

Pandemic Planning: Focus on Emerging Pathogens

UNC Health
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Region IV Regional Emerging Special Pathogen Treatment Center



October 30, 2023

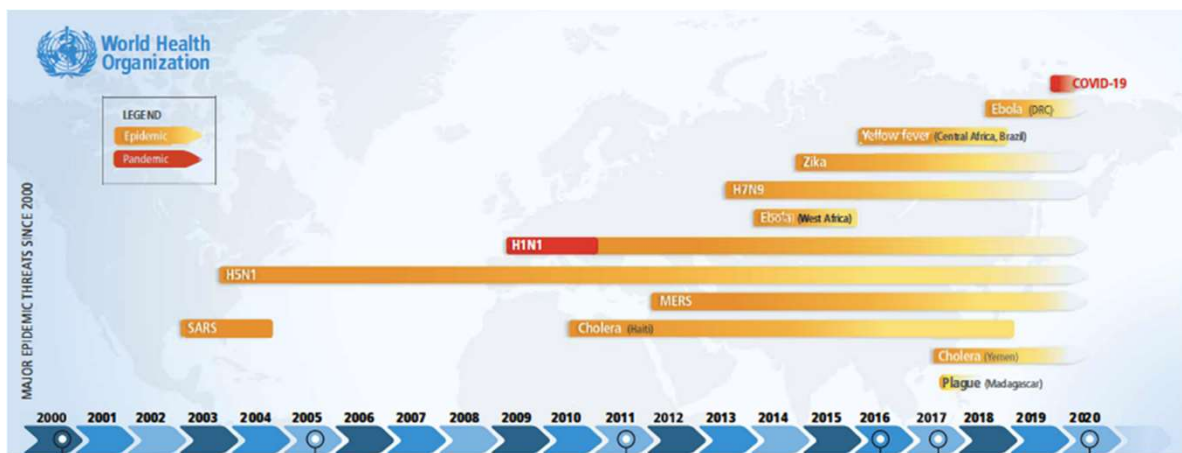
Definitions

- Emerging Disease: diseases that have newly appeared in the population, OR have existed but are rapidly increasing in incidence or geographic range
- Re-emerging Disease: diseases that were once a major health problem, declined dramatically, but are again becoming health problems
- Endemic: a “long-term” problem, never significantly declining (e.g., pneumonia)
- Epidemic: an increase in disease incidence over baseline
- Pandemic: Epidemic involving >2 continents (e.g., COVID-19, MPOX)

Basic Concepts in Infectious Disease Emergence

- Emergence of infectious disease is complex
- Diseases are dynamic, changing
- Most new infections are not caused by completely new pathogens (e.g., coronaviruses, influenzas)
- Agents involved in new and reemerging infections cross taxonomic lines (e.g., bats and Ebola Virus Disease, fleas and plague)
- Human behavior drives disease emergence
 - Social, economic, political, technologic, climatic, and environmental factors all shape disease patterns and influence emergence

Outbreaks over the past 20 years



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WHO Pandemic Threats – Priority Diseases

New in 2024

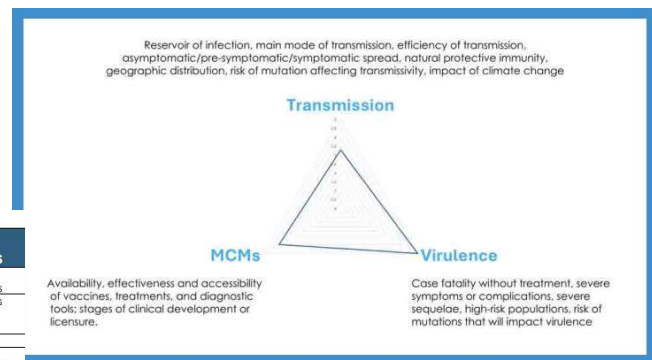
- Priority pathogens based on regions in the world
- WHO document: Pathogens Prioritization: A Scientific Framework for Epidemic and Pandemic Research Preparedness
- No long lists just the top 9 priority pathogens
- Determines a threat based on regions in the world
- Determines if a pathogen is a priority based on the risk of it becoming a Public Health Emergency of International Concern (PHEIC)

	2017	2018	2024		
Family	Priority Pathogens	Priority Pathogens	PHEIC risk	Priority Pathogens	Prototype Pathogens
Adenoviridae			Low-Medium		Recombinant Mastadenovirus
Adenoviridae			Low-Medium		Mastadenovirus blackbeard1 serotype 14
Anelloviridae			Low		
Arenaviridae	Arenaviral hemorrhagic fevers including Lassa Fever	Lassa Fever virus	High	Mammarenavirus lassaense	Mammarenavirus lassaense

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Prioritization Pathogens V6_0 https://cdn.who.int/media/docs/default-source/consultation-rdb/prioritization-pathogens-v6/final.pdf?sfvrsn=c98effa7_7&download=true2_who.int

WHO evidence elements to assess a pathogen's potential to cause a PHEIC or pandemic



