



Sexually Transmission of Zika Virus Infection: What We Know and What We Don't Know

John T. Brooks, MD

Senior Medical Advisor

National Center for HIV/AIDS, Viral Hepatitis, STD, and TB Prevention

Division of HIV/AIDS Prevention

Centers for Disease Control and Prevention

2016 STD Conference

September 21, 2016

Transmission of Zika virus

Documented

- Bite of an *Aedes aegypti* or *Ae. albopictus* mosquito
- Intrauterine and perinatal transmission
- Sexual transmission from infected men and women
- Laboratory exposure

Plausible

- Blood transfusion/tissue transplantation
- Breast milk



Aedes aegypti mosquito

Zika Symptoms and Outcomes

Most infections are asymptomatic or mild

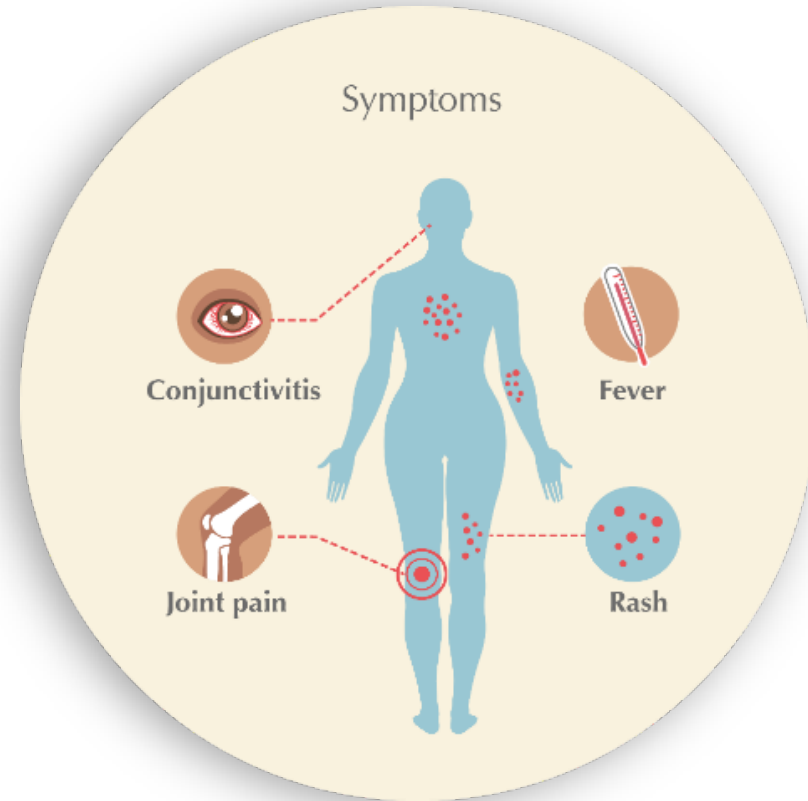
Symptoms develop 2-7 days after exposure

- Fever, rash, arthralgia, or conjunctivitis
- Last several days to a week

Severe and fatalities rare

- Demyelinating syndromes (GBS)

Infection appears to confer immunity



Populations of Greatest Concern

Pregnant women

- Microcephaly and other severe fetal brain defects¹

Women of reproductive age (age 15-44 years)

- 37% of pregnancies in the U.S. are unplanned²

After recovery from infection, there appears to be no risk to future pregnancies



Sexual Transmission of Zika

Suggested by at least two reports prior to current outbreak in the Americas

- Possible sexual transmission reported from U.S. in 2008¹
- Recovery of Zika by culture and detection by rRT-PCR in semen of symptomatically infected Tahitian man in 2013²
- Both men reported hematospermia

In early 2016, multiple case reports of sexually transmitted infections

- From travelers returning from areas with active Zika transmission to sex partners that had not traveled

Now reported from at least 11 countries including United States

1. Foy, 2011, Emerg Infect Dis **17**(5): 880-882. 2. Musso, 2015, Emerg Infect Dis **21**(2): 359-361.

How Can Zika Be Transmitted Sexually?

