Adenovirus-14 Outbreak in the UP, 2018

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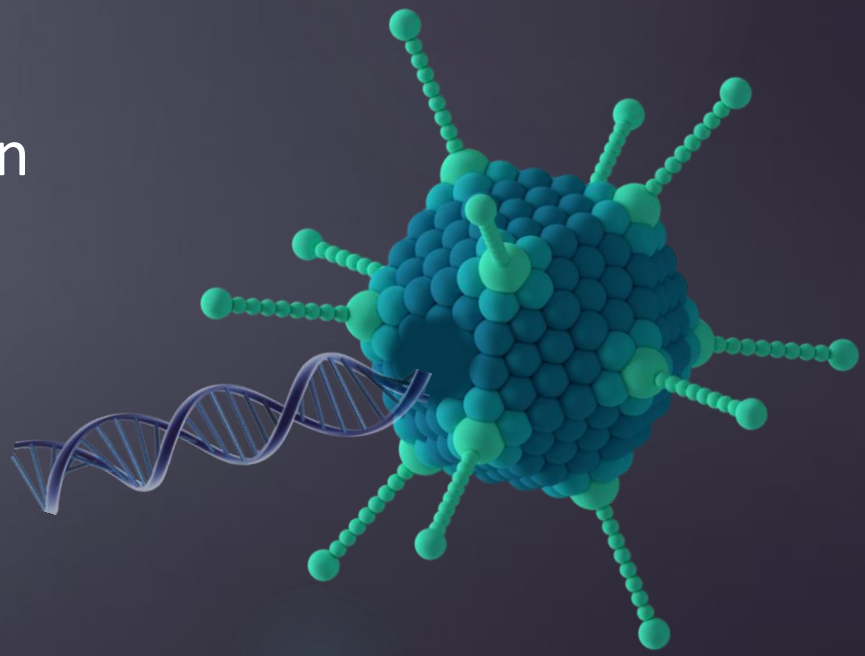
Adenovirus

- Different from other respiratory viruses
  - Medium-sized, non-enveloped icosahedral viruses with double-stranded DNA
  - Resistant to many common disinfectants
  - Can remain infectious for longer periods on environmental surfaces than influenza



Adenovirus

- Broad spectrum of illness in humans, including pneumonia, conjunctivitis, cystitis, gastroenteritis
- Severity of illness varies from asymptomatic infection to severe lower respiratory tract infection, viral sepsis, and even death in rare occasions
- Severe infections more likely in immunocompromised individuals, young children, and older adults

Adenovirus

- 7 species and >50 serotypes of HAdVs (human adenoviruses) have been identified
- Clinical manifestations, patterns of infection, and severity vary by species, subspecies, serotype, and genetic subtype

HAvD subgroup	Serotype	Type of infection
A	12, 18, 31	gastrointestinal, respiratory, urinary
B, type 1	**3, 7, 16, 21**	keratoconjunctivitis, gastrointestinal, respiratory, urinary
B, type 2	11, 14, 34, 35	gastrointestinal, respiratory, urinary
C	1, 2, 5, 6	respiratory, gastrointestinal including hepatitis, urinary
D	**8–10,13,15,17,19,20,22–30,32,33,36–39,42–49**	keratoconjunctivitis, gastrointestinal
E	**4**	keratoconjunctivitis, respiratory
F	40, 41	gastrointestinal
G	52	gastrointestinal

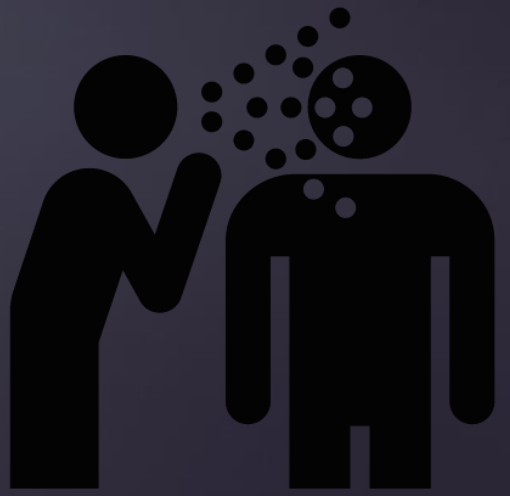
(Ghebremedhinet al., 2014)

Detection

- Identified using viral antigen detection, PCR to identify viral DNA, virus isolation, and serology
  - Adenovirus identified more often than in the past as facilities are adopting multiplex PCR respiratory viral panels (RVPs)
- Adenovirus typing usually performed by molecular methods
  - Few labs can undergo adenovirus strain determination and often request testing by CDC

Transmission

- Close personal contact
- Aerosols from coughing and sneezing
- Touching an object/surface with the virus, then touching mouth, nose, or eyes prior to washing hands
- Feces
- Water



Treatment and Prevention

- No specific treatment
- Generally mild w/o needing medical care in healthy individuals
- **Cidofovir** has been used for severe infections in people with immunocompromised conditions, but with side effects
  - Additional studies are needed to prove its efficacy
- Prevention is key
  - Wash hands with soap + water
  - Avoid touching eyes, nose, or mouth with unwashed hands
  - Avoid close contact with sick individuals
  - Stay home when sick
  - Cover mouth and nose when coughing/sneezing

