Mosquito-Borne Uveitis

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Mosquito Proboscis

Global Distribution of Aedes aegypti

Global Distribution of Aedes albopictus
Global Distribution of Aedes albopictus

Global Distribution of Aedes aegypti

Tropics: 36% of the Earth’s Landmass
One-Third of the Earth’s Population

http://education.nationalgeographic.org/encyclopedia/tropics/

Global Air Travel

Aegypti, Aegypti Albopictus, and Albopictus Occurrences
Heavily Interconnected

Malaria – 450,000 Deaths/year
- Measles
- Mumps
- Rubella
- Filariasis
- Pork tapeworm
- Hepatitis C

The Flaviviridae Family
- Enveloped viruses
- Icosahedral structures
- A positive sense, single-strand RNA genome (~12kb)
- Transcribed as a single polyprotein
- More than 100 different members
- Subdivided into:
  - Flavivirus (including Yellow fever, Japanese Encephalitis, West Nile, dengue, and Zika viruses)
  - Pestivirus
  - Hepacivirus (hepatitis C viruses)

http://www.utmb.edu/discoveringdenguedrugs-together/Diseases/Flaviviridae%20Family.asp
West Nile Virus

- Flavivirus genus
- Flaviviridae family
- Positive-sense, single stranded RNA virus
- ~ 12Kb.
Global Distribution of West Nile Virus

Courtesy Mr. Nicholas Jones, Uveitis, 2nd Edition, 2013

West Nile Virus – USA, 1999-2012
CDC ArboNET

Figure 2. Average annual incidence of West Nile Virus neuroinvasive disease, 1999-2012.
Cases of WNV Reported to the CDC by Year

<table>
<thead>
<tr>
<th>Year</th>
<th>Cases</th>
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<tbody>
<tr>
<td>2015</td>
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<td>2013</td>
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<td>2002</td>
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<td>2001</td>
<td>21</td>
</tr>
<tr>
<td>2000</td>
<td>66</td>
</tr>
<tr>
<td>1999</td>
<td>62</td>
</tr>
</tbody>
</table>

< 1 / 100,000 / year

Index Cases, NYC

Average Annual Incidence of WNV Human Neuroinvasive Disease by Decile, 1999 – 2012, USA CDC ArboNET

More Common in Elderly

Number of Cases of WNV Human Neuroinvasive Disease by week, 1999 – 2012, USA CDC ArboNET

More Common in Summer / Fall

2015 To Date
Cases reported to CDC ArboNET

Human - 1566

Mosquito

http://diseasemaps.usgs.gov/mapviewer/

West Nile Virus

CDC - Centers for Disease Control and Prevention

CDC ArboNET

West Nile Virus in the United States — A Historical Perspective and 5 Testing
**Systemic Disease**

- 2 – 14 day incubation
- 80% asymptomatic
- 15% symptomatic, WN Fever – self limited, ~ 1 week
  - Fever
  - Headache
  - Myalgia
  - Arthralgia
  - Malaise
  - Nausea
  - Vomiting
  - Skin Rash
  - Pharyngitis
- 5% WN Encephalitis – Severe headache, meningismus, confusion, stupor/coma, tremors, convulsions, paralysis, death – typically older or debilitated (diabetes).

**Ocular Disease**

- AC inflammation
- Vitreous inflammation
- Retinal vasculitis
- Retinitis
- Chorioiditis (ICGA)
- Multifocal chorioretinitis curvilinear pattern

*Early Lesions*

*Deep, Yellow-White*

*Multifocal Chorioretinitis*

*Often Curvilinear Pattern*

*Courtesy Prof. Moncef Khairallah*
Chorioretinal Lesions in Nonfatal Cases of West Nile Virus Infection

Ophthalmol 2003; 110:1732-1736

West Nile Virus Chorioretinitis

Ocular Manifestations of West Nile Virus Infection

International Journal of Medical Sciences

West Nile Virus Chorioretinitis

http://www.westcoastretina.com/WestCoastRetina/Feb-2014.html

Courtesy West Coast Retina

Courtesy K. Bailey Freund
Multifocal Chorioretinitis
Often Curvilinear Pattern
More on ICGA

West Nile Virus Lesions
Nerve Fiber Layer Distribution?

