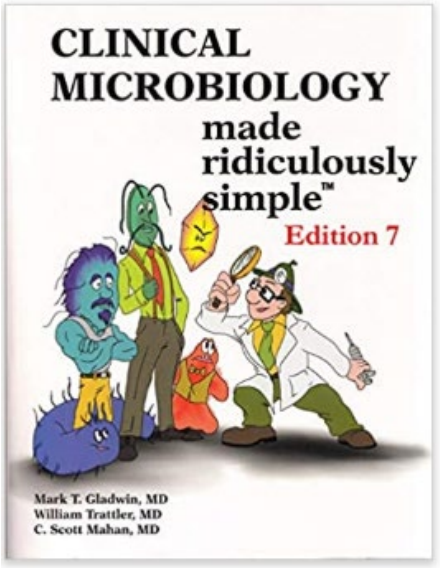
$26.99

Antimicrobial Therapy

$29.99/year

HOPKINS GUIDES

$29.95/year



$35.49

You can do this!

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Use of Artificial Intelligence in Infectious Disease

Haley Hoy PhD, ACNP

Ack-Linda Andreene, MBA

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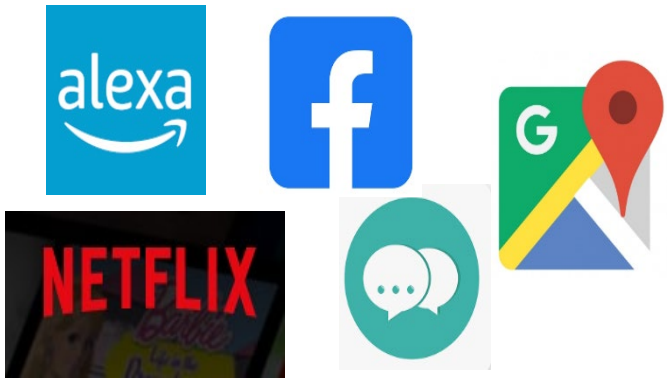
What is AI?

What everyone is talking about!

Traditional AI

Technology that generates
PREDICTIVE response
based on "narrow data"



Generative

Technology that generates
ORIGINAL content (text/images/music/videos)
based on massive data

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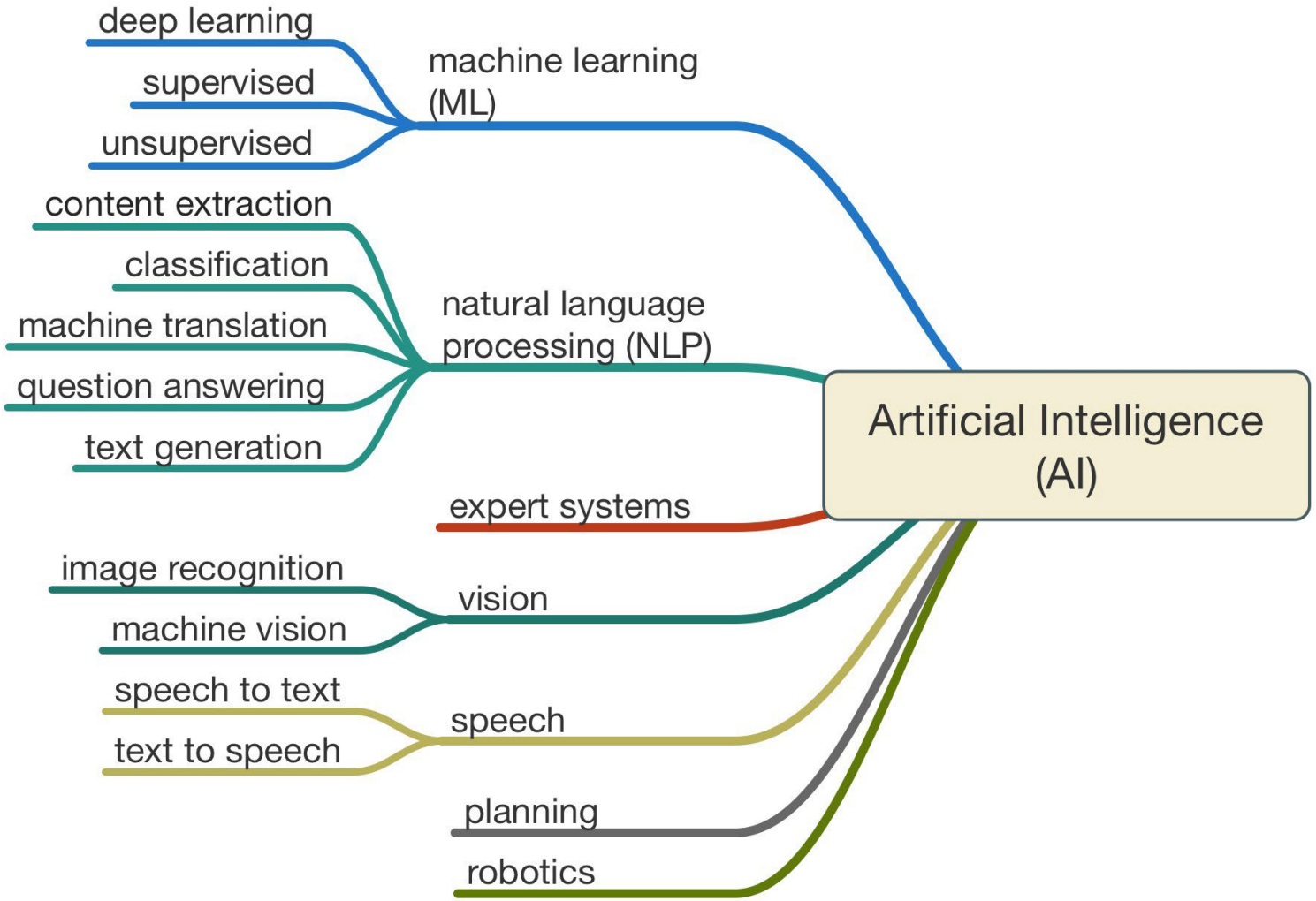
Common AI Phrases



