findings from the UK Millennium Cohort Study. J Epidemiol Commun H 2018;72:94-100.
44. Vazou S, Pesce C, Lakes K, Smiley-Oyen A. More than one road leads to Rome: a narrative review and meta-analysis of physical activity intervention effects on cognition in youth. Int J Sport Exerc Psychol 2019;17:153-78.
45. Else-Quest NM, Hyde JS, Goldsmith HH, Van Hulle CA. Gender differences in temperament: a meta-analysis. Psychol Bull 2006;132:33-72.
46. Nolen-Hoeksema S. Emotion regulation and psychopathology: the role of gender. Annu Rev Clin Psychol 2012;8:161-87.
47. Wanless SB, McClelland MM, Lan X, Son SH, Cameron CE, Morrison FJ, et al. Gender differences in behavioral regulation in four societies: the United States, Taiwan, South Korea, and China. Early Child Res Q 2013;28:621-33.
48. Veijalainen J, Reunamo J, Heikkilä M. Early gender differences in emotional expressions and self-regulation in settings of early childhood education and care. 2020. Early Child Dev Care. 2020. https://doi.org/10.1080/03004430.2019.1611045
49. Hill A, Degnan K, Calkins SD, Keane SP. Profiles of externalizing behavior problems for boys and girls across preschool: the roles of emotion regulation and inattention. Dev Psychol 2006;42:913-28.
50. Tomporowski PD, Pesce C. Exercise, sports, and performance arts benefit cognition via a common process. Psychol Bull 2019;145:929-51.
51. Chastin SF, Palarea-Albaladejo J, Dontje ML, Skelton DA. Combined effects of time spent in physical activity, sedentary behaviors and sleep on obesity and cardio-metabolic health markers: a novel compositional data analysis approach. PLoS One 2015;10:e0139984.
52. Barisic A, Leatherdale ST, Kreiger N. Importance of frequency, intensity, time and type (FITT) in physical activity assessment for epidemiological research. Can J Public Health 2011;102:174-5.

50 Years Ago in *The Journal of Pediatrics*

Therapy of Hemolytic Uremic Syndrome, a 50-Year Update

Kaplan BS, Katz J, Krawitz S, Lurie A, Path F. An Analysis of the Results of Therapy in 67 Cases of the Hemolytic-Uremic Syndrome. J Pediatr 1971;78:420-5.

An unknown syndrome of microangiopathy characterized by a triad of hemolytic anemia, thrombocytopenia, and acute kidney injury was described for the first time by Gasser et al in 1955, named the "hemolytic-uremic syndrome" (HUS). In the 1970s, the etiology and pathogenesis remained unclear. A postulated mechanism of renal injury was a consumption coagulopathy, suggesting that heparin could be useful, although it had no apparent effect on immediate survival and is no longer advised. Survival was better in patients treated with early peritoneal dialysis and now is seldom required because its indications are similar to other forms of acute kidney injury.[1]

In 1983, Karmali et al identified the etiologic toxin produced by the *Escherichia coli* serotype O157:H7, a critical discovery for future therapy, owing to the growing knowledge regarding its pathogenesis and complement interaction. Approximately 90% of cases in children are produced by the Shiga toxin-producing *E coli*, associated with a prodrome of diarrhea known as "hemorrhagic colitis." This toxin damages the cellular glycosphingolipid, increasing thrombin and fibrin levels, activating an inflammatory response responsible of extensive microangiopathic intravascular thrombosis and multiorgan failure particularly targeting the kidneys. The toxin has a high affinity for the membrane receptor in the glomerular endothelium and tubular cells, making dialysis a needed therapy in 50%-70% of cases.[2]

Antibiotic use for this disorder is controversial. Current recommendations suggest against antibiotic use, owing to a paradoxical increase in Shiga toxin production. The cornerstone of management for HUS is supportive care such as fluids and blood transfusion, including platelets when active bleeding takes place. Eculizumab, a humanized monoclonal antibody, blocks factor C5 activation and has a promising effect in complement-associated HUS.[3]

HUS is one of the most common causes of acute kidney injury in children. Overall mortality has decreased from 60% to less than 5% in the last half-century. Its proper identification is still essential to provide prompt supportive care.

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References

1. O'Brien AD, Lively TA, Chang TW, Gorbach SL. Purification of Shigella dysenteriae 1 (Shiga)-like toxin from Escherichia coli 0157:H7 strains associated with haemorrhagic colitis. Lancet 1983;1:573.
2. Karmali MA, Steele BT, Petric M, Lim C. Sporadic cases of haemolytic-uraemic syndrome associated with faecal cytotoxin and cytotoxin-producing Escherichia coli in stools. Lancet 1983;I:619-20.
3. Sheerin NS, Glover E. Haemolytic uremic syndrome: diagnosis and management. F1000Research 2019;8:1690.