Table 2. PB CD34+ cell count and achievement of target dose in a single collection (n=80).

PB CD34+ cell count (x 10^6/L)	2.0 x 10^6 CD34+ cells/kg
≤ 20.9	0%
> 20.9 < 32.5	50%
≥ 32.5	100%

a WBC ≥ 5.0 x 10^9/L is a sensible threshold to initiate CD34+ cell counts, and subsequently has been adopted in Taunton.

The PB CD34+ cell count is used to confirm that the harvest will yield sufficient CD34+ cells. If achievement of the target dose is predicted to be unlikely, the linear nature of the PB CD34+ cell count can be used to provide an indication of the number of collections needed.

For example, if 32.5 x 10^6/L predicts a PBSC yield of 2.0 x 10^6/kg, a PB CD34+ cell count of approximately 16.0 x 10^6/L suggests a PBSC yield of half the target dose (i.e.,1.0 x 10^6/kg), suggesting that at least two collections would be required. Similarly, a PB CD34+ cell count of 100 x 10^6/L would indicate a final yield of approximately three times the target yield (i.e., 6.0 x 10^6/kg).

Of course, this assumes that the PB CD34+ cell count will remain stable for the duration of the 'harvest window'. Any decrease in circulating CD34+ cells would extend the number of collections required. Similarly, an increase would reduce the the number of collections needed to achieve the target dose.

Owing to the dynamic nature of PB CD34+ cell mobilisation, the PB CD34+ cell count preceding each harvest was measured if more than one was needed. Updating the predicted yield permits optimum patient management by avoiding harvesting unnecessarily, or allows additional harvests to be performed if the PB CD34+ cell count is seen to be diminishing.

Importantly, we use PB CD34+ cell counts not only to predict the harvest yield on a particular day but also to ensure that stem cell mobilisation has occurred.

With a CD34 count usually available within an hour of receipt of a sample, delays in harvesting are minimal. The cost of routinely performing two or more leucapheresis procedures when one would have been sufficient (or should not have been commenced at all) far outweighs the cost of a CD34 count.

The present study aimed to assess the utility of the PB CD34+ cell count as a robust method to optimise the timing of apheresis in order to achieve the target dose in a single collection, or to provide accurate information about the number of procedures that would be required if one were insufficient (or if CD34+ cell mobilisation had occurred at all). The results showed that PB CD34+ cell counts can predict harvest yield, irrespective of treatment regime or patient weight.

In summary, PB CD34+ cell counts provide a realistic and cost-effective opportunity for improved utilisation of clinical and laboratory resources. A more effective service can be offered to the patient by minimising inconvenience and the need for unnecessary procedures (by avoiding harvesting too early or too late), and by identifying those patients unlikely to yield sufficient CD34+ cells to be of therapeutic value. □

We thank Dr Paul Ewings for statistical analysis of the data and Dr Steve Johnson for reading the text and suggesting improvements.

References

1 Schots R, Van Riet I, Damiaens S *et al*. The absolute number of circulating CD34+ cells predicts the number of hematopoietic stem cells that can be collected by apheresis. *Bone Marrow Transplantation* 1996; **17**: 509–15.

2 Elliott C, Samson DM, Armitage S *et al*. When to harvest peripheral blood stem cells after mobilization therapy : Prediction of CD34-positive cell yield by preceding day CD34-positive concentration in peripheral blood. *J Clin Oncol* 1996; **14**: 970–3.

3 Mohle R, Murea S, Pforsich M *et al*. Estimation of the progenitor cell yield in a leukapheresis product by previous measurement of CD34+ cells in the peripheral blood. *Vox Sang* 1996; **71**: 90–6.

4 Armitage S, Hargreaves R, Samson D *et al*. CD34 counts to predict the adequate collection of peripheral blood progenitor cells. *Bone Marrow Transplantation* 1997; **20**: 587–91.

5 Areman E, Meehan KR, Sacher RA. Preapheresis levels of peripheral blood CD34+ cells correlate with CD34+ peripheral blood progenitor cells in autologous patients. *Transfusion* 1997; **37**: 1217.