Persistence on Surfaces

- Adenovirus not generally destroyed by common disinfectants
- Disinfectants effective against adenovirus include:
  - ~1,900 ppm chlorine
  - 79.6% ethanol with 0.1% quaternary ammonium compound
  - 65% ethanol with 0.63% quaternary ammonium compound
  - 70% ethanol
- Here are some examples of products with an EPA registered kill claim against adenovirus that are known to be effective:
  - Clorox Disinfectant Spray
  - Clorox Clean-Up
  - Lysol Disinfectant Spray

Vaccine

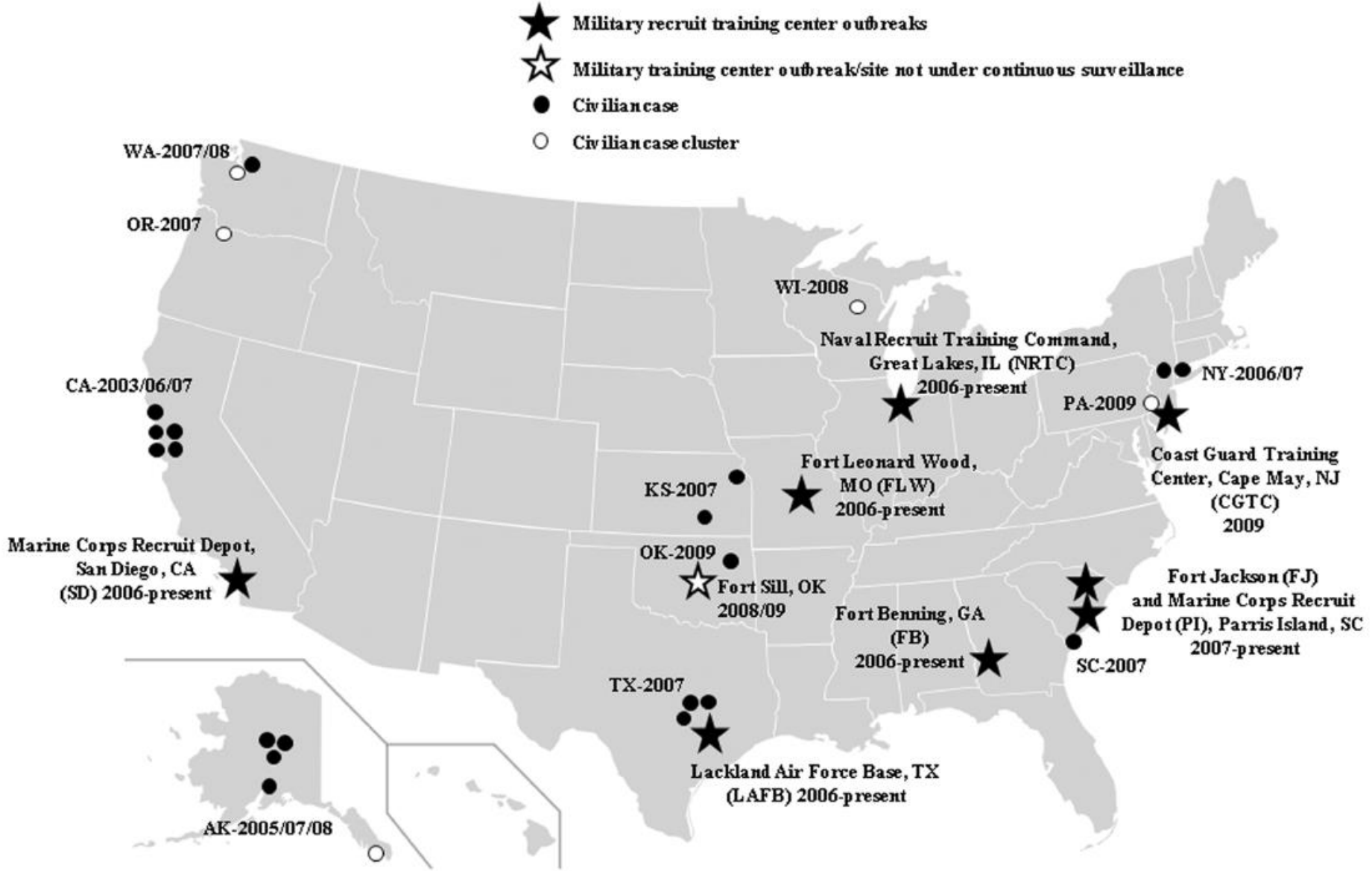
- There are currently no vaccines for adenovirus available for the general public
- Only approved for use among military personnel
  - 1971-1999 vaccine (against types 4 & 7) available to US military recruits, but stopped in 1999
  - March 2011 new live, oral vaccine approved by FDA for use among military personnel

HAdV serotype 14

- B2 subspecies
- First identified among military recruits in Netherlands in 1955
  - Caused military and civilian outbreaks of pharyngoconjunctival fever and mild respiratory tract disease through 1960s in Europe and Asia
- This prototype strain was referred to as the de Wit strain
  - Rare and had not identified in the Western Hemisphere by 1990s

