Arboviroses: des virus à risque chez les femmes enceintes

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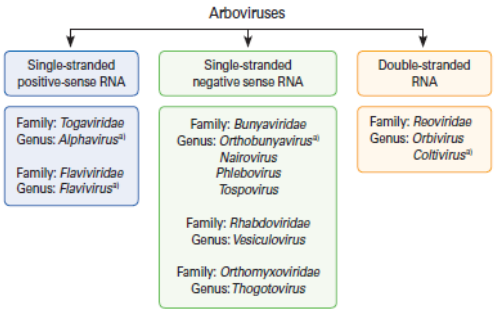
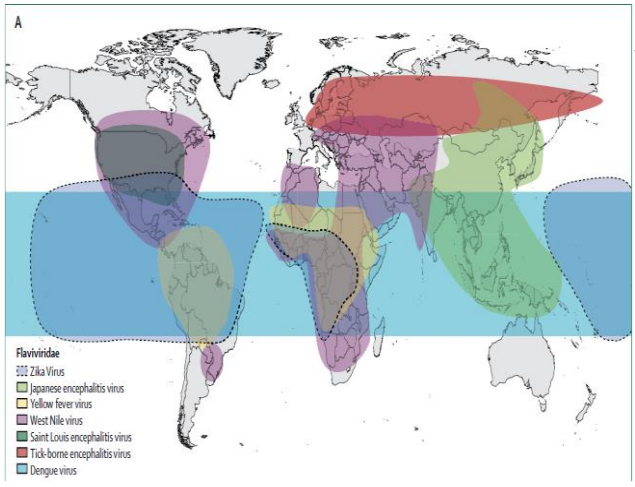
Les arboviroses

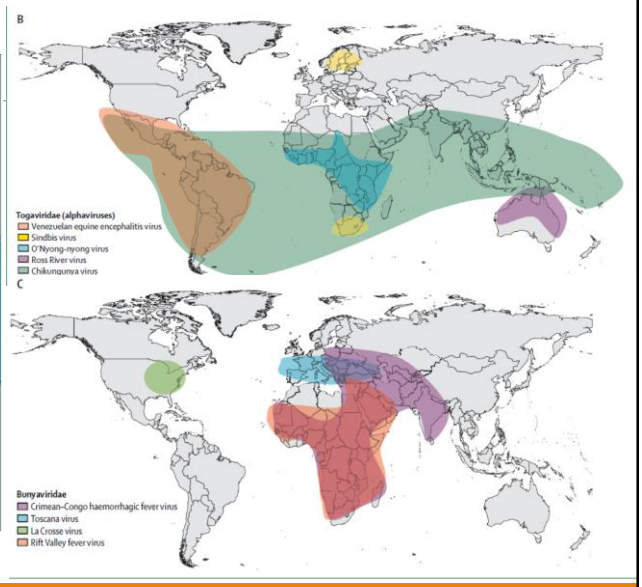
- Arbovirus= arthropode-borne virus
- >500 espèces et >100 pathogènes pour l'homme
- 6 familles
- vecteurs: moustiques+++ , tiques, phlébotomes, culicoïdes



