

Downloaded from UvA-DARE, the institutional repository of the University of Amsterdam (UvA)  
<http://hdl.handle.net/11245/2.45934>

---

File ID	uvapub:45934
Filename	amc2006.13.pdf
Version	unknown

---

SOURCE (OR PART OF THE FOLLOWING SOURCE):

Type	article
Title	Placental malaria and immunity to infant measles
Author(s)	S. Owens, G Harper, J. Amuasi, G. Offei-Larbi, J. Ordi, B.J. Brabin
Faculty	UvA: Universiteitsbibliotheek
Year	2006

FULL BIBLIOGRAPHIC DETAILS:

<http://hdl.handle.net/11245/1.426445>

---

*Copyright*

*It is not permitted to download or to forward/distribute the text or part of it without the consent of the author(s) and/or copyright holder(s), other than for strictly personal, individual use, unless the work is under an open content licence (like Creative Commons).*

---



## Placental malaria and immunity to infant measles

S Owens, G Harper, J Amuasi, G Offei-Larbi, J Ordi and B J Brabin

*Arch. Dis. Child.* 2006;91:507-508  
doi:10.1136/adc.2005.085274

---

Updated information and services can be found at:  
<http://adc.bmj.com/cgi/content/full/91/6/507>

---

*These include:*

### Rapid responses

You can respond to this article at:  
<http://adc.bmj.com/cgi/eletter-submit/91/6/507>

### Email alerting service

Receive free email alerts when new articles cite this article - sign up in the box at the top right corner of the article

---

### Topic collections

Articles on similar topics can be found in the following collections

[Other Infectious Diseases](#) (1577 articles)  
[Other Pediatrics](#) (1862 articles)

---

### Notes

---

To order reprints of this article go to:  
<http://www.bmjournals.com/cgi/reprintform>

To subscribe to *Archives of Disease in Childhood* go to:  
<http://www.bmjournals.com/subscriptions/>

## SHORT REPORT

## Placental malaria and immunity to infant measles

S Owens, G Harper, J Amuasi, G Offei-Larbi, J Ordi, B J Brabin

*Arch Dis Child* 2006;**91**:507–508. doi: 10.1136/adc.2005.085274

The efficiency of transplacental transfer of measles specific antibody was assessed in relation to placental malaria. Infection at delivery was associated with a 30% decrease in expected cord measles antibody titres. Uninfected women who received anti-malarial drugs during pregnancy transmitted 30% more antibody than those who received no antimalarial drugs.

Measles kills one million children each year, although a vaccine has been a component of the WHO Expanded Programme of Immunisation since 1985. The transplacental transfer of measles immunoglobulin G (IgG) from mother to fetus is a key component of infant immunity and partially determines the successful response to vaccination.<sup>1</sup> We previously reported that 10% of babies born to mothers with heavy *Plasmodium falciparum* infections failed to acquire protective levels of tetanus antibody, despite adequate maternal levels.<sup>2</sup> However, conflicting data on the effect of placental malaria on fetal acquisition of maternal antibodies were recently reported.<sup>3</sup> Malaria is known to disrupt the placental architecture, leading to a massive infiltration of monocytes, thickening of the basement membranes, and extensive fibrin deposition in the materno-fetal transfer membrane (syncytiotrophoblast).<sup>4</sup> Placental malaria is a leading cause of low birthweight in Africa, especially in primigravidae, who lose previously acquired immunity and become particularly susceptible to parasitisation.<sup>4</sup> We assessed the efficiency of transplacental transfer of measles antibody in 104 HIV negative mother-infant pairs living in Kumasi, Ghana, in relation to placental malaria and exposure to antimalarial drugs during pregnancy.

## METHODS

Consenting women who delivered vaginally at the Komfo Anokye Teaching Hospital, Kumasi, Ghana were enrolled between April and June 2003. Demographic and retrospective antenatal data were obtained by questionnaire and from the antenatal health card. Babies and placentae were weighed to the nearest 50 g. Hypertensive women and those delivering stillborn infants, multiple births, or infants with congenital abnormalities were excluded.

