Introduction and Brief Overview:

Objectives:

- Review Ebola Virus Disease (EVD):
  - Ebola Hemorrhagic Fever (EHF),
  - How this disease almost produced a world-wide pandemic,
  - Evolving ability to treat this pathogen,

- Discuss Chikungunya Fever, (CHIKF),
  - A significant disease that is being overlooked,
  - How this disease is moving into the US,
  - Current treatment pathways,

- Lassa & Marburg Fever,
- Compare SARS-CoV and MERS-CoV,
- Briefly look at EV D-68,
- Influenzas with ‘pandemic’ potential,
- Dengue fever,
- West Nile Virus Disease,
- Hanta virus disease,
Cases Treated in US:

- 1st 2 health care providers flown back to US and treated at Emory.
- 3rd health care provider flown back to US and treated in Nebraska.
- 4th health care provider flown back to US and treated at Emory Hospital.
- 5th person who may have been exposed, treated at the NIH.

Cases Treated in US:

- 7th victim, who cared for the Dallas index case, presented Friday October 10th, Dallas
- 8th victim, who cared for the Dallas index case, had positive Ebola test result on Oct 14th, Dallas,
  - Transferred to Emory Hospital/CDC on Oct 15th,
- 9th victim, tested positive on October 23rd, in NYC.
  - Received care at Bellevue Medical Center, Manhattan,
- 10th victim, transferred from Sierra Leone to the Omaha Nebraska Ebola referral hospital, 11-15-14.

Follow-Up:
Cases treated in the US:

- 4th Aid worker victim, a physician, treated at Emory in September.
- Returned in March with elevated intra-ocular pressures and inflammation?
- Intraocular fluid contained active Ebola virus.

Ebola Outbreak - 2013-2014:

- Ebola Hemorrhagic Fever:
  - Current Ebola outbreak first began in December 2013:
    - Patient ‘0’ now identified
      - 2 y/o boy in Guinea who died from the infection
  - Largest & longest outbreak ever recorded
  - WHO (August) has (August 2014) declared this outbreak as a “Public Health Emergency”.

Follow-Up:
Cases treated in the US:

- 12th victim
  - American health care worker
  - Treated at NIH
  - Transferred to NIH in March 2015,
  - Was working in West Africa
  - Recovered and discharged from care – April 2015
Ebola Outbreak – 2013-2014:

- Virus sequencing:
  - West African strain is a new variant of Ebola – Zaire.
- Ebola Zaire has had a 90% fatality rate in previous African outbreaks!
- Oct 15th: 'WHO' Assistant Director reports mortality rate for this variant of 'Zaire' in Guinea, Sierra Leone & Liberia:
  - ~ 70%
  - Possibility of 5000-10,000 new cases/week in these countries.

EHF Statistics – Aug. 2014:

- CDC.gov

EHF Statistics – to mid-April 2015:

- Current Ebola Outbreak – 2015 #’s:
  - EHF/EVD:
    - West Africa total cases – April 8th:
      - Total cases: 25,550
      - Lab confirmed cases: 14,827
      - Total deaths: 10,587

Ebola Outbreaks -2014:

- EHF/EVD:
  - Democratic Republic of Congo (DRC):
    - Separate outbreak identified,
    - Ebola variant strain is different than the West African strain!
  - Outbreak traced to single victim who became infected after preparing 'bushmeat'.

Current Ebola Outbreaks:

- DRC (October 5th, 2014):
  - Case Counts:
    - Total cases: 70
    - Total deaths: 43
    - Lab confirmed cases = 30

Unchanged on Oct 8th
Methods by which Ebola Can Enter the US:

- **Most probable:**
  - Arriving via air or other transport:
    - Purposeful repatriation for treatment,
    - Visitor returning and subsequently found to be infected,
    - Persons fearing they have the disease and coming to the US to avail themselves of advanced treatment,
    - Suicide terrorists who purposely infected themselves to spread infection in the US;
    - Category 'A' agent on CDC/homeland security watch list,
- **Less probable:**
  - Consuming infected imported 'bushmeat' in the US:
    - These items are still being illegally imported into the US and sold in specialty stores in major cities.
    - Eating infected bushmeat is how each outbreak in Africa has begun.
- **Least probable:**
  - Ebola Reston could again mutate back to a pathogenic form:
    - Has been present in the US since 1989.