Yun Go, Clin Exp Vacc Res 2014

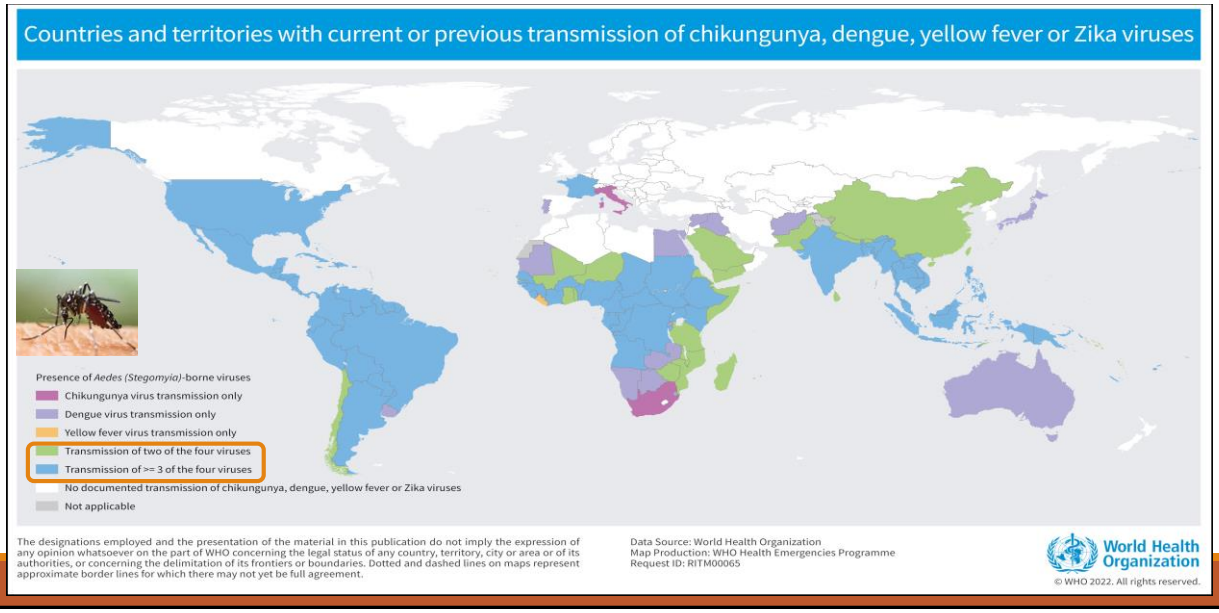
Répartition géographique: mondiale!





Charlier et col, Lancet child 2017

Répartition géographique: co-circulation



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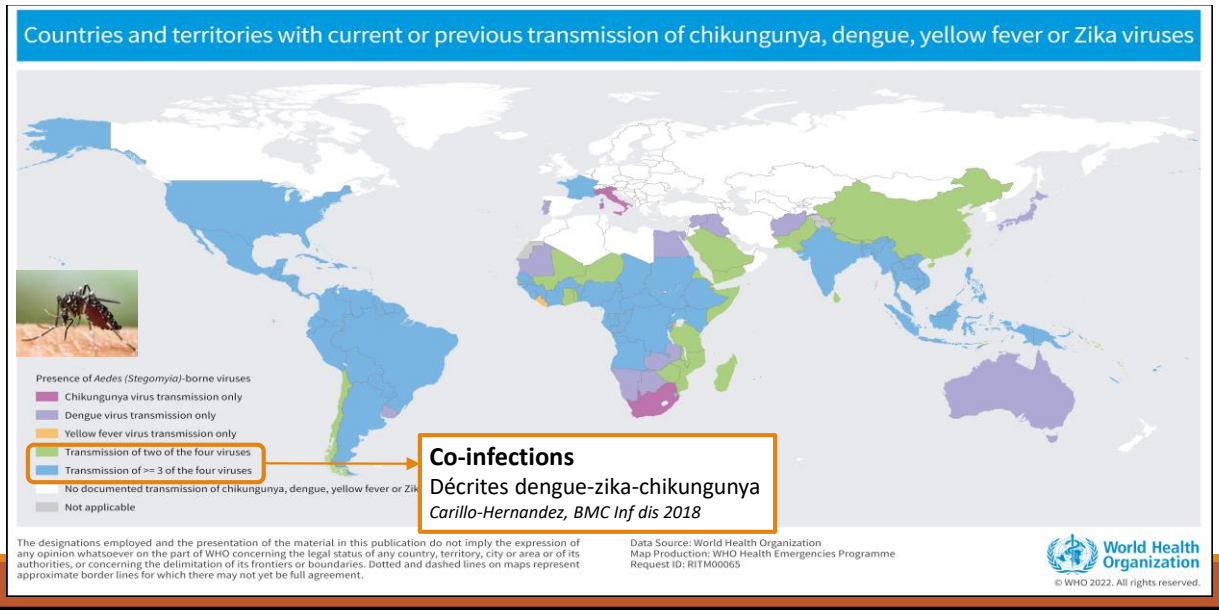

Co-infections
Décrites dengue-zika-chikungunya
Carillo-Hernandez, BMC Inf dis 2018

Grossesse et moustiques?