Maternal and cord blood samples (10 ml) were obtained by venepuncture at delivery. Placental biopsies were obtained from an off-centre position and stored in 10% formaldehyde in phosphate buffer. Paraffin embedded sections were stained with haematoxylin-eosin and examined by light microscopy under polarised light. Placental malaria infection was defined by the presence of parasites and malaria pigment into non-infected, active infection, and past infection.<sup>4</sup> Total IgG was assayed by laser nephelometry (Beckmann) and measles specific antibodies were measured by commercial enzyme linked immunoassay (ELISA). Anonymous HIV testing of maternal samples was undertaken by non-quantitative ELISA, and three HIV positive women were

excluded. Maternal and cord blood haemoglobin was measured on Hemocue®. Ethical approval was obtained from both participating institutions before fieldwork was undertaken.

Log<sub>10</sub> transformed cord measles antibody titres were regressed on log<sub>10</sub> transformed maternal titres, and placental histological classification fitted to the linear model.<sup>2,3</sup> The influence of key potential confounding variables (gestational age, birthweight, and maternal total IgG concentration) was assessed in a multivariate model. Ratios of cord:maternal antibody titres were calculated and then log<sub>10</sub> transformed, generating geometric mean transfer ratios as a measure of transfer efficiency.<sup>3</sup>

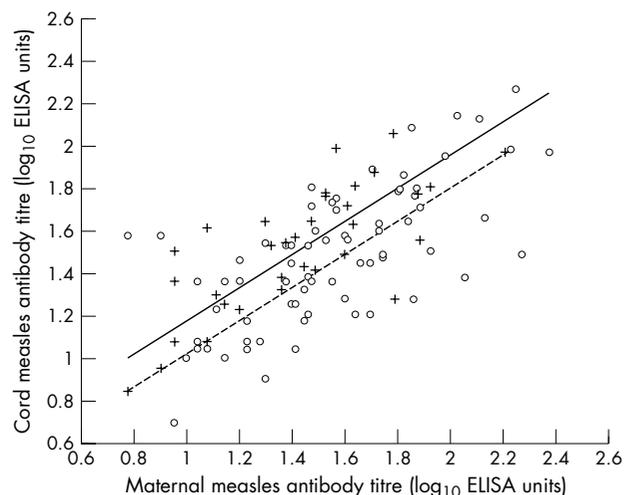
## RESULTS

Placental malaria infection was detected in 33 of 104 subjects (31.7%), active infection in 18 of 104 (17.3%), past infection in 15 of 104 (14.4%), and no infection in 71 of 104 (68.3%). Placental malaria prevalence among primiparae was 50% and among multiparae 20.3% (odds ratio = 3.92 (95% confidence interval (CI), 1.65 to 9.35)). There were no cases of cord parasitaemia. During pregnancy, 51.5% of subjects took antimalarial drugs for prophylaxis or for empirical malaria treatment. There were no significant differences in antenatal attendance, maternal age, parity, nutritional status (indicated by mid-upper arm circumference), and placental malaria prevalence at delivery between subjects who did and did not use antimalarial agents.

Placental infection was associated with reduced maternal haemoglobin (104 v 117 g/l;  $p < 0.001$ ), lower birthweight (2.85 v 3.08 kg;  $p = 0.019$ ), and increased geometric mean maternal total IgG (50.4 v 28.9 g/l;  $p < 0.001$ ). Placental infection was not significantly associated with geometric mean maternal measles antibody titres (65.8 v 50.4 ELISA units/l). The relation between cord and maternal antibody titres and placental malaria infection was defined under linear regression ( $R^2 = 0.46$ ;  $p < 0.001$ ) and is illustrated in fig 1. Placental histological classification slightly improved the model ( $R^2 = 0.49$ ;  $p < 0.001$ ) in multivariate analysis. Other confounding variables were insignificant and were excluded. The expected cord titre in active placental malaria infection was 70.5% (95% CI, 52.0% to 95.5%) of that expected with no placental infection, and in past infection, 68.7% (49.5% to 95.5%). The relation between antimalarial treatment and the transformed cord:maternal measles antibody transfer ratio is illustrated in fig 2. Among non-infected mothers, those who received antimalarial drugs during pregnancy transferred significantly more measles antibody than those who did not (geometric mean transfer ratios: 1.33 v 0.98 respectively;  $p = 0.046$ ).

