Biothreats and Emerging Infectious Diseases

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Biothreats and Emerging Infectious Diseases

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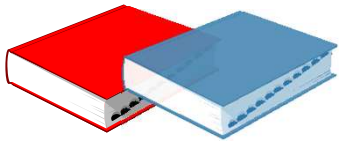
Biothreats

- Natural, accidental, intentional threats posed by a biological agent
- Bacterial, fungal, viral, and toxins they produce
- Examples: Anthrax, Smallpox

Emerging Infectious Diseases

- Infections that have newly appeared in the population, or have existed but are rapidly increasing in incidence or geographic range
- Examples: Mpox, Ebola, Dengue, Zika



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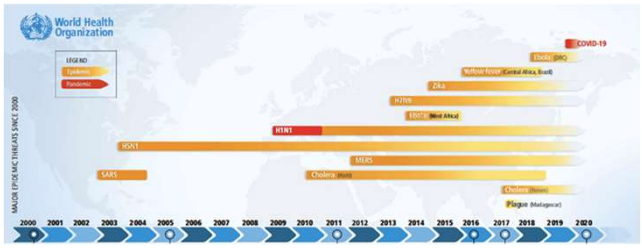
Threats and more threats



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NEW AND EMERGING MICROBIAL THREATS

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CDC, Biothreats (category A)	WHO 2015 (highly infectious pathogens)	WHO 2022 (highly infectious pathogens)	WHO 2022 (fungi, by priority group)	WHO 2024, Drug Resistant Bacteria Threats
• Anthrax (*Bacillus anthracis*) • Botulism (*Clostridium botulinum* toxin) • Plague (*Yersinia pestis*) • Smallpox (variola major) • Tularemia (*Francisella tularensis*) • Viral hemorrhagic fevers, including Filoviruses (Ebola, Marburg) and Arenoviruses (Lassa, Machupo)	• Crimean-Congo hemorrhagic fever • Filovirus diseases (e.g., EVD & Marburg) • Highly pathogenic emerging Coronaviruses relevant to humans (MERS CoV & SARS-CoV) • Lassa fever • Nipah • Rift Valley Fever • Preparedness for a new disease	• COVID-19 • Crimean-Congo hemorrhagic fever • Ebola virus disease • Marburg virus disease • Middle-East Respiratory Syndrome Coronavirus (MERS-CoV) and Severe Acute Respiratory Disease (SARS) • Nipah and Henipaviral diseases • Rift Valley Fever • Zika • "Disease X"	**Critical** • *Cryptococcus neoformans* • *Candida auris* • *Aspergillus fumigatus* • *Candida albicans* **High Priority** • *Nakaseomyces glabrata* spp. (*C. glabrata*) • *Histoplasma* • *Eumycetoma* agents • *Mucorales* • *Fusarium* spp. • *C. tropicalis* • *C. parapsilosis*	**Critical** • CR, *Acinetobacter baumannii* • CR, *Enterobacterales* • 3rdCeph R, *Enterbacterales* • Rif R, *M. tuberculosis* **High Priority** • FQ R, *Salmonella tyhphi* • FQ R, *Shigella* spp. • Vanc R, *E. faecium* • CR, *P. aeruginosa* • FQ R, *Salmonella* spp. • 3rd Ceph R, *N. gonorrhoeae* • FQ R, *N. gonorrhoeae* • MRSA

CDC, Centers for Disease Control and Prevention; WHO, World Health Organization

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FORCES PROMOTING EMERGING DISEASES THREATS

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- Travel
- Population increases/density
- Migration
- Climate change/Global warming
- Habitat destruction/encroachment
- Domestic animal population and amplification
- War/Conflict/Bioterror

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BASIC CONCEPTS IN INFECTIOUS DISEASE EMERGENCE

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- 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

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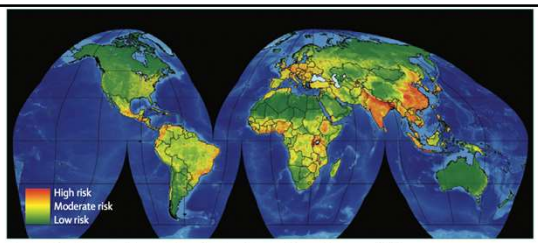

Figure 1: **Global hotspots for emerging infectious diseases that originate in wildlife**
A database of all known emerging infectious diseases[1] since 1940 was used to identify the most likely origins of each separate emergence event. Presence or absence of infections emerging from wildlife was analysed with logistic regression against a series of known drivers, including human population density, change in human population density, and wildlife diversity (mammalian species richness), gridded at 1 km² resolution. The global distribution of model outputs gives a measure of the likelihood of a region to generate a new zoonotic emerging infectious disease that originates in wildlife. Because previous pandemics have mainly originated in wildlife, these maps identify hotspots where the next pandemic is most likely to originate.

Lancet 2012; 380: 1956–65

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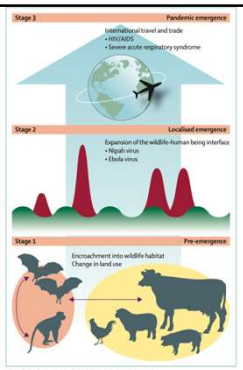

Figure 2: Emergence of pandemic zoonotic disease

Stage 1 is a pre-emergence state, in which naturally occurring microbes are transmitted between their animal reservoirs. Disturbances to the ecology of these populations (eg, due to changes in land use) change the dynamics of microbial transmission and can lead to a heightened risk of pathogen spillover to other non-human wildlife or livestock hosts (but not people).