Mère Nature

On sait qu'**une femme enceinte attire davantage les moustiques** (joie !). La grossesse entraîne des **modifications hormonales** et généralement, cela provoque une **hausse de la température corporelle**. Ce qui veut dire **plus de transpiration** et donc, intérêt accru des moustiques. Ils repèrent aussi le changement de l'odeur corporelle et **l'exhalation de CO^2** plus importante d'une femme enceinte.

magicmaman

Tout d'abord, si vous avez l'impression d'avoir plus de piqûres de moustiques depuis votre grossesse, vous n'êtes pas paranoïaque. "C'est une question de métabolisme, il augmente chez les femmes enceintes, surtout à partir du quatrième mois", nous explique Stéphane Gayet. "**La température corporelle augmente**, ainsi que **la ventilation pulmonaire**. Les moustiques sont surtout attirés par la chaleur et le gaz carbonique. Aussi, il semblerait que l'hyper production d'hormones sexuelles participe à cette

passionSanté

Pourquoi les femmes enceintes attirent-elles les moustiques ?

NEWS Des études ont montré que les femmes enceintes souffrent deux fois plus de piqûres de moustiques que celles qui ne le sont pas. Comment expliquer cela ?

Il y a plusieurs raisons : les femmes enceintes transpirent davantage, leur température corporelle augmente, leur odeur corporelle change et elles exhalent plus de dioxyde de carbone.

actu.fr

des études ont montré que les moustiques avaient une préférence pour **les gens à forte corpulence,** parce qu'ils produisaient plus de CO2. Selon ces précédentes études, les moustiques seraient aussi plus attirés par les **buveurs de bière** et les **femmes enceintes.**

Grossesse et moustiques?

- Études montrant sur-risque de piqures durant la grossesse par anophèle
  Lindsay, Lancet 2000
  Ansel, Trans R Soc Trop Med Hyg 2002
  Himeidan, Am trop Med Parasitol 2004
- Effet sueur, composition microbiote cutané, odeurs/composés volatils
  Dormont, J Chem Ecol 2021
  Omolo, PloS One 2021
  Busula, Med Vet Entomol 2017

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Grossesse et moustiques?

Molécules ou substances actives	Concentrations usuelles [concentration efficace min]	Arthropodes ciblés (par ordre alphabétique)	Avantages	Inconvénients	Enfants * (concentrations)	Femmes enceintes (concentrations)
Produits disposant d'une AMM (présence du numéro d'AMM sur l'étiquette) et un RCP						
DEET (N1,N-diéthyl-m-toluamide)	30 à 50 % [10 à 25 %]	Aoûtats, Culicoides, Moustiques, Phlébotomes, Simulies, Tiques dures.	Recul quant à son utilisation.	Huileux. Altère les plastiques. Irritant pour les yeux.	10 % entre 1 et 2 ans 30 % et plus à partir de 2 ans	≤ 30 % Uniquement en zone à risque élevé
IR3535 (N-acétyl-N-butyl-β-alaninate d'éthyle)	20 à 35 % [10-20 %]	Aoûtats, Culicoides, Moustiques, Phlébotomes, Stomoxes, Tiques dures.	Faible odeur. Non huileux. N'altère pas les plastiques. Efficace contre les tiques.	Durée d'efficacité sur *Anopheles* parfois moindre que le DEET aux concentrations ≤ 20 %	10 à 20 % entre 6 mois et 2 ans 35 % à partir de 2 ans	≤ 20 %
Produits autorisés au niveau européen, mais sans produit avec AMM en France						
Icaridine ou picaridine ou KBR3023 (Carboxylate de Sec-butyl 2-(2-hydroxyéthyl)pipéridine-1)	20 à 25 % [10-20 %]	Aoûtats, Culicoides, Mouches piqueuses (glossines et taons, ...), Moustiques, Puces, Tiques dures.	Large spectre d'activité. N'altère pas les plastiques. Faible odeur.	Pas aussi efficace que le DEET contre les tiques, certaines anophèles et les culicoides	10 % à 25 % partir de 24 mois	≤ 20 %
Produits en cours d'évaluation au niveau européen						
Huile d'*Eucalyptus citriodora*, hydratée, cyclisée (produit naturel, le PMD ou para-menthane-3,8 diol étant un produit de synthèse)**	10 à30 %	Culicoides, Mouches piqueuses, Moustiques, Tiques dures.	Large spectre d'activité.	Evaluation partielle, Moindre durée d'efficacité Forte odeur, Très irritant pour les yeux	Pas chez les enfants de moins de 3 ans***	≤ 10 %

