

clinically and biochemically distinct autosomal dominant form of familial hyperinsulinism.

Glaser B, et al. *N Engl J Med* 1998;338:226-230.

Editor's comment: Identification of this mutation in the glucokinase protein is another step in understanding glucose homeostasis. It is clear that different mutations within the same gene give rise to different phenotypes requiring different therapies. The Val203Ala mutation within the same gene results in loss of function and gives rise to maturity-onset diabetes mellitus. That particular glucokinase mutation has been identified in about 50% of individuals with gestational diabetes. By contrast, this new type of mutation leads to hyperinsulinism and hypoglycemia. This contrast illustrates that the domain of mutations within a gene can lead to striking differences in phenotypes.

Judith G. Hall, MD

2nd Editor's comment: Most patients with familial HI have a defect in the sulfonylurea protein resulting from a

SUR gene mutation. An excellent article to review in conjunction with this article is by Permutt et al, entitled "FHI: An Inherited Disorder of Spontaneous Hypoglycemia in Neonates and Infants" (*Diabetes Reviews* 1996;4:347-353). Permutt et al provide the foundation to better understand the etiologies and variations of familial HI, previously called leucine-sensitive hypoglycemia and/or nesidioblastosis.

Robert M. Blizzard, MD

Please Send Correspondence to:

Robert M. Blizzard, MD
University of Virginia
The Blake Center
1224 West Main Street
7th Floor, Suite 701
Charlottesville, VA 22903

Births After Intracytoplasmic Injection of Sperm Obtained by Testicular Extraction From Men With Nonmosaic Klinefelter's Syndrome

Klinefelter's syndrome results from the presence of an extra X chromosome (47,XXY) in males. It is a relatively common sex chromosomal abnormality, occurring in about 1 in 500 males. Some individuals with Klinefelter's syndrome are mosaics, ie, they have both 46,XY and 47,XXY cells. Individuals who are mosaic (46,XY/47,XXY) may have some degree of spermatogenesis and may be fertile, compared with nonmosaic Klinefelter men (47,XXY), who typically have azoospermia and infertility.

Palermo et al have reported 2 couples in which the nonmosaic Klinefelter's syndrome males had undergone testicular sperm extraction (followed by in vitro fertilization by intracytoplasmic injection of single sperm) and thereby were able to father healthy newborn infants.

In the case reports, the men were 32 years and 34 years old and their wives were 32 and 33 years old. Both women were healthy and normal, while both men had nonmosaic Klinefelter's syndrome (47,XXY). Both men had gynecoid habitus, gynecomastia, and bilateral atrophic testes. The first man had bilateral varicocele; the second man had a moderate-size left varicocele. Both men had high serum gonadotropin and low serum testosterone levels. Both men had only Sertoli cells on testicular biopsies. Three semen analyses of the first man showed normal volumes and fructose and a single abnormal nonmotile sperm in 1 semen specimen.

Analysis of the 3 semen samples from the second man revealed low volume, normal fructose, and no sperm.

Both women were given leuprolide (a gonadotropin-releasing hormone agonist) subcutaneously to inhibit gonadotropin secretion and then a combination of human menopausal gonadotropin and follicle-stimulating hormone intramuscularly. Oocytes (15 to 40) were retrieved by ultrasonographically guided transvaginal needle aspiration after intramuscular administration of chorionic gonadotropins.

Simultaneous testicular biopsies were performed in the men. Both men had received testolactone 3 months before having a testicular biopsy. After intracytoplasmic sperm injection and fertilization of oocytes, embryos (3 for each woman) were selected and transferred. Both couples refused preimplantation diagnosis.

Both women received daily intramuscular injections of 50 mg progesterone in oil until fetal heartbeats were confirmed by ultrasound. The ultrasound of the first woman at 32 days of embryo transfer revealed 2 asymmetric uterine sacs, only one of which had a fetal heartbeat. Ultrasound of the second woman showed 2 intrauterine sacs, both with fetal heartbeats. Amniocentesis at 20 weeks showed a fetal karyotype of 46,XY in the first pregnancy and fetal karyotype of 46,XX and 46,XY in the second pregnancy.