Stage 2 is localised emergence, either through self-limiting spillover events (green peaks and troughs, representing the rise and fall in numbers of infected people with time) or large- scale spillover (red peaks, representing spikes in the number of infected people with time), that leads to person-to-person transmission for a few pathogen generations.

In stage 3, some spillover events might lead to indefinitely sustained person-to-person outbreaks, international or global spread, and the emergence of a true pandemic.

The ultimate goal of successful pandemic prevention is to move the control point to stage 1.

Lancet 2012; 380: 1956–65

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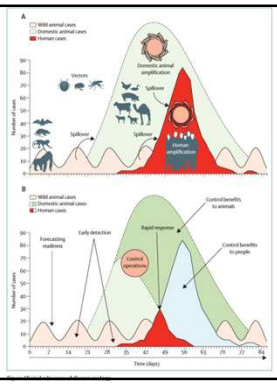

(A) Transmission of infection and amplification in people (bright red) occurs after a pathogen from wild animals (pink) moves into livestock to cause an outbreak (light green) that amplifies the capacity for pathogen transmission to people.

(B) Early detection and control efforts reduce disease incidence in people (light blue) and animals (dark green).

Spillover arrows shows cross-species transmission.

Lancet 2012; 380: 1956–65

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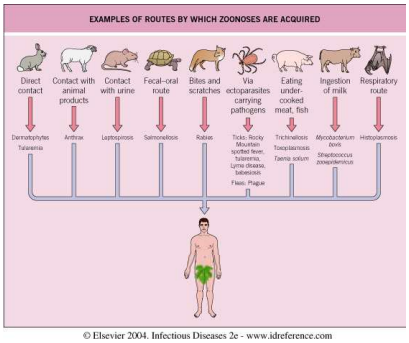

© Elsevier 2004. Infectious Diseases 2e - www.idreference.com

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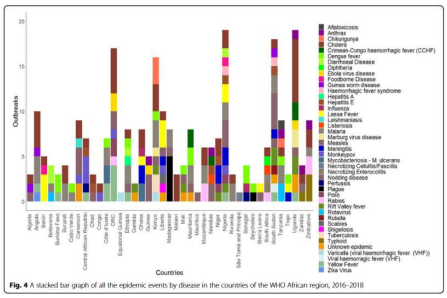
OUTBREAKS AND EPIDEMICS IN AFRICA, WHO, 2016-2018



https://d-nb.info/1208626124/34

Fig. 4 A stacked bar graph of all the epidemic events by disease in the countries of the WHO African region, 2016–2018

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WHO LIST OF PRIORITY DISEASES

- Arenaviral hemorrhagic fevers (including Lassa Fever)
- Crimean Congo Haemorrhagic Fever (CCHF)
- Filoviral diseases (including Ebola and Marburg)
- Middle East Respiratory Syndrome Coronavirus (MERS-CoV)
- Other highly pathogenic coronaviral diseases (such as Severe Acute Respiratory Syndrome, (SARS)
- Nipah and related henipaviral diseases
- Rift Valley Fever (RVF)
- Severe Fever with Thrombocytopenia Syndrome (SFTS)
- Zika

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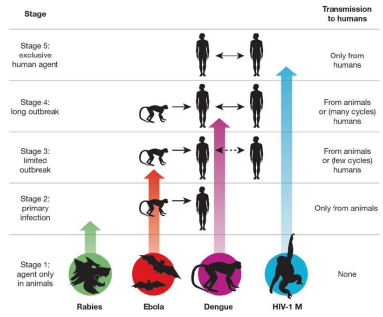

http://web.stanford.edu/group/parasites/ParaSites2012/Lassa%20Libby%20Burch

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HIGH CONSEQUENCE PATHOGENS

Viral Hemorrhagic Fevers

- Examples: Ebola, Lassa, Marburg, Crimean-Congo
- Isolation: Private room (ideally anteroom)
- Develop hot, warm and cold zones
- Dedicated lab equipment
- PPE: No skin exposed; impervious gown, double gloves, PAPR, boots, scrubs
- Safe PPE use (observed donning and doffing)
- Proper waste disposal
- Monitoring for illness among HCP providing care
- Vaccine availability: Depends on disease
- PEP: Depends on disease

High Consequence Aerosol Transmitted Pathogens

- Examples: Highly pathogenic avian influenza (H5, H7), novel coronaviruses, Andes
- Isolation: Airborne isolation room (ideally anteroom); direct out exhausted air, negative pressure, ≥12 air exchanges per hour
- PPE: Gloves, gown, N95 respirator, eye protection
- Monitoring for illness among HCP providing care
- Vaccine availability: Depends on disease
- PEP: Depends on disease

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HIGH CONSEQUENCE *HENIPAVIRUSES*, ASIA

	Nipah*	Hendra
Virus	*Paramyxoviridae*, genus *Henipavirus*	*Paramyxoviridae*, genus *Henipavirus*
Cases (mortality)	~600 (40%-75%)	Rare (<10 reported)
Location	Malaysia, Singapore, Bangladesh, India	Australia
Reservoir	Fruit bats (*Pteropus*, flying fox)	Fruit bats (*Pteropus*, flying fox)
Source(s)	Pigs	Horses
Transmission	Contact with body fluids/respiratory secretions	Contact with body fluids, infected animal
Person-to-person spread	Yes	No (but likely possible)
Nosocomial risk	Yes (in seeing of no or minimal PPE)	?
Prevention (vaccine)	No (in development)	No (vaccine licensed in Australia for horses)
Treatment	Supportive (monoclonal Abs under development)+	Supportive (monoclonal Abs under development)+; Ribavirin?
PEP	Remdesivir? (effective in nonhuman primates)	No
Infection prevention	Use VHF precautions^	Use VHF precautions (conservative)

