Infantile Spasms: Current Therapy and Progress

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Infantile spasms represent an age-dependent epileptic syndrome that usually begins between 4 and 6 months of life; onset is before the age of 12 months in about 90% of cases. The spasms are characterized by symmetric, bilateral, brief, and sudden contractions of the flexor or extensor muscle groups. The seizures may be resistant to treatment, and the syndrome frequently is associated with mental retardation.

In 14% to 38% of cases, infantile spasms are "cryptogenic," without identifiable underlying cause. However, the majority of patients have so-called "symptomatic" infantile spasms, with some identifiable pre-, peri-, or postnatal factor that underlies the syndrome: hypoxemia-ischemia, intrauterine infection, a cerebral malformation or degenerative disorder, tuberous sclerosis, a genetic abnormality, an inborn error of metabolism, an intracranial hemorrhage, traumatic delivery, head injury, or a central nervous system infection. Magnetic resonance imaging, detailed chromosomal analysis, and sophisticated metabolic screening have enhanced the differentiation of subtle symptomatic from true cryptogenic presentations.

Adrenocorticotropic hormone (ACTH) is the agent used most often to treat infantile spasms, but despite years of accumulated experience, neither the optimal dose nor the most appropriate duration of therapy has been well established. Typically, treatment consists of either medium- (100 IU/m^2 per day) or high-dose (150 IU/m^2 per day) ACTH injected intramuscularly for as few as 2 weeks or as many as 2 months. Common side effects include obesity, hypertension, and thrombocytopenia. Seizures that have responded to treatment with ACTH may relapse when the therapy is withdrawn; a second course of ACTH may be of benefit. More recently, it has been suggested that either low-dose (30 IU/m^2 per day) ACTH or oral prednisone may be as effective as medium- or high-dose ACTH.

Other agents used in the treatment of infantile spasms include sodium valproate, clonazepam, vitamin B6, and vigabatrin. Sodium valproate is the drug of second choice, when ACTH has failed, followed by clonazepam. High-dose vitamin B6 has been used both as monotherapy and as adjunctive therapy, usually after treatment with ACTH and in conjunction with sodium valproate. Vigabatrin, a new antiepileptic drug available in Europe, has proven especially effective in children who have tuberous sclerosis underlying their infantile spasms. Clearly, more effective and safer therapeutic agents need to be developed.

The long-term prognosis for children who have infantile spasms depends to a large extent on the underlying etiology. Children who have cryptogenic infantile spasms, but who have a normal neurologic and developmental history before the onset of spasms and a normal physical examination and neuroimaging prior to therapy, have the most hopeful prognosis; one third to one half of such children will be neurologically and cognitively normal at long-term follow-up. Likewise, response to therapy helps predict outcome. Children who respond to treatment have a better prognosis for cognitive development than those who do not. Still, of children who have the syndrome of symptomatic infantile spasms in which there is an identifiable underlying cause, about 50% will have residual motor impairment and 70% to 80% will be mentally retarded. In the past, mortality associated with infantile spasms was estimated to be as high as 25%; a more recent estimate is 5%, probably reflecting improved supportive medical care.

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Comment: "Infantile spasms" is a clinically descriptive term for a characteristic form of epilepsy, also called "salaam seizures" in the older literature. Typically, although not always, affected infants manifest the epilepsy with sudden, brief flexion of the neck and trunk, accompanied by adduction and flexion of the extremities, so that their hands meet in the midline and their heads bow, mimicking a "salaam" gesture. Early in the course of infantile spasms, a child's seizures may be as subtle as head nodding, which can be overlooked very easily as a signal of a serious disorder. When the fuller-blown spasms begin, they tend to occur in clusters, and some children may have hundreds of seizure clusters a day.

As characteristic as the clinical picture can be, so too is the electroencephalographic pattern associated with infantile spasms. Called "hypsarrhythmia," it consists of diffuse, disorganized, high-voltage slow waves with random multifocal spikes and sharp waves. Although not pathognomonic, hypsarrhythmia is typical of infantile spasms.

Part of the difficulty in assessing the effectiveness of treatment for infantile spasms is that even without therapy, both the typical seizure pattern and the hypsarrhythmic electroencephalogram tend to resolve with time. The bad news is that so many children, once their spasms have passed, are left with other epileptic disorders as well as with significant retardation.

Henry M. Adam, MD
Editor, In Brief

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