

Smith-Lemli-Opitz syndrome: Which laboratory test confirms the diagnosis?

Smith-Lemli-Opitz syndrome (SLOS) is a syndrome characterized by multiple malformations, dysmorphic features, mental retardation and behavioural abnormalities. This autosomal recessive defect of cholesterol synthesis is caused by mutations in the 7-dehydrocholesterol (7DHC) reductase gene and leads to a generalized cholesterol deficiency. A normal plasma cholesterol level does not rule out SLOS and should not be used as a screening test. The diagnosis of a confirmed case of SLOS is based on the demonstration of elevated plasma levels of 7DHC. This screening test should also be performed in affected individuals with a positive family history of SLOS, in families with a previous clinical diagnosis of SLOS without biochemical confirmation or in families with more than one similarly affected relative. Plasma 7DHC measurement is not routinely available, and a referral to a geneticist or a metabolic specialist is usually required. Biochemical genetics laboratories in Alberta, Ontario, Quebec and Newfoundland perform this diagnostic test. For patients with SLOS who are reported to the CPSP, funded plasma 7DHC measurement and mutation analysis for SLOS are available at McMaster University, Hamilton, Ontario through the Biochemical Genetic Laboratory and the Molecular Diagnosis Laboratory. SLOS may also be diagnosed by the measurement of tissue 7DHC and cholesterol levels or by direct 7DHC reductase activity assays. These tests, as well as retrospective or postmortem biochemical diagnoses performed on frozen or paraffin preserved tissue samples, neonatal blood spots and stored amniotic fluid or plasma, can be performed in some research laboratories. During the first year of the Canadian Paediatric Surveillance Program's surveillance of SLOS, nine confirmed new cases were reported, yielding an incidence of one in 37,100 births. All cases were reported in infants of white, European origin, suggesting that the incidence of SLOS in this population may be as high as one in 29,700 births. This number is most likely an underestimation, given that only one mildly affected patient was reported during the first year and that other patients may still remain undiagnosed.

The Canadian Paediatric Surveillance Program is a joint project of the Canadian Paediatric Society and Health Canada's Centre for Infectious Disease Prevention and Control that undertakes the surveillance of rare diseases and conditions in children. For more information, visit <<http://www.cps.ca/english/proadv/cpsp/cpsp.htm>> or <<http://www.cps.ca/francais/proadv/pcsp/pcsp.htm>>