*https://www.cdc.gov/hicpac/pdf/2023-November-HICPAC-Summary-508.pdf: ^Minimally: gown, gloves, eye protection, N95 or higher; +Remdesivir, Favipiravir, n102.4; Faus-Contino J, et al. Viruses 2024;16:179; Hegde ST, et al. JID 2024;229:733

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VIRAL HEMORRHAGIC FEVERS

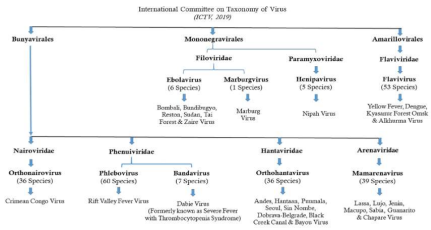

Fig. 1. Overview of VHF causing viruses.

Mariappan V, et al. Curr Res Virologic Sci 2021;2:100009

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VIRAL HEMORRHAGIC FEVERS WITH PERSON-TO-PERSON SPREAD (Nosocomial Risk)

	Ebola	Marburg	Lassa	Crimean-Congo	Andes
Virus	*Filoviridae, Ebolavirus*	*Filoviridae, Marburgvirus*	*Arenaviridae*	*Bunyaviridae*	Hantanvirus
Mortality	50%-90%	20-90%	Hospitalized=15%-20%	~3-30%	15%-30%
Location	Africa	Africa	Africa	Africa, Eastern Europe, Central Asia, Middle East	South America (Chile, Argentina)
Reservoir	Bats	Bats	*Mastomys* rodents	Multiple hosts	Wild rodents
Source(s)	Bats, multiple animals	Likely bat secretions	Rat urine	Ticks	Rodents
Transmission	Direct/Indirect contact*	Direct/Indirect contact*	Ingestion, inhalation^	Via ticks^	Bites, inhalation^
Incubation period (d)	6-12 (range, 2-21)	~7 (range, 2-14)	7-21	1-3 (tick bite); 3-7 (BBF)	7-14
Nosocomial risk	High	High	High (skin contact; body fluids)	Moderate	Low
Prevention (vaccine)	Yes (Zaire strain)	No	No	No	No
Treatment	Ab (Inmazab, Ebanga)	Supportive, Remdesivir?	Supportive, Ribavirin?	Supportive, Ribavirin?	Supportive
Infection prevention	VHF	VHF	VHF	VHF	Airborne isolation room+

*Also semen; ^Also direct/indirect contact; and possible aerosol; +PPE = N95, gown, gloves, eye protection

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Appendix A Update – South American Hemorrhagic Fevers*

Virus	Clinical Illness	Mortality	Modes of P2P transmission	Body fluids	Episodes of occupational ly-acquired transmission in healthcare	Proposed PPE and Patient Placement
South American Hemorrhagic Fevers (Arenaviruses) **Junin** (Argentine HF) **Machupo** (Bolivian HF) **Chapare** (Chapare HF) **Guanarito** (Venezuelan HF) **Sabia** (Brazilian HF)	**All:** flu-like illness **Junin:** absence of respiratory symptoms **Machupo:** may develop neurologic/hemorrhagic manifestations **Chapare:** may develop ARDS/multiorgan dysfunction **Guanarito:** respiratory symptoms, may develop neurological/hemorrhagic manifestations **Sabia:** may develop multiorgan dysfunction	**Junin:** 15-30%, 1% w/ Rx **Machupo:** 25% **Chapare:** 60% **Guanarito:** 33% **Sabia:** 50% Only Junin has vaccine (not available in US) No proven treatments for any	**Junin:** P2P transmission surmised in large-scale outbreaks **Machupo:** P2P transmission demonstrated in 1971, large-scale outbreaks **Guanarito:** Unclear; only one case of secondary transmission has been identified **Chapare:** Yes, via contact with body fluids (all) **Sabia:** not established	**Junin:** reported from oral swabs, urine, breastmilk, 7sexual transmission **Machupo:** blood/throat swab/post-mortem liver/spleen (viral cx) **Chapare:** 2019 outbreak w/ blood/urine/conjunctival/sperm +NP/OP +PCR and culture/NGS **Guanarito:** not established **Sabia:** not established	**Junin:** none **Machupo:** yes **Chaparo:** yes **Guanarito:** none **Sabia:** two lab accidents	Same as Ebola

Disclaimer: The findings and conclusions herein are draft and have not been formally disseminated by the Centers for Disease Control and Prevention and should not be construed to represent any agency determination or policy.

