EMERGING INFECTIOUS DISEASES: *C. auris*, Mpox, SARS-CoV-2, HPV, CRE

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Disclosures: PDI, Kinnos, slides modified from David J. Weber, MD, MPH

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- Focus on infection prevention
  - Role of environmental contamination in transmission
  - Frequency of environmental transmission
  - Hand hygiene
  - Surface/device disinfection

BASIC CONCEPTS IN DISEASE EMERGENCE

- Emergence of infectious diseases is complex
- Infectious diseases are dynamic
- Most new infections are not caused by genuinely new pathogens
- Agents involved in new and reemergent infections cross taxonomic lines
- The concept of the microbe as the cause of disease is inadequate and incomplete
- Human activities are the most potent factors driving disease emergence
- Social, economic, political, climatic, technologic, and environmental factors shape disease patterns and influence emergence
- Understanding and responding to disease emergence require a global prospective, conceptually and geographically
- The current global situation favors disease emergence

Wilson ME. Emerging Infectious Diseases 1995;1:39.

PREVENTING TRANSMISSION OF AN INFECTIOUS DISEASE REQUIRES UNDERSTANDING THE CHAIN OF TRANSMISSION

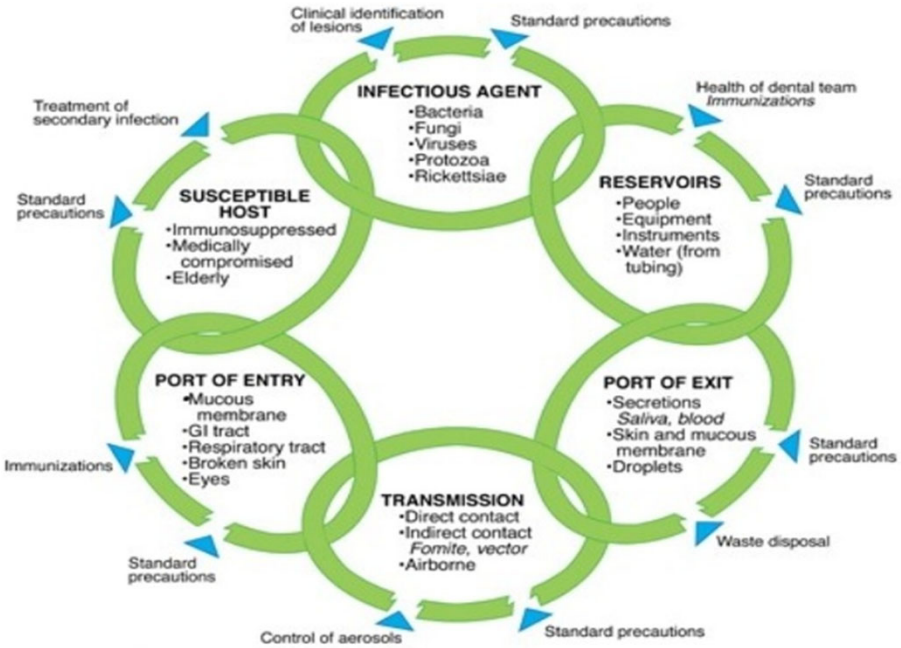

Table 1. Comparison of Pathogens Primarily Transmitted by Contact with Body Fluids (eg, Ebola virus) Versus Respiratory Droplets and Droplet Nuclei (eg, SARS-CoV-2)

Variable	Ebola Virus	SARS-CoV-2
Microbiology		
Year identified	1976	2019
Family	Filaviridae	Coronaviridae
Genome	RNA	RNA
Coat	Enveloped	Enveloped
Epidemiology		
Prevalence	Repeated outbreaks	Pandemic
Reservoir	Bats	Bats; research ongoing to identify additional potential reservoirs
Intermediate host	Primates and other animals	None demonstrated
Primary mode of transmission	Direct Contact: Contact with infectious body fluids	Respiratory droplets
Other modes of transmission	Indirect contact (ie, contaminated surfaces, devices), sexual, blood transfusion	Direct and indirect contact (ie, contaminated surfaces, devices)
Basic reproductive rate (R_0)	1.5–2.0[23]	1.8–3.6[24]
Asymptomatic and presymptomatic transmission	No	Yes
Incubation period	6–12 d (range, 2–21)	2–14 d
Case fatality rate	~50% (range, 25%-90%)	~15% among hospitalized patients
Treatment	Monoclonal antibody combination (atoltivimab, maftivimab, and odesivimab-ebgn)	Remdesivir, bamlanivimab
Infection prevention		
Nosocomial transmission involving HCP (HCP-to-HCP, HCP-to-patient, patient-to-HCP)	Yes	Yes
Laboratory biosafety level	BSL-4	BSL-2 (routine diagnostic testing); BSL-3 (virus isolation in cell culture)
Survival on surfaces	Hours to a few days	Hours to a few days
Antiseptic	60%–90% alcohol-based product	60%–90% alcohol-based product
Disinfectant	EPA, emerging virus claim (List "N")	EPA, emerging virus claim (List "N")
Special handling of used linens, patient waste	Yes	No
PPE worn by HCP (CDC)	1. Single-use (disposable) fluid-resistant gown that extends to at least mid-calf or single-use (disposable) fluid-resistant coveralls without integrated hood 2. Single-use (disposable) full face shield 3. Single-use (disposable) face mask 4. Single-use (disposable) gloves with extended cuffs. Two pairs of gloves should be worn. At a minimum, outer gloves should have extended cuffs.[25]	1. N95 respirator (or equivalent or higher-level respirator) or facemask (if a respirator is not available) 2. Eye protection (ie, goggles or a face shield that covers the front and sides of the face) 3. Single use (disposable), clean, nonsterile gloves 4. Single use (disposable) isolation gown or cloth gown.[26]
Pre-exposure prophylaxis	Vaccine	Vaccine
Postexposure prophylaxis	None approved for postexposure prophylaxis	None

Note. BSL, biosafety level; EPA, US Environmental Protection Agency; HCP, healthcare personnel.

Shenoy ES, Weber DJ. ICHE 2021;42:457-460

NEW AND EMERGING MICROBIAL THREATS

Biothreats (category A)	WHO 2015 (highly infectious pathogens)	WHO 2022 (highly infectious pathogens)	WHO Fungi (by priority group)	WHO 2017 Multidrug Resistant Microbes
• Anthrax (*Bacillus anthracis*) • Botulism (*Clostridium botulinum* toxin) • Plague (*Yersinia pestis*) • Smallpox (variola major) • Tularemia (*Francisella tularensis*) • Viral hemorrhagic fevers, including Filoviruses (Ebola, Marburg) Arenaviruses (Lassa, Machupo)	• Crimean-Congo hemorrhagic fever; • Filovirus diseases (i.e. EVD & Marburg) • Highly pathogenic emerging Coronaviruses relevant to humans (MERS Co-V & SARS) • Lassa Fever • Nipah; • Rift Valley Fever • Preparedness for a new disease	• COVID-19 • Crimean-Congo hemorrhagic fever • Ebola virus disease and Marburg virus disease • Lassa fever • Middle East respiratory syndrome coronavirus (MERS-CoV) and Severe Acute Respiratory Syndrome (SARS) • Nipah and henipaviral diseases • Rift Valley fever • Zika • "Disease X"	Critical • *Cryptococcus neoformans* • *Candida auris* • *Aspergillus fumigatus* • *Candida albicans* High • *Nakaseomyces glabrata* spp. (*C. glabrata*) • *Histoplasma* • Eumycetoma agents • Mucorales • *Fusarium* spp. • *C. tropicalis* • *C. parapsilosis*	Critical • CR *Acinetobacter baumannii* • CR *Pseudomonas aeruginosa* • CR or ESBL Enterobacterales High • VRE • MRSA, VISA, VRSA • FQ-R *Campylobacter* • FQ-R *Salmonella*

Key: EVD, Ebola virus disease; MERS, Middle East Respiratory Syndrome; SARS, Severe Acute Respiratory Syndrome; WHO, World Health Organization

Weber DJ, Rutala WA, Sickbert-Bennett EE. American J Infect Control 2023 (In press)

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EXOTIC INFECTIOUS DISEASES SEEN IN THE US

- Lassa virus (April 2014, MN): Returned traveler from Liberia (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6049013/pdf/ofy131.pdf)
  - Other imported cases: 2015, NJ; 2014, MN; 2010, 2004, NJ; 1989, IL – 3 died, 2 survived – an additional 3 patients cared for in US who were medical evacuees
- Mpox (July 2021, TX): US citizen recently returned from Nigeria (https://emergency.cdc.gov/han/2021/han00446.asp)
  - In 2003, 47 confirmed/probable cases reported from 6 states (IL, IN, KS, MI, OH); source = pet prairie dogs (reservoir Giant Gambian rats imported as pets)
- Ebola (September, 2014, 4 cases, 3 due to 2nd transmission): Source = Liberian national visit US from Liberia
- Rabies: From 1960 to 2018, 127 human rabies cases were reported in the US, with ~25% resulting from dog bites received during international travel. Of US acquired infections, 70% attributed to bat exposures (https://www.cdc.gov/rabies/location/usa/index.html) (https://www.cdc.gov/rabies/location/usa/surveillance/human_rabies.html)\
- Measles (multiple years): Outbreak index case often in traveler with expansion in unvaccinated cohorts
  - Measles remains a global threat to human health. In 2018, the WHO. WHO reported over 328,000 measles cases among 184 WHO member states, with the European Region reporting the most cases (25.6%) . Low vaccination coverage for measles is presumed to be responsible for recent increases (Angelo KM. J Travel Med 2019;26(6).

EXOTIC DISEASES ACQUIRED IN THE US

- Paralytic polio: New York
- Dengue, 2010-2017: US acquired cases were reported from HI, 250; FL,103: TX, 24; NY, 1 (https://www.cdc.gov/mmwr/volumes/69/wr/mm6906a1.htm)
- Malaria:
  - CDC: Outbreaks of locally transmitted cases of malaria in the United States have been small and relatively isolated (airport transmission), but the potential risk for the disease to re-emerge is present due to the abundance of competent vectors, especially in the southern states; occasional blood transfusion acquired cases (https://www.cdc.gov/malaria/about/us_transmission.html)
  - Since 2000, four outbreaks of autochthonous malaria transmission have been documented in the USA. The most recent outbreak occurred in Palm Beach County, Florida, in 2003 (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7808401/pdf/40475_2020_Article_224.pdf)
- Chikungunya virus: Local transmission has been identified in FL, TX, Puerto Rico, U.S. Virgin Islands (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5928745/pdf/tpmd170668.pdf)
- Chagas disease (*Trypanosoma cruzi*): Rare acquisition in US; 26 cases contracted in TX, 2013-2018 (https://asm.org/Articles/2021/April/Chagas-Disease-in-the-U-S-What-We-Know-About-the-K)
- Zika: No current local transmission - The last cases of local Zika transmission by mosquitoes in the continental US were in FL and TX in 2016-17 (https://www.cdc.gov/zika/geo/index.html)
- Cutaneous Leshmaniasis: Occasional cases of have been acquired in TX and OK (https://www.cdc.gov/parasites/leishmaniasis/epi.html)
- Plague (SW US): ~7 cases bubonic plague per year (range, 1-17); rare cases of pneumonia plague; source prairie dogs/ground squirrels
- Anthrax: Rare cases in US; 2006 via African drum hides, CA; previous 1976 (http://publichealth.lacounty.gov/acd/Diseases/Anthrax.htm)
- Leprosy: 150-250 cases in US per year (2323 new cases, 1994-2011); rate 14x higher among foreign born (Bezalel SA. Mayo Clinic 2019)

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KEY CONSIDERATIONS IN ASSESSING AND MANAGING THE THREAT OF AN EMERGING INFECTIOUS DISEASE

- Pathogen
  - Taxonomy (provides clues regarding transmission routes, environmental stability, germicide susceptibility)
  - Hosts
- Epidemiology
  - Locations of endemicity (i.e., locations in the world where sources or reservoirs reside)
  - Incubation period
  - Transmission routes
  - Infectivity (i.e., communicability)
  - Duration of infectivity
- Clinical
  - Symptoms
  - Signs
  - Risk factors for acquisition of infection
  - Morbidity
  - Mortality
  - Risk factors for morbidity and mortality
  - Diagnostic methods (sensitivity, specificity, biosafety)
  - Therapy (availability, efficacy, safety)

Weber DJ, Rutala WA, et al. Am J Infect Control 2016;44:e91-100

KEY CONSIDERATIONS IN ASSESSING AND MANAGING THE THREAT OF AN EMERGING INFECTIOUS DISEASE

- Infection Prevention
  - Environmental survival
  - Germicide susceptibility
  - Isolation recommendations
  - Recommended personal protective equipment
  - Pre-exposure prophylaxis (availability, efficacy, safety)
  - Postexposure prophylaxis (availability, efficacy, safety)
  - Recommended biosafety level in the laboratory
  - Recommended waste disposal (liquids and solids

- Managing a pandemic
  - Sensitive and specific (ideally rapid) diagnostic test
  - Early identification of patients
  - Protecting our healthcare personnel (appropriate isolation, PPE, donning, doffing)
  - Sufficient staff, inpatient/ICU beds, ventilators
  - Managing shortages
  - Rapid development and approval of therapeutics and vaccines

Weber DJ, Rutala WA, et al. Am J Infect Control 2016;44:e91-100

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- *C. auris*
- Mpox
- SARS-CoV-2
- HPV
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CANDIDA AURIS: AN OVERVIEW, CDC

- *Candida auris* is an emerging fungus that presents a serious global health threat for the following reasons:
  - *C. auris* is spreading geographically and increasing in incidence.
  - From 2019 to 2021, 17 states reported their first *C. auris* case and cases resistant to antifungal drugs tripled…now 35 states
  - *C. auris* may colonize patients for months to years (no method of decolonization). Infection (usually candidemia) has a high mortality (~60%).
  - It is often multidrug-resistant (e.g., echinocandins, triazoles, polyene [amphotericin B]). Some strains are resistant to all three available classes of antifungals.
  - It is difficult to identify with standard laboratory methods, and it can be misidentified in labs without specific technology. Misidentification may lead to inappropriate management.
  - It has caused multiple outbreaks in healthcare settings. For this reason, it is important to quickly identify *C. auris* in a hospitalized patient so that healthcare facilities can take special precautions to stop its spread.
- May 11, 2021: Updated tracking *C. auris* to include historical and current U.S. interactive maps and downloadable datasets
- July 19, 2021: Environmental Protection Agency (EPA) has created List P, a list of EPA-registered disinfectants effective against *C. auris*
- Current needs: (1) rapid diagnostics; (2) new drugs; (3) decolonization methods; (4) registered, easy to use and effective disinfectants; (5) other tools or protocols for treatment and prevention

https://www.cdc.gov/fungal/candida-auris/index.html
https://www.cdc.gov/fungal/candida-auris/researchers-and-industry-professionals.html

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CANDIDA AURIS: EPIDEMIOLOGY

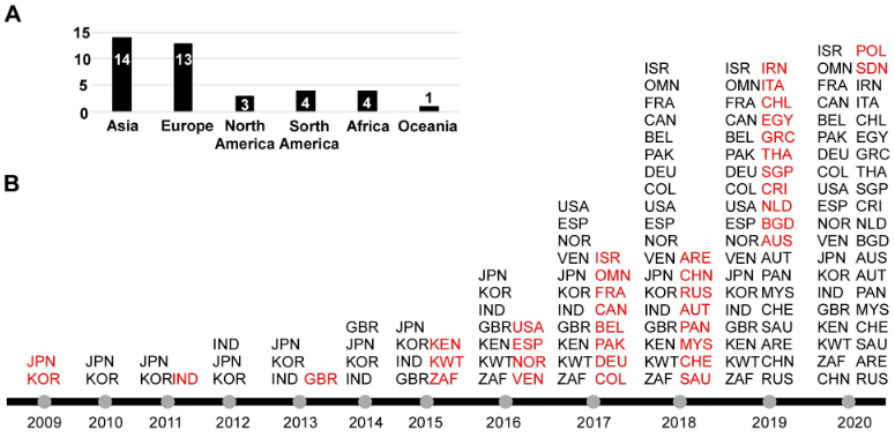


Fig 2. Countries with reported cases of *C. auris* infection or colonization from January 2009 to June 2020. (A) Number of countries belonging to each continent that have reported infection or colonization with *C. auris*. (B) Countries with reported cases from January 2009 to June 2020. The first reported case from each country is denoted in red text. ARE, United Arab Emirates; AUS, Australia; AUT, Austria; BEL, Belgium; BGD, Bangladesh; CAN, Canada; CHE, Switzerland; CHL, Chile; CHN, China; COL, Colombia; CRI, Costa Rica; DEU, Germany; EGY, Egypt; ESP, Spain; FRA, France; GBR, United Kingdom; GRC, Greece; IND, India; IRN, Iran; ISR, Israel; ITA, Italy; JPN, Japan; KEN, Kenya; KOR, Korea (South); KWT, Kuwait; MYS, Malaysia; NLD, the Netherlands; NOR, Norway; OMN, Oman; PAK, Pakistan; PAN, Panama; POL, Poland; RUS, Russia; SAU, Saudi Arabia; SDN, Sudan; SGP, Singapore; THA, Thailand; USA, United States of America; VEN, Venezuela; ZAF, South Africa.