Infections et grossesse

- **Tolérance immunitaire maternelle**
  - Susceptibilité accrue à certains agents pathogènes intracellulaires, notamment les virus, les bactéries intracellulaires et les parasites.
- **Passage transplacentaire des pathogènes**
  - Fœtopathies infectieuses congénitales
  - Séquelles selon le tropisme de l'agent pathogène
- **Modification physiologique de l'hémodynamique maternelle**
  - Augmentation de la fréquence cardiaque et de la consommation d'oxygène
  - Diminution de la capacité pulmonaire

Impact d'une infection
- Sur la mère
- Sur la grossesse/foetus
- Sur le bébé

adapté de Pr O Picone

Quels risques?

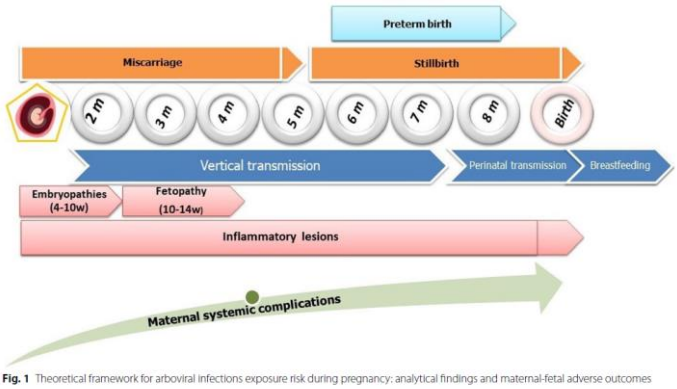

Fig. 1 Theoretical framework for arboviral infections exposure risk during pregnancy: analytical findings and maternal-fetal adverse outcomes

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Fausses-couches
Mort in utero
Prématurité

PPAG
Infections in utero
Malformations foetales
Infections péri et néo-natales

Infection maternelle sévère, décès

Quels risques?

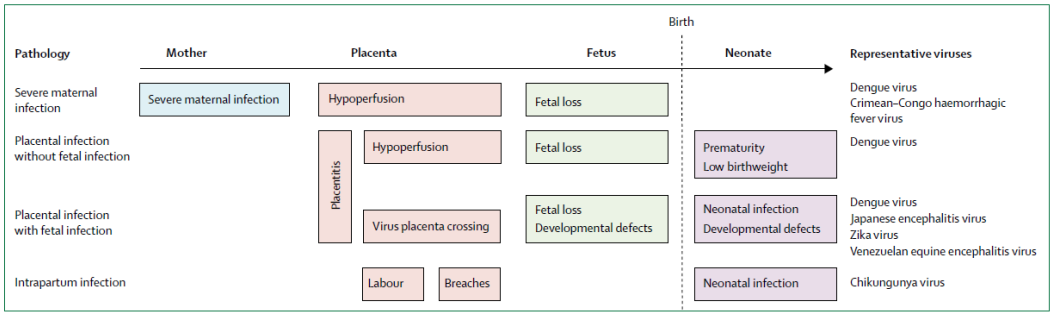

Figure 2: Patterns of pathophysiological events associated with adverse fetal or neonatal outcomes

