

EMERGING INFECTIOUS DISEASES IN ARIZONA

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Dr. Villarroel has nothing to disclose. Dr. Engelthaler has nothing to disclose.









WHAT ARE EMERGING INFECTIOUS DISEASES?



Emerging infectious diseases can be defined as infectious diseases that have newly appeared in a population or have existed but are rapidly increasing in incidence or geographic range.* [HIV, SARS, Lyme disease, E. coli O157:H7, Hantavirus, COVID]

*or are caused by the NIAID Category A, B, or C priority pathogens.



WHAT ARE <u>Re-</u>Emerging infectious diseases?



Re-emerging diseases are diseases that reappear after they have been on a significant decline in a more virulent form or in a new epidemiologic setting. [malaria, tuberculosis, pertussis, influenza, gonorrhea]



HOW LONG HAVE WE HAD RE-/EMERGING INFECTIOUS DISEASES?

Since the neolithic revolution (12,000 years ago), with the beginnings of domestication.

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Emerging Infectious Diseases in History

Year	Name	Deaths	Comments
430 BCE	"Plague of Athens"	~100,000	First identified trans-regional pandemic
541	Justinian plague (<i>Yersinia</i> <i>pestis</i>)	30–50 million	Pandemic; killed half of world population
1340s	"Black Death" (<i>Yersinia pestis</i>)	\sim 50 million	Pandemic; killed at least a quarter of world population
1494	Syphilis (Treponema pallidum)	>50,000	Pandemic brought to Europe from the Americas
c. 1500	Tuberculosis	High millions	Ancient disease; became pandemic in Middle Ages
1520	Hueyzahuatl (Variola major)	3.5 million	Pandemic brought to New World by Europeans
1793- 1798	"The American plague"	~25,000	Yellow fever terrorized colonial America
1832	2nd cholera pandemic (Paris)	18,402	Spread from India to Europe/Western Hemisphere
191 <mark>8</mark>	"Spanish" influenza	\sim 50 million	Led to additional pandemics in 1957, 1968, 2009
1976- 2020	Ebola	15,258	First recognized in 1976; 29 regional epidemics to 2020
1981	Acute hemorrhagic conjunctivitis	rare deaths	First recognized in 1969; pandemic in 1981
1981	HIV/AIDS	~ 37 million	First recognized 1981; ongoing pandemic





Major Categories of Emerging Infectious Diseases

Newly emerging infectious diseases	Diseases recognized in humans for the first time, e.g., HIV/AIDS (1981),	
	Nipah virus (1999), SARS (2002), MERS (2012), COVID-19 (2019)	
Re-emerging infectious diseases	Diseases that have historically infected humans but continue to re-appear	
	either in new locations (e.g., West Nile in the United States and Russia in	
	1999) or in resistant forms (e.g., methicillin-resistant Staphylococcus aureus)	
Deliberately emerging infectious	Diseases associated with intent to harm, including mass bioterrorism	
diseases		
Accidentally emerging infectious	Diseases created by humans that are released unintentionally, e.g., epizootic	
diseases	vaccinia and transmissible vaccine-derived polioviruses	



HOW DO THESE DISEASES "EMERGE"?

Most new pathogens are zoonotic (\rightarrow) .

Other diseases (re)emerge due to antimicrobial resistance, declines in vaccine coverage, new spread to new areas, etc.





HOW DO THESE DISEASES "EMERGE"?

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It's not just the microbial agent that is critical to emergence - it's also the host and environmental interactions.



WHAT FACTORS LEAD TO THE EMERGENCE OF A NEW DISEASE?

- Viral evolution, emergence*
- Increased contact with zoonoses
- Deforestation, hunting, bushmeat
- \circ $\,$ Increased host and vector density
- Urbanization, population growth
- Climate change
- Human mobility, air travel
- \circ $\,$ Insecurity, war, civil disruption $\,$
- Antibiotic resistance
- Inadequate supply of vaccines and drugs
- Disinformation, anti-vaccination

*Could occur naturally or through laboratories



HOW COMMON ARE SPILLOVER EVENTS?

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Spillovers of a virus from animals to humans are not as rare as scientists used to think. Here are some 45 possible human cases documented since November 2021.





Emerging Infectious Diseases - What, Where, How
History of Emerging Diseases in Arizona
Current Emerging Infectious Diseases in Arizona
Resources for Arizona Clinicians

WHAT ARE SOME EMERGING DISEASES WE'VE SEEN HERE?

