



## Case Studies from the Child Development Center

### Internationally adopted brothers with developmental delay

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NM, a 3 ½-year-old boy, was seen at the Child Development Center approximately six months after his adoption from a Central American country. He had lived with his biological mother for the first 2 years of life and then was placed in a foster home until the adoption. The adoptive parents had very little information about the biological family, but were told the biological mother was employed as a maid. There was no information about the pregnancy, birth or birth weight. When the adoptive parents first met NM, he was 2 ½ years old and weighed only 18 pounds. He was sick with intestinal parasites and could not walk. The adoptive parents then learned NM's 5-month-old biological brother, EM, was available for adoption and the couple made arrangements to adopt both boys together. The process of adoption took several months, during which NM was treated for parasites and gained some weight. When he arrived in the US, he weighed 21 pounds. Stool examination was negative for ova and parasites. Other screening tests showed no evidence of anemia, lead intoxication, hepatitis, tuberculosis or sexually transmitted diseases. EM also was examined and appeared to be a healthy infant.

Once he settled into his new home, NM's affect improved and he became very animated and happy. He started to say a few single words and he made appropriate sounds for trucks and cars. He enjoyed looking at books and he imitated his parent's activities around the house (pretending to sweep, vacuum and cook). His appetite was good, but he had a tendency to hold food in his cheeks. He learned to take off his clothes and he helped with dressing activities. NM became very attached to his parents and cried when he was left with a baby sitter. Although he had no trouble falling asleep, he awoke frequently with night terrors. His parents also noted that he had an unsteady gait. Despite NM's favorable adjustment to his adoptive home, the parents were concerned about his continuing developmental delays.

Physical examination revealed height and weight to be at the 10th percentile on US growth curves. His head circumference was at

the 25th percentile. There were no dysmorphic features or evidence of birth defects. Hearing and vision appeared to be intact, cardiac and respiratory examinations were normal, and the neurological examination was within normal limits. He was a curious and friendly boy who cooperated for all parts of the evaluation. Developmental examination found his motor, language and adaptive skills to be at a 21-month level.

Although delayed for his age, given his history of malnutrition, chronic parasitic infections and early deprivation, we decided to enroll NM in an early childhood program through the public school system. I made an appointment to see him again in about six months for follow-up.

At the next visit eight months later, his mother reported that NM was enjoying the early childhood program. He received speech, occupational and physical therapies. He still was having difficulty learning to talk. He only used two-word phrases and his speech was not very clear. His mother thought he understood only about half of what was said to him. His play patterns were very simple. His health continued to be good and his night terrors had diminished considerably. Repeat developmental testing showed about three months progress in eight months time. His mother also brought EM, now 21 months old. She reported that he, too, was delayed in development. He had just started walking alone and was starting to say single words. EM's physical examination revealed length at the 25th percentile, weight at the 50th percentile and head circumference at the 5th percentile. There were no dysmorphic features and neurological examination was normal. Developmental examination revealed that EM's skills were at a 12-15 month level.

Many children adopted overseas, especially those who experienced significant deprivation or ill health during early childhood, may be developmentally delayed when they arrive in the US. However, over the first 6-12 months, most children show rapid progress in their new home environments. In this case, despite the lack of any dysmorphic features, the absence of "catch up" development in the older boy, and the presence of a younger brother with developmental delay (who shared at least a common mother), suggested the possibility of an x-linked disorder.

Inside this issue:

*Internationally adopted brothers with developmental delay*

## Internationally adopted brothers with developmental delay *cont.*

Chromosome testing revealed both boys have full mutation fragile X syndrome. Subsequent psychological testing found both children to have moderate cognitive delay. Over the next several years, both children developed signs of ADHD and have responded well to stimulant medications. Neither child has significant emotional or behavioral problems.

Fragile X syndrome (Fra X) is the most common inherited cause of mental retardation with a prevalence of approximately 1:4,000 in the general population. The gene mutation consists of a tri-nucleotide expansion (CGG) on the X chromosome. Individuals with more than 230 CGG repeats have a "full mutation." The gene usually is methylated, preventing transcription and translation of the gene into the FMR1 protein. In each pregnancy, the mother may pass on the pre-mutation or the gene may expand to a full mutation. Because boys have only one X chromosome (which is always inherited from the mother), receipt of an expanded gene results in Fra X syndrome; receipt of the pre-mutation gene results in a "carrier" state. Girls who receive an expanded gene from their mother may have a spectrum of clinical symptoms depending on the extent to which the affected gene is expressed or suppressed due to Lyonization of one of the X chromosomes. Carrier males pass on the pre-mutation to all of their daughters but none of their sons.

The classic features of Fra X syndrome include a long face, prominent ears, prominent chin (prognathism) and enlarged testicles. However, prior to adolescence, affected boys may not appear particularly dysmorphic. Other associated findings include hyperextensible finger joints, double-

jointed thumbs, strabismus, mitral valve prolapse, sleep disturbance, cleft lip and palate and Pierre-Robin malformation sequence. Most boys with Fra X syndrome are mentally retarded, but up to 13 percent may have an IQ in the normal range. According to Merenstein et al. 1996, males with a full mutation that is fully methylated have a mean IQ of 41, whereas males who are mosaic (some cells with the permutation and some cells with the full mutation) have a mean IQ of 60, and males with a full mutation with only partial methylation (less than 50 percent methylation) have a mean IQ of 88 in adulthood. Over time, approximately 30 percent of males and females with Fra X syndrome experience a significant decline in IQ. Typically, they do not lose skills, but instead fail to develop abstract reasoning in line with their normally developing peers. ADHD symptoms, with hyperactivity, is seen in approximately 80 percent of affected boys and 35 percent of girls. Response to typical stimulant medications is favorable. About 15 percent of young children with this syndrome may be diagnosed with autism, although many improve with time and may no longer meet the criteria for autism as they reach mid-childhood. Finally, extreme shyness (social avoidance), anxiety and hypersensitivity to environmental stimuli are often prominent symptoms and may be very difficult to manage with either behavioral therapy or medications.

All children with suspected developmental delay, with or without dysmorphic features, should have chromosome testing, including fragile X molecular testing, as part of a comprehensive etiologic evaluation.

**References available upon request.**

*Case Studies from the Child Development Center* is a limited edition newsletter to help inform referring physicians and other professionals on the depth and breadth of pediatric communication and behavioral issues diagnosed and treated in the Child Development Center at Children's Hospital of Wisconsin.

It is written by Child Development Center staff and produced by Children's Hospital of Wisconsin in January, March, May, July, September and November.

It also is available online at [www.chw.org](http://www.chw.org), Child Development Center, Related Links.

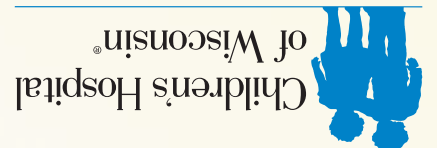
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