Biosafety Risk Assessment Fundamentals

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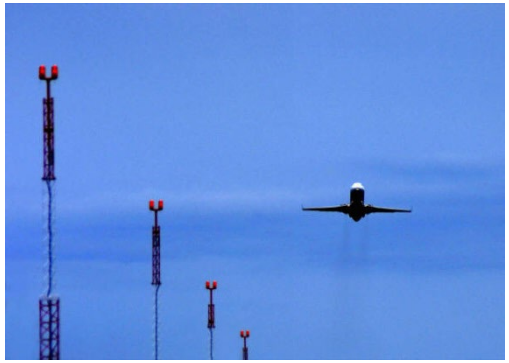
Objectives

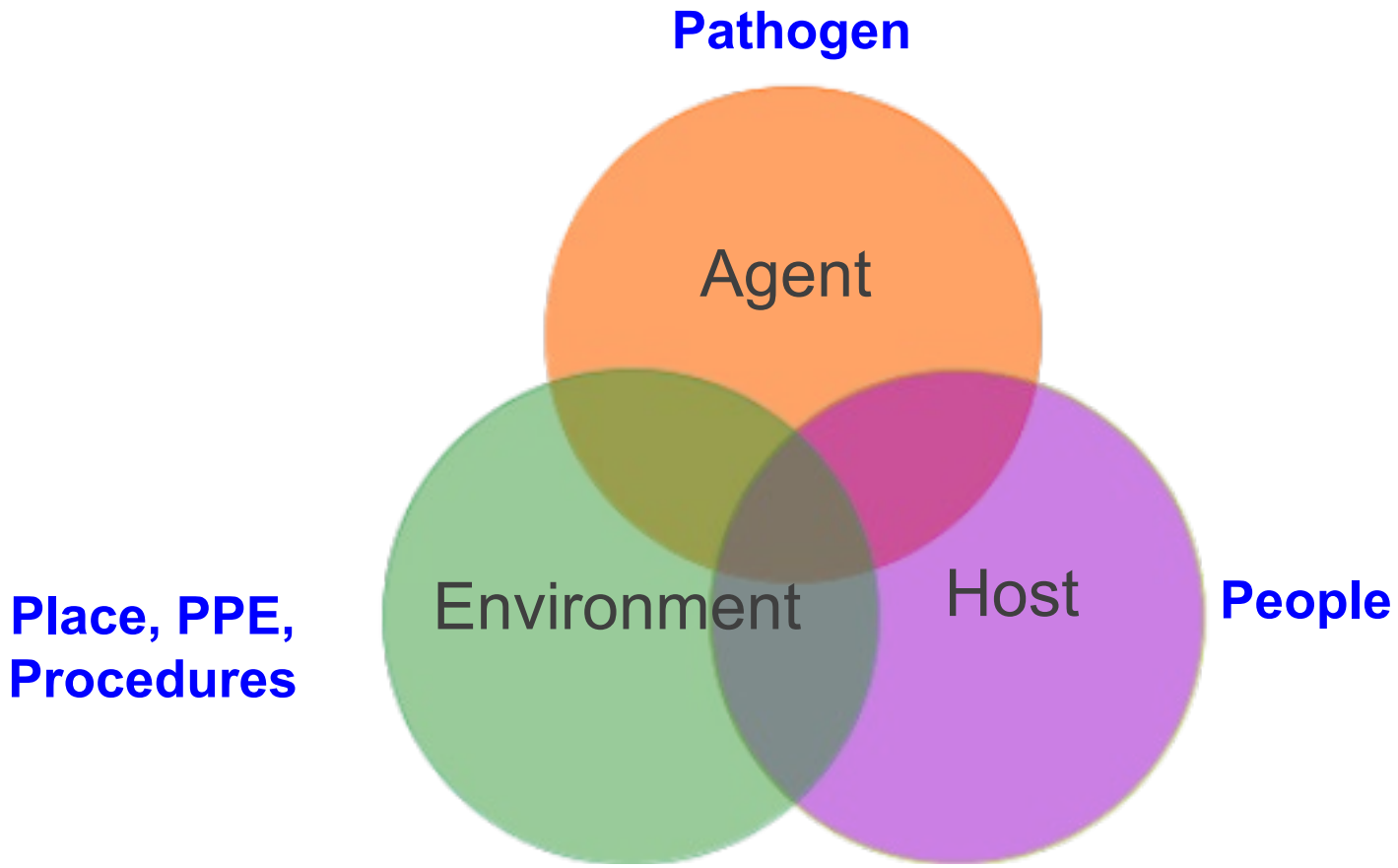
- Describe the basic steps of a risk assessment
- Determine reasons to perform a risk assessment
- Define risk mitigation
- Examples of risk assessments in the microbiology laboratory

Risk Assessment is not a new concept

- We conduct risk assessments all the time…



Risk of a Lab Acquired Infection is a combination of Factors



Source: B. Johnson, Anthology of Biosafety, IV, 2001

How do laboratorians get infected?

Needle stick/sharps
Inhalation of aerosols
Ingestion
Ocular/Mucosal splash or contact
Lab animal/vector exposure
Persons affected in adjacent workspace
Unknown route

D. L. Sewell. 1995. Clinical Microbiology Reviews. 8: 389-405.

What is Risk? Follow the steps

- ***Risk*** *is the likelihood of an undesirable event happening, that involves a specific hazard or threat and has consequences*

1. **Define the situation:**

   What work is occurring?

2. **Define the risks within the situation:**

   What can go wrong?

3. **Characterize the risks:**

   How likely is it to happen?

   What are the consequences?

Definitions

- **Risk Assessment (RA)** is a process that involves hazard identification and hazard control
- Risk assessment requires
  - knowledge of the hazards
  - understanding of the work, the environment, and the staff
  - management involvement and support

Definitions

Hazard is something that is intrinsically dangerous such as an object, a chemical, an infectious agent or a situation.

