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50 Years Ago in *THE JOURNAL OF PEDIATRICS*

The Liver in Juvenile Idiopathic Arthritis and the Evolution of Liver Function Tests

Schaller J, Beckwith B, Wedgwood RJ. Hepatic involvement in juvenile rheumatoid arthritis. J Pediatr 1970;77:203-10.

In 1970, prominent pediatric rheumatologist Jane Schaller et al reported 5 cases of hepatic involvement in what was then called juvenile rheumatoid arthritis. The authors described patients with acute-onset fevers, hepatosplenomegaly, rash, lymphadenopathy, and serositis who later developed arthritis. This was among the first description of liver disease in what is now more commonly known as juvenile idiopathic arthritis. Juvenile idiopathic arthritis is now recognized widely as a multisystem disorder, with numerous subsequent reports of liver involvement, from elevation in liver enzymes to acute liver failure.[1]

Highlighted in the paper was the then widely used bromsulfthalein (BSP) retention test as a marker of liver function, involving injection of BSP into patients and measurement of serum levels 45 minutes later. The result was expressed as percent retention (<5% considered normal).[2] It was used for several decades in clinical practice and in animal model research of hepatobiliary disorders. This author's mentors recall the BSP test as being cumbersome, unreliable, and a cause of anaphylactic reactions. Thus, it has fallen out of favor in clinical practice.

Historically, liver function tests refer to markers of cell injury (alanine aminotransferase, aspartate transaminase, and gamma-glutamyl transferase) and liver synthetic dysfunction (international normalized ratio, albumin, factor levels). As understanding of liver physiology has expanded over the last several years, so too has the need for more dynamic tests to truly assess liver function. Areas of study have included measurement of serum bile acids to evaluate enterohepatic circulation and tests of hepatic clearance using compounds such as BSP, indocyanine green, aminopyrine, caffeine, and lidocaine. Although the latter have shown promise in adults, there remain questions about feasibility and reliability in pediatrics. Thus, they are not commonly used in pediatric practice.[3] With continued advancements in pediatric hepatology, there will likely emerge within the next 50 years, novel, noninvasive, robust methods for the assessment of liver function.

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