


## Maternal-fetal infections: Why do they matter?

Caroline Charlier and Marc Lecuit 

Institut Pasteur, Biology of Infection Unit, Paris, France; Inserm U1117, Paris, France; French National Reference Center and WHO Collaborating Center for Listeria, Institut Pasteur, Paris, France; Necker-Enfants Malades University Hospital, Department of Infectious Diseases and Tropical Medicine, Institut Imagine, APHP; Université de Paris, Paris, France

The encounter of a pathogen and a pregnant host can happen at various steps of pregnancy and lead to a vast array of outcomes. Maternal infection can be more severe than in the general population, as reported for influenza [1], measles [2–4], dengue 5, or malaria [6]. Fulminant maternal infection may end pregnancy, as reported for Crimean-Congo hemorrhagic fever [7]. Some pathogens, such as *Listeria monocytogenes* and *Toxoplasma gondii*, are able to cross the placental barrier, replicate in the placenta and eventually infect the fetus [8,9]. The placental barrier may also be crossed at the time of delivery, and placental breaches allow maternal/fetal blood exchanges, leading to the vertical transmission of pathogens, such as Hepatitis B virus, and chikungunya virus [10]. At the fetal level, microbial tropism for fetal cells may account for specific teratogenic consequences, as recently evidenced by Zika virus-associated neuropathology [11]. The most successful medical intervention to tackle maternal-fetal infections and their dire consequences is the prevention of transmission, as controlling fetal infection once it is established is particularly challenging. In this respect, the history of how prevention of HIV congenital infection has been achieved is exemplary.

This “focus issue” aims at illustrating these issues with three major pathogens associated with maternal-fetal infections. Mysorekar *et al.* summarizes the scientific achievements achieved over the past 4 years regarding Zika virus, and present the current understanding of Zika’s neurotropism and its dramatic teratogenic consequences [11–14]. We detail the epidemiological and clinical features of maternal-fetal listeriosis and present its pathophysiology [8,9,15,16]. Finally, Blanche reviews the stunning achievements that led to the control of congenital HIV, which started in the mid-nineties when zidovudine was proven effective in reducing vertical infection, and continues with the ongoing efforts in screening and organizing the care of pregnant women at a global scale [17].

We hope that this “focus issue” which provides the readers with a targeted overview of maternal-fetal

infections will inspire clinicians and scientists interested in this important field to synergize the medical and scientific dimensions of their research.

### Disclosure statement

No potential conflict of interest was reported by the authors.

### ORCID

Marc Lecuit  <http://orcid.org/0000-0002-4491-1063>

### References

- [1] Rasmussen SA, Jamieson DJ, Bresee JS. Pandemic influenza and pregnant women. *Emerg Infect Dis.* 2008;14:95–100.
- [2] Atmar RL, Englund JA, Hammill H. Complications of measles during pregnancy. *Clin Infect Dis.* 1992;14:217–226.
- [3] Dyer I. Measles complicating pregnancy: report of 24 cases with three instances of congenital measles. *South Med J.* 1940;33:601.
- [4] Ogbuanu IU, Zeko S, Chu SY, et al. Maternal, fetal, and neonatal outcomes associated with measles during pregnancy: namibia, 2009–2010. *Clin Infect Dis.* 2014;58:1086–1092.
- [5] Machado CR, Machado ES, Rohloff RD, et al. Is pregnancy associated with severe dengue? A review of data from the Rio de Janeiro surveillance information system. *PLoS Negl Trop Dis.* 2013;7:e2217.
- [6] Nosten F, Rogerson SJ, Beeson JG, et al. Malaria in pregnancy and the endemicity spectrum: what can we learn? *Trends Parasitol.* 2004;20:425–432.
- [7] Charlier C, Beaudoin MC, Couderc T, et al. Arboviruses and pregnancy: maternal, fetal, and neonatal effects. *Lancet Child Adolesc Health.* 2017;1:134–146.
- [8] Lecuit M, Nelson DM, Smith SD, et al. Targeting and crossing of the human maternofetal barrier by *Listeria monocytogenes*: role of internalin interaction with trophoblast E-cadherin. *Proc Natl Acad Sci U S A.* 2004;101:6152–6157.

- [9] Disson O, Grayo S, Huillet E, et al. Conjugated action of two species-specific invasion proteins for fetoplacental listeriosis. *Nature*. 2008;455:1114–1118.
- [10] Gerardin P, Barau G, Michault A, et al. Multidisciplinary prospective study of mother-to-child chikungunya virus infections on the island of La Reunion. *PLoS Med*. 2008;5:e60.
- [11] Musso D, Ko AI, Baud D. Zika virus infection - after the pandemic. *N Engl J Med*. 2019;381:1444–1457.
- [12] Mysorekar IU, Diamond MS. Modeling Zika virus infection in pregnancy. *N Engl J Med*. 2016;375:481–484.
- [13] Liang B, Guida JP, Costa ML, et al. Host and viral mechanisms of congenital Zika syndrome. *Virulence*. 2019;10(1):768–775.
- [14] Gladwyn-Ng I, Cerdón-Barris L, Alfano C, et al. Stress-induced unfolded protein response contributes to zika virus-associated microcephaly. *Nat Neurosci*. 2018 Jan;21(1):63-71.
- [15] Charlier C, Perrodeau E, Leclercq A, et al. Clinical features and prognostic factors of listeriosis: the MONALISA national prospective cohort study. *Lancet Infect Dis*. 2017;17:510–519.
- [16] Charlier C, Disson O, Lecuit M. Maternal-neonatal listeriosis. *Virulence*. 2020;11(1):391–397.
- [17] Blanche S. Mini review: prevention of mother-child transmission of HIV: 25 years of continuous progress toward the eradication of pediatric AIDS? *Virulence*. 2020;11(1):14–22.