What We Know

- Zika can be sexually transmitted by men to their male or female sex partners
- Zika can also be transmitted by women to their male sex partners (1 case)
- Zika can be transmitted through vaginal and anal sex, and possibly fellatio
- Asymptomatic men can transmit Zika sexually

What We Don't Know

- If Zika can be transmitted through sexual contact between two women.
- If Zika can be transmitted through cunnilingus.
- If per-act transmission risks differ (e.g., anal vs. vaginal receptive sex)
- If symptomatically infected persons are more likely to transmit than asymptotically infected persons (i.e., do symptoms correlated with infectiousness?)

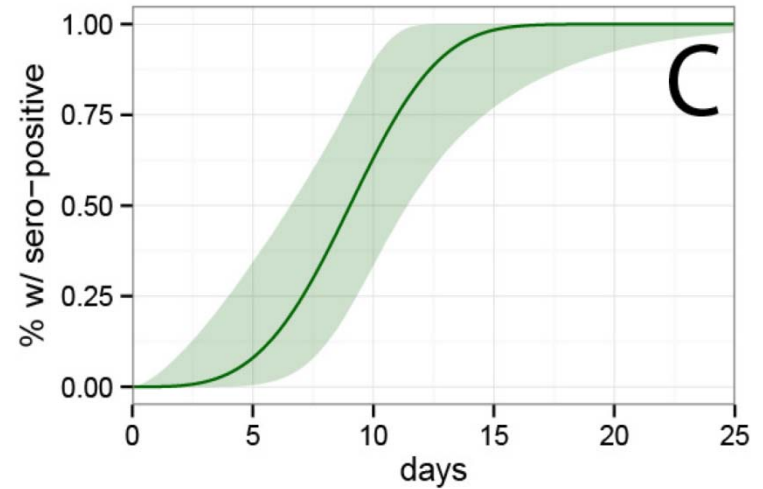
When and in What Body Fluids Can Zika be Detected?

Median serum incubation period 6 days¹

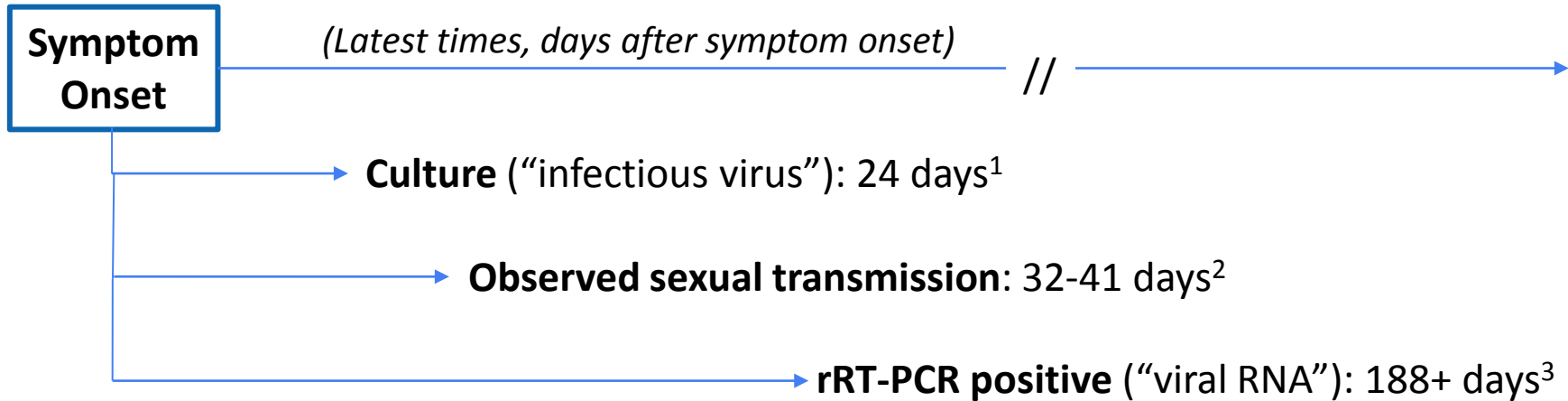
- 95% by 10-18 days

Virus cultured and detected by RT-PCR

- Serum
- Whole blood
- Urine
- Saliva
- Genital fluids (semen, cervicovaginal secretions)



