MAJOR ARTICLE

Revisiting the Role of Neutralizing Antibodies in Mother-to-Child Transmission of HIV-1

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We analyzed the association between mother-to-child transmission (MTCT) of human immunodeficiency virus type 1 (HIV-1) and maternal neutralizing antibodies to heterologous primary isolates of various HIV-1 clades, to test the hypothesis that protective antibodies are those with broad neutralizing activity. Our study sample included 90 Thai women for whom the timing of HIV-1 transmission (in utero or intrapartum) was known. The statistical analysis included a conditional logistic-regression model to control for both plasma viral load and duration of zidovudine prophylaxis. The higher the titer of neutralizing antibodies to a heterologous strain of the same clade, the lower the rate of MTCT of HIV-1. More specifically, high levels of neutralizing antibodies to the MBA (CRF01_AE) strain were associated with low intrapartum transmission of HIV-1. This suggested that such heterologous neutralizing antibodies may be involved in the natural prevention of late perinatal HIV transmission. These data are consistent with the hypothesis that the use of some antibodies might help to prevent perinatal HIV transmission, through passive immunoprophylaxis. Moreover, the study of humoral factors associated with MTCT of HIV-1 may identify correlates of protection that should help in the design of efficient HIV/acquired immunodeficiency syndrome vaccines.

Almost all pediatric HIV-1 infections are due to mother-to-child transmission (MTCT). In the absence of antiretroviral prophylaxis, transmission can occur during pregnancy (in utero), during labor and delivery (intrapartum), or through breast-feeding after birth [1]. Antiretroviral therapy during pregnancy and labor dramatically reduces the risk of in utero and intrapartum transmission [2, 3]. However, despite the use of chemoprophylaxis, some transmission can occur.

Identifying the factors associated with HIV-1 perinatal transmission and understanding their role has helped to define existing preventive interventions. The maternal plasma viral load has been unambiguously associated with MTCT; the higher the viral load, the higher the risk of MTCT [4–7]. However, 60%–80% of untreated infected mothers do not transmit infection, suggesting that other factors, including the host immune response to HIV, may be involved in preventing transmission. Various studies have used different methods in heterogeneous populations to address the still-debated role of maternal antibodies in MTCT [8–12]. Since the risk of transmission and its associated factors differ during pregnancy and during labor and delivery, it may also be important to consider when MTCT occurs. Although not all studies are in agreement, the type of maternal HIV variant transmitted seems to differ depending on the timing of transmis-

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sion, suggesting a selective pressure on the virus. Single or multiple major maternal variants are transmitted in utero, whereas minor variants are transmitted intrapartum [13, 14]. It has also been observed that infant-derived viruses are usually resistant to neutralization by their own mother's plasma [15, 16]. Finally, in some studies, a higher risk of MTCT has been found to be associated with higher levels of antibodies binding to several envelope epitopes (the immunodominant epitope of gp41 [IDE] and V3) [10, 17, 18], although a consensus has never been reached on this issue [19–21].

HIV-1 infection in newborns, at least that resulting from intrapartum transmission, occurs in the presence of passively transferred antibodies. MTCT therefore resembles natural challenge in an individual who has developed antibodies after immunization with a vaccine. This may make it possible to use MTCT to study the humoral response with the aim of identifying protective antibodies, since there is still a need in vaccine studies to determine correlates of protection. In the present study, we analyzed the association between neutralizing antibody titers and MTCT, with the following points and restrictions:

1. We did not use T cell line–adapted HIV strains, because they are artificially sensitive to neutralization [22].
2. We studied neutralizing antibodies to heterologous primary isolates of various clades, instead of studying neutralizing antibodies to homologous strains. Because infant-derived viruses are usually resistant to neutralization by their own mother's plasma [15, 16], this allowed us to test the hypothesis that protective antibodies are those with a broad neutralizing activity.
3. We performed the study in a homogeneous population of pregnant women of the same geographical origin (where the circulating strains belong to a largely predominant clade) and for whom we knew when transmission occurred—either in utero or intrapartum.
4. We performed control studies of antibodies to various HIV-1 antigens previously found to be associated with MTCT [17, 18].
5. The statistical analysis was adjusted for the 2 main confounding factors: plasma viral load and duration of zidovudine (ZDV) prophylaxis [23].

