

Hepatitis C in Children - Not the Same as in Adults

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Hepatitis C (HCV) is an RNA virus of Flaviviridae family. There are 6 major HCV genotypes and more than 50 subtypes. The extensive genetic heterogeneity of HCV and the lack of a vigorous T-cell response has made this an elusive virus to treat. Furthermore, the lack of symptoms until many years after acquisition has allowed this virus to insidiously invade our society. Decompensated liver disease from HCV is now the most common indication for liver transplantation.

In childhood, the virus rarely causes symptoms and many cases probably go unrecognized. It is estimated that there are a quarter million cases in the US, but the number may actually be much greater. Prevalence studies (*Committee on Infectious Diseases. AAP. Pediatrics 1998*) have found a seroprevalence of:

- ◆ 0.2% for children less than 12 years and
- ◆ 0.4% for those between 12 and 19 years

A concerted effort to establish the natural history in the pediatric population and the indications for treatment is now underway.

Prior to 1990, the predominant mode of transmission was through contaminated blood products. Now, the most common mode is vertical transmission. The risk of transmission is estimated to be approximately 5%, but is increased by comorbid states such as HIV where there is a 20% risk. Spontaneous clearance of the virus occurs in the first year for 25-50% of children. Horizontal transmission may also occur among household contacts and between children, but the incidence is so rare there are no restrictions for school, day care or sports.

Progression of liver disease may be influenced by the mode of acquisition and is also influenced by duration of disease. In general there is rare progression to decompensated liver disease in the pediatric population. Between 1995 and 2001 less than 1% of the pediatric liver transplants were for HCV. The histologic features are similar to those found in adult biopsies including lymphoid aggregates or follicles, sinusoidal lymphocytes and steatosis. However, children with who have other underlying illnesses such as thalassemia may have more significant and rapid liver damage. Data analysis of 211 thalassemic subjects with a mean age of 8.7 years followed for at least 4 years demonstrated that hepatic iron content and HCV were independent risk factors for liver fibrosis progression. Their concomitant presence resulted in striking progressive liver damage. In a second study, a group of patients treated for cancer at St. Jude's Children's Research Hospital had an incidence of cirrhosis of 8.5%. However, in general, most studies examining children have showed minimal progression of liver disease during childhood including those acquiring HCV from transfusions for congenital heart disease and leukemia. In a histologic series from Italy and Spain examining 80 children followed for a mean of 3.5 years: ± 4.3 years, the frequency and severity of bile duct damage increased with patient age. However, the overall necroinflammatory score was low, grade 1 or 2, and only 1 child had cirrhosis.

Despite the generally benign course during childhood, treatment is still a strong consideration. Early acquisition of HCV implies potentially long duration of disease and eventual liver damage. Additionally, there are social concerns and public health concerns. Parents have to wrestle with issues of how to discuss this disease with their child. Difficult situations frequently arise with friends, babysitters and schools. Furthermore the additional risk of vertical transmission to the next generation concerns many families. The typical

considerations involved in treatment decisions include these social concerns, along with an understanding of the natural history of the disease balanced against the chance of successful therapy.

Interferon is better tolerated than in adults and may have better sustained virologic response (SVR). SVR with monotherapy in multiple studies range from 33-45% and is strongly influenced by genotype. SVR for individuals with type 1 is less than 30% while type 2 is 70%. Few studies have been completed using combination therapy. In the most recent, 70 children ages 3 to 16 years received 3 MU per meter squared of interferon alfa-2b three times weekly along with ribavirin at a dose of 15 mg/kg per day for a period of 1 year. Treatment in children:

- ◆ less than 12 years was 57% SVR;
- ◆ Only 30% SVR in those older than 12 years.
- ◆ Those infected with genotype 1 was 38% SVR and 82% SVR for those with types 2 and 3.
- ◆ Adverse events led to discontinuation in only 7% of subjects.
- ◆ No data regarding peginterferon and ribavirin have been collected to date.

Caring for children with hepatitis C is particularly challenging. The natural history in the pediatric population is unclear. We have yet to fully understand which children are at risk for severe liver disease and who will respond to therapy. Ideally, the next decades will bring information and therapies that will effectively treat this disease for those in need and prevent it from being transmitted to others.

Editor's Note:

Key points and comments:

- ◆ Household transmission is rare but not absent.
- ◆ Most cases of HBV in children progress slowly
- ◆ Female children progress more slowly than male children
 - This is the same in adult patients
- ◆ Younger children respond better than older children to HCV medications
- ◆ Why treat children?:
 - Prevention of a chronic disease
 - Prevent HCC
 - Improves general well being
 - Social issues (school, peer relationships, dating, sex) may outweigh all other considerations

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