Risk is:

- the chance of injury or loss when exposed to a hazard.
- based on the probability of exposure and the severity of consequence from that exposure
- A prediction

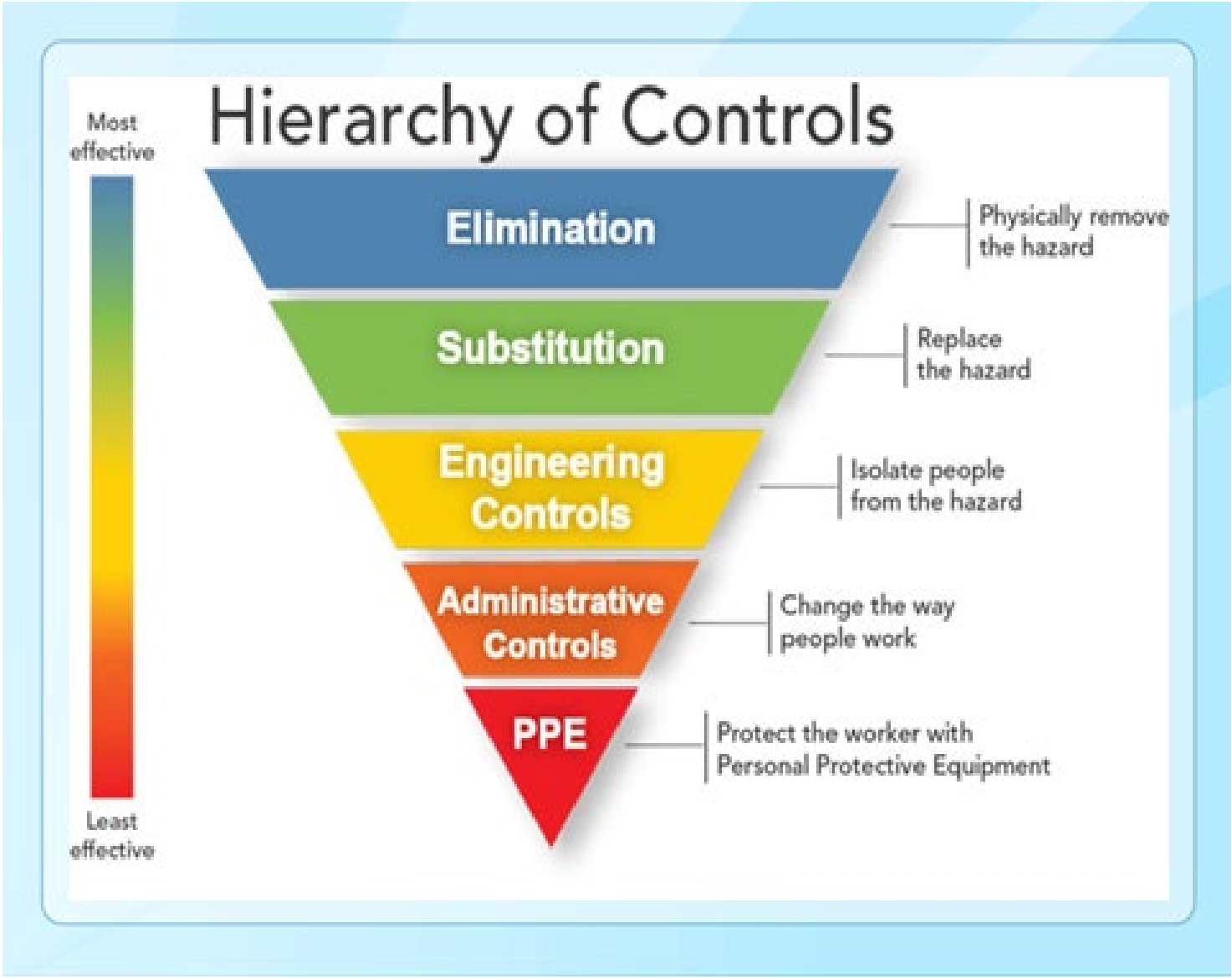
Risk Assessment Defined

- Process of identifying the hazards and evaluating the risks associated with biological agents and toxins, taking into account the adequacy of any exiting controls and deciding whether or not the risks are acceptable

Mitigation Defined

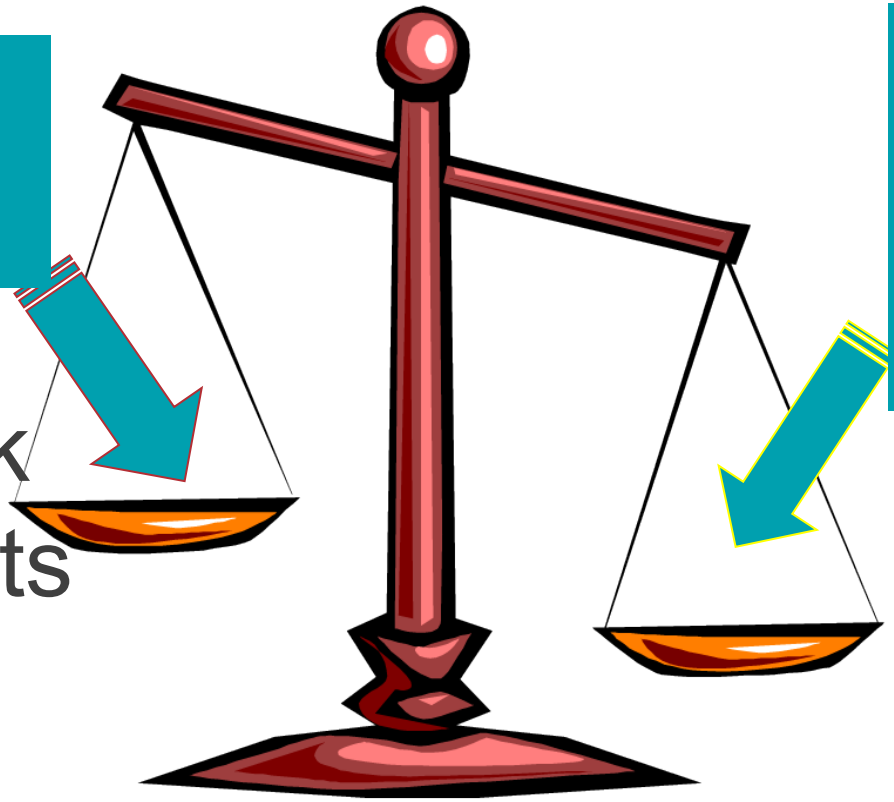
- Actions and control measures that are put into place to reduce or eliminate the risks associated with biological agents and toxins

