

Human error as well as errors of nature also complicate life, including life related to IVF. The Associated Press on July 10th released in newspapers around the world a report entitled "Test Tube Baby Mix-Up Causes Alarm: Birth of Black Babies to White Couple Raises Questions About Reliability of the Program". This

occurrence was in England. Such occurrences of error undoubtedly are very rare, but inevitably occur.

Life goes on, but not always without error. The positivities of what IVF has, does, and will accomplish, far outweigh the negativity of the errors of nature and man.

Robert M. Blizzard, MD

Hypovitaminosis D Prevalence and Determinants Among African American and White Women of Reproductive Age: Third National Health and Nutrition Examination Survey, 1988-1994

This study addressed the issue of the prevalence and the determinants of hypovitaminosis D among 1,546 African American and 1,426 white women of reproductive age (15-49). These women were not pregnant and participated in the Third National Health and Nutrition Examination Survey (1988 – 1994). Hypovitaminosis D was defined as serum 25-hydroxyvitamin D concentrations of < 37.5 nmol/L. The prevalence of hypovitaminosis D was 42.4% among African American women as compared to only 4.2% among white women. The presence of hypovitaminosis D was independently associated with low consumption of milk or cereal, less than ideal use of vitamin D supplements, cold seasons, urban residence, low body mass index, and use of oral contraceptives. Even among the 243 African Americans who consumed an adequate intake of vitamin D from supplements (>200 IU/d), 28.2% had hypovitaminosis D. The authors concluded that the high prevalence of hypovitaminosis D among African American women warrants further examination of the vitamin D recommendations for these women. The determinants of hypovitaminosis D among women should be considered when these women are advised regarding dietary intake and supplement use.

Nesby-O'Dell S, et al. *Am J Clin Nutr* 2002;76:187-192.

Editor's Comments: *The report by this group of investigators provided compelling data with irrefutable evidence that vitamin D deficiency constitutes a major unrecognized epidemic in many young black adult women and in 5% of white women of childbearing age. This survey might have shown a much higher prevalence of hypovitaminosis D if it had been performed in the winter. We may also assume that vitamin D deficiency*

might be equally prevalent among males of the same age and race, although this was not studied. This article clearly documents it is still currently possible to frequently find vitamin D deficiency in the United States, which plagued our ancestors during the 19th century. There are vulnerable populations, such as those who are not exposed to the benefits of sunlight irradiation, and in those who are dark skinned. The latter may not be able to synthesize sufficient vitamin D from the skin to prevent vitamin D deficiency, and may be in need of higher levels of vitamin D intake as compared to their white counterparts. Therefore, the recommendation to examine the dietary recommendations for young black women and men should be quickly undertaken. Since the black population has a high incidence of lactase deficiency and, therefore, not able to tolerate milk, oral vitamin D supplements may be needed.

In this study there were no measurements of parathyroid hormone levels or the active metabolic vitamin D (25-D hydroxy vitamin D), both of which are very sensitive indicators of calcium homeostasis and vitamin D deficiency. The high prevalence of hypovitaminosis D among "healthy young female adults" is important as vitamin D deficiency is associated with osteomalacia, bone pain, muscle aches, muscle weakness, and fibromyalgia. It also causes secondary hyperparathyroidism, which can precipitate and exacerbate osteoporosis by increasing mobilization of mineral and matrix from the skeleton. Therefore, there is reason for each of us to pay attention to an easily remedied medical problem that affects many of our patients whether they are adults or children.

Fima Lifshitz, MD

β-Cell Expression of IGF-I Leads to Recovery from Type 1 Diabetes

A method by which to reverse the process that leads to destruction of pancreatic islet cells and type 1 diabetes mellitus is the "Holy Grail" that all diabetologists seek.

In the present report from Barcelona, the investigators of the School of Veterinary Medicine and Gene Therapy Center succeeded in doing just that in an animal model

in which the key is selective overexpression of IGF-I in β -cells.

Transgenic mice were developed in which mouse IGF-I was linked to the rat insulin promoter and thus targeted to the β -cell, where IGF-I expression was many fold greater than in control animals. In these mice, at 6 months of age there was a 1.5 fold increase in β -cell mass but normal pancreatic insulin content. Circulating concentrations of IGF-I were comparable in control and transgenic animals. The latter did not develop hypoglycemia, hyperinsulinemia, or neoplasms and had normal life span and reproduction.