SUBJECTS, MATERIALS, AND METHODS

Study population. We compared baseline serum samples from randomly selected transmitting mothers (cases; $n = 28$) and nontransmitting mothers (controls; $n = 62$). The mothers participated in a clinical trial in Thailand assessing different ZDV treatment durations for the prevention of MTCT (Perinatal HIV Prevention Trial PHPT-1) [24]. The clinical trial compared 4 regimens of ZDV according to a factorial design: starting ZDV treatment in the mother at either 28 or 35 weeks gestation, and continuing for either 3 days or 6 weeks in the infant. The infants were not breast-fed. They were considered to be uninfected if 2 HIV DNA polymerase chain reaction test results were negative on 2 separate occasions after 1 month of age and were considered to be HIV infected if the test was positive on 2 separate occasions. We considered an infant to be infected in utero if the first test result, obtained within 3 days after birth, was positive, and we considered an infant to be infected intrapartum if the first test result was negative but the subsequent test results were positive. A previous analysis of this trial showed that high baseline maternal viral load and delayed maternal ZDV prophylaxis (starting at 35 weeks gestation, compared with 28 weeks) were independent predictive factors of HIV transmission [23]. The patients included in our substudy were classified according to the 2 principal risk factors of transmission: duration of maternal ZDV prophylaxis and maternal baseline plasma viral load (table 1).

The maternal blood samples used for serotyping and quantification of the neutralizing activity were collected at baseline, before initiation of ZDV prophylaxis. Typing of the maternal HIV strain was performed using a V3 serotyping assay highly specific for discriminating patients infected by B or CRF01_AE strains [25, 26]. All subsequent assays were performed blinded to the transmission status of the mother-infant pairs.

Neutralization assay. Neutralizing antibodies to 4 heter-

Table 1. Distribution of transmitters and nontransmitters according to maternal zidovudine (ZDV) prophylaxis duration and plasma viral load (VL).

	Maternal ZDV prophylaxis >8 weeks ($n = 45$)			Maternal ZDV prophylaxis ⩽8 weeks ($n = 45$)		
Patient group	Low VL	Medium VL	High VL	Low VL	Medium VL	High VL
Nontransmitters ($n = 62$)	24	8	5	14	7	4
All transmitters ($n = 28$)	1	4	3	4	4	12
In utero transmitters ($n = 11$)	0	0	2	3	2	4
Intrapartum transmitters ($n = 17$)	1	4	1	1	2	8

NOTE. Data are no. of subjects. The HIV-1 RNA load in plasma was measured using the Cobas Amplicor HIV-1 Monitor test (version 1.5; Roche Diagnostic Systems): low VL, <4.0 $\log_{10}$ copies/mL; medium VL, ⩾4.0 and <4.54 $\log_{10}$ copies/mL; high VL, ⩾4.54 $\log_{10}$ copies/mL.

ologous primary isolates were titrated by means of an assay using $CD4^+CXCR4^+CCR5^+$ HeLa cells harboring the *lacZ* reporter gene (P4P cells), as described elsewhere [27]. Strains were selected on the basis of the following criteria: (1) they belonged to different clades, including CRF01_AE and B, which are prevalent in Thailand; (2) they presented various phenotypes (X4, R5, dual-tropic); and (3) they were resistant to neutralization [27]. The strains included KON (CRF02_AG, X4), FRO (B, X4), GIL (F, R5), and MBA (CRF01_AE, R5X4). Virus stocks were prepared by passaging isolates only once or twice on phytohemagglutinin-stimulated peripheral blood mononuclear cells. The same stock of each isolate was used for the entire study. Titers of neutralizing antibodies were determined as the dilution of serum that resulted in a 90% decrease in the number of infected cells 2 days after infection with 100 $TCID_{50}$. Titrations were performed in duplicate, and the results are expressed as mean values. This assay also allows the identification of antibody-dependent enhancement, although the possible mechanisms of enhancement that the assay detects were not identified [27]. Enhancing properties of antibodies were defined as at least a 2-fold increase in infectivity when compared with negative controls.

