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Reply to Callen

To the Editor:

In our recent article in the *Journal* (Yang et al. 1997), we showed that an interstitial deletion of 17p11.2 had arisen after meiotic recombination in a carrier of an apparently balanced paracentric inversion (PAI; with breakpoints at 17p11.2 and 17p13.3). Considering all the cytogenetic and molecular evidence, especially the facts that (*a*) the breakpoints of the proband's interstitial deletion "flanked" the proximal breakpoint of the paternal PAI (the proximal Smith-Magenis syndrome (SMS) markers were deleted in spite of not being inverted), (*b*) some markers involved in the PAI were not deleted (the *PMP22* locus), and (*c*) the position of the recombination in paternal meiosis was mapped within the immediate vicinity of the resulting deletion, we proposed a model of unequal crossing-over at the base of an inversion loop.

In response to our article, Callen has raised an interesting point. He proposes an alternate explanation, wherein pairing at meiosis, followed by recombination between an *insertion*-bearing and the normal chromosome 17 homologue could result in the interstitial chromosomal deletion observed in the proband. We agree that a within-arm direct or inverted *insertion* is an important differential diagnosis in cases of suspected paracentric inversions, given the significantly enhanced risk of chromosomal imbalance associated with the former. However, although within-arm insertions (direct or inverted) can result in deletion or duplication of the inserted sequence (Gardner and Sutherland 1996), they cannot result in a concurrent deletion of non*inserted* sequences (proximal SMS markers) and sparing of *inserted* sequences (*PMP22* markers).

Taken together, the data seem to favor our hypothesis of an unequal crossing-over at meiosis, as proposed in our article. However, it should be noted that we have yet to formally exclude Callen's proposal—or even the possibility that the deletion arose de novo as a result of a slightly more proximal (unequal) recombination in 17p11.2.

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Anticipation in Familial Hodgkin Lymphoma

To the Editor:

Anticipation in childhood malignancy has been described by several investigators (Horwitz et al. 1996; Plon 1997). On the basis of 21 parent-child pairs with acute myelogenous leukemia and 9 parent-child pairs with chronic lymphocytic leukemia identified from the literature, Horwitz et al. rejected the hypothesis that there was no age-at-onset difference between the two generations, in either data set. Several published data sets were pooled to test whether there is a difference in parent-child pairs affected with Hodgkin lymphoma (HL). Because the occurrence of HL parent-child pairs is a rare event, several published data sets were pooled to test whether there is a difference, in cancer age at onset, between parents and children who are affected with HL. Thirty parent-child pairs with confirmed di-