https://doi.org/10.1371/journal.ppat.1008921.g002

Du H, et al. PLOS Pathogens 2020: Oct 22

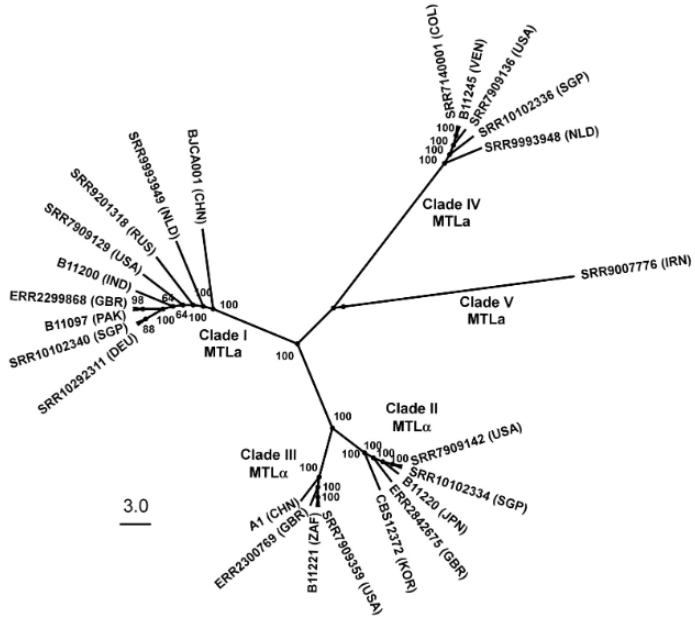
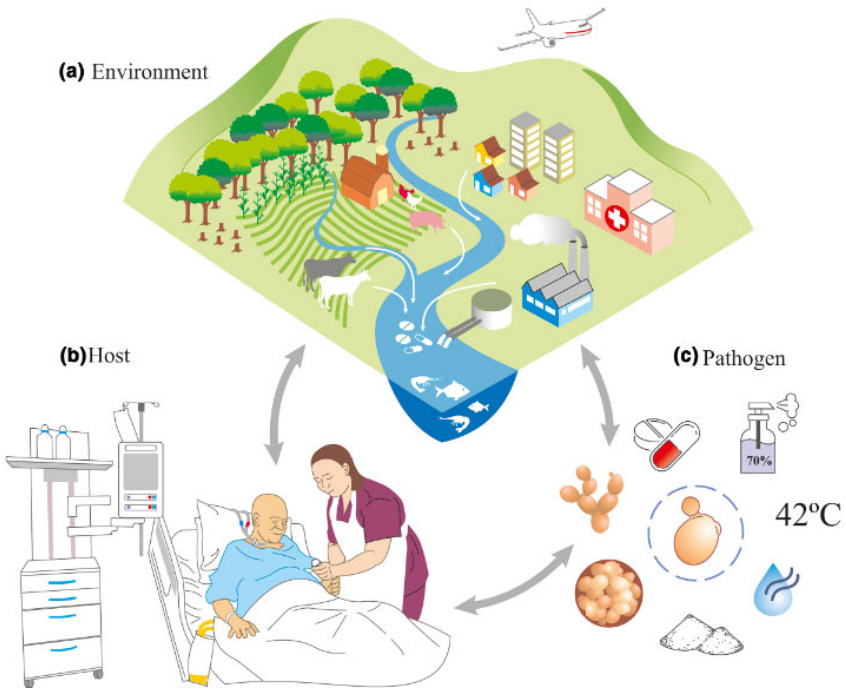


Fig 4. Five clades of *C. auris*. The phylogenic tree was generated with the program RAxML v7.3.2 using SNPs. The GTR model, gamma distribution, and 1,000 bootstraps were used to construct the phylogenetic relationships. The MTL are also included for each clade. CHN, China; COL, Colombia; DEU, Germany; GBR, United Kingdom; GTR, generalized time reversible; IND, India; IRN, Iran; JPN, Japan; KOR, Korea (South); MTL, mating type loci; NLD, the Netherlands; PAK, Pakistan; RUS, Russia; SGP, Singapore; SNPs, single-nucleotide polymorphisms; USA, United States of America; VEN, Venezuela describe the country where the strain was first isolated; ZAF, South Africa.

Clades have unique genetic and biochemical characteristics

On the emergence, spread and resistance of *Candida auris*: host, pathogen and environmental tipping points

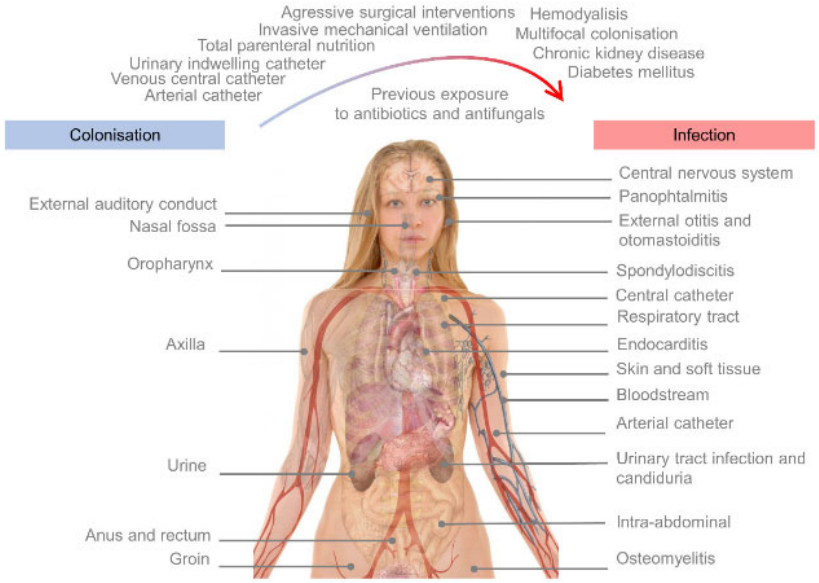


Chakrabarti A, Sood P. J Med Microbiol 2021;70:001318

Potential host–pathogen–environmental factors driving the emergence and spread of *C. auris*. (a) Environmental degradation caused by deforestation, expanded land use, industrial farming, aquaculture, human travel and climate change have probably disrupted and amplified the environmental niche of *C. auris*, bringing it closer to humans. An exponential increase in antimicrobial use in medicine, agriculture, animal husbandry and industry (white arrows) have also likely induced *C. auris* to acquire multiple resistance mechanisms. (b) Critically ill patients exposed to multiple invasive procedures and broad-spectrum antimicrobials are increasing in our hospitals and are susceptible to *C. auris*. Within hospitals *C. auris* contaminates and persists on inanimate surfaces and medical equipment, causing horizontal spread and outbreaks. (c) As a pathogen, *C. auris* exhibits high-level resistance to antifungals and some hospital disinfectants, tolerates temperatures up to 42 °C, resists desiccation, thrives in high-salt environments like human skin and sweat, forms robust biofilms, and switches into azole-resistant aggregative forms. These properties make *C. auris* a hardy nosocomial pathogen.

CANDIDA AURIS: EPIDEMIOLOGY

- First isolated in 2009 from ear discharge of a female patient in Japan; now reported in >45 countries worldwide
- Healthcare-associated outbreaks common
- Mortality ~65%-70%
- Primarily infects the usual spectrum of compromised individuals including those with uncontrolled diabetes mellitus, chronic renal diseases, neutropenia, and those on immunosuppressive therapy, broad-spectrum antimicrobials, and those with indwelling medical devices, or at extremes of age.
- Causes an array of human diseases ranging from fungemias, surgical/nonsurgical wound infections, urinary tract infections, meningitis, myocarditis, skin abscesses, to bone infections.



Bandara N, Smaranayake L. Med Mycology 2022;60:myac008; Lone S, Ahmad A 2019;62:620-637; Garcia-Bustos V, et al. Microorganisms 2021;9:2177

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TRANSMISSION AND PERSISTENCE OF *CANDIDA AURIS*

- Colonization of patients
  - Colonization of patients is common; multiple sites involved (Biswal 2017)
- Role of HCP
  - HCP may be colonized; uncommon (Schelenz 2017)
  - HCP hands may transiently carry *C. auris* (Biswal 2017)
- Role of environment
  - Environmental contamination common (Lesho 2018, Biswal 2017, Schelenz 2017, Valladhaneni 2016): mattresses, furniture, sinks, and medical equipment
  - Prolonged environmental survival on environmental surfaces; >14 days (Piedrahita 2017, Welsh 2017)
  - Prolonged survival (>7 days) on contaminated bedding (Biswal 2017)

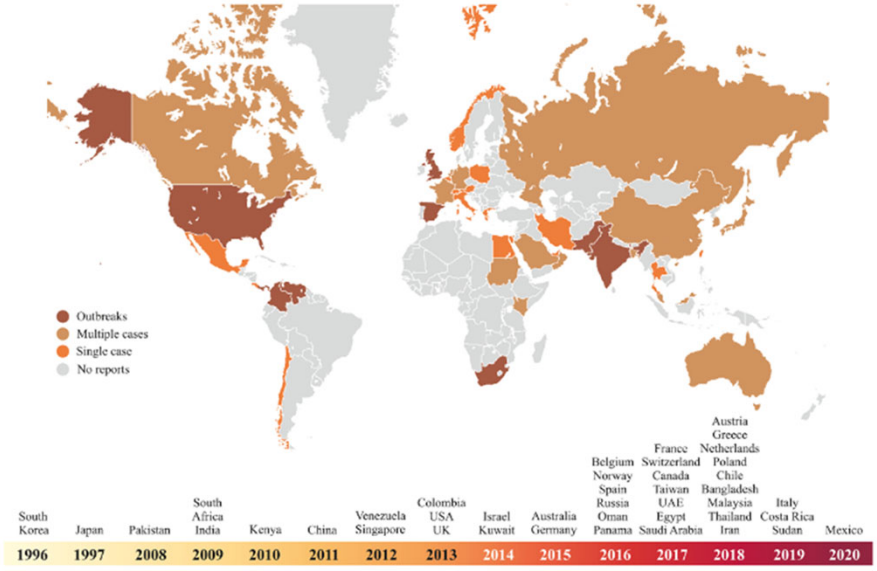
Hallmarks Making *Candida auris* a Major Public Health Issue and Proposed Interventions

Hallmark	Threat	Control/Prevention
Increased prevalence, unknown origin	Continuous increase in the future leads to emergence of *C. auris* as a frequent cause of nosocomial infections	Investigate potential sources/reservoirs, conduct epidemiological surveys in large prospective cohorts
Simultaneous emergence on different continents	Worldwide dissemination leads to pandemics of *C. auris* infection	Investigate environmental sources/reservoirs
Misidentification by diagnostic laboratories	Lack or delayed recognition of clinical cases leads to occult outbreaks	Improve development and access to new diagnostic tools (MALDI-TOF mass spectrometry, molecular techniques), improve training of laboratory personnel
Biofilm formation, persistence/survival in the environment	Interhuman transmission leads to nosocomial outbreaks	Screen patients, create hospital hygiene plans (isolation/disinfection), improve decontamination of surfaces (sporicidal agents)
Antifungal resistance (intrinsic or rapidly inducible)	Emergence of multidrug- or pan-drug–resistant strains leads to outbreaks with high mortality rate	Limit antifungal drug overuse, develop of novel antifungal therapies

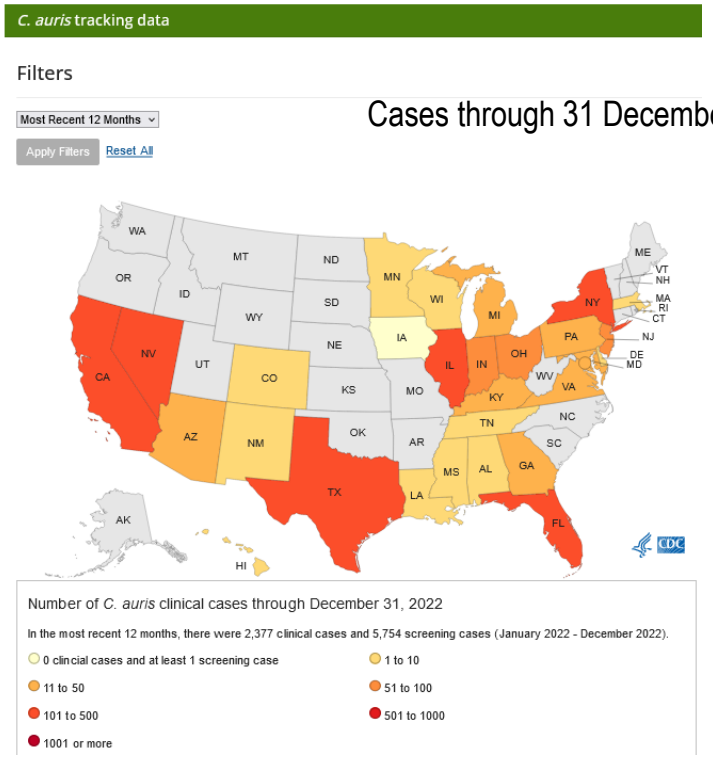
Abbreviation: MALDI-TOF, matrix-assisted laser desorption ionization–time of flight.

Lamoth F, Kontoyiannis DP. JID 2018;217:516

C. auris SURVEILLANCE, WORLDWIDE & US (CDC)



Chakravbarti A, Sood P. J Med Microbiol 2021;70:001318



International Multicentre Study of *Candida auris* Infections

- Retrospective observational multicentre study, 10 centers, 5 countries
- Significant risk factors for *C. auris* infection include the age group of 61–70 years (39%), recent history of ICU admission (63%), diabetes (63%), renal failure (52%), presence of CVC (91%) and previous history of antibiotic treatment (96%). *C. auris* was commonly isolated from blood (76%).
- All-cause crude mortality rate after 30 days was 37%. Antifungal therapy was associated with a reduction in mortality (OR:0.27) and so was source removal (OR:0.74). Contact isolation precautions were followed in 87% patients.

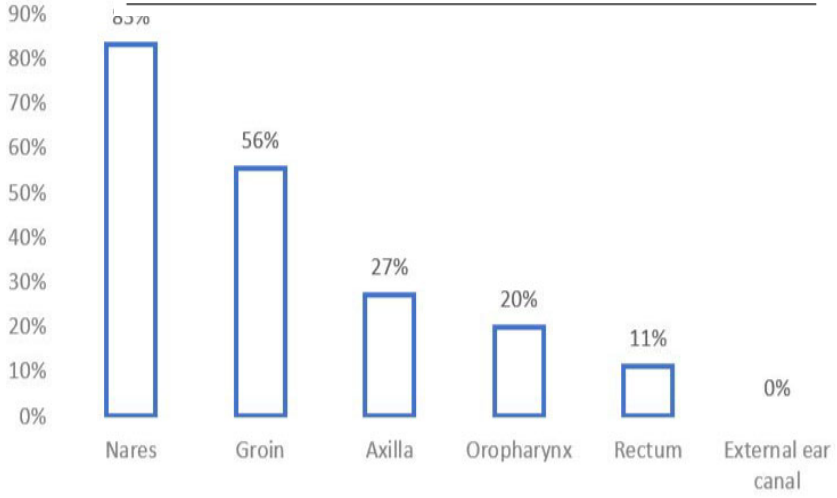
Table 2. Time from admission to positive culture.

No. of Days	Patient No.	Patient %
≤2 days	5	9%
3–7 days	8	15%
8–14 days	8	15%
15–30 days	17	31%
>1 month	16	30%

Pandya N, et al. J Fungi 2021;7:878

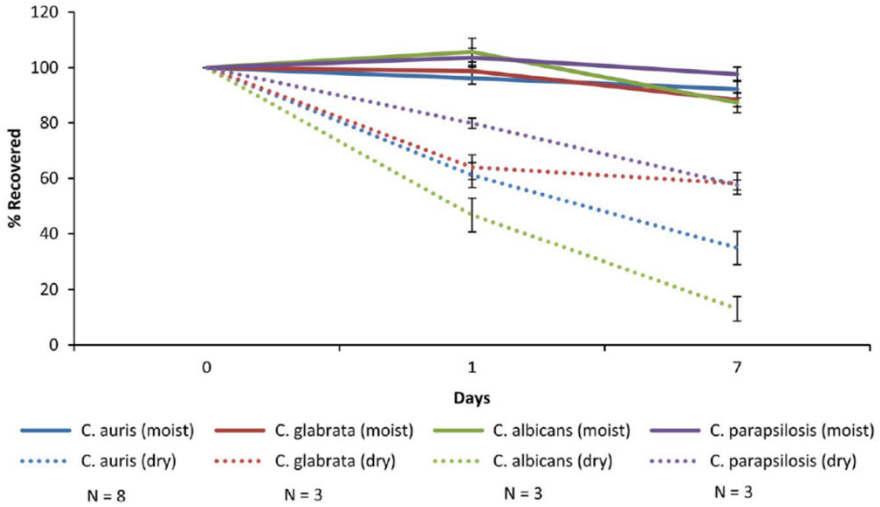
Table 4. Analysis to determine the risk factors for mortality among *C. auris* cases.

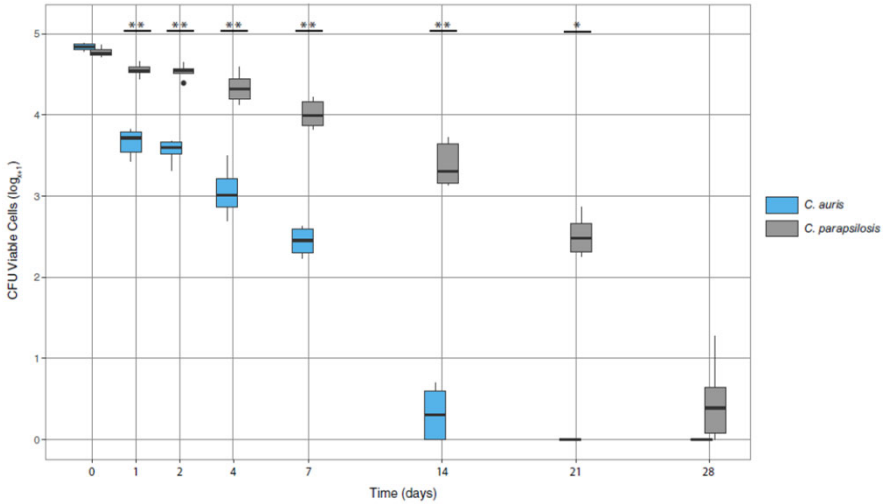
Risk Factor	Group-1 (Expired Patients)	Group-2 (Patients with Other Outcome)	Odds Ratio
Renal failure	67%	40%	3.0
Congestive Heart Failure	46%	17%	4.23
Invasive ventilator	75%	63%	1.74
Haemodialysis	63%	17%	8.33
Total parenteral Nutrition	33%	13%	3.25
Central Venous Catheter	100%	83%	4.60
Candidemia	88%	67%	3.5
Bacterial co-infection	58%	40%	2.1



ENVIRONMENTAL SURVIVAL OF *CANDIDA AURIS*

Persists for 7 days on moist or dry surfaces





Piedrahita C, et al. ICHE 2017;38:1107-1109

Welsh RM, et al. J Clin Microbiol 2017;55:2996-3005

NOSOOCOMIAL OUTBREAK OF *C. auris*

(Biswal M, et al. JHI 2017;97:363-370)

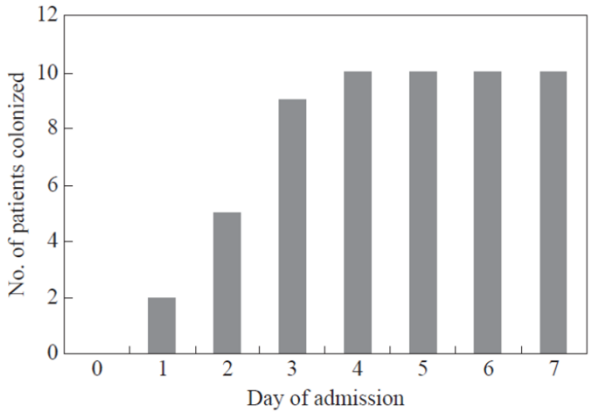


Figure 3. Time to *Candida auris* acquisition after intensive care unit admission.

