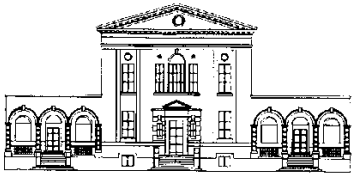
Zika testing in pregnant and pregnancy planning women: the role of partners' testing



Giuseppe Ippolito,

Giuseppina Liuzzi, Concetta Castilletti, Francesco Vairo, Maria R. Capobianchi, Antonino Di Caro, Licia Bordi, Emanuele Nicastri

National Institute for Infectious Diseases Lazzaro Spallanzani-Rome, Italy

giuseppe.ippolito@inmi.it

WHO Collaborating Center for clinical care, diagnosis, response and training on Highly Infectious Diseases

World Health Organization

Early Detection

The FASTER
We Know What It Is

Rapid Response

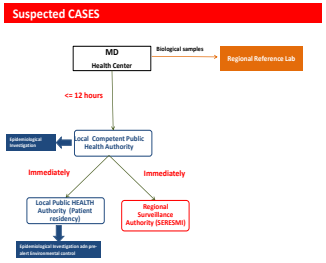
The FASTER We Can Take Appropriate Action

The knowledge of Zika virus can be used to consider the effect on:

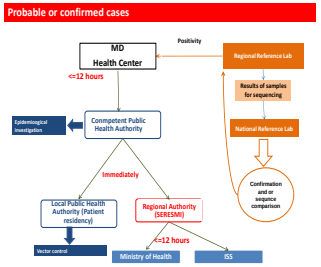
1. risk assessment
2. clinical presentation
3. transmission
4. diagnostics
5. clinical management
6. public health measures

The Arbovirus surveillance system in Lazio Region

- Integrated laboratory Surveillance
- Enhanced surveillance in the Lazio Region
  - Notification of suspect cases
  - Pre alert of the vector control services
  - Constant evaluation of cases by the Regional Reference Lab
  - Evaluation of vector control measures
  - Training and awareness increase in HCWs
  - **Zika included in the surveillance since May 2015**

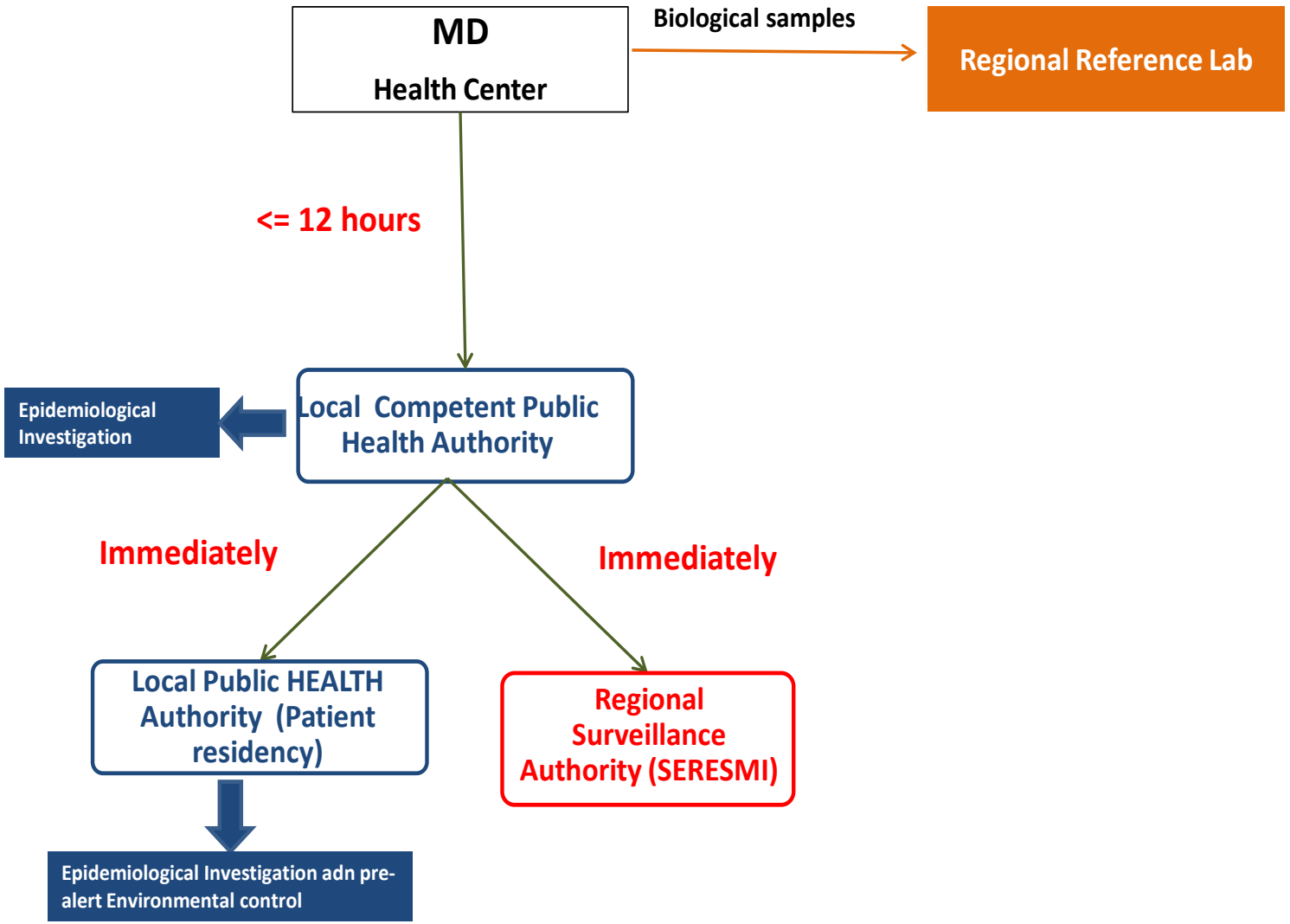


SERESMI



The Arbovirus surveillance system in Lazio Region

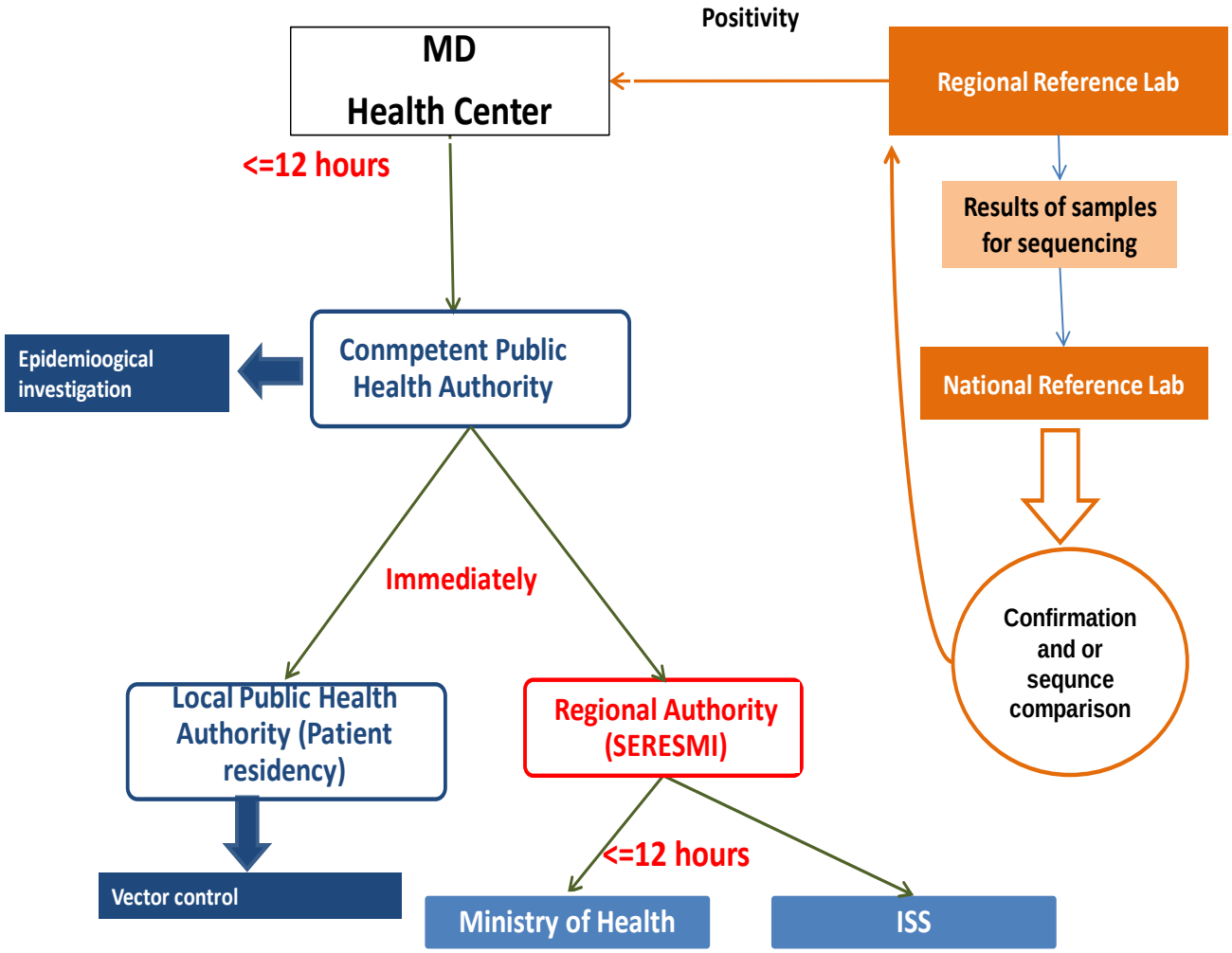
Suspected CASES



SERESMI

The Arbovirus surveillance system in Lazio Region

Probable or confirmed cases



SERESMI

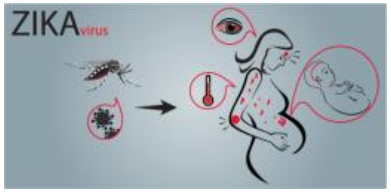
Zika Americas Alert Timeline

1 February 2016
WHO declares that the recent association of Zika infection with clusters of microcephaly and other neurological disorders constitutes a Public Health Emergency of International Concern.

