No Spinal Deformity Seen After Cervical Fusion

BY SHERRY BOSCHERT
San Francisco Bureau

SAN FRANCISCO — Seventeen children under the age of 6 who underwent occipital cervical fusion using transarticular screws showed normal growth and alignment of the spine an average of 28 months later, Richard C.E. Anderson, M.D., said at a meeting on pediatric neurologic surgery.

The study found no evidence of unintended fusion to adjacent spinal segments in treated children.

DR. ANDERSON

Children with atlantoaxial or occipitocervical instability often need surgery to stabilize the spine, but not much is known about the long-term effects of spinal fusion in children younger than 9 years, whose spines are still growing. Patients in this retrospective study averaged 5 years in age at the time of atlantoaxial (C1-C2) or occipitocervical fusion and have been followed for 13-54 months so far. The study compared plain radiographic and CT images taken immediately after surgery with images from both modalities taken at the most recent follow-up.

All patients fused successfully and maintained straight or lordotic spinal shapes, with most spines staying the same or evolving from straight to a lordotic curvature. One went from lordotic to straight, said Dr. Anderson of Columbia University, New York.

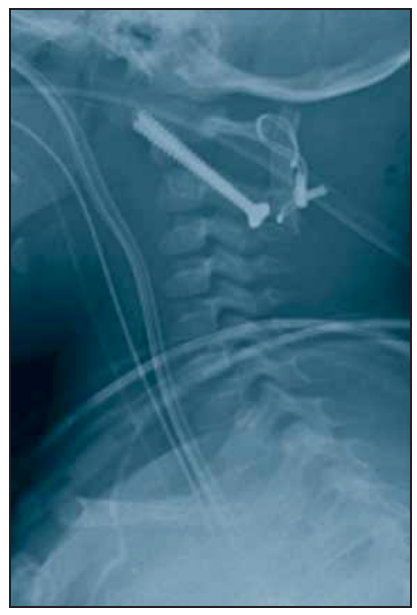
The degree of lordosis in a neutral position increased by 12 degrees, from 15 degrees postoperatively to 27 degrees, a nonsignificant increase that trended toward statistical significance, he said. Of the overall spinal growth, an average of approximately 34% occurred within the fusion construct, suggesting normal growth of the spine.

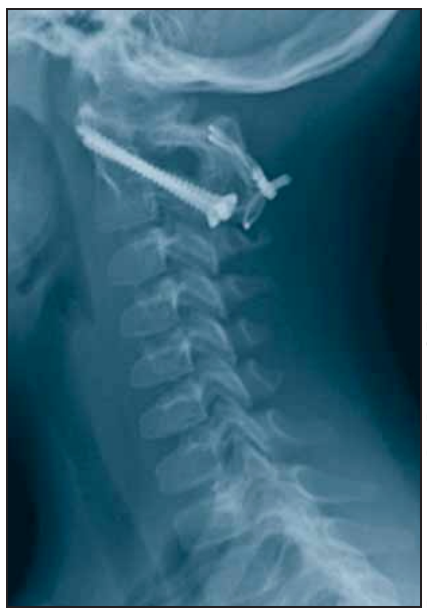
The follow-up imaging showed no kyphosis, osteophyte formation, or long-term instability. "Some previous papers have commented on an unusually high incidence of unintended fusion to adjacent spinal segments," but this study found no evidence of this, he said at the meeting, jointly sponsored by the American Association of Neurological Surgeons and the Congress of Neurological Surgeons.

A subset analysis of five patients with longer follow-up—more than 48 months each—found similar results. These patients averaged 4 years in age at the time of surgery and were followed for a mean of 50 months.

The preliminary long-term results suggest that there's no increased risk for spinal deformity in children under age 6 undergoing C1-C2 or occipital-C2 fusion. Longer follow-up is needed until their spines reach maturity, and better CT data would be helpful, Dr. Anderson said.

"Really, we want to know how the spinal canal grows," among other things, he said. ■





PHOTOS COURTESY DR. RICHARD C.E. ANDERSON

Lateral plain x-ray immediately after C1-C2 fusion (left). After 4 years and 28% vertical growth, there is no deformity to cervical alignment (right).