Mitigation


Hierarchy of Controls
Most effective
Least effective
Elimination
Physically remove the hazard
Substitution
Replace the hazard
Engineering Controls
Isolate people from the hazard
Administrative Controls
Change the way people work
PPE
Protect the worker with Personal Protective Equipment

Risk Assessment Goals:
Balancing risk and work performance

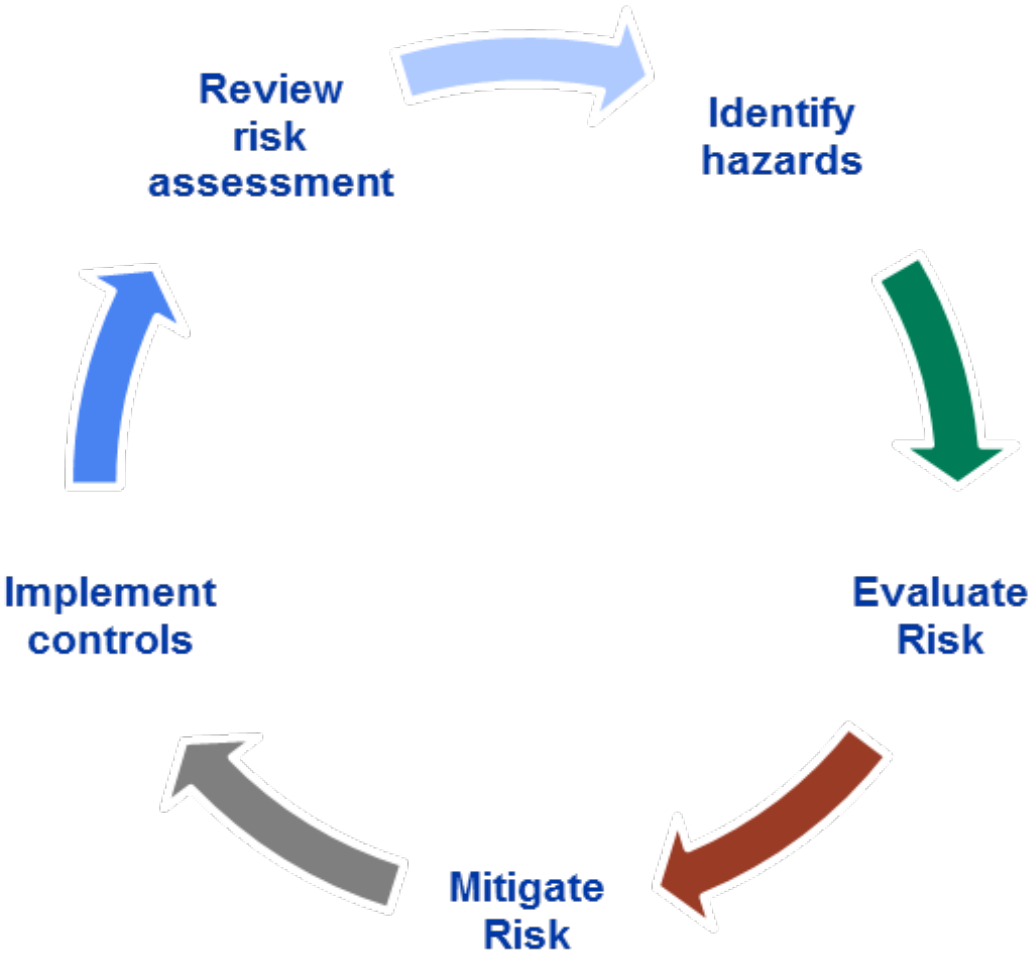
Practices implemented to mitigate risk



Performance of work in an accurate and efficient manner.

Review Risk Assessments Annually

Risk Assessment Process



Risk Assessment Outcome

- Prevent laboratory-acquired infections (LAIs) from:
  - Direct contact (spills/splashes) to mucous membranes
  - Inhalation of aerosols
  - Percutaneous inoculation from cuts, sharps, vectors, non-intact skin
  - Ingestion
  - Indirect contact (contamination from fomites*)

*Fomite - an inanimate object (as a computer, doorknob, phone or work surface) that may be contaminated with infectious organisms and serve in their transmission

Who performs the risk assessment?

- *Ideally,* a multidisciplinary team
  - Laboratory staff
  - Management/supervisors
  - Health and safety specialists (biosafety, occupational health …)
  - Facility staff
  - Scientists with unique expertise & experience
    - Microbiologists, molecular biologists, chemists
    - Veterinarians
    - Others

Who should be lead the RA?

- Qualifications of the lead assessor:
  - Knowledge of the facility, safety principles, modes of transmission, hazards, and local, state and federal regulations.
  - Problem-solving skills
  - Practical experience

When to perform the risk assessment?

- Before work begins
- Whenever there is a move or renovation
- Changes in personnel
- New infectious agent or reagent
- New equipment
- Repeat when changes are to made in agents, practice, employees or facilities

When to perform the risk assessment? (cont.)

