

# Sexually Transmitted Zika Virus Infection

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# What is Zika Virus?

Single-stranded,  
enveloped RNA virus

Member of the *Flaviviridae*  
family

- Yellow fever
- West Nile
- Dengue
- St. Louis encephalitis



# Incubation Period and Symptoms

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- Incubation period of 3–14 days
- Most infections (~80%) are asymptomatic
- Most common symptoms
  - Fever
  - Rash – very common, often but not always itchy
  - Joint pain
  - Conjunctivitis (red eyes)
- Other symptoms include muscle pain and headache



*Photo by Nacho Doce/REUTERS. From:  
<http://www.pbs.org/newshour/updates/how-many-zika-infected-infants-will-develop-microcephaly-and-other-faqs/>*



# How Zika is transmitted?



**Most people get Zika from a mosquito bite**



More members in the community become infected



A mosquito bites a person infected with Zika virus



The mosquito becomes infected



A mosquito will often live in a single house during its lifetime



More mosquitoes get infected and spread the virus



**Other, less common ways, people get Zika:**



**During pregnancy**

A pregnant woman can pass Zika virus to her fetus during pregnancy. Zika causes microcephaly, a severe birth defect that is a sign of incomplete brain development



**Through sex**

Zika virus can be passed through sex from a person who has Zika to his or her sex partners



**Through blood transfusion**

There is a strong possibility that Zika virus can be spread through blood transfusions

# Zika virus disease — United States, 2016

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- US States & DC

Total: 5,102

- Locally acquired mosquito-borne cases reported: 224
- Travel-associated cases reported: 4,830
- Laboratory acquired cases reported: 1
- Sexually transmitted: 46



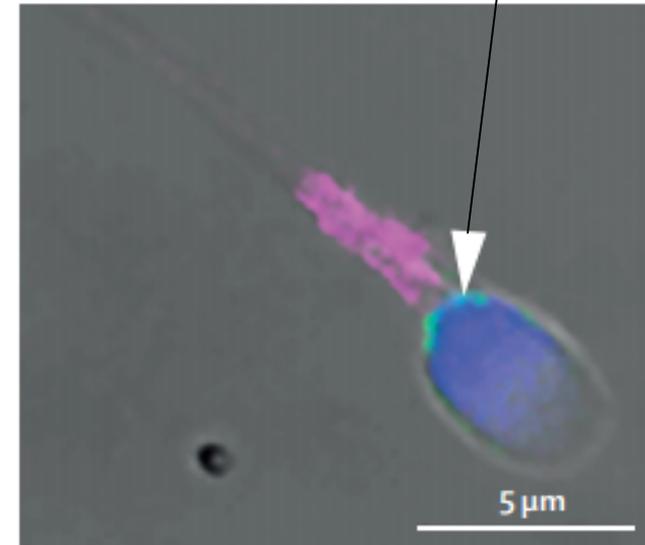
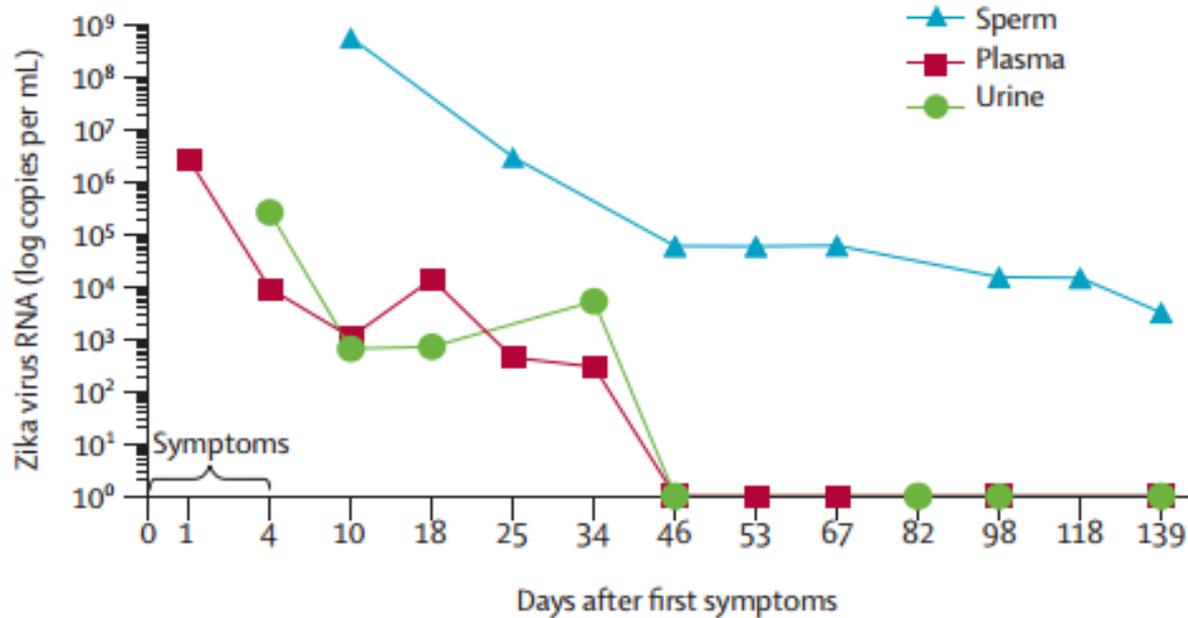
# Zika virus in semen and spermatozoa

