"During the second World War it was my privilege to serve as a Clinical Chemist in the Canadian Naval Hospital in Halifax. In the period from 1942-1946 laboratory analyses were performed on about 200 cases of hepatitis. Serum proteins were approximated by specific gravity in copper sulfate solutions. By 1947, I was back in Toronto as Assistant Professor of Pathological Chemistry and C. J. Bardawill, a recent graduate in medicine, was my first graduate student. His assigned research project was to study biochemical abnormalities in experimental liver injury. We needed a simple, rapid, and accurate method for serum proteins and the biuret reaction seemed to offer the best prospects. Bardawill gained useful analytical experience by comparing several biuret reagents and we settled on a modified version of Weichselbaum's 'dilute' reagent. The paucity of data on the behavior of these reagents (and some unfounded reservations on my part concerning the analytical prowess of my colleague) prompted me to investigate in more detail the factors affecting the behavior of biuret reagents stabilized with tartrate. These experiments were performed between January and June of 1948 and the paper was sent for publication in July.

"Also, as a result of my war-time Hospital experience, I had persuaded the Dean of Medicine to support the establishment of a Clinical Investigation Laboratory in our Department under my supervision. Its purpose was to foster the investigation of pathological conditions in patients, by a collaboration between members of the Clinical Departments and members of the Department of Pathological Chemistry. Maxima David was the technologist in this laboratory. She had a clever idea that instead of setting up a separate serum dilution for total protein, we could use an aliquot of the sodium sulfate dilution immediately after mixing. This proved correct, the method was thus improved and she earned her right to co-authorship. Bardawill obtained his Master's degree and went on to become a fine internist; his death at an early age was a sad loss for Canadian medicine.

"The success of our biuret method for serum proteins resulted in large measure from the timing of its publication. Here was a clearly established procedure in a major journal that any laboratory interested in serum proteins could set up and use. Hospital laboratory services were developing all around the world. Many clinical studies must have included measurements of serum proteins, thus accounting for the numerous citations. We ordered a modest 300 reprints and ran out of them within weeks. My hope is that the method has made a significant contribution to the care and welfare of patients."

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This Week’s Citation Classic

The properties of stabilized biuret reagents were investigated in order to define the optimal concentrations of copper, alkali, tartrate and potassium iodide. An 'ideal' reagent and a simple procedure are described for the determination of total protein, albumin and globulins in serum or plasma. [The SCI® indicates that this paper has been cited over 6,430 times since 1961.]