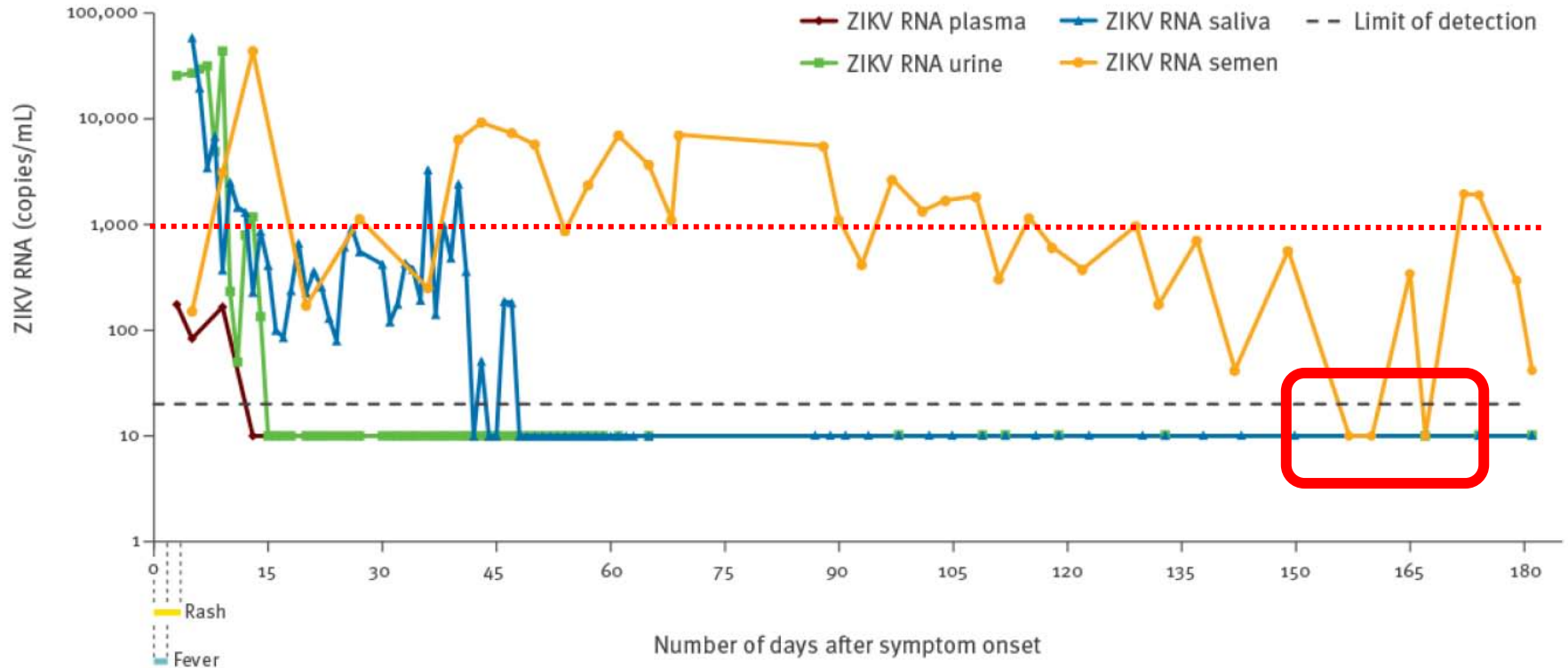
Zika Virus in Semen and Risk of Sexual Transmission



1. D'Ortenzio, 2016, N Engl J Med; Jun 2;374(22):2195-8. doi: 10.1056/NEJMc16044492. Freor, 2016, Euro Surveill; Jun 9;21(23). doi: 10.2807/1560-7917.ES.2016.21.23.30254. 3. Barzon, 2016, Euro Surveill; 21(32);pi=30316 11-August-2016

Prolonged Detection of Zika Viral RNA in Semen

A. Duration of symptoms and ZIKV RNA load in the patient's plasma, urine, saliva and semen samples (by real-time RT-PCR)



Zika Virus in Semen and Risk of Sexual Transmission

What does detection of Zika viral RNA mean in terms of infection risk?