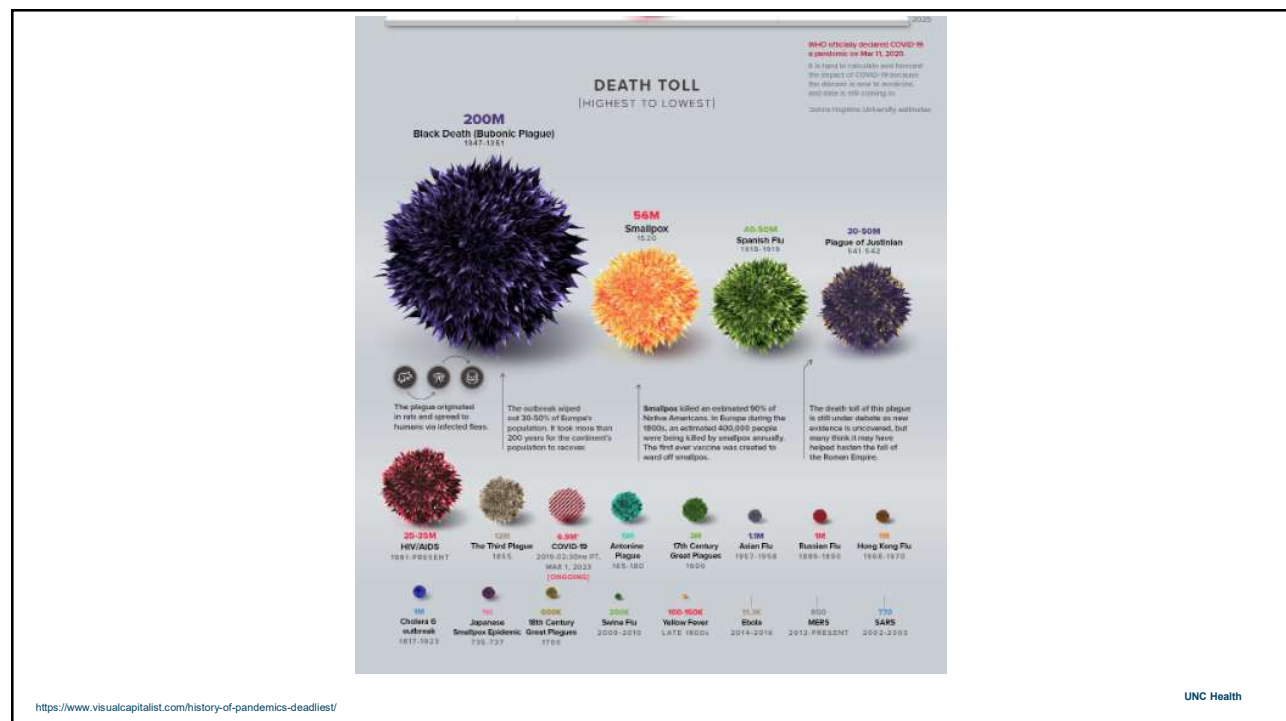
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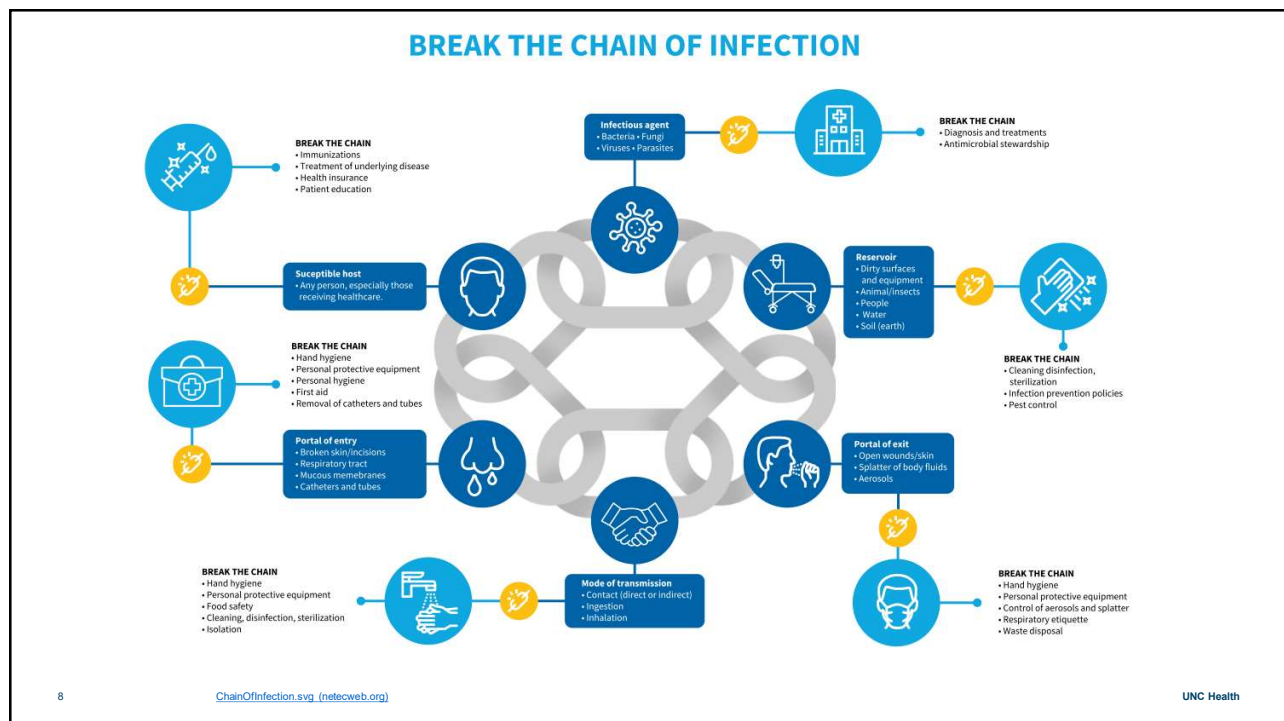
What's Increasing Our Risk?



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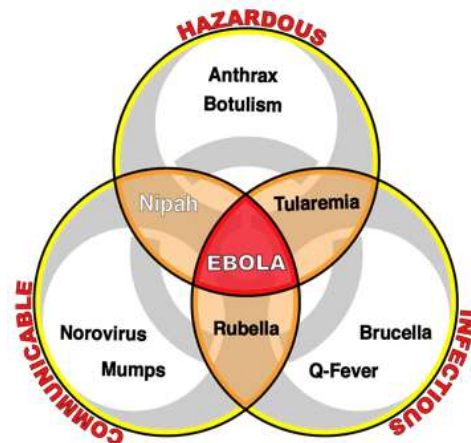
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What is a special pathogen?

