authors should have reported the uncertainty of their estimates considering that their calculations were based on only 28 and 37 cases. This could have been done by calculating AUC values and the 95% confidence interval for the ROC curves used for selection of their cutoff values. We are also surprised that the authors did not discuss why their cutoff value was 10 times higher than the cutoff value from a large prospective study.5

The role of IVIg in the treatment of FNAIT is still a matter of debate, and hence it is surprising that the authors do not make reference to the recent studies by Giers et al8; these authors could not find any effect of IVIg when given to either the mother or the fetus. The results of the treatment with IVIg and steroids are surprisingly good and may have been because of selection bias.

Response

Prediction of the fetal status in noninvasive management of alloimmune thrombocytopenia

Fetal/neonatal alloimmune thrombocytopenia is a severe disease with devastating outcome in severely affected infants. Antenatal interventions suggest the most deleterious consequence, intracranial hemorrhage (ICH), is preventable without known risks for the mother and child. In these circumstances the most challenging issues include development of maternal testing to reliably predict fetal status and allow noninvasive antenatal strategies. Our study is the first to report information both on fetal platelet count and maternal alloantibody concentrations with 3 regime therapies. Only HPA1b/1b women with a subsequent managed pregnancy after an index case leading to diagnosis, a complete obstetrical and sibling history, data on fetal and neonatal status, and analysis of these factors may explain apparent discrepancies between our results and other reports (retrospective versus prospective studies; among the anti–HPA-1a immunized mothers referred to our unit, 20% are not HLA DRB3*0101).

Case reports may overestimate the clinical severity we observed. However the severity of clinical presentation and percentage of primigravida in newly diagnosed cases were very similar to previous larger cohort retrospective reports2-4. When biologic markers were analyzed careful consideration was given to (1) gestation range. The alloantibody concentration analysis was reviewed only with the first treated pregnancy of each mother (2) severity of the disease, platelet count < 50 × 10⁹/L (3) timing of maternal samplings: at delivery means samplings done on delivery and NOT during the postnatal period. As reported elsewhere,5 we observed a noticeable increase in the postpartum concentration; therefore certain samples were excluded from analysis in the index cases (4) methodology used for alloantibody concentration (expressed as IU/mL as mentioned in “Methods” not observed by Sachs et al3).

These factors may explain apparent discrepancies between our results and other reports (retrospective versus prospective studies; among the anti–HPA-1a immunized mothers referred to our unit, 20% are not HLA DRB3*0101).

Cases were referred to our unit for therapy counseling; IVIG courses and steroids were therefore given without noticeable variations over the period of time and carefully controlled.

The goal of antenatal management is the prevention of severe fetal thrombocytopenia, with in utero ICH in 80% of cases. A safe fetal platelet count > 50 × 10⁹/L may allow vaginal delivery. For ethical reasons no randomized controlled trials have been done for therapy against no treatment. Therefore, only observational studies are available. Reports, in some hundreds of cases,7 are in favor of maternal therapy with IVIG ± steroids. Giers et al8 report cases with repeated fetal blood samplings (FBS) before each IVIG course potentially playing a role in boosting the maternal immunization possibly explaining the poor results.

In this study without blind allocation the measure of the treatment effect was absence of ICH and the neonatal platelet count. To prevent ICH, the 3 therapeutic regimens were effective. Though each treatment had a failure rate, it is noticeable that combined therapy had the lowest percentage of neonates requiring postnatal therapy. The statistical analysis gave similar results even if siblings are not taken into account (only 51% of the index
untreated cases were first newborns not as noted by Sachs et al1). This confirms that samples are independent.

At present the only available antenatal method to confirm response to therapy is FBS, which has a significant complication rate. Maternal alloantibody concentration threshold before therapy allows considering FBS for only 23.1% of the women, constituting considerable progress (NPV 76.9% and not 75% as noted by Sachs et al1). When followed during pregnancy over a greater number of cases (43 cases) it is still predictive of therapy failure (Table 1).

In view of the rarity of this condition, collaborative studies are needed to accrue meaningful data and improve noninvasive strategies.

**Table 1. Follow-up of the maternal anti–HPA-1a antibody concentrations during managed pregnancies**

<table>
<thead>
<tr>
<th>Weighted AUC, IU/mL</th>
<th>Newborn platelet count, × 10^9/L</th>
<th>&lt; 50</th>
<th>≥ 50</th>
<th>P</th>
<th>Se, %</th>
<th>Sp, %</th>
<th>PPV, %</th>
<th>NPV, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>24, n</td>
<td></td>
<td>5</td>
<td>23</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥ 24, n</td>
<td></td>
<td>10</td>
<td>5</td>
<td>.0049*</td>
<td>66.7</td>
<td>82.1</td>
<td>66.7</td>
<td>82.1</td>
</tr>
</tbody>
</table>

n indicates number of newborns; Se, Sensitivity; Sp: Specificity; PPV, positive predictive value; and NPV, negative predictive value.

*P < .05 (CI for α – risk of 5%)

References

Response: prediction of the fetal status in noninvasive management of alloimmune thrombocytopenia

Gerald Bertrand, Moustapha Drame, Corinne Martageix and Cecile Kaplan