*Presented at CDC HICPAC meeting, 22 August 2024

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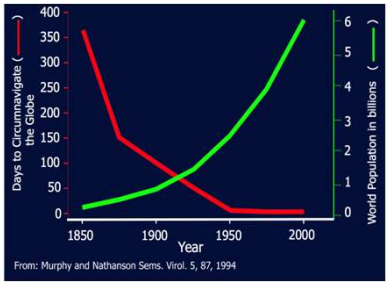
Speed of Global Travel in Relation to World Population Growth



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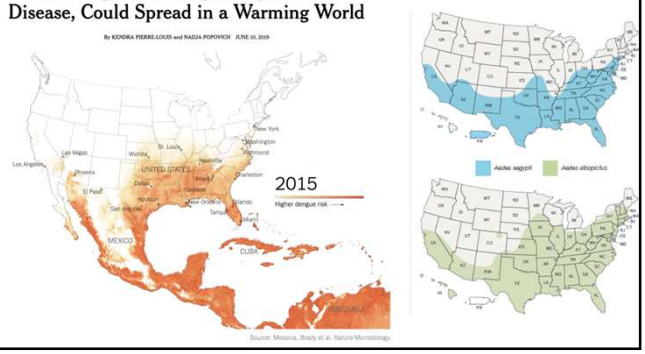
How Dengue, a Deadly Mosquito-Borne Disease, Could Spread in a Warming World



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EXOTIC DISEASES ACQUIRED IN THE US

- 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
- Inhalation anthrax: Rare cases in US; 2006 via African drum hides, CA; previous 1976 (http://publichealth.lacounty.gov/acd/Diseases/Anthrax.htm)
- Polio: Cases in 2022 in New York (derived from polio vaccine strain 2)

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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
- Monkeypox (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)
  - 2021, large global outbreak
- 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).

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EMERGING DISEASES IN THE US

DISEASE (source)	CASES	OUTCOME	YEAR
West Nile virus (Israel)	Thousands	Endemic (US)	1999
SARS (China)	8096 (8 US, 1 UNC)	Controlled	2003
Monkeypox (Africa)	71	Controlled	2003
Novel flu, H1N1 (Mexico)	Thousands	Endemic (Worldwide)	2009
MERS-CoV (Arabian Peninsula)	Hundreds	Epidemic (Arabian area)	2014
Enterovirus D68	Hundreds (13 UNC)	Epidemic (US)	2014
Ebola	Thousands (1 US)	Epidemic (West Africa)	2014-15
COVID-19	Tens of millions (US)	Epidemic to Endemic	2019-present
Monkeypox	Thousands	Epidemic	2022

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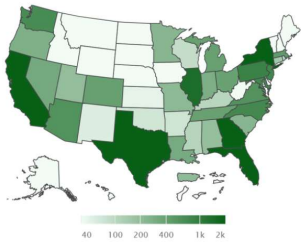
2022-2023 Spread of Mpox in U.S.

- The first U.S. case was confirmed in May 2022.
- At first, spread was associated with international travel.
- More than 30,000 U.S. cases have been reported; new cases are declining.
- Most cases have been in gay, bisexual, & other men who have sex with men.
- Cases have also been reported in men who do not have sex with men, cisgender and transgender women, transgender men, gender-diverse people, children, and teens.



Data as of February 8, 2023

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MPX: 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 (virus detected by PCR) 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
  - Deaths have been reported, most commonly late stage HIV

Infection Prevention

- Single patient room (special air handling, not required); dedicated bathroom
- AIIR: Aerosol generating procedures
- PPE: Gown, gloves, eye protection, N95 respirator
- Appropriate waste management (linens and other contaminated objects may transmit infection)
- Disinfection: EPA registered disinfectant with an emerging viral pathogens claim

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

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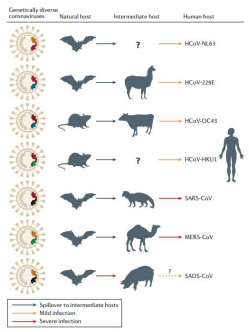
Origin and evolution of pathogenic coronaviruses

TIMELINE: EMERGING NIDOVIRUSES

Virus	Species	Emergence
HCoV-NL63 (Alpha)	Human	500-800 years
HCoV-229E (Alpha)	Human	200-300 years
HCoV-OC43 (beta)	Human	~120 years
PEDV	Porcine	~29 years
PRRSV	Porcine	~29 years
BCoV	Bovine	~24 years
SARS-CoV*	Human	~20 years
MERS-CoV*	Human	~12 years
SADS-CoV (HKU2)	Porcine	~7 years
SARS-CoV-2*	Human	~4 years



Cui J, et al. Nature Rev Microbiol 2019;17:181

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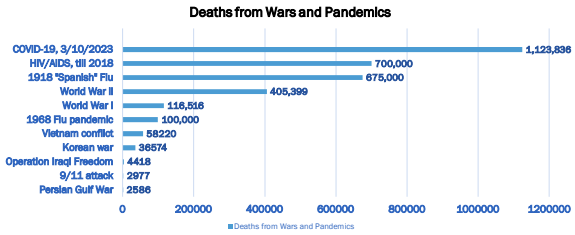
Deaths from COVID-19 and Other Pandemics and Wars, US



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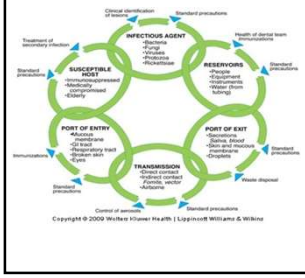
PREVENTING TRANSMISSION OF AN INFECTIOUS DISEASE REQUIRES UNDERSTANDING THE CHAIN OF TRANSMISSION



Virus/Bx	Ebola Virus	SARS-CoV-2
Microbiology		
Year identified	1976	2019
Family	Filoviridae	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 reproduction rate (R_0)	1.5-2.0[27]	1.4-3.6[28]
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	10%, emerging virus claim (List "N")	10%, 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 (knee-length if 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.[31]	1. N95 respirator (or equivalent or higher level of protection) or powered air-purifying respirator (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.[32]
Pre-exposure prophylaxis	Vaccine	Vaccine
Postexposure prophylaxis	None approved for postexposure prophylaxis	None