Interim Guidelines for Pregnant Women During a Zika Virus Outbreak — United States, 2016

Emily E. Petersen, MD[1]; J. Erin Staples, MD, PhD[2]; Dana Meaney-Delman, MD[3]; Marc Fischer, MD[2]; Sascha R. Ellington, MSPH[1]; William M. Callaghan, MD[1]; Denise J. Jamieson, MD[1]

22 January 2016
Pregnant women with a history of travel to an area with Zika virus transmission and who report two or more symptoms consistent with ZIKV disease should be tested for Zika virus infection

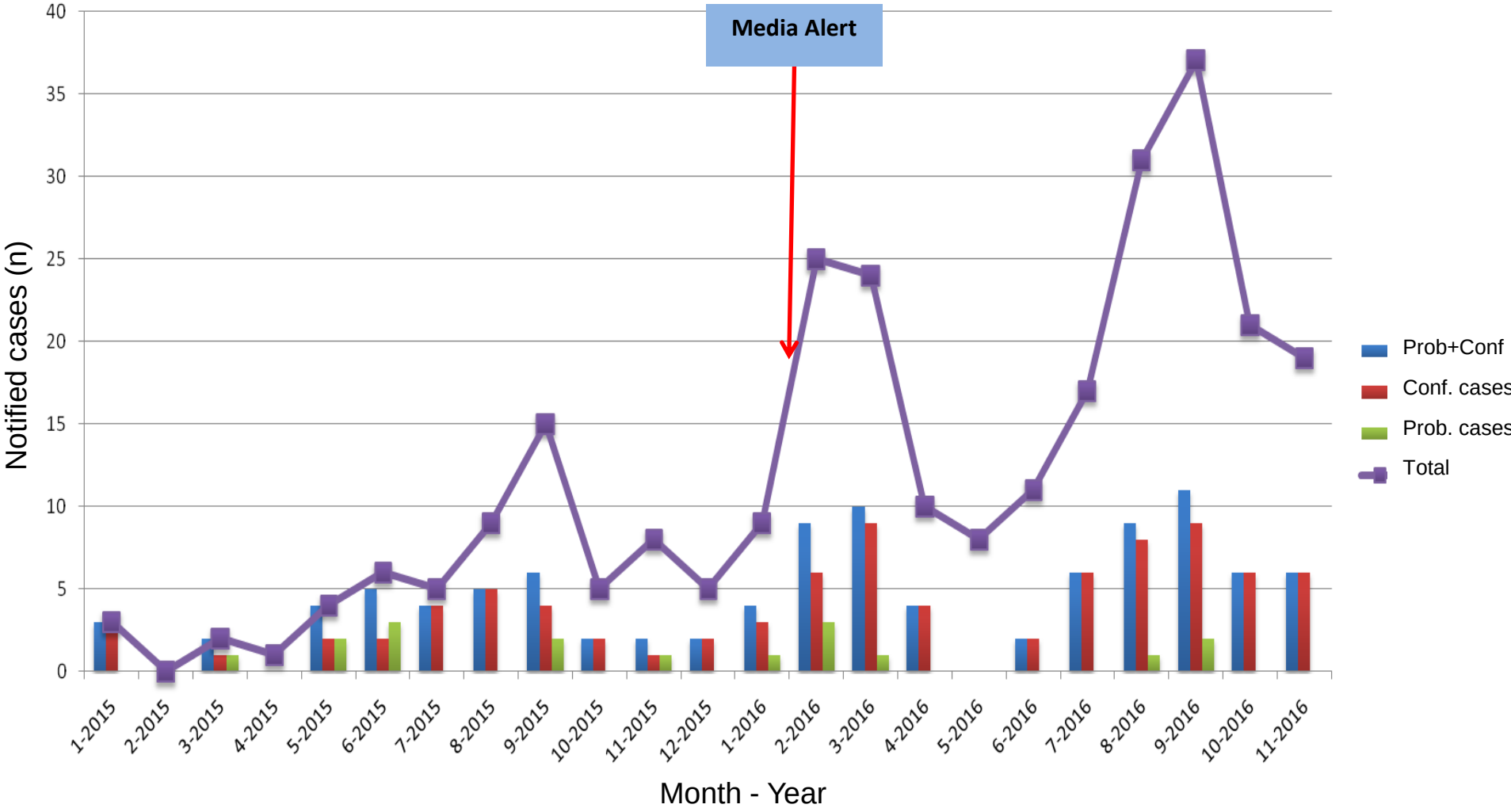


28 November 2015
Brazil detects Zika virus genome in the blood and tissue samples of a baby with microcephaly

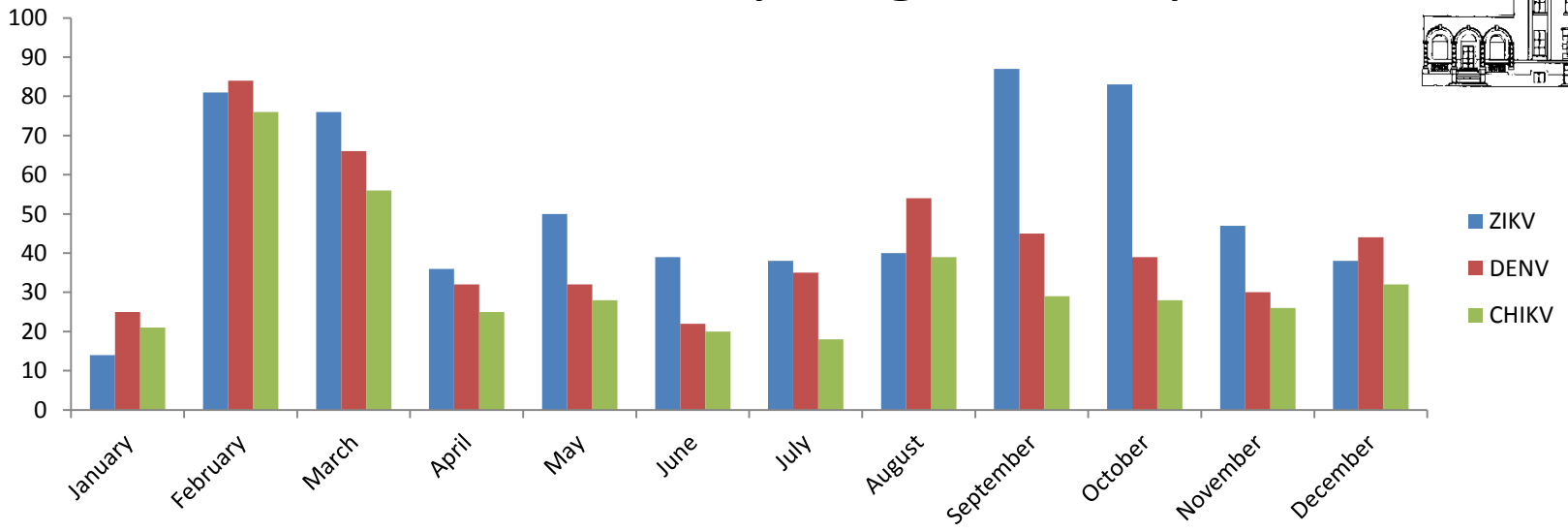
21 January 2016
Brazil reports 3,893 suspected cases of microcephaly, including 49 deaths.