Contamination of *Candida auris* on environmental samples and carriage on healthcare workers' hands

Samples	MICU	CCU	Trauma ICU	NSW
Environmental				
No. of samples	68	10	189	37
C. auris-positive samples	7	0	17	0
Handwash samples (HCWs)				
No. of samples	41	13	79	12
C. auris-positive samples	2	0	2	0

MICU, medical intensive care unit; CCU, cardiac care unit; ICU, intensive care unit; NSW, neurosurgical ward; HCW, healthcare worker.

C. auris frequently isolated from axilla, groin, rectum and oropharynx; colonization can occur rapidly and persists

Colonization rate by *Candida auris* of different body sites

Site	Oral	Rectal	Axilla	Groin
Trauma ICU				
No. of samples	89	83	158	168
Growth of *C. auris*	4 (4.4%)	15 (18%)	62 (39.2%)	34 (20.2%)
MICU				
No. of samples	38	35	38	38
Growth of *C. auris*	6 (15.7%)	3 (8.5%)	10 (26.3%)	2 (5.2%)
Total	10/95 (10.5%)	18/118 (15.2%)	72/196 (36.7%)	36/206 (17.4%)

ICU, intensive care unit; MICU, medical intensive care unit.

First hospital outbreak of the globally emerging *Candida auris* in a European hospital

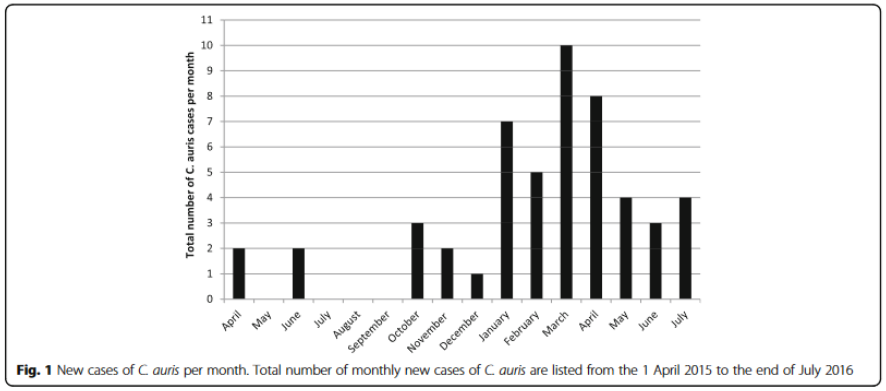


Fig. 1 New cases of *C. auris* per month. Total number of monthly new cases of *C. auris* are listed from the 1 April 2015 to the end of July 2016

CDC

- The risk of *C. auris* infection to otherwise healthy people, including healthcare personnel, is very low.
- At this time, HCP do not need to be tested for *C. auris* unless they are identified as a possible source of transmission to patients

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

- As healthcare workers (HCW) have been implemented in the transmission of other *Candida* species in the past we have undertaken an extensive staff screening program involving doctors, nurses, physiotherapists, catering and cleaning staff, dieticians, a Chaplin and ward administrators. Staff hands (agar impression plates), nose, axilla, groin and throat swabs were analyzed for the presence of *Candida*. Only one out of 258 HCW screened were found to have a *C. auris* positive nose swab (all other samples were negative). This nurse had been caring for a heavily *C. auris* colonized patient. After a five-day decolonization protocol with chlorhexidine washes, nasal ointment and oral nystatin medication (as described below) repeat microbiology samples were negative suggesting transient carriage only

Schelenz S, et al. Antimicrob Resistant Infect Control 2016;5:35

Characteristics of clade-III *Candida auris* colonization and infection in southern California, 2019–2022

- Background: 5 genomic clades – clade I (first isolated South Asian) = highest frequency of **antifungal resistance; clades I, III (African), and IV (South Am)= frequency associated with outbreaks. V (Iran), II (East Asian). Clades have unique genetic and biochemical** characteristics. Single common ancestor and descendants called a clade.
- 45 patients identified from late 2019 to early 2022 in CA (mortality = 18%)
- Most had tracheostomy or were from facility with known outbreak, 15% identified through passive surveillance
- 8 (18%) had a history of COVID-19
- 13 (29%) had bloodstream infection (likely to have central line)

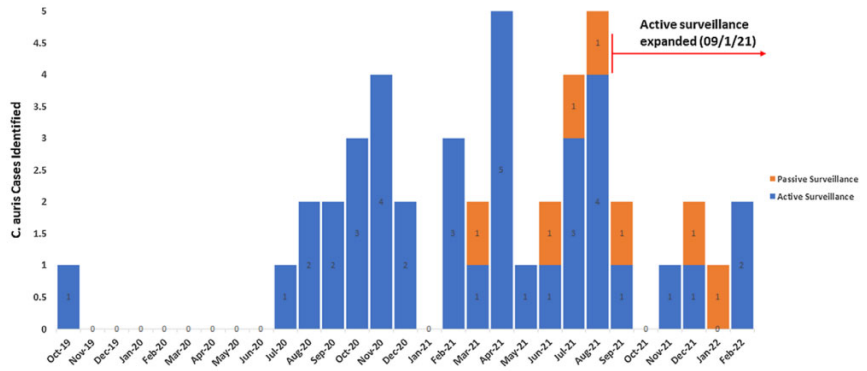


Fig. 2. Timeline and positive *C. auris* cases identified by either active or passive surveillance.

De St. Maurice A, et al. ICHE 2022;1-9

Table 2. Characteristics of Patients (n=13) with Invasive *C. auris*

Characteristic	No. (%)
Comorbidities	13 (100)
Chronic respiratory failure	8 (61)
End-stage renal disease	4 (31)
Diabetes	9 (69)
Cirrhosis	1 (8)
Malignancy	1 (8)
Known history of *C. auris* prior to infection	8 (62)
Received treatment for *C. auris* infection	12 (92)[a]
***C. auris* antifungal treatment**	
Caspofungin	11 (85)
Anidulafungin	1 (8)
Liposomal amphotericin[b]	1 (8)
Site of infection	
Blood	9 (69)
Urine	3 (23)
Pleural fluid	3 (23)
Tracheal aspirate	2 (15)
Wound	2 (15)

[a]For 1 patient, the blood culture grew *C. auris* after the patient died; therefore, the patient did not receive treatment.
[b]One patient received combination therapy with caspofungin and liposomal amphotericin.

Susceptibility of *C. auris* and *C. albicans* to 21 germicides used in healthcare facilities

- Goal: Assess susceptibility of *C. auris* to germicides
- Methods: Disc-based quantitative carrier testing
- Results: All of the FDA-cleared high-level disinfectants have a registration claim >1 minute (e.g., 8–45 minutes). In summary, with the exception of a water-based QAC and a 1:50 dilution of sodium hypochlorite, our data demonstrate that most disinfectants (10 of 13, 77%) used in healthcare facilities are effective (>3-$\log_{10}$ reduction) against *C. auris*.

Germicide name	Manufacturer, Location	Active Ingredient	Formulation Tested	Classification	*C. auris*[a]	*C. albicans*[a]
Purell Advanced instant hand sanitizer	GOJO, Akron, OH	70% ethanol	Undiluted	Antiseptic	4.0	2.5
Betadine solution	Purdue Products, Stamford, CT	10% povidone–iodine/1% iodine	Undiluted	Antiseptic	2.5	2.3
Medicated Soft 'N Sure	Steris, St. Louis, MO	0.5% triclosan	Undiluted	Antiseptic/Handwash	1.4	1.7
Soft Care Defend	Diversey, Charlotte, NC	1% chloroxylenol	Undiluted	Antiseptic/Handwash	2.8	3.9
Avagard	3M, St Paul, MN	1% chlorhexidine gluconate solution, 61% ethyl alcohol	Undiluted	Antiseptic/Surgical hand scrub	2.0	1.9
Scrub-Stat 2%	Ecolab, St Paul, MN	2% chlorhexidine gluconate solution	Undiluted	Antiseptic/Surgical hand scrub/handwash	1.6	2.8
Scrub-Stat 4%	Ecolab, St Paul, MN	4% chlorhexidine gluconate solution	Undiluted	Antiseptic/Surgical hand scrub/handwash	1.9	3.5
Isopropyl rubbing alcohol 70% USP	Medichoice, Mechanicsville, VA	70% isopropyl alcohol	Undiluted	Antiseptic/Disinfectant	3.8	4.1
Solution of hydrogen peroxide 3% USP	Medichoice, Mechanicsville, VA	3% hydrogen peroxide	Undiluted	Antiseptic	1.4	1.8
Austin's A-1 bleach 1:10	James Austin Co, Mars, PA	5.25% sodium hypochlorite (~6,100–6,700 ppm)	1:10 dilution	Disinfectant	4.1	4.0
Austin's A-1 bleach 1:50	James Austin Co, Mars, PA	5.25% sodium hypochlorite (~1,245 ppm)	1:50 dilution	Disinfectant	1.6	1.5
Vesphene IIse	Steris, St Louis, MO	9.09% o-phenylphenol, 7.66% p-tertiary amylphenol	1:128 dilution	Disinfectant	4.1	3.6
Hydrogen peroxide cleaner disinfectant	Clorox, Oakland, CA	1.4% hydrogen peroxide	Undiluted	Disinfectant	4.1	4.1
Lysol disinfectant spray	Reckitt Benckiser, Parsippany, NJ	58% ethanol, 0.1% QAC[b]	Undiluted	Disinfectant	3.8	4.1
A-456 II disinfectant cleaner	Ecolab, St Paul, MN	21.7% QAC[c]	1:256 dilution	Disinfectant	1.7	1.5
Super Sani-Cloth wipe	PDI, Orangeburg, NY	55% isopropyl alcohol, 0.5% QAC[d]	Undiluted[f]	Disinfectant	3.9	4.1
Prime Sani-Cloth wipe	PDI, Orangeburg, NY	28.7% isopropyl alcohol, 27.3% ethyl alcohol, 0.61% QAC[e]	Undiluted[f]	Disinfectant	4.1	4.1

Rutala WA, et al. ICHE 2019;40:380-382

List P: Antimicrobial Products Registered with EPA for Claims Against *Candida auris* (contact times, product dependent)

- Sodium Hypochlorite (1-3 min)
- Hydrogen peroxide and peracetic acid (1-3 min)
- Hydrogen Peroxide, Peracetic Acid and Octoanoic Acid (4 min)
- Dodecylbenzenesulfonic acid (1-1.25 min)
- Isopropyl Alcohol and Quaternary Ammonium Compound (1 min)
- Isopropyl Alcohol, DDAC and ADBAC (2 min)
- Hydrogen Peroxide (1-5 min)
- Quaternary Ammonium Compounds (10 min)
- Sodium dichloro-s-triazinetrione (2 min)
- Ethanol, Isopropyl Alcohol and DDAC (1 min)
- Isopropyl Alcohol and Quaternary Ammonium Compounds (2 min)

Caveats

- List P displays 30 approved products
- All products are ONLY approved for "hard non-porous surfaces"
- Contact times vary by class and specific product
- Products include sprays, wipes and liquids
- Some products are ready to use; others may require dilution
- Per CDC, if products on List P are not accessible or otherwise suitable, interim guidance permits use of an EPA-registered disinfectant active against *C. difficile* (List K)
- Follow manufacturer's use recommendations

https://www.epa.gov/pesticide-registration/list-p-antimicrobial-products-registered-epa-claims-against-candida-auris
https://www.cdc.gov/fungal/candida-auris/c-auris-infection-control.html

SUSCEPTIBILITY OF *C. auris* TO UV

- UV-C efficacy assessed against MRSA, *C. auris*, *Candida* sp., and MRSA[1]
  - *C. auris* less susceptible to UV-C than MRSA; similar but slight less susceptible than *C. difficile*
  - Increasing exposure time (10 to 20 to 30 min) resulted in enhanced killing; at 20 min, >4.5 $\log_{10}$; at 30 min >6 $\log_{10}$
- Pulsed xenon efficacy assess against *C. auris*[2]
  - 99.4% reduction in *C. auris* CFU after 5min at 1m and 99.6% after 10min at 2m
- Killing of *C. auris* by UV-C: Importance of exposure time and distance[3]
  - Maximal effect of *C. auris* killing found at 30min exposure at 2m (maximal killing, >5 $\log_{10}$). With half the time or twice the distance, efficacy diminished to ~10 and ~50-fold, respectively. At suboptimal exposure times and distance, strains from Japan/Korea more sensitive to UV-C killing than from Venezuela, Spain and India.
- Clade-specific variation in susceptibility of *C. auris* to UV-C[4]
  - Increased susceptibility of *C. auris* belonging to clades I, II and IV with increasing UV exposure time. *C. auris* isolates susceptible to UV-C were mostly nonaggregating, but the isolates that were more resistant to UV exposure formed aggregates.
- Efficacy of relatively low-cost UV-C devices against *C. auris*[5]
  - Some low-cost devices provided effective decontamination. *C. auris* from clades III and IV were less susceptible that from clades I and II.
- Inactivation of C. *auris* by UV-C[6]
  - With an organic load (FCS), *C. auris* reduction ($\log_{10}$) were; 4.57 direct line of sight, 2.41 indirect line of sight
- UV-C disinfection using a robot for routine cleaning[7]
  - UV-C inhibited growth of *C. auris* in the lag phase, but not in the presence of rim shadows; *C. auris* not effectively killed by standard UV cycle

[1]Cadnum JL, et al. ICHE 2018;39:94; [2]Maslo C, et al. BMC ID 2019;19:540; 3 de Groot T, et al. Mycoses 2019;62:408; [4]Chatterjee P, et al. ICHE 2020;41: 1384; [5]Pearlmutter BS, et al. ICHE 2021, 1-5; [6]Rutala WA, et al. ICHE 2021, 1-3; 7 Astrid F, et al. Antimicrob Resist Infect Control 2021;10:84

Key interventions recommended (or to be considered) by select governmental agencies to prevent transmission of *Candida auris*

Agency (country/ region)	Active surveillance population	Hand hygiene	Isolation	Transmission-based precautions	Environmental disinfection	Additional special measures	Reference
Centers for Disease Control and Prevention (USA)	Contacts of newly identified case patients. Patients with an overnight stay in a healthcare facility outside of the USA in the previous year	Alcohol-based hand rub, or soap and water if hands are visibly soiled	Single room or cohorting with another patient with *C. auris*	Standard and contact precautions, for the duration of colonization, perhaps indefinitely	Use a disinfectant active against *Clostridioides difficile* spores	Minimize the number of care providers	[91]
Public Health England (UK)	Patients admitted from affected hospitals within the UK or from hospitals in countries reporting outbreaks. Close contacts in intensive care settings or contacts of patients prior to implementation of isolation procedures	Soap and water followed by alcohol-based hand rub	Single room or cohorting for colonized or infected patients or pending screening from high-risk areas	Contact precautions	Post-discharge terminal cleaning with sodium hypochlorite disinfectant, with or without no-touch disinfection	Single-use medical equipment; chlorhexidine skin washes for critically ill patients, mouth gargle with chlorhexidine, and topical nystatin and terbinafine at key sites	[92]
European Centre for Disease Prevention and Control (Europe)	Patients recently admitted or transferred from hospitals with detected *C. auris* case. Close contact patients	–	Single room or cohorting	Contact precautions	Post-discharge terminal cleaning with chlorine-based disinfectants, hydrogen peroxide or other disinfectants with fungicidal activity	Staff cohorting. Single-use equipment or cohorting of equipment among cases	[61•]
Centre for Opportunistic, Tropical and Hospital Infections (South Africa)	Routine screening on admission not recommended	Soap and water followed by alcohol-based hand rub	Single room or cohorting	Standard and contact precautions	Environmental cleaning with a chlorine-based disinfectant and consider hydrogen peroxide vapor for no-touch disinfection after terminal cleaning	Off-unit procedures should be scheduled for last case of the day, followed by thorough cleaning	[93]

Synder GM Wright SB. Curr Infectious Dis Report 2019;21:19

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Evaluation of Hospital Floors as a Potential Source of Pathogen Dissemination

Deshpande et al. AJIC 2017. 45:336.