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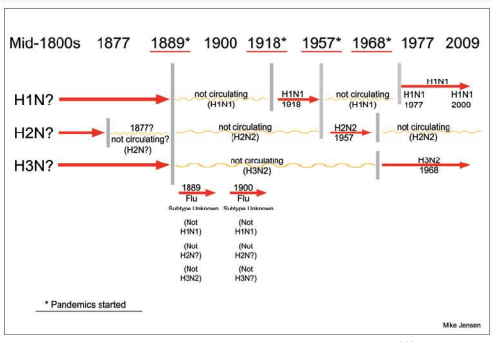

Pineo R, et al J Developing Societies. 2021.

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INFLUENZA TYPE A VIRUSES

UNC SCHOOL OF MEDICINE

- Influenza A viruses are divided into subtypes on the basis of two proteins on the surface of the virus: hemagglutinin (HA) and neuraminidase (NA). There are 18 known HA subtypes and 11 known NA subtypes. In birds, 16 HA and 9 NA subtypes have been identified. (Two additional subtypes, H17N10 and H18N11, have been identified in bats.)
- Influenza A viruses have been detected and are known to circulate in seven different animal species or groups, including humans, wild water birds, domestic poultry, swine, horses, dogs and bats. Equine (horse) influenza A(H3N8) virus routinely circulates and can cause illness in horses, and canine (dog) influenza A(H3N2) virus routinely circulates and can cause illness in dogs.
- Highly Pathogenic Avian Influenza (HPAI): Highly pathogenic avian influenza viruses cause severe disease and high mortality in infected poultry. Include: A (H5) and A(H7) – 90% to 100% mortality in chickens, usually within 48 hours
- Avian influenza A viruses rarely infect people. Five subtypes of avian influenza A viruses are known to have caused human infections (H5, H6, H7, H9, and H10 viruses). The most frequently identified subtypes of avian influenza A viruses that have caused human infections are H5, H7 and H9 viruses. Specifically, A(H5N1) and A(H7N9) viruses have caused the majority of avian influenza A virus infections reported in people, with HPAI A(H5N6) and LPAI A(H9N2) viruses also causing human infections in recent years
- H5N1 viruses: There are nine known subtypes of A(H5) viruses - [A(H5N1), A(H5N2), A(H5N3), A(H5N4), A(H5N5), A(H5N6), A(H5N7), A(H5N8), and A(H5N9)]. Sporadic A(H5) virus infections of humans have occurred, such as with HPAI A(H5N1) viruses associated with poultry outbreaks in many countries. 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.

https://www.cdc.gov/flu/avianflu/influenza-a-virus-subtypes.htm

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H5N1 INFLUENZA

27 Total Reported Human Cases in the United States During 2024

*18 of the 27 H5 human cases reported in the US have been confirmed as H5N1 | Learn More

Human Case Summary during the 2024 outbreak, by state and exposure source

Exposure Source

State	Cattle	Poultry	Unknown	State Total
California	13	0	0	13
Colorado	1	9	0	10
Michigan	2	0	0	2
Missouri	0	0	1	1
Texas	1	0	0	1
Source Total	17	9	1	27

Detections in Animals

- **10,420** wild birds detected as of 10/15//2024 | Full Report
- **51** jurisdictions with bird flu in wild birds
- **103,474,481** poultry affected as of 10/18/2024 | Full Report
- **48** states with outbreaks in poultry
- **323** dairy herds affected as of 10/18/2024 | Full Report
- **14** states with outbreaks in dairy cows

- All California cases have occurred in dairy workers on affected farms.
- All available data so far suggests sporadic instances of animal-to-human spread.
- The source of the exposure in one case, which was reported by Missouri on September 6, could not be determined. Serological testing of the contacts of the Missouri case are pending (some of which were symptomatic but not tested while ill).

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H5N1 OUTBREAKS (mammalian animal to animal)

- Background: H5N1 first detected at goose farm in China in 1996; first big poultry outbreak in Hong Kong in 1997 (first documented human death); ~2005 spilled over into migratory birds; new variant (2.3.4.4b) emerged in 2022 (likely less virulent in humans than earlier variants that had human mortality of ~50%)
- New England seals: H5N1, clade 2.3.4.4b [Puruyear W, et al. https://doi.org/10.1101/2022.07.29.501155]
  - Location = MA, ME; Date = January 2022; Bird outbreak peaks, march and June; Beginning in June, seal carcasses (17/29) found to positive for H5N1
- Mink farm: H5N1, clade 2.3.4.4b (mutation $T_{271}A$ in PB_2 gene) [Aguero M, et al. Euro Surveill 2023;28(3)]
  - Location = Northwest Spain; Date = October 2022; Single farm (50,000 minks involved); outbreak due to presumed wild bird to mink transmission
  - No mink-to-human transmission
- Wild bears: H5N1 [https://fwp.mt.gov/homepage/news/2023/jan/0117---three-grizzly-bears-test-positive-for-highly-pathogenic-avian-influenza]
  - Location = Montana; Date = Fall 2022; Symptoms = neurologic (blindness, disorientation)
- Wild animals: H5N8 [Floyd T, et al. Emerg Infect Dis 2021:27:2856]
  - Location = UK rehabilitation center; Date = November 2020; Animals = 5 swans, 1 fox, 5 seals; No human infection