Titration of antibodies to IDE, V3, and p24. Antibodies to various HIV antigens were titrated by ELISA. Antigens were the following: a synthetic peptide covering the IDE (RVLAVERYLKDQQLLGIWGCSGKLICTTAV, cyclic); an equimolar mixture of 30-aa peptides representing the V3 consensus sequences of subtypes A, B, C, D, and CRF01_AE [25]; and a recombinant p24 produced in *Escherichia coli* (provided by F. Mallet, UMR CNRS-BioMérieux, Lyon, France). The wells of polyvinyl microtiter plates (Falcon; Beckton-Dickinson) were coated, by incubation for 20 h at 37°C (100 μL/well), with the IDE peptide (1 μg/mL), with the mixture of the V3 peptides (0.5 μg/mL each), or with p24 (1 μg/mL), dissolved in 0.01 mol/L sodium phosphate buffer (PBS) (pH 7.4). The wells were then washed 3 times with PBS containing 0.5% Tween 20 (PBS-TW), and the uncoated sites were saturated with PBS containing 2% newborn calf serum (NBCS) for 1 h at 37°C (200 μL/well). After 3 washes with PBS-TW, 100 μL of the mothers' serum, diluted in 0.01 mol/L PBS containing 0.75 mol/L NaCl, 10% NBCS, and 0.05% Tween 20 (PBS-TW-NBCS), was added to the wells and incubated for 1 h at 20°C. Preliminary studies determined the serum dilutions as those that produced absorbance values in the dynamic range for most serum samples. These dilutions were 1:2500 for antibodies to IDE and to p24 and 1:500 for antibodies to V3. After 5 washes with PBS-TW, peroxidase-conjugated goat $F(ab')_2$ anti-human immunoglobulin (TAGO) (100 μL of a 1:5000 dilution in PBS-TW-NBCS) was added and incubated for 30 min at 20°C. The wells were washed 5 times with PBS-TW, and antibody binding was detected by incubation with hydrogen peroxide-*o*-phenylenediamine (H_2O_2-OPD) for 30 min at room temperature. The color development was stopped with 2N H_2SO_4, and the absorbance was measured at 492 nm. The same pool of serum samples from 10 unexposed HIV-negative individuals was used as a negative control in each run (3 replicates). The cutoff value was calculated as the mean for the negative controls plus 0.05, a value that corresponds to at least 3 SDs when 200 serum samples from HIV-1–uninfected individuals are tested. For each sample and antigen, the results were expressed as the ratio of absorbance of the sample to the cutoff value (absorbance ratio).

Statistical analysis. The analysis aimed to test the association between antibody titers and overall as well as in utero and intrapartum transmission, adjusting for known risk factors of transmission. Antibody titers below the limit of detection were assigned values of half the limit of detection. Continuous variables were compared among transmitters and nontransmitters by use of the Kruskal-Wallis test, and categorical variables were compared using Fisher's exact test. We used a conditional logistic-regression model to adjust for the 2 principal risk factors of transmission: baseline viral load (divided into 3 categories: <4.00, 4.00–4.54, and ⩾4.54 $\log_{10}$ copies/mL) and ZDV prophylaxis duration (longer or shorter than the median duration, 8 weeks). In this model, the neutralizing titers were

Table 2. Baseline characteristics of the patients included in this neutralization substudy, according to factors known to be associated with HIV-1 mother-to-child transmission, compared with those of the patients who did not participate in the substudy.

	Patients participating in the neutralization substudy			Patients not participating in the neutralization substudy			
Characteristic	T (n = 28)	NT (n = 62)	P^a	T (n = 69)	P^b	NT (n = 1214)	P^c
CD4 cell count, cells/mm^3	290 (160–398)	340 (230–530)	.05	343 (230–430)	.20	363 (240–510)	.77
Viral load, $\log_{10}$ copies/mL	4.59 (4.07–4.93)	3.67 (3.27–4.29)	.0001	4.38 (3.87–4.75)	.20	3.89 (3.33–4.46)	.42
Duration of ZDV prophylaxis, days	35 (23–67)	72 (34–82)	.007	39 (28–76)	.32	59 (32–79)	.18

NOTE. Data are medians (interquartile ranges). NT, nontransmitters; T, transmitters; ZDV, zidovudine.

[a] T vs. NT participating in the neutralization substudy (Kruskal-Wallis test).

[b] T in the neutralization substudy vs. T in the original study population who were not included (Kruskal-Wallis test).

[c] NT in the neutralization substudy vs. NT in the original study population who were not included (Kruskal-Wallis test).