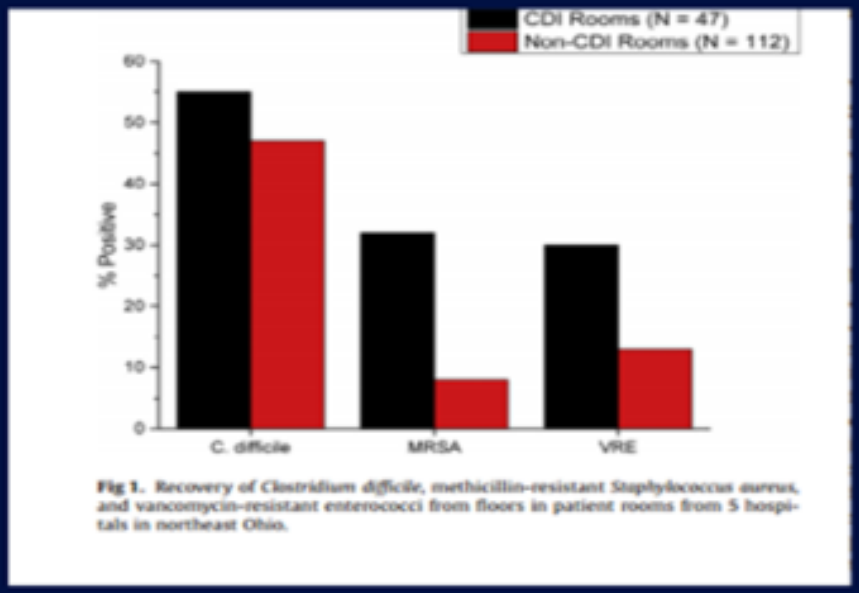


Fig 1. Recovery of *Clostridium difficile*, methicillin-resistant *Staphylococcus aureus*, and vancomycin-resistant enterococci from floors in patient rooms from 5 hospitals in northeast Ohio.

- 318 floors sites sampled in 159 rooms
- *C. difficile* most frequently isolated
- MRSA and VRE isolated more frequently from CDI rooms
- 41% (100) had objects (personal-clothing, phone chargers; medical-BP cuff, call button) in contact with floor
- Of 31 objects on floor, 18% MRSA, 6% VRE, 3% Cd bare/glove cultures positive
- Demonstrates potential for indirect transfer of pathogens to hands from fomites on floor

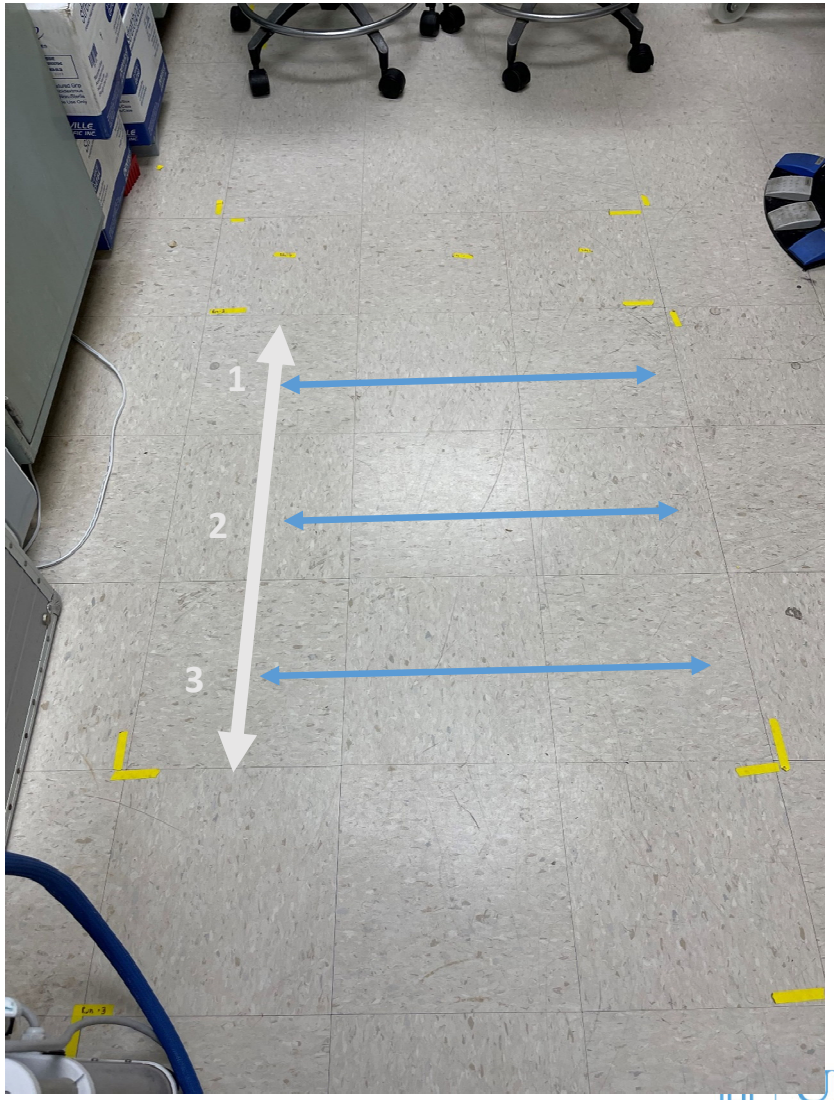
Inactivation and/or Physical Removal of *Candida auris* from Floors by Detergent Cleaner, Disinfectants, Microfiber and UV

Rutala, Bolomey, Cadnum, Donskey, 2023

- Contaminated floors may be source of transmission of *C. auris*
- Since floors may be a source of *C. auris* contamination of hands, strategies for inactivating or removing *C. auris* from floors were investigated
- A detergent cleaner, disinfectants, microfiber and UV-C were investigated.

C. auris Experimental Procedure

- Inoculate tiles with 10^5 to 10^6 *C. auris* (CDC #0385; clade 4) in 5% FCS (one 12x12 inch tile inoculated/spread to cover the tile)
- Recovery from control/untreated tiles was ~4 logs
- Groups
  - Prominence detergent
  - Virex 256
  - Spore Defense
  - Water
  - Unwiped controls
- To compare microfiber with cotton mop pads they were immersed in the test product.
- Soak microfiber/cotton with liquid and wring out excess
- Tiles wiped 3 times covering the inoculated tile and 2 adjacent tiles as shown by blue lines
  - The purpose of wiping the 2 adjacent tiles was to assess the potential for transfer of C. auris to uninoculated tiles)
- Sample each tile
- Plate dilutions on Sabaurouds plates to quantify
- Repeat experiment three times
- A 10-minute UV-C light (UVDI device) exposure was used for comparison



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Inactivation and/or Physical Removal of Candida auris from Floors by Detergent Cleaner, Disinfectants, Microfiber and UV

Rutala, Bolomey, Cadnum, Donskey, 2023

	Type of mop	Log Reduction On Tile 1 (SEM)	Transfer to tile 2 (SEM)	Transfer to tile 3 (SEM)
Prominence detergent	Microfiber	3.69 ± 0.15	0.00 ± 0.00	0.16 ± 0.00
	Cotton	3.69 ± 0.16	0.50 ± 0.33	0.00 ± 0.00
Virex 256	Microfiber	3.26 ± 0.28	0.16 ± 0.16	0.26 ± 0.14
	Cotton	3.69 ± 0.18	0.00 ± 0.00	0.00 ± 0.00
Spore Defense	Microfiber	3.85 ± 0.00	0.00 ± 0.00	0.00 ± 0.00
	Cotton	3.69 ± 0.20	0.00 ± 0.00	0.00 ± 0.00
Water	Microfiber	3.51 ± 0.33	0.34 ± 0.22	0.09 ± 0.09
	Cotton	2.45 ± 0.74	0.50 ± 0.33	1.00 ± 0.33
UV	N/A	3.85 ± 0.00	N/A	N/A

- The sporicidal disinfectant with microfiber and UV-C reduced *C. auris* on the floor to undetectable levels (Table 1) and did not allow transfer to adjacent tiles.
- Microfiber with water, detergent and the 2 disinfectants reduced *C. auris* by >3-$\log_{10}$ or 99.9% on tile 1.
- Cotton mop pads with the 2 disinfectants and the detergent reduced *C. auris* by >3-$\log_{10}$ on tile 1, but cotton mop pads with water did not.
- Microfiber and/or cotton mops transferred *C. auris* to uninoculated tiles when used with water, the detergent, and the quaternary ammonium compound, but no transfer to uninoculated tiles occurred with the sporicidal disinfectant.

Inactivation and/or Physical Removal of Candida auris from Floors by Detergent Cleaner, Disinfectants, Microfiber and UV

Rutala, Bolomey, Cadnum, Donskey, 2023

- Contamination of surfaces in *C. auris* patient rooms is common and has been associated with patient-to-patient transmission.
- *C. auris* is inactivated by many disinfectants but it is not rapidly inactivated by a commonly used floor disinfectant (i.e., a quaternary ammonium compound diluted in water).
- Since floors may be a source of pathogen contamination on hands,6 and quaternary ammonium compounds are not rapidly effective against *C. auris*, we investigated other strategies for inactivating or removing *C. auris* on floors.

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Inactivation and/or Physical Removal of Candida auris from Floors by Detergent Cleaner, Disinfectants, Microfiber and UV

Rutala, Bolomey, Cadnum, Donskey

- Our data demonstrated the most effective method to eliminate C. auris from floors is UV-C and a sporicidal disinfectant. Sporicidal disinfectants have been shown to inactivate *C. auris* and provide an option to eliminate *C. auris* from floors.
- Water, detergent, and a non-sporicidal disinfectant (with no *C. auris* claim) cross-contaminated uncontaminated surfaces from an inoculated tile. This demonstrated that when C. auris was not inactivated by the floor "treatment" procedure, the mop (cotton or microfiber) will physically move the C. auris from a contaminated to clean surface, as *C. auris* remained viable and the potential for hand contamination was not eliminated.

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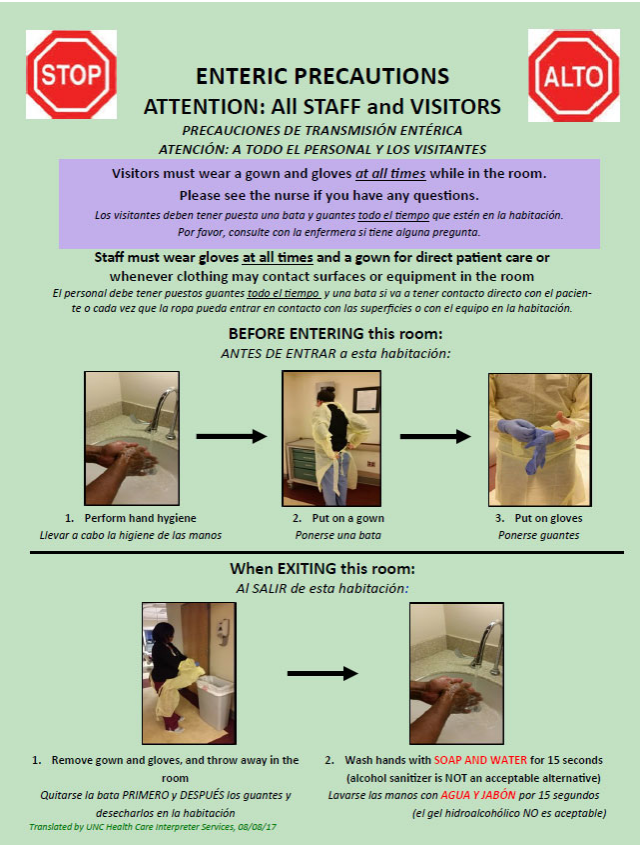
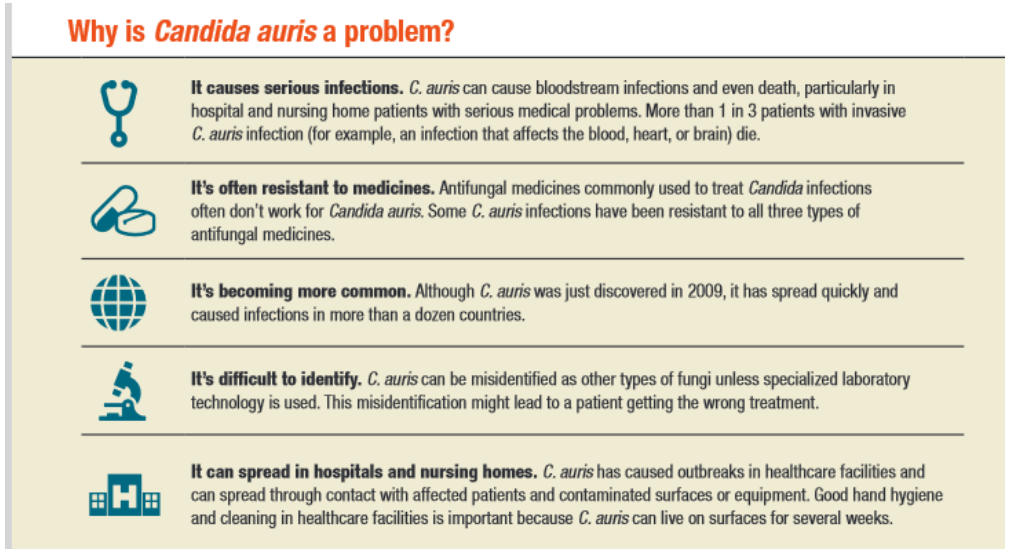
UNC Medical Center strategy for control:

- Patient's chart flagged before arrival to UNC Medical Center.
- Service lines caring for the patient have been communicated with directly.
- Infection Prevention has partnered with nursing staff, environmental services, patient transport, ICU transport, house supervisors, patient logistics center and ancillary areas the patient may visit.
- Patient placed on Enteric Precautions to ensure proper room cleaning daily with bleach and bleach + UV upon discharge.
- Alcohol based hand rubs are effective.
- Microbiology lab has been notified and has developed algorithm for identification.



CDC FACT SHEET



Why is *Candida auris* a problem?

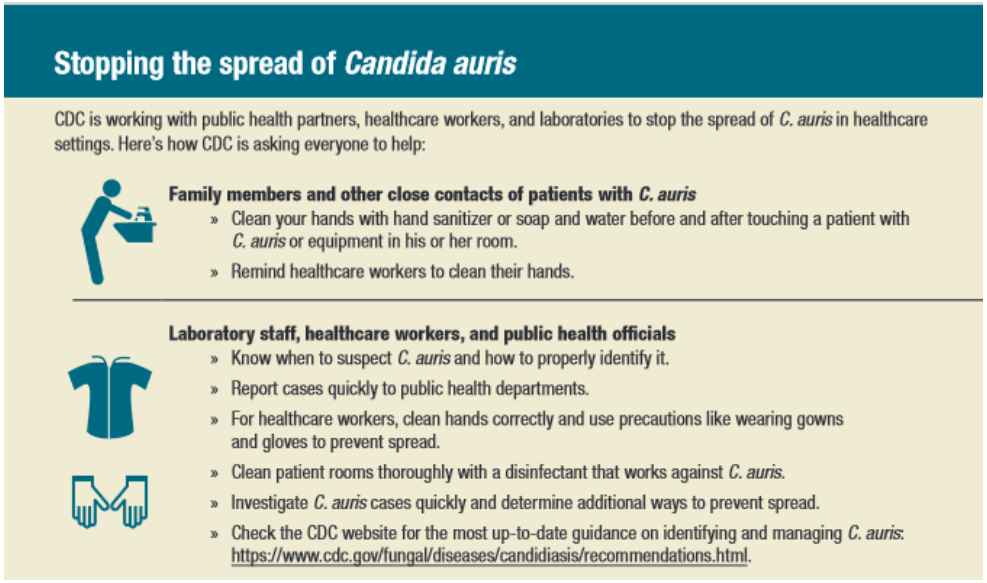
It causes serious infections. *C. auris* can cause bloodstream infections and even death, particularly in hospital and nursing home patients with serious medical problems. More than 1 in 3 patients with invasive *C. auris* infection (for example, an infection that affects the blood, heart, or brain) die.

It's often resistant to medicines. Antifungal medicines commonly used to treat *Candida* infections often don't work for *Candida auris*. Some *C. auris* infections have been resistant to all three types of antifungal medicines.

It's becoming more common. Although *C. auris* was just discovered in 2009, it has spread quickly and caused infections in more than a dozen countries.

It's difficult to identify. *C. auris* can be misidentified as other types of fungi unless specialized laboratory technology is used. This misidentification might lead to a patient getting the wrong treatment.

It can spread in hospitals and nursing homes. *C. auris* has caused outbreaks in healthcare facilities and can spread through contact with affected patients and contaminated surfaces or equipment. Good hand hygiene and cleaning in healthcare facilities is important because *C. auris* can live on surfaces for several weeks.



Stopping the spread of *Candida auris*

CDC is working with public health partners, healthcare workers, and laboratories to stop the spread of *C. auris* in healthcare settings. Here's how CDC is asking everyone to help:

Family members and other close contacts of patients with *C. auris*

- Clean your hands with hand sanitizer or soap and water before and after touching a patient with *C. auris* or equipment in his or her room.
- Remind healthcare workers to clean their hands.

Laboratory staff, healthcare workers, and public health officials

- Know when to suspect *C. auris* and how to properly identify it.
- Report cases quickly to public health departments.
- For healthcare workers, clean hands correctly and use precautions like wearing gowns and gloves to prevent spread.
- Clean patient rooms thoroughly with a disinfectant that works against *C. auris*.
- Investigate *C. auris* cases quickly and determine additional ways to prevent spread.
- Check the CDC website for the most up-to-date guidance on identifying and managing *C. auris*: https://www.cdc.gov/fungal/diseases/candidiasis/recommendations.html.

https://www.cdc.gov/fungal/diseases/candidiasis/pdf/Candida_auris_508.pdf

Infection Prevention and Control for *Candida auris*

- Hand Hygiene: HCP should follow standard hand hygiene practices. Alcohol-based hand sanitizer (ABHS) is the preferred hand hygiene method for *C. auris* when hands are not visibly soiled. If hands are visibly soiled, wash with soap and water.
- Transmission Based Precautions: Private room with bathroom, contact isolation (gloves & gown)
  - Duration of precautions: Patients often remain colonized with *C. auris* for many months, perhaps indefinitely, even after an acute infection (if present) has been treated and resolves. Continue precautions for entire duration of stay.
  - CDC does not recommend routine reassessments for *C. auris* colonization. At this time, no specific intervention is known to reduce or eliminate *C. auris* colonization.
- Disinfection: *C. auris* can persist on surfaces in healthcare environments for days to months.
  - Perform thorough routine (at least daily) and terminal cleaning and disinfection of patients' rooms and other areas where patients receive care (e.g., radiology, physical therapy) using an appropriate disinfectant. Clean and disinfect shared or reusable equipment (e.g., ventilators, physical therapy equipment) after each use. Label cleaned and disinfected equipment as such and store it away from dirty equipment. Data indicate that products solely dependent on quaternary ammonia compounds (QACs) are NOT effective. Use an EPA–registered hospital-grade disinfectant effective against *C. auris* (List P). Consider a "no touch" method (e.g., UV-C) as a supplement to standard disinfection.
- Other: 1) Educate HCP about appropriate precautions; 2) Ensure adequate supplies are available; 3) Monitor compliance with HH & disinfection (provide feedback); 4) Ensure proper signage on door; 5) Flag the patient's record; 6) Consider patient screening and lab surveillance.

