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This Week's Citation Classic

Brock D J H & Sutcliffe R G. Alpha-fetoprotein in the antenatal diagnosis of anencephaly and spina bifida. *Lancet* 2:197-9, 1972. (University Dept. Human Genetics, Western Gen. Hosp., Edinburgh, Scotland]

This paper showed that it was possible to make antenatal diagnoses of anencephaly and spina bifida by measurement of amniotic fluid alpha-fetoprotein concentrations. This introduced a new category of at-risk mothers to antenatal diagnosis. [The ***SCI***® indicates that this paper has been cited over 310 times since 1972.]

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"In the early 1970s Roger Sutcliffe and I were investigating the origin of amniotic fluid protein. If most were of fetal origin we thought that it might prove useful for antenatal diagnosis. However, we were able to show fairly convincingly that the majority of protein derived from the maternal serum. The exception was alpha-fetoprotein (AFP).

"We had gone to considerable trouble to raise an antiserum against human AFP to allow us to make a series of measurements on its concentration in amniotic fluid. As we were interested in fetal abnormalities, we asked ourselves whether there were any particular disorders where one might anticipate a change in amniotic fluid AFP concentration. Once the question was posed in this way, the answer was blindingly obvious: the open neural tube defects such as spina bifida and anencephaly. The anatomical deformities in these abnormalities made it seem fairly likely to us that both fetal serum and fetal cerebrospinal fluid components passed directly into the amniotic fluid. Our reasoning suggested that we should get at least statistically significant increases in AFP, since the protein was known to be present at high levels in fetal serum.

"Fortunately we had been collecting amniotic fluids from a variety of pregnancies for a number of years. In our first experiment we set up five anencephalic amniotic fluids against five controls. The results were extraordinary. All five anencephalic fluids had such high AFP concentrations that they had gone completely off scale. My technician reported that the experiment had not worked and would have to be repeated, but both Roger and I knew that we had stumbled onto something important.

"We assembled as many other relevant amniotic fluids as we could, measured feverishly, and wrote a paper, which was accepted and published all within the space of three months. Almost as an aside, we tossed in the statement in the final paragraph that we could see no reason why this procedure should not eventually be applied to maternal blood and thus available to all pregnant women. I can't think how we arrived at that idea, which in terms of existing knowledge was absurd, but it has turned out to be exactly right.

"Within a week of the appearance of our paper a colleague had his technician in my laboratory learning the new procedure. Within a year AFP analysis was being carried out on all amniotic fluids in the United Kingdom and was an accepted part of the standard procedure of antenatal diagnosis. There were really no problems in the passage of a research technique into routine clinical usage. Recently, several articles have been published on the topic.[1-4]

"The paper was much cited in the early years because it opened up a new field of antenatal diagnosis. However, it has now become such an accepted procedure that one rarely sees 'Brock and Sutcliffe (1972).' The moral is to enjoy your moment of glory; it won't last."

1. Brock D J H. Prenatal diagnosis of neural tube defects. *Eur. J. Clin. Invest.* 7:465-72, 1977.
2. Feto-specific proteins in prenatal diagnosis. *Mol. Aspects Med.* 3:433-553, 1980.
3. **Brock D J H, Barron L, Duncan P, Scrimgeour J B & Watt M.** Significance of elevated mid-trimester maternal plasma alpha-fetoprotein values. *Lancet* 1:1281-2, 1979.
4. Report of the UK collaborative study on alpha-fetoprotein in relation to neural tube defects. *Lancet* 1:1323-33, 1977.