Viral Hemorrhagic Fever (VHF):

- Caused by 5 distinct families of RNA viruses:
  - Arenaviridae:
    - Lassa fever, Lujo virus, Argentine, Bolivian, Brazilian & Venezuelan hemorrhagic fevers,
  - Bunyaviridae:
    - Hanta virus disease, Crimean-Congo hemorrhagic fever, Rift Valley fever and others,
  - Filoviridae:
    - Ebola, Marburg,
  - Flaviviridae:
    - Dengue fever, yellow fever, & some tick-borne encephalitis
  - Rhabdoviridae:
    - Hemorrhagic fever.

Ebola Virus Disease:

- Caused by 4 of 5 viruses in the genus *Ebolavirus*, family *Filoviridae*, order *Mononegavirales*:
  - Bundibugyo virus,
  - Ebola Zaire:
    - Zaire – (most virulent strain, 90% fatality rate),
  - Sudan virus,
  - Tai Forest virus,
  - Ebola-Reston strain; (Reston Virginia)
    - Not currently disease-producing in humans.

Ebola - Zoonotic & Vector-borne!

- Monkeys, pigs, and bats:
  - Are reported as commonly infected animals.
- Fruit bats:
  - Are thought to be non-affected virus carriers,
  - And the most likely reservoir for the disease.

Ebola Virus:

- Single-stranded, negative-sense, RNA virus:
  - 18,959 – 18,961 nucleotides in length,
- RNA-dependent, RNA polymerase necessary for viral transcription and replication:
  - Source of mutations.
Could Domestic Pets be infected or become carriers?

- Several studies have found seropositive antibodies to Ebola strains in non-primate vertebrates;
  - Most specifically bats, pigs and dogs, (see references below)
  - There are some case reports suggesting that pigs can develop Ebola disease;
  - There are currently no reported studies on carrier status and/or infection in domestic animals such as dogs or cats.

References:
- Olsen SH, et al, Emerg Health Threats J, 2012;5:9134,

Transmission:

- Ebola cycle:
  - Transmission:
    - Equatorial animal "Bushmeat" consumption
    - Currently thought that the 1st victim in an outbreak connects the disease from an infected animal,
    - Then disease is transmitted person-to-person by contact with infected bodily fluids.

CDC.gov

Pathogenesis:

- Main initial targets of Ebola viral infection;
  - Endothelial cells of blood vessel walls,
  - Macrophages,
  - Monocytes,
  - Liver cells,

- Viral replication overwhelms protein synthesis of infected cells & host immune defenses;
  - Virus invades the immune system (neutrophils) and transported throughout the body by these cells;
  - Lymph nodes, liver, lungs, spleen, and other targets,

- Viral damage to endothelial cell walls leads to loss of vascular integrity and leads to bleeding,

- Damage to the liver leads to clotting diatheses,

- Damage to immune system leads to immunocompromise,

- Dropping WBC counts may be prognostic factor of outcome,


Incubation Period:

- Ebola Virus Disease (EVD):
- Ebola Hemorrhagic Fever (EHF):

- Incubation period:
  - Usually 2 days to 3 weeks
  - after contracting the virus.

- Long incubation period allows for extended travel after virus contact;
- Victims can travel to different continents and present in unexpected locales with acute symptoms.


Human-to-Human Transmission:

- Ebola:
  - During incubation period:
    - Victim is not contagious
    - until (at least) the onset of initial symptoms;
  - Fever most common, (87.1%)*
    - * 1 recent, observational study;
    - NEJM – Oct 2014,

Screening - Transmission:

- Ebola Screening – Airports:
  - Infrared thermometers,
  - Can only identify those with symptom onset = fever.

Ebola Screening:

- Early signs & symptoms:
  - Fever,
  - Headache
  - Joint and muscle aches

- Followed by:
  - Weakness
  - Diarrhea
  - Vomiting
  - Stomach pain
  - Lack of appetite


EHF Presentation:

- Other signs & symptoms:
  - Rash
  - Red eyes
  - Hiccups
  - Cough
  - Sore throat
  - Chest pain
  - Difficulty breathing
  - Difficulty swallowing
  - Bleeding internally and externally.