- Changes in manufacturer or supplier of consumable materials (PPE, containers, waste disposal materials, media)
- Recent accident, LAI, theft or security violation
- National or regional changes in disease status (endemicity of disease or disease eradication)

Work plan to complete the risk assessment

Engage Everyone

Create a risk assessment matrix for the agent, protocols and staff susceptibility to disease

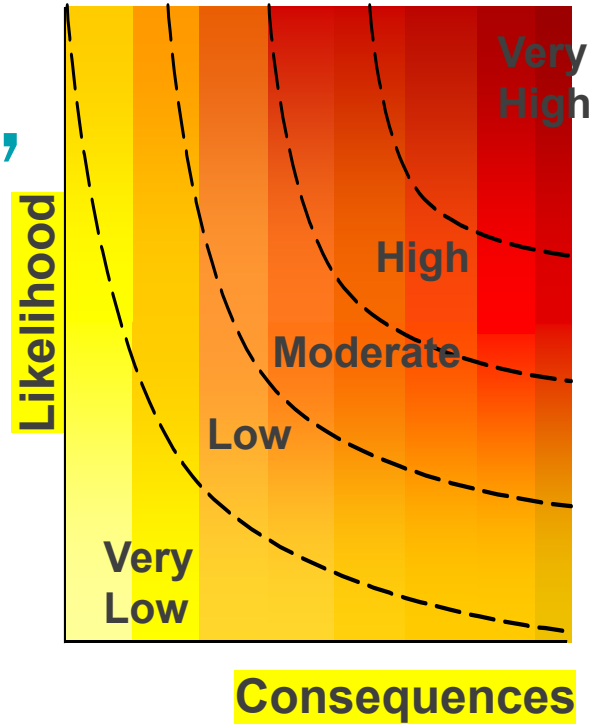
Identify lab procedure hazards through a protocol driven risk assessment

Determine appropriate biosafety level and risk mitigation steps

Evaluate staff competency and utilization of safety equipment

Review assessment with staff and management

Relationship of Likelihood, Consequences and Time



How likely is this to happen?

Occurrence

What are the consequences?

Time

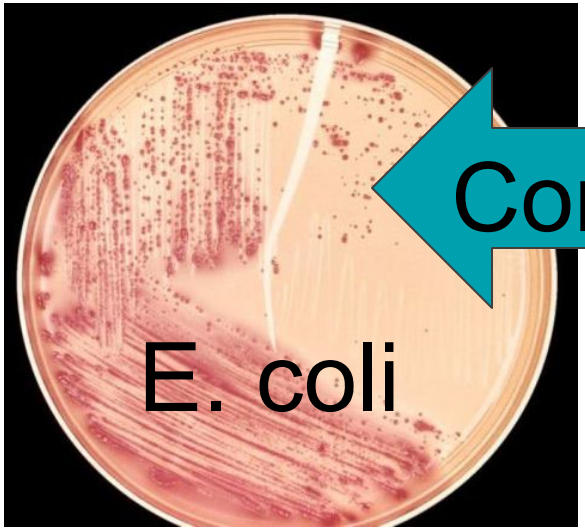
- Likelihood of infection from the biological agents
- Likelihood of an exposure based upon the work practice

- Consequences of infection/exposure to an at- risk host

Example: Specimen receiving

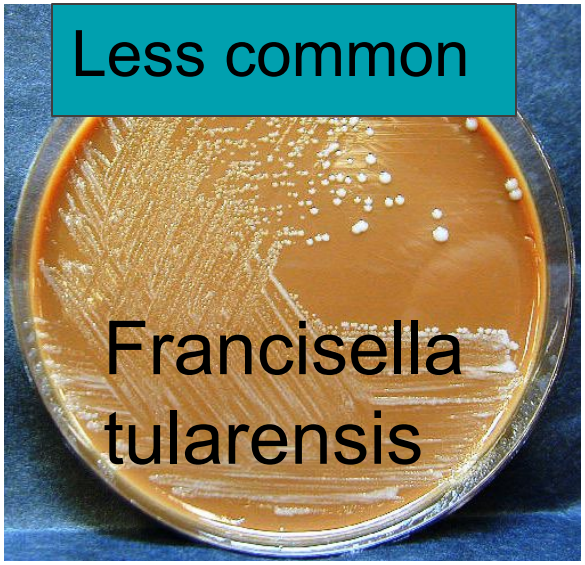
- What can go wrong during specimen receiving?
- How likely is it? What factors did you consider in assessing the likelihood?
- What are the consequences? What factors did you consider in assessing the consequences?
- What mitigation measures should you put in place to make the risks of specimen receiving acceptable?

Start with the Pathogens seen

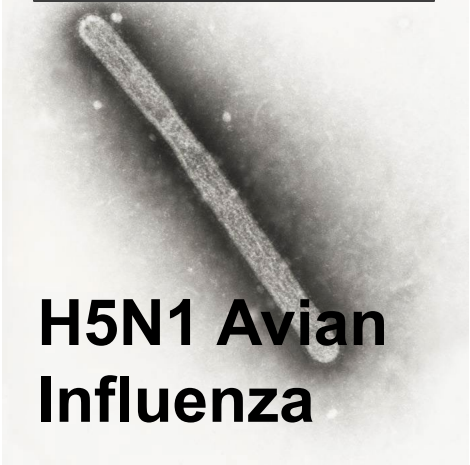


Common

Less common

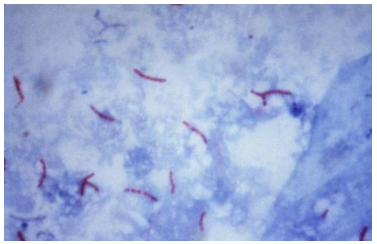


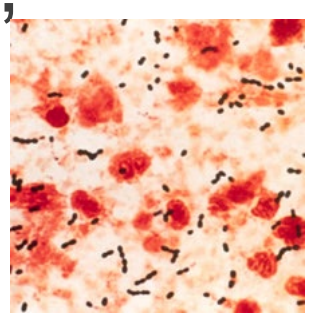
Emerging

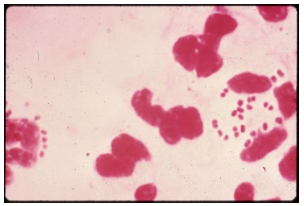


Estimate Risk based on Pathogen

- Infective dose
- Contagiousness
- Stability in the environment with regards to temperature, light, pH, desiccation, humidity, and life cycle
- Incubation period
- Infectious period
- Modes of transmission





