UW TASP tele-antimicrobial stewardship program | echo

Antifungal Stewardship

Erica Stohs, MD, MPH

May 15, 2018

This presentation is intended for educational use only, and does not in any way constitute medical consultation or advice related to any specific patient.

Outline

- What is antifungal stewardship?
- Opportunities
  - Immunocompromised
  - Immunocompetent: Target *Candida*
- *Candida* Resistance

Antifungal Stewardship

- Goal: Optimize the use of antifungals to achieve the best outcomes while minimizing adverse events and limiting selection pressures that drive resistance.
- Right drug, right dose, right duration, right patient
- Challenges:
  - Diagnostics vary (timing, sensitivity, specificity)
  - →Overutilization & high costs
  - Immunocompromised patients

Pfaller, MA et al. *Medical Mycology* 2016;54: 1-22.
Ananda-Rajah et al. *Current Opinion in ID* 2012; 25(1): 107-15.

How We Use Antifungal Drugs

Prophylaxis Empiric Targeted Definitive

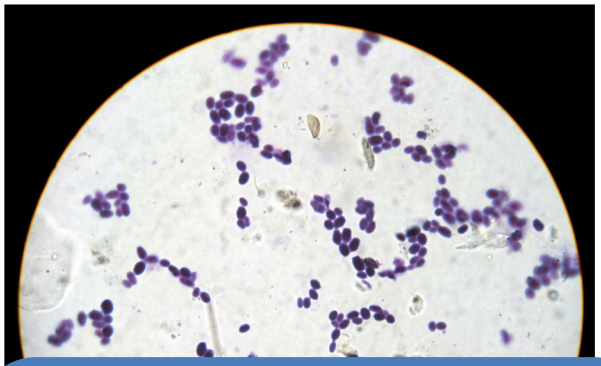
Depends on the host:

How We Use Antifungal Drugs

Prophylaxis Empiric Targeted Definitive

Depends on the disease:

Puln



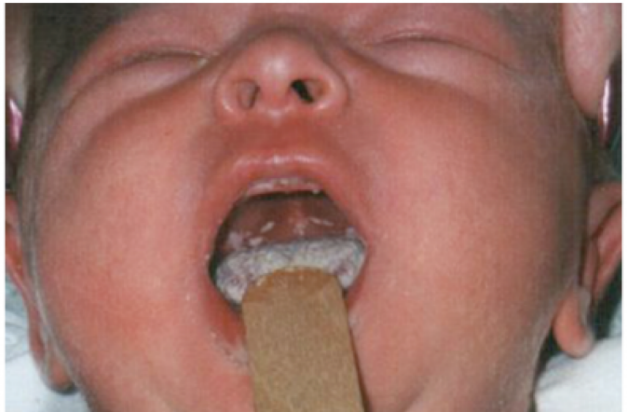
Daily Costs:
Posaconazole: $500
Voriconazole: $200

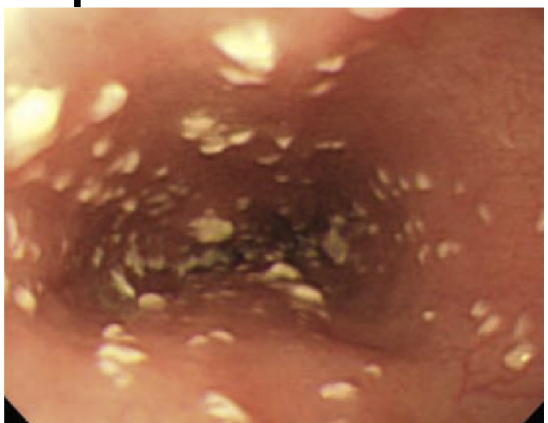
Daily Costs:
Micafungin: $62
Fluconazole: $4