HAdV serotype 14

- Emerged as a significant pathogen in the U.S. in 2006 for several clusters of severe lower respiratory tract disease in both military and civilian settings
  - Community outbreak in Oregon resulted in 29 hospitalizations and 7 deaths
  - A U.S. military training facility outbreak resulted in 23 hospitalizations and 1 death



(Kajon et al., 2007)

ADENOVIRUS 14 OUTBREAK IN THE UPPER PENINSULA

SCOTT SCHREIBER

REGION 8 EPIDEMIOLOGIST

MICHIGAN DEPARTMENT OF HEALTH AND HUMAN SERVICES

INITIAL NOTIFICATION

- Friday, August 24 @ 10:25am - MCHD nurse receives call from Infectious Disease physician at UPHS-Marquette
  - 4 cases of adenovirus admitted in past week
  - 2 severely ill: sisters, reside in neighboring county, one transferred for ECMO and other intubated in ICU
- Notifications to MCHD Medical Director, Regional Epi, MDHHS Respiratory Epi
- Specimens to be shipped to MDHHS Bureau of Labs for additional testing

ADENOVIRUS CLUSTER – ADDITIONAL CASES

- Monday, August 27
  - Late call from UPHS IC to MDHHS – coworker (casino) of one of the adenovirus cases was admitted at neighboring hospital. Thinking legionellosis, asked to test for adeno
- Tuesday, August 28
  - Medical Director contact to OSF IC
    - additional OSF inpatient identified from the weekend – also works at same casino
- Cluster of severe illness + association with casino

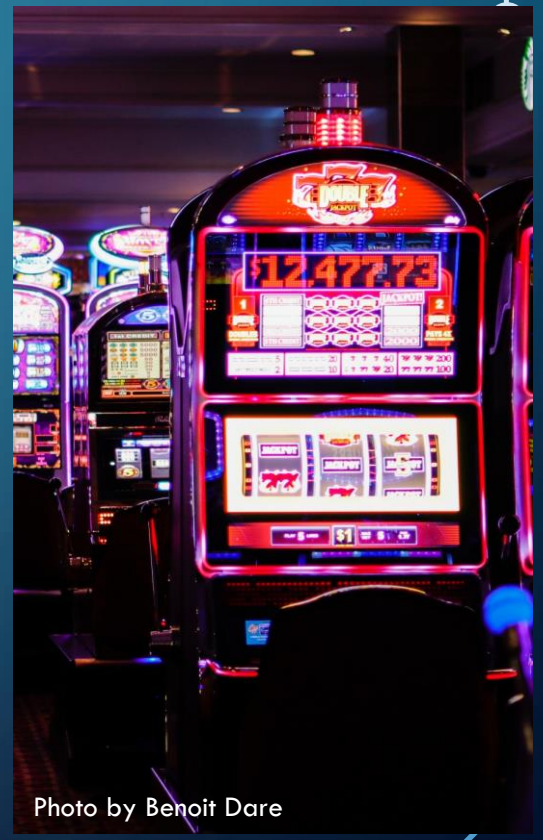


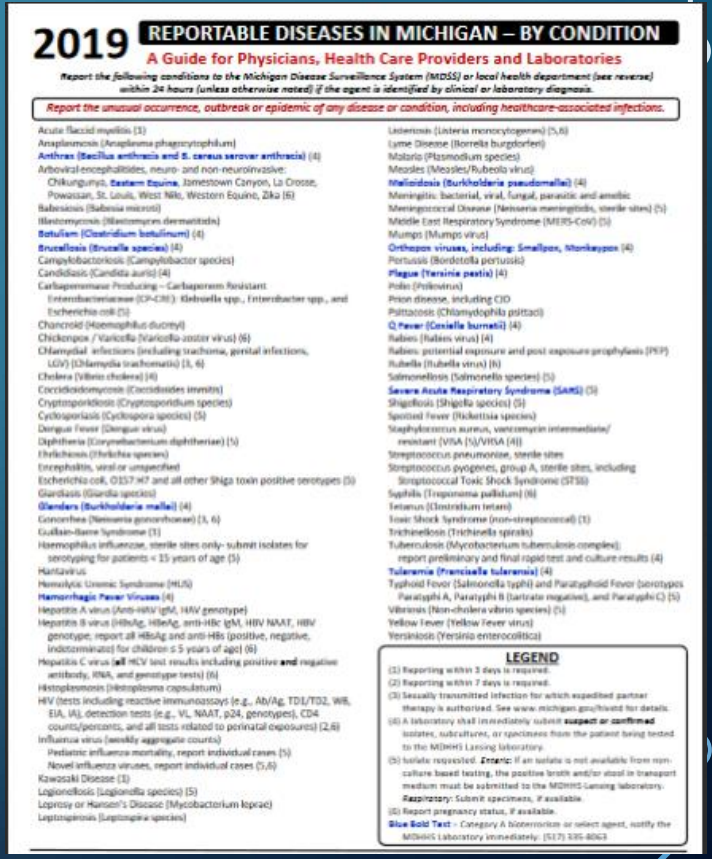
Photo by Benoit Dare

CASINO AND TRIBAL JURISDICTION

- Native American tribes recognized as independent, sovereign nations
  - Do not fall under the jurisdiction of local or state health departments
- No health-related position at casino
- August 28 - Tribal health clinic director contacted by LHJ Medical Director and served as liaison to casino, tribal leadership
  - Notified of cluster, health-related guidance shared