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

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CONCLUSIONS: *CANDIDA AURIS*

- *C. auris* is a growing worldwide threat due to high mortality, resistance to many antifungals, and difficulties in laboratory identification
- *C. auris* is capable of prolonged environmental survival; contamination of hospital surfaces is common
- *C. auris* killed by most hospital disinfectants but has reduced susceptibility to some low-level disinfectants (QACs in water) and to UV-C (use settings for *C. difficile*); *C. auris* is susceptible to alcohol-based antiseptics
- References
  - Weber DJ, Rutala WA, Sickbert-Bennett EE. Emerging Infectious Diseases, Focus on Infection Prevention, Environmental Survival and Germicide Susceptibility: SARS-CoV-2, Mpox, and *Candida auris*. Am J Infect Control 2023 (In press)
  - Rutala WA, Kanamori H, Gergen MF, Sickbert-Bennett EE, Weber DJ. Inactivation of *Candida auris* and *Candida albicans* by ultraviolet-C. Infect Control Hosp Epidemiol. 2022 Oct;43(10):1495-1497.
  - Rutala WA, Kanamori H, Gergen MF, Sickbert-Bennett EE, Weber DJ. Susceptibility *of Candida auris* and *Candida albicans* to 21 germicides used in healthcare facilities. Infect Control Hosp Epidemiol. 2019 Mar;40(3):380-382.
  - Weber DJ, Sickbert-Bennett EE, Kanamori H, Rutala WA. New and emerging infectious diseases (Ebola, Middle Eastern respiratory syndrome coronavirus, carbapenem-resistant *Enterobacteriaceae*, *Candida aur*is): Focus on environmental survival and germicide susceptibility. Am J Infect Control. 2019 Jun;47S:A29-A38.
  - Rutala WA, Gergen MF, Sickbert-Bennett EE, Anderson DJ, Weber DJ; CDC Prevention Epicenters Program. Antimicrobial activity of a continuously active disinfectant against healthcare pathogens. Infect Control Hosp Epidemiol. 2019 Nov;40(11):1284-1286.

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EMERGING INFECTIOUS DISEASES: *C. auris*, Mpox, SARS-CoV-2, HPV, CRE

- *C. auris*
- Mpox
- SARS-CoV-2
- HPV
- CRE

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ZOONOTIC DISEASE THREATS

Table 1. Importance of selected zoonotic diseases.

Disease	No. of US[a] cases in 1990–1998	Bioterrorism potential[b]	Infection control concern
Andes virus pulmonary syndrome	Not reportable	+	++
Anthrax	1	+++	+
B virus infection	Not reportable	None	+
Hemorrhagic fever (due to filoviruses and arenaviruses)	Not reportable	+++	+++
Monkeypox	Not reportable	?	++
Plague	80	+++	+++
Q fever	Not reportable	++	+
Rabies	25	None	+

NOTE. +++, high concern; ++, moderate concern; +, low concern; ?, unknown.

[a] Some zoonotic diseases, although not reportable nationally, may be reportable in individual states.

[b] Data are from [5].

Weber DJ, Rutala WA. Clin Infect Dis 2001;32:446

Table 2. Zoonotic diseases: mode(s) of transmission and risk of human-to-human transmission.

Disease	Pathogen	Mode(s) of transmission	Risk of human-to-human transmission
Hantavirus pulmonary syndrome	Andes virus	Inhalation of host rodent feces, urine, or saliva	Undefined; epidemiological and molecular evidence supports hypotheses regarding person-to-person transmission
Anthrax	*Bacillus anthracis*	Direct contact with contaminated animal products (e.g., hides), inhalation of spores, or ingestion of contaminated food	Rare cases of human-to-human transmission via direct contact with cutaneous lesions; risk of infection via inhalation from contaminated clothes and/or patient items
B virus infection	Cercopithecine herpesvirus 1	Direct contact with macaques (e.g., animal bites or scratches, cage scratch, or contaminated sharp injury); direct contact with infected cell culture	Rare; only a single case reported following direct contact with herpetic lesion
Hemorrhagic fever	Multiple agents[a]	Direct contact with potentially infective material (e.g., blood, vomitus, stool, or tissue)	High; person-to-person transmission common; nosocomial transmission frequent
Monkeypox	*Orthopoxvirus*	Contact with lesions; droplet transmission (?)	Attack rate among household contacts (unvaccinated), ~10%
Plague	*Yersinia pestis*	Flea bite; cat scratch; inhalation	High for pneumonic plague; theoretical for cutaneous plague (via inhalation from aspiration or wound irrigation); risk of infection via inhalation from contaminated clothes and/or patient items
Q fever	*Coxiella burnetii*	Contact with products of conception; inhalation	Rare; single case of human-to-human transmission (obstetrician); risk of infection via inhalation from contaminated clothes and/or patient items
Rabies	Rhabdovirus	Animal bites or scratches; rarely, mucous membrane contamination with animal saliva, aerosol transmission while spelunking or in a laboratory, or corneal transplantation; exposure frequently unknown	Animal-to-human transmission via nonintact skin and mucosal contact with saliva is well documented; human-to-human transmission theoretically possible; anecdotal reports of human-to-human transmission; nosocomial transmission not reported

NOTE. ?, unknown.

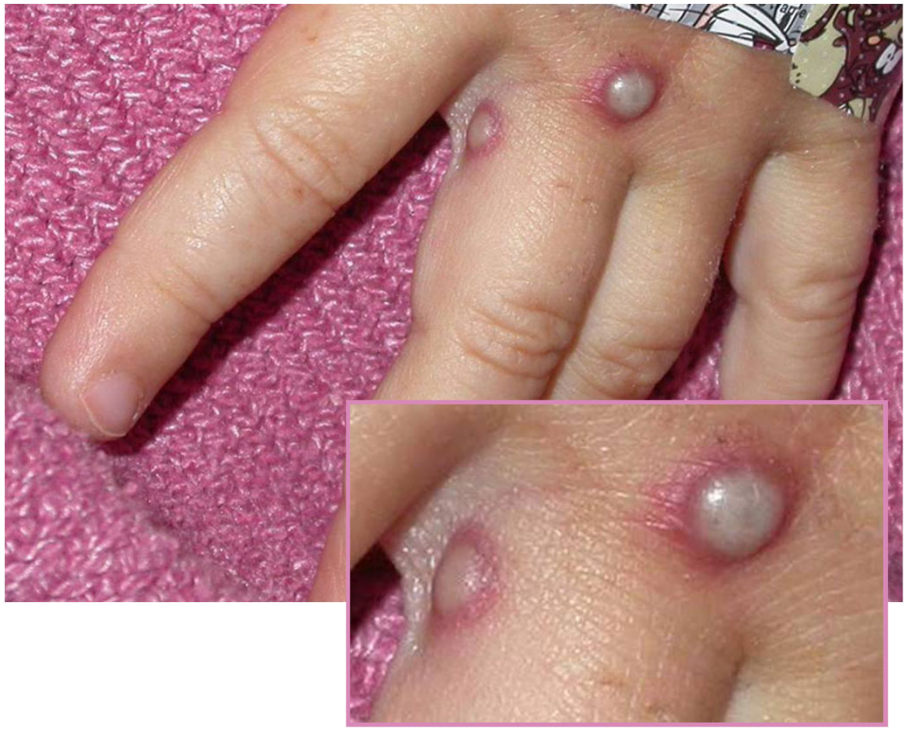
[a] Including Ebola, Marburg, Lassa, Crimean-Congo hemorrhagic fever, Argentine hemorrhagic fever, and Bolivian hemorrhagic fever viruses.

MPOX: KEY FEATURES

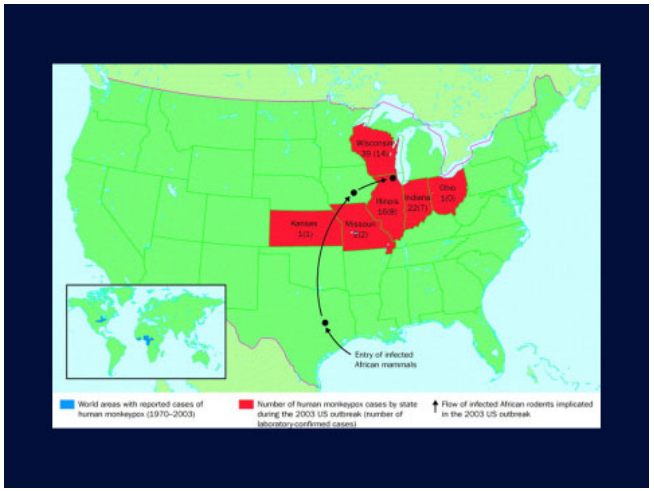
- Pathogen: Mpox virus; member of the Orthopoxvirus genus
- Reservoir: Unclear (rodents and non-human primates?)
- Infectiousness: Ro: ~1.3
- Duration of infectivity: Until all skin lesions have fallen off leaving healthy skin
- Incubation period: ~8.26 days (95% CI; 7.55, 8.97 days)
- Transmission mechanisms: : Animal-to-human (e.g., bite, scratch); human-to- human via skin-to-skin contact, droplet, vertical (transplacental, mother-to-fetus; congenital); fomites (e.g., contaminated clothes, bedding); needlestick
- Pre-symptomatic transmission: Rare; Asymptomatic transmission, unclear
- Environmental survival: Prolonged (potentially months)
- Diagnosis: Samples obtained from skin lesions (PCR)
- Pre-exposure prophylaxis: Yes (Jynneos vaccine)
- Post-exposure prophylaxis: Yes (Jynneos vaccine)
- Isolation: Private room (airborne isolation room for aerosol generating procedures); PPE, N95, gloves, gowns, eye protection
- Antiseptics = Alcohol waterless product; Disinfectants = disinfectants listed by the EPA, list Q
- Therapy: Follow recommendations of CDC

2003 MPOX OUTBREAK IN U.S.

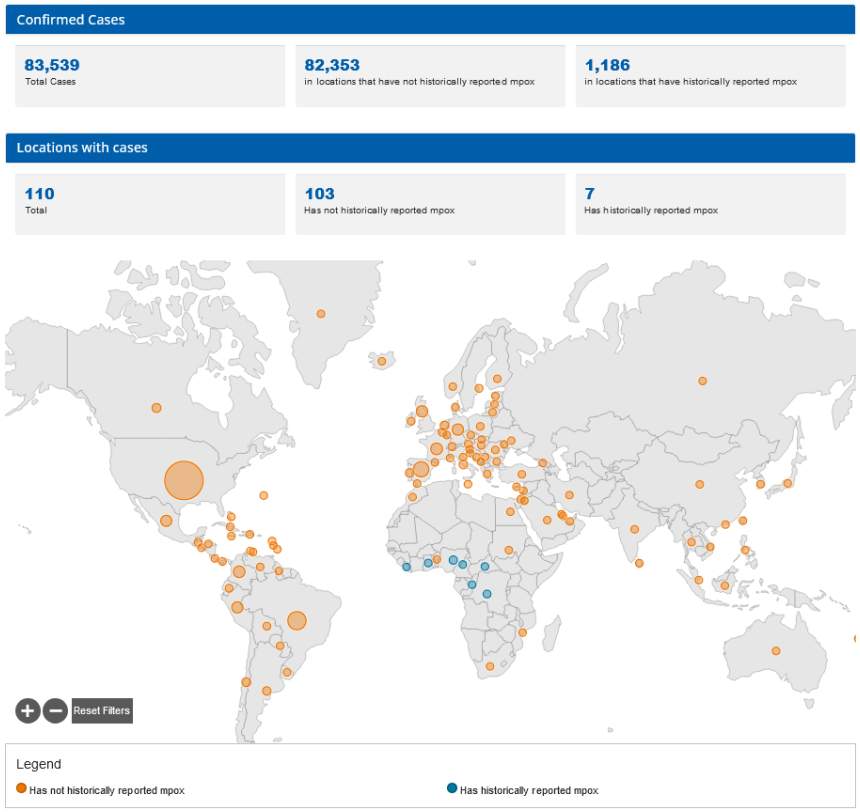
Child: Secondary lesions 5/27/03, adjacent to primary inoculation site on left hand

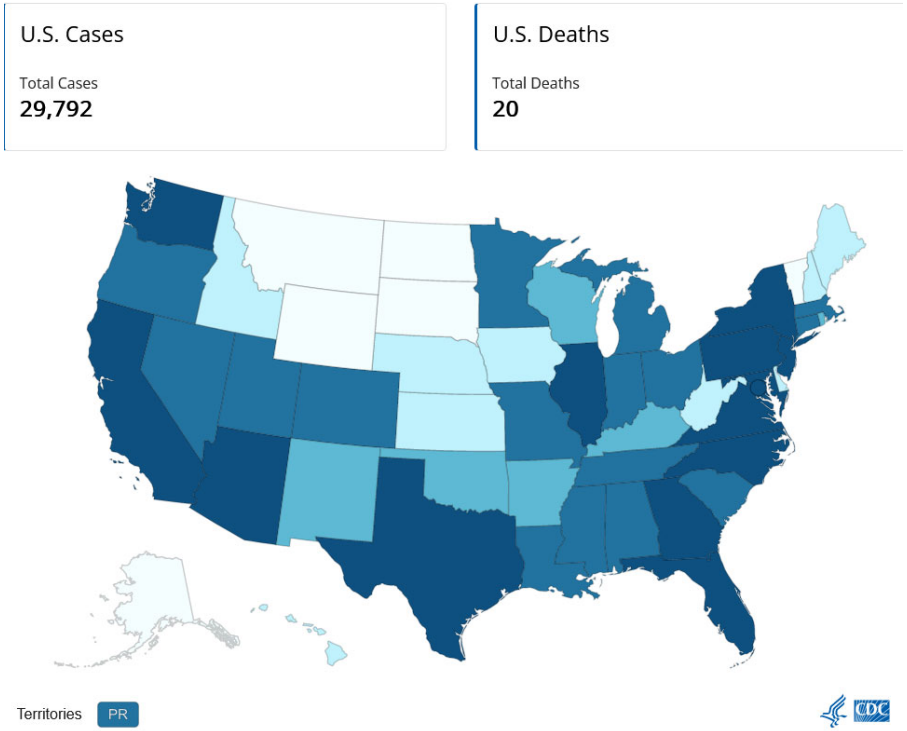


- Outbreak: May 13 to June 20, 2003
- Index case, 3-year old female hospitalized after prairie dog bite with cellulitis at bite site and disseminated lesions (also fever, chills, lymphadenopathy, cough, headache, and conjunctivitis; prairie dog died
- Reservoir: Gambian rats
- Source: Prairie dogs (all 47 cases contact with prairie dogs), Rabbit
- Six states: IL, IN, KS, MI, OH, WI
- Largest outbreak outside of Africa led to 47 human infections
- No human-to-human transmission; No deaths (fatality rate 1-10%)



2022 MPOX Outbreak, Global Map & US

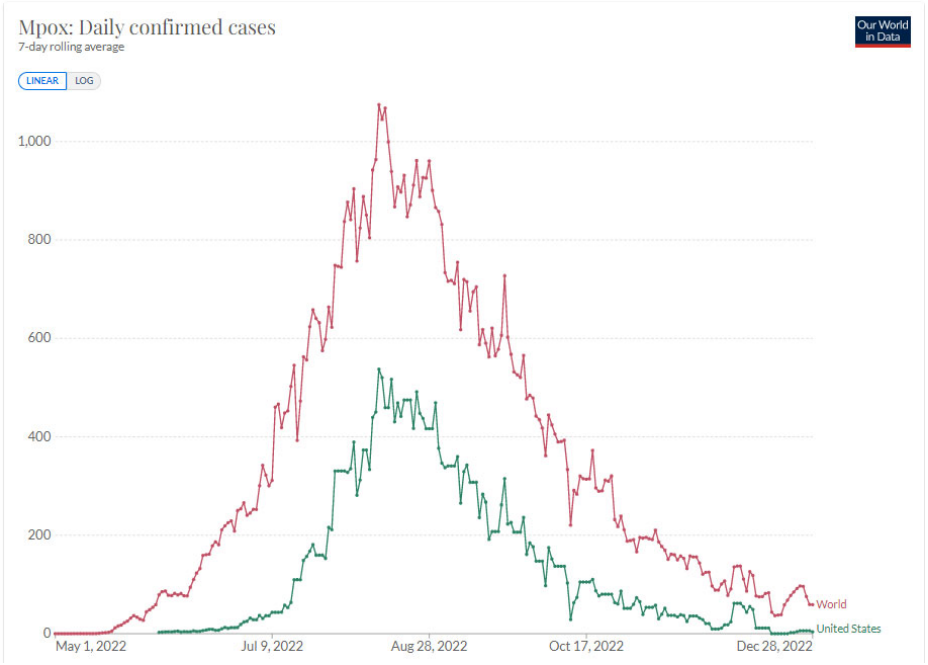


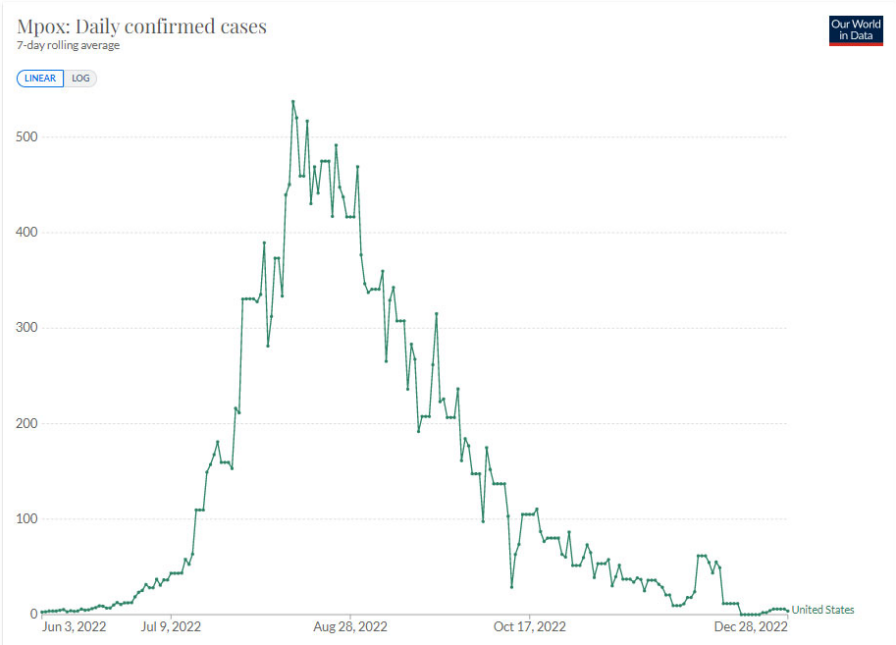


Deaths uncommon (US=20); hospitalizations infrequent (US, 8%) and most commonly for pain relief

https://www.cdc.gov/poxvirus/monkeypox/response/2022/index.html

MPOX OUTBREAK CURVES: WORLDWIDE & US





Cases peaked in August 2022, then steep decline conc among persons with multiple sex partners and primarily gay and bisexual men and trans women. Many persons in these populations got immunity from virus either vaccine or recovery.