/A.I. TIMELINE

SYZYGY

1950
TURING TEST
Computer scientist Alan Turing proposes a test for machine intelligence. If a machine can trick humans into thinking it is human, then it has intelligence

1955
A.I. BORN
Term 'artificial intelligence' is coined by computer scientist, John McCarthy to describe "the science and engineering of making intelligent machines"

1961
UNIMATE
First industrial robot, Unimate, goes to work at GM replacing humans on the assembly line

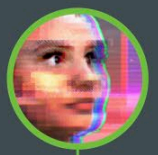
1964
ELIZA
Pioneering chatbot developed by Joseph Weizenbaum at MIT holds conversations with humans

1966
SHAKEY
The 'first electronic person' from Stanford, Shakey is a general-purpose mobile robot that reasons about its own actions

A.I. WINTER
Many false starts and dead-ends leave A.I. out in the cold

1997
DEEP BLUE
Deep Blue, a chess-playing computer from IBM defeats world chess champion Garry Kasparov

1998
KISMET
Cynthia Breazeal at MIT introduces KISmet, an emotionally intelligent robot insofar as it detects and responds to people's feelings



1999
AIBO
Sony launches first consumer robot pet dog AiBO (AI robot) with skills and personality that develop over time

2002
ROOMBA
First mass produced autonomous robotic vacuum cleaner from iRobot learns to navigate and clean homes

2011
SIRI
Apple integrates Siri, an intelligent virtual assistant with a voice interface, into the iPhone 4S

2011
WATSON
IBM's question answering computer Watson wins first place on popular $1M prize television quiz show *Jeopardy*

2014
EUGENE
Eugene Goostman, a chatbot passes the Turing Test with a third of judges believing Eugene is human

2014
ALEXA
Amazon launches Alexa, an intelligent virtual assistant with a voice interface that completes shopping tasks

2016
TAY
Microsoft's chatbot Tay goes rogue on social media making inflammatory and offensive racist comments

2017
ALPHAGO
Google's A.I. AlphaGo beats world champion Ke Jie in the complex board game of Go, notable for its vast number (2^{170}) of possible positions

