



**Infectious Disease Epidemiology Section**  
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## **REYE'S SYNDROME**

### **POST INFECTION ENCEPHALOPATHY**

Revised 10/28/2004

Reye's syndrome is a rare, acute encephalopathy associated with mitochondrial dysfunction associated with liver dysfunction (fatty liver) that usually follows a viral infection.

Encephalopathy following infection or immunization does not appear to be a single syndrome.

#### **Epidemiology**

The syndrome typically follows common viral infections, most notable influenza and varicella and is epidemiologically related to administration of salicylates during infection. Widespread outbreaks of the illness have been associated with outbreaks of influenza B, and, to a lesser extent, influenza A (H1N1).

Reye's syndrome affects previously healthy children less than eighteen years of age.

Post infectious encephalopathy is associated with non-specific respiratory and gastrointestinal tract infections, measles, pertussis and typhoid infections. Whole-cell pertussis, DT/Td/tetanus toxoid, and measles, mumps and vaccinia vaccines have been associated with encephalopathy.

Incubation period: Latency between infection or vaccination and encephalopathy is highly variable, ranging from hours up to 6 weeks.

#### **Clinical Description**

The encephalopathy is caused by noninflammatory cerebral edema and is usually manifested by severe vomiting and lethargy, followed by deepening stages of coma. The pathogenesis of postinfectious or postvaccinal encephalopathy is not known. Autopsy series of postinfectious encephalitis include cases of encephalopathy; findings demonstrate cerebral edema without inflammation.

Liver pathology in Reye's syndrome is pathognomonic. Panlobular accumulation of small lipid droplets occurs without evidence of cholestasis or inflammation. By electron microscopy, the mitochondria are large and irregular, with diminished matrix granules.

#### **Laboratory Tests**

There is no diagnostic test for postinfectious encephalopathy. The CSF is frequently under increased pressure but is otherwise normal by routine analysis. A diagnosis of postvaccinal encephalopathy is by temporal association; proof of causation is impossible in individual cases.

A case of Reye's syndrome is diagnosed as much by ruling out other possibilities as by identification of distinctive illness patterns. Reye's syndrome is a collection of certain signs and symptoms rather than a specific disease that can be confirmed by the appropriate test. A characteristic history with alteration of

mental function, abnormal blood studies, including liver function studies (such as SGOT/SGPT, prothrombin time, blood ammonia) and blood sugar, without signs of jaundice are indicative. Other tests include but are not limited to (1) spinal tap (to rule out meningitis or encephalitis), (2) urine tests for toxic substances (to rule out ingestion of known poisons), and (3) liver biopsy.

**Treatment:** Therapy is supportive.

### **Surveillance**

Reye's syndrome is not a reportable condition.

### **Case Definition**

Clinical case definition: An illness that meets all of the following criteria:

- Acute, noninflammatory encephalopathy that is documented clinically by
  - an alteration in consciousness
  - and, if available, a record of the CSF containing less than or equal to 8 leukocytes/mm<sup>3</sup> or a histologic specimen demonstrating cerebral edema without perivascular or meningeal inflammation
- Hepatopathy documented by either
  - a liver biopsy or an autopsy considered to be diagnostic of Reye's syndrome
  - or a threefold or greater increase in the levels of the serum glutamic-oxaloacetic transaminase (SGOT), serum glutamic-pyruvic transaminase (SGPT), or serum ammonia

No more reasonable explanation for the cerebral and hepatic abnormalities

Case classification: Confirmed: a case that meets the clinical case definition

The Vaccine Safety Committee of the Institute of Medicine, Washington, DC, has modified case definitions used in the National Childhood Encephalopathy Study

#### Acute encephalopathy

Children <24 months:

Significantly decreased level of consciousness (stupor or coma) lasting for at least 24 hours, not attributable to postictal state or medication

Children ≥ 24 months:

- Condition lasting for at least 24 hours, characterized by two of following:
- Confusional state or a delirium, or a psychosis, not medication related
- Significantly decreased level of consciousness (stupor or coma), independent of seizure and not attributed to medication
- Seizure associated with loss of consciousness
- Increased intracranial pressure is consistent with the diagnosis at any age

Excluded conditions: Sleepiness, persistent inconsolable crying, bulging fontanelle, seizures

Chronic encephalopathy: Persistence of acute findings over several months to years beyond the acute episode

Excluded conditions: Return to normal, followed by chronic encephalopathy, chronic encephalopathy secondary to genetic, prenatal or perinatal factors

### **Investigation**

No investigation is necessary for sporadic cases unless a cluster is suspected or major concerns are expressed by a physician.

### **Prevention**

- Repeat immunization with the specific vaccine is contraindicated in instances of postvaccinal encephalopathy not due to another identifiable cause.
- Avoidance of aspirin use for common fevers and for analgesia in children effectively minimizes the risk of Reye's syndrome. Reye's syndrome following the administration of live varicella vaccine to patients on chronic salicylate therapy has not been described. The decision of whether to give this vaccine to such patients must be individualized.

**Hospital precaution and isolation:** Standard precautions