Table 3. Neutralizing antibodies to KON, FRO, GIL, and MBA in transmitting mothers (T) and nontransmitting mothers (NT).

Strain	No. (%) of subjects with detectable neutralizing antibody			P^a
	T (n = 28)	NT (n = 62)	Total (n = 90)	
KON (CRFO2_AG)	17 (61)	41 (66)	58 (64)	.64
FRO (B)	14 (50)	23 (37)	37 (41)	.26
GIL (F)	4 (14)	20 (32)	24 (27)	.12
MBA (CRF01_AE)	13 (46)	44 (71)	57 (63)	.03
0 strain	3 (11)	12 (19)	15 (17)	
1 strain	9 (32)	7 (11)	16 (18)	
2 strains	10 (36)	16 (26)	26 (29)	
3 strains	5 (18)	19 (31)	24 (27)	
4 strains	1 (4)	8 (13)	9 (10)	

[a] T vs. NT (Fisher's exact test).

transformed into categorical variables—"0" if the titer was >20, "1" if the titer was 10–20, and "2" if the titer was <10—for the titers of antibodies to the KON, FRO, GIL, and MBA strains; and "0" if the titer was in the upper third of the distribution, "1" if the titer was in the middle third, and "2" if the titer was in the lower third, for antibodies to V3, IDE, and p24.

RESULTS

Baseline maternal characteristics according to factors known to be associated with HIV-1 MTCT. Transmission was observed in 18% (8/45) of women in the long-duration ZDV prophylaxis group and in 44% (20/45) of women in the short-duration group (table 1). Eleven neonates were infected in utero, and 17 were infected intrapartum. Short duration of maternal ZDV prophylaxis, high maternal viral load, and low CD4 cell count were predictors of MTCT in this subsample (table 2). This was consistent with the results of previous analyses including all patients who had participated in the original clinical trial. Moreover, the subsample included in the present study was comparable to the original study population (table 2). The gestational age at sample acquisition was similar for transmitters and nontransmitters (median, 25.5 and 25.7 weeks, respectively; $P = .5$, Kruskal-Wallis test), as was the median time from sample acquisition to delivery (13.7 weeks for both groups).

Neutralizing antibody and MTCT. Of the 90 samples, 15 (17%) showed no neutralizing activity at all to any of the 4 viruses tested, whereas 59 (66%) showed neutralizing activity to at least 2 strains (table 3). At least 3 of the 4 viruses were neutralized by 27 (44%) of 62 serum samples from nontransmitters but by only 6 (21%) of 28 serum samples from transmitters ($P = .06$, Fisher's exact test). Determination of the frequency of neutralization showed that the ability to neutralize the 3 strains KON, FRO, and GIL was not significantly different between transmitting and nontransmitting mothers (table 3). However, neutralizing antibodies to MBA were detected more often in nontransmitting mothers (71%) than in transmitting mothers (46%) ($P = .03$). Enhancement of infection was not observed with any of the serum samples.

Comparison of antibody titers according to HIV transmission. The titers of neutralizing antibodies to KON, FRO, and GIL were not statistically different between transmitting and nontransmitting mothers ($P = .45$, $P = .16$, and $P = .06$, respectively; Kruskal-Wallis test). However, titers of antibodies to MBA were higher in nontransmitting mothers ($P = .006$) (figure 1*A*). The association between high titers of neutralizing antibodies to MBA and a lower rate of HIV transmission was also significant when conditional logistic regression was used ($P = .01$), after adjustment for the 2 principal risk factors, viral load and duration of ZDV prophylaxis. We found the same significant association between a lower rate of transmission and higher titers of neutralizing antibodies to MBA ($P = .009$, Krus-