## DISCUSSION

Placental malaria was associated with impaired transplacental transfer of measles antibody in this study. Antenatal antimalarial drug exposure was associated with improved transfer in women uninfected at delivery. Such women were likely to have been infected earlier in pregnancy but cleared



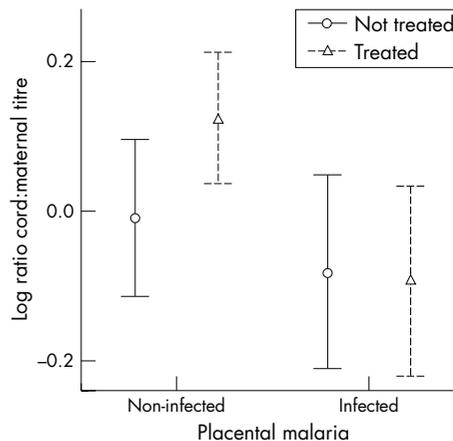
**Figure 1** Scatterplot of  $\log_{10}$  transformed cord/maternal measles antibody titres. Regression lines are fitted according to placental infection. Broken line and crosses: infected placentas; continuous line and circles, non-infected placentas.

the parasites more effectively, limiting placental pathology and improving the transfer capacity of the syncytiotrophoblast. Antimalarial drug exposure may have represented demographic confounding but no evidence for this was detected in the variables examined, and exposure was irrelevant in women infected at delivery. Potential interactions between placental malaria and HIV co-infection<sup>3</sup> were avoided in this HIV seronegative sample.

Reduced concentration of measles antibody at birth is critical in determining early susceptibility and severity of measles infection in infants, as well as the timing of effective measles vaccination. In Malawi between 1996 and 1998, 51% of infants with measles were less than 9 months of age and 17% less than 6 months.<sup>5</sup> Improved malaria control in pregnancy has substantial benefits for the mother and the baby, which may include a reduced risk of measles in early infancy. Studies of infant measles susceptibility in relation to placental malaria and maternal antibody transfer are warranted.

#### ACKNOWLEDGEMENTS

We thank Dr K A Danso and the staff and patients of the Labour Unit, KATH and Dr David Jeffreys, MRC Laboratories, The Gambia, for comments and statistical advice. This work was supported by the European Commission Research Directorates General Fifth Framework (contract PREMA-EU-ICA4CT-2001-1110012), the Liverpool School of Tropical Medicine and Academic Medical Centre, University of Amsterdam.



**Figure 2** Box plot of cord:maternal measles antibody titre according to placental malaria infection status and history of antimalarial drug treatment during pregnancy.

#### Authors' affiliations

**S Owens**, MRC Laboratories, Atlantic Road, Fajara, The Gambia  
**S Owens, G Harper, B J Brabin**, Child and Reproductive Health Group, Liverpool School of Tropical Medicine, Liverpool, UK  
**J Ordi**, Department d'Anatomia Patologica, Universitat de Barcelona, Barcelona, Spain  
**J Amuasi, G Offei-Larbi**, Komfo Anokye Teaching Hospital, Kumasi, Ghana  
**B J Brabin**, Emma Kinderziekenhuis, Academic Medical Centre, University of Amsterdam, Netherlands  
 Competing interests: none declared

Correspondence to: Professor Bernard Brabin, Child and Reproductive Health Group, Liverpool School of Tropical Medicine, Pembroke Place, Liverpool L3 5AQ, UK; [b.j.brabin@liv.ac.uk](mailto:b.j.brabin@liv.ac.uk)

Accepted 1 March 2006

#### REFERENCES

- Caceres VM, Strebel PM, Sutter RW.** Factors determining prevalence of maternal antibody to measles virus throughout infancy: a review. *Clin Infect Dis* 2000;**31**:110–19.
- Brair ME, Brabin BJ, Milligan P, et al.** Reduced transfer of tetanus antibodies with placental malaria. *Lancet*, 1994 **22**, **343**:208–9.
- Scott S, Cumberland P, Shulman CE, et al.** Neonatal measles immunity in rural Kenya: the influence of HIV and placental malaria infections on placental transfer of antibodies and levels of antibody in maternal and cord serum samples. *J Infect Dis* 2005;**191**:1854–60.
- Brabin BJ, Romagosa C, Abdelgalil S, et al.** The sick placenta—the role of malaria. *Placenta* 2004;**25**:359–78.
- Yamaguchi S, Dunga A, Broadhead RL, et al.** Epidemiology of measles in Blantyre, Malawi: analyses of passive surveillance data from 1996 to 1998. *Epidemiol Infect* 2002;**129**:361–9.