Charlier et col, Lancet child 2017

Types d'atteintes en cas d'arbovirose

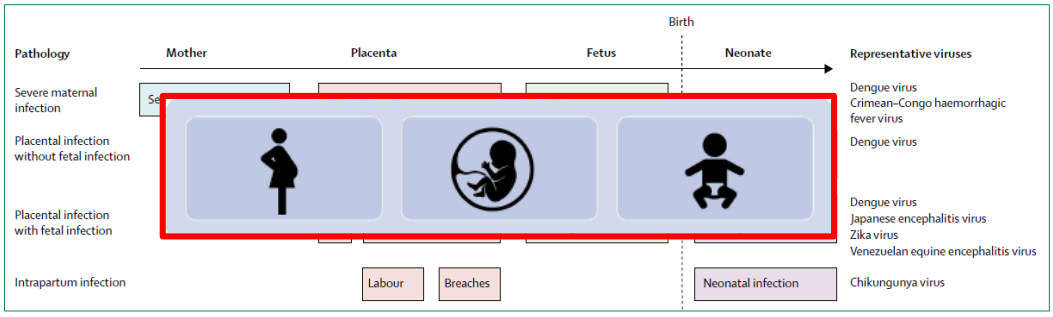

Figure 2: Patterns of pathophysiological events associated with adverse fetal or neonatal outcomes

Charlier et col, Lancet child 2017

Arboviroses et grossesse

	Severe maternal complication	Malformation (teratogenic)	Miscarriage	Stillbirth	Premature deliveries	Neonatal severe infection	Neonatal neurodevelopmental and Neurosensory Alterations	Long-term neurodevelopmental delays occurred
Zika virus	Rare	●	●	●	–	●	●	●
Dengue Virus	●	–	●	●	●	●	–	–
Chikungunya virus	Rare	–	●	●	●	●	●	●
Venezuelan Equine Encephalitis Virus	Rare	●	●	●	●	No data	●	No data
West Nile Virus	●	●	●	–	–	●	●	–
Rift Valley fever virus	●	No data	●	●	–	●	No data	–
Yellow fever virus	●	–	No data	No data	No data	●	No data	No data
Japanese encephalitis virus	●	No data	●	No data	No data	●	No data	No data
	● Documented risk		● Suspected risk	–	Assessed not documented			

Fig. 2 Fetal and neonatal consequences of arboviral infections during pregnancy

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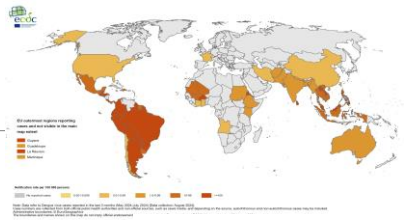
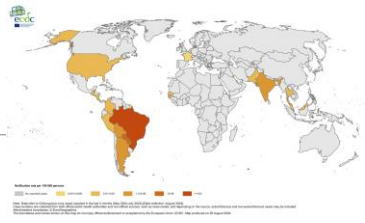
Focus sur la dengue



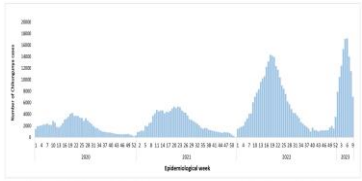
- OMS: 13M cas et 8500 décès rapportés depuis début 2024
- Estimation entre 100 et 400M infections annuelles
- 50% population mondiale exposée
- Grossesse
  - Formes sévères mère avec sur-mortalité maternelle OR ≈ 4
  - Hémorragies péri-partum
  - FC, mort in utero, mort néo-natale OR ≈ 3
  - Prématurité, PPAG OR ≈ 1,5
  - Nné: Ac maternels, nouvel épisode + grave

Howard-Jones Microorganism 2023
Contopoulos-Ioannidis, PLOS Neg Trop Dis 2018
Brar, Arch Gyn Obst 2021
Paixiao, Lancet Inf Dis 2016

