"Of Pregnancy and Progeny" (1980), by Norbert Freinkel [1]

By: Castagnetti, Blaise

Norbert Freinkel's lecture "Of Pregnancy and Progeny" was published by the American Diabetes Association's journal *Diabetes* in December of 1980. In the lecture, Freinkel argued that pregnancy [2] changes the way that the female body breaks down and uses food. Through experiments that involved pregnant women as well as infants, Freinkel established the body's maternal metabolism and how it affects both the mother and the infant. Freinkel's main focus of research in the latter part of his life was diabetes, specifically in pregnant women. Diabetes occurs in around one to three percent of all pregnancies, which is 30,000 to 90,000 women a year in the US. Freinkel's article indicates that pregnancy [2] influences the metabolism in all pregnant females and that pregnancy [2] complicated by diabetes is only an exaggeration of what occurs in all pregnant women. Subsequently, many doctors more closely monitored pregnant women and their blood sugar and insulin levels, as doctors were informed that all pregnant women have the capacity to become diabetic.

Freinkel held several different teaching positions at Northwestern Medical School, was the head of several clinics, and was the director of the Center for Endocrinology, Metabolism, and Nutrition. Freinkel briefly discusses the first published series about diabetes in pregnancy [2]. In 1882, James Matthews Duncan compiled twenty-two cases of diabetic pregnant women and observed how diabetes affected the fetuses and infants of those women. The twenty-two cases observed by Duncan occurred in fifteen women, four of whom died during the course of pregnancy [2]. Nineteen women had fetuses that became viable [3], meaning they could live outside of the womb [4], and of those, seven of the fetuses and infants died before birth or in the weeks right before or after birth.

In 1980, Freinkel originally gave "Of Pregnancy and Progeny" as a lecture at the Northwestern University [5] Medical School in Chicago, Illinois. He dedicated his lecture to Frederick Banting, a Canadian medical scientist who co-discovered the hormone [6] insulin. After giving the lecture, the journal *Diabetes* printed the lecture in their journal. "Of Pregnancy and Progeny" has ten sections. The first five are focused mainly on the pregnant woman, while the last five sections are focused on the fetus [7] and infant. Through his lecture, Freinkel outlined the history of diabetes and pregnancy [2]. In earlier times, if a woman had diabetes before becoming pregnant, she was advised that her condition may severely complicate the pregnancy [2]. Diabetic women rarely gave birth because of the fear of future complications for both themselves and the infants.

In the beginning of the lecture, Freinkel describes the effects of the conceptus, or having an embryo in the uterus [8], on maternal and insulin metabolism, as well as affirming the hypothesis of accelerated starvation. He reported that insulin levels increase late in human pregnancy [2] and increase only modestly in early pregnancy [2]. Accelerated starvation is a process that occurs in the body after a pro-longed fast, where the body's blood sugar levels are low. It is a metabolic process that is considered normal in the human body when low blood sugar levels occur. Freinkel cited the works of Phillip Felig and Jon Tyson in dictating that humans [9] naturally display features of accelerated starvation using their experiment of accelerated starvation on rats.

In section three, Freinkel talks about the special features of accelerated starvation. Freinkel describes his accelerated starvation experiment on women that were thirty-two to thirty-eight weeks pregnant and on non-pregnant women. These women were all matched by age and size. In his experiment, Freinkel gave all the women a standard dinner at six PM. After dinner, the women would not be allowed to eat breakfast the following morning to get an accurate fasting blood sample. Freinkel took blood samples from the women at twelve, fourteen, sixteen, and eighteen hours after fasting. Freinkel observed that all of the pregnant women showed signs of low blood sugar, whereas the non-pregnant women displayed normal blood sugar levels. Freinkel concluded that skipping breakfast has major metabolic implications for women who are late in their pregnancy [2] and that the tendency for accelerated starvation is present at all times during the late stages of pregnancy [2].

In the next section of the article, Freinkel details what happens in the body when food is eaten during the latter stages of pregnancy [2]. Freinkel had conducted another fasting experiment of his that he discusses in the article. In the experiment, Freinkel gave an oral dosage of glucose to pregnant women fourteen hours after their dinner the night before. His experiment showed that there was a greater rise in blood sugar and triglyceride, which is a main constituent of body fat. In his writing, Freinkel infers that fat metabolism increases in cases of fasting and ingestion of glucose in pregnant women. The levels of glucose in the blood are correlated with the original levels at the time of glucose administration. That shows that the levels of

glucose in the blood after a night of fasting and an oral dose of glucose are similar to the levels of glucose in the blood after a meal.