11 November 2015
Brazil declares a national public health emergency as increasing cases of microcephaly.

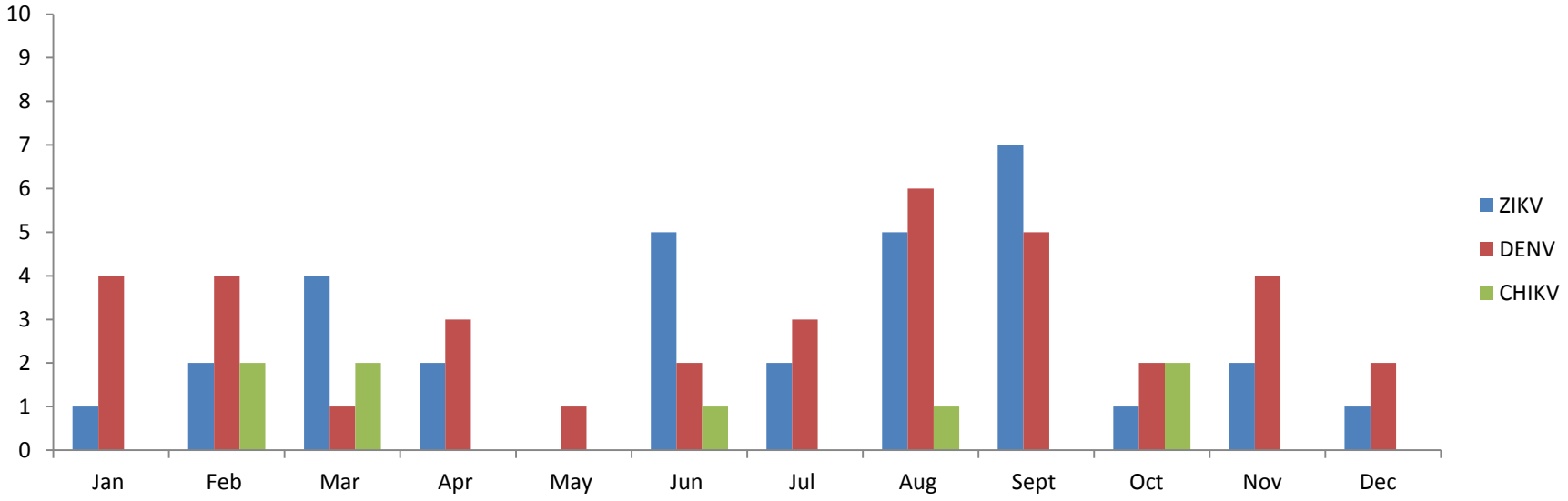
Effect of media alert on the number of notified cases: temporal trend in Lazio region



Arbovirus laboratory diagnosis requests

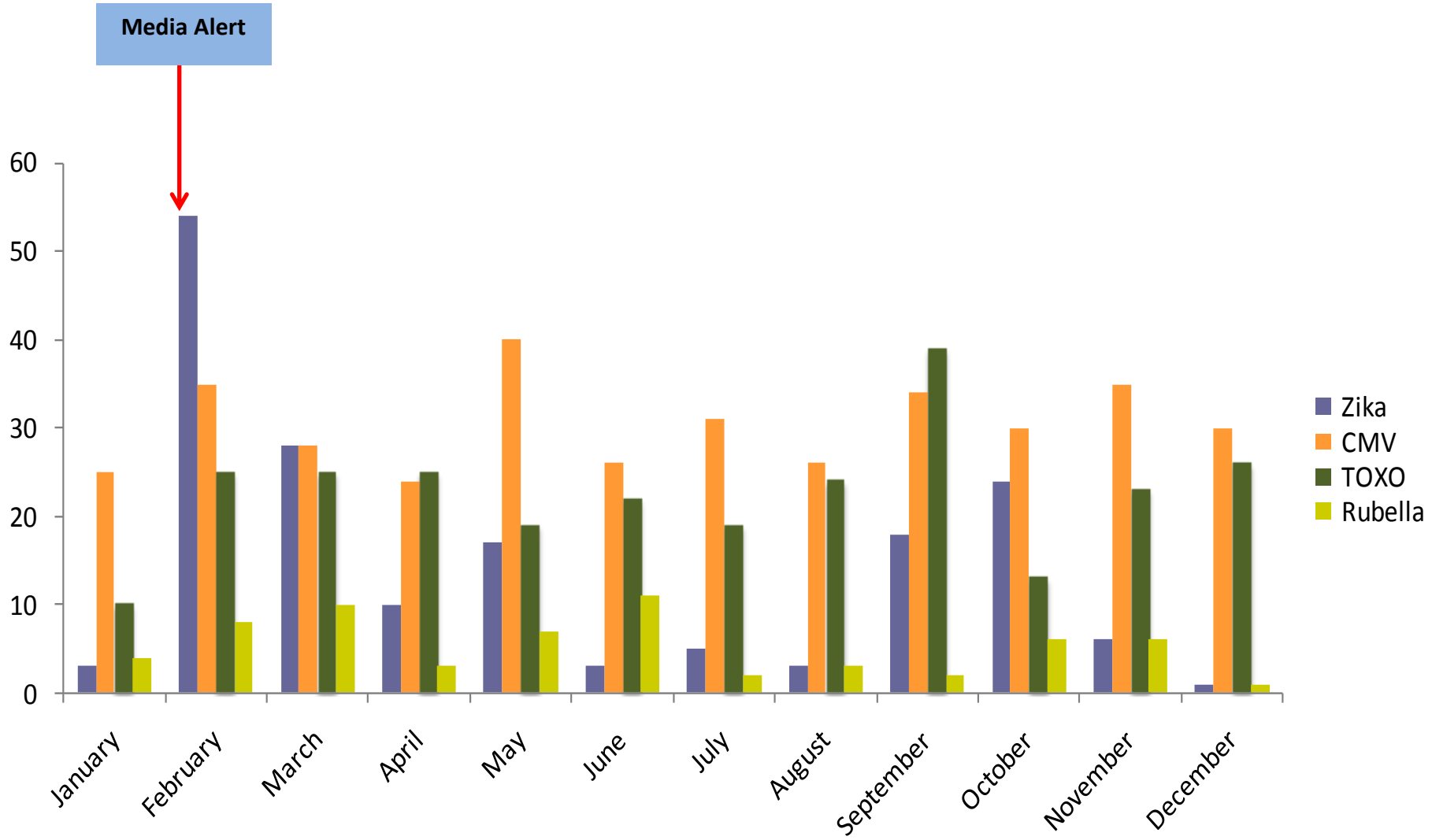


Arbovirus positive cases



Antenatal and Perinatal Infectious Diseases Unit

Antenatal and Perinatal Infectious Diseases Unit: Main reasons for consultation - year 2016



National Institute for Infectious Diseases
Lazzaro Spallanzani – IRCCS , Rome. Italy

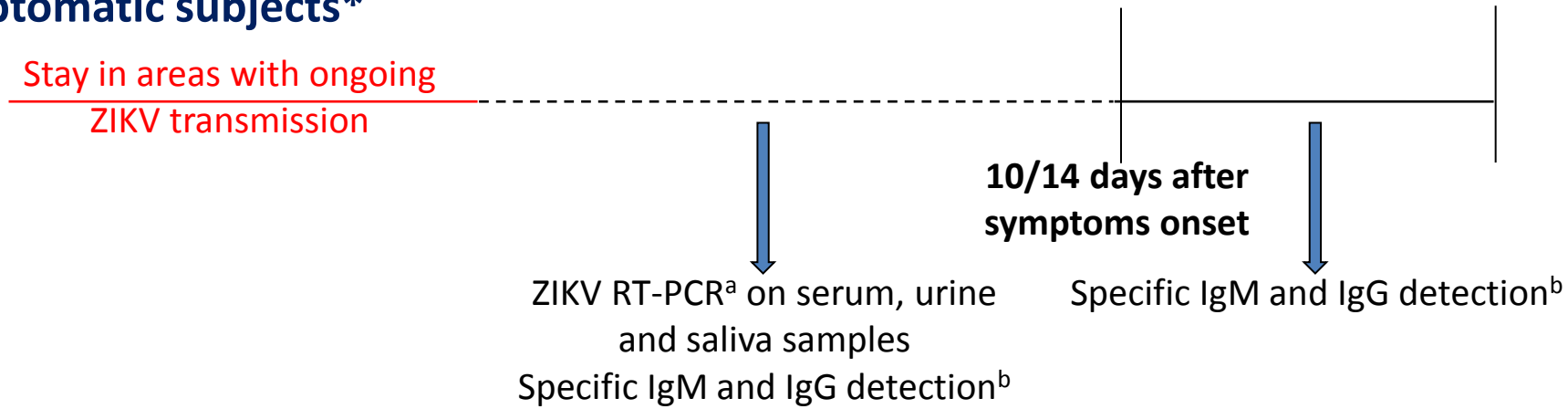
Since February 4, 2016, in parallel with the enhanced surveillance system, INMI implemented an **expanded testing algorithm** involving:

- all pregnant women with history of travel in a ongoing transmission area during the current pregnancy whether symptomatic or not
- all exposed partners of pregnant women
- couples planning pregnancy

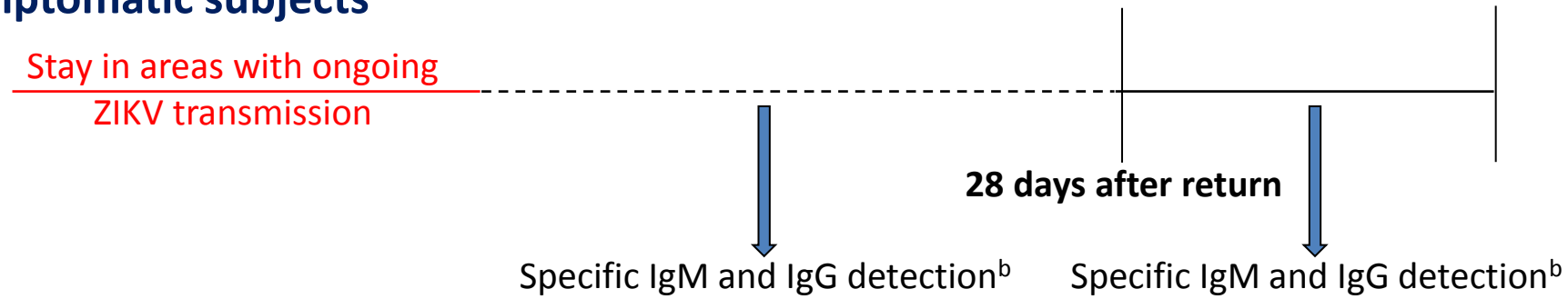
INMI Testing algorithm – 4 february 2016

