

Verner J V & Morrison A B. Islet cell tumor and a syndrome of refractory watery diarrhea and hypokalemia. *Amer. J. Med.* 25:374-80, 1958.
[Depts. Medicine and Pathology, Duke Univ. Med. Ctr., Durham, NC]

This paper reports two patients with a fatal syndrome of watery diarrhea, hypokalemia, and benign islet tumors. We theorized that secretions of these tumors were causative and that early diagnosis and surgical removal might result in cure. [The SCI® indicates that this paper has been cited in over 310 publications since 1958.]

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Groundwork for this research actually began during my internship at Duke University where medical department house staff were required to make in-depth presentations at a "Sunday School." My topic that year was hypokalemia, and a continuing fascination with and study of the subject ultimately led to this and other clinical reports. The ambience of the department at that time under Gene Stead challenged us to think creatively about patients, and clinical research was strongly encouraged.

Three years later, as chief resident, I was at the hospital six days and nights a week, seeing or reviewing every patient admitted to the medical wards. In addition, I had requested the laboratory to alert me to all patients anywhere in-house with hypokalemia. It was in this way that I came in contact with the first of two patients reported in the paper. I saw him on the surgical service just one hour prior to his death and was puzzled to find a man supposedly recovering from routine inguinal herniorrhaphy dying from a cholera-like diarrhea with the peculiar com-

ination of terminal uremia and profound hypokalemia. At the clinicopathological conference, the clinical diagnosis, "probable chronic laxative abuse," struck me as preposterous. When an acorn-sized, benign, nonbeta islet tumor shown on a slide was described as "an incidental finding of no known clinical significance," I experienced a "eureka" happening and knew intuitively that it was that very tumor which had caused the patient's death.

A.B. Morrison of the Department of Pathology and I discussed the case, and he became as intrigued with the pathological findings as I was with the clinical ones. Although conception of the new syndrome had taken place, a second case was needed to substantiate the birth. A short time later, I was reviewing the chart of a 19-year-old man recently discharged after his 19th Duke Medical Center admission for diarrhea and hypokalemia. Discovering that he had missed his appointment with a Duke psychiatrist, I called his home only to find that he had been hospitalized elsewhere and died with severe diarrhea. Autopsy materials obtained by Morrison revealed a benign islet tumor.

Next came the arduous precomputer review of the literature and the thrill of finding that the syndrome had not previously been described. After many midnight hours of writing and rewriting, we submitted the paper to Stead. Recognizing its importance, he not only sent it to his favorite journal, where it was published rather quickly, but also encouraged me to present it in Atlantic City to the American Federation for Clinical Research.

The paper has been cited often because it made possible the diagnosis of a rare and previously unknown syndrome, now often referred to as the Verner-Morrison Syndrome. Diagnosis was soon followed by a pioneering surgical cure,¹ better clinical definitions of the syndrome,² identification of tumoral secretory products, such as VIP (vasoactive intestinal polypeptides),³ and recent reports of increasing numbers of useful agents for medical treatment of inoperable cases.^{4,5}

1. Chears W C, Thompson J E, Hutcheson J B & Patterson C O. Pancreatic islet tumor with severe diarrhea. *Amer. J. Med.* 29:529-33, 1960. (Cited 55 times.)
2. Verner J V & Morrison A B. Endocrine pancreatic islet disease with diarrhea: report of a case due to diffuse hyperplasia of nonbeta islet tissue with a review of 54 additional cases. *Arch. Intern. Med.* 133:492-500, 1974. (Cited 130 times.)
3. Bloom S R, Polak J M & Pearse A G E. Vasoactive intestinal peptide and watery diarrhea syndrome. *Lancet* 2:14-16, 1973. (Cited 310 times.)
4. Bonfills S. New somatostatin molecule for management of endocrine tumours. *Gut* 26:433-7, 1985.
5. Oberg K, Funa K & Alm G. Effects of leukocyte interferon on clinical symptoms and hormone levels in patients with mid-gut carcinoid tumors and carcinoid syndrome. *N. Engl. J. Med.* 309:129-33, 1983.