EARLY CHALLENGES

- Adenovirus is not a required reportable disease
  - Unknown what the normal background is for the time of year
  - Testing capabilities changing at hospital labs (Multiplex PCR Respiratory Virus Panel)
- How to best track cases
  - Decision early to enter individually as Unusual Outbreak or Occurrence + utilize outbreak identifier



2019 REPORTABLE DISEASES IN MICHIGAN – BY CONDITION

A Guide for Physicians, Health Care Providers and Laboratories

Report the following conditions to the Michigan Disease Surveillance System (MDSS) or local health department (see reverse) within 24 hours (unless otherwise noted) if the agent is identified by clinical or laboratory diagnosis.

Report the unusual occurrence, outbreak or epidemic of any disease or condition, including healthcare-associated infections.

Acute flaccid myelitis (1)
Anaplasmosis (Anaplasma phagocytophilum)
Anthrax (Bacillus anthracis and B. cereus serover anthracis) (4)
Arboviral encephalitides, neuro- and non-neuroinvasive:
Chikungunya, **Eastern Equine**, Jamestown Canyon, La Crosse, Powassan, St. Louis, West Nile, Western Equine, Zika (6)
Babesiosis (Babesia microti)
Blastomycosis (Blastomyces dermatitidis)
Botulism (Clostridium botulinum) (4)
Brucellosis (Brucella species) (4)
Campylobacteriosis (Campylobacter species)
Candidiasis (Candida auris) (4)
Carbapenemase Producing – Carbapenem Resistant Enterobacteriaceae (CP-CRE): Klebsiella spp., Enterobacter spp., and Escherichia coli (5)
Chancroid (Haemophilus ducreyi)
Chickenpox / Varicella (Varicella-zoster virus) (6)
Chlamydial infections (excluding trachoma, genital infections, LGV) (Chlamydia trachomatis) (3, 6)
Cholera (Vibrio cholerae) (4)
Coccidioidomycosis (Coccidioides immitis)
Cryptosporidiosis (Cryptosporidium species)
Cyclosporiasis (Cyclospora species) (5)
Dengue Fever (Dengue virus)
Diphtheria (Corynebacterium diphtheriae) (5)
Ehrlichiosis (Ehrlichia species)
Encephalitis, viral or unspecified
Escherichia coli, O157:H7 and all other Shiga toxin positive serotypes (5)
Giardiasis (Giardia species)
Glanders (Burkholderia mallei) (4)
Gonorrhea (Neisseria gonorrhoeae) (3, 6)
Guillain-Barre Syndrome (3)
Haemophilus influenzae, sterile sites only- submit isolates for serotyping for patients < 15 years of age (5)
Hantavirus
Hemolytic Uremic Syndrome (HUS)
Hemorrhagic Fever Viruses (4)
Hepatitis A virus (Anti-HAV IgM, HAV genotype)
Hepatitis B virus (HBsAg, HBeAg, anti-HBc IgM, HBV NAAT, HBV genotype; report all HBsAg and anti-HBs (positive, negative, indeterminate) for children ≤ 5 years of age) (6)
Hepatitis C virus (**all** HCV test results including positive **and** negative antibody, RNA, and genotype tests) (6)
Histoplasmosis (Histoplasma capsulatum)
HIV (tests including reactive immunoassays (e.g., Ab/Ag, TDI/TDI, WB, EIA, IA), detection tests (e.g., VL, NAAT, p24, genotypes), CD4 counts/percents, and all tests related to perinatal exposures) (2,6)
Influenza virus (weekly aggregate counts)
Pediatric influenza mortality, report individual cases (5)
Novel influenza viruses, report individual cases (5,6)
Kawasaki Disease (1)
Legionellosis (Legionella species) (5)
Leprosy or Hansen's Disease (Mycobacterium leprae)
Leptospirosis (Leptospira species)
Listeriosis (Listeria monocytogenes) (5,6)
Lyme Disease (Borrelia burgdorferi)
Malaria (Plasmodium species)
Measles (Measles/Rubeola virus)
Melioidosis (Burkholderia pseudomallei) (4)
Meningitis: bacterial, viral, fungal, parasitic and amebic
Meningococcal Disease (Neisseria meningitidis, sterile sites) (5)
Middle East Respiratory Syndrome (MERS-CoV) (5)
Mumps (Mumps virus)
Orthopox viruses, including: Smallpox, Monkeypox (4)
Pertussis (Bordetella pertussis)
Plague (Yersinia pestis) (4)
Polio (Poliovirus)
Prion disease, including CJD
Psittacosis (Chlamydophila psittaci)
Q Fever (Coxiella burnetii) (4)
Rabies (Rabies virus) (4)
Rabies: potential exposure and post exposure prophylaxis (PEP)
Rubella (Rubella virus) (6)
Salmonellosis (Salmonella species) (5)
Severe Acute Respiratory Syndrome (SARS) (5)
Shigellosis (Shigella species) (5)
Spotted Fever (Rickettsia species)
Staphylococcus aureus, vancomycin intermediate/ resistant (VISA (5)/VRSA (4))
Streptococcus pneumoniae, sterile sites
Streptococcus pyogenes, group A, sterile sites, including Streptococcal Toxic Shock Syndrome (STSS)
Syphilis (Treponema pallidum) (6)
Tetanus (Clostridium tetani)
Toxic Shock Syndrome (non-streptococcal) (1)
Trichinellosis (Trichinella spiralis)
Tuberculosis (Mycobacterium tuberculosis complex); report preliminary and final rapid test and culture results (4)
Tularemia (Francisella tularensis) (4)
Typhoid Fever (Salmonella typhi) and Paratyphoid Fever (serotypes Paratyphi A, Paratyphi B (tartrate negative), and Paratyphi C) (5)
Vibriosis (Non-cholera vibrio species) (5)
Yellow Fever (Yellow Fever virus)
Yersiniosis (Yersinia enterocolitica)