Pregnant women's partners and couples planning pregnancy

Symptomatic subjects*



Asymptomatic subjects*



***Differential diagnosis for Chikungunya, Dengue 1-4, and Yellow Fever**

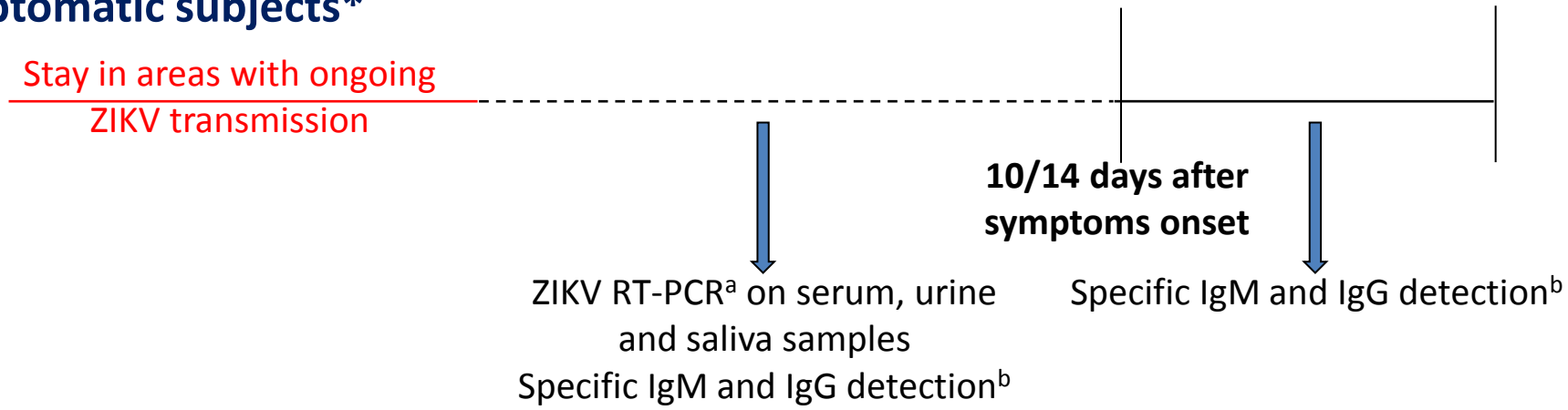
[a]Zika Virus real-time RT-PCR and confirmation of positive results with a pan-flavivirus NS5 nested RT-PCR and sequencing

[b]Indirect immunofluorescence assay and confirmation of positive results with PRNT also against Dengue2 and Yellow fever viruses

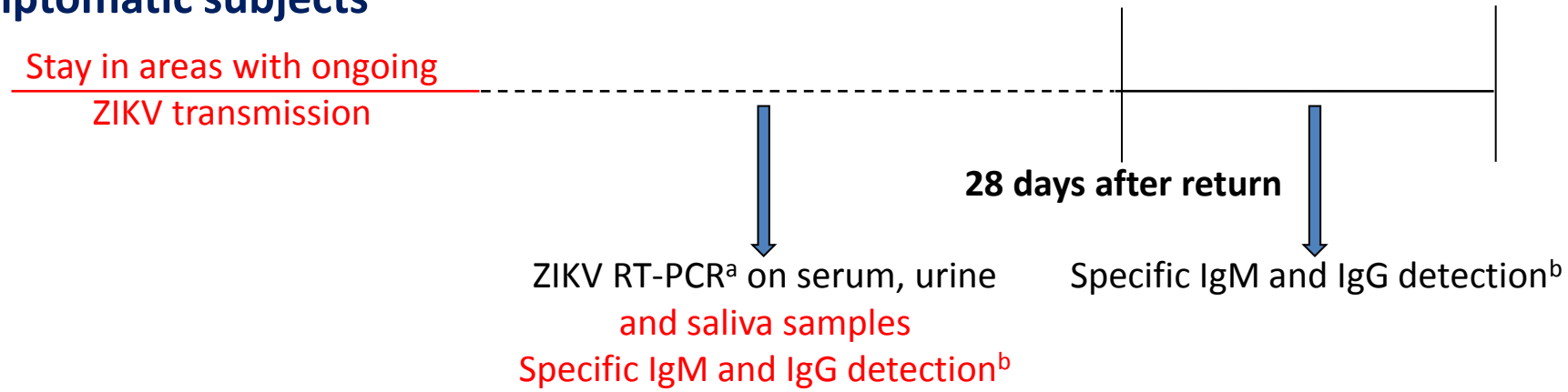
INMI Testing algorithm – 4 february 2016

Pregnant women

Symptomatic subjects*



Asymptomatic subjects*

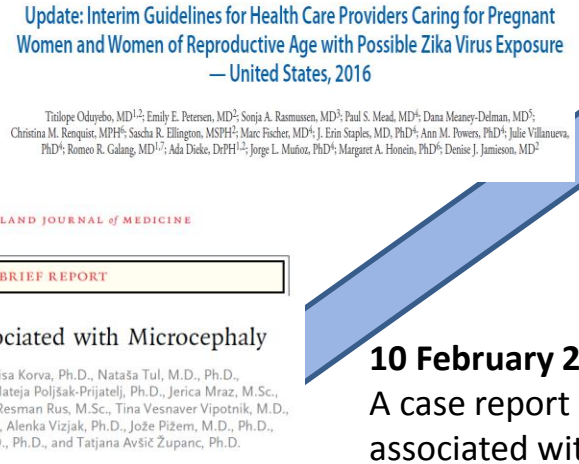


***Differential diagnosis for Chikungunya, Dengue 1-4, and Yellow Fever**

[a]Zika Virus real-time RT-PCR and confirmation of positive results with a pan-flavivirus NS5 nested RT-PCR and sequencing

[b]Indirect immunofluorescence assay and confirmation of positive results with PRNT also against Dengue2 and Yellow fever viruses

Testing guidance timeline (CDC)



Update: Interim Guidelines for Health Care Providers Caring for Pregnant Women and Women of Reproductive Age with Possible Zika Virus Exposure — United States, 2016

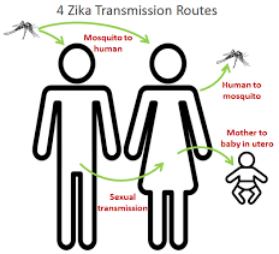
Titilope Oduyebo, MD[1,2]; Emily E. Petersen, MD[2]; Sonja A. Rasmussen, MD[3]; Paul S. Mead, MD[4]; Dana Meaney-Delman, MD[5]; Christina M. Renquist, MPH[6]; Sascha R. Ellington, MSPH[2]; Marc Fischer, MD[4]; J. Erin Staples, MD, PhD[4]; Ann M. Powers, PhD[4]; Julie Villanueva, PhD[4]; Romeo R. Galang, MD[1,7]; Ada Dieke, DrPH[1,2]; Jorge L. Muñoz, PhD[4]; Margaret A. Honein, PhD[6]; Denise J. Jamieson, MD[2]

The NEW ENGLAND JOURNAL of MEDICINE

BRIEF REPORT

Zika Virus Associated with Microcephaly

Jernej Mlakar, M.D., Misa Korva, Ph.D., Nataša Tul, M.D., Ph.D., Mara Popović, M.D., Ph.D., Mateja Poljšak-Prijatelj, Ph.D., Jerica Mraz, M.Sc., Marko Kolenc, M.Sc., Katarina Resman Rus, M.Sc., Tina Vesnaver Vipotnik, M.D., Vesna Fabjan Vodušek, M.D., Alenka Vizjak, Ph.D., Jože Pižem, M.D., Ph.D., Miroslav Petrovec, M.D., Ph.D., and Tatjana Avšič Županc, Ph.D.



12 February 2016
Testing can be offered to pregnant women without clinical illness consistent with Zika virus disease.
If performed, testing should include Zika virus IgM.
Testing should be performed 2–12 weeks after travel.

10 February 2016
A case report describes severe fetal brain injury associated with Zika virus infection in a woman who became pregnant in Brazil in February 2015.
Mlakar J et al 2016 NEJM

2 February 2016
The United States reports a case of sexual transmission of Zika infection in Texas.

Evolution of testing algorithm for pregnant women+partners residing in/returning from epidemic areas

	Pregnant women	Partner of pregnant	Couples planning pregnancy
	CDC	CDC	CDC
Jan '16	Test only symptomatic, **IgM; RT-PCR (serum)**	Not considered	Not considered

Evolution of testing algorithm for pregnant women+partners residing in/returning from epidemic areas (INMI vs CDC)

	Pregnant women		Partner of pregnant		Couples planning pregnancy	
	CDC	INMI	CDC	INMI	CDC	INMI
Jan '16	Test only symptomatic, **IgM; RT-PCR (serum)**	Test both symptomatic and asymptomatic **IgG/IgM, RT-PCR (serum+urine, saliva)**	Not considered	Not considered	Not considered	Not considered

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Febr	Test both symptomatic, **IgM; RT-PCR (serum)** and asymptomatic, **IgM**	"	No indication to test; Counseling	Offering test regardless of symptoms, **IgG/IgM, RT-PCR (serum+urine, saliva)**	No indication to test; Counseling	Offering test to both members of the couple

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April	As February	"	"	"	"	"
July	Test all possible exposures (including sexual), **IgM; RT-PCR (serum + urine)**	"	"	"	"	"

6 months later Excluding saliva

SISTEMA SANITARIO REGIONALE
IRCCS LAZZARO SPALLANZANI

REGIONE LAZIO

Istituto Nazionale per le Malattie Infettive
Struttura Complessa Laboratorio di Virologia e Laboratori di Biosicurezza
Direttore: D.ssa M.R. Capobianchi
e-mail: maria.capobianchi@inmi.it; Tel. 0655170434 Fax 065594555

Istruzioni operative per l'invio di campioni relativi alla diagnosi di infezione da arbovirus al Laboratorio di Riferimento Regionale

Ai fini degli accertamenti relativi alle infezioni da arbovirus, si riportano le istruzioni operative su tipologia di campioni, modalità di trasporto, consegna dei campioni diagnostici al Laboratorio di Virologia dell'INMI "L. Spallanzani". Si precisa che le istruzioni specifiche per l'infezione da virus West Nile sono state compilate in un documento dedicato.