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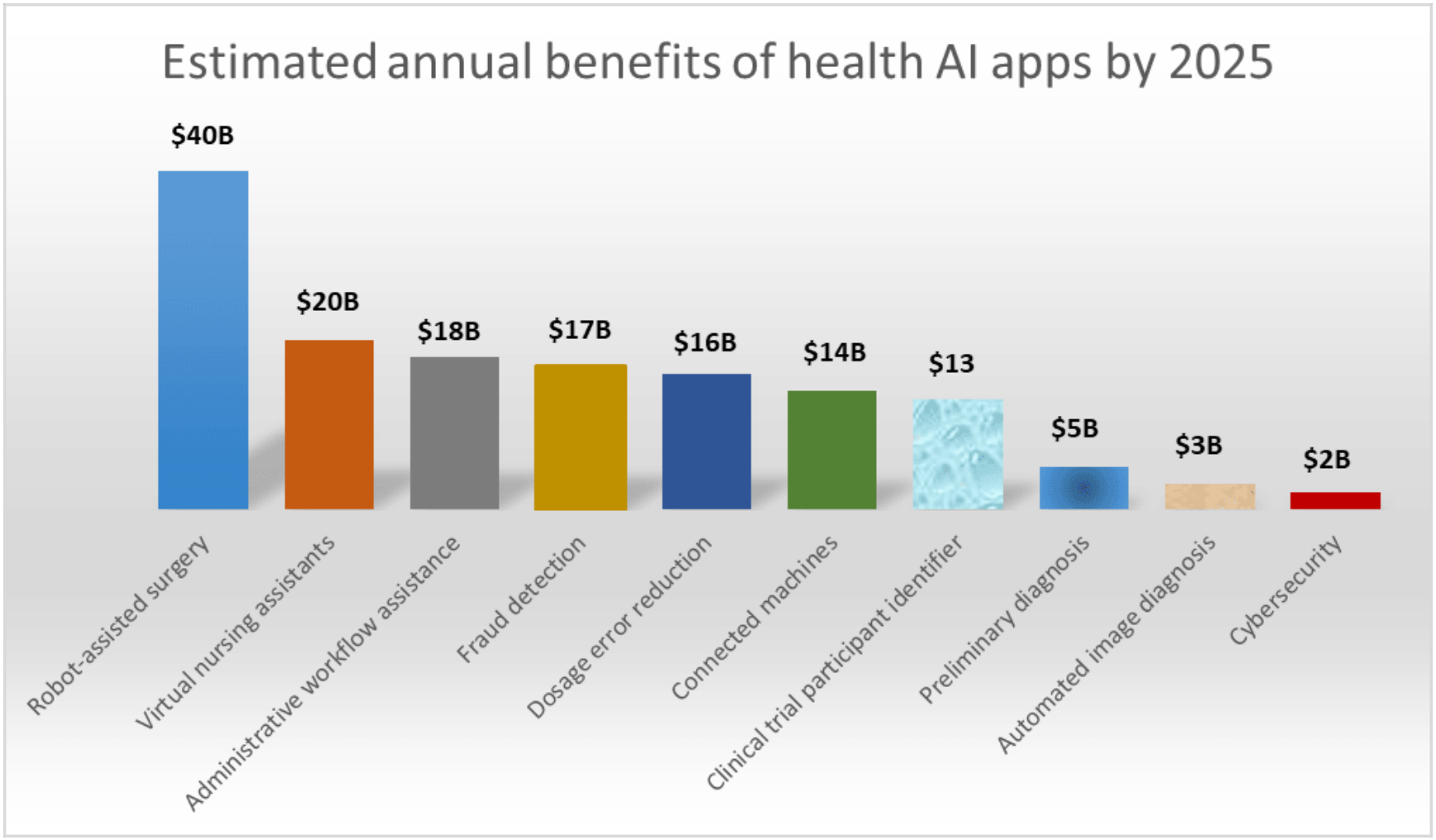
Health AI