6 Bandarenko N, Sims LC, Brecher ME. Circulating CD34+ cell counts are predictive of CD34+ peripheral blood progenitor cell yields. *Transfusion* 1997; **37**: 1218–20.

7 D'Arena G, Musto P, Cascavilla N *et al*. Circulating CD34+ absolute cell number is the best single parameter to predict the quality of leukapheretic yield. *Bone Marrow Transplantation*. 1998; **22**: 215–6.

8 Chapple P, Prince HM, Quinn M *et al*. Peripheral blood CD34+ cell count reliably predicts autograft yield. *Bone Marrow Transplantation* 1998; **22**: 125-130.

9 Yu J, Leisenring W, Bensinger WI *et al*. The predictive value of white cell or CD34+ cell count in the peripheral blood for timing apheresis and maximizing yield. *Transfusion* 1999; **39**: 442–50.

10 Benjamin RJ, Linsley L, Fountain D *et al*. Preapheresis peripheral blood CD34+ mononuclear cell counts as predictors of progenitor cell yield. *Transfusion*. 1997; **37**: 79–85.

11 Gratama JW, Orfao A, Barnett D *et al*. Flow cytometric enumeration of CD34+ haematopoietic stem and progenitor cells. *Cytometry* 1998; **34**: 128–42.

Placental transfer of measles antibodies in Nigerian mothers

A. ADEIGA, R. O. AKINOSHO, R. A. AUDU, J. ONYUEWUCHE and *O. OYEWOLE

*Nigerian Institute of Medical Research, P.M.B 2013, Yaba – Lagos; and *Federal Laboratory and Disease Control Services, Federal Ministry of Health, Lagos, Nigeria*

Measles is a major health problem of childhood in developing countries, despite the immunisation of children against the disease.[1] Factors such as ignorance, malnutrition, non-immunisation, delay in seeking medical attention and intra-uterine fetal infection from the exposed mother have

contributed to the high morbidity and mortality rate of measles infection.[2-4] Vaccine failure is another factor in the high morbidity rate of measles.[5,6] The failure of children to seroconvert the live measles vaccine, as observed in kwashiorkor children, also helps to propagate the disease.[7]

Normally, babies will acquire measles antibody across the placenta during gestation, and this provides protection until they are immunised at nine months.[3] However, a study of 20 babies (aged between one month and nine months) revealed that 88% had no protective antibody at six months and all were susceptible to measles at nine months.[8,9] This could result from either the transfer of low levels of measles antibody across the placenta or the possibility that intra-uterine infection overwhelms the measles antibody and renders it ineffective.[10]

In a community study,[3] women exposed to measles infection during pregnancy had a prenatal mortality rate of 15%, compared with 4% for women not exposed to measles. This type of prenatal infection was suggested as the cause of measles in babies aged one to two months.[11]

The present study aims to establish the pattern of measles immunity in babies of women exposed to an environment in which measles is endemic.

Forty-two pregnant women gave informed consent and were enrolled in the study. Inclusion criteria were that they must be in the first trimester of pregnancy and that a complete antenatal record be kept to delivery. The study group was monitored through case notes and assessment of clinical condition at each clinic visit. Babies were examined for underweight or infection at delivery.

Blood was collected by venepuncture during antenatal consultation. Cord blood was collected at delivery and sera were separated and stored at –20°C until used.

A haemagglutination inhibition (HI) technique was used to carry out the measles antibody assay. Briefly, an initial measles antigen titration was performed in phosphate-buffered saline (PBS) to find the haemagglutinating titre of the antigen. Serum samples were adsorbed with 50% Rhesus monkey erythrocytes overnight to remove non-specific agglutinins, prior to measles antibody titration. Serial two-fold dilutions (1 in 4 to 1 in 2048) of treated samples were prepared in PBS (pH 7.2) in a multi-welled plate. Equal volumes (25 µL) of each serum dilution and 4HAI units of measles antigen were mixed. This was incubated for 1 h at room temperature, following which 0.5% washed monkey erythrocytes were added as an indicator. This was followed by further incubation at 37°C for 1 h.