Si riportano di seguito le informazioni generali sull'invio dei campioni diagnostici, ribadendo che, in base a quanto sopra espresso, è essenziale che il medico richiedente consulti il laboratorio per concordare le indagini più appropriate e la tipologia di campione da inviare.

1.Tipologia dei campioni da inviare

Fase della malattia	Tipologia di campione	Tipologia di contenitore
Fase acuta sintomatica *(Entro i primi 5 giorni dall'esordio)*	- Sangue/EDTA per RT-PCR	- Provetta sterile infrangibile (almeno 4 ml)
	- Sangue senza anticoagulanti per RT-PCR e sierologia	- Provetta sterile infrangibile (almeno 4 ml)
	- Urine	- Contenitore infrangibile sterile (provetta o contenitore per urinocultura. Almeno 5 ml)
	- Saliva o Tampone salivare	- Tampone floccato in terreno di trasporto virale (almeno 2 ml, non contenente inattivanti) in flacone infrangibile.
	- Liquor *(in caso di sintomatologia neurologica)*	- Contenitore infrangibile sterile (almeno 1 ml)
	In base alla valutazione congiunta con il laboratorio ed alla presentazione clinica, possono essere inviati campioni biologici aggiuntivi, quali: - Liquido seminale, tampone vaginale, altro	- Da concordare con il Laboratorio

Rev3 del 08/11/2016

RAPID COMMUNICATIONS

Detection of Zika virus RNA in whole blood of imported Zika virus disease cases up to 2 months after symptom onset, Israel, December 2015 to April 2016

Y Lustig [1], E Mendelson [1,2], N Paran [3], S Melamed [3], E Schwartz [4]
1. Central Virology Laboratory, Ministry of Health, Tel-Hashomer, Israel
2. School of Public Health, Sackler Faculty of Medicine, Tel-Aviv University, Israel
3. Israel Institute for Biological Research, Ness-Ziona, Israel
4. Institute of Tropical Medicine, Sheba Medical Ctr. Tel Hashomer, Israel

Correspondence: Yaniv Lustig (yaniv.lustig@sheba.health.gov.il)

Citation style for this article:
Lustig Y, Mendelson E, Paran N, Melamed S, Schwartz E. Detection of Zika virus RNA in whole blood of imported Zika virus disease cases up to 2 months after symptom onset, Israel, December 2015 to April 2016. Euro Surveill. 2016;21(26):pii=30269. DOI: http://dx.doi.org/10.2807/1560-7917.ES.2016.21.26.30269

Article submitted on 15 June 2016 / accepted on 30 June 2016 / published on 30 June 2016

Prolonged Detection of Zika Virus in Vaginal Secretions and Whole Blood

Kristy O. Murray, Rodion Gorchakov, Anna R. Carlson, Rebecca Berry, Lilin Lai, Muktha Natrajan, Melissa N. Garcia, Armando Correa, Shital M. Patel, Kjersti Aagaard, Mark J. Mulligan

Emerging Infectious Diseases • www.cdc.gov/eid • Vol. 23, No. 1, January 2017

Evolution of testing algorithm for pregnant women+partners residing in/returning from epidemic areas (INMI vs CDC)

	Pregnant women		Partner of pregnant		Couples planning pregnancy	
	CDC	INMI	CDC	INMI	CDC	INMI
Jan '16	Test only symptomatic, **IgM; RT-PCR (serum)**	Test both symptomatic and asymptomatic **IgG/IgM, RT-PCR (serum+urine, saliva)**	Not considered	Not considered	Not considered	Not considered
Febr	Test both symptomatic, **IgM; RT-PCR (serum)** and asymptomatic, **IgM**	"	No indication to test; Counseling	Offering test regardless of symptoms, **IgG/IgM, RT-PCR (serum+urine, saliva)**	No indication to test; Counseling	Offering test to both members of the couple
April	As February	"	"	"	"	"
July	Test all possible exposures (including sexual), **IgM; RT-PCR (serum + urine)**	"	"	"	"	"
Nov	"	+ **whole blood for RT-PCR**	"	"	"	"
Jan '17	As July '16, possible use also of **whole blood for RT-PCR**	"	"	"	"	"

6 months later Excluding saliva

Antenatal and Perinatal ID Unit

199
Women Consulted
(pregnant or planning pregnancy)

148
Women urndewent
Arboviral test

110
Partners
Counsulted and Tested

3
ZIKV+

14
Previous
flavivirus

1
CHIKV+

1
Previous
CHIKV

22
Previous
flavivirus

1
DENV+

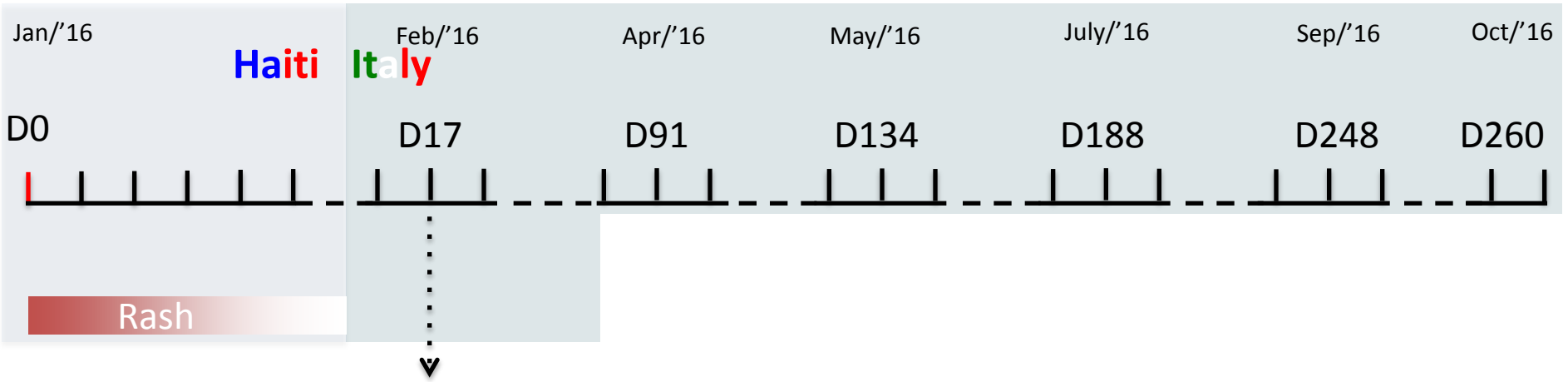
1
Previous
CHIKV

Zika virus testing outcome among persons tested at INMI L. Spallanzani, 2016

Testing outcome	ZIKV-associated symptoms° No. (%)	No symptoms No. (%)	Total No. (%)
Pregnant or planning pregnancy women (Tot.)	**22 (100)**	**126 (100)**	**148 (100)**
• Acute Zika virus infection	0 (0.0)	0 (0.0)	0 (0.0)
• Acute Dengue virus infection	1 (4.5)	0 (0.0)	1 (0.7)
• Acute Chikungunya virus infection	0 (0.0)	0 (0.0)	0 (0.0)
• Recent Unspecified flavivirus infection	6 (27.3)	17 (13.5)	23 (15.5)
• Previous Chikungunya virus infection	1 (4.5)	0 (0.0)	1 (0.7)
• No infection	14 (63.6)	109 (86.5)	123 (83.1)
Pregnant or planning pregnancy partners (Tot.)	**15 (100)**	**95 (100)**	**110 (100)**
• Acute Zika virus infection	2 (13.3)	1 (1.1)	3 (2.7)
• Acute Dengue virus infection	0 (0.0)	0 (0.0)	0 (0.0)
• Acute Chikungunya virus infection	1 (6.7)	0 (0.0)	1 (0.9)
• Recent Unspecified flavivirus infection	1 (6.7)	13 (13.7)	14 (12.7)
• Previous Chikungunya virus infection	0 (0.0)	1 (1.1)	0 (0.0)
• No infection	11 (73.3)	80 (84.2)	91 (82.7)

° Fever, rash, arthralgia.