Focus sur le chikungunya



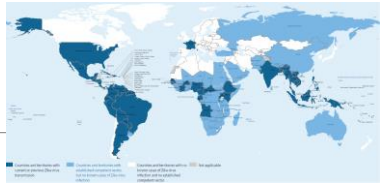
- OMS 5M cas rapportés depuis 2015, 100 pays
- Reprise circulation en Amérique du Sud depuis 2022 et intensification en 2023 et en 2024
- Grossesse:
  - Infections néo-natales sévères: méningo-encéphalites, CIVD, hémorragies…
  - Transmission verticale: impact++en périnatal
  - FC, prématurité faibles



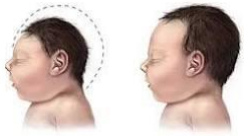
Source: PAHO/WHO Health Information Platform for the Americas (PLISA per its acronym in Spanish) as provided by Ministries and Institutes of Health of the countries and territories of the Region of the Americas. Washington DC: PAHO.

Hcini, Trop Dis Travel Med 2024
Silveira-Faria, Braz J Inf Dis 2024
Musso, NEJM 2018
Pomar, BMJ 2019

Focus sur le zika



- Amérique du Sud reste le 1er continent touché,
- même si circulation en baisse depuis 2017
- Transmission décrite Asie et Afrique
- Grossesse:
  - « infection congénitale dévastatrice »
    - Plus infection précoce durant la grossesse + transmission et +gravité
    - Perte fœtale ≈7-14%
    - Atteintes neuros ≈15-30%: microcéphalies, calcifications intra-craniennes,ventriculomégalies….
  - Nné: Syndrome Zika congénital
    - Microcéphalies, anomalies oculaires, surdité, convulsions…
    - Impact sur son développement



Howard-Jones, Microorganism 2023
Alvarado-Domenech, J Pediat 2022
Musso, NEJM 2018
Pomar, BMJ 2019

Sites de détection et transmission:
ce qui est corrélé…ce qui est documenté

Table 2 Site of detection of arboviruses in maternal, fetal annexes, and in different neonatal samples according to virus type

	Site of detection of RNA		
Virus	**Mothers**	**Fetal annexes**	**Fetus or neonates**
ZIKV	Saliva, urine, blood (whole blood, serum, plasma), anal fluid, cervical mucus, vaginal fluid, breast milk, solid organ transplantation, CSF	Amniotic fluid, placenta, membranes, umbilical cord	Cord blood, urine, neonatal blood, CSF, brain
DENV	Breast milk, seminal fluid, saliva, urine, blood, solid organ transplantation, CSF	Amniotic fluid, placenta, umbilical cord	Neonatal blood, urine
JEV	No data	Placenta	Brain, liver
WNV	Blood, serum, urine, brain, CSF, milk	Placenta, umbilical cord	Blood
YFV	Blood	No data	Serum samples
CHIKV	Breast milk, seminal fluid, saliva, urine, blood, amniotic fluid, placenta, membranes, CSF	Amniotic fluid, placenta	Blood
VEEV	Blood, throat swabs, human serum	Amniotic fluid	Brain tissue from aborted and stillborn human fetuses
OROV	blood	No data	No data

The identification of the virus at a site does not mean that it can be considered as a possible source of contamination (e.g., *ZIKV* has been found in breast milk without being a confirmed mode of neonatal contamination)

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Table 1 Summary of the current state of knowledge of mother-to-child transmission of arboviruses

	Vertical transmission during pregnancy	Perinatal transmission	Breastfeeding
ZIKV	Documented in first, second trimester, and third trimester	rare	Not documented
DENV	Documented: Low incidence	Documented	Not documented
CHIKV	Documented: Low incidence	Documented with intrapartum viremia	Not documented
VEEV	Documented: Rate unknown	No data	Not documented
OROV	No data	No data	No data
YFV	No data	Documented: Rate unknown	Not documented
WNV	Documented rare	Suspected	Not documented
RVFV	Documented: Unknown incidence	Documented: Rare	Not documented
JEV	Documented: Rare	Documented: Rare	No data

Vertical transmission primarily refers to transmission during pregnancy, while perinatal transmission encompasses the period around the time of childbirth and may include labor, delivery, and breastfeeding

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Sites de détection et transmission:
ce qui n'est pas clairement corrélé…