The plate was then examined. Even haemagglutination was recorded as a positive reaction, while a button of erythrocytes at the base of the well indicated a negative reaction. The titre at which positive and negative reactions occurred was noted.

Both the maternal and cord sera showed HI measles antibodies. However, three immune status groups emerged from the result. This classification was based on the fetal:maternal ratio of the pair of sera tested.

The first group comprised 14 mother/cord pairs that showed a ratio <1. Measles antibody in the sera of mothers in this group was significantly higher than that found in the cord sera ($P < 0.05$; Table 1).

Correspondence to: Dr Adesina Adeiga
Email: aadeiga@yahoo.com

Table 1. Group 1 patients with fetal:maternal antibody ratio <1.

Mother's antibody titre (reciprocal titre)	Cord blood antibody titre (reciprocal titre)	Fetal: maternal ratio	Malaria during pregnancy
256	64	0.25	No
512	64	0.13	Yes
512	128	0.25	Yes
128	8	0.06	Yes
256	16	0.06	Yes
256	64	0.25	No
256	64	0.25	No
512	128	0.25	No
1024	128	0.13	Yes
1024	128	0.13	Yes
256	16	0.06	Yes
256	8	0.03	Yes
256	64	0.25	Yes
2048	256	0.13	No

The second group comprised nine mother/cord pairs that showed a ratio >1. In this group, maternal measles antibody was found to be lower than the level in the cord sera, although the difference was not significant ($P > 0.05$; Table 2).

The third group comprised 19 mother/cord pairs that showed a ratio of 1, indicating that an efficient transfer of HI measles antibody from mother to fetus had taken place (Table 3).

Babies acquire measles antibody from their mothers across the placenta. This provides protection until the baby is immunised against the disease at nine months.[12] The study reported here was conducted to assess the levels of measles antibody acquired by babies during gestation.

Results revealed three groups of immune status based on fetal:maternal ratio. Group 1 (ratio <1) had a lower level of measles antibody in cord sera than in the mothers' sera, indicating inefficient transfer as a result of either placental insufficiency or pathology.[13] Among the factors reported to cause placental defect is malaria, which has been shown to affect the transfer of tetanus antibody to the fetus during malaria infection in pregnancy.[14,15]

Although 22 (52%) of the mothers studied had malaria infection during pregnancy, there was no relationship with the transfer of measles antibody because only nine of the mothers in group 1 had malaria. Thus, it is difficult to attribute the low level of measles antibody in the cord sera to malaria alone. The consequence of lowered measles antibody transfer to babies is the risk of measles infection prior to immunisation at nine months. Such early infection has been reported in babies between four and six months old.[9,10]

Group 2 (ratio >1) had a higher level of measles antibody in cord sera than that in the mothers' sera. Intra-uterine measles infection could be the cause of such high measles antibody levels in these babies, perhaps due to the exposure to measles of mothers with depressed or compromised immunity, leading to high viraemia. The consequence of this intrauterine infection can be prenatal fetal death, as shown in one study[3] to account for a 15% death rate.

Table 3. Group 3 patients with fetal:maternal ratio equal to 1.

Mother's antibody titre (reciprocal titre)	Cord blood antibody titre (reciprocal titre)	Malaria during pregnancy
128	128	Yes
128	128	Yes
64	64	No
256	256	No
256	256	Yes
128	128	Yes
128	128	No
128	128	Yes
512	512	Yes
256	256	No
128	128	No
256	256	Yes
256	256	No
256	256	Yes
256	256	Yes
256	256	No
256	256	Yes
128	128	No
256	256	No

Table 2. Group 2 patients with fetal:maternal ratio >1.