Partner A
Timeline infection and virological data

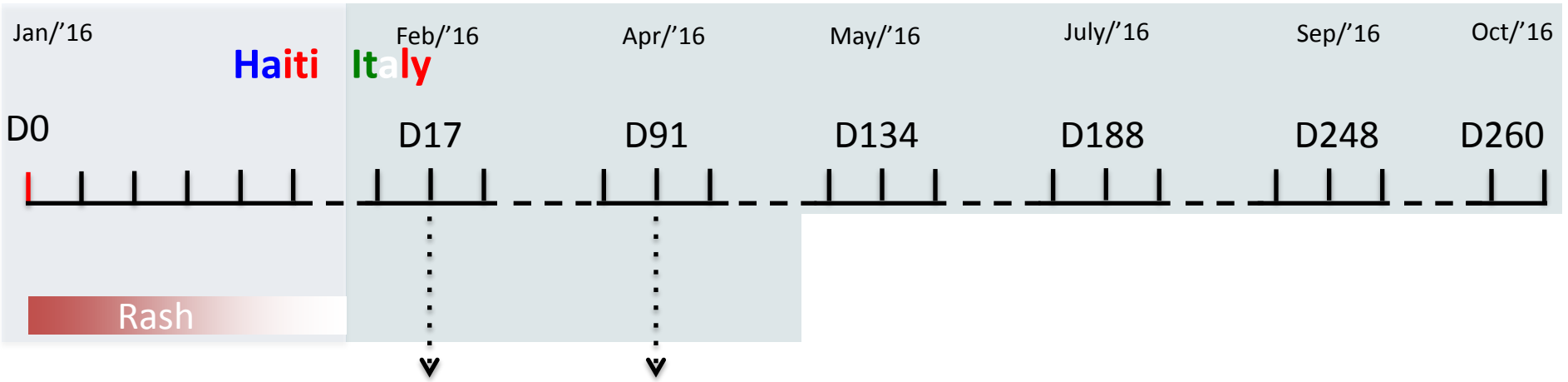


Anti ZIKV IgM (IFA)	**1:160**
Anti ZIVK IgG (IFA)	**1:640**
Anti ZIKV MNT	**1:160**
ZIKV RT-PCR serum	**Neg**
ZIKV RT-PCR saliva	**Pos (36,4)§**
ZIKV RT-PCR urine	**Neg**
ZIKV RT-PCR semen	**NT**

IFA: indirect immunofluorescence assay; MI

§Threshold cycle in parenthesis;

Partner A
Timeline infection and virological data

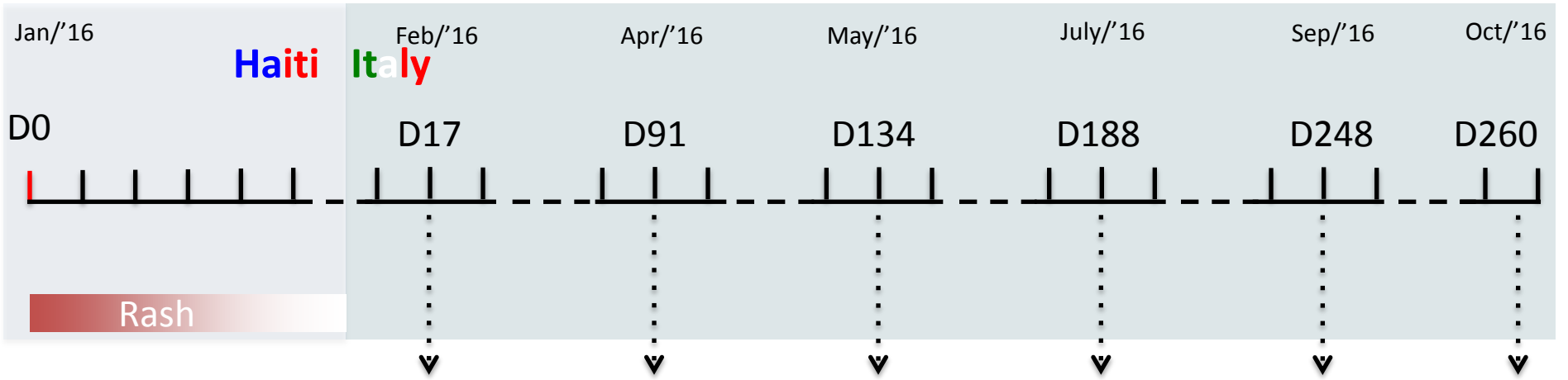


Anti ZIKV IgM (IFA)	**1:160**	**1:40**
Anti ZIVK IgG (IFA)	**1:640**	**1:1280**
Anti ZIKV MNT	**1:160**	**≥1:320**
ZIKV RT-PCR serum	**Neg**	**Neg**
ZIKV RT-PCR saliva	**Pos (36,4)§**	**Pos (35,4)**
ZIKV RT-PCR urine	**Neg**	**Pos (36,1)**
ZIKV RT-PCR semen	**NT**	**Pos (29,6)**

IFA: indirect immunofluorescence assay; MNT: microneutra

§Threshold cycle in parenthesis;

Partner A
Timeline infection and virological data



Anti ZIKV IgM (IFA)	**1:160**	**1:40**	**1:20**	**<1:20**	**<1:20**	**NT**
Anti ZIVK IgG (IFA)	**1:640**	**1:1280**	**1:2560**	**1:640**	**1:640**	**NT**
Anti ZIKV MNT	**1:160**	**≥1:320**	**≥1:320**	**NT**	**NT**	**NT**
ZIKV RT-PCR serum	**Neg**	**Neg**	**Neg**	**NT**	**NT**	**NT**
ZIKV RT-PCR saliva	**Pos (36,4)§**	**Pos (35,4)**	**Neg**	**NT**	**NT**	**NT**
ZIKV RT-PCR urine	**Neg**	**Pos (36,1)**	**Neg**	**NT**	**NT**	**NT**
ZIKV RT-PCR semen	**NT**	**Pos (29,6)**	**Pos (32,5)**	**Pos (30,2)**	**Neg**	**Neg**

IFA: indirect immunofluorescence assay; MNT: microneutralization test; NT: not tested

§Threshold cycle in parenthesis;

Nicastri et al, Eurosurv 2016

Persistent detection of Zika virus RNA in semen for six months after symptom onset in a traveller returning from Haiti to Italy, February 2016

E Nicastri [1], C Castilletti [1], G Liuzzi [1], M Iannetta [1], MR Capobianchi [1], G Ippolito [1]
1. National Institute for Infectious Diseases 'Lazzaro Spallanzani', IRCCS, Rome, Italy

Correspondence: Concetta Castilletti (concetta.castilletti@inmi.it)

Citation style for this article:
Nicastri E, Castilletti C, Liuzzi G, Iannetta M, Capobianchi MR, Ippolito G. Persistent detection of Zika virus RNA in semen for six months after symptom onset in a traveller returning from Haiti to Italy, February 2016. Euro Surveill. 2016;21(32):pii=30314. DOI: http://dx.doi.org/10.2807/1560-7917.ES.2016.21.32.30314

Article submitted on 06 July 2016 / accepted on 09 August 2016 / published on 11 August 2016

Infection dynamics in a traveller with persistent shedding of Zika virus RNA in semen for six months after returning from Haiti to Italy, January 2016

L Barzon [1,2], M Pacenti [2], E Franchin [1,2], E Lavezzo [1], M Trevisan [1], D Sgarabotto [3], G Palù [1,2]
1. Department of Molecular Medicine, University of Padova, Padova, Italy
2. Microbiology and Virology Unit, Padova University Hospital, Padova, Italy
3. Transplant Infectious Disease Unit, Padova University Hospital, Padova, Italy

Correspondence: Luisa Barzon (luisa.barzon@unipd.it)

Prevention of sexual transmission of Zika virus

Interim guidance update

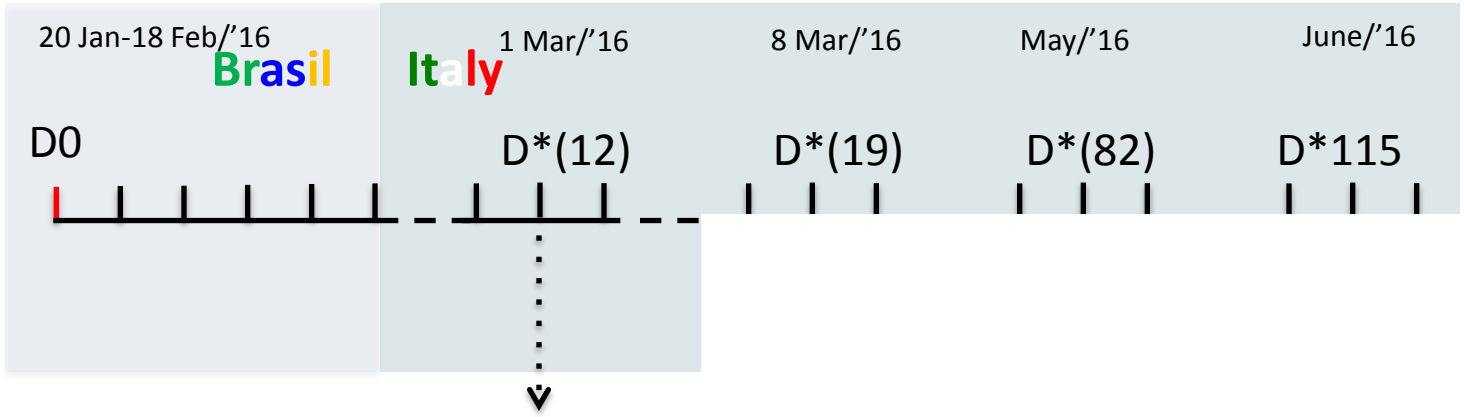
6 September 2016

WHO/ZIKV/MOC/16.1 Rev.3

World Health Organization

[c] The recommendation on adoption of safer sex practices or considering abstinence for 6 months is a conservative measure. Although documented cases have shown persistence of ZIKV RNA in semen longer than the 62 days (and up to 188 days) adopted for the calculation of 6 months (3 times 62 days), we are maintaining the recommendation given 1) that sexual transmission of ZIKV has not been reported after 41 days of symptom onset; 2) the limited data on the duration of ZIKV in semen; and 3) the lack of knowledge on whether ZIKV is infectious after it is found in semen following a long period after symptom onset (24 days is the maximum period up to which the virus has been cultured).