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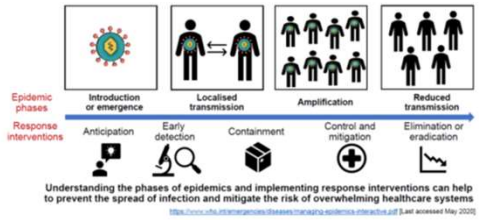
FOUR PHASES OF EPIDEMICS AND RESPONSE INTERVENTIONS



Understanding the phases of epidemics and implementing response interventions can help to prevent the spread of infection and mitigate the risk of overwhelming healthcare systems

https://www.who.int/emergencies/diseases/managing-epidemics-interactive.pdf [Last accessed May 2020]

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KEY CONSIDERATIONS IN ASSESSNG THE THREAT OF AN EMERGING INFECTIOUS DISEASE

- Pathogen
  - Taxonomy (provides clues regarding transmission routes, environmental stability, germicide susceptibility)
  - Host
- Epidemiology
  - Locations of endemicity (ie, locations in the world where sources or reservoirs reside)
  - Incubation period
  - Transmission routes
  - Infectivity (ie, 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)

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KEY CONSIDERATIONS IN ASSESSNG THE THREAT OF AN EMERGING INFECTIOUS DISEASE

- General
- Have a comprehensive facility plan for managing a highly communicable emerging infectious disease.
- Nestle the plan for emerging infectious diseases within the general disaster plan.
- Base the plan on the route(s) of transmission for the infectious agent.
- Incorporate the incident command structure in the plan.
- Periodically train key personnel on the plan.
- The plan should include care of single patients (eg, Ebola) and managing large number of patients in an epidemic (e.g., novel influenza).
- Incorporate communications with local and state health department officials.
- Infection control
  - 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)

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UNC HOSPITAL PREPAREDNESS: HIGHLY COMMUNICABLE DISEASES

- Critical issues
  - Surge capacity
  - Maintaining adequate staffing
  - Provision of essential services/supplies
- Additional issues
  - Surveillance
  - Diagnosis
  - Protecting personnel
  - Occupational health
  - Stockpiling PPE
  - Triage of limited supplies/beds
  - Security

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BIOLOGIC WARFARE: HISTORY

- 300 BC: Greeks pollute wells and drinking water with animal corpses
- 1346, Kaffa: Attacking Tatar force catapulted cadavers of plague victims into city – outbreak of plague led to defeat
- 1763, Fort Pitt, North America: Blankets from smallpox hospital provided to Native Americans – resulted in epidemic of smallpox among tribes in Ohio River valley
- 1932-45, Manchuria: Japanese military physicians infected 10,000 prisoners with biological agents (*B. anthracis, Y. pestis, V. cholerae*, *Salmonella* spp., *Shigella* spp.) – 11 Chinese cities attacked via food/water contamination, spraying via aircraft

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BIOTERRORISM: WHY NOW?

- SecDef William Cohen, March 1998, Heritage Foundation
  - Our American military superiority presents a paradox…because our potential adversaries know they can't win in a conventional challenge to the U.S. forces, they're much more likely to try unconventional or asymmetrical methods, such as biologic or chemical weapons
- Richard Betts, Council on Foreign Relations
  - Nuclear arms have great killing capacity but are hard to get; chemical weapons are easy to get but lack such killing capacity; biological agents have both qualities.

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TRENDS FAVORING BIOLOGICAL WEAPONS

- Biological weapons have an unmatched destructive potential
- Technology for dispersing biologic agents is becoming more sophisticated
- The lag time between infection and appearance of symptoms generally is longer for biological agents than with chemical exposures
- Lethal biological agents can be produced easily and cheaply
- Biological agents are easier to produce clandestinely than are either chemical or nuclear weapons
- Global transportation links facilitate the potential for biological terrorist strikes to inflict mass casualties
- Urbanization provides terrorists with a wide array of lucrative targets
- The Diaspora of Russian scientists has increased the danger that rogue states or terrorist groups will accrue the biological expertise needed to mount catastrophic terrorist attacks
- The emergence of global, real-time media coverage increases the likelihood that a major biological incident will induce panic

Heritage Foundation

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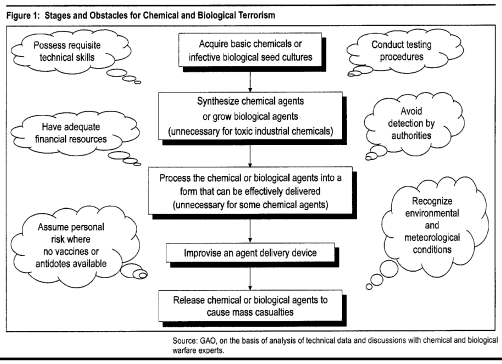

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CENTERS FOR DISEASE CONTROL BIOTERRORIST AGENTS: CATEGORY A

- Easily disseminated or transmitted person-to-person
- High mortality, with potential for major public health impact
- Might cause public panic and social disruption
- **Require special action for public health preparedness**
- **Viruses**: Variola major (smallpox), filoviruses (e.g., Ebola, Marburg), arenaviruses (e.g., Lassa, Machupo)
- **Bacteria**: *Bacillus anthracis* (anthrax), *Yersinia pestis* (plague), *Francisella tularensis* (tularemia)
- **Toxins**: *Clostridium botulinum* toxin (botulism)