- Hantavirus Pulmonary Syndrome
- West Nile Virus Disease
- Plague
- Dengue
- C. auris
- o Zika
- COVID-19
- \circ CRE
- Mpox
- Arguably: Cocci



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Hantavirus Outbreak - 1993

- May 1993 outbreak of unexplained ARDS in the Four Corners Region
- Unknown pathogen / unknown source
- Mystery disease killed > 70% of cases especially young healthy adults
- Clinical course to death = <u>rapid!</u>
- Outbreak caused intense public panic
- Political pressure 1
- Stress level PH agencies/staff was extreme!









SLIDE FROM CRAIG LEVY







Engelthaler et al, 1999, Emerg Infect Dis



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Adapted from: Engelthaler et al, 1999, Emerg Infect Dis



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C. auris cases in Arizona | All time

2022 C. auris cases

Grand Total	205
Clinical	53
Screening	152

2023 Year-to-date *C. auris* cases

Grand Total	162
Clinical	93
Screening	69





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Preliminary draft, ADHS CRE and C. aureus Report, 2023

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For example, this is a mixed culture of *Candida glabrata* (purple), *Candida tropicalis* (navy blue), and *Candida auris* (white, circled in red) on CHROMagar Candida.



Candida auris on CHROMagar Candida, here, for example, displays multiple color morphs.

Increasing Threat of Spread of Antimicrobial-resistant Fungus in Healthcare Facilities

Print

OF HEALTH SERVICES

Press Release

For Immediate Release: Monday, March 20, 2023 **Contact:** <u>Media Relations</u> (404) 639-3286

Candida auris (C. auris), an emerging fungus considered an urgent antimicrobial resistance (AR) threat, spread at an alarming rate in U.S. healthcare facilities in 2020-2021, according to data from the Centers for Disease Control and Prevention (CDC) published in the Annals of Internal Medicine. Equally concerning was a tripling in 2021 of the number of cases that were resistant to echinocandins, the antifungal medicine most recommended for treatment of *C. auris* infections. In general, *C. auris* is not a threat to healthy people. People who are very sick, have invasive medical devices, or have long or frequent stays in healthcare facilities are at increased risk for acquiring *C. auris*. CDC has deemed *C. auris* as an urgent AR threat, because it is often resistant to multiple antifungal drugs, spreads easily in healthcare facilities, and can cause severe infections with high death rates.









Note: Bars with similar labels may be different lengths due to rounding.



https://www.nytimes.com/2020/07/08/briefing/arizona-mary-trump-facebook-your-wednesday-briefing.html

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Average cases during phases of the pandemic

Surveillance data dashboard

Weekly Summary Severity Year by Year Trends

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https://www.azdhs.gov/covid19/data/index.php

COVID Variant Update

Newest "Variant of Interest": BA.2.86/JN.1

- Becoming dominant in Europe
- CDC US: 8.8%
- AZ: 6/214 (2.8%) since Nov 1
- Unusual L455S spike mutation
- All Variants are still Omicron and act like Omicron – high transmission, low severity
 - No known increase in severity
 - Likely evading antibodies from previous vaccination/infection


Variants are Just Mutation Vehicles

- Variants are selected for because mutations provide advantage
 - Typically antibody escape
- Mutations are recurring as antibodies lose binding effectiveness
- These mutations are becoming cyclical, unlike variants, which become extinct



COVID Wastewater Surveillance - AZ



https://pathogen-intelligence.tgen.org/VECTRSurveillance/flagstaff/





WHAT NEW DISEASES ARE COMING TO ARIZONA?



Cryptococcus decagattii ("VGVI") An Endemic AZ Cryptococcus?

Environmental Cryptococcus gattii





Cryptococcus: The Naming Complex



Hagen et al, Fung Gen Biol, 2015



C. gattii shows up in Arizona

- In 2011, a Tucson veterinarian identified a *Cryptococcus* positive cat; confirmed as *C. gattii* by a veterinary reference lab in CA
- A local hospital in the Phoenix metro region identified two *C. gattii* immunocompromised patients in late 2019 (pulmonary; meningitis)
- A third human clinical case of *C. gattii* found in AZ in 2021 (meningitis)
- TGen and ADHS confirm all samples as belonging to the "VGVI" clade

C. gattii phylogeny



microorganisms

Communication

Phylogenomic Placement of American Southwest-Associated Clinical and Veterinary Isolates Expands Evidence for Distinct *Cryptococcus gattii* VGVI