At two months of age, administration of streptozotocin (STZ) led to the development of insulinitis, hyperglycemia, hypoinsulinemia, and death at four months of age in the control groups from two strains of mice (C57BL and CD-1) utilized. In the C57BL mice which overexpressed IGF-I only in the β -cell, STZ led to transient modest hyperglycemia, impaired insulin secretion, mild but reversible insulinitis, and subsequent normal life span. In the CD-1 transgenic mice, hyperglycemia and hypoinsulinemia following STZ were extreme, but again transient with long term survival (Figure). After recovery from hyperglycemia, the growth was normal in the β -cell-targeted IGF-I transgenic animals.

Histological examination in C57BL mice revealed a mild decrease in islet β -cells and budding of insulin containing cells from pancreatic ductal epithelium. Thus, IGF-I appeared to at least partially protect β -cells from destruction while also increasing generation of new β -cell precursors. Since the β -cell IGF-I receptor is found on the β -cell membrane, the high levels of IGF-I synthesized by the β -cell specific IGF-I transgenic mice must be acting in a paracrine or autocrine manner to protect β -cells insulted by STZ.

Histological examination in the CD-1 mice revealed much less severe insulinitis in the transgenic STZ treated mice than in the control STZ treated animals. There was slow recovery from insulinitis, but with β -cell proliferation and neogenesis, blood sugar and insulin serum levels were restored to normal.

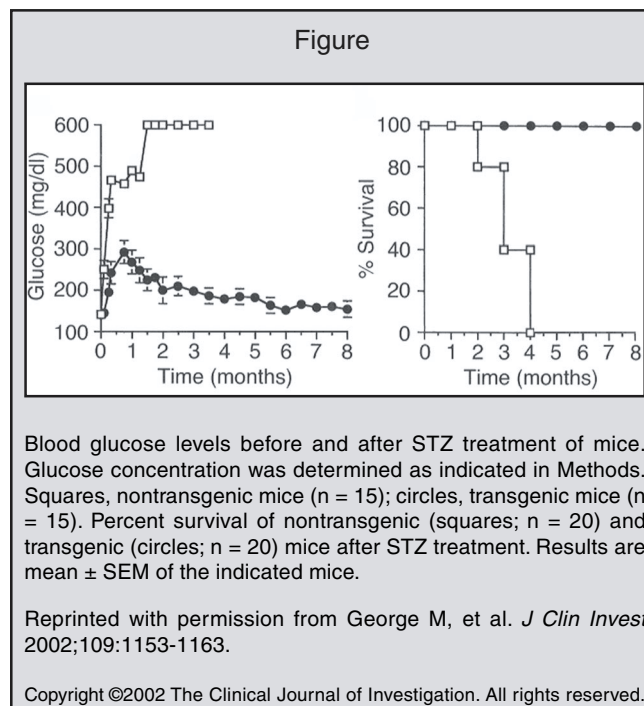
The authors concluded that co-expression of IGF-I and insulin in β -cells protected these cells from permanent destruction by STZ by increasing resistance to the inflammatory insult itself, augmenting β -cell division, and encouraging differentiation of new β -cells. They suggest that IGF-I may be a candidate gene for

transfer to pancreatic β -cells in the gene therapy of patients developing type 1 diabetes mellitus.

George M, et al. *J Clin Invest* 2002;109:1153-1163.

Editor's Comment: *This exciting paper raises the possibility that IGF-I might be capable of halting the progression of β -cell loss in patients developing type 1 diabetes mellitus if a method can be found to target this growth factor to the insulted β -cell in the intact patient. Perhaps equally feasible, and possibly even more beneficial, might be the insertion of IGF-I into the β -cells of patients at risk for development of type 1 diabetes mellitus to "protect" or to help them recover from the anticipated insults in the future that will lead to insulinitis. The latter objective may be more useful because the present experiments, which were successful, were conducted in animals that had high IGF-I pancreatic islet contact before the STZ insult. Such an approach would, hopefully, simulate the successful experiment recorded in this article.*

Allen Root, MD



Growth and Maturation in Marfan Syndrome

The Marfanoid habitus is well known to pediatric clinicians; it is characterized by tall, asthenic habitus. In Marfan Syndrome (MFS), there is multi-organ involvement including eye, heart and muscular/skeletal abnormalities. Erkula et al, largely from Johns Hopkins

data, have retrospectively compiled growth pattern data on 180 clinically diagnosed MFS patients. They have generated growth charts and growth velocity charts for infant, children and adolescent males and females. Not unexpectedly, males and females with MFS are larger