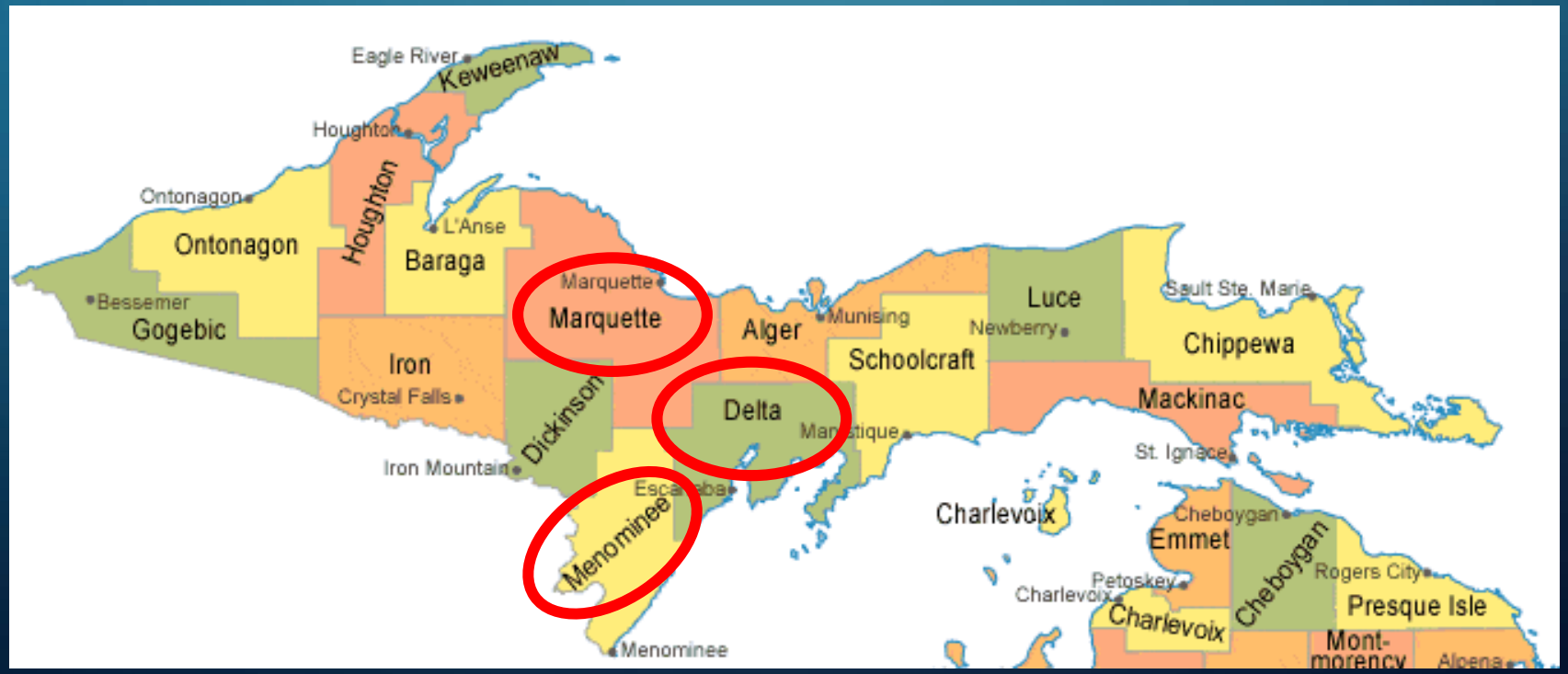
LEGEND

(1) Reporting within 3 days is required.
(2) Reporting within 7 days is required.
(3) Sexually transmitted infection for which expedited partner therapy is authorized. See www.michigan.gov/hivstd for details.
(4) A laboratory shall immediately submit **suspect or confirmed** isolates, subcultures, or specimens from the patient being tested to the MDHHS Lansing laboratory.
(5) Isolate requested. **Enteric:** If an isolate is not available from non-culture based testing, the positive broth and/or stool in transport medium must be submitted to the MDHHS Lansing laboratory. **Respiratory:** Submit specimens, if available.
(6) Report pregnancy status, if available.
Blue Bold Text - Category A bioterrorism or select agent, notify the MDHHS Laboratory immediately: (517) 335-8063

