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**Purpose:** To present the results of a 21-year (1982 to 2003) longitudinal study of 260 patients with urea cycle disorders (UCDs) following a total of 975 hyperammonemic episodes, and quantify survival and symptoms associated with these events.

### Key takeaways:

- First hyperammonemic episode was reported in 34% of patients at 0 to 30 days of age (neonatal onset) and 66% of patients at  $\geq 31$  days of age (late onset).
- Patients with neonatal-onset disease had the worst outcome; 35% of patients were alive at final follow-up (approximately 11 years after the start of the study period).
  - Of the 26 deaths in this group, 22 were within the first 2 months of life and only 1 patient died after 3 years of age (age 6).
- Patients with late-onset disease had better outcomes, with 78% to 87% alive at final follow-up.
- In females with ornithine transcarbamylase (OTC) deficiency, 92% of all hyperammonemic episodes occurred after 2 years of age.
- Episodes were preceded by the following: illness in 58%; noncompliance with diet in 15%; noncompliance with medication in 10%; and major life events (such as surgery, accidents, school stress, pregnancy) in 10%.
- In 76% of all episodes (and 80% of first episodes), patients presented with neurological symptoms at the time of hospital admission. Other notable presenting signs and symptoms included infection (reported in 34% of episodes) and vomiting (30%).

### Conclusions:

- Neurological signs were expected and confirmed to be the most common presenting symptom. Surprisingly, only 63% of patients reported a decreased level of consciousness and only 19% presented with vomiting at the time of their first episode.
- The high incidence of infection (34%) as a presenting symptom underscores the importance of careful 'sick-day' monitoring and treatment of patients with UCDs, and supports a hypothesis that catabolic stress (eg, from a viral illness) is a more significant risk factor for hyperammonemia than an increased dietary intake of protein.
- The survival data from this study were encouraging, with at least 50% of the patients alive at 5 years.