UWTASP
tele-antimicrobial stewardship program

Let's Focus on Candidiasis

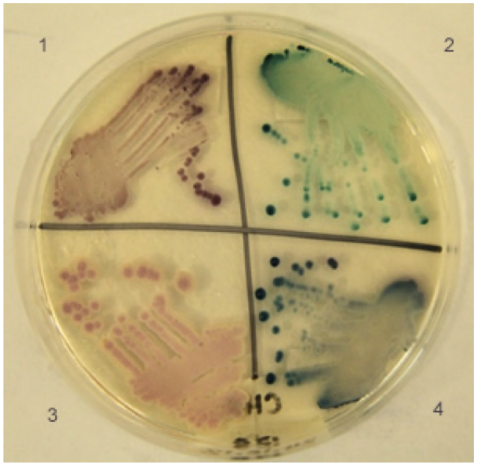
- Fungal infection caused by yeasts from genus *Candida*
- Most common species: *Candida albicans*
- NORMALLY lives on mucous membranes (oropharynx, esophagus, vagina) without causing infections
- Overgrowth can lead to symptoms

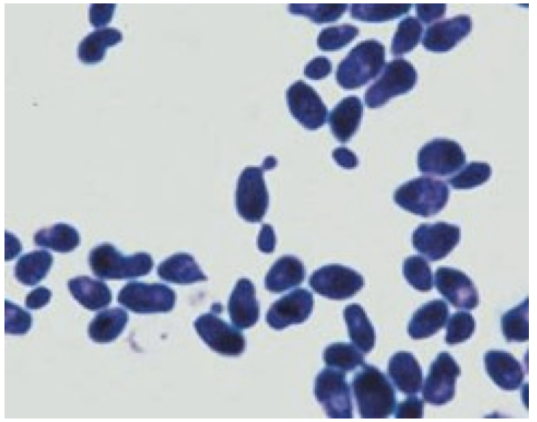




Invasive Candidiasis

- Candidemia
- 4th most common cause of health-care associated bloodstream infections in the US
  - 46,000 / year
  - Each case results in 3-13 days of additional hospitalization
  - Est. $6k – 29k additional costs per case → Millions of $$ annually





https://www.cdc.gov/drugresistance/threat-report-2013/index.html

Invasive Candidiasis

- Over 15 distinct Candida species, but >90% of invasive disease is caused by these 5:

Species	% of total by surveillance program (No. of isolates)		
	SENTRY[a] (860)	PATH[b] (3,648)	CDC[c] (2,209)
C. albicans	47	42	41
C. glabrata	18	27	27
C. parapsilosis	18	16	18
C. tropicalis	11	9	9
C. krusei	1	3	2
Other	5	3	3

Risk Factors for Candidemia

Pfaller, M. et al. *Clin Micro Reviews* 2007;20(1): 133-63.

RISK FACTOR	ROLE
Antibiotics - number & duration	IV access & ↑colonization
Corticosteroids	Immunosuppression ↑↓
Age (extremes)	Immunosuppression
Chemotherapy / malignancy / neutropenia	Immunosuppression
Gastric acid suppression	↑colonization
Indwelling catheter	IV access
TPN	IV access, hyperglycemia, possible contamination
Surgery	Route, IV access
Mechanical ventilation	Route
Renal failure / Hemodialysis	IV access, immunosuppression
Malnutrition	Immunosuppression
Hospital or ICU stay, duration	Exposure to factors above

Case 1

- A 66 yo M is mechanically ventilated in the ICU following a MVA where he sustained abdominal trauma. On day 7 after two days of high fevers, his blood culture is reportedly growing yeast.
- What should you start empirically?

A. Micafungin 100 mg IV
B. Fluconazole 400 mg IV
C. Caspofungin 50 mg IV
D. A or C

Case 1

- A 66 yo M is mechanically ventilated in the ICU following a MVA where he sustained abdominal trauma. On day 7 after two days of high fevers, his blood culture is reportedly growing yeast.
- What should you start empirically?

A. **Micafungin 100 mg IV**
B. Fluconazole 400 mg IV
C. Caspofungin 50 mg IV
D. A or C

Clinical Infectious Diseases
IDSA GUIDELINE

Clinical Practice Guideline for the Management of Candidiasis: 2016 Update by the Infectious Diseases Society of America

Candidemia Treatment in Non-neutropenic Patients:

Echinocandins: (strong rec, high-quality evidence)

- Micafungin 100 mg daily
- Caspofungin 70 mg load, then 50 mg daily
- Anidulafungin 200 mg load, then 100 mg daily

Fluconazole IV or PO 800 mg load, then 400 mg daily

- IF not critically ill
- AND unlikely to have fluc-resistant *Candida*

Case 1 – Part 2

- While you await speciation for the previous patient, you note that *Candida* grew from cultures from the patient's endotracheal tube and urine from his foley catheter. He has a R IJ central venous catheter from which the blood culture was drawn.
- What lines or tubes need to be removed or exchanged ASAP?

