Chikungunya

Aedes, joints

Epidemiology and natural history

- Aedes mosquito carrier, ssRNA virus
- First recorded outbreak *probably* in 1779
- Isolated in 1952 during epidemics in East Africa (Tanganyika)
- Endemic in tropical Africa and Asia, particularly in India, Southeast Asia, East Africa
- Re-emerged in 2005
- Introduced to Caribbean islands in 2013
- Introduced to U.S. (Florida) in 2014 by transmission through *Aedes* mosquito
- Epidemics are *sudden, explosive,* and *unpredictable*

Transmission

- Not just in travelers anymore
- *Aedes* mosquito (present in southeastern U.S.)
- Birds, cattle, monkeys, and other vertebrates as reservoirs
- Possible transmission during childbirth and theoretically during blood transfusions

Prevention

- No vaccine
- Permethrin-treated bite-proof long-sleeves and trousers + mosquito repellent

Clinical presentation

- Incubation 3-7 days
- ***Abrupt onset of erratic, incapacitating, relapsing arthralgia***
- Fever, headache, back pain, myalgia, symmetric arthralgia
- Possibly Guillain-Barre and CN palsies as a result (not unique to Chikungunya)
- Skin: pruritic + macular/maculopapular rash on throax with facial edema
- Acute Sx normally subside within a week

Diagnosis

- Clinical + **Epidemiology**
- Serology (see CDC guidelines)
  - Viral RNA can be isolated in serum within 8 days
    - Antibodies develop after 1 week
  - Red top tube
  - Viral isolation requires a level 3 biosafety lab
- Bloodwork
  - CBC (lymphopenia, thrombocytopenia)
  - Liver panel (elevated)
  - Cr (elevated)

Treatment

- Supportive
- No proven effect of antivirals
- NSAIDs may make arthralgia worse: controversial
  - Pain caused by virus itself, not inflammatory reaction

Clinical Course and Complications

- Usually resolves in 1 week
- Recurrent joint pains for >= 1 year

Case #1

- 45yo female presents to clinic 9 days after returning from a family visit in Hyderabad, India complaining of 3-day duration of feeling feverish with join pain.

Case #1

- HPIx:
  - Trip to India for 3 weeks
  - Feverish+fatigued+itching since 3 days ago
  - Hasn't been able to do much since
  - Bilateral knee pain started yesterday out of the blue and is unbearable; OTC analgesics don't help much

Case #1

- Physical Exam
  - Vitals: T 39.8, P 89 reg, RR 17 95% oRA, BP 142/85
  - CV N
  - Resp N
  - Abdo N
  - MSK: exquisite tenderness on bilateral knee ROM, unable to perform
  - Skin: macular rash over trunk

Case #1

- Try NSAIDs and Acetaminophen for Sx relief
- Otherwise rest and rehydration

Malaria

Anopheles, Plasmodium, relapsing fever

Malaria

- *Plasmodium falciparum, vivax, ovale, malariae* → infect erythrocyte → relapsing and recurring fever and chills
- Named based on the belief that the bad air from Rome peripheral marshes were causing the fever

Epidemiology

- *P. falciparum* most common and deadly in Africa
- High prevalence in sub-Saharan Africa
- Kills 660,000/year, mostly children
- Endemic in most tropics: if it has nice forests, there's probably malaria there!
- Greatest transmission, morbidity, mortality in Africa where *P. falciparum* is most common
- Elsewhere, *P. vivax* is most common

Epidemiology

- Can occur in returning travelers up to months after return and in any age
- **Most common** cause of febrile illness in returning travelers from tropics