Research Into Autism Genetics Slated for Funding Increase

BY JEFF EVANS
Senior Writer

Federal health agencies have teamed up with private organizations and government health agencies in Canada and Ireland to provide funding for research into the genetic basis of susceptibility to autistic spectrum disorders.

The coalition, headed by the National Institute of Mental Health, has made $21 million available to researchers and requested grant applications titled "Identifying Autism Susceptibility Genes."

Rather than fund the collection of new data sets on autism spectrum disorders, the coalition wants researchers to submit applications that focus on using large data sets of more than 1,000 pedigrees that already have been assembled. These data sets should have adequate statistical power to detect autism susceptibility loci, according to the NIMH.

The call for research asks investigators to determine the functional significance of any genes or gene variants identified during analysis of larger data sets.

Studies have located several chromosomal regions associated with autism, but few specific genes have been identified.

The call for more research asks investigators to determine the functional significance of any genes or gene variants that are identified during the analysis of the large data sets.

The identification of new genes or gene variants may help researchers to subdivide the autism spectrum disorders into distinct disorders with different molecular mechanisms.

Some of the grant applications also may address the possibility that not all heritable traits of autism directly involve alterations in the genetic code.

Heritable changes that do not alter the DNA sequence include epigenetic mechanisms such as imprinting, DNA methylation, and changes in chromatin or protein conformations; they could potentially regulate gene expression and play an important etiologic role in the disorder.

The coalition consists of four other institutes in the National Institutes of Health besides the NIMH, as well as the Canadian Institutes of Health Research, the Health Research Board (Ireland), the Southwest Autism Research and Resource Center, Cure Autism Now, and the National Alliance for Autism Research.

The coalition expects to fund two to three organizations to participate during the 5-year project. ■

For more information or to request applications, go to http://grants1.nih.gov/grants/guide/rfa-files/RFA-MH-05-007.html.

Immune Dysregulation Found in Autism Spectrum Disorder Patients

BY KERRI WACHTER
Senior Writer

BUDAPEST, HUNGARY — Children with autism spectrum disorders appear to have immune responses different from those of healthy children, according to data presented at the 4th International Congress on Autoimmunity.

"There is evidence now for an immune dysregulation in children with autism, compared with children in the general population," said Paul Ashwood, Ph.D., of the University of California, Davis.

There was no sign of immune dysregulation when mononuclear cells from children with ASD were stimulated with MMR vaccine antigens.

In a study of 31 children with autism spectrum disorders (ASD) and 19 typically developing control children aged 2-5 years, the children with ASD had abnormal levels of several cytokines in response to stimulation with three antigens, compared with the control children.

The study adds weight to the idea that autism has an immune component. There are several previous reports of both increased autoimmunity and immune response deficits in children with autism spectrum disorders.

"However, a lot of these reports are conflicting, and there is no consensus so far," Dr. Ashwood said.

In this study, Dr. Ashwood and colleagues isolated and stimulated peripheral blood mononuclear cells for 48 hours with phytohemagglutinin, lipopolysaccharide, and vaccine antigens from tetanus and MMR. Analysis was performed for 18 cytokines. At baseline, cytokine levels were similar in the children with ASD and the control children.

Following stimulation with phytohemagglutinin, the children with ASD had statistically significantly lower levels of IL-2, IL-6, IL-10, and IL-12 than the control children.

There was also a trend toward higher levels of IL-13 and granulocyte macrophage-colony stimulating factor—which stimulates the precursor cells of granulocytes, macrophages, and eosinophils—among the children with ASD than the control children.

A similar pattern was seen after stimulation with lipopolysaccharide. Children with ASD had lower levels of IL-12 and a slight increase in granulocyte macrophage-colony stimulating factor, compared with the control children.

Stimulation with tetanus antigens resulted in lower levels of IFN- , IL-1- , IL-12, and granulocyte macrophage-colony stimulating factor in the children with ASD, compared to the control children.

There was no difference between the groups after stimulation with MMR vaccine antigens. The researchers are planning to investigate cytokine and chemokine response to individual components of the MMR vaccine. ■