Internal & External Bleeding:

Ebola Hemorrhagic Fever:

- Sign of severe infection,
- External bleeding:
  - Can potentially be seen from all vascularized locations:
    - Mucus membranes,
    - Conjunctiva,
    - Orifices,

Differential Diagnosis:

- Malaria,
- Typhoid fever,
- Typhus,
- Dengue fever,
- Shigellosis,
- Lassa fever,
- Yellow fever
- Leptospirosis,

Infection Risk?

- When, after developing initial symptoms, does a victim become an infection risk to those he/she comes in close contact with?
- There is currently no evidence-based human research to help answer this question.
- Current protocols are based on anecdotal observation during previous and the current outbreak!
- The answer is related to ‘viral load’!
Ebola:

- Viral load of a symptomatic Ebola victim with developed infection is significant!
  - ~10 Billion virions in a drop of infected blood or other bodily fluids.
- For comparison, a ‘drop’ of infected blood from an untreated HIV patient with AIDS can have ~ 1 million virions.


Viral Load?

- When, after initiation of symptoms, does this huge viral load begin to appear?
- The answer currently is not known?

Diagnostic Tests for Ebola Infection:

- Serology testing:
  - Antigen-linked, Enzyma-linked, Immunosorbent Assay (ELISA)
  - IgG ELISA,
- Molecular testing:
  - Polymerase Chain Reaction (PCR),
  - Virus Isolation & Culture,
  - Or;
  - Quarantine, watch and wait.

Rush to find rapid test:

- Need a test that only requires a few drops of blood, and can be performed locally and rapidly.
- In Africa currently takes days to deliver blood sample to a testing lab
  - Then takes days to obtain result.

Recent Test Developments:

- Genalyte reports development of a 10-minute Ebola test.
  - The test is based on a proprietary silicon chip technology.
  - A paper test, developed by researchers at Harvard-MIT, can distinguish strains of Ebola.
  - The test is reported to be inexpensive,
  - To be completed in minutes
  - and doesn’t require refrigeration or shipping samples.
- FDA approved (Oct 25th) Biofire Defense’s test utilizing their FilmArray technology,
  - Reported to have a 1 hour turnaround.
- WHO approved in February 2015, a 15 minute screening test for Ebola
  - Requires confirmatory testing
  - (missing ~ 8% of Ebola patients)

Acute Management:

- Absolute isolation:
  - with full universal precautions,
  - For all symptomatic victims,
  - All persons who had direct, unprotected contact with a victim;
  - Once victim symptoms (such as fever) appear,
  - Should be isolated and tested for Ebola!
  - Isolation is currently the only way to contain the disease and stop it’s spread!

Morin, M, Los Angeles Times, Science, August 5, 2014
http://news.sciencemag.org/health/2015/02/rapid-test-ebola-now-available
Acute Management:

**Ebola Virus Disease**

- Supportive care;
  - Rehydration,
  - Electrolyte balance,
  - Oxygen,
  - Blood pressure management,
  - Bleeding;
  - Blood replacement,
  - Anticoagulants early – DIC prevention,
  - Procoagulants – late – prevent massive exsanguination,
- Secondary infection control,
- Management of complications,

Specific, Targeted Interventions:

**Ebola Virus Disease**

**Specific, Targeted Therapies:**

- Until current outbreak:
  - Ebola considered an ‘orphan’ disease;
  - There was little interest in developing agents to combat this infection.
  - Some funds available in EU via ‘orphan disease’ classification.

**Acute Mgt. Options:**

- Transfusions from Ebola survivors:
  - Blood-borne antibodies,
  - In the US; these are plasma transfusions.

Specific, Targeted Interventions:

**Ebola Virus Disease**

**Specific Interventions:**

**Acute Mgt. Options:**

- Transfusions from Ebola survivors:
  - Blood-borne antibodies,
  - In the US; these are plasma transfusions.