Surveillance & Infectious Disease Epidemiology

MULTI-COUNTY

- Cases and healthcare facilities were across two jurisdictions and three counties
  - Statewide MDSS access for LHJs would have been helpful

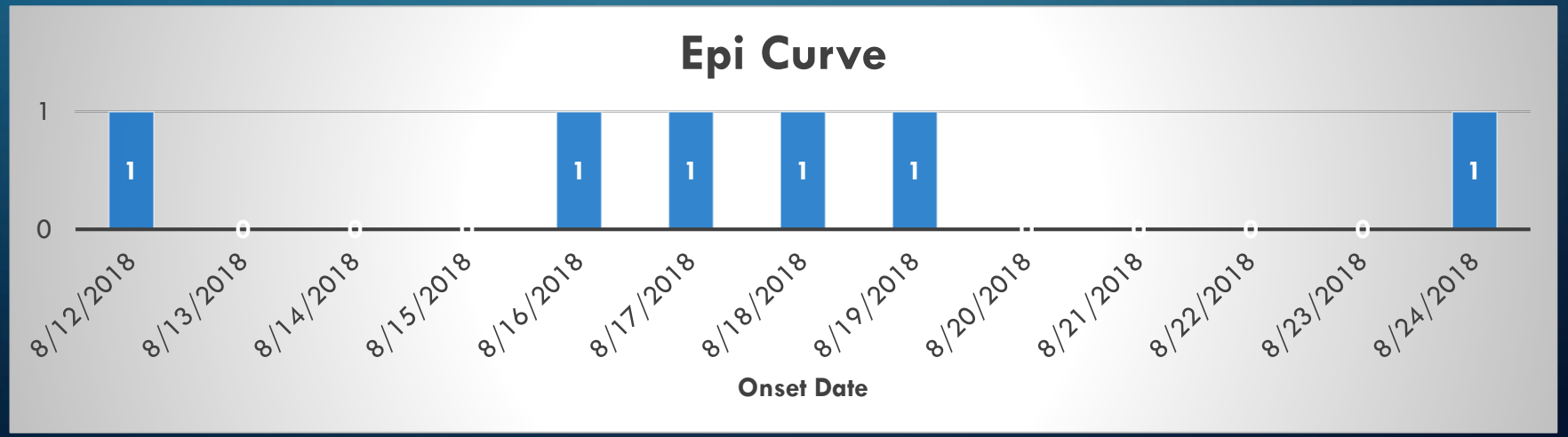


ADENOVIRUS CLUSTER – CONTINUED…

- Thursday, August 30
  - Adenovirus + PCR results on two cases from OSF
  - 6 total cases, 4 w/ casino connection
  - Joint decision (LHJ, MDHHS) to send out statewide HAN and provider letter – HAN will include name and location of casino
  - MCHD/PHDM Medical Director contact to Tribal health clinic regarding prevention measures and HAN/provider letter
    - Enhanced cleaning, encouraging ill employees to stay home, placement of hand sanitizer throughout, and active surveillance of food service individuals for illness

EPIDEMIOLOGY SO FAR

- 6 cases adenovirus positive
  - 33% female, age range 45-62 (mean 53)
  - Residence: Delta (3), Marquette (2), Menominee (1)
  - Cough, SOB, fever, hypoxic respiratory failure
  - Most w/ comorbidities and tobacco use