Mother's antibody titre (reciprocal titre)	Cord blood antibody titre (reciprocal titre)	Fetal: maternal ratio	Malaria during pregnancy
256	512	2	No
64	256	4	No
128	1024	8	Yes
128	256	2	Yes
256	512	2	No
128	256	2	Yes
128	256	2	No
128	256	2	No
256	512	2	No

Babies with high measles antibody need to be monitored for antibody titre at nine months before immunisation as derived measles antibody may prevent the babies from developing active immunity, thereby leading to vaccine failure.[16]

Group 3 (ratio = 1) showed evidence of adequate transfer of measles antibody to the babies from their mothers. However, those with high measles antibody should still be monitored for the reasons given above.

Malaria was recorded among the pregnant women studied, but there was no evidence of its effect on the transfer of measles antibodies. Hence, malaria cannot be totally implicated in the poor antibody transfer in group 1. Also, no relationship was shown between antibody level and other parameters investigated (e.g., birth weight, parity). □

References

1 Fagbule, Orifunmishe F. Measles and childhood mortality in semi-urban Nigeria. *Afr J Med Med Sci* 1988. **17**(3): 181–5.

2 Adu FD, Ikusika A, Omotade O. Measles outbreak in Ibadan: clinical, serological and virological identification of affected children in selected hospitals. *J Infect* 1997; **35**(3): 241–5.

3 Aaby P, Bukh J, Lisse IM, Siem E, Silva M. Increased prenatal mortality among children of mothers exposed to measles during pregnancy. *Lancet* 1988; 5:1 (8584): 516–9.

4 Samb B, Aaby P, Whittle HC *et al*. Serologic status and measles attack rates among vaccinated and unvaccinated children in rural Senegal. *Pediatr Infect Dis J* 1995; **14**(3): 203–9.

5 Williams JA. Measles infection following immunization. A report of 49 cases in Lagos, Nigeria. *Afr J Med Med Sci* 1971; **2**: 159–63.

6 Hirose M, Hidaki Y, Miyazaki C, Ueda K, Yoshikawa H. Five cases of measles secondary vaccine failure with confirmed seroconversion after measles vaccination. *Scand J Infect Dis* 1997; **29**: 187–90.

7 Powel GM. Response to live attenuated measles vaccine in children with severe kwashiorkor. *Ann Trop Paediatr* 1982; **2**: 143–5.

8 Kiepiela P, Coovadia HM, Loening WE, Coward P, Abdool-Karim SS. Loss of maternal measles antibody in black South African infants in the first year of life – Implications for age of vaccination. *S Afr Med J* 1991; **79**(3): 145–8.

9 Babaniyi OA, Parakoyi DB, Aiyedun BA, Bello MA. Loss of maternally acquired measles antibody during infancy in Ilorin Nigeria. *J Trop Pediatr* 1995 **41**(2); 115–7.

10 Dabbis F, Waldman RJ, Mann GE, Commenges D, Madza G, Jones TS. Loss of maternal measles antibody during infancy in African city. *Int J Epidemiol* 1989; **159**(4): 610–5.

11 Mukhtar AA, Aisanag MS. Measles in a two-month-old baby and his mother in Juba, Sudan. *East Afr Med J* 1989; **66**: 74–5.

12 Harry T, Ogunmekan D. Optimal age for vaccinating Nigerian children against measles. I Neonatal antibody profile and subsequent susceptibility to measles. *Trop Geogr Med* 1981; **33**(4): 375–8.

13 Chandra RK. Levels of IgG subclasses, IgA, IgM and tetanus antitoxin in paired maternal and fetal sera: findings in healthy pregnancy and placenta insufficiency In: Henning WA, ed. *Materno-fetal transmission of immunoglobulins*. Cambridge: University Press, 1975: 77.

14 Brabin J. The risks and severity of malaria in pregnant women. In: *WHO Applied Field Research Report in Malaria Reports*. 1991. No 1.

15 Brair ME, Brabin BJ, Milligan P, Maxwell SM, Hart CA. Reduced transfer of tetanus antibodies with placental malaria. *Lancet* 1994; **343**: 208–9.

16 Albrecht P, Ennis FA, Saltzman EJ, Krugman S. Persistence of maternal antibody in infants beyond 12 months: mechanism of measles vaccine failure. *J Pediatr* 1977; **91**: 715–8.