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CLASS A BIOTHREATS: KEY FACTS

Disease	Incubation Period (d)	Transmission	Person-to-person spread	Mortality	PrEP	PEP	Treatment
Inhalation anthrax	1-6 (range, 1-60)	Inhalation {contact, ingestion, injection}^	No	Very high (~45% despite therapy)	Yes; vaccine	Yes; vaccine, antibiotics	Yes; vaccine, antibiotics & antitoxin
Smallpox	10-14	Aerosol, contact	Yes; +++	~35%	Yes; JYNNEOS vaccine	Yes; Vaccine, antivirals	Yes; antivirals
Pneumonic plague	1-6	Aerosol {contact, vector}^	Yes, ++	~50%	No	Yes, antibiotics	Yes; antibiotics
Tularemia	3-7 d (range, 1-14)	Aerosol, vector, ingestion	No	5%-15% (untreated); <2%, treated	No	Yes, antibiotics	Yes; antibiotics
VHF*	2-21 d^	Aerosol, contact, vector+	Yes, ++	Variable (but high);	Possibly^	Possibly^	Possibly^
Botulism	12-36 hours (6hr-10d)	Aerosol {ingestion, contact}	No	40-50% (untreated); 5%-10%, treated	No	No	Yes; antoxin, antitoxin

d, days; PEP, post-exposure prophyaxis; PrEP, pre-exposure prophyaxis;
*Includes Ebola, Lassa, Crimean-Congo (characteristics depend on infecting pathogen; ^{other transmission mechanisms unlikely when used as biothreat
Special contact & airborne = smallpox, VHF; Aerosol (mask) = pneumonia plague; Contact = Cutaneous anthrax; None = Tularemia, botulism

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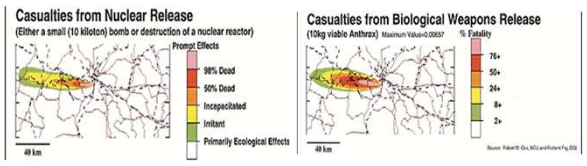
EFFECTS FROM A NUCLEAR RELEASE OR BIOWEAPON RELEASE



Siegrist, Emerging Infectious Diseases 1999

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CENTERS FOR DISEASE CONTROL BIOTERRORIST AGENTS: CATEGORY B

- Moderately easy to disseminate
- Moderate morbidity and low mortality
- **Require improved diagnostic capacity & enhanced surveillance**
- **Viruses**: Alphaviruses (VEE, EEE, WEE)
- **Bacteria**: *Coxiella burnetii* (Q fever), *Brucella spp*. (brucellosis), *Burkholderia mallei* (glanders) , *B. pseudomallei* (melioidosis), *Rickettsia prowazekii* (typhus fever), Chlamydia psittaci (psittacosis)
- **Toxins**: *Rinus communis* (caster beans) ricin toxin, *Clostridium perfringens* episolon toxin, *Staphylococcus* enterotoxin B
- **Food/waterborne pathogens**: *Salmonella spp*., *Vibrio cholerae*, *Shigella dyseneriae*, *E. coli* 0157:H7, *Cryptosporidium parvum*, etc.

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CENTERS FOR DISEASE CONTROL BIOTERRORIST AGENTS: CATEGORY C

- Availability
- Ease of production and dissemination
- **Potential for high morbidity and mortality and major public health impact**
- Emerging agents such as Nipah virus and hantavirus

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SOURCES OF BIOTERRORISM

- Biological warfare
- State sponsored terrorism
- International terrorist groups
- National cults
- The deranged "loner"

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BIOLOGICAL WARFARE: IMPACT

[release of 50 kg agent by aircraft along a 2 km line upwind of a population center of 500,000 – Christopher et al., JAMA 278;1997:412]

Agent	Downwind reach, km	No. dead	No. incapacitated
Rift Valley fever	1	400	35,000
Tick-borne encephalitis	1	9,500	35,000
Typhus	5	19,000	85,000
Brucellosis	10	500	125,000
Q fever	>20	150	125,000
Tularemia	>20	30,000	125,000
Anthrax	>20	95,000	125,000

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CHARACTERISTICS OF BIOWARFARE

- Potential for massive numbers of casualties
- Ability to produce lengthy illnesses requiring prolonged and intensive care
- Ability of certain agents to spread via contagion
- Paucity of adequate detection systems
- Presence of an incubation period, enabling victims to disperse widely
- Ability to produce non-specific symptoms, complicating diagnosis
- Ability to mimic endemic infectious diseases, further complicating diagnosis

US Army, Biologic Casualties Handbook, 2001

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STEPS IN MANAGEMENT

1. Maintain an index of suspicion
2. Protect thyself
3. Assess the patient
4. Decontaminate as appropriate
5. Establish a diagnosis
6. Render prompt therapy
7. Practice good infection control
8. Alert the proper authorities
9. Assist in the epidemiologic investigation
10. Maintain proficiency and spread the gospel

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DETECTION OF OUTBREAKS

- Epidemiologic clues
- Medical clues
- Syndromic surveillance
- Other
  - Intelligence reports
  - Claims of release
  - Discovery of munitions or tampering
  - Increased numbers of pharmacy orders for antibiotics
  - Increased number of 911 calls