Our World in Data – *https://ourworldindata.org/monkeypox*

MONKEYPOX

- History: First recognized in 1958 (captive primates); first human cases in 1970-71 (Zaire); endemic in regions of Africa; increasing cases in Africa in recent years likely to decreasing prevalence of smallpox vaccine recipients; 2003 US outbreak, 71 cases
- 2022 outbreak:86,956 cases worldwide; 30,347 cases in US; >100 countries (February 2023); cases substantially reduced, late summer
- Transmission: 1) Direct contact with body fluids or lesions; 2) Respiratory (droplet transmission) - no data on risk if patient has pneumonia; 3) Sexual? (unknown if via semen or vaginal fluids); 4) Vertical (transplacental; mother-to-fetus); 5) Indirect (via fomites) such bedding & clothes[1,4] or eating utensils[2]
- Nosocomial transmission to HCP has been reported[3,4,5,6]
- Smallpox virus (Monkeypox surrogate) environmental survival: at the ambient temperature of 25.8-26.4°C and 85-90° relative humidity, the virus in crusts survived only 8 weeks but at lower temperatures and relative humidities the survival time was considerably prolonged[7]; survival in cotton may be as long as 18 months[8]
- Smallpox, disinfectant susceptibility: ethanol, isopropanol, 60-95% ≤1min
- Vaccinia: Sodium hypochlorite, QAUT plus CHG inactivating virus at all concentrations tested[10]

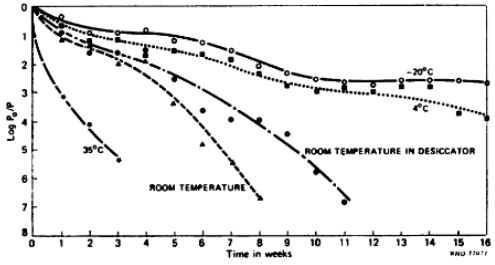


Fig. 1. Fall in log titre of variola virus with time under different environmental conditions.

[1]Harris E. JAMA 2022 27 May; [2]Nolen LD, et al. Am J Trop Med Hyg 2015;93:410; [3]Adler H, et al. Lancet ID 2022;24 May; [4]Vaughan A, et al. EID 2020;26:782; [5]Learned LA, et al. Am J Trop Med Hyg 2005;73:428; [6]Yinka-Ogunleye A, et al. Lancet ID 2019;19:872; [7]Huq F. Bull WHO 1976;54:3571; [8]MacCallum FO, McDonald JR. Bull WHO 1957;16:247; [9]Tanabe I et al. Appl Environ Microbiol 1976;32:209; [10]de Oliveira TML, Rehfeld LS, et al. Am J Trop Med 2011;85:152

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MPOX: SUMMARY OF NEW INFORMATION

- Current outbreak largest ever recorded; however, outbreak curve has dramatically decreased
- Outbreak due to a new clade (clade IIb)
- Main transmission mechanism is skin-to -skin contact (others: droplet ; requires prolonged exposure, fomites [shared eating utensils, contaminated bedding/clothes], transplacental and congenital)
- Mpox virus DNA can be detected in wastewater – may be useful as a monitoring tool (similar to polio and SARS-CoV-2)
- Great majority of cases in men who have sex with men (MSMs); NC ~700 cases, at risk population in NC = 15,700
- Most patients in current outbreak have atypical symptoms compared to classic (endemic) MPX
- Testing: Available at health departments (free) and many commercial labs (capacity, ~70,000-80,000 tests per week)
- UNC-CH performing “in house” diagnostic tests for UNC Health
- Jynneos vaccine available for pre-exposure (PreP) and post-exposure prophylaxis (PEP)
  - UNC has provided PreP to our microbiologists performing mpox testing; PreP also being provided in ID clinic
  - FDA has authorized ID administration at 1/5 dose to expand supply (based on limited data; one 2015 paper)
  - Recent papers demonstrate effectiveness of vaccine in preventing mpox
- Tecovirimat (TPOXX) available for treatment: Only case series available regarding effectiveness.

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MPOX: ROUTES OF TRANSMISSION

- Animal-to-human via bite/scratch, direct contact, and indirect contact (cleaning cages, animal products)
  - Primates, rodents (squirrels, prairie, woodchucks), pigs, opossums
- Human-to-animal (dog, greyhound; current outbreak)
- Human-to-human
  - Respiratory secretions (droplet transmission) – prolonged face-to-face contact (no data regarding risk from patients with pneumonia)
  - Direct contact (skin-to-skin) with body fluids or body lesions
    - Auto-inoculation possible (e.g., Skin lesion to eyes)
  - Indirect contact/fomites (drinking or eating from same dish, contact with contaminated linens)
  - Sexual: Direct contact, unknown if via semen or vaginal fluids
  - Vertical (transplacental) or at deliver (congenital): May lead to fetal demise
- Mortality: The case fatality rate for the Central African clade is 1-10% versus <3% for the West African clade
  - Likely an overestimate (biased by severity)
  - Currently outbreak expected mortality <1%; highest risk immunocompromised, pregnant women, young children

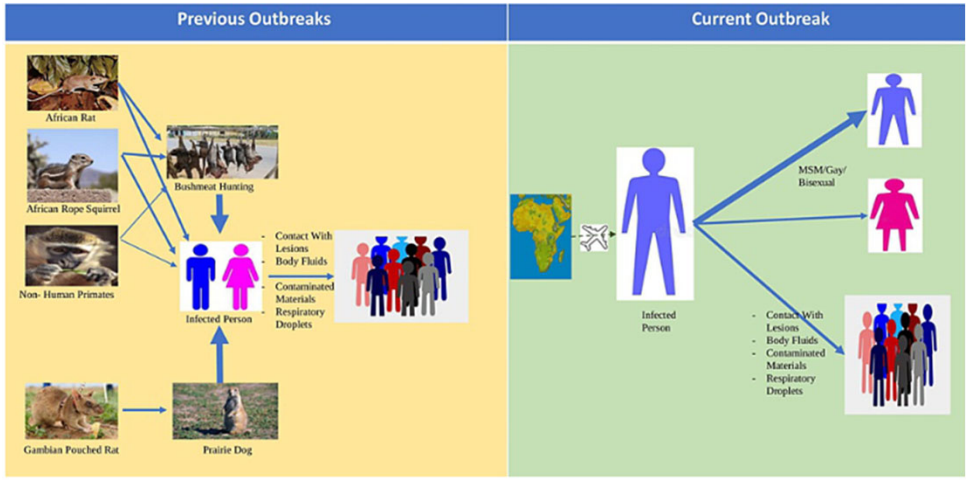

FIGURE 3: Changes in the transmission mode of monkeypox over the decades

MSM: men who have sex with men

Thin Arrow: low association; Thick Arrow: higher association

Titanji BK, et al. Open Forum Infectious Diseases 2022;21 June
Bunge EM, et al. PLOS Neglected Tropical Diseases 2022:11 February;
Reynolds MG, et al. Curr Opin Virology 2018;28:108-115; CDC
Khalil A, et al. Ultrasound Obstet Gynecol 2022;2 June
Alakunle E, et al. Viruses 2020;12:1257
Seang S, et al. Lancet 2022;10 August
Singh S, et al Cureus 2022:14(11);e31109

Surface Contamination Associated With Mpox Infected Persons

Setting	Frequency of Positive Surfaces (PCR)	Frequency of Positive Surfaces (Culture)	Reference
Household	70% (21/30)	0% (0/30)	Pfeiffer JA, at al.
Household	87% (27/31)	23% (7/31)	Morgan CN, et al
Household	88% (37/42)	60% (6/10)	Atkinson B, et al
Hospital rooms	93% (55/60)	50% (2/4)	Gould S, et al.
Hospital rooms	Frequent	Not assessed	Norz D, et al.
Hospital room	Frequent	14% (1/7)	Marimuthu et al.
Hospital rooms]	100% (9/9)	Not assessed	Muller et al.

Chart developed by WHO working group of Mpox virus environmental survival and disinfection
Weber DJ, Rutala WA, et al. Am J Infection Control 2023 (In press)

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MPOX: INFECTION CONTROL IN HEALTHCARE SETTINGS,CDC

- Precautions: In addition to Standard Precautions, if a patient seeking care is suspected to have mpox infection, additional infection control precautions (as described below) should be implemented. Infection prevention and control personnel should be notified immediately. Activities that could resuspend dried material from lesions (e.g., use of portable fans, dry dusting, sweeping, vacuuming) should be avoided.
- Patient placement: A patient with suspected or confirmed mpox infection should be placed in a single-person room with a dedicated bathroom; special air handling is not required. Transport and movement of the patient outside of the room should be limited to medically essential purposes. If the patient is transported outside of their room, they should use well-fitting source control (e.g., medical mask) and have any exposed skin lesions covered with a sheet or gown. Intubation, extubation, and any procedures likely to spread oral secretions should be performed in an airborne infection isolation room.
- PPE for HCP: Gown, gloves, eye protection, NIOSH-approved particulate respirator equipped with N95 filters or higher
- Environmental Control: Standard cleaning and disinfection procedures should be performed using an EPA-registered hospital-grade disinfectant with an emerging viral pathogen claim. Soiled laundry (e.g., bedding, towels, personal clothing) should be handled in accordance with recommended standard practices, avoiding contact with lesion material that may be present on the laundry. Management of food service items should also be performed in accordance with routine procedures.
- Duration of isolation: Those with confirmed mpox infection should have recommended isolation precautions for mpox maintained until all lesions have crusted, those crusts have separated, and a fresh layer of healthy skin has formed underneath.
- Management of exposures: See CDC webpages
- Other: To date, there have been no confirmed reports of mpox virus transmission from medical products of human origin (MPHO) including blood transfusion, organ transplantation, or implantation, transplantation, infusion, or transfer of human cells, tissues, or cellular or tissue-based products (HCT/Ps).

https://www.cdc.gov/poxvirus/monkeypox/clinicians/infection-control-healthcare.html#anchor_1653508869481; 31 Oct. 2022

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EMERGING INFECTIOUS DISEASES: *C. auris*, Mpox, SARS-CoV-2, HPV, CRE

- *C. auris*
- Mpox
- SARS-CoV-2
- HPV
- CRE

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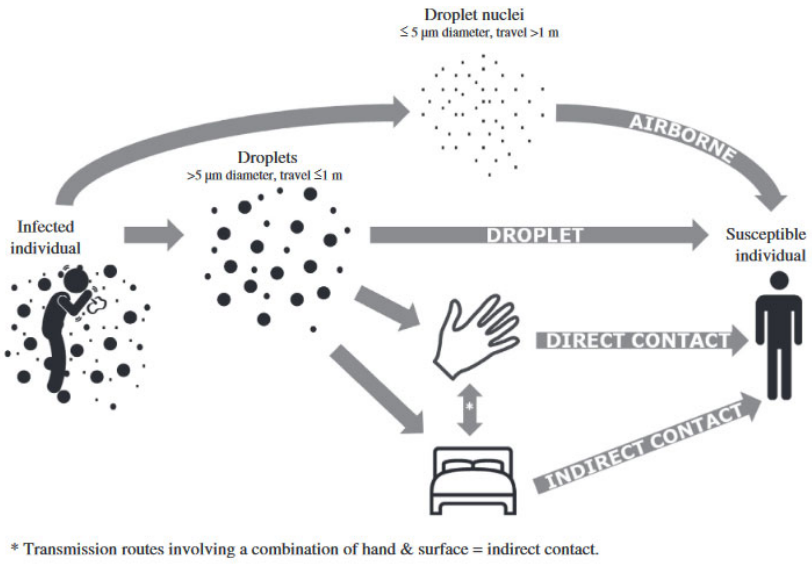
TRANSMISSION OF SARS CoV-2



Otter JA, et al. J Hosp Infect 2016;92:235-50

- Aerosol/Droplet (≤6 feet) most important mode of transmission
- Aerosol (>6 feet) demonstrated indoor with directional airflow and poor ventilation (less important than short distance transmission)
- Other modes: Direct contact and indirect (via the contaminated environment)
  - Elevator button in an apartment building (less likely aerosol remaining in elevator) (Xie C, et al. BMC Public Health 2020;5 August)
  - Elevator buttons or restroom taps in a mall (Cai J, et al. Emerg Infect Dis 2020;26:1343-1345)
  - Toilet on aircraft (Bae SH, et al. Emerg Infect Dis 2020;26:Nov.)
- Pre-symptomatic (i.e., up to 48 hours before person develops symptoms) and asymptomatic transmission well documented – important in maintaining pandemic
- Transmission via blood not demonstrated; via stool (very rare; two outbreaks linked to plumbing)
- **Prevention - In hospital, adhere to Universal Pandemic Precautions**

Role of Healthcare Surface Environment in SARS-CoV-2 Transmission

Kanamori, Weber, Rutala, Clin Infect Dis, In press

- Centers for Disease Control & Prevention says the virus spreads from person to person mainly through respiratory droplets from coughing, sneezing or talking in close proximity to each other, but the CDC has also said it may be possible for a person to get COVID-19 by touching a surface or object that has the virus on it and then touching their own mouth, nose or possibly their eyes. CDC clarified while it is still possible that a person can catch it from touching a contaminated surface, it's "not thought to be the main way the virus spreads."

Role of Healthcare Surface Environment in SARS-CoV-2 Transmission

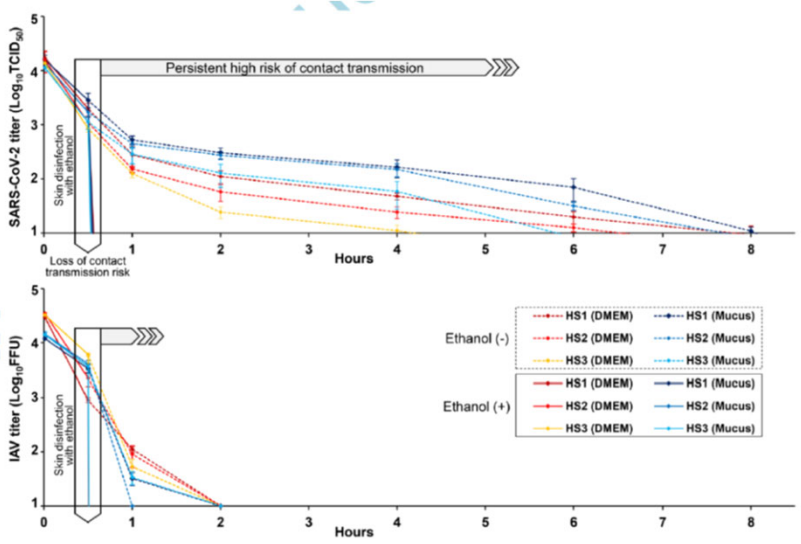
Kanamori, Weber, Rutala, Clin Infect Dis, https://doi.org/10.1093/cid/ciaa1467, 28 September 2020

- Survival on environmental surfaces
  - Hours to days (SARS-CoV-2)
  - Depends on experimental conditions such as viral titer (10^7 higher than real life) and volume of virus applied to surface, suspending medium, temperature, relative humidity and surface substrates
  - Human coronavirus 229E persist on surface materials at RT for at least 5 days
  - SARS-CoV-2 can be viable on surfaces for 3 days (plastic, stainless steel ~2-3 days, cardboard ~24h)
  - Suggest transmission of SARS-CoV-2 may occur

RATIONALE FOR HAND ANTISEPSIS AND SURFACE/SHARED DEVICE DISINFECTION

- Goal: Assess survival of SARS-CoV-2 and influenza A virus (IAV) on human skin and surfaces
- SARS-CoV-2 survived hours on human skin; longer survival time on surfaces; IAV does not survive as well as SARS-CoV-2
- Both SARS-CoV-2 and IAV in the mucus/medium on human skin were completely inactivated within 15s by 80% ethanol

	Survival time[1], hour, median (95% CI)				Half-life time[2], hour, median (95% CI)			
	IAV (DMEM)	SARS-CoV-2 (DMEM)	IAV (Mucus)	SARS-CoV-2 (Mucus)	IAV (DMEM)	SARS-CoV-2 (DMEM)	IAV (Mucus)	SARS-CoV-2 (Mucus)
Stainless steel	11.56 (10.11-13.22)	84.29 (54.01-119.56)	1.73 (1.57-1.91)	64.51 (52.35-77.73)	6.78 (5.84-7.97)	32.62 (16.80-56.68)	0.86 (0.76-0.98)	25.53 (18.45-34.24)
Borosilicate glass	10.61 (9.18-12.27)	85.74 (56.27-119.80)	1.73 (1.58-1.88)	61.23 (49.03-74.44)	6.13 (5.22-7.29)	33.24 (17.59-56.49)	0.85 (0.76-0.96)	23.63 (17.16-31.86)
Polystyrene	6.07 (5.05-7.27)	58.07 (37.76-81.95)	1.96 (1.76-2.18)	35.92 (29.58-42.67)	3.04 (2.40-3.87)	22.58 (11.64-41.24)	0.91 (0.80-1.04)	13.17 (10.26-17.35)
Human skin (HS total)	1.82 (1.65-2.00)	9.04 (7.96-10.22)	1.69 (1.57-1.81)	11.09 (10.22-12.00)	0.80 (0.72-0.90)	3.53 (3.02-4.16)	0.77 (0.71-0.84)	4.16 (3.79-4.58)