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case-reports de transmission DENG, WNV via allaitement?
Desgraupes, Viruses 2021, MMWR 2002

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Sites de détection et transmission:
ce qui n'est pas connu…(pas encore)

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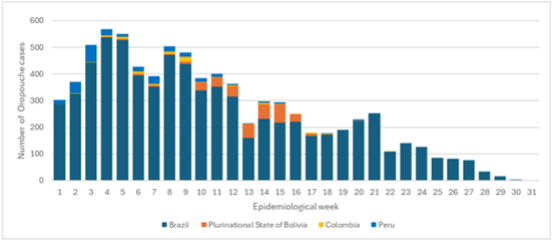
Disease Outbreak News

Oropouche virus disease - Region of the Americas

23 August 2024



Brazil has reported one fetal death and one miscarriage in the state of Pernambuco, as well as four cases of newborns with microcephaly, identified through retrospective studies in the states of Acre and Pará indicating possible cases of vertical transmission of OROV infection and their consequences.[2] Three additional possible cases of vertical transmission are being investigated in the state of Pernambuco. Despite the evidence of vertical transmission of OROV (polymerase chain reaction [PCR] positivity on tissues from pregnancy loss reported), it cannot be concluded that OROV is the cause of the fetal deaths, and investigations are still ongoing.

As of 30 July 2024, five cases of possible vertical transmission have been identified in Brazil: four cases of stillbirth and one case of spontaneous abortion in the state of Pernambuco, as well as four cases of newborns with microcephaly in the states of Acre and Pará. The investigations are ongoing(1).

Cuba reported its first Oropouche outbreak in June 2024 with 500 confirmed cases and over 10,000 suspected cases according to PAHO by September 23. While this outbreak did not lead to severe cases, it marked an unprecedented geographic expansion of the virus. In the Dominican Republic, 33 cases, including 3 deaths, have been confirmed to date, according to PAHO as of September 23.

Transmission sexuelle?

Table 1. Arboviruses with the potential to be sexually transmitted between humans as determined by apparent sexually acquired cases or the presence of the virus in the reproductive tract or sexual secretions.

Virus	Number of Reported Cases Suspected to have Occurred by Sexual Transmission	Evidence of the Virus in the Human Reproductive Tract or Sexual Secretions			References
		Virus Isolation	Antigen Detection	Nucleic Acid Detection	
Bunyavirales					
Crimean-Congo hemorrhagic fever virus	5 [a]	NT	NT	+	[19–23]
Heartland virus	0	NT	+	NT	[28]
Rift Valley fever virus	0	–	NT	+	[32]
Severe fever with thrombocytopenia syndrome virus	0	NT	NT	+	[30]
Flaviviridae					
Dengue virus	2	NT	NT	+	[48–51]
West Nile virus	1 [a]	–	+	+	[52–54]
Yellow fever virus	0	NT	NT	+	[55]
Zika virus	Many	+	+	+	[4,5,7–14,47,56–71]
Togaviridae					
Chikungunya virus	0	NT	NT	+	[72]

NT, not tested; +, positive; –, negative. [a] Occurred in an endemic region, so the virus could have been acquired by vector-borne transmission.

Blitvich et al, Viruses 2020

Transmission sexuelle?

Table 1. Arboviruses with the potential to be sexually transmitted between humans as determined by apparent sexually acquired cases or the presence of the virus in the reproductive tract or sexual secretions.

Virus	Number of Reported Cases Suspected to have Occurred by Sexual Transmission	Evidence of the Virus in the Human Reproductive Tract or Sexual Secretions			References
		Virus Isolation	Antigen Detection	Nucleic Acid Detection	
Bunyavirales					
Crimean-Congo hemorrhagic fever virus	5 [a]	NT	NT	+	[19–23]
Heartland virus	0	NT	+	NT	[28]
Rift Valley fever virus	0	–	NT	+	[32]
Severe fever with thrombocytopenia syndrome virus	0	NT	NT	+	[30]
Flaviviridae					
Dengue virus	2	NT	NT	+	[48–51]
West Nile virus	1 [a]	–	+	+	[52–54]
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Blitvich et al, Viruses 2020

agence de la biomédecine

Recommandations professionnelles

Pour la prise en charge en assistance médicale à la procréation (AMP), en préservation de la fertilité et en don de gamètes

des patients exposés au risque d'infection par le virus Zika

Nouvelle version du 9 février 2018 (V5)

Haut Conseil de la santé publique

AVIS

relatif aux mesures de prévention des risques liés au virus Zika et au virus de la dengue dans le domaine de l'assistance médicale à la procréation (AMP).