- One other case of up to 181 days; outliers?
- Documented 4 cases with negative follow-up at 56-99 days
- All attempts to culture virus from late samples have been unsuccessful

How Much of a Risk Does Zika in Semen Pose?

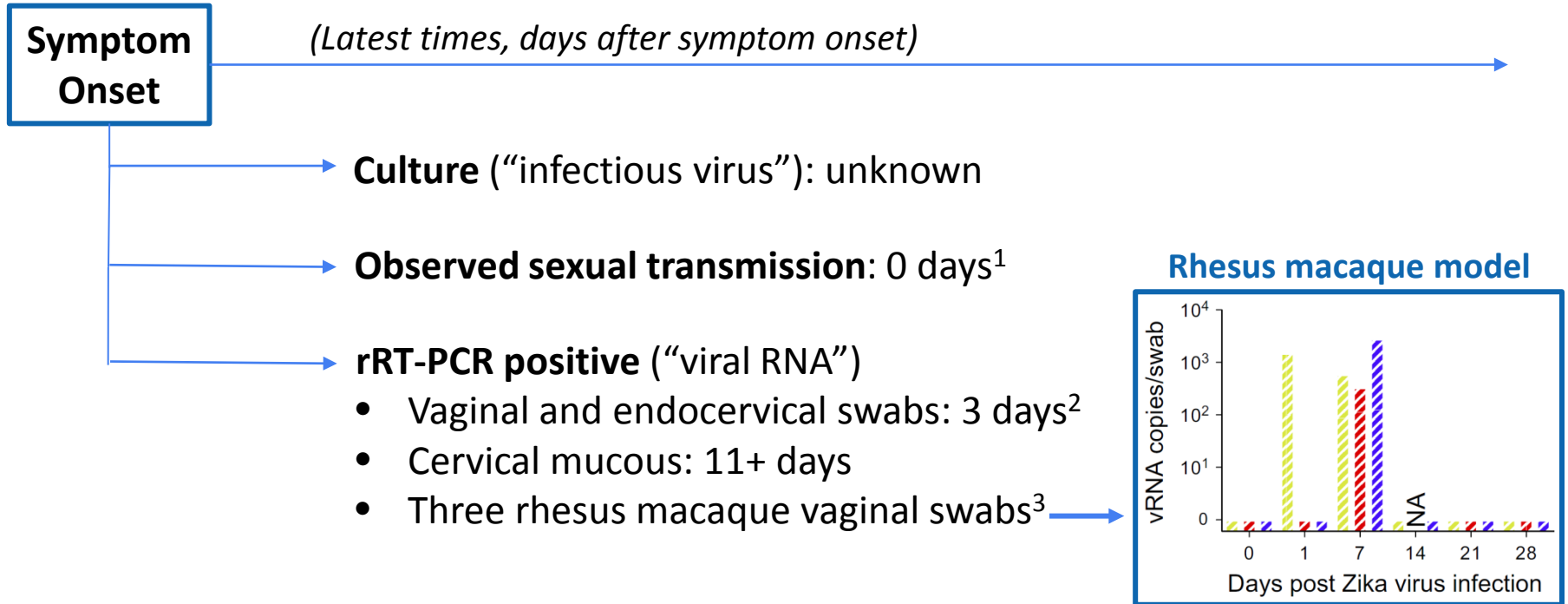
What We Know

- Zika has not been cultured from semen > 30 days after illness onset.
- Of the few sexually transmitted infections observed, most have occurred < 60 days after illness onset.
- Zika viral RNA has been persistently detected in semen > 180 days after illness onset.

What We Don't Know

- What is the incidence of Zika viremia in semen (both infected men with and without symptoms)?
- How long can virus capable of *transmitting infection* remain in semen?
- Where is virus replicating?
- What is the pattern of viremia in semen (steady decline or intermittent)?
- Can anything be done to speed resolution of semen viremia?