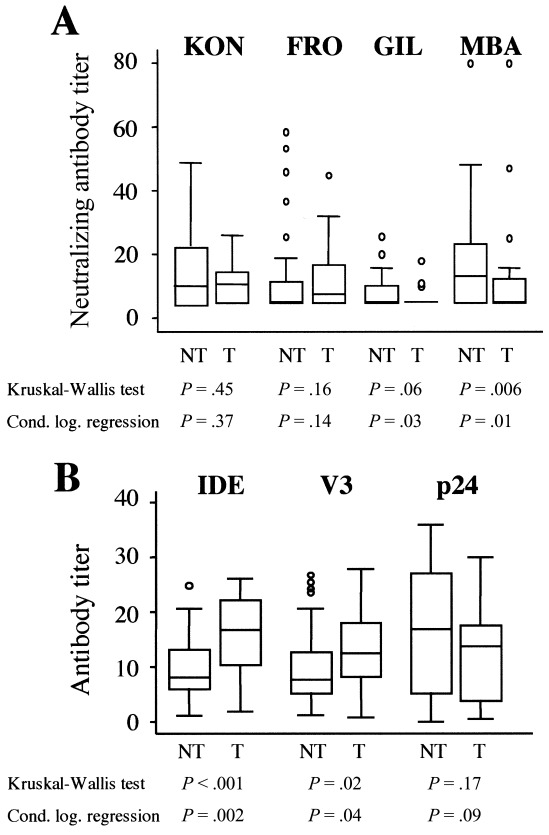

Figure 1. Comparison of antibody titers in transmitting (T) versus nontransmitting (NT) mothers. The distribution of antibody titers is shown for neutralizing antibodies *(A)* and antibodies to IDE, V3, and p24 *(B)*. The antibody titers in panel B correspond to the absorbance ratios. For each distribution, the horizontal lines represent the 10th, 25th, 50th (median), 75th, and 90th percentiles.

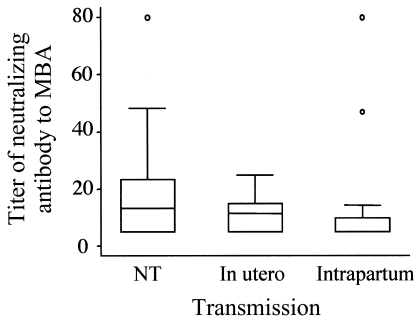

Figure 2. Comparison of titers of neutralizing antibodies to the MBA (CRF01_AE) strain in nontransmitting (NT) and in transmitting mothers according to time of transmission (in utero or intrapartum). Box plots show the distribution of maternal antibody titers. For each distribution, the horizontal lines represent the lower adjacent 25th, median, 75th, and upper adjacent percentiles.

kal-Wallis test; $P = .01$, conditional logistic regression) when the analysis was restricted to only the 81 CRF01_AE-infected mothers. The association between neutralizing antibodies to the highly neutralization-resistant strain, GIL, and transmission was of borderline significance ($P = .06$, Kruskal-Wallis test; $P = .03$, conditional logistic regression).

Of the 28 infected newborns, 11 were infected in utero and 17 were infected intrapartum. The mothers who transmitted the virus intrapartum had significantly lower levels of neutralizing antibodies to MBA, compared with nontransmitting mothers ($P = .008$, Kruskal-Wallis test; $P = .02$, conditional logistic regression) (figure 2). In contrast, levels of neutralizing antibodies to MBA were not significantly different between mothers who transmitted the virus in utero and those who did not ($P = .42$, Kruskal-Wallis test; $P = .53$, conditional logistic regression). The significant association between low levels of neutralizing antibodies to MBA and intrapartum transmission of HIV-1 still held after we restricted the analysis to the mothers infected with CRF01_AE strains ($P = .03$, conditional logistic regression).

The median absorbance ratios of antibodies to IDE were 16.8 and 8.3 among the transmitters and nontransmitters, respectively. This difference was statistically significant ($P < .001$, Kruskal-Wallis test; $P = .002$, conditional logistic regression) (figure 1*B*). We also found that a high reactivity to V3 was associated with transmission ($P = .02$, Kruskal-Wallis test; $P = .04$, conditional logistic regression). No significant difference in serum reactivity to p24 between transmitters and nontransmitters was seen ($P = .17$, Kruskal-Wallis test; $P = .09$, conditional logistic regression). Although the titers of antibodies to IDE were higher in mothers who transmitted the virus in utero than in nontransmitting mothers ($P = .005$, Kruskal-Wallis test), this was not confirmed by conditional logistic regression ($P = .23$). Similarly, despite there being a significant difference between the mothers who transmitted the virus intrapartum and those who did not ($P < .001$, Kruskal-Wallis test), this was not confirmed by conditional logistic regression ($P = .22$).