- 32 y/o health man returning from French Guyana
- Sx: Moderate fever, maculopapular rash, myalgia, arthralgia
- Dx: positive Zika RNA in plasma and urine at 2d after sx onset
- Dengue and CHIK PCR negative
- Semen (11), blood (10), and urine (5) samples collected for 141 days after sx onset
- All semen samples positive
  - Viral load 8.6 log copies/mL → 3.5 log copies/mL
- Blood and urine samples positive to day 37
- Additional 2 of 5 patients positive in semen on Days 69, 115



# Zika virus infects spermatozoa

Zika virus



Mansuy JM, et. al. Zika virus in semen and spermatozoa. Lancet Infect Dis, 2016. 16(10): p.1107.



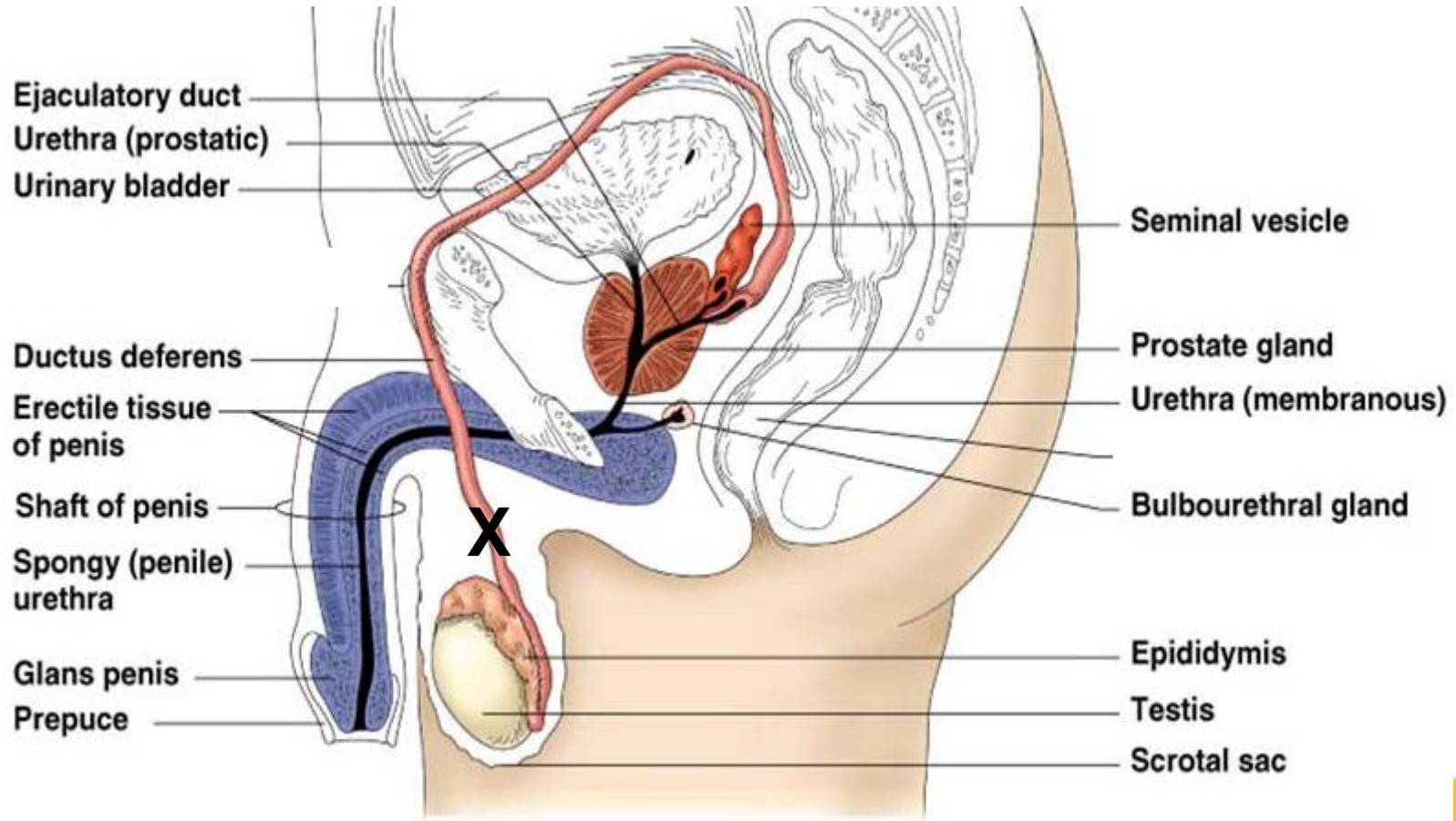
# Sexual transmission of Zika virus from a vasectomized man

