it is of interest that the case discussed here (III-2) was judged to be normal at birth, was sent home, and suffered an apneic event at 5 d of age (Schanen et al. 1998).

Therefore, the search for the RTT gene receives a further stimulus from the prospect of its use not only for diagnostic testing of young females who exhibit symptoms suggestive of RTT but also for investigation of unexplained neonatal death or infantile apnea and failure to thrive in males. The genotyping data reported here narrow the unexcluded regions of the X chromosome and focus the gene search to a small interval on Xp and the distal long arm.

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CAROLYN SCHANEN[1] AND UTA FRANCKE[2]
[1]*Department of Pediatrics and the Mental Retardation Research Center, UCLA School of Medicine, Los Angeles; and* [2]*Howard Hughes Medical Institute, Stanford*

Electronic-Database Information

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Address for correspondence and reprints: Dr. Carolyn Schanen, Department of Pediatrics and the Mental Retardation Research Center, UCLA School of Medicine, 10833 Le Conte Avenue, MDCC 22-398, Los Angeles, CA 90095-1752. E-mail: schanen@ucla.edu

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Alternative Interpretation of Reported Paracentric Inversion

To the Editor:

In the recent article in the *Journal*, entitled "Molecular Analysis of Deletion (17)(p11.2p11.2) in a Family Segregating a 17p Paracentric Inversion: Implications for Carriers of Paracentric Inversions," Yang et al. (1997) describe a patient with an interstitial deletion of the short arm of chromosome 17, del(17)(p11.2p11.2). The father of the patient carried a chromosome rearrangement of 17p, which was interpreted as a paracentric inversion, inv(17)(p11.2p13.3). The deletion was considered to arise from an unequal crossing-over event associated with the formation of an inversion loop at meiosis.

An alternative cytogenetic explanation for the father's karyotype is a direct or inverted intrachromosomal insertion of a region from 17p11.2 to 17p13.1, into band p13.3 of the short arm of chromosome 17—that is, ins(17)(p13.3p11.2p13.1) or ins(17)(p13.3p13.1p11.2). Pairing at meiosis, with recombination within the insertion, can result in either deletion of the inserted segment or duplication of the inverted segment (see Gardner and Sutherland 1996). Therefore, an intrachromosomal insertion is a logical explanation for the del(17) observed in the patient reported by Yang et al. This is compatible with the observed banding pattern of the father's rearranged chromosome 17 and does not require any unusual mechanism of "unequal crossing-over" to generate the observed chromosome abnormality. Therefore, this case does not provide evidence for a risk of viable chromosome abnormalities being generated from a parental paracentric inversion.

DAVID F. CALLEN
Department of Cytogenetics and Molecular Genetics
Women's and Children's Hospital
North Adelaide, Australia

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Address for correspondence and reprints: Dr. David F. Callen, Department of Cytogenetics and Molecular Genetics, Women's and Children's Hospital, 72 King William Road, North Adelaide, SA 5006, Australia. E-mail: dcallen@dcallen.mad.adelaide.edu.au

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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.

Sanjay I. Bidichandani,[1] Antonio Baldini,[2] and Pragna I. Patel[1,2,3]

Departments of [1]Neurology and [2]Molecular and Human Genetics, and [3]Division of Neuroscience, Baylor College of Medicine, Houston

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Address for correspondence and reprints: Dr. Pragna I. Patel, Department of Neurology, NB431A, Baylor College of Medicine, One Baylor Plaza, Houston, TX 77030. E-mail: pragna@bcm.tmc.edu

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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-