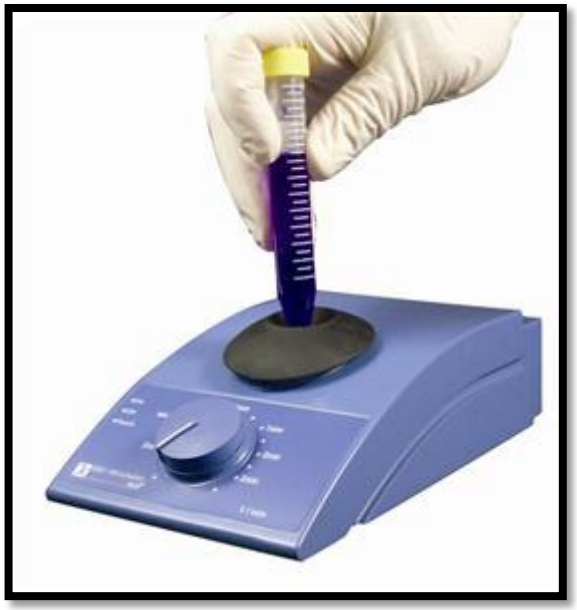


Risk Assessment Matrix for Agent Hazards*

Risk factors	Degree of Laboratory Risk		
Agent Hazards	**Low to Moderate**	**Moderate to High**	**High**
Pathogenicity	Mild to moderate disease (***Salmonella typhimurium***)	Moderate to serious disease (***Mycobacterium tuberculosis***)	Severe disease (**Herpes virus B**)
Virulence	Mild to moderate disease or low infectivity	Severe disease or moderate infectivity	Lethal disease or high infectivity
Infective dose	$>10^6$ IU (***Vibrio cholerae***)	10^6 – 100 IU (**Influenza A virus**)	<100 IU (***Francisella tularensis***)
Transmission	Indirect contact (contact with contaminated surfaces, animal bedding)	Direct contact (droplet, tissue, fluid, secretion contact with mucous membranes; ingestion)	Inhalation or percutaneous inoculation (needle stick)

*adapted from D.O. Fleming ,personal communication

Protocol Driven Risk Assessment



- The lab activity drives the level of containment
  - Ex. HIV amplification increases the risk of exposure and leads to an increase in the level of containment (BSL3 practices)

Risk Assessment Matrix for Protocol Hazards

Protocol Hazards	Low Risk	Moderate Risk	High Risk
Agent Concentration	$<10^3$ IU/ml	$10^3 – 10^6$ IU/ml	$>10^9$ IU/ml
Suspension Volume	<1 ml	1 ml – 1 L	>1 L
Generate droplets & droplet nuclei	Streaking “smooth” agar	Pipetting	Flaming an inoculating loop
Protocol Complexity	Standard repetitive procedures	Periodic change in procedures	Frequent change and complex procedures
Use of Animals	Use of safe animal care practices	Necropsies; large animals handling	Aerosol challenge protocols
Use of Sharps		With protective devices - safety sharps	Without protective devices

Activities

Average Bacteria Recovered from Aerosol Generating Procedures

Procedures	Average Bacteria CFU recovered/ft from air during the procedure
Opening petri dish	0
Opening screw capped test tube	4
Picking colony from plate	0.005
Streaking on smooth agar plate	0.26
Pipette inoculating test tube	0.26
Syringe and needle withdrawal from rubber-cap bottle	16.0

Source: Kruse, R.H. et. Al. Biological Safety Cabinetry. Clinical Microbiology Reviews. 1991.4:207-241.

Risk Assessment Matrix for Susceptibility to Disease

Risk factors	Degree of Laboratory Risk		
Susceptibility to Disease	**Low to Moderate**	**Moderate to High**	**High**
Potential for Exposure	Visitor to lab	Lab worker in room where agent is handled	Lab worker who handles agent
Individual Susceptibility	Effective immunization	Immunocompetent	Compromised immune status
Availability of vaccine or other prophylaxis	Yes	Less effective prophylaxis	No
Availability of effective treatment	Yes	Treatment offers some value	No

Mitigation Control Measures

- **Engineering Controls**: Physical changes to work stations, equipment, materials, production facilities, or any other relevant aspect of the work environment that reduce or prevent exposure to hazards
- **Administrative Controls**: Policies, standards and guidelines used to control risks
- **Practices and Procedures**: Processes and activities that have been shown in practice to be effective in reducing risks
- **Personal Protective Equipment**: Devices worn by the worker to protect against hazards in the laboratory

Advantages/Disadvantages

Control Measure	Advantages	Disadvantages
Engineering	Efficient, eliminates hazard	Cost, complexity
Administrative	Authority approach	Indirect approach, primarily addresses the human factor
Practices & Procedures	SOP based (standardized approach)	Training and supervision requirements
PPE	Ease of use, relative cost	Does not eliminate hazard, PPE fails exposure happens, uncomfortable, limits ability

Mitigation used in combination

Engineering Controls	Administrative Controls	Practices and Procedures	Personal Protective Equipment (PPE)
BSC	Policy on when to use the BSC	Training and competency on BSC use	Gloves, gowns, face shields, eye protection, respirator
BSL-3	When is it mandated to work in the BSL-3	Written SOP on when to work in the SOP	Required protection to work in the BSL-3