A. Endotracheal tube
B. Foley catheter
C. Central venous catheter and repeat blood cultures
D. All of the above

Case 1 – Part 2

- While you await speciation for the previous patient, you note that *Candida* grew from cultures from the patient's endotracheal tube and urine from his foley catheter. He has a R IJ central venous catheter from which the blood culture was drawn.
- What lines or tubes need to be removed or exchanged ASAP?

A. Endotracheal tube
B. Foley catheter
C. **Central venous catheter and repeat blood cultures**
D. All of the above

Clinical Infectious Diseases
IDSA GUIDELINE

Clinical Practice Guideline for the Management of Candidiasis: 2016 Update by the Infectious Diseases Society of America

Candidemia in Non-Neutropenic Patients
CVCs should be removed as early as possible when source is presumed to be the CVC and can be removed safely (strong rec, mod evidence)
ETT: Growth from resp. secretions usually indicates colonization and rarely requires treatment (strong, mod)
Indwelling bladder catheters should be removed whenever feasible as they are predisposing factors. (strong, low) -Asymptomatic Candiduria: does NOT require treatment.* -Symptomatic Candiduria: can treat based on organism

*Excludes patients about to undergo urologic procedure & VLBW infants.

Case 1- Part 3

- Two days later, the patient's culture from before grows *Candida albicans* susceptible to fluconazole. Repeat blood cultures are clear.
- What changes, if any, should you make?

A. Switch micafungin to fluconazole 400 mg IV/PO
B. Continue micafungin 100 mg IV daily
C. Ask ophthalmology to see your patient
D. No changes
E. A & C

Case 1- Part 3

- Two days later, the patient's culture from before grows *Candida albicans* susceptible to fluconazole. Repeat blood cultures are clear.
- What changes, if any, should you make?

A. Switch micafungin to fluconazole 400 mg IV/PO
B. Continue micafungin 100 mg IV daily
C. Ask ophthalmology to see your patient
D. No changes
E. **A & C**

Clinical Infectious Diseases
IDSA GUIDELINE

Clinical Practice Guideline for the Management of Candidiasis: 2016 Update by the Infectious Diseases Society of America

Candidemia in Non-Neutropenic Patients

Transition from echinocandin to fluconazole (within 5-7 days) for clinically stable patients who are fluconazole-susceptible. (Strong/mod)

- If C. glabrata, use high dose fluconazole 800 mg IV or PO

All non-neutropenic candidemic patients should have a dilated ophthalmologic exam to r/o endopthalmitis (Strong/low)

Recommended duration of therapy for candidemia without metastatic complications is **2 weeks** after documented clearance of blood cultures. (Strong, mod)

Should prophylaxis be used to prevent invasive candidiasis in the ICU?

