Are clinical pathology labs ready for emerging infectious diseases

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Lessons from COVID Pandemic

We were neither ready, nor prepared

Clinical pathology laboratory
- No diagnostic tests
- Not enough tests available
- No sample collection kits

Hospitals and medical centers
- Lack of treatment
- No standard protocol for patient isolations , medical waste disposal
- Lack of masks, face shields, goggles
- Lack of sufficient personnel (many in quarantine, others afraid and not working

SARS-CoV-2 and COVID-19 background

- Was first detected in Wuhan China, associated with a live market
- Live markets can be associated with transmission of novel disease
- Wild animals sold in live markets may transmit diseases to which humans have no immunity
- SARS-CoV-2 is related to SARS-COV-1, MERS, and 4 "common cold" viruses
- COVID-19 has killed many more people than SARS-1 and MERS combined

Major questions when dealing with a new disease

- How rapidly can an accurate diagnostic test be developed?
- How quickly can a vaccine can be developed?
- How fast can drug(s) for treatment can be developed or repurposed?
  - Repurposing advantagious because drugs are already FDA-approved and can be used off label with fewer studies.

Diagnostic Tests

Cell Culture:
virus culture (CDC discouraged virus culture due to danger to inexperienced personell)

Nucleic acid amplification tests (PCR: NAAT)
NAATs were developed very rapidly, but the problems were:
- large scale production of test kits
- ramping up instruments manufacturing (PCR machines)

Antigen Tests:
- not as sensitive and specific as PCR assays
- false positives and false negatives
- cheaper but and faster than PCR
- good for inexperienced personnel, including possibly, the patients themselves

Antibody tests:
- not for general use: not for the diagnosis of acute disease.
- some can distinguish COVID patient vs vaccinated individuals
- can help in the diagnosis of Long Covid and MIS-C (the related kids disease)

Vaccination: mRNA technology

- Pfizer
- Moderna
- AstraZeneka

Vaccine hesitation
- microchips
- magnetic effect

GeneXpert set up at DMC Emergency Rooms

COVID Testing at DMC Core Microbiology Lab

Challenges:

- Staff
- Machines with high throughput
- Reagent .....Allocation

BSL3: Type B2 biosafety cabinet

End of Covid:

Next topic: *Candida auris*

Discovered in Japan (from an ear infection; hence auris) in 2009; now worldwide

May be resistant to all 3 groups of antifungals

Often causes fungemia, but can be latent and thus disseminate easily

Appeared at the DMC in 2022

We were looking for it, and screened all yeast isolates for *C. auris* one week per month for several years.

Identification Method	Organism *C. auris* can be misidentified as
Vitek 2 YST*	*Candida haemulonii* *Candida duobushaemulonii*
API 20C	*Rhodotorula glutinis* (characteristic red color not present) *Candida sake*
API ID 32C	*Candida intermedia* *Candida sake* *Saccharomyces kluyveri*
BD Phoenix yeast identification system	*Candida haemulonii* *Candida catenulata*
MicroScan	*Candida famata* *Candida guilliermondii*** *Candida lusitaniae*** *Candida parapsilosis***
RapID Yeast Plus	*Candida parapsilosis***

Candida auris

Diagnosis:

Matrix-assisted Lazer Desorption time of flight (Maldi-tof) is accurate

Large hospital systems have this instrumentation, too expensive for small hospitals

Diseases:

Severe, invasive infections in very ill patients

- usually blood, wound
- can colonize, be isolated from urine, respiratory
- can contaminate fomites/hospital rooms
- can cause hospital-based outbreaks

Resistance: to many or all antifungals and must be susceptibility tested

Keep out of hospitals:

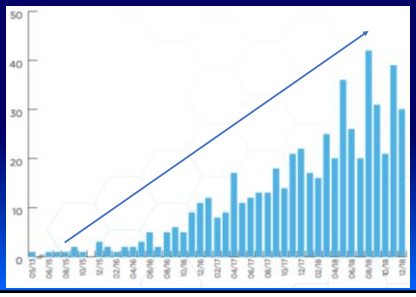
Screen patients w/ history of recent hospitalization

e.g. admitted from nursing homes

Must isolate for several days until *C. auris* can be ruled out

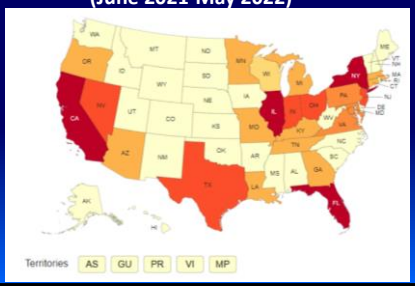
Origin of *C. auris* isolates in US

Cases of *C. auris* in US (2015-2018)

