

This Week's Citation Classic

Shelley H J. Glycogen reserves and their changes at birth and in anoxia.
Brit. Med. Bull. 17:137-43, 1961.
[Nuffield Inst. Medical Res., Univ. Oxford, Oxford, England]

This paper describes the changes in tissue glycogen concentration which occur during fetal life and the first few days after birth. Large amounts accumulate in the liver and skeletal muscles of many species as a store for use after birth. The high concentration in the heart enables the fetus to survive for long periods without oxygen. [The SCIP® indicates that this paper has been cited over 265 times since 1961.]

Heather J. Shelley
University of Oxford
Nuffield Institute for Medical Research
Headington Oxford OX3 9DS
England

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"This was a review paper and one reason it has been cited so often is that reviews make convenient references. Another is that the timing was right. It was becoming clear that not only the survival but also the quality of the newborn child could be affected by events occurring before and immediately after birth. Evidence was accumulating that lack of oxygen or glucose during the perinatal period could cause permanent brain damage and clinicians were anxious to prevent this.

"The article summarized data showing that the fetus accumulates glycogen during the latter part of gestation and suggested that if these reserves were deficient, the newborn's chances of normal survival would be jeopardized. This suggestion was followed by a great deal of more sophisticated research, aimed at discovering whether I was right, how carbohydrate metabolism was regulated in the fetus and newborn, and whether it could be modified to their advantage, a debate which is still in progress.

"I did not foresee my debut as 'the glycogen girl.' In 1956 I was a research assistant investigating the aetiology of pregnancy toxæmia in sheep. My attention was focused on the mother's glycogen reserves, but the Institute's director, G.S. Dawes, had become intrigued by the ability of fetal and newborn animals to survive for long periods without oxygen, an ability which was lost with increasing maturity. The phenomenon had been described by Robert Boyle,¹ but the mechanism was still obscure. Energy was obtained by anaerobic glycolysis and Claude Bernard had noted the presence of glycogen in fetal tissues. It seemed possible that the amount available to a vital organ could be a factor limiting survival. To our delight, we found a good correlation between anoxic survival and the glycogen content of the heart. We compared data from fetal lambs, rodents, and, thanks to the generosity of the National Institutes of Health, rhesus monkeys studied in Puerto Rico, one of the more glamorous places to pursue research. The monkey data were added to the graphs just before the paper went to press, the day we came back from San Juan.

"The next task was to see if the animal data were applicable to man. The review included values obtained at abortion, but babies near term could only be studied *post mortem*. Having no medical qualifications, and being pregnant myself by then, I was wholly dependent on the help of clinical colleagues in three large hospitals. Their generous collaboration enabled me to confirm its relevance, and the work was a good example of how clinical data can be interpreted in the light of animal experiments. I am still working in the field, investigating the response of the fetus to hypo and hyperglycemia, in the hope that the treatment of pregnant women and their children can be improved still further. More recent reviews have been prepared by myself² and W.W. Hay, Jr.³

1. Boyle R. New pneumatical experiments about respiration. *Phil. Trans.* 5:2011-31, 1670.
2. Shelley H J, Bassett J M & Milner R D G. Control of carbohydrate metabolism in the fetus and newborn. *Brit. Med. Bull.* 31:37-43, 1975.
3. Hay W W, Jr. Fetal glucose metabolism. *Semin. Perinatol.* 3:157-76, 1979.