

## Citation Classics

**Van Handel E & Zilversmit D B.** Micromethod for the direct determination of serum triglycerides. *Journal of Laboratory Clinical Medicine* 50:152-57, 1957.

**A microprocedure for the direct determination of triglyceride concentrations in biologic specimens is presented. The method depends on the quantitative removal of phosphatides from the sample and the subsequent determination of esterified glycerol. The procedure has been tested on whole blood and plasma. [The SC<sup>®</sup> indicates that this paper was cited 1,440 times in the period 1961-1975.]**

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"In the early fifties, Don Zilversmit was working on the turnover of phospholipids at the University of Tennessee, while I was working on the chemistry of phospholipids at the University of Amsterdam. This shared interest led to my appointment at the University of Tennessee. Had Memphis offered an ocean beach, it might have lasted longer than the three years it did. Ironically, the team became best known for removing from serum, in one swoop, the phospholipids to which we had both dedicated our lives.

"To study the mechanism of absorption in dogs, we used the then available I 131 labeled fat. In order to test whether the label would stick during absorption, we needed a way to measure serum triglycerides. Determinations then in use were done by difference, extracting and weighing the total lipids, and subtracting whatever value was determined for cholesterol, cholesterol esters, and phospholipids. Since triglycerides constitute only a small fraction of this total, these determinations often yielded negative values. We therefore designed a 'micro-method for the direct determination of

serum triglycerides,' based on the glycerol rather than on the fatty acid moiety of the molecule. Had we been able to mix I 131 with C 14 labeled triglycerides, the non-validity of the I 131 labeling would have been immediately apparent, and the chemical method unnecessary. The I 131 method sank, the triglyceride method rose.

"To make the paper acceptable to a clinical journal, we determined 'normal values' in 12 students. Twenty years and millions of determinations later, the average value in the population is still the same.

"In 1957, the term 'triglyceride' could not be found in the index of any clinical text-book. Within a few years, 'high triglycerides' became a common household scare-word along with high cholesterol and high glucose.

"The need for automation in clinical chemistry required a modification which combines a specific lipase with a glycerol dehydrogenase and avoids solvent extraction and heating. However, the 1957 method is still widely used, in spite of my 'improvement' published in 1961.<sup>1</sup> This 1961 cluster (information science jargon for a buster) is yearly siphoning off enough citations to knock the 1957 mother paper just off the list of 50 most cited papers.

"Don Zilversmit, now at Cornell, is still working on problems related to mammalian lipids and lipoproteins. I moved to the Entomological Research Center in Vero Beach, Florida, and have been working on insect metabolism ever since. I have published several other methods which are frequently cited. There has always been a much greater demand for my method papers than for my biological results, except when I started the title of an article with the word 'sex.'<sup>2</sup> Perhaps the readers expected again an original method, easily taught to technicians.

"Serum triglycerides seem to be a permanent feature on the clinical scene. What is the significance of this determination? I don't know. Check with your doctor."

1. **Van Handel E.** Suggested modifications of the micro determination of triglycerides. *Clinical Chemistry* 7:249-51, 1961.

2. .... Sex as regulator of triglyceride metabolism in the mosquito. *Science* 134:1979-80, 1961.