INFECTIOUS DISEASES

TRIAL OF IMMUNE GLOBULIN IN INFANT BOTULISM

A 5-year, randomized, double-blind, placebo-controlled trial of the orphan drug Human Botulism Immune Globulin Intravenous (BIG-IV) in 122 infants in California with confirmed infant botulism (75 caused by type A *Clostridium botulinum* toxin, and 47 by type B toxin) was conducted at the California Department of Health Services, Richmond, CA; National Botulism Surveillance and Reference Laboratory, CDC and P, Atlanta; and Division of Biostatistics, University of California, Berkeley. Eligible infants had acute flaccid paralysis consistent with infant botulism and had been hospitalized for <3 days. Infants treated with BIG-IV showed significant reductions in hospital stay, time in intensive care, duration of mechanical ventilation, duration of tube or intravenous feeding, and hospital charges. In a 6-year nation-wide, open-label study, infants treated with BIG-IV within 7 days of admission had a mean hospital stay of 2.2 weeks, and early treatment shortened the length of stay significantly more than later treatment. No serious adverse events were attributable to BIG-IV. (Arnon SS, Schechter R, Maslanka SE et al. Human botulism immune globulin for the treatment of infant botulism. **N Engl J Med** February 3, 2006;354:462-471). (Reprints: Dr Arnon, California Department of Health Services, 850 Marina Bay Pkwy, Rm E-361, Richmond, CA 94804).

COMMENT. The diagnosis of infant botulism may be difficult and requires a high index of suspicion. One infant in the trial who died 5 months after receiving placebo was subsequently found to have Werdnig Hoffman disease. The authors comment that infant botulism was suspected at admission in only half of the patients enrolled in the randomized trial. Three-quarters of the infants needed intensive care, and half needed mechanical ventilation. Serious complications included nosocomial *C difficile* infection with pseudomembranous colitis and toxic shock in one infant, and one patient required surgical repair of tracheal stenosis after intubation. BIG-IV has a half-life of 28 days and will neutralize for 6 months the botulinum toxin absorbed from the colon of an infant (Johnson RO, Clay SA, Arnon SS. Diagnosis and management of infant botulism. **Am J Dis Child** 1979;133:586-593).

Three infants with a relapsing form of infant botulism (IB) were reported from the Children's Hospital of Philadelphia (Glauser TA et al. **Ann Neurol** 1990;28:187-189). None had been re-exposed to honey or breast milk. Honey has been implicated in several cases in the USA (Arnon SS. **Annu Rev Med** 1980;31:541). Over 600 cases of IB were reported in the US in a 14 year period, the disease being endemic in California, Utah, and Pennsylvania. The disease is rare in the United Kingdom, only 2 cases reported up to 1989 (Smith GE et al. **Arch Dis Child** 1989;64:871-872). Differential diagnoses include neonatal myasthenia gravis, infectious polyneuritis, congenital myopathy, infantile spinal muscular atrophy, and organic phosphate intoxication. Aminoglycoside antibiotics may exacerbate the paralysis and hypotonia. Most patients with IB recover, but recovery appears to be accelerated and complications lessened by use of BIG-IV.