Zika Virus in Cervicovaginal Secretions



1. Davidson, 2016, *MMWR Morb Mortal Wkly Rep.* 2016;65(Early Release July 15, 2016) 2. Prisant, 2016, *Lancet Infect Dis*, Jul 11. pii: S1473-3099(16)30193-1. doi: 10.1016/S1473-3099(16)30193-1. 3. Dudley, 2016, *Nature Comm*; Jun 28;7:12204. doi: 10.1038/ncomms12204.

What Risk is Posed by Zika in Cervicovaginal Fluids?

What We Know

- There is a paucity of data
 - One case report with samples
- Single female → male transmission¹
 - Exposure near symptom onset
 - Menses imminent
 - Male uncircumcised

What We Don't Know

- What is the incidence of Zika viremia in cervicovaginal secretions (both infected men with and without symptoms)?
- How long can virus capable of *transmitting infection* remain in cervicovaginal secretions?
- What is the source of virus?
- What is the pattern of viremia (steady decline or intermittent)?

1. Davidson, 2016, MMWR Morb Mortal Wkly Rep. 2016;65(Early Release July 15, 2016).



ZIKA AND SEX: HOW TO PROTECT YOURSELF AND YOUR LOVED ONES, IF YOU OR YOUR PARTNER HAVE BEEN IN AN AREA WITH ZIKA

IF YOU ARE:	IF YOU ARE:	IF YOU ARE:
Pregnant	Planning to get pregnant	Not planning or able to get pregnant
WHAT TO DO:	WHAT TO DO:	WHAT TO DO:
Use condoms* or do not have sex	Wait to get pregnant. Use condoms* or do not have sex	Consider using condoms or not having sex
FOR HOW LONG:	FOR HOW LONG:	FOR HOW LONG:
For the entire pregnancy	If traveler is male: And has Zika illness/symptoms, at least 6 months after symptoms started And has no Zika illness/symptoms, at least 8 weeks after return from travel	If traveler is male: And has Zika illness/symptoms, at least 6 months after symptoms started And has no Zika illness/symptoms, at least 8 weeks after return from travel
	If traveler is female: And has Zika illness/symptoms, at least 8 weeks after symptoms started And has no Zika illness/symptoms, at least 8 weeks after return from travel	If traveler is female: And has Zika illness/symptoms, at least 8 weeks after symptoms started And has no Zika illness/symptoms, at least 8 weeks after return from travel
WHY:	WHY:	WHY:
To prevent infection in the mother and birth defects in the baby	To prevent infection in the mother and birth defects in the baby	To prevent getting Zika

*For this algorithm, condoms refer to all barriers that prevent infection during sex including male and female condoms and dental dams. Sex is defined as vaginal, anal, or oral sex and the sharing of sex toys.



ZIKA AND SEX: HOW TO PROTECT YOURSELF AND YOUR LOVED ONES, IF YOU OR YOUR PARTNER LIVE IN AN AREA WITH ZIKA

IF YOU ARE:	IF YOU ARE:	IF YOU ARE:
Pregnant	Planning to get pregnant	Not planning or able to get pregnant
WHAT TO DO:	WHAT TO DO:	WHAT TO DO:
Use condoms* or do not have sex	Talk to a healthcare provider to discuss and plan the pregnancy	Consider using condoms or not having sex
FOR HOW LONG:	FOR HOW LONG:	FOR HOW LONG:
For the entire pregnancy	As long as there is Zika in the area	As long as there is Zika in the area
WHY:	WHY:	WHY:
To prevent infection in the mother and birth defects in the baby	To prevent infection in the mother and birth defects in the baby	To prevent getting Zika

*For this algorithm, condoms refer to all barriers that prevent infection during sex including male and female condoms and dental dams. Sex is defined as vaginal, anal, or oral sex and the sharing of sex toys.