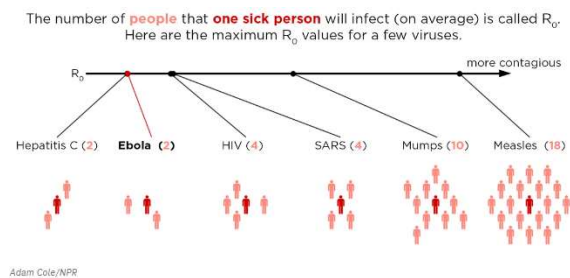
- Highly contagious (communicable)
- Highly hazardous
- Highly infectious
- Very few pathogens have all 3 characteristics!



Cieslak TJ, Herstein JJ, Kortepeter MG, Hewlett AL. A Methodology for Determining Which Diseases Warrant Care in a High-Level Containment Care Unit. Viruses. 2019;11(9):773. Published 2019 Aug 22. doi:10.3390/v11090773

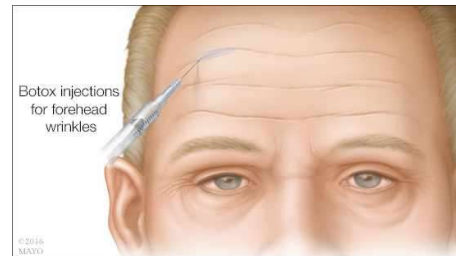
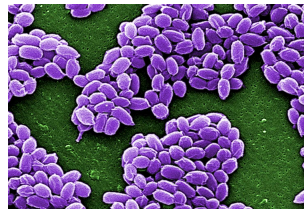
Highly Contagious

- How many people will it infect?
- Expressed in terms of the reproductive number, R_0
- The number of secondary cases resulting from a single primary case in the absence of medical interventions
- “Epidemic threshold” – pathogens with a R_0 greater than 1 have the capability to cause an outbreak
- Influenza: 1.3
- Mpox: 2.1
- Polio: 5-7
- COVID-19: 2.9 (ancestral strain)



Highly Hazardous

- Measured by morbidity and mortality
- Inhalation anthrax has a mortality rate close to 100%
 - Not very infectious: ID₅₀ estimated at 8,000 – 40,000 spores
 - Not transmissible P2P
- *Clostridium botulinum* is also highly hazardous (but neither infectious nor contagious)



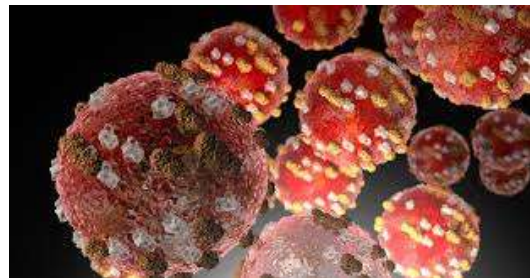
Highly Infectious

- **How much of the pathogen will it take to make someone sick?**
 - Usually measured by the infectious dose needed to infect 50% of a given population (ID₅₀)
 - Lower number indicates greater infectious nature of a pathogen
- **SARS-CoV-2: estimated to be <100 viral particles**
- **Influenza A: >790 viral particles**
- **RSV: 160-640 viral units**
- **Norovirus: 10-18 viral particles**
- **Shigella: 10-200 organisms**
- ***Mycobacterium tuberculosis*: <10 bacilli**
- ***S. aureus*: at least 100,000 organisms**
- ***Coxiella burnetii* (Q-fever): 1 bacterial cell**

Pathogen	Mechanism of PTP Spread	ID ₅₀
Ebola	Blood & Body Fluids	1-10 aerosolized organisms
Marburg	Blood & Body Fluids	1-10 aerosolized organisms
Lassa	Blood & Body Fluids	1-10 aerosolized organisms
Lujo	Scant data; Presumably Blood & Body Fluids	No data
Junin	Blood & Body Fluids	No data
Machupo	Blood & Body Fluids	No data
Guanarito	Scant data; Presumably Blood & Body Fluids	No data
Sabia	No data	No data
CCHF	Blood & Body Fluids	No data
SARS	Respiratory Droplets; Possibly Droplet Nuclei	No data
MERS	Respiratory Droplets; Possibly Droplet Nuclei	No data
H5N1 Influenza	Respiratory Droplets; Possibly Droplet Nuclei	1000 viral particles ²

A fourth consideration: effective medical countermeasures

- **Immunizations (prevent it)**
- **Therapeutics (treat it)**
- **Example: Measles**
 - One of the most communicable diseases known
 - R_0 12-18
 - Highly hazardous
 - Over 136,000 worldwide deaths in 2022
 - Highly infectious
 - 0.2 organisms by intranasal spray (lab setting)
 - Medical countermeasure: immunizations
 - 75% decrease in mortality since the turn of the century
 - Does not require biocontainment level care, but only airborne precautions



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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, et al. Am J Infect Control 2016;44:e91-100 UNC Health

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)
- Post-exposure 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, et al. Am J Infect Control 2016;44:e91-100 UNC Health

What's Increasing Our Risk?