DISCUSSION

In the present study, we analyzed, with an emphasis on neutralizing antibodies, the association between the humoral response to HIV-1 in infected pregnant women and MTCT. We used a subsample of women who participated in a randomized clinical trial in Thailand and received different regimens of ZDV for the prevention of MTCT [24]. We tested 2 hypotheses. First, if maternal neutralizing antibodies effectively prevent MTCT, then they should also neutralize a broad spectrum of HIV primary isolates in vitro. This would mean that infection in vivo with major variants present in the mothers' blood and genital tract should be inhibited. This would also apply to distantly related minor variants that escape immune pressure. Therefore, we analyzed the neutralization of primary isolates of various clades, including heterologous isolates of the prevalent clades in Thailand, instead of analyzing the neutralization of autologous viruses. Second, if neutralizing antibodies are involved in preventing MTCT, this should occur primarily when passively transferred IgGs reach a sufficient level in the fetus, toward the very end of the pregnancy. Therefore, the neutralizing antibodies should be most effective in preventing intrapartum transmission. This fetal/neonatal situation resembles natural challenge in the presence of preexisting antibodies. Therefore, it may help in identifying antibodies that should be raised with future anti-HIV vaccine candidates.

Our study was conducted in a homogeneous population of pregnant women in Thailand [24]. Unlike other settings, such as Africa or some European countries [28, 29], the genetic diversity of HIV in Thailand is still limited, because of the relatively recent introduction of a dominant clade, CRF01_AE [30]. This homogeneous population limited the impact of viral genetic diversity in the analysis. Because maternal plasma viral load and duration of ZDV prophylaxis were strongly associated with the transmission of HIV-1 [4–7, 18, 23], we used a conditional logistic regression model to adjust for these 2 principal risk factors.

More nontransmitting mothers than transmitting mothers harbored antibodies with a broad neutralization spectrum. However, 1 mother transmitted the virus despite having antibodies with a broad neutralization spectrum. Also, despite having no detectable neutralizing activity in their plasma, 12 mothers did not transmit the virus (table 3). This emphasizes that, if neutralizing antibodies are involved in MTCT, they are only part of a complex, multifactorial biological process. Titers of neutralizing antibodies to the MBA (CRF01_AE) strain were significantly higher in nontransmitting mothers than in transmitting mothers, even after analysis was restricted to the subgroup of CRF01_AE-infected mothers. No difference was seen for neu-

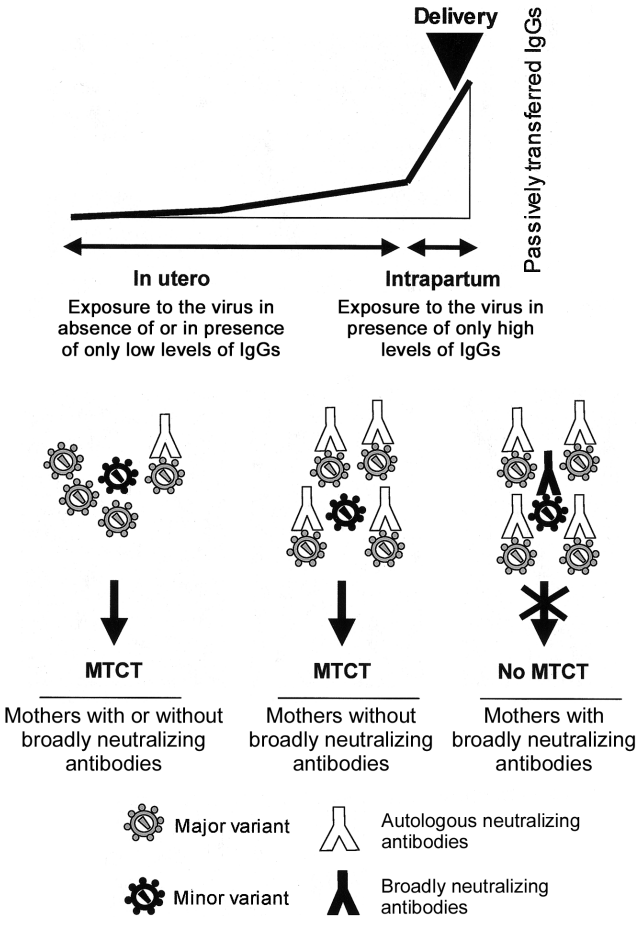

Figure 3. Hypothetical schematic representation of the possible role of neutralizing antibodies in preventing mother-to-child transmission (MTCT) of HIV-1. During in utero exposure, multiple or major variants would be transmitted independently of the presence or absence of neutralizing antibodies in the mother's blood. During intrapartum exposure, major variants would be neutralized by passively transferred autologous neutralizing antibodies. However, minor variants would be transmitted in the absence of broadly neutralizing antibodies but could be neutralized in babies whose mothers harbor broadly neutralizing antibodies.