Hirose R, et al. Clin Infect Dis. 2020 Oct 3

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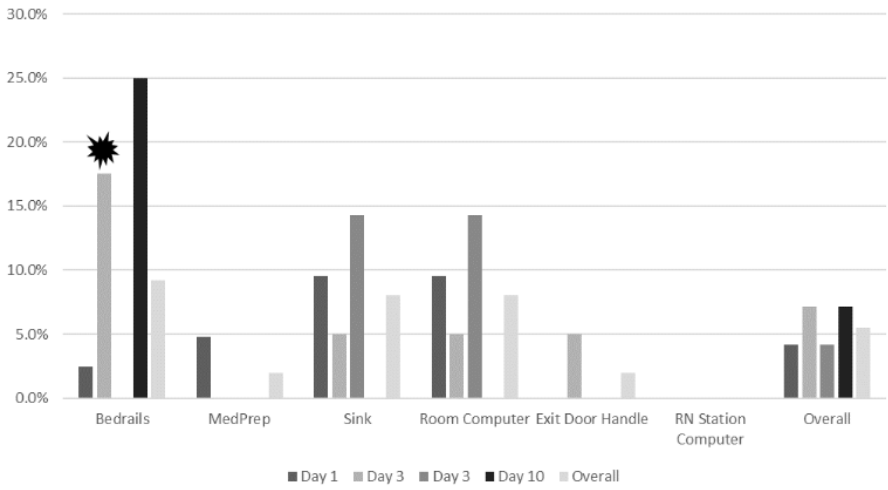
SARS-CoV-2 Environmental contamination in hospital rooms is uncommon using viral culture techniques

- We assessed environmental contamination of inpatient airborne isolation rooms housing COVID-19 patients in a dedicated COVID-19 unit. Contamination with SARS-CoV-2 was found on 5.5% (19/347) of surfaces via RT-PCR and 0.3% (1/347) of surfaces via cell culture. Environmental contamination is uncommon in hospitals rooms; RNA presence is not a specific indicator of infectious virus.
- A total of 347 individual samples were obtained from 20 patient rooms and screened for SARS-CoV-2 RNA;140 on day 1, 140 on day 3, 48 on day 6, and 14 on day 10. Overall, 19 (5.5%) samples were positive via RT-PCR;9 from bedrails (9.2%), 4 from sinks (8.0%), 4 from room computers (8.0%), 1 from the medical prep area (2.0%) and 1 from the exit door handle (2.0%). Notably, all nursing station computer samples were negative (Figure 1). Of the 19 positive samples, 6 were from day 1, 10 on day 3, 2 on day 6 and 1 on day 10. All 19 SARS-CoV-2 RNA positive samples were screened for infectious virus via cell culture. Notably, only one (0.3%) sample, obtained on day 3 from the bedrails of a symptomatic patient with diarrhea and a fever, demonstrated cytopathic effect and the harvested inoculates were SARS-CoV-2 RT-PCR positive, indicating viral growth.



Warren BG, ..Weber DJ, et al. Clin Infect Dis 2022;12 January

Role of Healthcare Surface Environment in SARS-CoV-2 Transmission

Kanamori, Weber, Rutala, Clin Infect Dis, https://doi.org/10.1093/cid/ciaa1467, 28 September 2020

- CDC recommends that an EPA-registered disinfectant on the EPA's List N that has qualified under the emerging pathogen program for use against SARS-CoV-2 be chosen for the COVID-19 patient care.
- List N has >450 entries and 32 different active ingredients

Table 1: Inactivation of viruses by different types of physical disinfectants.

Disinfection	Concentration	Virus	Strain isolate	Retention time	Reduction of viral infectivity (log_{10})	Reference
UVC (254 nm)	Dose of 3 J/m^2	SARS-CoV-2	Isolate FFM-1	11–34 min	1.0	[9]
UVC (254 nm)	Dose of 7 J/m^2	SARS-CoV-2	Isolate FFM-1	11–34 min	2.0	[9]
UVC (254 nm)	Dose of 28 J/m^2	SARS-CoV-2	Isolate FFM-1	11–34 min	3.0	[9]
UVC (254 nm)	Dose of 140 J/m^2	SARS-CoV-2	Isolate FFM-1	11–34 min	6.0	[9]
UVC (254 nm)	Dose of 6.9 J/m^2	SARS-CoV-2	—	2 h	1.0	[10]
UVB (300 nm)	Dose of 1400 J/m^2	Vaccinia virus	—	2 h	2.0	[11]
UVC (254 nm)	Dose of 0.2 J/cm^2	SARS-CoV-2	Frankfurt 1	—	≥3.4	[12]
UVC (254 nm)	Dose of 0.2 J/cm^2	CCHFV	Afg09-2990	—	≥2.2	[12]
UVC (254 nm)	Dose of 0.2 J/cm^2	NiV	Malaysia	—	≥4.3	[12]
UVC (222 nm)	Dose of 0.56 mJ/cm^2	HCoV	229E	—	1.0	[13]
UVC (222 nm)	Dose of 0.39 mJ/cm^2	HCoV	OC43	—	1.0	[13]
Pulsed-xenon ultraviolet light	—	SARS-CoV-2	USA-WA1/2020	2 min	>4.54	[14]
Visible light plus MB (plasma units)	120 J/cm^2	MERS-CoV	EMC/2012	—	≥3.3	[12]
Visible light plus MB (plasma units)	120 J/cm^2	EBOV	Mayinga-76	—	≥4.6	[12]
Gamma irradiation	1 mrad	SARS-CoV-1	Strain Tor 2	5 s	>4.0	[15]
Dry heat	90°C	Poliovirus	Strain Sabin	1 min	>4.6	[16]
Dry heat	90°C	Adenovirus	Type 5	1 min	3.9	[16]
Dry heat	60°C	CCV	SP-80 strain	1 min	1.56	[17]
Dry heat	60°C	MHV	RV-13 strain	1 min	2.87	[17]
Dry heat	80°C	CCV	SP-80 strain	1 min	>4.04	[17]
Dry heat	80°C	MHV	RV-13 strain	1 min	>3.88	[17]
Dry heat	56°C	SARS-CoV	Isolate FFM-1	30 min	≥5.01	[18]
Dry heat	60°C	SARS-CoV	Isolate FFM-1	30 min	≥5.01	[18]
Dry heat	4°C	PEDV	Strain CV777	120 min	0.0	[19]
Dry heat	40°C	PEDV	Strain CV777	120 min	1.0	[19]
Dry heat	56°C	PEDV	Strain CV777	10 min	1.0–1.7	[20]
Dry heat	56°C	MERS-CoV	MERS-CoV strain Hu/France-FRA2_130569/2013 (FRA2)	30 s	0.1–0.9	[21]
Dry heat	56°C	CCV	Strain S378	30 min	≥5.01	[22]
Moist heat	90°C	Poliovirus	Strain Sabin	1 min	>5.0	[18]
Moist heat	90°C	Adenovirus	Type 5	1 min	>4.1	[18]

CCHFV: Crimean-Congo haemorrhagic fever virus; NiV: Nipah virus; EBOV: Ebola virus; MB: methylene blue; SARS: severe acute respiratory syndrome; MERS: Middle East respiratory syndrome; MHV: mouse hepatitis virus; CCV: canine coronavirus; HCoV: human coronavirus; TGEV: transmissible gastroenteritis virus; PEDV: porcine epidemic diarrhoea virus.

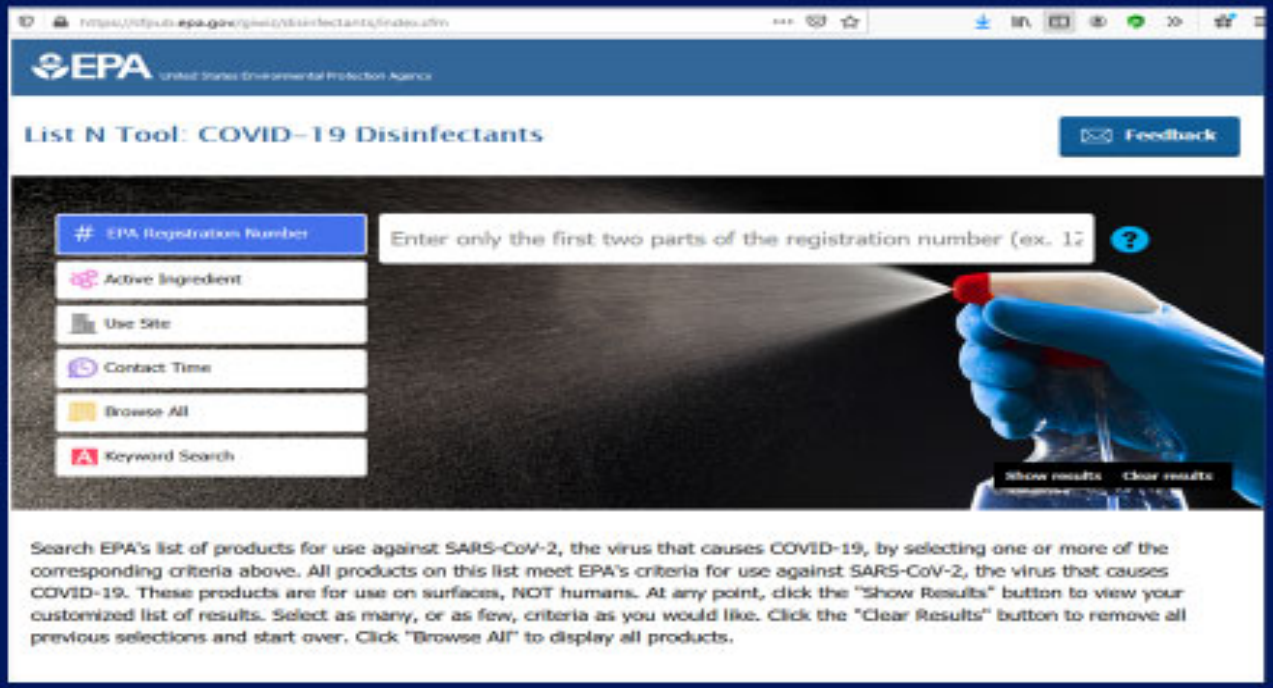
Table 2: Inactivation of viruses by different types of chemical disinfectants.

Disinfection	Concentration	Virus	Strain isolate	Contact time	Reduction of viral infectivity (log_{10})	Reference
Ethanol	95%	SARS-CoV	Isolate FFM-1	30 s	≥5.5	[23]
Ethanol	80%	MERS-CoV	Strain EMC	30 s	>4.0	[24]
Ethanol	70%	Poliovirus	Strain Sabin	1 min	2.1	[16]
Ethanol	70%	Adenovirus	Type 5	1 min	2.4	[16]
2-Propanol	100%	SARS-CoV-2	Isolate FFM-1	30 s	≥3.31	[23]
2-Propanol	70%	SARS-CoV-2	Isolate FFM-1	30 s	≥3.31	[23]
Desderman (78% ethanol)	78%	SARS-CoV-2	Isolate FFM-1	30 s	≥5.01	[23]
Sterillium (45% 2-propanol and 30% 1-propanol)	45% and 30%	SARS-CoV-2	Isolate FFM-1	30 s	≥2.78	[23]
Hydrogen peroxide	Vapor of unknown concentration	TGEV	Purdue strain type 1	2-3 h	4.9–5.3	[25]
Hydrogen peroxide	0.5%	HCoV	Strain 229E	1 min	>4.0	[26]
Hydrogen peroxide	0.5%	Influenza A virus	PR-8	1 min	>4.75	[26]
Hydrogen peroxide	0.5%	HCoV	Type 37	1 min	>4.25	[26]
Benzalkonium chloride	0.04%	HCoV	Strain 229E	1 min	<3.0	[27]
Didecyldimethylammonium chloride	0.0025%	CCV	Strain S378	3 d	>4.0	[28]
Sodium hypochlorite	2500 ppm	Poliovirus	Strain Sabin	10 min	4.5	[16]
Sodium hypochlorite	2500 ppm	Adenovirus	Type 5	10 min	ND	[16]
Sodium hypochlorite	10 ppm	CCV	SP-80 strain	10 min	0.9	[17]
Sodium hypochlorite	100 ppm	CCV	SP-80 strain	10 min	1.05	[17]
Sodium hypochlorite	0.5–0.6%	Ebola virus	—	10 min	1.1	[29]
Sodium hypochlorite	0.5%	HIV	—	1 min	≥7	[29]
Formaldehyde	0.7%	SARS-CoV	Isolate FFM-1	2 min	>3.01	[18]
Formaldehyde	1%	SARS-CoV	Isolate FFM-1	2 min	>3.01	[18]
Glutaraldehyde	0.5%	SARS-CoV	Isolate FFM-1	2 min	>4.01	[18]
Glutaraldehyde	2%	HCoV	Strain 229E	1 min	>3.0	[27]
Glucoprotamin	26%	SARS-CoV	Isolate FFM-1	2 min	>1.68	[27]
Magnesium monoperphthalate	0.5%	SARS-CoV	Isolate FFM-1	30 min	>4.5	[27]
PVP-I surgical scrub (7.5 g/L available iodine)	7.5 g/L	MERS-CoV	Isolate HCoV-EMC/2012	15 s	4.64	[30]
PVP-I skin cleanser (4 g/L available iodine)	4 g/L	MERS-CoV	Isolate HCoV-EMC/2012	15 s	4.97	[30]
PVP-I gargle and mouthwash (1 g/L available iodine)	1 g/L	MERS-CoV	Isolate HCoV-EMC/2012	15 s	4.30	[30]
Povidone-iodine	0.23%	SARS-CoV	Isolate FFM-1	15 s	4.60	[4]
Povidone-iodine	0.23%	MERS-CoV	Isolate HCoV-EMC/2012	15 s	4.40	[4]
Povidone-iodine	0.23%	Influenza virus A	H1N1	15 s	5.67	[4]

ND: not done; SARS: severe acute respiratory syndrome; MERS: Middle East respiratory syndrome; MHV: mouse hepatitis virus; CCV: canine coronavirus; HCoV: human coronavirus; TGEV: transmissible gastroenteritis virus.

List N Tool: COVID-19 Disinfectants

https://cfpub.epa.gov/giwiz/disinfectants/index.cfm



List N Tool: COVID-19 Disinfectants

32 Active Ingredients

- Ethyl alcohol
- Hydrogen peroxide
- Hypochlorous acid
- Isopropyl alcohol
- Peracetic acid
- Phenolic
- Quaternary ammonium

SARS-CoV-2: CONCLUSIONS

- SARS-CoV-2 can survive on various surfaces for minutes to hours
- SARS-CoV-2 mRNA can often be detected on hospital rooms surfaces; viable SARS-CoV-2 is infrequently detected
- Coronaviruses can be efficiently inactivated by physical and chemical disinfectants at different concentrations (70, 80, 85, and 95%) of isopropanol (70 and 80%) in less than or equal to 60 s and 0.5% hydrogen peroxide or 0.1% sodium hypochlorite within 1 minute. Additionally, glutaraldehyde (0.5-2%), formaldehyde (0.7-1%), and povidone-iodine (0.1-0.75%) could readily inactivate coronaviruses. Moreover, dry heat at 56°C, ultraviolet light dose of 0.2 to 140 J/cm2, and gamma irradiation could effectively inactivate coronavirus.
- EPA cleared disinfectants (List N) - EPA expects products on List N to kill all strains and variants of the coronavirus SARS-CoV-2 (COVID-19) when used according to the label directions. See: https://www.epa.gov/coronavirus/about-list-n-disinfectants-coronavirus-covid-19-0.
  - Minimum contact time reported among similar products (contact times varies among products; review MFU): Hydrogen peroxide/oxtanoic acid/peracetic acid, 0.25 min; Quaternary ammonium/isopropanol, 0.5 min; Hydrogen peroxide, 0.5 min; Sodium hypochlorite, 0.5 min; Hydrogen peroxide/peracetic acid, 1 min; Isopropanol, 1 min; Quaternary ammonium compounds, 1 min; Phenolic, 3 min
- SARS-CoV-2 highly susceptible to UV-C

Fadaei A. ScientificWorldJournal 2021;Oct 25:9342748

UNC SCHOOL OF MEDICINE

EMERGING INFECTIOUS DISEASES: *C. auris*, Mpox, SARS-CoV-2, HPV, CRE

- *C. auris*
- Mpox
- SARS-CoV-2
- HPV
- CRE

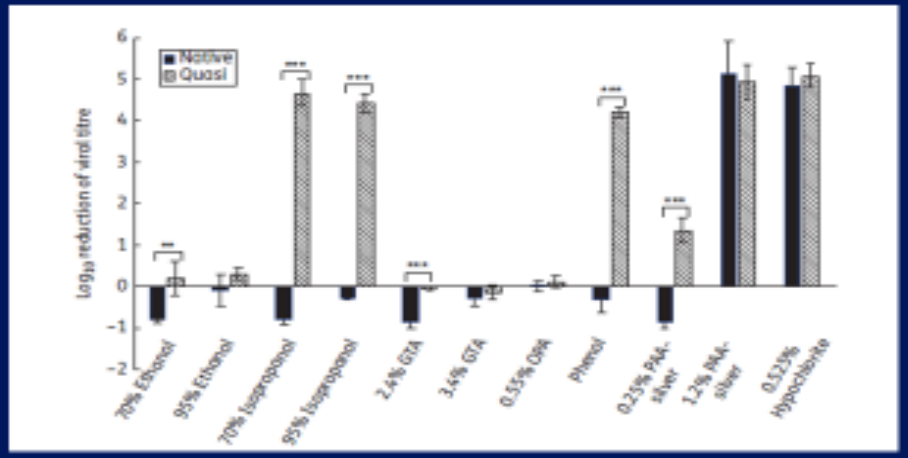
UNC SCHOOL OF MEDICINE

Human Papillomavirus

- **Human Papillomavirus (HPV)**
  - **HPV is transmitted through sexual contact**
  - **Medical devices can become contaminated**
  - **If adequate disinfection of devices does not occur, the next patient may be at risk for HPV infection**
  - **Based on one publication, there are currently no FDA-cleared HLDs that are effective against HPV**