- **More than 900 new viruses identified since 2009**
- **Human encroachment on natural habitats**
- **Climate change**
- **Wet markets**
- **"Jump Zones"**
 - Areas with the greatest risk of viruses jumping from bats to humans
 - West Africa: 1 in 5 people at risk; exploitation of natural resources
 - China & Laos: where COVID-19 began, and where scientists have found the closest relatives in wildlife to the virus responsible for the current pandemic
 - India: Almost half a *billion* people live in fast-expanding jump zones, the most of any nation
 - Brazil: the most land at risk of any country



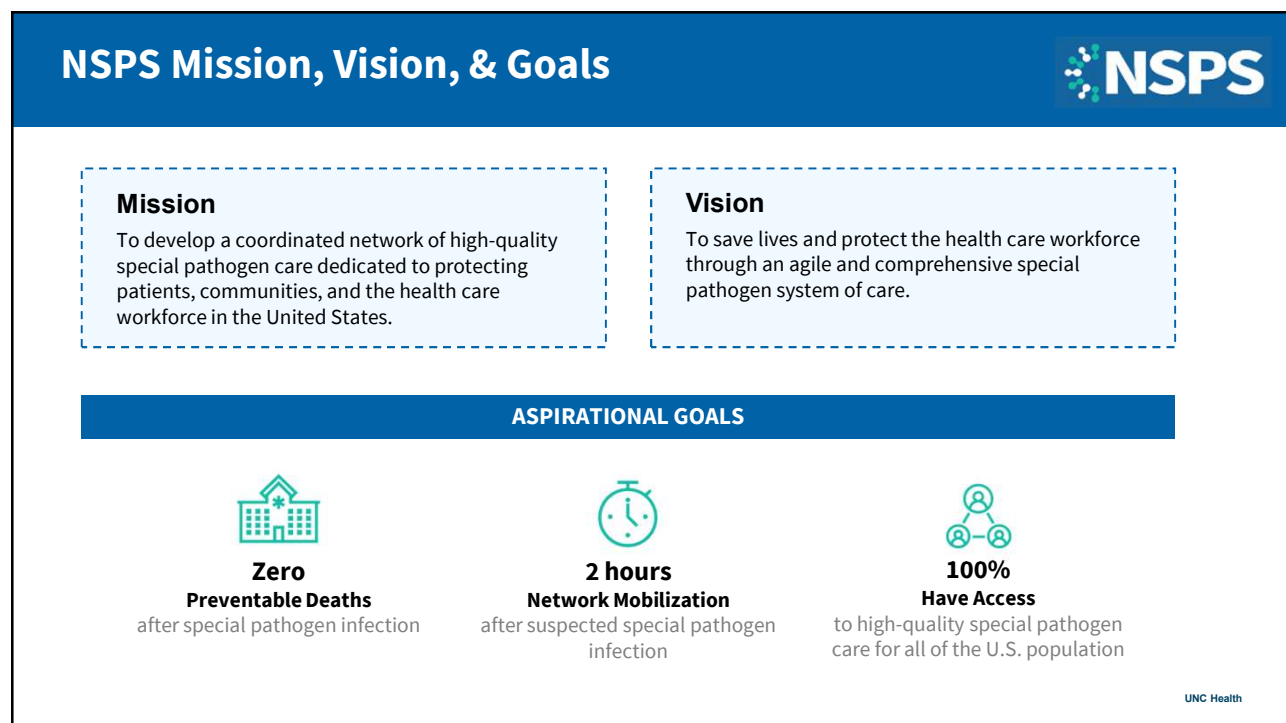
NSPS Overview



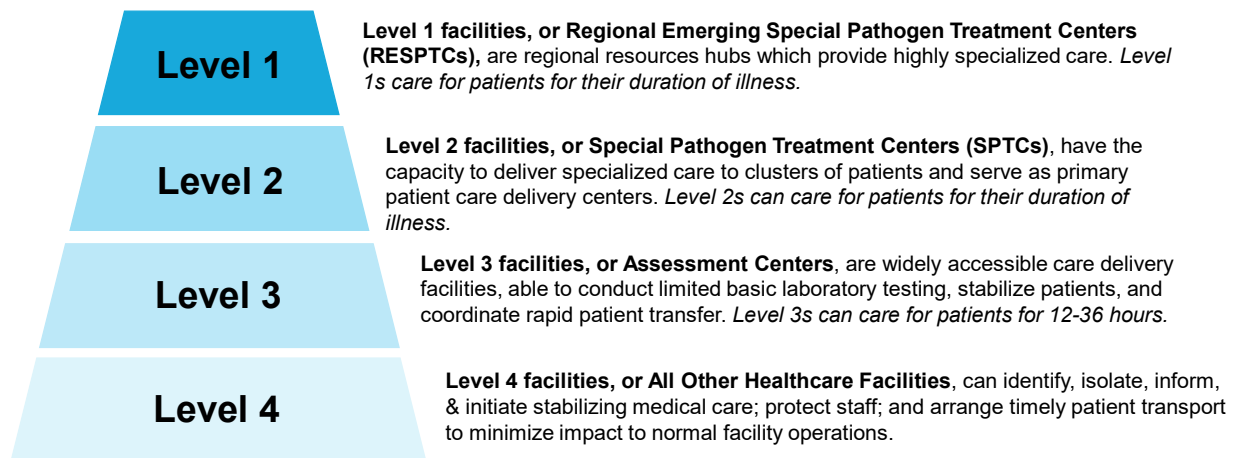
What is the NSPS?

The National Special Pathogen System (NSPS) is a tiered System of Care with four facility levels (e.g., Level 1, Level 2, Level 3, Level 4) that have increasing capabilities to care for suspected or confirmed patients with High Consequence Infectious Diseases (HCIDs).