Partner B
Timeline infection and virological data



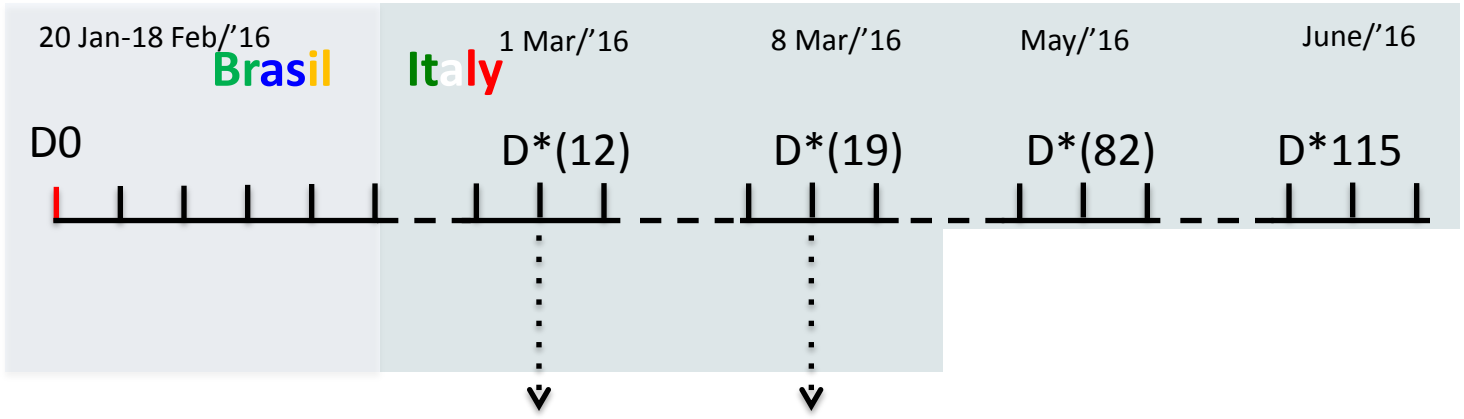
Anti ZIKV IgM (IFA)	**1:80**
Anti ZIKV IgG (IFA)	**1:320**
ZIKV RT-PCR serum	**Neg**
ZIKV RT-PCR saliva	**Neg**
ZIKV RT-PCR urine	**Neg**
ZIKV RT-PCR semen	**Pos (27.7)§**

*Asymptomatic subject; days from last possible exp

IFA: indirect immunofluorescence assay; RT-PCR: rev

§Threshold cycle in parenthesis;

Partner B
Timeline infection and virological data



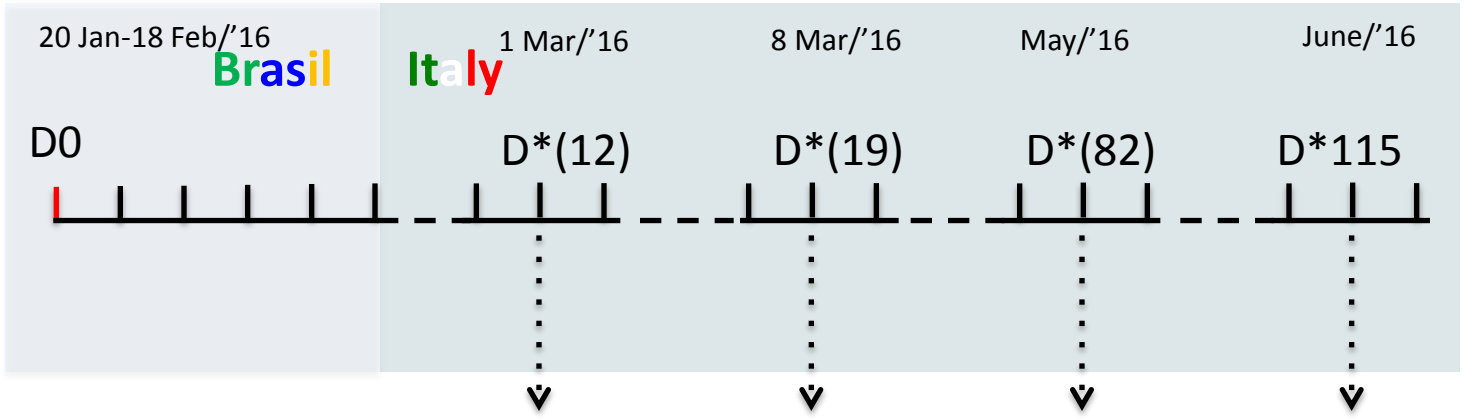
Anti ZIKV IgM (IFA)	**1:80**	**1:40**
Anti ZIKV IgG (IFA)	**1:320**	**1:640**
ZIKV RT-PCR serum	**Neg**	**Neg**
ZIKV RT-PCR saliva	**Neg**	**Neg**
ZIKV RT-PCR urine	**Neg**	**Neg**
ZIKV RT-PCR semen	**Pos (27.7)§**	**Pos (42.0)**

*Asymptomatic subject; days from last possible exposure

IFA: indirect immunofluorescence assay; RT-PCR: reverse transcriptic

§Threshold cycle in parenthesis;

Partner B
Timeline infection and virological data



Anti ZIKV IgM (IFA)	**1:80**	**1:40**	**1:20**	**1:20**
Anti ZIKV IgG (IFA)	**1:320**	**1:640**	**1:640**	**1:320**
ZIKV RT-PCR serum	**Neg**	**Neg**	**Neg**	**NT**
ZIKV RT-PCR saliva	**Neg**	**Neg**	**Neg**	**NT**
ZIKV RT-PCR urine	**Neg**	**Neg**	**Neg**	**NT**
ZIKV RT-PCR semen	**Pos (27.7)§**	**Pos (42.0)**	**Neg**	**Neg**

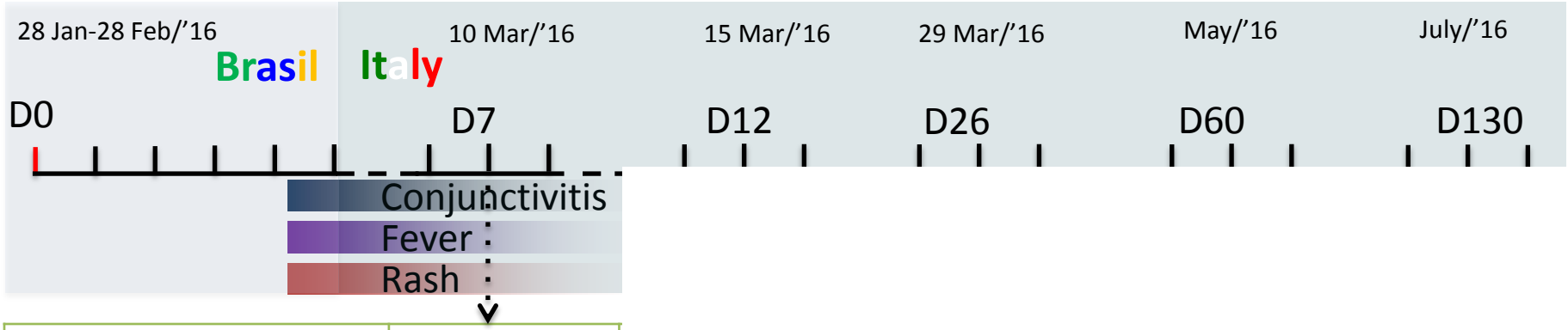
*Asymptomatic subject; days from last possible exposure

IFA: indirect immunofluorescence assay; RT-PCR: reverse transcription Polymerase Chain Reaction; NT: not tested

§Threshold cycle in parenthesis;

Partner C (vaccinated for Yellow Fever)

Timeline infection and virological data



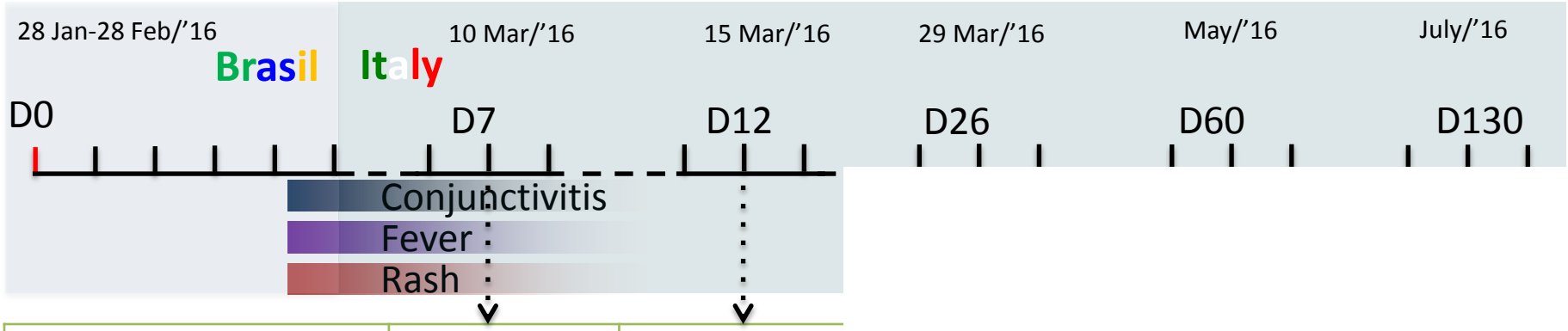
Anti ZIKV IgM (IFA)	**weak pos.**
Anti ZIKV IgG (IFA)	**1:80**
Anti YFV IgM (IFA)	**<1:20**
Anti YFV IgG (IFA)	**1:320**
Anti DENV IgM (IFA)	**<1:20**
Anti DENV IgG (IFA)	**1:80**
ZIKV RT-PCR serum	**Neg**
ZIKV RT-PCR saliva	**Pos (34.2)§**
ZIKV RT-PCR urine	**Neg**
ZIKV RT-PCR semen	**Neg**