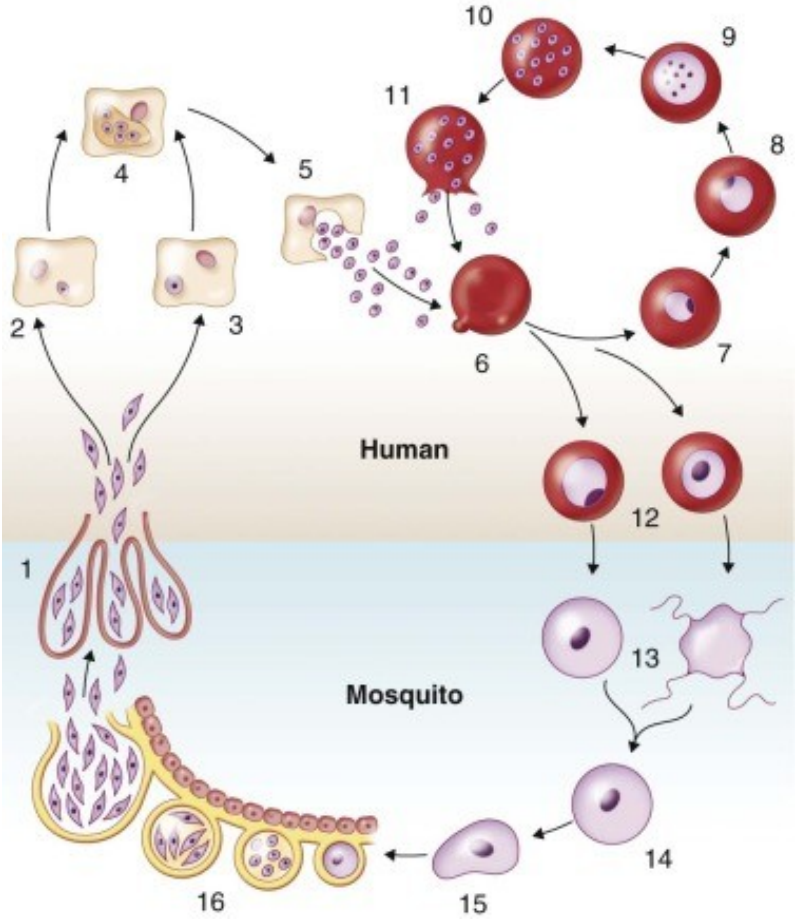
Transmission

- *Anopheles* mosquito in endemic areas
- Bite at night

Pathophysiology

- Anopheles feeding → inject sporozoite → infect hepatocyte → release merozoite → infect erythrocytes → develop and re-release in cycles (24-72h)
- Therefore:
  - Relapsing fever every 24-72h
  - Possibility of chronic liver infection

Pathophysiology - Life cycle



Pathophysiology tidbits

- *P. falciparum* can mediate cytoadherence where erythrocytes bind to ligands on endothelial cells, thus not passing through spleen
- Other species of Plasmodium don't mediate cytoadherence, infect fewer erythrocytes, and cause less severe disease

Death

- Common cause of death = severe anemia

Clinical presentation

- Uncomplicated Malaria
- Severe *P. falciparum* malaria
- Complicated non-*P. falciparum* malaria

Clinical Presentation

- **Fever**, no fever, **fever**, no fever, **fever**...no fever
- Hx suggestive of lack of protective caution and travel to endemic areas
- Incubation time varies (most commonly within 1-2 months in non-immune)

Diagnosis

- Hx
- Thick blood smear
  - Microscopic visualization of parasites with Giesma stain in lysed erythrocytes
- Antigen detection
  - Histidine-rich protein-2 only expressed by *P. falciparum*
  - Plasmodial LDH and aldolase produced by all human malarial species
- PCR

Treatment

- Artemether–lumefantrine combo as first line in many countries, effective for both *P. falciparum* and non-*P. falciparum*
- Chloroquine for non-*P. falciparum* Central America and Caribbean (low resistance)
- Ultimately, referral to Infectious diseases is the best course of action

Clinical Course and Complications

- Uneventful recovery with appropriate treatment
- Mortality 0.1% in uncomplicated malaria
- Worst outcomes due to delay in recognition and initiation of appropriate therapy