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The Tiered System of Care



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Facility Overviews			
			
LEVEL 1	LEVEL 2	LEVEL 3	LEVEL 4
<ul style="list-style-type: none"> Can safely identify, isolate, initiate stabilizing medical care, perform required laboratory testing, and inform local public health partners Can activate internal processes for confirmed patients from nearby Level 2, 3, or 4 facilities within two hours time, coordinate transfer within four hours time, and are able to admit suspect or confirmed high consequence infectious disease (HCID) patients at the direction of the Administration for Strategic Preparedness and Response (ASPR) within eight hours time; these may be repatriated US citizens from OCONUS, inter-regional air/ground transports or transfers from a lower tier of the National Special Pathogen System (NSPS) Represents the capacity to hospitalize HCID patients, provide all levels of care up to and including critical care for the duration of their illness, and support continued follow up care when isolation is no longer required When patient volumes exceed Level 1 facility capacity, supports, in collaboration with ASPR and the NSPS Coordinating Body, coordination, and communication amongst other area Level 1 and 2 facilities for optimal patient placement, quality care, and resource utilization Provides care for adult, pediatric, and neonatal patients and must be prepared to offer labor and delivery services if necessary 	<ul style="list-style-type: none"> Can safely identify, isolate, initiate stabilizing medical care, and perform limited basic laboratory testing, and inform local public health partners Can activate internal processes for suspect case(s) from nearby Level 3 or 4 facilities within two hours time, and coordinate transfer within four hours time, and are able to admit suspect or confirmed HCID patients at the direction of ASPR within eight hours time Represents the capacity to hospitalize HCID patients for the duration of their illness and support continued follow up care when isolation is no longer required When patient volumes exceed Level 2 facility capacity, the Regional Emerging Special Pathogen Treatment Centers (RESPTCs) will support collaboration, coordination, and communication among other area Level 1 and 2 facilities for optimal patient placement, quality care, and resource utilization Can be adult focused and/or pediatric focused. Obstetric care is preferred but not required for capability of Level 2 	<ul style="list-style-type: none"> Can safely identify, isolate, initiate stabilizing medical care, and perform limited basic laboratory testing, and inform local public health partners Can activate internal processes for suspect case(s) from nearby Level 4 facilities within two hours time, and coordinate transfer within four hours time. Can safely provide medical care for 12-36 hours and should initiate transfer after stabilization if/when the suspect case rules in for an HCID and/or potentially meets other criteria for transfer Maintains transfer relationships with Level 2 and RESPTCs to support inpatient care for suspect HCID patient who rule-in for HCIDs Can be adult focused and/or pediatric focused 	Considerations to Meet Accreditation Standards <ul style="list-style-type: none"> Can safely identify, isolate, initiate stabilizing medical care, and inform local public health partners. Can safely initiate transfer after stabilization if/when the suspect case rules in for an HCID and/or potentially meets other criteria for transfer. Can be any type of health care facility (e.g., hospitals, urgent cares, nursing homes, etc.) Can be focused on any patient population (i.e., adult, pediatric)

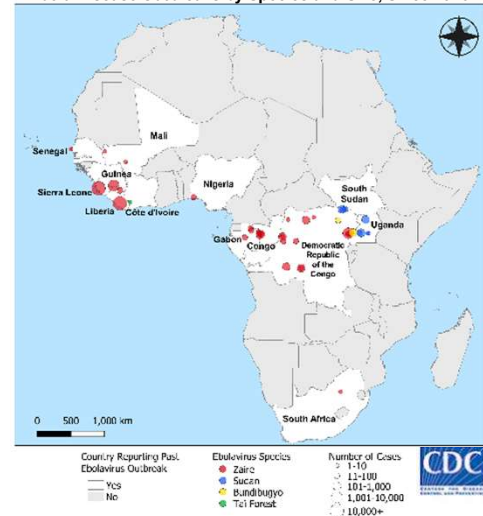
Mitigating the Risk: Staff - Stuff - Space

- Staff – who will care for patients in a pandemic
 - Do you have a team of specialized staff?
 - Do you have a staff who are Subject Matter Experts (SMEs) in pandemic care?
 - Emergency Management teams
- Stuff
 - PPE
 - What types?
 - How much?
 - Where is it stored?
 - Dedicated equipment
- Space
 - Where will you care for patients?
 - Do you have space to store extra PPE in the event of an outbreak or pandemic?
 - Do you have training space?
 - What will you do with your waste if it is Category A?

Ebola Virus Disease (EVD)

- **Acute viral hemorrhagic illness**
 - Discovered in 1976
 - Infects humans & non-human primates
- **Reservoir:** unknown, but presumed to be forest-dwelling fruit bats or non-human primates
- **Incubation period:** 2-21 days
- **Not infectious when asymptomatic***
- **Transmitted through direct & indirect contact**
 - Can persist on surfaces for long periods of time
 - Dry surfaces (doorknobs, counter tops): several hours
 - Bodily fluids (blood): several days
- **Recent outbreaks (2022)**
 - DRC (April – July)
 - DRC (August – September)
 - Uganda (September 2022 – January 2023)
 - [Sudan ebolavirus strain – no vaccine available](#)

Ebola Disease Outbreaks by Species and Size, Since 1976



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Ebola Virus Disease (EVD)

• Signs & Symptoms

- Fever
- Aches & pains (headaches, muscle/joint pain)
- Weakness & fatigue
- Sore throat
- Loss of appetite
- GI: abdominal pain, diarrhea, vomiting
- Unexplained bruising bleeding, hemorrhaging

- Wet vs. Dry

• Clinical management of Ebola disease should focus on supportive care of complications:

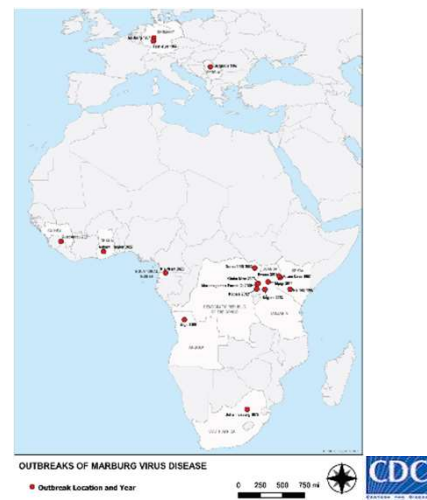
- Hypovolemia
- Electrolyte abnormalities
- Hematologic abnormalities
- Refractory shock
- Hypoxia
- Hemorrhage
- Septic shock
- Multiorgan failure
- DIC