**Other Acute Mgt. Options:**

- Other emerging treatments:
  - ‘Antisense’ technology:
    - small interfering RNAs (siRNAs) and phosphorodiamidate morpholino oligomers (PMOs)
    - targeting the Zaire Ebola virus.
Other Acute Management:

**Ebola Virus Disease**

- **Favipiravir:**
  - Japanese anti-influenza drug;
  - Fujifilm Holdings Corp
  - Appears effective in an Ebola mouse model,
  - Has been given to a French aid worker (nun) who contracted Ebola while working in Liberia, (patient survived).
  - FDA-approved trial to begin in Africa – December 2014,
  - There are now oral (200mg) and IV preparations,


- **Amiodarone, dronedarone & verapamil:**
  - Block entry of filoviruses (including Ebola), into cells - in vitro,
  - These classes of drugs are multi-ion channel inhibitors and adrenoceptor antagonists,
  - Currently believed that “anti-filovirus effect” occurs via this mechanism,
  - Drugs worked at usual therapeutic doses,


- **Estrogen receptor drugs (clomiphene & toremifene):**
  - Inhibit the progress of Ebola virus, in infected mice,
  - Study funded by USAMRIID & NIH,


Other Possible Acute Mgt. Options:

**‘Serendipity’ agents:**

- **Estrogen receptor drugs (clomiphene & toremifene):**
  - Inhibit the progress of Ebola virus, in infected mice,
  - Study funded by USAMRIID & NIH,

Other Possible Mgt. Options:

**Tekmira Pharmaceutical’s TKM-Ebola:**

- Utilized on 3rd US aid worker flown to Nebraska Medical Center in September,
  - Combination of small interfering RNA’s targeting 3 of the 7 proteins in Ebola,

  - [http://www.sciencedaily.com/releases/2015/04/150422135748.htm](http://www.sciencedaily.com/releases/2015/04/150422135748.htm)

- **April 22nd 2015 - Edition of Nature:**
  - TKM-Ebola successful in treating Ebola infected animal models;
  - Treated animals all survived and healthy
  - All controls expired of the disease.


Other Possible Mgt. Options:

**BCX4430:**

- Broad-spectrum, small molecule antiviral drug
- Developed by BioCryst
- Testing at USAMRIID
- Approved for Phase 1 trials
- Beginning late in 2014,

**Lamivudine:**

- Antiviral agent for HIV/AIDS;
- Reported in September to have been successfully utilized in 13 of 15 Ebola-infected patients in Liberia as part of a combination therapy,
Other Possible Acute Mgt. Options:

**Ebola Virus Disease**

- **NCBI-NIM-NIH:**
  - **AVI-7537**
  - Antisense RNA oligomer (19mer).
  - Targets the VP24 gene of the Ebola virus.
  - Companion drug being developed to target Marburg virus.
  - Developed by Sarepta Therapeutics, a Cambridge biotech firm.

  [http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3509674](http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3509674)

- **Russia – October 2014:**
  - **Triazavirin**, an antiviral drug candidate created by the Ural Biopharmaceutical Technology Center;
  - Approved, by the Russian Health Ministry, for emergency use against Ebola.
  - Original, published studies of agent are for H1N1.

  [http://tch.dni.com/content/2014/10/12/yekaterinberg_scientists_develop_drug_to_fight_ebola_39715.html](http://tch.dni.com/content/2014/10/12/yekaterinberg_scientists_develop_drug_to_fight_ebola_39715.html)

- **GSK’s method splices components of the Zaire strain of the Ebola virus into a chimp adenovirus, (closely related to a human adenovirus strain that causes upper respiratory tract infections).**
  - "The (Trojan horse) adenovirus infects cells in a vaccinated animal, causing them to take up the gene and produce Ebola proteins. This primes the immune system to attack the proteins of Ebola viruses when an infection occurs."


- **Another vaccine candidate at the NIH**
  - Bethesda campus.
  - Developed by the Public Health Agency of Canada Microbiology Laboratory.
  - Sept – 2014:
    - FDA approved a trial in 40 healthy human volunteers for this method. (VRC 207),
    - Clinicaltrials.gov - NCT02231866.
  - A small U.S. drug maker, NewLink Genetics,
    - Holds the license.
  - April 2015:
    - Sierra Leone – clinical trial begun
    - 6000 health care workers in 5 high risk districts of the country will receive vaccine.


Vaccine Candidates:

- **rVSV-ZEBOV:**
  - Another vaccine candidate at the NIH
    - Bethesda campus.
  - Developed by the Public Health Agency of Canada Microbiology Laboratory.
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    - FDA approved a trial in 40 healthy human volunteers for this method. (VRC 207),
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[Other Possible Acute Mgt. Options:](#)

**Ebola Virus Disease**

- **October 2014 - China:**
  - has approved JX-06,
  - for emergency use in the treatment of Ebola Virus Disease.
  - 'small molecule' drug.
  - developed in part by the Chinese military.
  - Sihuan Pharmaceutical Holdings Group Ltd has signed an agreement with Chinese research Academy of Military Medical Sciences (AMMS) for drug development.
  - There are millions of Chinese nationals living in Africa, with around 10,000 in the worst affected countries - Sierra Leone, Guinea and Liberia.