Prevention

- Insecticide repellent
- Sleeping in screened rooms or insecticide-impregnated bed nets
- Prophylactic drug therapy
  - Chloroquine in Central America and Caribbean
  - Daily Malarone, weekly mefloquine, or daily doxycycline
- **NO** preventive mechanism is fully protective
- **Keep** it in your differential

Case #2

- 45yo male presents to clinic with 2 week hx of recurrent fevers.
- Just returned from a trip from Republic of Congo 2 months ago
- Otherwise has been fine since arrival
- Does not remember mosquito bites
- Used mosquito protection measurements

Case #2

- Feels feverish abou every other day
- Says he’s never been good with pills

Case #2

- Most likely diagnosis: Malaria

Case #2

- Specific work-up
  - Thick blood smear
  - Malaria antigen detection
    - Histidine-rich protein-2
    - Plasmodium aldolase and LDH
- Refer to Infectious Diseases

Zika

Aedes, Viral, Pregnancy

Epidemiology

- Flavivirus discovered in 1947 in Uganda near Zika forest, described in 1952
- Transmitted by *Aedes aegypti* and *A. albopictus* mosquito species
  - As you've noticed, ***Aedes*** is probably always the correct answer
- Introduced to Brazil possibly by Tahiti soccer team during 2014 Confederation Cup (based on isolated strains)

Transmission

- Vertical
  - Mother to fetus
  - Detected in breast milk, but no reports of transmission
- Horizontal
  - Sexual
  - Blood transfusions

Clinical presentation

- Incubation 3-12 days
- Maculopapular pruritic rash
- Low grade fever
- Arthritis/arthralgia
- Conjunctivitis
- Myalgia
- Headache

Clinical presentation

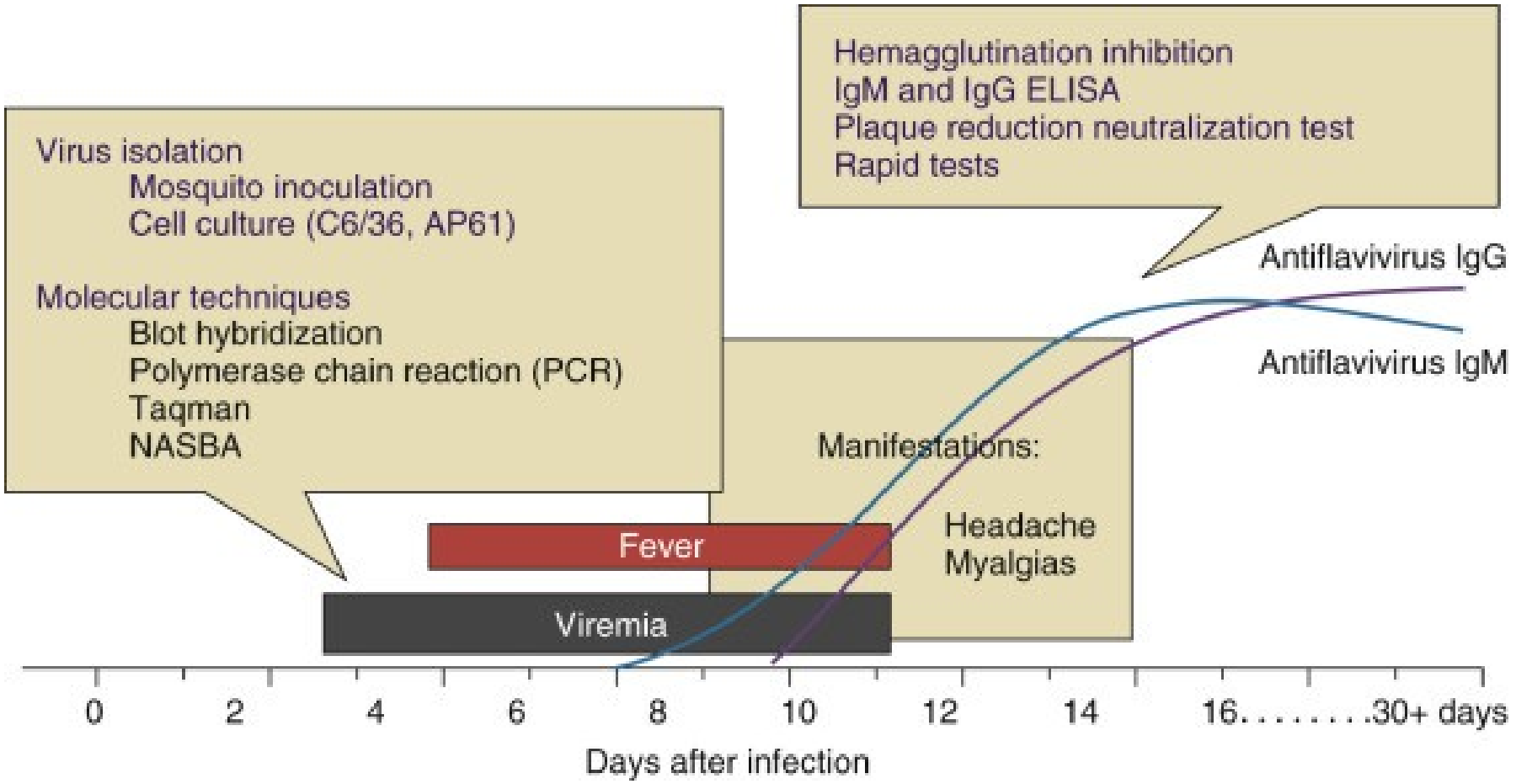
- Sounds familiar?
- Typically looks like another self-limited viral illness