- Couple traveled to Maldives in early 2016
- Man's sx: fever, rash, headache, weakness, myalgias
  - Onset 17 days after travel started & 4 days after return
- Unprotected sexual intercourse 11 days after return
- Woman's sx: fever, itchy rash, conjunctivitis, weakness, arthritis in ankles/wrists/knees
  - Onset 31 days after travel started, 18 days after return, 8 days after unprotected sexual intercourse
- Man's semen positive by PCR for Zika RNA on day of illness #47, 69, and 96.
  - Zika RNA from Day 69 semen able to infect cell culture

Arsuaga, M., et al., *Probable sexual transmission of Zika virus from a vasectomised man*. Lancet Infect Dis, 2016. 16(10): p. 1107.

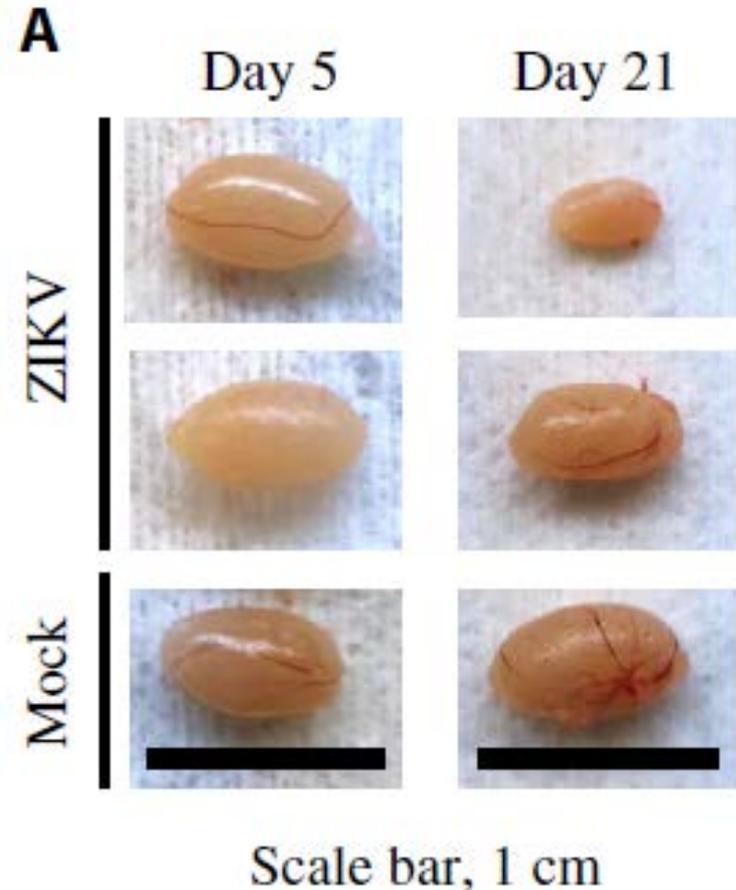


# Possible sources of Zika virus in male genitourinary tract



# Can Zika virus cause testicular atrophy?

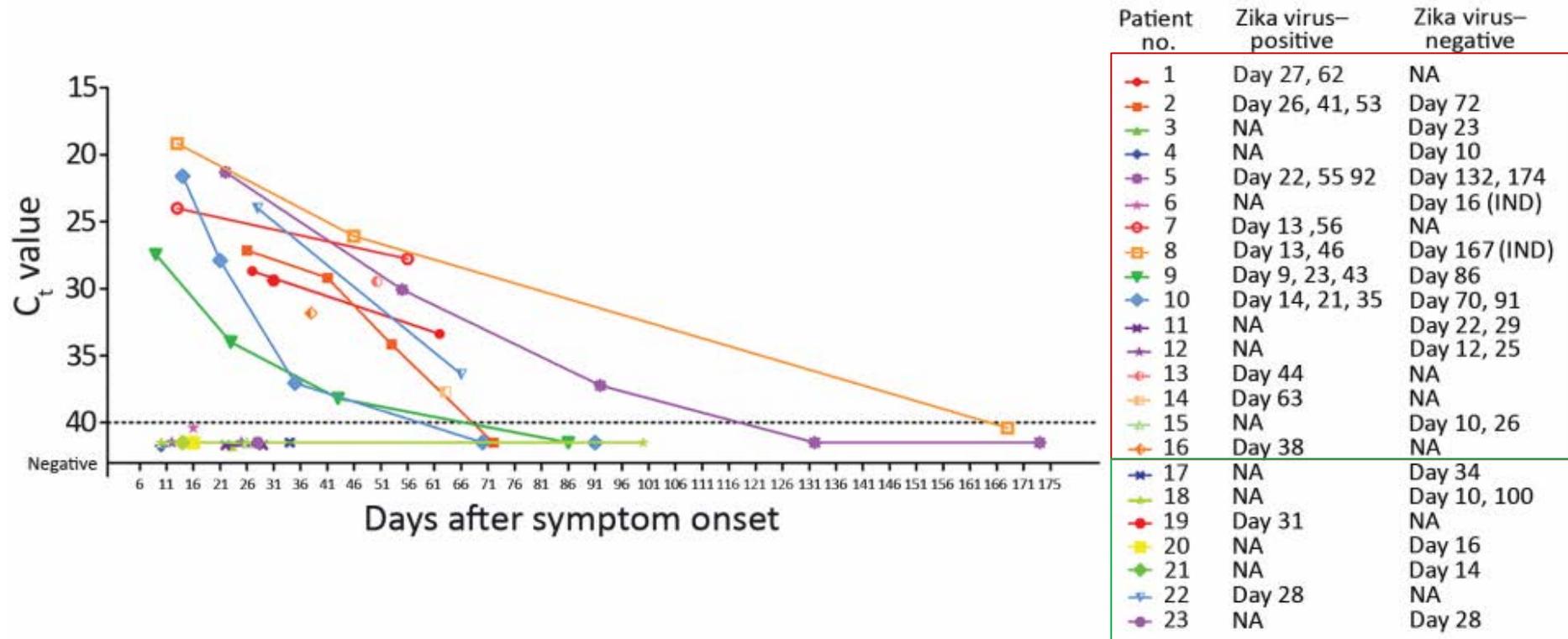
- Mouse study showed viral RNA in testicular Leydig cells
  - Generate testosterone
  - Support sperm production
- Reduced testosterone levels, even at 21d post-infection
- Testicular atrophy



Uraki R, et. al. Zika virus causes testicular atrophy. *Sci Adv*, 2017. 3(2): p. e1602899.