[Other Possible Acute Mgt. Options:](#)

**Ebola Vaccine Candidates:**

- **ChAd3:**
  - NIH reported that 4 monkeys that had been immunized against Ebola with an experimental vaccine did not contract the disease with subsequent Ebola exposure at 2 months post vaccination;
  - Booster shot required.
  - Human safety trials began in September:
    - OkaIos/GlaxoSmithKline & USAMRIID working with NIH on vaccine development.
    - NIAID/GSK vaccine candidate,
    - Clinicaltrials.gov - NCT02231866


Vaccine Candidates:

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  - Approved, by the Russian Health Ministry, for emergency use against Ebola.
  - Original, published studies of agent are for H1N1.

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  - "The (Trojan horse) adenovirus infects cells in a vaccinated animal, causing them to take up the gene and produce Ebola proteins. This primes the immune system to attack the proteins of Ebola viruses when an infection occurs."

Vaccine Candidates:

- Johnson & Johnson reports (Oct. 2014)
  - Will begin safety testing in early January.
  - Vaccine combination candidate.

- The New Brunswick, N.J., company is spending up to $200 million to speed up production of the vaccine,
  - which it licensed in part from a Danish company last month.

- If safety tests are successful, the company hopes to begin large clinical trials in May 2015.

Targeted Mgt. Options:

- Some of these agent candidates have been emergently given to victims during the current outbreak,
  - None have completed the usual, accepted research pathways!

- Therefore, in reality, none are ready for ‘prime time’!

Immunity?

- Are survivors of Ebola infection immune from re-developing the disease;
  - If re-exposed to the virus?

- It is currently hypothesized that there is adequate antibody cross-reactivity among the different strains of Ebola (5 currently known) to yield acute, generalized immunity;
  - Length of immunity is not known?

- However:
  - Only limited ‘in-vitro’ and animal testing has been performed.

Could Ebola Reston be utilized as an Ebola Vaccine?

- As a ‘desperation’ measure, yes:
  - But;
    - Vaccinating humans with a live Ebola virus is a bad idea!
    - The virus could mutate back to its pathogenic form;
      - Ebola Zaire,
    - It could combine with other single-stranded RNA viruses to mutate into a more virulent strain with respiratory spread encoding, (genetic shift),
    - NIH and WHO estimate that ~1% of a vaccinated population would die from unforeseen complications of live virus vaccination.

Prevention:

- Isolation of all symptomatic victims!
  - Droplet & fluid protection,
  - Absolute universal precautions with symptomatic infected victims,
  - Standard disinfectants;
    - are reported to kill Ebola on contaminated surfaces,
  - Avoid outbreak areas.

USAMRIID:

- Level IV biohazard required for handling Ebola

- Management of protective ‘gear’ is a critical part of prevention!

- All elements of donning, working with, and removal of protective gear:
  - Should be repetitively practiced,
  - Before utilizing this equipment in a live ‘hot zone’ situation!
Prevention:

• Contamination and infection during removal of protective equipment:
  • Now thought, by some, to be one of the chief pathways of infection among workers caring for Ebola victims.
  • Many are now recommending ‘eyes-on’ supervised and assisted removal of protective equipment:
    • After ‘hot zone’ exposure,
    • By ‘de-con-only’ personnel.
  • CDC has accepted this revision to its procedure recommendations as of 10-25-14.

Need for Prevention:

• Genetic Shift!
  • The more Ebola infection spreads (greater # of victims infected),
  • the more chance (Mathematical probability) of encountering another different single-stranded RNA viral disease in an infected host;
  • Influenza virus, coronavirus, etc.,
  • if that other viral disease is encoded for respiratory spread,
  • And – if a genetic shift event occurs,
  • (Reassortment = phenotypic change),
  • Then – Ebola can become an airborne infection!