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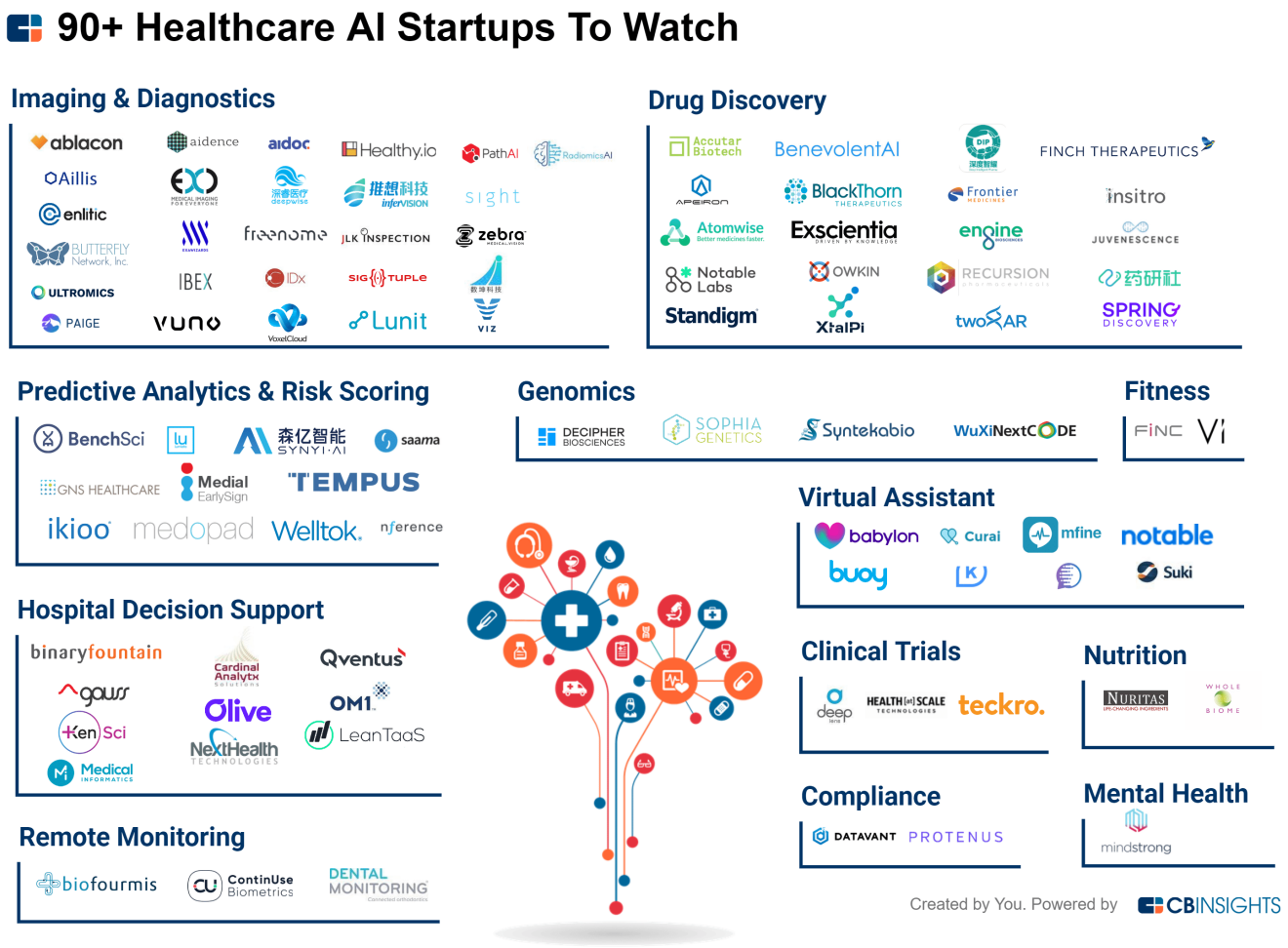
Health AI