ENDOSCOPE REPROCESSING: CHALLENGES
Susceptibility of Human Papillomavirus
J Meyers et al. J Antimicrob Chemother, Epub Feb 2014

- Most common STD
- In one study, FDA-cleared HLD (OPA, glut), no effect on HPV
- Finding inconsistent with other small, non-enveloped viruses such as polio and parvovirus
- Further investigation needed: test methods unclear; glycine; organic matter; comparison virus
- Conversation with CDC: validate and use HLD consistent with FDA-cleared instructions (no alterations)



Human Papillomavirus

- Two recently published studies identified methodological artifacts (did not use refined virus) and question the validity of the original results.
  - Ozbun et al. EBioMedicine 2021;63:103165. Showed OPA treatment inactivated refined HPV 31 raft virus, xenograft-derived HPV 11, recombinant quasivirus HPV 11, HPV 16 and HPV 31
  - Egawa et al. EBioMedicine 2021; 63:103177. Showed that refined raft-derived HPV18 and HPV pseudovirus and mouse papilloma virus were inactivated
- Based of findings by Ozbun and Egawa, we believe that aldehydes are effective against HPV

HLD Inactivate Papillomavirus

Egawa et al. EBioMedicine 2021;63

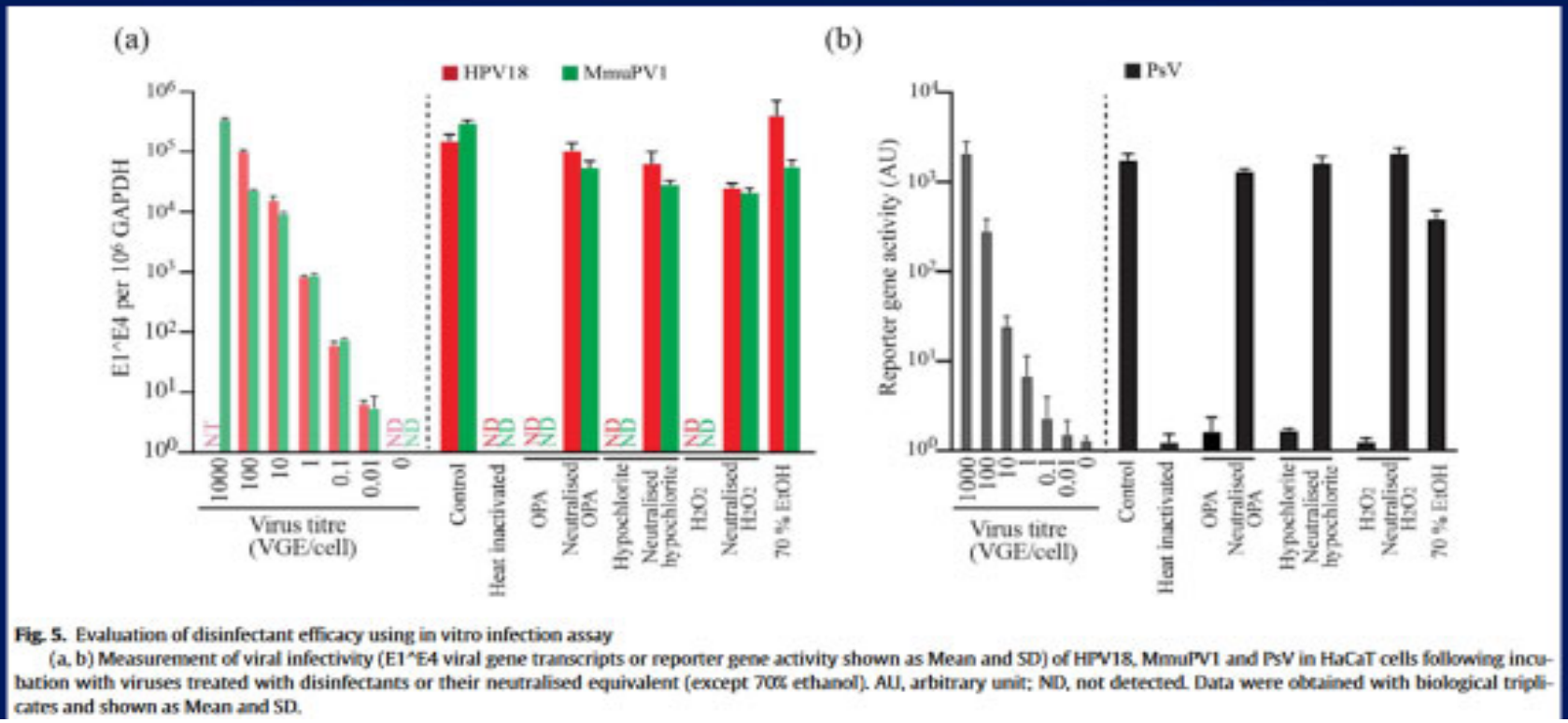


Fig. 5. Evaluation of disinfectant efficacy using in vitro infection assay

(a, b) Measurement of viral infectivity (E1^E4 viral gene transcripts or reporter gene activity shown as Mean and SD) of HPV18, MmuPV1 and PsV in HaCaT cells following incubation with viruses treated with disinfectants or their neutralised equivalent (except 70% ethanol). AU, arbitrary unit; ND, not detected. Data were obtained with biological triplicates and shown as Mean and SD.

EMERGING INFECTIOUS DISEASES: *C. auris*, Mpox, SARS-CoV-2, HPV, CRE

- *C. auris*
- Mpox
- SARS-CoV-2
- HPV
- CRE

UNC SCHOOL OF MEDICINE

Carbapenem-Resistant Enterobacterales

- Main reservoir: GI tract
- Mechanism of transmission: Person-to-person via direct and indirect contact
- Multiple outbreaks have occurred from contaminated endoscopes
- Sinks have been demonstrated to be a reservoir of CRE
- CRE isolated from the environment
- CRE are often resistant to multiple classes of antibiotics, limiting treatment
- Contact Precautions: private room, gown and glove when caring for patient

CRE: ENVIRONMENTAL CONTAMINATION

- Device related outbreaks
  - Endoscopes (Muscarella LF, BMJ Open Gastroenterol 2019;6:e000282; Bourigault C, et al. JHI 2018;99:422; Rutala WA, Weber DJ. AJIC 2016;44:e47))
  - Bronchoscopes (Mehta AC, et al. Chest 2020;157:454)
- Hospital rooms
  - Sink drains (Kotay SM, et al. Appl Environ Micro 2019;85:e01997; Buchan BW et al. AJIC 2019;47:98; Kotsanas D, et al. Med J Aust 2013;198:267))
  - Faucets (Gordon AEK, et al. CID 2017;65:1431)
- Hospital room surfaces (#1 = Tanner WD, et al. CID 2021;72:S8; #2 = Shams AM, et al. ICHE 2016;37:1426)
  - #1) 6 hospitals (2 academic hospitals, 4 VAs); MDRO rooms = Patients on contact precautions for an MDRO (left table)
  - #2) 9 acute care hospitals, 2011-2013, rooms of patients on contact precautions, *K. pneumonia* (ESBL or CRE)

Table 2. Percent of Rooms with Specific MDRO Contamination by Room Type

	MDRO Detected						
Room Type	None (%)	*C. difficile* (%)	MRSA (%)	VRE (%)	CRE (%)	CRA (%)	Number of Rooms, n
Control	88.0	1.3	4.3	6.8	0	0	234
CP *C. difficile*	78.7	4.3	4.3	12.8	0	0	47
CP MRSA[a]	64.5	2.2	23.2	15.2	0.7	0	138
CP VRE	69.0	0	3.4	31.0	0	0	29
CP CRE	66.7	0	0	33.3	0	0	3
Any CP	68.4	2.4	16.3	16.3	0.5	0	209
Number of rooms, n	348	8	44	50	1	0	443

MDRO CP rooms (n = 10 rooms) or control rooms with MDRO contamination (n = 9 rooms) based on more than 1 microorganism are represented in the table multiple times.

Abbreviations: CP, contact precautions; CRA, carbapenem-resistant *Acinetobacter*; CRE, carbapenem-resistant *Enterobacteriaceae*; MRSA, methicillin-resistant *Staphylococcus aureus*; VRE, vancomycin-resistant enterococci.

[a] Room type MRSA includes patients with previous positive MRSA surveillance and MRSA clinical tests combined because the distribution across contamination was similar.

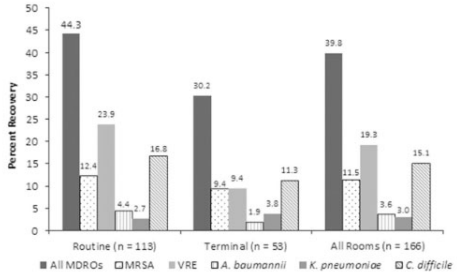


FIGURE 3.
Percent recovery of each target multidrug-resistant organism (MDRO) and all MDROs from routine cleaned, terminal cleaned, and all rooms.

UNC SCHOOL OF MEDICINE

CRE: FREQUENCY OF ENVIRONMENTAL CONTAMINATION AND SURVIVAL OVER TIME

TABLE 1. Contamination on Surfaces in Rooms Housing a Patient with CRE

Room Site Cultured (No.)	CRE Positive, No. (%)[a]	CRE, mean CFU (range)[b]
Bed rail (15)	2 (13.3)	45 (43–47)
Overbed table (15)	1 (6.7)	3
Chair #1 arm (12)	0 (0.0)	...
Sink (15)	2 (13.3)	14.5 (11–18)
Toilet (11)	2 (18.2)	7 (4–10)
Bathroom floor (10)	1 (10.0)	5
Supply cart (11)	1 (9.1)	2
Linen hamper (12)	0 (0.0)	...
Mobile computer (3)	0 (0.0)	...
Chair #2 arm (3)	0 (0.0)	...
Bedside table (3)	0 (0.0)	...
Toilet cabinet (4)	0 (0.0)	...
Floor outside toilet cabinet (4)	1 (25.0)	2
Ventilator counter (1)	0 (0.0)	...
Total (119)[c]	10 (8.4)	5.1 (2–47)

CFU, colony forming units; CRE, carbapenem-resistant *Enterobacteriaceae*.
[a]Considered positive if ≥1 of the 5 Rodac plates had positive growth (ie, area sampled = 120 cm^2).
[b]Mean and range calculated only for CRE culture positive sites.
[c]For one site cultured, technical difficulties prevented assessing growth. Thus total was 119 sites instead of 120 sites.

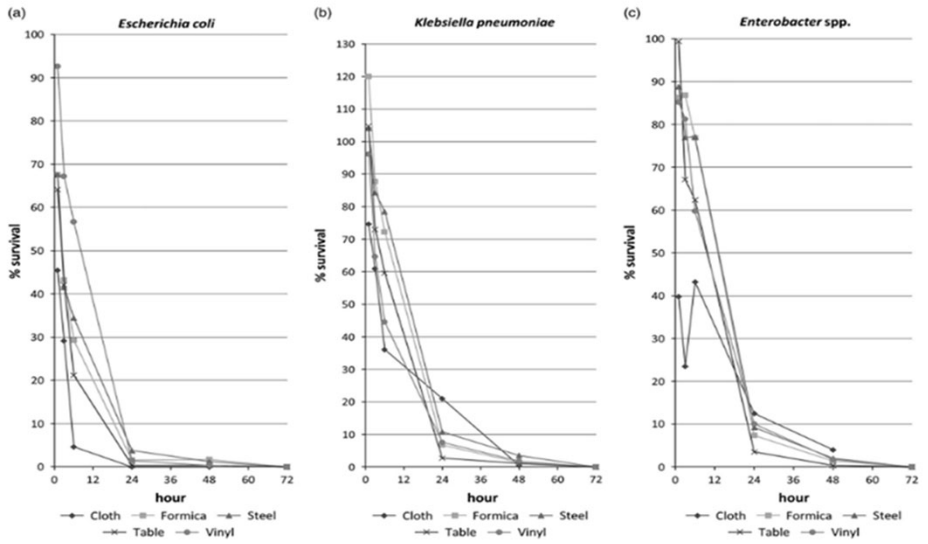


FIGURE 1. a. Survival of Carbapenem-Resistant *Escherichia coli* on 5 Different Environmental Surfaces. b. Survival of Carbapenem-Resistant *Klebsiella pneumoniae* on 5 Different Environmental Surfaces. c. Survival of Carbapenem-Resistant *Enterobacter* spp. on 5 Different Environmental Surfaces

Weber DJ, Rutala WA, et al. ICHE 2015;36:590-593

Germicidal Activity against Carbapenem/Colistin-Resistant *Enterobacteriaceae* Using a Quantitative Carrier Test Method

Abstract

Susceptibility to germicides for carbapenem/colistin-resistant *Enterobacteriaceae* is poorly described. We investigated the efficacy of multiple germicides against these emerging antibiotic-resistant pathogens using the disc-based quantitative carrier test method that can produce results more similar to those encountered in health care settings than a suspension test. Our study results demonstrated that germicides commonly used in health care facilities likely will be effective against carbapenem/colistin-resistant *Enterobacteriaceae* when used appropriately in health care facilities

>3-$\log_{10}$ reduction (CRE, 1min, 5% FCS, QTC)

- 0.20% peracetic acid
- 2.4% glutaraldehyde
- 0.5% Quat, 55% isopropyl alcohol
- 58% ethanol, 0.1% Quat
- 28.7% isopropanol, 0.06% p-tertiary amylphenol
- ~5,250ppm chlorine
- 70% isopropanol
- 70% ethanol (hand rub)
- O.65% hydrogen peroxide, 0.15% peroxyacetic acid
- Accelerated hydrogen peroxide; 1.4% and 2.0%
- Quat; 0.085% QACs (not *K. pneumoniae*)

Kanamori H, Rutala WA, et al. AAC 2018;62:e00318-18

EMERGING INFECTIOUS DISEASES: C. auris, Mpox, SARS-CoV-2, HPV, CRE

- Focus on infection prevention
  - Role of environmental contamination in transmission
  - Frequency of environmental transmission
  - Hand hygiene
  - Surface/device disinfection

CONCLUSIONS

- SARS-CoV-2
  - The COVID-19 pandemic has led to >1 million deaths in US; SARS-CoV-2 is now endemic
  - SARS-CoV-2 can survive on hands and environmental surfaces for hours
  - The principle means of SARS-CoV-2 transmission is via aerosols; contaminated surfaces and fomites play a small role
  - As an enveloped virus, SARS-CoV-2 is inactivated by antiseptics (e.g., 60-90% alcohol) and EPA approved hospital disinfectants
- Human papillomavirus (HPV)
  - HPV is a very common sexually transmitted pathogen; HPV is the major cause of cervical cancer (it also causes vaginal, rectal and oral cancers)
  - Although concern has been raised that HVP is not inactivated by glutaraldehyde and ortho-phthalaldehyde, more recent data suggests that all high-level disinfectants inactivate HPV
- *Candida auris*
  - *C. auris* is a growing worldwide threat due to high mortality, resistance to many antifungals, and difficulties in laboratory identification
  - *C. auris* is capable of prolonged environmental survival; contamination of hospital surfaces is common
  - *C. auris* killed by high-level disinfectants but has reduced susceptibility to some low-level disinfectants (QACs in water) and to UV-C (use settings for *C. difficile*); *C. auris* is susceptible to alcohol-based antiseptics
- Carbapenem-resistant *Enterobacterales* (CRE)
  - CRE outbreaks are most commonly linked to contaminated duodenoscopes and to sinks
  - CRE do not survive well in the environment; CRE have similar susceptibility profile to antiseptics/disinfectants as non-resistant strains
- Mpox
  - Skin-to-skin contact; prolonged environmental survival; EPA List Q (emerg viral pathogens) disinfectants; hand hygiene, alcohol-based rubs

THANK YOU


WE'VE GOT A NEW ONE!
NORTH AMERICA
MONKEY POX
WEST NILE VIRUS
MAD COW
SARS
caglecartoons.com

EMERGING PATHOGENS AND INFECTIOUS DISEASE THREATS

- Polio: US and UK
- Measles: Outbreak in Ohio (in unvaccinated or inadequately vaccinated persons)
- Ebola: Outbreak, Uganda (9/20/22-12/13/22): 142 confirmed cases with 55 deaths (CFR, 39%); 22 deaths in probable cases; 19 infections in HCP (7 deaths) – current outbreak strain not covered by current therapies or vaccine
- Marburg (Cases – Ghana reported in July)
- *Candida auris*: Worldwide and US increase in cases with multiple outbreaks reported
- Avian influenza (9/2/22), H5N1, US: Wild birds, 2189; poultry ~41,000,000; humans, 1 (4/28/22); states, 45
  - Human infections with HPAI A(H5N1) virus have been reported in 19 countries since 2003, resulting in severe pneumonia and death in more than 50% of cases. Human infections with HPAI A(H5N6) virus have been reported since 2014 from two countries with death occurring in more than 40% of cases, and human infections with HPAI A(H5N8) virus were reported from one country in 2021.
  - Others: Influenza A(H6), influenza A(H7), influenza A(H9), influenza A(H10)
- *Burkholderia pseudomallei*: 2 human cases with local acquisition reported from TX (soil samples negative); 7/22, CDC reported agent in soil and water samples from Gulf Coast region of Miss.; 2021, 4 cases in US linked to contaminated aromatherapy room spray

Hall CM, et al. PLOS One 2022;29 July; CDC press release 7/27/22