Testing

Recommended to establish diagnosis of infection

- Patient with fever, rash, arthralgia, or conjunctivitis and either :
 - Onset during or within 2 weeks of travel to an area with active transmission
 - Epidemiologic link to laboratory-confirmed case through vertical transmission, sexual contact, or association in time and place
- Offer testing to all asymptomatic pregnant women with a history of either:
 - Travel to or residency in an area with active transmission during pregnancy
 - Sexual contact with a potentially infected person (e.g., recently returned traveler or person living in an area with ongoing transmission), whether she or her sex partner have had or develop any symptoms of illness

Testing

Not recommended to establish absence of infection

Falsely negative results might be falsely reassuring that there is no risk of sexual and lead to inadvertent sexual exposure of fetus to Zika

- Serum RT-PCR: Zika viral RNA has been detected in semen when no longer detectable in serum and urine (utility of whole blood under consideration)
- Serum IgM: testing window is limited and not well defined (estimated to be positive around 2-12 weeks after infection)
- Whole blood RT-PCR: promising but not yet available
- Semen testing: all RT-PCR and culture are done under research protocols only

CDC Studies of Zika Virus in Semen and Other Body Fluids

U.S. study of returned male travelers diagnosed with Zika

- Semen and urine
- Every 2 weeks up to 6 months after onset
- Self-collection, self-mailer
- Project Director: Alison Hinckley, cue0@cdc.gov/[970-221-6400](tel:970-221-6400)

Puerto Rico study of men and women diagnosed with Zika (ZiPer)

- Blood, saliva, urine, semen, and vaginal swabs
- Symptomatic and asymptomatic men and women
- Specimens weekly for 4 weeks then biweekly until negative twice
- Recruiting 350 patients with up to 5 household contacts each
- Email ZIPER@cdc.gov

What Else Do We Know and Not Know?

What is the contribution of sexual transmission to the burden of Zika infections?

- Difficult to discern where both exposures are occurring simultaneously.

Can kissing transmit Zika?

- Unlikely given the disproportionate male:female ratio of sexually transmitted infections (predominately transmitted from men, predominately symptomatic)

Is Zika spreading unobserved through the population through sex?

- Unlikely given that it is a time-limited infection, unlike traditional STDs that may continue to be transmitted for long periods until diagnosed and treated

Have there been any sexual transmitted infections of pregnant women?

- Yes and CDC is monitoring the outcomes of all pregnant women diagnosed

Summary

Zika may be first flavivirus observed to be transmitted through sex

We have learned a lot about sexual transmission of Zika but knowledge gaps remain, especially to inform prevention recommendations

Key questions include:

- Correlation of infectiousness with viral RNA titers
- Contribution of sexual transmission to burden of Zika virus infections
- Biology of Zika infection in human male and female genitourinary tract

Balancing principles of precaution and proportionality is a challenge

CDC Resources and Materials

- CDC sexual transmission webpage - <http://www.cdc.gov/zika/hc-providers/clinical-guidance/sexualtransmission.html>
- Interim Guidelines – http://www.cdc.gov/mmwr/volumes/65/wr/mm6529e2.htm?s_cid=mm6529e2_e
- Fact sheets/Posters - <http://www.cdc.gov/zika/fs-posters/index.html>
- Infographics - <http://www.cdc.gov/zika/comm-resources/infographics.html>
- How use to condoms and dental dams infographic - <http://www.cdc.gov/condomeffectiveness/index.html>

CDC's Response to ZIKA

ZIKA AND SEXUAL TRANSMISSION



BASICS OF ZIKA VIRUS AND SEX



How Zika is spread through sex

- Zika can be passed through sex from a person who has Zika to his or her sex partners. Sex includes vaginal, anal, and oral sex and the sharing of sex toys.
- Zika can be passed through sex, even if the infected person does not have symptoms at the time. It can be passed from a person with Zika before their symptoms start, while they have symptoms, and after their symptoms end and may also be passed by a person who never develops symptoms.
- Zika can remain in semen longer than in other body fluids, including vaginal fluids, urine, and blood.



Studies are underway to find out

- How long Zika stays in the semen and vaginal fluids of people who have Zika.
- How long Zika can be passed to sex partners.
- If Zika passed to a pregnant woman during sex has a different risk for birth defects than Zika transmitted by a mosquito bite.



Thank you!

For more information, contact CDC
1-800-CDC-INFO (232-4636)
TTY: 1-888-232-6348 www.cdc.gov

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