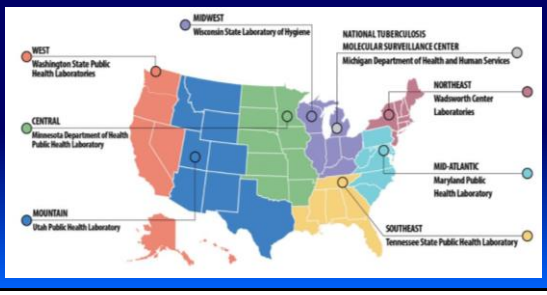


Reported clinical cases of *Candida auris* (June 2021-May 2022)

Cases
- 0
- 1-10
- 11-50
- 51-100
- 101-500



Antimicrobial Resistance (AR) Laboratory Networks



WAYNE STATE
Center for Emerging and Infectious Diseases

Established at Wayne State University School of Medicine in early 2022
Funded by MDHHS grant

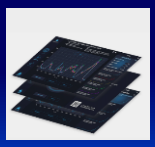
Areas of activity;
- Study and combat infectious diseases and prepare for future pandemics
- Surveillance of Multi-Drug Resistance Organisms (MDROs)
- Outbreak investigation (LTACs and nursing homes for C. auris)
- Vaccine studies
- Training and education, workshops, etc.
- Innovative research

Preparing for the next pandemic and new pathogens

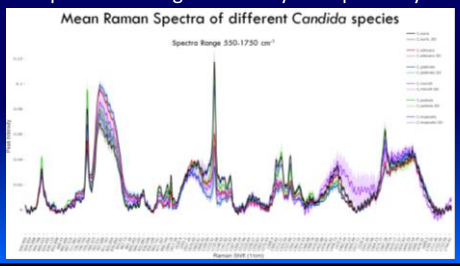
To be ready, we need to identify the risk areas and develop diagnostic tests, vaccines, and treatments. Current risk areas are
- Respiratory infections including COVID/ FluA/B/RSV
- Candida auris
- Monkeypox
- Multi- Drug Resistant Organisms (MDROs)

Work to control and mitigate the current concerns in infectious diseases
- rapid identification of antibiotic-resistant human pathogens and their mechanism of resistance
- stringent infection-prevention measures to control the spread of resistant organisms
- emphasis on expanded surveillance programs for early identification of outbreaks

Fully automated, reagent-free, Raman Spectroscopy system for rapid detection of pathogens in point of care settings



Detecting *C. auris* and distinguishing it from other Candida species with high sensitivity and specificity



Antibiotic resistance in bacteria
Multi-Drug Resistant Organisms (MDROs)

VRSA (2022) Michigan vs all other states

MI: first VRSA isolated here

VRSA in MI: 50%
Other 49 states combined: 50%

The carbapenemase family of β-lactamases

Penicillins	Cephalosporins	Cephamycins	Carbapenems	Monobactams
Benzyl-penicillin	Cephalothin 1st	Cefoxitin	Imipenem	Aztreonam
Methicillin	Cefamandole 2nd	Cefotetan	Meropenem	
Ampicillin	Cefuroxime 2nd	Cefmetazole	Ertapenem	
Carbenicillin	Cefotaxime 3rd		Doripenem	
Mezlocillin	Ceftazidime 3rd			
Ticarcillin	Ceftriaxone 3rd			
	Cefepime 4th			

KPCs hydrolyze all
- Penicillins
- Cephalosporins
- Cephamycins
- Carbapenems
- Monobactams

How to treat CRE infections

Avycaz (ceftazidime + avibactam)

Vabomere (meropenem +vaborbactam)

Zerbaxa (ceftolozane + tazobactam)

What can be done?

Screen, screen, screen
Antibiotic stewardship
Rapid detection (molecular test platforms)

Monkeypox

- known in Africa for decades
- a viral zoonosis (not from monkeys, but can spread to and from them)
- related to small pox
- remote small pox vaccine does not protect
- transmission by close contact
- not usually lethal but can cause hospitalization/death
- No specific treatment. For severe cases, CDC recommends ticovirimat (available via clinical trials and expanded access protocol from CDC), brincidofovir, vaccinia immune globulin, and cidofovir.
- Diagnostic PCR tests available at Quest and Labcorp

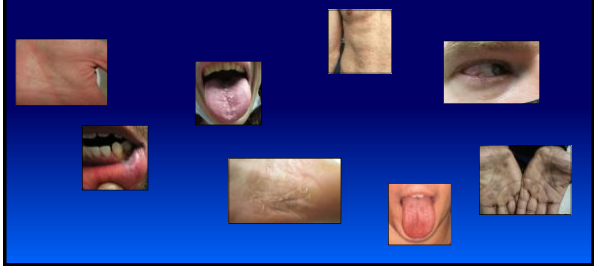
There is a vaccine (JYNNEOS) but…

Limited availability through health departments

Recommended by CDC
if you were exposed to monkeypox within the last 14 days
(you had close physical contact with someone who was diagnosed with monkeypox)
OR you think you may be at risk for monkeypox (MSM)

Many unknowns
- What ab level provides protection?
- How long protection last?
- Best route of administration?

Syphilis is back



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