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50 Years Ago in *THE JOURNAL OF PEDIATRICS*

Wilson's Disease Remains a Great Masquerader

Slovis TH, Dubois RS, Rodgerson DO, Silverman A. The varied manifestations of Wilson's disease. Pediatr 1971;78:578-74.

A century after the initial description of "hepatolenticular degeneration," Wilson's disease remains a rare entity with variable manifestations requiring a high index of suspicion for diagnosis. The authors described this inherited disorder of copper metabolism owing to an undetermined genetic defect. They illustrate the clinical findings in various Wilsonian phenotypes—acute and chronic liver disease, fulminant liver failure with hemolytic crisis, neuropsychiatric disorder, as well as asymptomatic siblings.

In 1993, the genetic defect in *ATP7B* was identified. The resultant mutant protein leads to decreased excretion of copper in bile and accumulation in the liver with subsequent copper release into the bloodstream and deposition in other organs.[1] Contemporary diagnostic algorithms have been developed incorporating clinical measures described by the authors—low ceruloplasmin level, increased urine copper, pathognomonic Kayser-Fleischer rings, and hepatic iron quantification on biopsy as the gold standard. More than 500 *ATP7B* mutations have been identified, and genetic testing has improved the diagnostic process, particularly for asymptomatic relatives.

Therapeutic options have expanded and include the chelating agents D-penicillamine and trientine, as well as zinc blockade of enteral copper absorption. One described patient was the first described recipient of a liver transplant for Wilson's disease. Currently, liver transplantation is a well-established treatment for end-stage liver disease and fulminant liver failure, with almost 900 transplants performed in the US for Wilson's disease over the last 30 years.[2] It is the only chronic disease granted the highest priority (status 1A) on the waitlist for those with fulminant failure, because transplantation remains the sole life-saving option for these patients. Emerging technologies, such as gene therapy, aimed at correcting the *ATP7B* mutation, may change the landscape of Wilson's disease.[3] Most important for favorable outcomes in these patients is early recognition of varied presentations, just as described 50 years ago.

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