Candida auris – resistant fungus

- First identified in Japan in 2009, in the ear canal of a 70-year-old woman.
- *C. auris* has spread rapidly around the globe, emerging in at least five continents, with the first UK case detected in 2013.
- Causes severe disease in hospitalized patients
- Can be Resistant to all three classes of antifungals: azoles, polyenes, echinocandins
- Difficult to identify
- Can spread to other patients

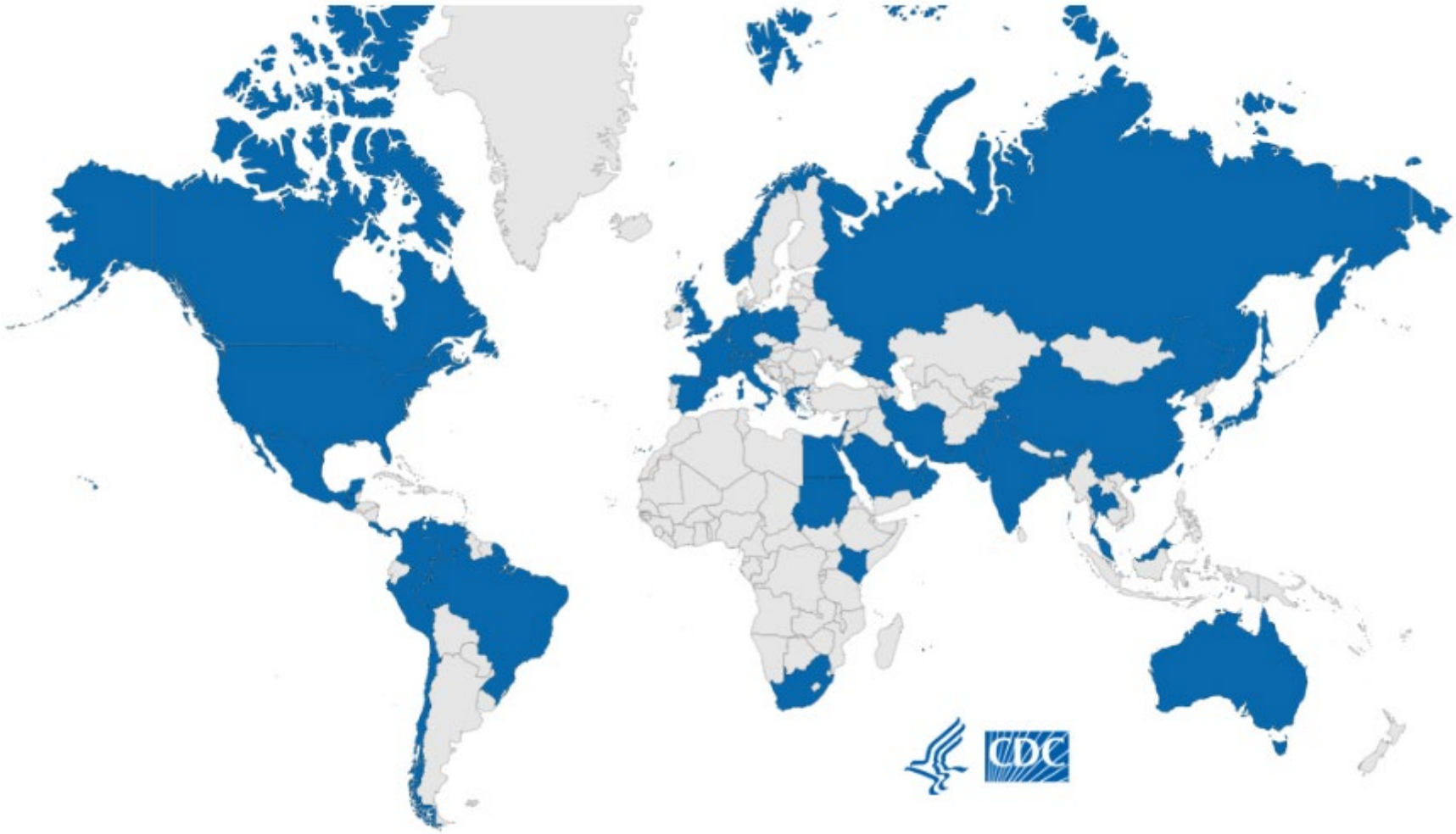
Why is *C. auris* an emerging threat?

- *C. auris* has been identified from many body sites including bloodstream, urine, respiratory tract, biliary fluid, wounds, and external ear canal.
- Many clinical laboratories do not typically speciate isolates from non-sterile sites since presence of *Candida* in these sites may represent colonization rather than infection.
- *C. auris* is important to identify even from a non-sterile body site because presence of *C. auris* in any body site can represent wider colonization, posing a risk for transmission and requiring implementation of infection control precautions.