# Presence and persistence of Zika virus RNA in semen of men with Zika virus infection — United Kingdom, 2016



Atkinson B, et. Al. Presence and persistence of Zika virus RNA in semen, United Kingdom, 2016. Emerg Infect Dis, 2017. 23(4): 611–615.



# Important conclusions from UK Semen Study

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- Zika virus can persist in semen for several weeks to months after recovery from symptomatic infection
- Zika virus RNA persistence in semen is not consistent
  - 43.5% lacked detectable RNA on 1<sup>st</sup> sample (all but 1 tested within 28 days of symptom onset)
- No obvious differences in terms of age, travel hx, symptoms



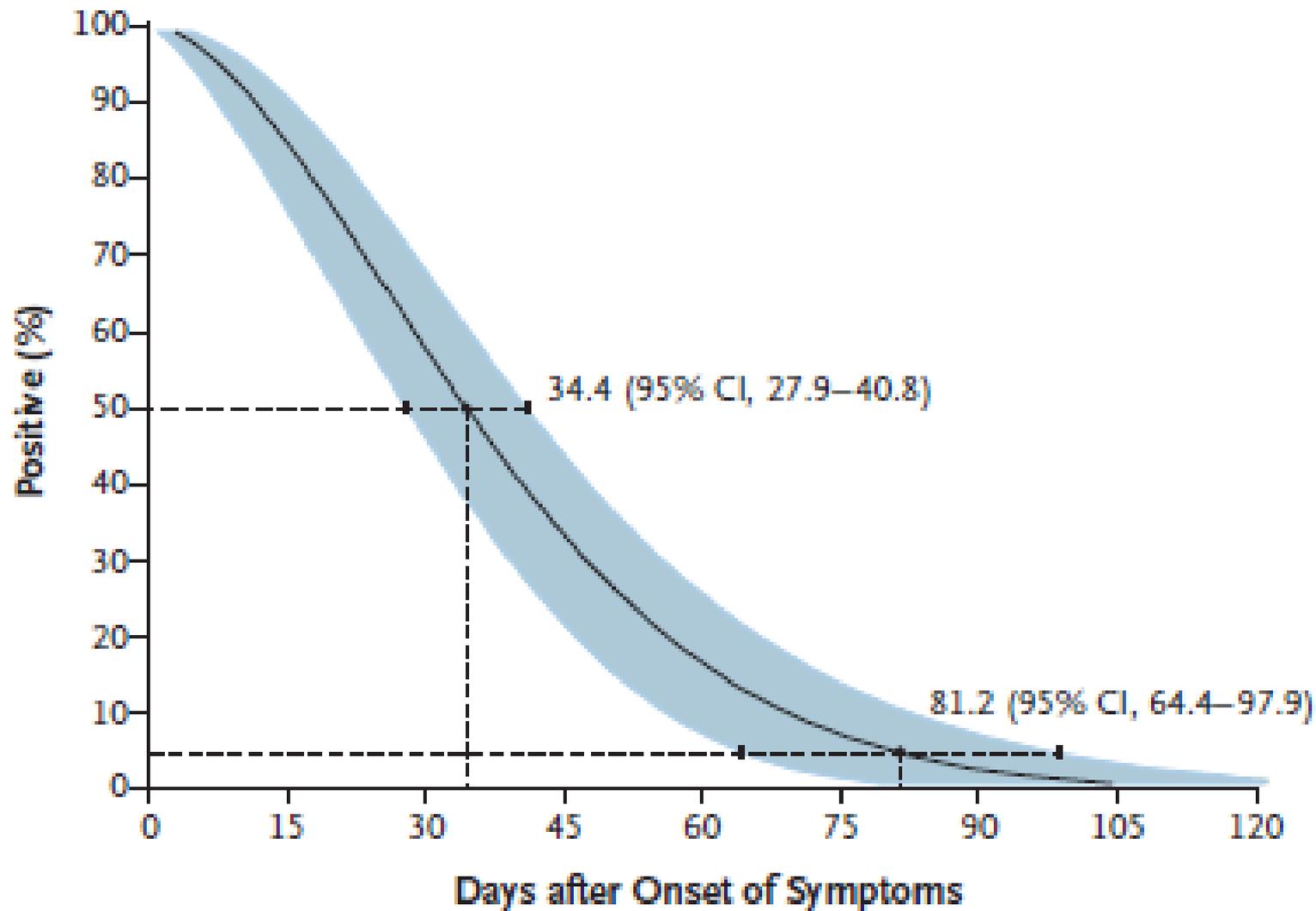
# Persistence of Zika virus in body fluids — preliminary report