IFA: indirect immunofluorescence assay; NT: r

§Threshold cycle in parenthesis;

Partner C (vaccinated for Yellow Fever)

Timeline infection and virological data



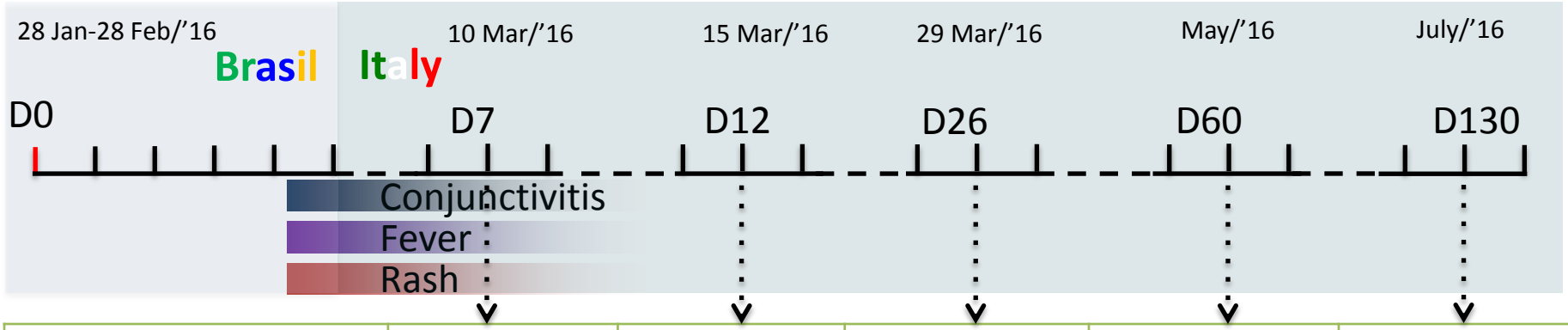
Anti ZIKV IgM (IFA)	**weak pos.**	**1:80**
Anti ZIKV IgG (IFA)	**1:80**	**1:320**
Anti YFV IgM (IFA)	**<1:20**	**<1:20**
Anti YFV IgG (IFA)	**1:320**	**1:80**
Anti DENV IgM (IFA)	**<1:20**	**<1:20**
Anti DENV IgG (IFA)	**1:80**	**1:80**
ZIKV RT-PCR serum	**Neg**	**Neg**
ZIKV RT-PCR saliva	**Pos (34.2)§**	**Neg**
ZIKV RT-PCR urine	**Neg**	**Pos (27.5)**
ZIKV RT-PCR semen	**Neg**	**Neg**

IFA: indirect immunofluorescence assay; NT: not tested

§Threshold cycle in parenthesis;

Partner C (vaccinated for Yellow Fever)

Timeline infection and virological data

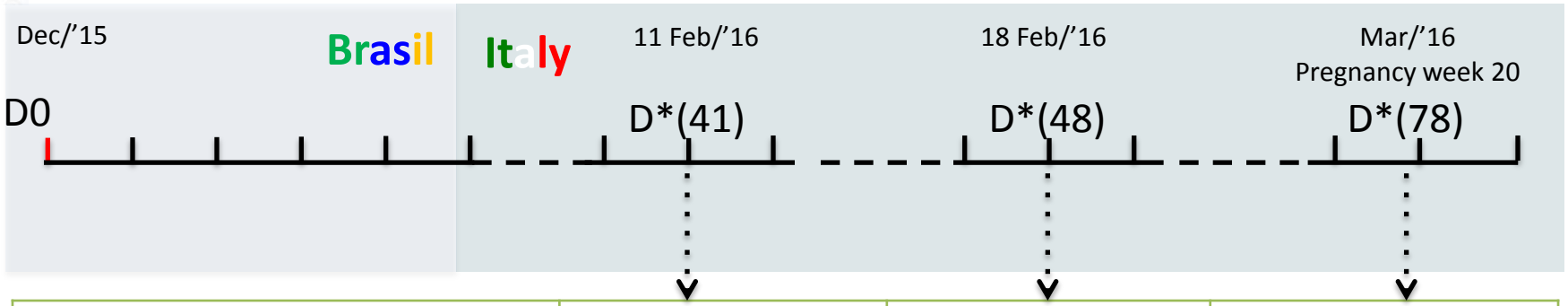


Anti ZIKV IgM (IFA)	**weak pos.**	**1:80**	**1:80**	**1:40**	**<1:20**
Anti ZIKV IgG (IFA)	**1:80**	**1:320**	**1:128**	**1:1280**	**1:2560**
Anti YFV IgM (IFA)	**<1:20**	**<1:20**	**NT**	**NT**	**NT**
Anti YFV IgG (IFA)	**1:320**	**1:80**	**NT**	**NT**	**NT**
Anti DENV IgM (IFA)	**<1:20**	**<1:20**	**NT**	**NT**	**NT**
Anti DENV IgG (IFA)	**1:80**	**1:80**	**NT**	**NT**	**NT**
ZIKV RT-PCR serum	**Neg**	**Neg**	**Neg**	**Neg**	**NT**
ZIKV RT-PCR saliva	**Pos (34.2)§**	**Neg**	**Neg**	**Neg**	**NT**
ZIKV RT-PCR urine	**Neg**	**Pos (27.5)**	**Neg**	**Neg**	**NT**
ZIKV RT-PCR semen	**Neg**	**Neg**	**Pos (28.3)**	**Pos (31.7)**	**Neg**

IFA: indirect immunofluorescence assay; NT: not tested

§Threshold cycle in parenthesis;

Asymptomatic pregnant woman with undetermined recent flavivirus infection virological data



Anti ZIKV IgM (IFA)	**<1:20**	**<1:20**	**<1:20**
Anti ZIKV IgG (IFA)	**1:160**	**1:320**	**1:2560**
Anti ZIKV MNT	**1:10**	**1:10**	**1:10**
Anti DENV IgM (IFA)	**<1:20**	**<1:20**	**<1:20**
Anti DENV IgG (IFA)	**1:320**	**1:320**	**1:1280**
Anti DENV MNT	**1:10**	**1:10**	**1:10**
ZIKV RT-PCR serum	**Neg**	**Neg**	**NT**
ZIKV RT-PCR Urine	**Neg**	**Neg**	**NT**
ZIKV RT-PCR Amniotic fluid	**NT**	**NT**	**Neg**
Anti ZIKV IgM Amniotic fluid	**NT**	**NT**	**<1:2**
Anti ZIKV IgG Amniotic fluid	**NT**	**NT**	**1:10**

* Asymptomatic subject; days from last possible exposure

IFA: indirect immunofluorescence assay; MNT: microneutralization test; NT: not tested

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JAMA | Original Investigation

Birth Defects Among Fetuses and Infants of US Women With Evidence of Possible Zika Virus Infection During Pregnancy

Margaret A. Honein, PhD; April L. Dawson, MPH; Emily E. Petersen, MD; Abbey M. Jones, MPH; Ellen H. Lee, MD; Mahsa M. Yazdy, PhD; Nina Ahmad, MD; Jennifer Macdonald, MPH; Nicole Evert, MS; Andrea Bingham, PhD; Sascha R. Ellington, MSPH; Carrie K. Shapiro-Mendoza, PhD; Titilope Oduyebo, MD; Anne D. Fine, MD; Catherine M. Brown, DVM; Jamie N. Sommer, MS; Jyoti Gupta, MPH; Philip Cavicchia, PhD; Sally Slavinski, DVM; Jennifer L. White, MPH; S. Michele Owen, PhD; Lyle R. Petersen, MD; Coleen Boyle, PhD; Dana Meaney-Delman, MD; Denise J. Jamieson, MD; for the US Zika Pregnancy Registry Collaboration

Among 442 completed pregnancies, 6% overall had a fetus or infant with evidence of a ZIKV-related birth defect, primarily microcephaly with brain abnormalities.

Among women with possible Zika virus infection during the first trimester, 11% had a fetus or infant with a birth defect.

The proportion of fetuses or infants with birth defects by maternal symptom status was 6% for asymptomatic women and 6% for symptomatic women

Conclusions

- Expanded testing opportunity implemented since February 2016
- Expanded testing strategy identified 3 ZIKV mild/asymptomatic cases which would have been missed outside the context of prenatal testing for exposed women
- Challenging diagnosis in women with previous flavivirus infection (IgG); one case underwent amniocentesis
- Weak IgM response in pregnant women (as for CMV, rubella, etc)
- Prolonged viral shedding in the semen highlights the important role of partner testing in order to prevent sexually transmitted ZIKV infection.
- Healthcare services should consider ZIKV for family planning in couples with history of travel in areas with ongoing transmission
- Based on the knowledge opportunity offered by the ZIKV model, continued support of these activities will be critical in curtailing potential adverse outcomes related to evolving epidemics