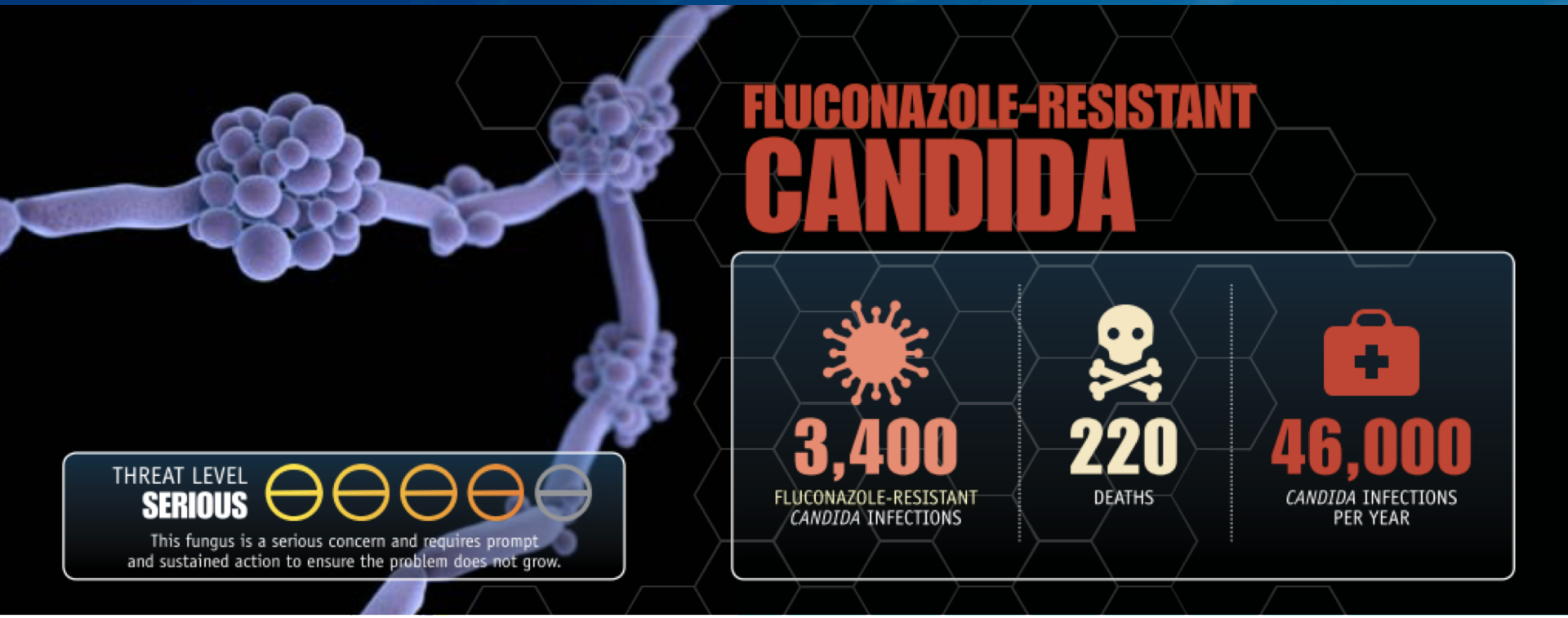
Clinical Infectious Diseases

IDSA GUIDELINE

Clinical Practice Guideline for the Management of Candidiasis: 2016 Update by the Infectious Diseases Society of America

- Weak evidence for fluconazole or echinocandin prophy
- Consider for high-risk/ICU patients if >5% invasive candidiasis
- Half the studies ↓ candidemia but no diff in mortality
- None looked at possibility of ↑ resistant Candida

Resistant Candida



- Identified by CDC as one of 12 serious antimicrobial resistance threats in their 2013 report.
- Who gets these?

Risk Factors for Candidemia

Pfaller, M. et al. *Clin Micro Reviews* 2007;20(1): 133-63.

