

This Week's Citation Classic

Huggett A St. G & Nixon D A. Use of glucose oxidase, peroxidase, and o-dianisidine in determination of blood and urinary glucose. *Lancet* 2:368-70, 1957. [Dept. Physiol., Univ. London, and Dept. Physiol., St. Mary's Hosp. Med. Sch., London, England]

A method for estimating glucose specifically by the use of a fungal oxi-dase preparation and a chromogenic oxygen acceptor was described. It has proved of considerable value for the measurement of blood glucose in clinical medicine, as well as in other fields. [The SC[®] indicates that this paper has been cited over 1,045 times since 1961.]

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"It is very sad that neither Professor Huggett, FRS, nor Dr. D.A. Nixon is alive to learn of the request for this *Citation Classic*. By the mid -1960s, both men realised that the paper was often referred to, and a number of scientists also visited the laboratory to discuss the method with them. The frequent citation of this paper is not difficult to understand for it provided a method for measuring glucose specifically and this has had widespread daily use in clinical medicine. It can perhaps best be regarded as a 'classical' method since it has now been in use for 20 years.

"Huggett's main interest was foetal and placental physiology, and his development of Caesarian section during late pregnancy of sheep and goats enabled him and his colleagues to study functions of the living foetus while still attached to the mother.

"In these investigations, Huggett and Nixon made many estimates of blood glucose in both foetal and maternal circulations. Since the blood of the sheep foetus contains fructose as well as glucose, the glucose was determined as the difference between total reducing power, measured by reduction of copper, and a direct estimate of fructose. Clearly a direct estimate of glucose was desirable. In 1956, a method based on the enzymic oxidation of glucose to gluconic acid with simultaneous production of hydrogen peroxide, which in turn, in the presence of peroxidase, acted on a chromophore whose oxidation product could be determined colourimetrically was discovered by A.S. Keston and J.D. Teller.^{1,2} Keston applied his reagent to filter paper for testing urinary glucose. Teller modified the reagent and used it to test for glucose in blood plasma or serum. Huggett and Nixon modified Teller's method and worked out details suitable for estimating glucose in deproteinised blood and in decolourised urine using glucose oxidase prepared from *Penicillin notatum*. Their procedure requires a reagent simple to prepare, a constant temperature bath at 37°C, and a colourimeter or spectro-photometer. Colour develops in an hour and is stable for several hours."

1. **Keston A S.** Specific colorimetric enzymatic analytical reagents for glucose. *Abstracts of papers of the 129th meeting of the American Chemical Society, 8-13 April 1956, Dallas, Texas.* Washington, DC: American Chemical Society, 1956. p. 31-2C.
2. **Teller J D.** Direct, quantitative, colorimetric determination of serum or plasma glucose. *Abstracts of papers of the 130th meeting of the American Chemical Society, 16-21 September 1956, Atlantic City, New Jersey.* Washington, DC: American Chemical Society, 1956. p. 69C.