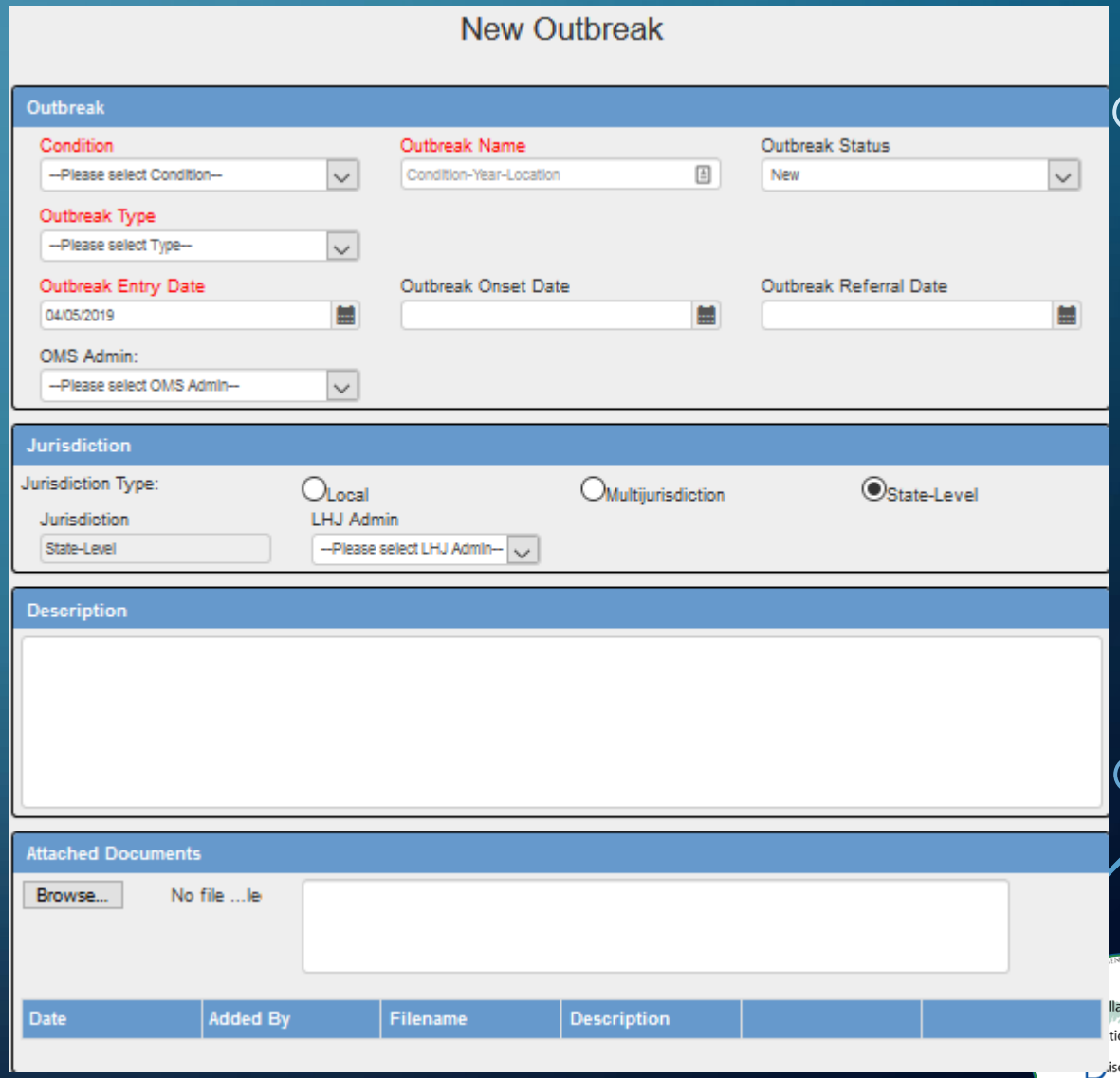
EXTERNAL NOTIFICATIONS - FRIDAY, AUGUST 31 -

- HAN sent
  - Email only, also sent to WI contacts (both within and separate from system)
- Provider letters sent
  - Include adeno in differential, report hospitalized cases
- LHJ and MDHHS discuss and decide on media release, casino will be named
    - Call from TV media about HAN content prior to media release

MIHAN
Michigan Health Alert Network

SHARED LINE LISTS

- September 6 – begin sharing line lists between MDHHS and LHJ
  - Lack of appropriate case detail fields
  - CDC results not sent into MDSS
  - In hindsight, OMS would have worked well for this
    - Secure
    - LHJ and MDHHS access