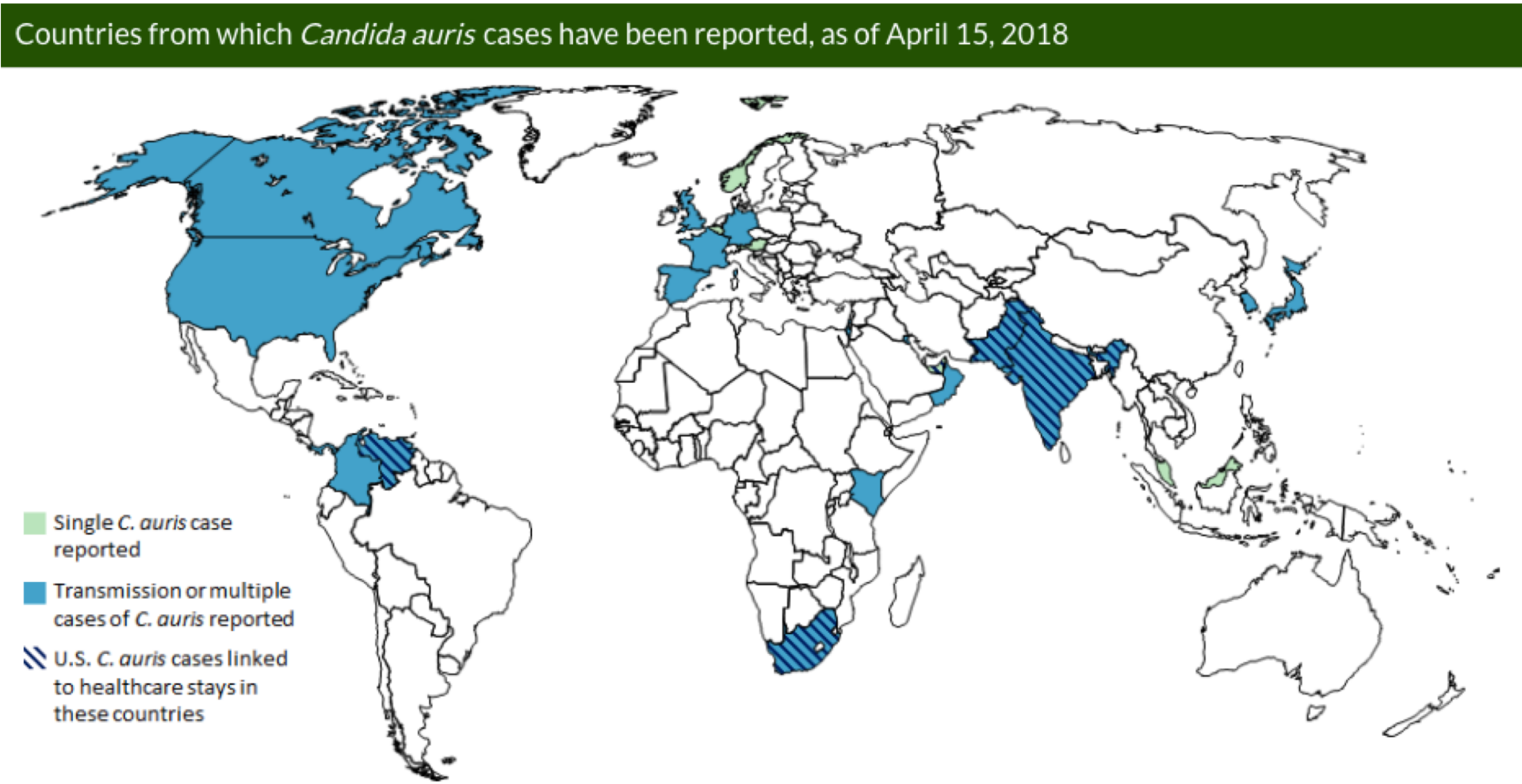
RISK FACTOR	ROLE
Antibiotics - number & duration	IV access & ↑colonization
Corticosteroids	Immunosuppression ↑↓
Age (extremes)	Immunosuppression
Chemotherapy / malignancy / neutropenia	Immunosuppression
Gastric acid suppression	↑colonization
Indwelling catheter	IV access
TPN	le
Surgery	
Mechanica	
Renal failu	
Malnutrition	Immunosuppression
Hospital or ICU stay, duration	Exposure to factors above

Stem cell transplant patients in particular

- Use fluconazole prophylaxis
- Tend to be non-*C. albicans* species
- Up to 20% C. glabrata resistant to fluconazole

Hamdy, RF e al. *Virulence* 2016;8(6): 658-72.