28 avril 2022

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Sur la base des données de la bibliographie et des très rares cas rapportés de transmission de la dengue par voie sexuelle, il n'y a pas de recommandation particulière à envisager pour les personnes ayant recours à une AMP. En effet, aucun risque n'a été rapporté à ce jour chez des couples exposés en zone de circulation active de la dengue (Ile de La Réunion ou Antilles).

Transmission sexuelle?

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Replication-Competent Oropouche Virus in Semen of Traveler Returning to Italy from Cuba, 2024. Castilletti C, Huits R, Mantovani RP, Accordini S, Alladio F, Gobbi F.

Published in *Emerg Infect Dis* on 7 octobre 2024.
https://doi.org/10.3201/eid3012.241470

A febrile man in Italy who had traveled to Cuba in July 2024 was diagnosed with Oropouche fever. Reverse transcription PCR detected prolonged shedding of Oropouche virus RNA in whole blood, serum, urine, and semen. Sixteen days after symptom onset, replication-competent virus was detected in semen, suggesting risk for sexual transmission.

Blitvich et al, Viruses 2020

Arboviroses en voyage…mais pas seulement…

	Geographical area	Main vectors	Maternal risk	Antenatal consequences of mother-to-child transmission	Perinatal consequences of mother-to-child transmission
Crimean-Congo haemorrhagic fever virus (CCHFV)	Europe (southeast and eastern), Africa, Middle East, countries south of the 50th parallel	Midge (*Culicoides* spp); tick (>30 species involved)	Documented increased risk of severe infection: increased mortality (34%[48])	Transmission documented, incidence unknown; four miscarriages at 4–19 weeks of gestation (fetuses untested);[48] stillbirths with maternal death[48,49]	Documented, incidence unknown; one case of documented fatal neonatal infection[50]
Tahyna virus (TAHV)	Europe, Africa, Asia	Mosquito (*Culex* spp)	No data	No data	No data
Toscana virus (TOSCV)	Europe	Sandfly (*Phlebotomus* spp)	No data	No data	No data
Tick-borne encephalitis virus (TBEV)	Northern Europe and northern Asia (in a belt extending from eastern Europe to Japan)	Tick (*Ixodes* spp)	peu cas décrits formes sévères poss	Prématurité transmission verticale non détectée	No data
West Nile virus (WNV; also known as Kunjin virus in Oceania)	Worldwide, most prevalent in America and Africa, low prevalence in Europe	Mosquito (*Culex* spp)	+sévère méningoencéphalites	Rare congenital abnormalities (~4%): lissencephaly, meningoencephalitis, cerebral atrophy, chorioretinitis, coarctation of the aorta	Uncertain; two cases with encephalitis that developed 6–10 days after birth (maternal symptoms 21–6 days before delivery, no documentation of viral infection at birth);[35] one case with transient rash at birth and positive IgM 1 month later (maternal symptoms at birth)[35]

Charlier et col, Lancet child 2017
Bjonholm, NMNI 2022
Velay, EID 2023
OTIS, NIH 2023
Howard-Jones, Microorganism 2023

En conclusion arboviroses et grossesse

- Une problématique émergente
- Il n'y a plus de région du monde épargnée
- Risques quelque soit le terme de la grossesse
- pour la mère/pour le nouveau-né qui vivent en zone d'endémie
- pour la femme enceinte qui voyage et son partenaire
- Les données sont évolutives….
- …au fur et à mesure des épidémies


Merci pour
votre attention