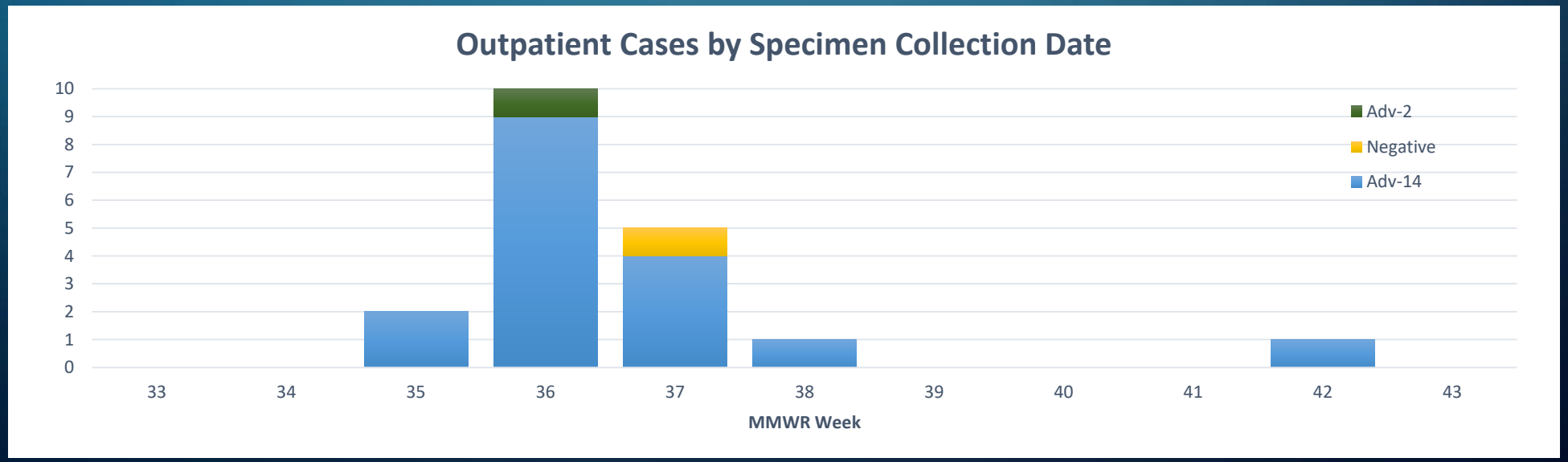


ADENOVIRUS CLUSTER – CONTINUED…

- September 5 – Adenovirus-14 confirmed by CDC in 2 cases
- September 10 – notified of first death (Sept. 7)
- September 20 – Up to 13 cases + for adenovirus (4 Marquette)
- September 26 – media release to update on cluster and death
- September 27 – second death due to adenovirus
- October 3 – LHJ/MDHHS call to review cases, discuss media release
  - No change in guidance, decided not to do another release

OUTPATIENT TESTING

- September 4 – outpatient testing started at UPHS and OSF
- 17 outpatient positive for Adv-14
  - Age range 5-75 years (mean 26.8)
  - Specimen collection date: 9/1-10/16
  - 59% of cases noted active or passive tobacco exposure



ADENOVIRUS CLUSTER – CONTINUED…

- October 10 – Additional CDC results
  - 31 total specimens tested (14 inpatient/17 outpatient)
    - 25 positive for Adeno-14, 5 negative, 1 Adeno-2
    - All Marquette county residents negative so far – 2 were part of initial cluster
- October 17 – after 3 weeks with no new cases, 2 new suspect cases admitted.
- October 18 – Provider and media release sent out
- October 22 – third death reported. New suspect cases are adenovirus positive, Marquette residents, and have no association with the casino
- November 5 – Final call with CDC

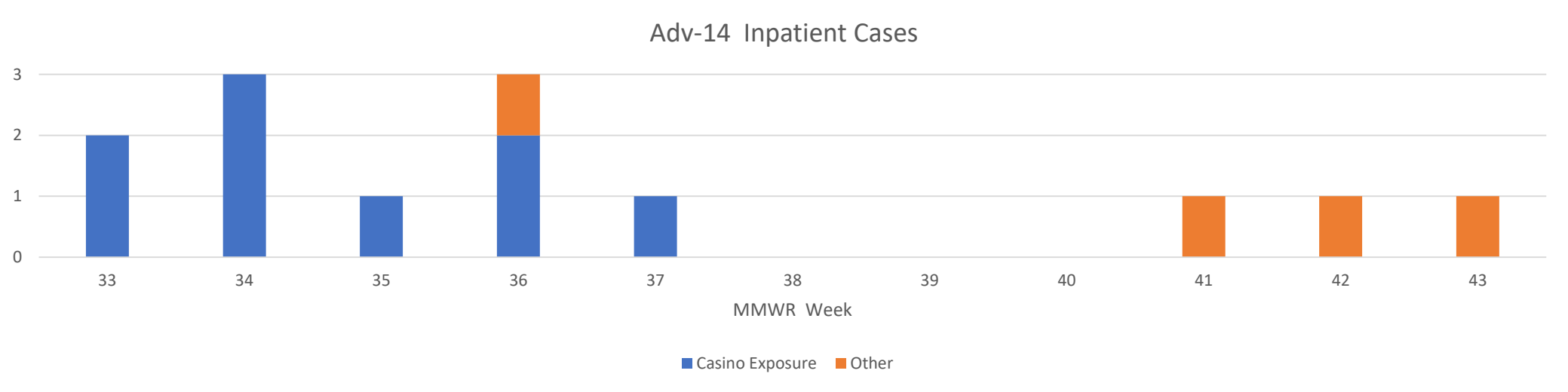
ACTIVE SURVEILLANCE – LATE OCTOBER

October 25 – direct contact to neighboring hospitals regarding adenovirus testing and any positives

DICKINSON	PORTAGE	SCHOOLCRAFT
7 tests run in September, all negative	1 negative, had been sent to Marquette, no in house adeno test	1 positive case in child Tested on Biofire, unknown how many total tests were run

EPIDEMIOLOGY FINAL

- 14 inpatient positive for Adv-14
  - 57% female, age range 45-76 years (mean 57.5)
  - Onsets: 8/12/18-10/21/18
  - 3 deaths, 7 ICU
  - 8/14 (57%) w/ casino exposure, 6 were employees
  - 11/14 (79%) known tobacco use
  - Residence: Delta (10), Marquette (3), Menominee (1)



SUMMARY

- Successes
  - Communication great throughout
    - IC nurses were essential and excellent at keeping public health updated
    - Multi-agency: PHDM, MCHD, MDHHS, BoL, Tribal, CDC
- Challenges
  - Changing Case Definition
  - Surveillance of a non-reportable, sharing line lists (use OMS)
  - Role of the casino in transmission?
  - Frequency of public updates? Potential to further alarm public without benefit

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THANK YOU!