Spurious . . .?

Multifocal Chorioretinitis
Often Curvilinear Pattern

Courtesy Prof. Moncef Khairallah
Systemic and Intraocular Manifestations of West Nile Virus Infection
Seema Garg, MD, PhD, and Lee M. Jampol, MD

IV. Ophthalmic manifestations of WNV infection
A. Chorioretinitis
   1. Case 1
   2. Case 2
   3. Case 3
   4. Case 4
   5. Case 5 and 6
   6. Case 7
   7. Case 8
   8. Uveitis without chorioretinitis
      1. Case 9
   C. Ocular retinal vasculitis
      1. Case 10
      2. Case 11
   D. Congenital choriotinal scarring
      1. Case 12
   E. Optic neuritis
      1. Case 13
      2. Case 14

Neuroretinitis – Retinitis Vascular Occlusion

Ischemic and Hemorrhagic Retinal Vasculitis Associated with West Nile Virus Infection
Seema Garg, MD, PhD,a Lee M. Jampol, MD,a John F. Wilson, MD,b Ivan R. Batlle, MD,b Helmut Buetter, MD
Dengue Virus

- Flavivirus genus
- Flaviviridae family
- Positive-sense, single stranded RNA virus
- ~ 11Kb.

Global Distribution of Dengue Virus

50-100M New Cases per Year

Courtesy Mr. Nicholas Jones, Uveitis, 2nd Edition, 2013
**Systemic Disease**

- 2 – 14 day incubation
- Asymptomatic
- Non-specific febrile illness
- Classic Dengue fever
  - High Fever
  - Severe Headache
  - Myalgia
  - Arthralgia
  - Malaise
  - Nausea
  - Vomiting
  - Maculopapular Skin Rash
- 10% - Dengue Hemorrhagic Fever Shock Syndrome

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**Cases of Dengue Reported to the CDC by Year**

- **2015 YTD**
  - < 1/100,000/year
  - Mostly Florida and Texas

- **2014**
  - Imported: 642
  - Locally Acquired: 33

- **2013**
  - Imported: 772
  - Locally Acquired: 554

- **2012**
  - Imported: 654
  - Locally Acquired: 554

- **2011**
  - Imported: 243
  - Locally Acquired: 1552

- **2010**
  - Imported: 642
  - Locally Acquired: 10,969

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**2015 To Date**

Cases reported to CDC ArboNET

- **Locally Acquired**
  - 33 Cases

- **Imported**
  - 364
Ocular Disease

75% Bilateral
May be Serotype Specific

- Subconjunctival hemorrhage
- AC inflammation
- Vitreous inflammation
- Retinal hemorrhage
- Retinal vasculitis
- Retinal vascular occlusion
- Retinitis
- Deep retinal spots / foveolitis
- RPE mottling
- Serous retinal detachment
- Choroiditis (ICGA)

Prevalence of Dengue Maculopathy in Patients Hospitalized for Dengue Fever

Dengue Virus
Subconjunctival Hemorrhage
Platelet Counts < 50,000/ul

Hemorrhage
Yellow-White Lesions

Dengue-Associated Maculopathy

Eye Bank of the Netherlands

Ophthalmology 2007;114;1743-1747

Dengue Virus
Active Lesions

 Courtesy Dr. Stephen Teoh

Dengue Virus
Active Lesions

 FA

 Courtesy Dr. Stephen Teoh

Dengue Virus
Active Lesions

 ICGA

 Courtesy Dr. Stephen Teoh

Dengue Virus
Active Lesions

 Courtesy Dr. Stephen Teoh
Dengue Virus Infection

**Active Lesions**

"Foveolitis" Courtesy Dr. Stephen Teoh

**Inactive Lesions**

Courtesy Dr. Padmamalini Mahendradas

**Dengue retinochoroiditis**

Khalid Tabbara

*From the Department of Ophthalmology, The Eye Center and The Eye Institute in Research in Ophthalmology, Riyadh, Saudi Arabia.*