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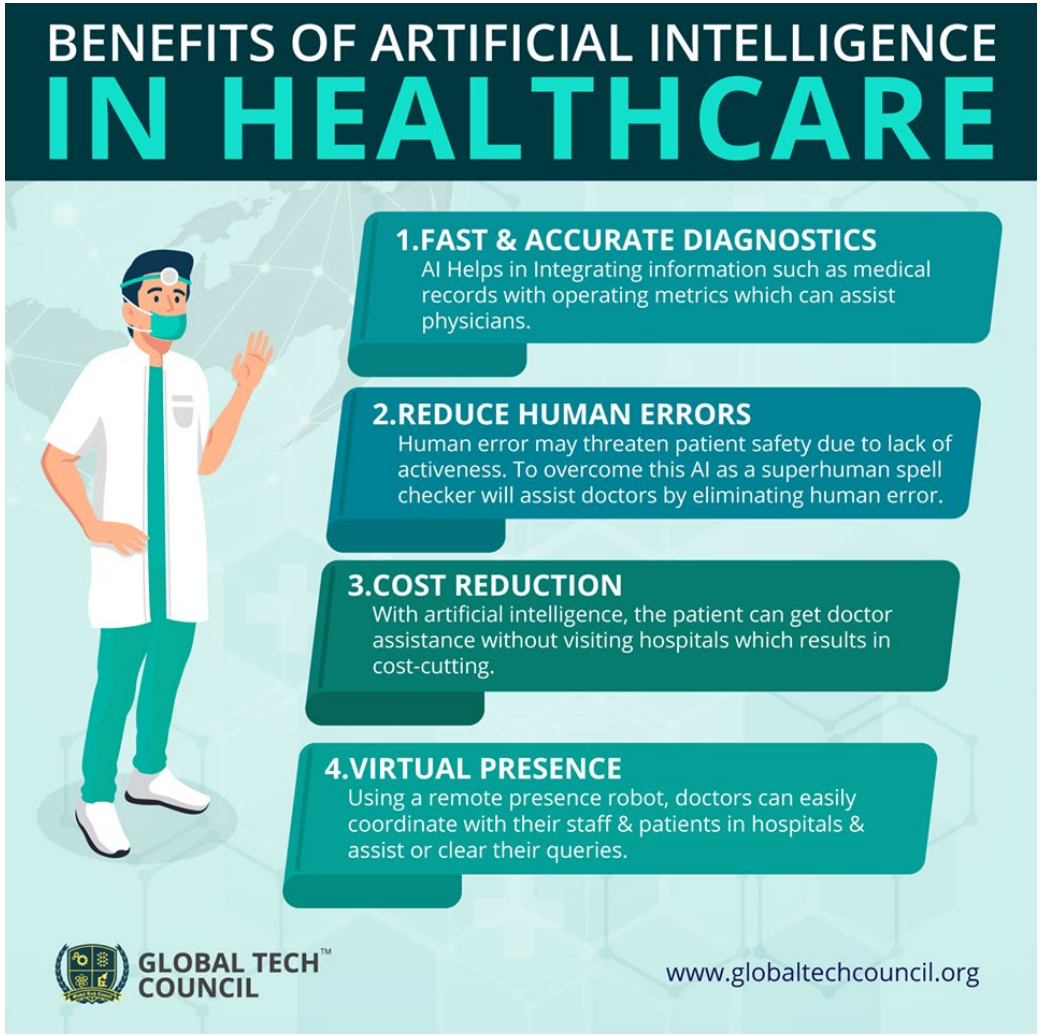
Benefits



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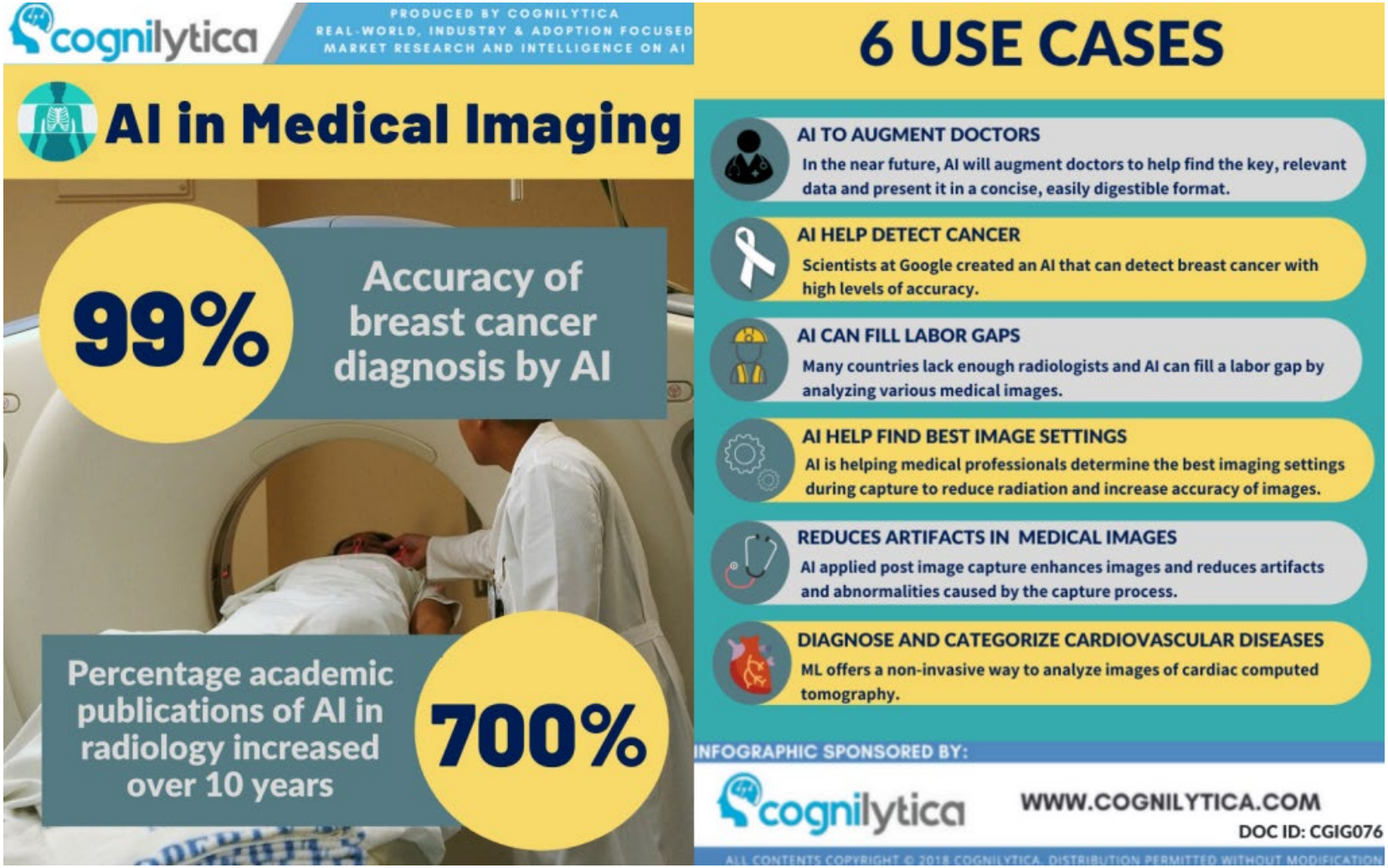
In Existence