Stop increasing case load:

Reassortment Event:

Chikungunya Virus Disease:

Chikungunya Fever (CHIKF):

• First recognized in Africa in 1950’s,

• Name means “to become contorted” or ‘that which bends up’ in Makonde or possibly Bantu dialects.
CHIKF - Transmission:

• Zoonotic,

• In Africa, virus is maintained and transmitted in a cycle between non-human primates, small mammals (bats & monkeys) and Aedes mosquitoes;
  – *Aedes aegypti* and *Aedes albopictus*,


CHIKF Virus Transmission:

• Human disease generally occurs via transmission from bite of a vector mosquito;
  – *Aedes aegypti* or *Aedes albopictus*,

http://www.cdc.gov/chikungunya/transmission/index.html

Re-emergence:

• In 2000 - 2005 CHIKF began re-emerging in epidemics beginning in Africa and around the Indian Ocean;
  – Found to be due to viral genome mutations that allow viral replication in *Aedes* (and possibly other) mosquito vectors,
    • Thus virus infection is transmitted and re-transmitted *directly* by mosquitos.


CHIK Virus Transmission:

• Direct person-to-person transmission
  • Is not thought to generally occur,

• Maternal-fetal transmission;
  • Has been reported,

• Transmission via infected blood;
  • Has been hypothesized?

http://www.cdc.gov/chikungunya/transmission/index.html

• Beginning in 2006-2007 cases and local transmission began to be seen in France and Italy.
• More recently disease has migrated to the Caribbean Islands
  – And then to continental US.
Vector Mosquitoes in US:

- Distribution of Aedes mosquitoes

US Cities with Worst Mosquito Infestations:

- 1. Atlanta
- 2. Chicago
- 3. Washington, DC
- 4. Detroit
- 5. Houston,
- 6. Raleigh-Durham, NC
- 7. Boston,
- 8. Dallas-Fort Worth,
- 9. Charlotte, NC
- 10. Nashville, TN
- 11. Memphis, TN
- 12. Grand Rapids, Michigan
- 13. Miami-Fort Lauderdale,
- 14. Richmond-Petersburg,
- 15. Minneapolis-St. Paul
- 16. New York
- 17. Cleveland-Akron
- 18. Greenville-Spartanburg, SC, & Ashville, NC
- 19. Albany, NY
- 20. Knoxville, TN

May 1st 2015:
- 1,414,451 total cases in the Americas
- Increase of 42,891 cases in last 2 weeks.

New Chikungunya Cases Reported:

- May 5th, 2015:

Epidemiology:

- Numbers of victims affected are difficult to quantify, as CHIKF is currently not a reportable disease:
  - Islands in which the disease has spread have documented up to 1/3 of inhabitants infected & symptomatic, during initial epidemics.

Asymptomatic Infection:

- Current evidence suggests somewhere between 10-20% of infected individuals do not develop symptoms;
  - However they still can transmit disease if bitten by and re-transmit virus to a mosquito during acute infection.
Incubation period is variable, generally ~ 2-12 days post infection;
- Majority of cases developing symptoms 1-3 days post infection.

Transmission:
- The incubation period allows for infected victims to travel to other countries before symptoms develop;
- Such as returning home from a trip or vacation.

CHIKF:
- Disease has many characteristics similar to Dengue Fever ('breakbone fever'), and is transmitted by the same vector (Aedes Mosquito),
- Many public health officials retrospectively now feel that many historic disease outbreaks attributed to Dengue may have been CHIKF;
  - Disease may be even more prevalent than previously thought.

Could it be possible for victim to be simultaneously infected by both Dengue and Chikungunya?
- Dengue is also a single-stranded RNA virus.
- Some believe that the wide variation in reported symptoms are caused by multiple infective agents, simultaneously transmitted by the same vector;
  - Aedes mosquitoes.

Signs & Symptoms:
- 2 phases of disease:
  - Acute illness phase,
  - Late phase,
Acute Illness Phase:
– Generally abrupt onset of initial symptoms;
  • High fever, polyarthralgia, (87-98%),
    – Fever & joint pain are the most commonly reported symptoms
  • backache, headache, fatigue
    – Most symptoms appear with 4-7 days,
  • Macular or maculopapular rash, (40-50%)
    – Extremities, trunk, face
  • Generalized pruritus (25%),
  • Nausea, vomiting, diarrhea, abdominal pain (15-47%).