tralizing antibodies to the KON and FRO heterotypic strains. We saw an association between higher titers of neutralizing antibodies to the highly neutralization-resistant GIL strain and a lower risk of MTCT. This suggests that the detection of relevant neutralization determinants shared by multiple clades may be possible by use of this highly resistant strain.

Our data unambiguously showed that higher titers of neutralizing antibodies to a heterologous strain of the same clade were associated with a lower rate of MTCT of HIV-1. This suggests that such antibodies may have a role in the prevention of infection. A previous study conducted in Thailand did not find any correlation between maternal antibodies at delivery and vertical transmission of HIV-1, except for a trend toward a higher titer of neutralizing antibodies against a subtype B T cell line–adapted isolate [31]. However, it is difficult to compare the data from this previous study and our data, since the studies were performed using different isolates that may have different levels of susceptibility to neutralization. Therefore, it will be important to confirm our observation in different settings, using, for instance, a similar Thai population with several B and CRF01_AE primary isolates as indicator strains, as well as another population in which a different clade predominates, such as clade C in South Africa.

We found that higher levels of antibody binding to the IDE and V3 regions of the HIV-1 envelope were associated with an increased rate of transmission. This was also seen in previous studies performed in Africa [10, 17] and Europe [18]. Although a consensus has never been reached on this issue, this association raises questions concerning the possibility that these antibodies are surrogate markers for an unknown risk factor for transmission or that they are deleterious in themselves. Such antibodies may enhance infection and, therefore, transmission. However, although the neutralization assay has been shown to be able to detect enhancing antibodies [27], none of the 90 serum samples tested enhanced infection in vitro, which does not support this hypothesis. Alternatively, these highly immunogenic epitopes may be more efficient as antigenic decoys in certain patients, therefore diverting their humoral responses away from more functionally relevant envelope epitopes.

A high level of neutralizing antibodies to MBA was the most significant humoral factor associated with a lower risk of MTCT in our study. The difference was highly significant between nontransmitters and intrapartum transmitters. Viruses transmitted intrapartum are frequently minor variants of those present in the mother, revealing a strong selective pressure. In contrast, viruses transmitted in utero are more likely to be single or multiple major maternal variants [13]. This is consistent with the results of our study. Although it is impossible to know when in utero transmission occurred in each case, on the basis of the known kinetics of passively transferred IgGs during pregnancy, it can be assumed that it occurred in the presence of lower levels of maternal antibodies than those present during intrapartum transmission. That higher levels of neutralizing antibodies to the MBA (CRF01_AE) strain were associated with lower rates of intrapartum transmission of HIV-1 but were not associated with in utero transmission suggests that the reduction in intrapartum HIV transmission risk may involve heterologous neutralizing antibodies. It can be suggested that passively transferred heterologous neutralizing antibodies should be able to neutralize minor variants that are not neutralized by the autologous antibodies (figure 3). Oral challenge studies in animals that mimic peri- and postpartum HIV transmission have shown that passive hyperimmune serum or a combination of neutralizing human monoclonal antibodies may completely protect against perinatal HIV transmission [32–37]. This, as well as our study of the humoral factors associated with MTCT

of HIV-1 during the natural course of infection, strongly suggests that some antibody specificities are able to prevent perinatal HIV transmission. The risk of MTCT of HIV has been greatly reduced by antiviral chemotherapy. Although this is a major advance in the management of HIV/AIDS, the potential toxicities of the treatments and the development of drug resistance may limit the long-term efficacy of antiretroviral prophylaxis [2, 38]. Combining immunoprophylaxis and chemoprophylaxis to prevent MTCT of HIV-1 is an alternative treatment that should be considered [39–41]. As well as passive immunization, the study of humoral factors associated with MTCT of HIV-1 may allow the identification of correlates of protection and deleterious immune responses, thus aiding the design of efficient HIV/AIDS vaccines.

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