• Pathogen-specific Treatments

- Inmazeb
- Ebanga

Marburg Virus Disease (MVD)

- **Acute viral hemorrhagic illness**
 - Discovered in 1967
 - Infections humans & non-human primates
- **Reservoir: Cave-dwelling fruit bats**
 - Route of transmission from bats to humans is unknown, but the virus has been found in bat oral secretions, urine, and feces (guano)
 - Spread between humans via direct and indirect contact
 - Survives 4-5 days on contaminated surfaces
- **Incubation period: 2-21 days**
- **Not infectious when asymptomatic**
- **Current outbreaks (2024)**
 - Rwanda September 27, 2024 – ongoing

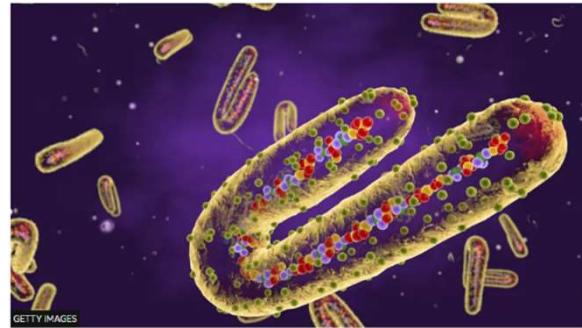


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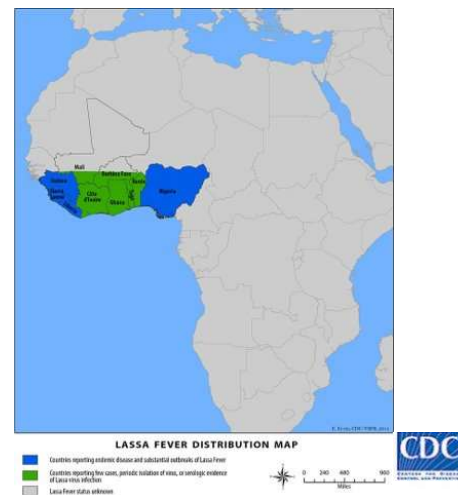
Marburg Virus Disease (MVD)

- **Signs & Symptoms**
 - Sudden onset with fever, chills, headache, myalgia
 - Around day 5: maculopapular rash (usually on trunk)
 - Nausea, vomiting, diarrhea, sore throat, abdominal pain
 - Increasing severity: jaundice, pancreatitis, weight loss, delirium
- **Treatments**
 - EA-IND mAb is available
 - Remdesivir
- **Supportive therapy:**
 - intravenous fluids
 - electrolyte replacement
 - supplemental oxygen
 - blood and blood product replacement



Lassa Fever

- **Arenaviral hemorrhagic fever**
 - First case identified in 1969
 - Infects humans
- **Spread by the common African rat excreta**
 - Transmitted by inhalation, digestion, and direct contact with broken skin
- **Incubation:** 6-21 days
- Approximately 80% of patients are asymptomatic or experience only mild febrile illness
- Disease is more severe in persons who are pregnant



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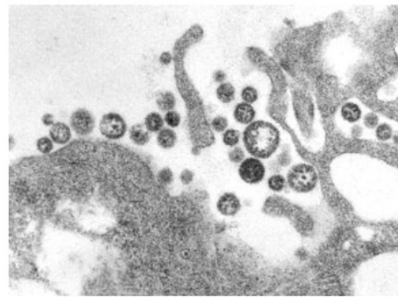
Lassa Fever

• Signs & symptoms (severe illness)

- Hemorrhaging from gums, eyes, or nose
- Respiratory distress
- Vomiting
- Facial swelling
- Hearing loss
- Encephalitis

• Treatment

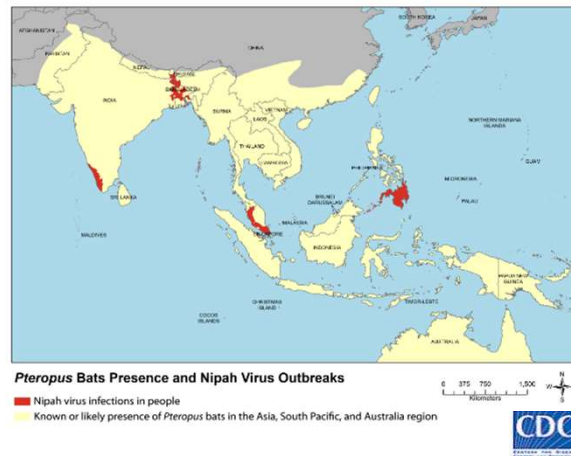
- Ribavirin
- Supportive care
- Consider co-infection



CDC

Nipah Virus (NiV)

- First discovered in 1999
- Known to primarily infect humans and pigs
- Spread by fruit bats (flying foxes) via saliva and urine
- Transmission occurs by:
 - Direct contact with infected animals
 - Consuming foods made with contaminated animal products
 - Person to person via direct contact and respiratory secretions
- Incubation period: 4-32 days
- Recent outbreaks:
 - Jan-Feb 2023 (Bangladesh)



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Nipah Virus (NiV)

•Signs & symptoms

- Initial
 - Fever, headache, cough, sore throat, vomiting, difficulty breathing
- Severe
 - Confusion, seizures, encephalitis, acute respiratory distress, coma
- Long term
 - Persistent convulsions, personality changes