Next, Freinkel discusses the differences in blood sugar levels in women who were fed compared to women who fasted. Freinkel observed that the variation in blood sugar levels between meals were much greater for pregnant women in comparison to women who were not pregnant. To help regulate blood sugar levels, Freinkel reports that injections of regular insulin concurrently with meals was an effective option. The results from that treatment of insulin injections were yet to be determined, because according to Freinkel, his study was too small to justify extravagant extrapolations.

In the sixth and seventh sections of the article, Freinkel examines the effects of the maternal fuels, which comprise of sugars, amino acids, etc., on the development of the placenta [10] and fetus [7]. Between 1951 and 1976, the perinatal mortality rate of pregnancies complicated by diabetes reduced from 17.7 percent to 12.0 percent, a reduction [11] of about one third. Freinkel stresses that the placenta [10] and the fetus [7] are developed in an environment that is solely derived from maternal fuels. Thus, maternal fuels and insulin are the main deciding factor for the developing environment of the placenta [10]. Freinkel concludes that the process occurs naturally in all pregnant women, with the only difference being that the body's metabolic breakdown of glucose is exaggerated.

In the eighth section, Freinkel discusses the implications for gestational diabetes. In the article, Freinkel defines gestational diabetes as glucose intolerance with onset during pregnancy [2]. Freinkel observed through his research that pregnant women who are also diabetic display symptoms of insulin retardation [12] in response to doses of oral glucose. In that section, Freinkel also compared the infant weights of pregnant women with and without gestational diabetes. The study's results indicated that there is a correlation between the birth weights of infants born to diabetic women compared to the weights of infants born to normal women. Infants born to diabetic women were heavier than those born to non-diabetic women.

Freinkel evaluated the Jørgen Pedersen hyperglycemia-hyperinsulinism hypothesis in the next section of the article. The Pedersen hypothesis suggests that fetal overgrowth is related to the glucose transported from the mother to the placenta [10], which then stimulates the release of insulin by the fetal cells. Freinkel observed fifty-eight gestational diabetics, and 106 normal women during weeks thirty-two to thirty-six of pregnancy [2]. He was able to determine that glucose and triglyceride levels have a significant correlation in birth weight in the infants of gestational diabetics. However, normal glucose levels have no correlation to birth weight. He also came to the conclusion that gestational diabetics have undeniable disturbances in all major classes of insulin-dependent foodstuffs. With that new conclusion, Freinkel states that gestational diabetes must be viewed as a disorder of total fuel metabolism. Freinkel also reports that the Pedersen hypothesis should be modified according to these new findings.

Finally, in the last section of the article, Freinkel discusses fuel-mediated teratogenesis. Teratogenesis is the process by which birth malformations of an embryo or fetus [7] are formed. Changes in maternal insulin levels can affect a variety of changes in the fetus [7], by mediating changes in the fetal fuels. Freinkel sought to extend the fuel-mediated possibilities to include different forms of teratogenesis. Freinkel mentions a study by Gian-Paolo Revelli about the developmental effects on children whose mothers had experienced famine during pregnancy [2] caused by a German blockade that lasted from October 1944 to May 1945. The study found that people who experienced famine during the last trimester [13] of pregnancy [2] and the first few months of life had significantly lower obesity rates, compared to famine experienced in the first two trimesters which resulted in more obese offspring.

Freinkel's lecture described what he had been researching for decades leading up to the lecture. Freinkel contextualized gestational diabetes by comparing the infants born to diabetic and non-diabetic pregnant women, explaining that the physiological interactions occur in all pregnancies but are more amplified in gestational diabetics. That knowledge informed the practices of doctors, resulting in practices that emphasize monitoring blood sugar and insulin levels in all pregnant women and practices in which pregnant women are advised that the occurrence of diabetes is especially critical during pregnancy [2]. Women are advised what to eat and what not to eat. Furthermore, they are informed that exercise can help regulate blood sugar levels and prevent diabetes during pregnancy [2].

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Subject

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