Juan Monroy-Nieto ¹, Jolene R. Bowers ¹, Parker Montfort ¹, Guillermo Adame ², Constanza Giselle Taverna ³, Hayley Yaglom ¹, Jane E. Sykes ⁴, Shane Brady ², A. Brian Mochon ^{5,6}, Wieland Meyer ^{7,8}, Kenneth Komatsu ² and David M. Engelthaler ^{1,*}



Monroy-Nieto et al, 2022

MDPI

C. decagattii (VGVI) in the Southwest: Epidemiology and Ecology

- 1. No available epi data on exposure or travel
- 2. Multiple veterinary cases (cat) identified in northcentral Tucson
- 3. Working hypotheses:
 - 1. Local rodent/small mammal reservoir, eg, woodrat nests (ala hyrax middens)
 - 2. Decaying local flora, eg, decaying cactus hollows (ala decayed trees in PNW and Amazon)
 - 3. Other vertebrate reservoir/vector (eg, birds, bats)
 - 4. Other microclimate-habitat in desert southwest
- 4. Currently, we still know very little



Cryptococcus gattii spp. in Arizona



Clinical Suspicion of C. gattii

- Currently, C. gattii is considered a communicable disease of public health significance <u>not explicitly reportable</u> in Arizona
- Given the need to understand the epidemiology of this fungal pathogen, if there is suspicion of a clinical case:
 - Report to local and state public health
 - Collect travel history and other relevant epidemiologic information (e.g., contact with animals)
 - Submit clinical specimens for diagnostic testing (various options, but nucleic acid detection and culture is best)
- TGen is working with ADHS, commercial laboratories, and veterinarians to genomically characterize any AZ *C. gattii* isolates.

The High Path Avian Influenza Panzootic

High Path Avian Flu – Emerging Zoonoses?



High Path Avian Influenza (H5N1) - Animal





Reported HPAI A(H5N1) Animal Outbreaks* Reported to the World Organisation for Animal Health (WOAH), Jan 2022-Sept 2023





Positive Birds in AZ

- Condors (21), Vulture
- Hawks, Owls
- Cormorants
- Geese
- Ducks
- Grackle, Jay
- Chickens
- Pelicans
- Ibis
- Rhea



High Path Avian Influenza (H5N1) - Humans

Kandiel et al, 2023 Nature Comms

- 17 Human cases since 2022 8 serious, 4 deaths
 - Dominantly from clade 2.3.4.4b
- Nearly all associated with close bird contact
 - No human-to-human or mammal-to-human spread known
- 1 mild US case in CO
- Susceptible to all human influenza antivirals
- No human Ab protection against H5, but significant N1 cross-protection
- North American lineage reassorted with other avian strains
 - Increased virulence in mammals, but not increased transmission
 - Appear to bind poorly to human sialic acid receptors
- Risk for co-infection with human or swine strain



Or maybe we just make it more transmissible, on purpose ...

Science	Current Issue	First release papers	Arc	chive	Ab	out 🗸
HOME > SCIENCE > VOL. 336, NO. 6088 > AIRBORNE TRANSMISSION	OF INFLUENZA A/H5N1 VIRUS	BETWEEN FERRETS				
👌 🕴 SPECIAL ISSUE REPORT		f	У	in	ġ	f @
Airborne Trenemiesien of	Influenze		v:.			

Airborne Transmission of Influenza A/H5N1 Virus Between Ferrets

SANDER HERFST, EEFJE J. A. SCHRAUWEN, MARTIN LINSTER, SALIN CHUTINIMITKUL, EMMIE DE WIT, VINCENT J. MUNSTER, ERIN M. SORRELL, THEO M. BESTEBROER, DAVID F. BURKE, DEREK J. SMITH, GUUS F. RIMMELZWAAN, ALBERT D. M. E. OSTERHAUS, AND RON A. M. FOUCHIER fewer Authors Info & Affiliations

SCIENCE · 22 Jun 2012 · Vol 336, Issue 6088 · pp. 1534-1541 · DOI: 10.1126/science.1213362

Rapid communication

nature

Explore content v About the journal v Publish with us v

nature > letters > article

Letter Open access Published: 02 May 2012

Experimental adaptation of an influenza H5 HA confers respiratory droplet transmission to a reassortant H5 HA/H1N1 virus in ferrets

Masaki Imai, Tokiko Watanabe, Masato Hatta, Subash C. Das, Makoto Ozawa, Kyoko Shinya, Gongxun Zhong, Anthony Hanson, Hiroaki Katsura, Shinji Watanabe, Chengjun Li, Eiryo Kawakami, Shinya Yamada, Maki Kiso, Yasuo Suzuki, Eileen A. Maher, Gabriele Neumann & Yoshihiro Kawaoka