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DETECTION OF BT OUTBREAKS: EPIDEMIOLOGIC CLUES

- A rapidly increasing disease incidence
- Unusual clustering of disease for the geographic area
- Disease occurrence outside of the normal transmission season
- Simultaneous outbreaks of different infectious diseases
- Disease outbreak in humans after recognition of disease in animals
- Unexplained number dead animals or birds
- Disease requiring for transmission a vector previously not seen in the area
- Rapid emergence of genetically identical pathogens from different geographic areas

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DETECTION OF BT OUTBREAKS: MEDICAL CLUES

- Unusual route of infection
- Unusual age distribution or clinical presentation of common disease
- More severe disease and higher fatality rate than expected
- Unusual variants of organisms
- Unusual antimicrobial susceptibility patterns
- Any patient presenting with a disease that is relatively uncommon and has bioterrorism potential

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THE PROBLEM OF NEEDLES IN HAYSTACKS

- Outbreak severe acute respiratory infections
  - MERS, SARS, H5N1, H7N9, HxNy…
- Viral hemorrhagic fevers (VHF)
  - Ebola, Marburg, Lassa fever, Rift Valley, CCHF, bunyavirus
- Intentional release
  - Anthrax, smallpox, ricin
- Naturally occurring severe infections
  - Bacterial: Plague, tularemia, melioidosis
  - Viral: Adenovirus, parainfluenza, RSV

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DEVELOPING A BT PLAN

- Recognition of infection
- Incident command system
- Communication with public health
- Triage of patients
- Decontamination of patients
- Maintaining clean and contaminated areas
- Proper patient isolation
- Post-exposure prophylaxis
- Treatment
- Control/screening of visitors
- Immunization of HCWs
- Internal communications
- Availability of diagnostic tests
- Availability of PPE

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INFECTION CONTROL ISSUES FOR SELECTED AGENTS OF BIOTERRORISM

Disease	Incubation period (days)	Person-to-person transmission	Infection control precautions
Inhalational anthrax (see Chapter 185)	2–43*	No	Standard
Botulism (see Chapter 25)	12–72 hours	No	Standard
Primary pneumonic plague (see Chapter 176)	1–6	Yes	Droplet
Smallpox (see Chapter 151)	7–17	Yes	Contact and airborne
Tularemia (see Chapter 177)	1–14	No	Standard
Viral hemorrhagic fevers (see Chapter 183)	2–21	Yes	Contact and airborne
Viral encephalitides (see Chapter 23)	2–14	No	Standard
Q fever (see Chapter 235)	2–14	No	Standard
Brucellosis (see Chapter 180)	5–60	No	Standard
Glanders	10–14	No	Standard

* Based on limited data from human outbreaks; experimental animal data support clinical latency periods of up to 100 days

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DEVELOPING A BT PLAN

- Have a written BT preparedness plan
- Assess the feasibility and viability of the plan
- Disseminate the plan and ensure familiarity by all key stakeholders
- Use elements of daily practice as the backbone of the plan
- Incorporate internal mechanisms for intensified surveillance
- Ensure appropriate internal and external mechanisms of communication
- Test the plan periodically through drills
- Incorporate flexibility and build redundancy for key components
- Address logistics involving surge capacity
- Emphasize community preparedness

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THE MISSION: 4 EYES FOR BIOTHREATS

- IDENTIFY
  - Clinicians & microbiologists
- ISOLATE
  - Clinicians, infection control, hospital admin
- INFORM
  - Clinicians/labs to public health authorities, government, media
- INVESTIGATE
  - Police, internal security, governments, international agencies

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WE HAVE A DUTY TO BE PREPARED

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13 U.S. Regional Emerging Special Pathogen Treatment Centers

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UNC – Regional Emerging Special Pathogen Treatment Center (RESPTC)

- Serve as leading providers of care to sustain and improve healthcare system preparedness for emerging special pathogens
- Hospitals with enhanced capability and capacity to care for highly infectious diseases
- Act as regional hubs for the National Special Pathogen System
- Provide training and support to healthcare facilities within Region IV
- Build emerging special pathogen research capacity

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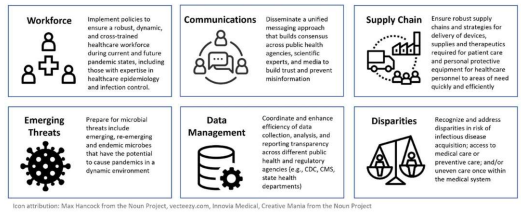
PANDEMIC PLANNING: SHEA RECOMMENDATIONS

UNC SCHOOL OF MEDICINE



Icon attribution: Max Hancock from the Noun Project, vecteezy.com, Innovia Medical, Creative Mania from the Noun Project

Figure 1. Topics selected by the SHEA Pandemic Preparedness workgroup for policymakers.

Hsu VP, et al. ICHE 2024:1-3

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WE HAVE A DUTY TO BE PREPARED

2011, NYC, Attack by hijacked planes

1995, Tokyo, Attack subways with Sarin by Aum Shinriko cult

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THANK YOU!!

UNC SCHOOL OF MEDICINE

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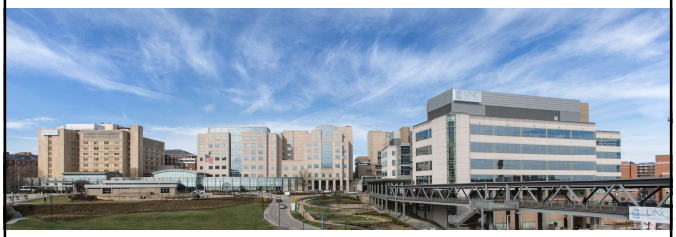
Thank You



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