**Active Lesions**

Courtesy Prof. Khalid Tabbara

**Inactive Lesions**

Courtesy Prof. Khalid Tabbara
Dengue Virus
Active Lesions

Dengue Virus
+ 9 Months, Inactive

Dengue Virus
Active Lesions – Retinitis / Intraretinal Hemorrhage

Dengue Virus
Active Lesions – Retinitis / Intraretinal Hemorrhage

Courtesy Dr. Srinivasan Sanjay

Courtesy Dr. Srinivasan Sanjay

Courtesy Prof. Chee Soon Phaik

Courtesy Prof. Chee Soon Phaik
Dengue Virus
Active Lesions – Vasculitis

Dengue Virus
Active Lesions – Vasculitis

Dengue Virus
Active Lesions – Foveolitis

Chikungunya

- Alphavirus genus
- Togaviridae family.
- Positive-sense, single stranded RNA virus
- ~ 12Kb.
Described in 1953, East Africa
Tanzania Mozambique

In “Makonde,” Chikungunya means “to walk bent over.”
A reference to the stooped posture of many sufferers.

Global Distribution of Chikungunya

2015 To Date
Locally Acquired
152
Imported
538

http://diseasemaps.usgs.gov/mapviewer/
Chikungunya

Courtesy Mr. Nicholas Jones, Uveitis, 2nd Edition, 2013
**Systemic Disease**

- 2 – 14 day incubation
- Acute
  - Fever
  - Headache
  - Low back pain
  - Severe joint pain
  - Myalgia
  - Malaise
  - Nausea
  - Vomiting
- Severe – multi-organ failure, CNS involvement, death

**Ocular Disease**

- AC inflammation +/- high IOP
- Vitreous inflammation
- Retinal hemorrhage
- Retinal vasculitis
- Retinal vascular occlusion
- Retinitis
- Neuroretinitis
- Serous retinal detachment
- Choroiditis (ICGA)

*In “Makonde,” Chikungunya means “to walk bent over.”*

*Courtesy Dr. Padmamalini Mahendradas*
Ocular Involvement Associated With an Epidemic Outbreak of Chikungunya Virus Infection

PRAJNA LALITHA, SIVAKUMAR RATHNAM, KRISHNADAS BANSHIRE, SHANMUGAM MAHESHKUMAR, RAJENDRAKISHOR VIJAYAKUMAR, AND PADMAKAR SATHE

Common
- AC / Vitreous cell
- Neuritis
- Retinitis +/- SRD

<table>
<thead>
<tr>
<th>Site of Involvement</th>
<th>No.</th>
<th>%</th>
</tr>
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<tbody>
<tr>
<td>Nongranulomatous anterior uveitis</td>
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<td>27.03</td>
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<tr>
<td>Panuveitis</td>
<td>6</td>
<td>16.21</td>
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<tr>
<td>Granulomatous anterior uveitis</td>
<td>1</td>
<td>2.70</td>
</tr>
<tr>
<td>Optic neuritis</td>
<td>4</td>
<td>10.81</td>
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<tr>
<td>Lagophthalmos and VIIth nerve palsy</td>
<td>3</td>
<td>8.11</td>
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<tr>
<td>Retinal vasculitis</td>
<td>3</td>
<td>8.11</td>
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<tr>
<td>Retinal soft exudates</td>
<td>2</td>
<td>5.41</td>
</tr>
<tr>
<td>Binocular retinoschisis</td>
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<td>2.70</td>
</tr>
<tr>
<td>Rubeotic</td>
<td>1</td>
<td>2.70</td>
</tr>
<tr>
<td>CMO</td>
<td>1</td>
<td>2.70</td>
</tr>
<tr>
<td>Multifocal choroiditis with CME</td>
<td>2</td>
<td>5.41</td>
</tr>
<tr>
<td>Exudative retinal detachment</td>
<td>2</td>
<td>5.41</td>
</tr>
<tr>
<td>Total</td>
<td>37</td>
<td>100</td>
</tr>
</tbody>
</table>

CMO = central macular edema, CMO = central retinal artery occlusion.