Diagnosis

- By paired urine and serum RNA (first analyte), NAT (6wks), IgM (up to 12wks) testing
- Endemic? Clinical diagnosis
- Otherwise, follow the most current CDC* guidelines for testing (is updated frequently)
  - Anyone with possible Zika virus **exposure** who has or recently experienced **symptoms** of Zika
  - **Symptomatic pregnant** women with possible Zika virus exposure
  - **Asymptomatic pregnant** women with ongoing possible Zika virus **exposure**
  - **Pregnant** women with possible Zika virus **exposure** who have a fetus with prenatal **ultrasound** findings consistent with **congenital Zika virus infection**
  - **May** be considered for **asymptomatic pregnant** women with possible **exposure** but not ongoing (**travelers**)

* https://www.cdc.gov/zika/hc-providers/testing-guidance.html

Diagnosis


Hemagglutination inhibition
IgM and IgG ELISA
Plaque reduction neutralization test
Rapid tests
Virus isolation
Mosquito inoculation
Cell culture (C6/36, AP61)
Molecular techniques
Blot hybridization
Polymerase chain reaction (PCR)
Taqman
NASBA
Antiflavivirus IgG
Antiflavivirus IgM
Manifestations:
Headache
Myalgias
Fever
Viremia
0
2
4
6
8
10
12
14
16. . . . . .30+ days
Days after infection

Treatment

- No vaccine
- No treatment

Clinical Course and Complications

- ITP (rare)
- Microcephaly in infant (vertical transmission)
- Guillain-Barre syndrome

Prevention

- Mosquito repellent, bed nets, etc.

Flash cases

- 26yo female went on a trip with partner, thinks she caught the flu. Urine bHCG negative. Screen?

Flash cases

- 26yo female went on a trip with partner, thinks she caught the flu. Urine bHCG negative. Using contraception. Screen?
- No – not pregnant

Flash cases

- 40yo male went to South Sudan for a 2 week trip. Feels ill, flu-like. Screen?

Flash cases

- 40yo male went to South Sudan for a 2 week trip. Feels ill, flu-like. Screen?
- No - male

Flash cases

- 50yo male with flu-like illness and fever and joint pain. Just returned from Cambodia. What should be on your mind as a possible diagnosis?

Flash cases

- 50yo male with flu-like illness and fever and joint pain. Just returned from Cambodia. What should be on your mind as a possible diagnosis?
- Chikungunya – tropical south east Asia + joint pain