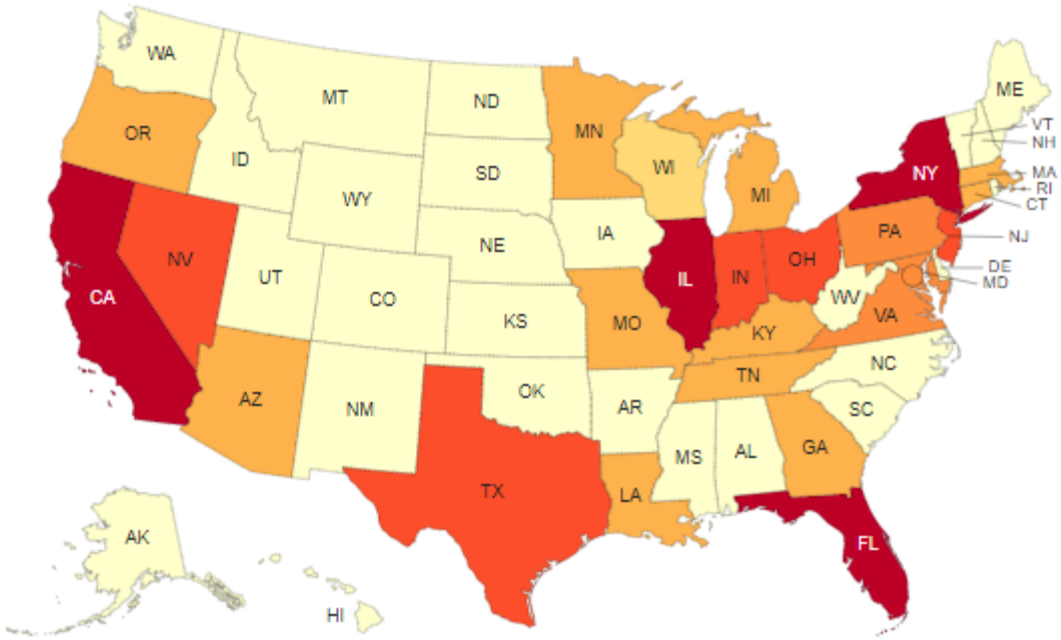
Epidemiology of *C. auris*

Countries from which *Candida auris* cases have been reported, as of February 15, 2021

This map is no longer being updated given how widespread *C. auris* has become.



Reported clinical cases of *Candida auris*, June 1, 2021-May 31, 2022



Number of Clinical Cases

- No cases reported
- 0 clinical cases, but ≥1 screening case
- 1 to 10
- 11 to 50
- 51 to 100
- 101 to 500

Territories AS GU PR VI MP

Epidemiology of *C. auris*

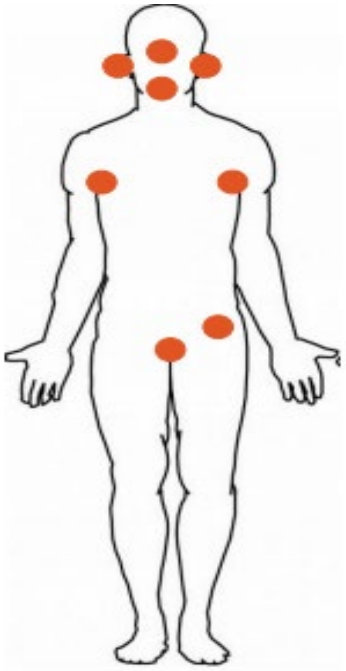
- As of May 31, 2021 , there have been a total of 2,386 confirmed cases of *C. auris* reported
- The majority of cases have been reported in New York, Illinois and California
  - Ex. An outbreak in NYC
    - 51 clinical cases of *C. auris*
    - 61 screening case-patients, which were identified for surveillance purposes
    - Epidemiologic links between cases reflected an interconnected web of facilities

Candida auris Infections

- Can spread easily in healthcare facilities through direct contact with infected or colonized patients and through contaminated surfaces and equipment
- *C. auris* can cause serious infections, such as bloodstream infections and other types of invasive infections particularly in patients in hospitals and nursing homes
- Antifungal medications regularly used to treat this infection often do not work because some *C. auris* isolates are resistant to all three major classes of antifungal medications
- More than 1 in 3 patients die within a month of *C. auris* infection

Candida auris Colonization

- It is possible for an individual to be asymptomatic and colonized with *C. auris*
- Primarily on skin but other body sites and nares can become colonized
- Can be persistent, may take months to years to clear
- At this time no decolonization strategies
- Can lead to:
  - Invasive infection
  - Transmission to others



Patient Risk Factors

- Typically affects the sickest of the sick
  - Ventilator-dependent
  - Tracheostomies
  - Colonized with other multi-drug resistant organisms
  - Recently received antibiotics and antifungals

- Healthcare abroad
  - A history of an overnight stay in a healthcare facility outside the United States
  - History of ambulatory surgery or hemodialysis outside of the United States in the previous 12 months
  - Patient has a history of an overnight stay in a hospital or skilled nursing facility in New York City, New Jersey, or Chicago within the previous 12 months

Reasons for Public Health Concern

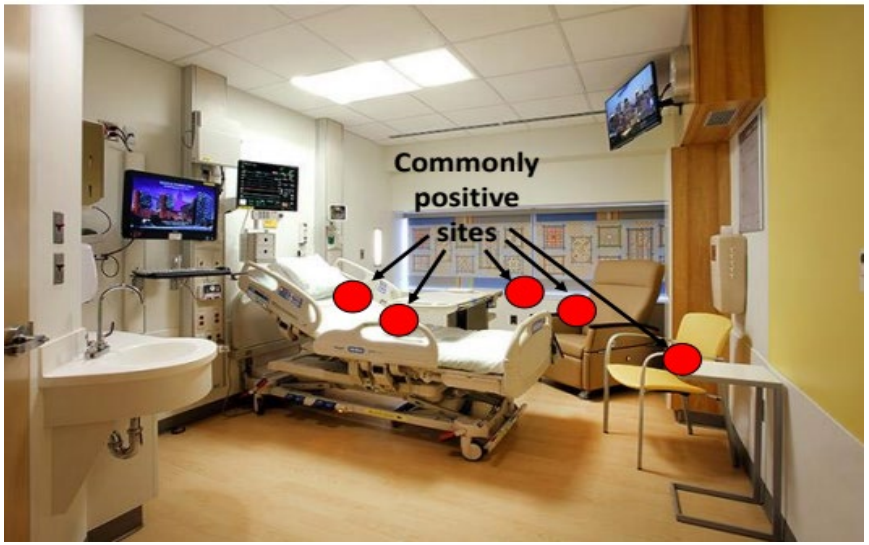
- C. auris is an antifungal resistant organism
- Can colonize skin
- Can contaminate the environment
- Can spread in healthcare settings

Problems with lab identification

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*
BD Phoenix yeast identification system	*Candida haemulonii* *Candida catenulata*
Microscan	*Candida famata* *Candida guilliermondii* (no hyphae/pseudohyphae present on cornmeal agar) *Candida lusitaniae* (no hyphae/pseudohyphae present on cornmeal agar) *Candida parapsilosis* (no hyphae/pseudohyphae present on cornmeal agar)

Facilities that detect *C. auris*

- All laboratories, especially laboratories serving healthcare facilities where cases of *C. auris* have been detected should do the following:
    - Review past microbiology records (as far back as 2015, if possible) to identify cases of confirmed or suspected *C. auris*.
    - Conduct prospective surveillance to identify and report *C. auris* cases in the future.



