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50 Years Ago in *THE JOURNAL OF PEDIATRICS*

Measurement of Urinary Catecholamine Excretion in Patients with Neuroblastoma

Voorhess ML. Neuroblastoma with normal urinary catecholamine excretion. J Pediatr 1971;78(4):680-3.

Neuroblastoma, the most common extracranial solid tumor of childhood, originates from primitive sympathetic ganglion cells. Although primary tumors are typically localized to the adrenal medulla, neuroblastoma may arise from prevertebral sympathetic ganglia and paraganglia in the cervical, thoracic, retroperitoneal, or pelvic regions. As Voorhess observed 50 years ago, tumors that compress the spinal cord can feature suppressed tyrosine metabolism and therefore have normal excretion of catecholamines, including dopamine and norepinephrine, which are further degraded to homovanillic acid (HVA) and vanillylmandelic acid (VMA), respectively. Elevated levels of HVA and VMA, identified in the urine or blood of approximately 90% of patients of neuroblastoma, can confirm a diagnosis, often before the results from tissue biopsy and/or ^{123}I-mIBG nuclear imaging.

Catecholamines associated with neuroblastoma metabolism have been evaluated for applications beyond confirming the diagnosis. In studies from abroad, mass screening programs assessed urinary HVA and VMA in all infants and identified many cases of neuroblastoma that would not otherwise have been clinically evident, in part because some patients have spontaneous resolution of their disease. Such screening has not been associated consistently with a decrease in the death rate owing to neuroblastoma and is, therefore, not used today. However, post-treatment surveillance of urinary HVA and VMA is part of the standard of care for survivors of neuroblastoma and results may provide an early signal of disease recurrence. Further, biologically aggressive tumors generate higher levels of urinary catecholamines, and studies are ongoing to identify how to apply these findings, including absolute values and ratios of catecholamines, as prognostic and therapeutic biomarkers.

The measurement of urine catecholamine degradation products remains integral for the management for patients with neuroblastoma, offering a rapid, noninvasive, and safe approach for diagnosis and monitoring, and novel applications with urine, such as a catecholamine metabolite panel and exosomal molecular profiling, are now being investigated.[1,2] The next decade is sure to reveal further insights into our biologic understanding of this potentially lethal disease.

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