Predominant Acute Symptoms:
• Fever - can be extremely high;
  – Up to 104°F Fahrenheit
• Pain - can be severe and prolonged;
  – (Chikungunya = “that which bends up”)

Late Phase:
• Late stage signs & symptoms;
  – A variable % of patients develop late-stage symptoms;
  • Arthralgias or musculoskeletal pains – most frequent long-lasting signs,
  • Other signs & symptoms include:
    • Fever, fatigue, headaches, neuropathic pain, cerebral disorders, sensorineural impairments, dysesthesia and/or paraesthesia, digestive disorders, cutaneous disorders, synovitis, tunnel syndromes, bursitis & joint inflammation, hemorrhage, pericarditis, myocarditis, pneumonias, Guillain-Barre,

Diagnosis:
• Common laboratory tests include:
  • Virus isolation;
    • Most accurate, but takes several weeks,
  • Molecular Testing:
    • RT-PCR:
      • Amplifies several Chikungunya-specific genes,
      • Takes one to two days.

Serological diagnosis:
• ELISA assay looking for CHIK-specific IgM levels,
  • Requires large amount of blood,
  • Posits in 3-5 days,
  • False positives can occur.

Differential Diagnosis:
• Other viral fevers
  • Dengue fever
  • West Nile fever
  • O’nyong-nyong fever
  • Ross River fever
  • Sindbis fever
  • Crimean Congo fever
  • Bubonic plague fever
  • Malaria fever
  • Ebola fever
• Hematological infections
  • Kaposi sarcoma infection
  • Lassa fever
  • Leishmaniasis
  • Chagas disease
  • Tuberculosis
  • HIV
  • Hepatitis B
  • Hepatitis C
  • Hepatitis D
  • Hepatitis E
  • Herpes simplex
• Parasitic infections
  • Malaria
• Bacterial infections
  • Leptospirosis

Clinical Management:

Acute Phase:

• There are currently no specific medications or interventions for acute CHIKF:

Acute Phase:

• Management is symptom-based, supportive interventions:
  • Fever control,
  • Maintain hydration,
  • Pain management,
  • Other supportive, symptom-specific management,

Ribavirin:
• May be helpful in those who have had more than 2 weeks of arthritis; symptoms
  • Case report data

Chloroquine:
• May be helpful for those with chronic arthritis?
  • Case report data

Steroids:
• Do not appear to be useful!

http://www.chikungunyavirusnet.com/treatment.html
http://en.wikipedia.org/wiki/Chikungunya

http://www.sciencedaily.com/releases/2011/03/110322115224.htm

Immunity?

• Circulating antibodies to CHIK virus are found in former victims of infection.

• It is thought that ‘natural’ exposure to the CHIK virus with antibody response;
  – Results in some degree of immunity from subsequent infections.

• But, this has not been well studied.

Chikungunya Vaccine Development:

• August 2014:  
  • NIH just completed a phase ‘0’ vaccine trial with 25 healthy adult volunteers;
  • Experimental vaccine candidate elicited neutralizing antibodies in all 25 subjects.

• March 2015:  
  • European vaccine phase 1 safety trial of 42 healthy volunteers completed;
  • Vaccine was reported to be well-tolerated and produced the desired immune response, even at the lowest dose.

• Vaccine produced as an R&D collaboration between Themis Bioscience GmBH and the Institut Pasteur (Paris).

Prevention:

• Avoid mosquito bites!

• Suppress mosquito infestation in ‘at-risk’ areas.

http://www.sciencedaily.com/releases/2014/08/140814192112.htm
http://www.cidrap.umn.edu/news-perspective/2015/03/chikungunya-vaccine-looks-promising-phase-1-trial
Prevention:

- Genetically engineered *Aedes aegypti* Mosquitoes:
  - British biotech company Oxitec:
  - Transmit a gene during reproduction that kills their offspring

- Goal is to stop spread of dengue fever & Chikungunya,
  - WHO estimates of 100 million dengue fever cases/year in 100 tropical & subtropical countries,
    - > 10 million children,
    - 25,000 Dengue-related deaths/year

- Mosquitoes already released in 4 countries:
  - Cayman Islands,
  - Malaysia,
  - Brazil,
  - Panama,

[Web links]
http://www.scientificamerican.com/article/genetically-engineered-mosquitoes/

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The End?

Or:

Have A Nice Day?

That's All Folks. That's all Folks!