

Neural Tube Defects

For the current Issue of *International Pediatrics*, Dr. Prats has written a Review Article entitled "Surgical Management of Congenital Spinal Lesions." These abnormalities are collectively known as neural tube defects or within the context myelodysplasia or spinal dysraphism. All these terms refer to the abnormal formation of some of the elements of the spinal cord, the exiting nerve roots, or coverings thereof (the meninges and bony elements).

There has been recent national and international attention to neural tube defects primarily for two reasons: their prevention with the use of periconceptional vitamin supplements (folic acid) and the use of intrauterine surgery for preterm closure.

Prevention

Professor Richard Smithells and his colleagues first reported on the association of neural tube defects and folic acid.¹ However, it was a decade later when the United States Public Health Service made an official recommendation.² The American Academy of Pediatrics has recently reinforced this recommendation that all women capable of becoming pregnant consume 400 microgram of folic acid daily to prevent neural tube defects.³ It is thought that only one in three women consume this much folic acid on a regular basis and thus, a major educational program is going to be necessary to achieve these goals.⁴ Although most investigators believe that the periconceptional use of folic acid supplementation will prevent 50%^{3,5} to 70%⁶ of neural tube defects, there have been reports that have failed to show a convincing reduction.⁷

The exact mechanism of folic acid and neural tube defects remains elusive, but there is an experimental model and some evidence that a defect in homocysteine metabolism may play a role.⁸ A recent review article on neural tube defects has highlighted much of this ongoing discussion, but, suffice it to say, that all medical practitioners should be educating our patients about the importance of folic acid in the diet of child bearing women.⁹

Intrauterine Repair

The second area of great interest, and controversy, has been the use of intrauterine repair of menigomyeloceles. Intrauterine surgery has been technically possible in the experimental animal for quite some time.¹⁰ The paralysis seen in children with neural tube defects (myelomeningocele) may be due to the myelodysplasia itself, or may be due in part

to a spinal cord injury caused by exposure of the neural tube to the intrauterine environment. This has been shown in the fetal rat, pig and sheep fetuses.^{11,12} The group from Vanderbilt University has had a significant experience with closing menigomyeloceles in utero¹³ and has reported that these children have benefited not only with respect to motor function, but also with a decreased incidence of shunt-dependent hydrocephalus and hindbrain herniations.¹⁴⁻¹⁶ Other centers, such as Philadelphia Children's Hospital, have had some modest experience with this surgery. Although it is still too early to make too many definitive statements regarding the efficacy, indications, risks, and long term effects, it is an interesting and exciting concept in the treatment of children with neural tube defects.

References

1. Smithells RW, Nevin NC, Seller MJ, et al. Further experience of vitamin supplementation for prevention of neural tube defect recurrences. *Lancet*. 1983;1:1027-31.
2. Recommendations for the use of folic acid to reduce the number of cases of spina bifida and other neural tube defects. *MMWR Morb Mortal Wkly Rep*. 1992;41(RR-14):1-7.
3. Folic acid for the prevention of neural tube defects. American Academy of Pediatrics. Committee on Genetics. *Pediatrics*. 1999;104:325-7.
4. Van der Pal-de Bruin KM, deWalle HE, Jeeninga W, et al. The Dutch' Folic Acid Campaign - have the goals been achieved? *Paediatr Perinat Epidemiol*. 2000;14(2):111-7.
5. McDonnell RJ, Johnson Z, Delaney V, et al. East Ireland 1980-1994: Epidemiology of neural tube defects. *J Epidemiol Community Health*. 1999;53(12):782-8.
6. Molloy AM, Mills JL, Kirke PN, et al. Folate status and neural tube defects. *Biofactors*. 1999;10:291-4.
7. Rosano A, Smithells D, Cacciani L, et al. Time trends in neural tube defects prevalence in relation to preventive strategies: an international study. *J Epidemiol Community Health*. 1999; 53:630-5.
8. Manning SM, Jennings R, Madsen JR. Pathophysiology, prevention, and potential treatment of neural tube defects. *Ment Retard Dev Disabil Res Rev*. 200;6:6-14.
9. Botto LD, Moore CA, Khoury MJ, et al. Neural tube defects. *NEJM*. 1999;341:1509-19.
10. Michejda M. Intrauterine treatment of spina bifida: primate model. *A Kinderchir*. 1984;39:259-61.
11. Hefez DS, Aryanpur J, Rotellini NA, et al. Intrauterine repair of experimental surgically created dysraphism. *Neurosurgery*. 1993;32:1005-10.
12. Meuli M, Meuli-Simmen C, Hutchins GM, et al. In utero surgery rescues neurological function at birth in sheep with spina bifida. *Nat Med*. 1995;1:342-7.
13. Mangels KJ, Tulipan N, Bruner JP, et al. Use of bipedicular advancement flaps for intrauterine closure of myeloschisis. *Pediatr Neurosurg*. 2000;32:52-6.

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14. Bruner JP, Tulipan N, Paschall RL, et al. Fetal surgery for myelomeningocele and the incidence of shunt-dependent hydrocephalus. *JAMA*. 1999;282:1819-25.
 15. Tulipan N, Hernanz-Schulman M, Lowe LH, et al. Intrauterine myelomeningocele repair reverses preexisting hindbrain herniation. *Pediatr Neurosurg*. 1999;31:137-42.
 16. Tulipan N, Bruner JP, Hernanz-Schulman M, et al. Effect of intrauterine myelomeningocele repair on central nervous system structure and function. *Pediatr Neurosurg*. 1999;31:183-8.

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