Discrepancies in hemoglobin levels

To the Editors: Danskin and Neilson (Danskin FH, Neilson JP. Twin-to-twin transfusion syndrome: what are appropriate diagnostic criteria? AM J OBSTET GYNECOL 1989;161:365-9) in reporting 178 consecutive twin pregnancies commented on the difficulties in the diagnosis of twin-to-twin transfusion syndrome. In their article they state that venous blood samples were usually taken from the neonates on the first day of life. We would like to point out that this method may misdiagnose the fetal hemoglobin level.

We recently checked and noted discrepancies in hemoglobin concentrations in blood collected from the umbilical vein at delivery and in the first day of neonatal life. In 12 cases of twin pregnancy umbilical venous cord blood samples were collected at delivery and the hemoglobin estimations were compared with results from venous blood samples taken on the first day of life. Discrepancies were present in 21 of the 24 infants delivered. In the eight neonates delivered small-for-gestational-age (SGA) all had a higher value in the neonatal specimen (mean difference, 34.3 gm/L ± SD 33.0; range, 8 to 108 gm/L; $p < 0.05$). In the neonates delivered appropriate-for-gestational-age (AGA) this difference was not so evident (mean difference, 12.5 gm/L ± SD 15.1; range, 0 to 59 gm/L; $p < 0.005$). In these cases there was an increase in eight, there was no change in three, and there was a decrease in hemoglobin level in five. The mean difference for SGA neonates was significantly higher than that seen in the AGA neonates ($p < 0.05$). We suggest that the hemoglobin changes result from the rapid changes in the state of hydration in the first day of life and these changes are greater in SGA infants.

We conclude that studies that rely on differences in hemoglobin and hematocrit levels to confirm the diagnosis of twin-to-twin transfusion in the presence of monochorionic placentation should be performed on cord blood samples collected at the time of delivery. The data of Danskin and Neilson may not be accurate in diagnosis of the true incidence of twin-to-twin transfusion syndrome.

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Response declined

Cytogenetic uncertainties surrounding the fragile X in Martin-Bell syndrome

To the Editors: The fragile site of Xq27 first noted by Lubs[1] and later appreciated by clinical geneticists for its diagnostic significance in Martin-Bell syndrome, remained a simple curiosity during the early 1970s.[2] In recent years, many laboratories have vigorously tried to modify their methods because specific tissue culture conditions are required for the expression of the fragile site at Xq27. Consequently, many more fragile sites in the human genome have been observed. Telomeric structural changes similar in appearance to the fragile X site on the long arm of chromosomes with identical morphology to the X chromosome have created a perplexing dilemma. These sites have been incorrectly misinterpreted as fragile X in a number of patients. One such example is chromosome 6, which also has a fragile site at q26 and is often a source of error.

There are persons who have a mixed population of cells with fragile site X(q27) and fragile site 6(q26) creating difficulties in the determination of an accurate estimate of the population with fragile X cells.[3] There are some persons who have gone undetected because of an extremely low percentage of cells with fragile site on chromosome X. The task remains arduous because various patients exhibit cells with a large range (1% to 50%) of fragile X. Thus it is suggested that if fragile X occurs in >0.7% of cells in males and >1.5% of cells in females from a single culture, then this probably indicates a specific fragile X expression.[4]

Routinely, the fragile X chromosome has been identified with the G-banding method. However, the harsh treatment-effect of trypsin during G-banding often results in poor morphology of the fragile sites. Consequently, the fragile X chromosome can escape detection, especially in cases with low incidence of expression.[5,6] Alternatively, if only conventional staining (solid stain) is used, chromosome 6 can be misinterpreted as a fragile X.

In our experience the conventional staining method remains highly practical in estimating the incidence of cells with fragile X. Conventionally stained metaphases can be rapidly destained and then restained by the Q-banding technique for positive chromosomal identification of those metaphases with fragile sites (Fig. 1). This confirmative approach is highly efficient, especially in subjects with a very low percentage of cells with fragile X or those who have fragile sites that involve other autosomes. With use of this approach six of 100 cases referred to our laboratory for confirmation were determined to have been erroneously identified as fragile X. A wrong diagnosis will have serious consequences, especially in cases that are identified by prenatal diagnosis, although it is understood that the absence of fragile X does not exclude the possibility of X-linked mental retardation in fetuses.

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