Open Access



María José Ruano¹ , Manuel del Valle Arrojo³ , Ricardo Fernández-Antonio⁴ 🛅, Antonio Manuel Souto⁵ , Pedro Tordable⁵ , Julio Cañás⁵ , Francesco Bonfante² , Edoardo Giussani² , Calogero Terregino² , Jesús Javier Orejas⁶

A Note on Chronic Wasting Disease



Prions

- Infectious misfolded protein that causes other proteins to misfold
- Transmissible Spongiform Encephalopathies (TSE)
- Non-microbial infections
- Spread by ingestion/infection of brain/CSF material
- Cognitive loss, muscle twitching/spasms 100% fatal
- Mad Cow Disease U.K. 1990's
- Chronic Wasting Disease is a major problem in deer and elk in North America



CWD: A Soon to Emerge Zoonotic Disease?



CWD Spongiform Encephalopathy Credit: Photo by Elizabeth Williams, CSU

DENGUE: REMERGING VECTOR W/ EMERGING ARBOVIRUS

> Emerg Infect Dis. 1997 Apr-Jun;3(2):241-2. doi: 10.3201/eid0302.970223.

The reemergence of Aedes aegypti in Arizona

D M Engelthaler, T M Fink, C E Levy, M J Leslie

PMID: 9204311 PMCID: PMC2627602 DOI: 10.3201/eid0302.970223



Notes From the Field

First Evidence of Locally Acquired Dengue Virus Infection — Maricopa County, Arizona, November 2022

 Melissa Kretschmer, MA¹; Jennifer Collins, MPH¹; Ariella P. Dale, PhD¹; Brenna Garrett¹; Lia Koski, MPH¹; Karen Zabel, MSN¹; R. Nicholas Staab, MD¹; Katie Turnbow¹; Judah Nativio, MS¹; Kelsey Andrews¹;
 William E. Smith, MS¹; John Townsend²; Nicole Busser²; James Will²;
 Kathryn Burr, DVM^{1,3,4}; Forrest K. Jones, PhD^{4,5}; Gilberto A. Santiago, PhD⁵; Kelly A. Fitzpatrick, MSPH⁵; Irene Ruberto, PhD³; Kathryn Fitzpatrick, MPH³; Jessica R. White, DrPH¹; Laura Adams, DVM⁵; Rebecca H. Sunenshine, MD^{1,6}

2021













Emerging Infectious Diseases - What, Where, How
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WHAT AZ SYSTEMS CAN DETECT EMERGING DISEASES?

1. AZ LABORATORY SURVEILLANCE

- a. Laboratory reportable conditions (<u>list</u>)
- b. Virologic surveillance (e.g. influenza strains)
- c. Bacteriologic surveillance (e.g. gonococcal resistance)
- d. Genomic surveillance (e.g. EV-D68)

2. AZ HUMAN SURVEILLANCE

- a. Clinician Reportable conditions (<u>list</u>)
- b. School, Childcare, Shelter reportable conditions (<u>list</u>)
- c. Biosense ED surveillance (e.g. search for Ebola cases)
- d. The Astute Clinician



Arizona Administrative Code ⁺ Requires Providers to:	Arizona	Administrative	Code ⁺ I	Requires I	Providers to:
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Report Communicable Diseases