•Treatment

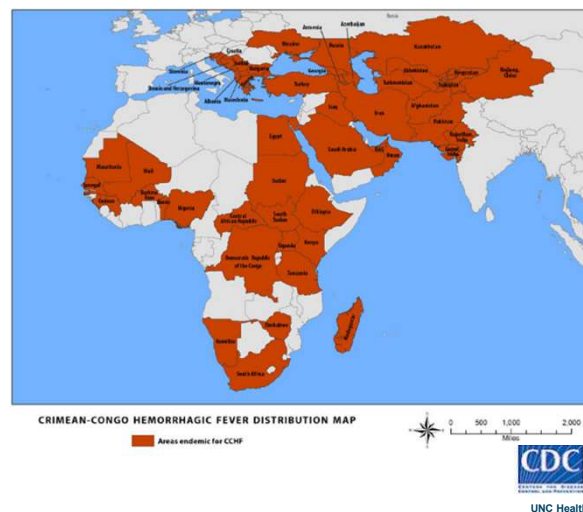
- Supportive care
- EA-IND mAb



NIAID Integrated Research Facility

Crimean-Congo Hemorrhagic Fever Virus (CCHF)

- **First recognized in 1944**
- **Ticks act as both a reservoir and a vector**
- **Human transmission occurs via exposure to an infected tick or infected animal blood**
 - Also known to occur through improperly sterilized medical equipment
 - Human-to-human transmission via infected bodily fluids
- **Length of incubation period depends on how the virus was acquired**
 - Tick bite: 1-3 days
 - Other blood/bodily fluid exposure: 5-6 days
- **Recent outbreaks**
 - 2022, Iraq
 - 2023, Georgia, Senegal, Namibia, Macedonia (single patient & HCW)



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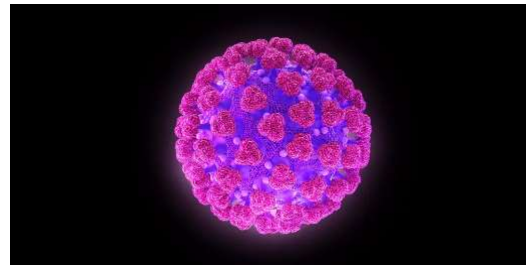
Crimean-Congo Hemorrhagic Fever Virus (CCHF)

- **Signs and symptoms**

- Sudden onset
 - Headache, fever, back & joint pain, stomach pain, vomiting
- Followed by red eyes, flushed face, and petechiae on palate
- Petechiae may progress to ecchymoses and other hemorrhagic findings
- Severe illness
 - Hepatitis, rapid kidney deterioration, liver failure, or pulmonary failure

- **Treatment**

- Supportive care
- Ribavirin



UTMB SPECTRE Program

New World Arenaviruses – South American Hemorrhagic Fevers

- **Very similar presentation**
 - Initial malaise, conjunctival injection, retro-orbital pain followed by sustained by moderate fever and GI symptoms
 - Hemorrhage, neurological involvement, leukopenia and thrombocytopenia are more often seen in the South American HFs than in Lassa fever
- **About 30% of patients develop more severe hemorrhagic or prominent neurologic manifestations, or secondary bacterial infections**
 - Hemorrhage most commonly seen in skin & mucous membranes (GI tract), intracranium, kidneys, pericardium, spleen, adrenal glands, and lungs
- **Incubation period of 6-14 days**
- **Spread via contact with excretions of an infected rodent**
 - Contaminated food
 - Broken skin
 - Inhalation of particles from excrement
- **P2P transmission rare or unconfirmed for some viruses**
- **Surveillance and reporting lower priorities due to:**
 - COVID-19
 - National health system collapse (Venezuela)

Junin (Argentinian HF)

- **Isolated in 1958 and first found in corn harvesters in the Argentinian pampas**
 - Region currently at risk includes upwards of 5 million people
- **Reservoir is the drylands vesper mouse**
- **Transmission usually occurs via inhalation of contaminated mouse excrement in dry dust**
- **3 phases: prodromal, neurologic hemorrhagic, and convalescence**
 - Hemorrhagic symptoms + seizures
- **Treated with ribavirin and plasma (if available & given early)**
- **CFR 15-30%**
- **Candid #1 vaccine**
 - 95-98% efficacy with up to 10 years of protection, resulting in very few cases today



Figure 21-2. Geographic distribution of Junin virus in Argentina. Hyperendemic areas are shown in pink. Radoshitzky, Sheli & Kuhn, Jens & Jahrling, Peter & Bavari, Sina. (2018). HEMORRHAGIC FEVER-CAUSING MAMMARENAVIRUSES.

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"Species of mammals known to be infected with [REDACTED] viruses to date: ferret, mink, European otter, North American river otter, marine otter, European badger, skunk, Virginia opossum, Amur leopard, Amur tiger, mountain lion, fisher, European polecat, lynx, bobcat, domestic cat, red fox, coyote, racoon, racoon dog, South American bush dog, American black bear, brown bear, grizzly bear, Kodiak bear, domestic pig (serology only), grey seal, harbour seal, fur seal, sea lion, porpoise, bottlenose dolphin, short-beaked common dolphin, white sided dolphin, dogs, Japanese raccoon dogs, Beech marten, Caspian seals, Asiatic black bear, Chilean dolphin, Burmeister's porpoise."

