

# This Week's Citation Classic

**Gordon R S, Jr.** Exudative enteropathy: abnormal permeability of the gastrointestinal tract demonstrable with labelled polyvinylpyrrolidone. *Lancet* 1:325-6, 1959. [Lab. Cellular Physiology and Metabolism, National Heart Institute, US Public Health Service, Bethesda, MD]

PVP labeled with  $^{131}\text{I}$  was shown to be a practical diagnostic test for the recognition of hypoproteinemia due to loss into the digestive tract. [The SCI® indicates that this paper has been cited over 280 times since 1961.]

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"This investigation exemplifies the virtues of serendipity, and the merits of having a large and varied scientific and clinical research endeavor under one roof at the National Institutes of Health. F. Bartter admitted a patient with 'hypercatabolic hypoproteinemia' for studies of nitrogen balance. I saw her with the intention of measuring her levels of free fatty acids (my research interest at that time), and guessed that her 'hypercatabolism' might really be due to loss of plasma proteins into the gut, followed by digestion and absorption of amino acids. With the help of J. Davidson (who was set up for duodenal intubations) and E. Middleton (who had prepared rabbit antiserum to human albumin for a study of chylomicrons), I tested her duodenal juice for albumin and got a strongly positive result. This observation was the beginning of a collaborative effort to study conditions associated with gastrointestinal protein loss.

"It was not difficult to postulate that an injectable, recognizable, nonbiodegradable macromolecule such as radioactive PVP would be a good diagnostic agent. It was difficult to make one; in fact, the commercial manufacturer of

PVP said it could not be done. It could be, but only with the continued help of another colleague, H. Fales, a knowledgeable and well-equipped organic chemist. After almost a year, I was ready to test the same patient, whose continued participation was also essential to the project, with  $^{131}\text{I}$ -PVP. It worked. Whereas normals excreted only traces of an injected dose in their stools, hers were highly radioactive.

"I then began preparing labeled PVP on a regular monthly schedule. The assistance of W. Briner, pharmacist, was invaluable in sterilizing, safety testing, and calibrating the product. With his facilities, we could scale up the monthly production, and offer experimental quantities of the material to investigators all over the world who had reported patients who appeared to have a similar condition. Wide distribution of the diagnostic agent led to other studies which showed how many diseases could result in the same pathophysiology.<sup>1</sup> This is the main reason for the frequent citation of my initial small study. I believe that the paper is also cited because of my mention of our use of disposable paint cans for collecting and handling feces for laboratory examination, avoiding most of the unpleasantness of transferring, homogenizing, and disposing of samples.

" $^{131}\text{I}$ -pvp has since been supplanted by other diagnostic agents, usually human albumin labeled with  $^{51}\text{Cr}$ . The condition has come to be known as protein-losing gastroenteropathy, and knowledge of its many etiologies is still expanding. It was all initiated by a chance observation on an unusual patient in an unusually diversified research environment—a study which could never have been planned.

"Recently, T.A. Waldmann prepared a chapter on this subject in the book *Gastroenterology*.<sup>2</sup>

1. Waldmann T A, Steinfeld J L, Dutcher T F, Davidson J D & Gordon R S, Jr. The role of the gastrointestinal system in "idiopathic hypoproteinemia." *Gastroenterology* 41:197-207, 1961. [Citation Classic. *Current Contents/Clinical Practice* (15): 16, 14 April 1980.]
2. Waidmann T.A. Protein-losing enteropathies. (Bockus H L, ed.) *Gastroenterology*. Philadelphia: W.B. Saunders, 1975. Vol. II. p. 361-85.