to the Local Health Department

		-			1.1	
* *0	Amebiasis	2	Glanders		0	Respiratory disease in a health care institution or correctional facility
	Anaplasmosis	-	Gonorrhea		1)*	Rubella (German measles)
2	Anthrax	0	Haemophilus influenzae, invasive dise	ease	0	Rubella syndrome, congenital
1	Arboviral infection		Hansen's disease (Leprosy)		0*0	Salmonellosis
-	Babesiosis	0	Hantavirus infection		0	Scabies
-	Basidiobolomycosis	D	Hemolytic uremic syndrome		0*0	Shigellosis
2	Botulism	0*0	Hepatitis A		2	Smallpox
0	Brucellosis	-	Hepatitis B and Hepatitis D		D	Spotted fever rickettsiosis (e.g., Rocky Mountain spotted fever)
=*0	Campylobacteriosis	-	Hepatitis C			Streptococcal group A infection, invasive disease
	Chagas infection and related disease (American trypanosomiasis)	1 *0	Hepatitis E			Streptococcal group B infection in an infant younger than 90 days of ag invasive disease
	Chancroid		HIV infection and related disease		-	Streptococcus pneumoniae infection (pneumococcal invasive disease)
0	Chikungunya	0	Influenza-associated mortality in a cl	hild	1	Syphilis
	Chlamydia trachomatis infection	0	Legionellosis (Legionnaires' disease))	E*0	Taeniasis
0*	Cholera	D	Leptospirosis		-	Tetanus
-	Coccidioidomycosis (Valley Fever)	0	Listeriosis		-	Toxic shock syndrome
-	Colorado tick fever	-	Lyme disease		D	Trichinosis
0	Conjunctivitis, acute	0	Lymphocytic choriomeningitis		Ð	Tuberculosis, active disease
-	Creutzfeldt-Jakob disease		Malaria		Ø	Tuberculosis latent infection in a child 5 years of age or younger (positive screening test result)
0*0	Cryptosporidiosis	2	Measles (rubeola)		2	Tularemia
0	Cyclospora infection	0	Melioidosis		D	Typhoid fever
-	Cysticercosis	2	Meningococcal invasive disease		D	Typhus fever
0	Dengue	0	Mumps		D	Vaccinia-related adverse event
0	Diarrhea, nausea, or vomiting	2	Novel coronavirus infection (e.g., SA	RS or M	MERS) 🖀	Vancomycin-resistant or Vancomycin-intermediate Staphylococcus aureu
2	Diphtheria	0	Pertussis (whooping cough)		-	Varicella (chickenpox)
	Ebrlichiosis	2	Plague		⊕*0	Vibrio infection
2	Emerging or exotic disease	2	Poliomyelitis (paralytic or non-paraly	ytic)	2	Viral hemorrhagic fever
-	Encephanus, parasiuc		Psittacosis (ornithosis)		-	West Nile virus infection
0	Encephalitis, viral	D	Q fever		2	Yellow fever
0	Escherichia coli, Shiga toxin-producing	2	Rabies in a human		@*O	Yersiniosis (enteropathogenic Yersinia)
E*0	Giardiasis	D	Relapsing fever (borreliosis)		D	Zika virus infection
Key:			1		Submit a repo woman.	rt within one working day if the case or suspect case is a pregnant
1	Submit a report by telephone or through an electronic reporting system authorized by the Department within 24 hours after a case or suspect case is diagnosed, treated, or detected or an occurrence is detected.			D		rt within one working day after a case or suspect case is diagnosed, tected.
*			is any nosed, neared, or acceled,	-	C	rt within five working days after a case or suspect case is diagnosed,
					Submit a report within 24 hours after detecting an outbreak.	





WHAT AZ SYSTEMS CAN DETECT THESE DISEASES?

We cannot overstate the importance of THE ASTUTE CLINICIAN.

If you are observing an unusual clinical occurrence - please call us.

A clinician call is often the catalyst for us detecting a new disease or significant outbreak. Clinicians are a critical piece of the public health system.



WHAT ARE RESOURCES AVAILABLE TO AZ CLINICIANS? (URGENT)

C Local Health Department



- Local Health Departments
 - Maricopa: 602-506-6767
 - Pima: 520-724-7797
 - Pinal: 866-960-0633
 - Coconino: 928-679-7272



Home | Contact Us
Arizona Health Alert Network (AzHAN) is an application used to distribute
important public health alerts to public health officials and healthcare
professionals. AzHAN is a secure web-based application that is available
24/7/365.
If you are interested in receiving important public health alerts, please click on the Register Now
button below to register.
REGISTER NOW



WHAT ARE RESOURCES AVAILABLE TO AZ CLINICIANS?



- AZ Valley Fever Annual Report
- <u>AZ West Nile Virus Webpage/Data</u>
- AZ Respiratory Virus Dashboards
- AZ COVID-19 Dashboard
- AZ COVID Seq Dashboard
- AZ Infectious Disease Data
- AZ Valley Fever Toolbox

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- CDC West Nile Virus Tutorial (free CME)

- <u>Arizona Infectious Disease</u> <u>Society Conference 2024</u>
- <u>COCCI Study Group</u>
 <u>Conference 2024 (date tbd)</u>
- <u>AZID 2024</u>

TAKE HOME FROM DR. VILLARROEL

- 1. Clinicians play a critical role in identifying the emergence of a new disease.
- 2. Clinicians need to know their resources and who to call.

for some extra reading...





How do pandemics begin? There's a new theory — and a new strategy to thwart them



TAKE HOME FROM DR. ENGELTHALER

- 1. New pathogens and their disease will continue to emerge and remerge (although we don't need to help them along)
- 2. We need faster and smarter tools to gain intel on these pathogens to allow us to respond ... faster and smarter





THANK YOU

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