Chikungunya Fever

20/30 20/30
+ Two Months
Oral CST, Topical CST, Topical Cyloplegic / Mydriatic

20/20 20/20

Chikungunya Fever

20/30 20/50
20/20 20/20

Courtesy Prof. Richard Rosen
Chikungunya Fever

Presentation

20/20
20/20

4 WEEKS

20/40
20/30

16 WEEKS

20/40
20/40

Courtesy Dr. Annie Mathai and Dr. Nidhi Relhan

Ocular Manifestations Associated with Chikungunya

Am J Ophthalmol 2007; 144:552-556

Vision at Last Visit Variable
**Zika Virus**

- Flavivirus genus
- Flaviviridae family
- Positive-sense, single stranded RNA virus
- ~ 12Kb.
How Zika Spread – 70-year Migration

Africa       Southeast Asia       Pacific Islands       Americas


Systemic Disease

• 1 in 5 symptomatic
• 2 to 10 day incubation
• Non-specific febrile illness
• Fever
• Arthralgias
• Maculopapular Skin Rash

Maculopapular Rash


**Testing**

- Serum PCR within 7 days
- Thereafter serum PRNT (Plaque Reduction Neutralization Technique) assay.
- Antibody crossreactivity with Dengue, WNV, etc


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**Risk of Local Zika Transmission:**
- Year Round
- Seasonal


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**US – Brazil Travel Routes**


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**Zika Risk**

Zika Risk

Maculopapular Rash

Conjunctivitis

Child with Microcephaly, Recife, Brazil
Zika virus in Brazil and macular atrophy in a child with microcephaly

"Severe Macular Neuroretinal Atrophy"

10 Microcephalic Infants

- 65% RPE Alterations
- 25% Optic Disc Hypoplasia
- 15% RPE Atrophy
- 15% Optic Disc Pallor
- 40% Exophoria
- 20% Esophoria
- 10% Horizontal Nystagmus
RPE Alterations

Atrophic Lesions

Courtesy Dr. Camila Ventura of the Altino Ventura Foundation in Recife,

Optic Disc Hypoplasia - Signs
1) Small disc
   (Disc-foveal distance > 3 DD)
2) "Double-ring sign"
3) +/- Vascular tortuosity

http://www.nature.com/eye/journal/v19/n5/images/6701857f15.jpg

Increased Frequency
- First Trimester Exposure
- Smaller Cephalic Perimeter

40 Infants with Microcephaly
Zika + Mothers (64% symptomatic)
37 eyes (46%) of 22 patients (55%) with findings

- RPE Mottling (28%)
- Optic Disc Hypoplasia (18%)
- Increased cip/Disc (11%)
- RPE Atrophy (8%)
- Optic Disc Pallor (8%)

Expanded Spectrum of Congenital Ocular Findings in Microcephaly with Presumed Zika Infection

Ophthalmology 2016;123:1788-1794
Zika virus-related hypertensive iridocyclitis

Bruno M. Fontes

Iridociclite hipertensiva associada à infecção por Zika virus

39-year-old Male Physician
- Known Zika Infection
- Blurred vision one week later
- 20/40 OU
- IOP 40 mmHg OD; 28 mmHg OS
- 1+ AC reaction OU
- Cleared with topical CST and cycloplegic/mydriatic

40s-year-old man
- Rash and Conjunctivitis x 2 days
- Serum PCR, IgM, PRNT +; AC PCR + Zika
- 20/20 OD; 20/40 OS
- IOP normal
- Tr + AC reaction OD; 2+ OS
- Cleared with topical CST and cycloplegic/mydriatic

Serologically Confirmed Zika-Related Unilateral Acute Maculopathy in an Adult

64-year-old man
- Erythematous rash / arthritis for 10 days after mission work in Haiti

February, 2016

20/20

Courtesy Dr. Will Parke
February, 2016
3/200 for 3 days
IOP Normal

“Ring of Gray Perifoveal Coloration in Roughly a ‘Bull’s-Eye’ shape”

Courtesy Dr. Will Parke

February, 2016
3/200 for 3 days

RPE Alterations

Courtesy Dr. Will Parke

00:28.36

02:33.14

02:33.14

00:28.36

Courtesy Dr. Will Parke

Courtesy Dr. Will Parke
Unilateral Acute Idiopathic Maculopathy (+Coxsackie)

- Conjunctivitis
- AC inflammation (+/- hypertensive)
- RPE Alterations / Atrophy
- Optic Disc Hypoplasia (Neonates)
- UAIM-like outer retinal inflammation

Ocular Disease

- Adult Conjunctivitis
- Anterior Uveitis
- UAIM
Zika Ophthalmic Images Courtesy of

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