- 150 participants prospectively assessed (55 men) in PR
- All PCR-positive in urine or blood
- Serum, urine, saliva, semen, vaginal secretions collected weekly x 1 month, then at 2, 4, 6 months
  - Tested by PCR
  - Serum tested for ZIKV IgM by ELISA
- ZIKV RNA present in at least 1 semen specimen in 31 (56%) of participants

Paz-Bailey, G., et al., *Persistence of Zika Virus in Body Fluids - Preliminary Report*. N Engl J Med, 2017.



# Time to loss of ZIKV RNA in semen



# Suspected Female-to-male transmission

- Woman in 20s returned to NYC from travel to endemic Zika area → abdominal cramping and HA while awaiting flight
- Condomless vaginal sex w/ male partner after arriving NYC same day
- Next day: fever, fatigue, rash, myalgia, arthralgia, back pain, swelling of extremities, numbness/tingling hands & feet
  - Also began menses – “heavier than usual”
- 2 days later: blood and urine collected; Zika PCR+; Zika IgM-
- Male partner: 7d after sex → fever, rash, arthralgia, conjunctivitis
- 3 days later: man’s urine Zika PCR+; serum PCR-; IgM-
- Man denied travel, mosquitoes, other sex



# What about the female urogenital tract?

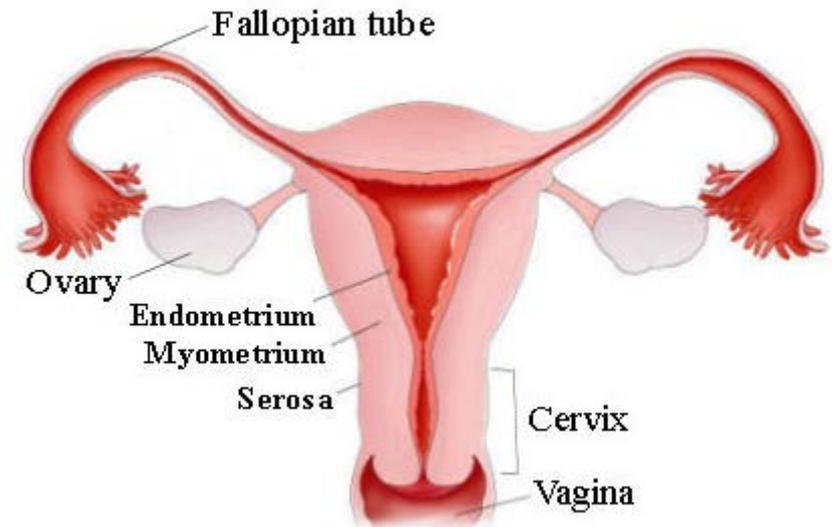
- French woman in 40s, HIV+ (controlled) w/ CD4 >500
- Travel to Martinique & Guadeloupe x 4 wks in summer 2016
- Day of return, sx onset: lethargy, myalgia → pruritic rash, abdominal pain, diarrhea, conjunctivitis, fever (38.1)
- Vaginal swabs collected
- Plasma, urine, & vaginal swabs + by PCR for ZIKV on Day 3
  - Virus from vaginal swabs able to infect cell culture
- Vaginal swab on day 10 negative by PCR
- Husband always asymptomatic (but 100% condom use)

Penot P, et. al. Infectious Zika virus in vaginal secretions from an HIV-infected woman, France, August 2016



# Infection of the female urogenital tract

- Detected in cervical mucus, endocervical swab, and genital swab 3 days after sx onset in symptomatic French woman<sup>1</sup>
- Endometrial cells likely ZIKV target, either via uterine vasculature (in viremic woman) or by sexual viral infection
  - Potential source of spreading virus to placenta during pregnancy<sup>2</sup>



<sup>1</sup>Prisant N, *et al.* Zika virus in the female genital tract. *Lancet Infect Dis.* 2016,16(9):1000–1.