Risk Assessment Matrix for *Candida auris*

Risk factors	Degree of Laboratory Risk		
Agent Hazards	**Low to Moderate**	**Moderate to High**	**High**
Pathogenicity		Severe disease for immunocompromised	
Virulence	Non-lethal disease or high infectivity		
Infective dose	Unknown		
Transmission	Contamination of environment		

*adapted from D.O. Fleming ,personal communication

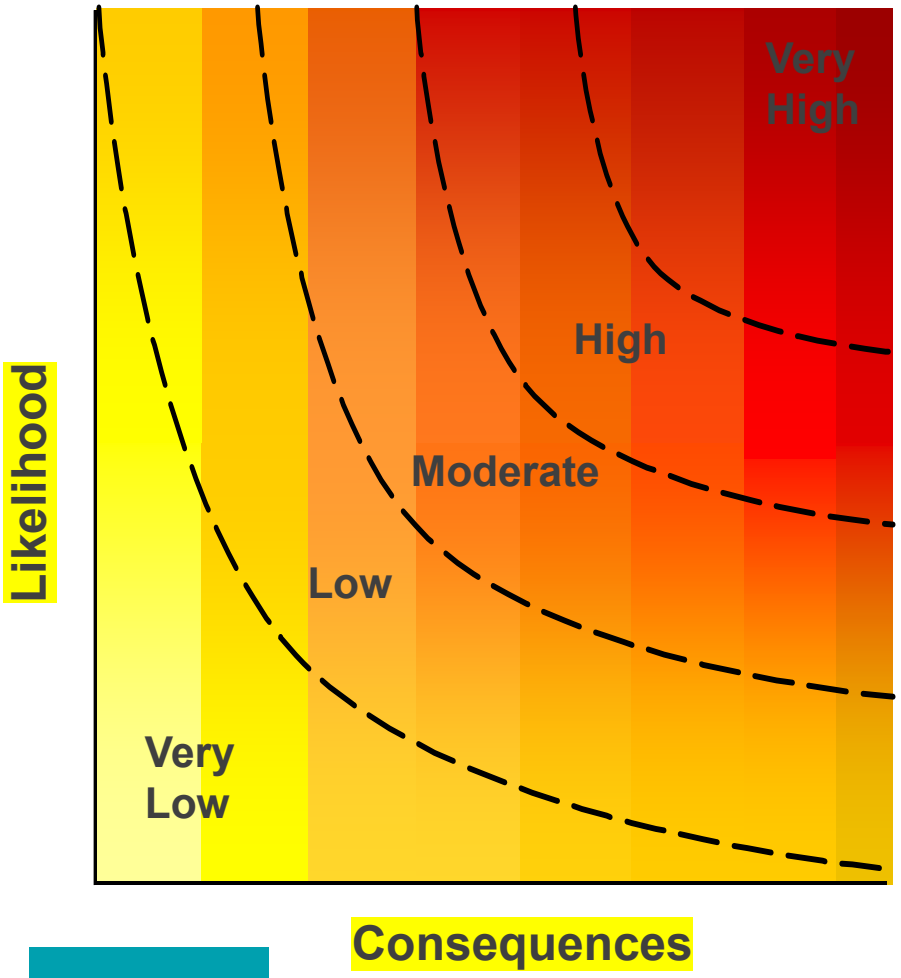
Risk Assessment Matrix for *Candida auris*

Protocol Hazards	**Low Risk**	**Moderate Risk**	**High Risk**
Agent Concentration	>10^9 IU/ml		
Suspension Volume	<1 ml	1 ml – 1 L	
Generate droplets & droplet nuclei	Making a suspension for identification on bench top		
Protocol Complexity	Standard repetitive procedures		
Use of Animals	NA	NA	NA
Use of Sharps	NA	NA	NA

Risk Assessment Matrix for *Candida auris*

Risk factors	**Degree of Laboratory Risk**		
Susceptibility to Disease	**Low to Moderate**	**Moderate to High**	**High**
Potential for Exposure	Others in the lab	Manipulating agent	
Individual Susceptibility	Immunocompetent	Compromised immune status	
Availability of vaccine or other prophylaxis	No		
Availability of effective treatment		Yes – but difficult to treat	

Consider these Lab Situations



- A culture plate on which is growing colonies of *Candida auris* is dropped to the floor in the laboratory

Risk Assessment Matrix

		Consequences				
		Insignificant (1) No injuries / minimal financial loss	**Minor (2)** First aid treatment / medium financial loss	**Moderate (3)** Medical treatment / high financial loss	**Major (4)** Hospitable / large financial loss	**Catastrophic (5)** Death / massive financial loss
Likelihood	**Almost Certain (5)** Often occurs / once a week	Moderate (5)	High (10)	High (15)	Catastrophic (20)	Catastrophic (25)
	Likely (4) Could easily happen / once a month	Moderate (4)	Moderate (8)	High (12)	Catastrophic (16)	Catastrophic (20)
	Possible (3) Could happen or known it to happen / once a year	Low (3)	Moderate (6)	Moderate (9)	High (12)	High (15)
	Unlikely (2) Hasn't happened yet but could / once every 10 years	Low (2)	Moderate (4)	Moderate (6)	Moderate (8)	High (10)
	Rare (1) Conceivable but only on extreme circumstances / once in 100 years	Low (1)	Low (2)	Low (3)	Moderate (4)	Moderate (5)