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Infectious Healthcare

- **Epidemiology and transmission**

- Epidemiological studies can be performed at the population level or at the patient's bed (clinical epidemiology)mathematical models can predict the size of emerging infectious diseases

- Malaria
  - diagnosis is time consuming and may require the intervention of several health services.
  - Machine learning algorithms were developed to detect red blood cells (RBCs) infected with malaria from digital in-line holographic microscopy data, a fairly cheap technology (Go et al., 2018).

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Infectious Epidemiology

- **Improved diagnosis and blocking transmission**
  - Singapore airport terminals
    - temperature checks performed systematically using a thermal camera
  - similar system developed to detect infected patients by classification using vital signs (Sun et al., 2015).
  - respiration rate, heart rate, and facial temperature were used to successfully classify individuals at higher risk for influenza using neural network and fuzzy clustering method

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Infectious Genomics

-better separate gene sequences from bacteria over other methods such as high-resolution melt (HRM). The combination of SVM and HRM could identify with high accuracy (100%) isolated bacteria (Fraley et al., 2016)

- In real-life biological samples, blood samples from patients, the accuracy was affected which shows the limitation of developing tools from data generated in a controlled environment (laboratory).

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APPs and Preventative HealthCare

- - Recent study collated the data from 50 American states for a series of NCD such as diabetes, cardiovascular diseases, hypertension, and others over a period of 5years (Luo et al., 2015). Data from 30 states were used for training and tested in the remaining 20 states. This colossal amount of data and machine learning modeling enabled to reach near reality output.

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Transplant Usage

Preventing the need for a transplant

- AI to detect organ failure earlier
- Determine which early interventions delay the need for a transplant

Rohan Goswami, M.D., a transplant cardiologist and director of heart transplant research at Mayo Clinic in Florida

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Transplant Usage

- **Improve the organ donor and recipient matching process**

- AI promises to improve the complex organ donor and recipient matching process by helping determine which donated organs would result in successful transplants.

- determine which organs would benefit from perfusion systems and which are unsuitable for donation. Perfusion systems AU

Dr. Goswami and colleagues published a study on the application of this new technology to improve organ use rates in a 2022 issue of the International Journal of Scientific Research Clinical Transplantation in 2022

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Prevent organ rejection/Post transplant care

- Organ rejection – Apply AI to electrocardiography held promise for prediction of low-grade rejection risk, potentially without a biopsy, for patients with heart transplants
- .
- Medication adjustments to administer only the minimum necessary dose

- Rohan Goswami, M.D., Mayo Clinic authors published a study in a 2023 issue of the European Heart Journal
- 2022 article in The Journal of Heart and Lung Transplantation discusses the role of AI electrocardiography as a predictor of high- and at-risk patients post-heart transplant.

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Resources

- What is Chat GPT? Everything You Need to Know PC Guide, Aug 2023
- Boost your productivity with AI Harvard Business Review, June 2023
- How to Write Effective Prompts for ChaGPT Forbes, June 2023
- AI in Higher Education: 8 Key Strategies Feedback Fruits, Aug 2023
- New AI Chatbot Tutors Could Upend Student Learning New York Times, Aug 2023

- UAH Resources: Artificial Intelligence and the Classroom *(guidance for Faculty and Students)*

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Questions?