<sup>2</sup>Pagani I, *et al.* Human endometrial stromal cells are highly permissive to productive infection by Zika virus. *Sci Rep*, 2017. 7:44286.



# Zika virus genital tract shedding in five women of childbearing age

## Results of RT-PCR for ZIKV by Time After Onset of Clinical Symptoms, days

	1–2	4–5	8–9	12–13	15–17	21–27
Blood	100% (3/3)	100% (2/2)	20% (1/5)	0% (0/2)	0% (0/4)	0% (0/5)
Urine	33% (1/3)	100% (2/2)	75% (3/4)	100% (1/1)	25% (1/4)	40% (2/5)
Vaginal Secretion	100% (1/1)	100% (2/2)	40% (2/5)	50% (1/2)	0% (0/4)	0% (0/5)
Cytobrush	100% (1/1)	100% (2/2)	25% (1/4)	50% (1/2)	0% (0/4)	0% (0/5)
Cervical mucus	0% (0/1)	100% (2/2)	75% (3/4)	100% (2/2)	0% (0/4)	0% (0/4)

# Zika transmission via anal sex

- Male w/ travel to Venezuela x 1 week in January 2016
- 2 days after return: fever, pruritic rash, conjunctivitis x 3d
- Condomless insertive anal sex with male partner 1d before and 1d after symptom onset
- Day 7: partner w/ fever, myalgia, HA, lethargy, malaise
  - Few days later: pruritic rash, conjunctivitis, & arthritis
- Both negative by PCR on serum, urine, and saliva
- Both Zika IgM positive with confirmatory PRNT
- Semen collected at Days 24 (Pt. 1) and 17 (Pt. 2) negative by PCR at CDC; Pt. 1's semen equivocal by PCR at DCHHS

Deckard DT, *et al.* Male-to-male sexual transmission of Zika virus — Texas, January 2016. *MMWR Morb Mortal Wkly Rep* 2016;65:372–374.



# High infection rates in macaques after intravaginal or intrarectal inoculation

- 2 species of macaques experimentally inoculated with Zika virus at a dose similar to what might be found in semen
- Virus introduced non-traumatically, under anesthesia, into either vagina or rectum
  - 50% vaginal introductions resulted in detectable RNA in bloodstream (most infectious)
  - 100% rectal introductions resulted in detectable RNA in bloodstream (most infectious)
- No macaques developed symptomatic infections
- Magnitude of viremia likely high enough to infect mosquitoes
- Sexual transmission could extend duration of epidemic

Haddow AD, *et al.* High infection rates for adult macaques after intravaginal or intrarectal inoculation with Zika virus. *Emerg Infect Dis.* 2017.



# Summary Zika virus detection times

Body Fluid	Range of viral detection times in relation to symptom onset
Serum	2 days before – 34 days after
Urine	2 days before – 91 days after
Saliva	2 days before – 91 days after
CSF	7 days after
Semen	3 – 188 days after
Vaginal secretions	≤13 days after

Moreira J, *et al.* Sexually acquired Zika virus: a systematic review. *Clin Microbiol Infect.* 2017, 23(5):296–305.



# Sexual transmission & prevention messages

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- Zika can be passed through vaginal, anal, and oral sex and through sharing of sex toys
- Zika virus can stay in semen longer than in other body fluids, which means men can pass Zika sexually for longer
- Infected people can pass Zika through sex even without symptoms and before, during, and after symptom onset
- Condoms (both male and female) can reduce the chance of getting Zika virus from sex
- Not sharing sex toys can reduce the risk of spreading Zika to sex partners



# Unanswered questions

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- Maximum time virus lasts in semen
- Maximum time *infectious* virus lasts in semen
- Does risk of sexual transmission differ for symptomatic vs. asymptomatic persons?
- Would testing of semen offer any benefit given concern for intermittent shedding?
- Impact of other STIs on risk of sexual transmission
- Long term impact of infection on future fertility



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# QUESTIONS?