-WHO, 7/12/2023



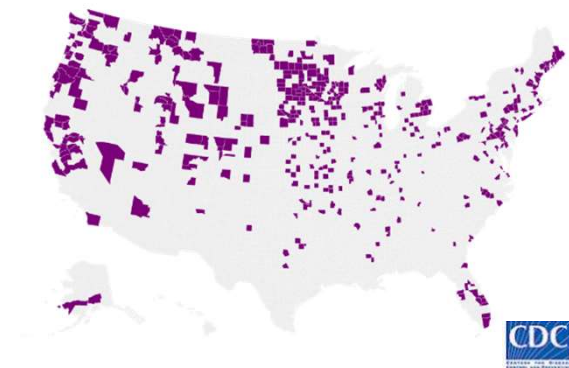
**Answer:
Highly Pathogenic
Avian Influenza
H5N1**

Novel Influenza A(H5N1)

•Highly Pathogenic Avian Influenza (HPAI)

•First outbreak occurred in Hong Kong, 1997

- Spillover from chickens to humans
- Spread to other parts of the world through trade & bird migration
- Transmission to other mammals also noted
- **Rare, limited human-to-human transmission (household)**
- **Exposure occurs via direct contact with infected birds**
- **Incubation period:** 2-5 days on average
- **Current Situation**
 - 17 human infections in US since 2022, 16 since 2024
 - 1 case with no exposure to animals
 - 5 states with reported cases



Novel Influenza A(H5N1)

- **Signs & symptoms**

- **Initial (approx. 3 days after exposure)**

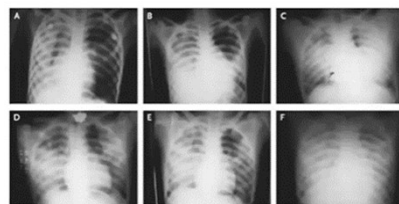
- Fever, cough, sore throat
- Dyspnea due to lower respiratory involvement often develops early

- **Severe (approx. 6 days after exposure)**

- Hypoxia
- Severe pneumonia
- Leukopenia
- ARDS
- Multiorgan dysfunction

- **Treatment**

- Oseltamivir
- Supportive care



Hien N. Engl J Med 2004



T. Uyeki, CDC, September 2005

37-yr woman, illness day #7 Admission CXR

Illness day #10; died day #11



21-yr male, illness day #5 Admission CXR

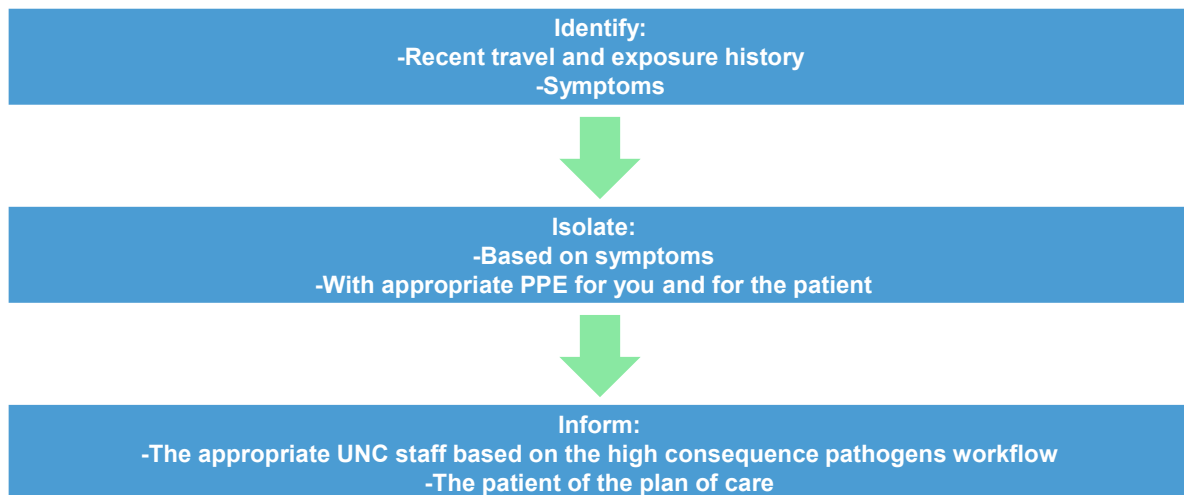
Illness day #12; survived (not ventilated)

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3 Steps to Safety Success: Identify, Isolate, Inform



Identify: Early Recognition is KEY

- **Early detection = better protection**
- **Visual cues of a potentially infectious person**
 - Facial cues
 - Puffy face
 - Droopy eyes
 - Dark eyes
 - Red nose
 - Body language
 - Posture
 - Skin
 - Pale or flushed
 - Diaphoretic



Identify: Early Recognition is KEY

If a patient looks sick...

Take steps to protect yourself and others

- **Put on PPE**
- **Give the patient a mask**
- **Prepare for what's next**

Identify: Early Recognition is KEY

What are we going to ask?

- Do you have any signs of infection?
- Have you traveled lately?
- Is there a difference in treatment?



Isolate

- **What PPE to use for what pathogen of concern**

- Generally, special airborne-contact PPE (or higher)

- **Where to place the patient (and how to get them there)**

- Which route? Stretcher or wheelchair? How many transporting?
- Room preparation
 - What stays in the room & what leaves?
 - Supplies
 - Bathroom?

- **Who has interacted with the patient?**

- **Review IP practices**

- **Waste management**

- What are we doing with all the PPE and used supplies?

Preventing future pandemics

- Identify threats early – Identify, Isolate, Inform
- Combat mis- and disinformation
- Engage the community – this is where outbreaks begin and end
- Work with local partners on training and education for special pathogens
- Understand your PPE inventory and how it is tracked
 - Is it real-time tracking?
 - How often is the inventory updated?
- Does your organization have plans for a surge of patients?
 - Staffing plan
 - Bed plan
 - Outpatient clinic plan
 - Waste management plan



“The worst potential bio-terrorist is nature itself”
Anthony Fauci