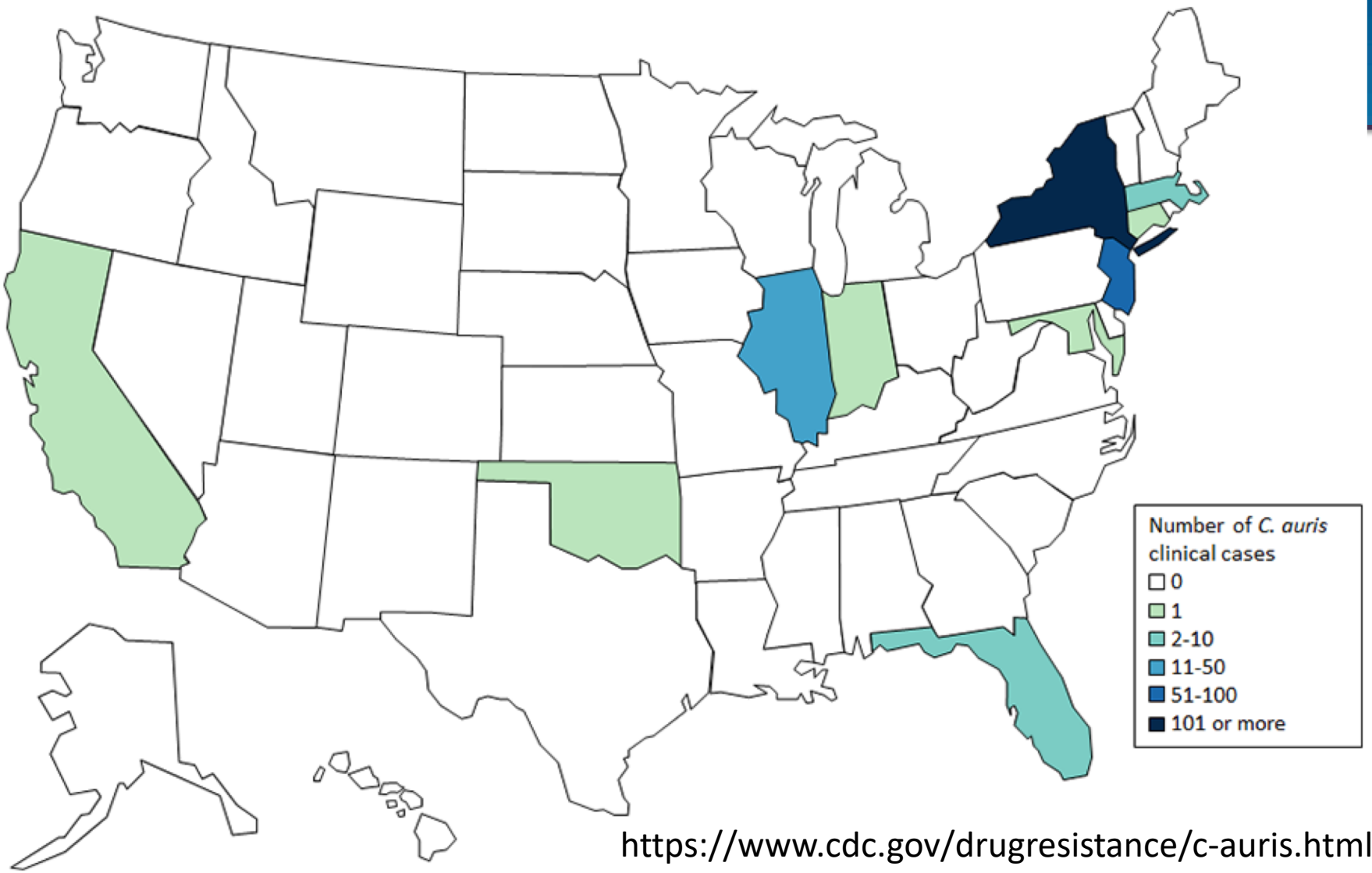
Resistant Candida: C. auris



https://www.cdc.gov/fungal/candida-auris/tracking-c-auris.html

UWTASP
tele-antimicrobial stewardship program

U.S. Map: Clinical cases of *Candida auris* reported by state, United States, as of October 31, 2017



https://www.cdc.gov/drugresistance/c-auris.html

Cases are categorized by the state where the specimen was collected. Most probable cases were identified when laboratories with current cases of *C. auris* reviewed past microbiology records for *C. auris*. Isolates were not available for confirmation. Early detection of *C. auris* is essential for containing its spread in healthcare facilities.

Candida auris, cont

- Who is at risk?
  - Recent surgery, diabetes, use of broad-spectrum antibiotics and antifungal use.
  - Recent nursing home stay and lines/tubes (CVC, feeding tubes, etc.) are at highest risk
  - All ages (pre-term infants to elderly)
- 30-60% patients with invasive C. auris have died.
- Echinocandins are still first line
- Standard & Contact Precautions, Hand Hygiene

https://www.cdc.gov/fungal/candida-auris/

Questions

- How does the lab identify *Candida auris*?
- How much invasive *Candida* do you see?
- Do you see areas your hospital could improve with regard to antifungal use/overuse?