A healthy boy was born to the first couple; he had a birth weight of 2,778 g at 38.5 weeks gestation. Two healthy children, a 2,551-g boy and a 2,410-g girl, were born by cesarean section to the second couple.

Palermo G, et al. *N Engl J Med* 1998;338:588-590.

Editor's comment: Assisted reproductive technology has become increasingly important and has revolutionized the treatment of infertility. Preimplantation diagnosis is now possible in which DNA can be analyzed from a single blastomere. This allows selection of disease-free embryos for transfer to the uterus. In the pregnancies described above, the parents chose to take no risk of loss at that stage, but

opted for more conventional prenatal diagnosis by amniocentesis. Intracytoplasmic sperm injection is a relatively new development in assisted technology and provides new hope for couples in whom in vitro fertilization has failed or when there is paucity of viable sperm. This technique is quite promising for nonmosaic Klinefelter's syndrome men, who may now be able to have their own biologic children through this new technology. Interestingly, the number of men recognized to be infertile has been increasing for more than a decade. Precise diagnosis of male infertility will help to provide options to couples.

Judith G. Hall, MD

Screening for Retinopathy in the Pediatric Patient With Type 1 Diabetes Mellitus

Diabetic retinopathy is the leading cause of blindness in the United States, in patients between the ages of 20 to 74 years. Individuals with type 1 diabetes mellitus are at a high risk for developing diabetic retinopathy. The American Academy of Pediatrics has recently published a statement regarding recommendations for ophthalmologic evaluation of asymptomatic children with type 1 diabetes mellitus.

The statement provides background about diabetic retinopathy and the rationale for the ophthalmologic examination for diabetic retinopathy. An examination schedule for diabetic retinopathy for asymptomatic individuals with type 1 diabetes mellitus also is suggested (Table).

The objective and goals of the statement are to (1) develop a program for assessing children with type 1 diabetes mellitus on a regular basis to prevent diabetic retinopathy as part of the diabetic management; (2) identify children who may be at risk for developing diabetic retinopathy; (3) refer patients appropriately for ophthalmologic examination; and (4) educate individuals with diabetes and their families regarding the benefits of good diabetic control. The members of the committee believe referral to an ophthalmologist for follow-up is essential because ophthalmologists are much better able to detect early retinopathy than primary care physicians. HMOs often are reluctant to refer patients to ophthalmologists for such exams, and this poor practice is unacceptable.

Sections of Endocrinology and Ophthalmology American Academy of Pediatrics. *Pediatrics* 1998;101:313-314.

Editor's comment: The American Academy of Pediatrics guidelines will be useful for pediatricians and pediatric endocrinologists taking care of children with type 1 diabetes mellitus. Good control of diabetes mellitus is a

first step in preventing diabetic retinopathy. Prompt laser eye surgery can prevent further visual deterioration and delay the onset of blindness as a result of diabetic retinopathy.

Judith G Hall, MD

Suggested Ophthalmologic Examination Schedule for Asymptomatic Pediatric Patient With Type 1 Diabetes

INITIAL DISCUSSION

Within the first year after diagnosis, child and/or parents should receive counseling by a pediatrician or pediatric endocrinologist regarding the need for ophthalmologic examination and early intervention.

INITIAL EXAMINATION BY AN OPHTHALMOLOGIST*

3 to 5 years after diagnosis if >9 years of age

FOLLOW-UP EXAMINATION†

Annually

DURING PREGNANCY

During first trimester, then every 3 months until delivery

* Poor control or deterioration may indicate an earlier initial examination. An ophthalmologic examination also should be performed in poorly controlled patients before intensification of therapy.

† Abnormal findings will dictate more frequent follow-up examinations.