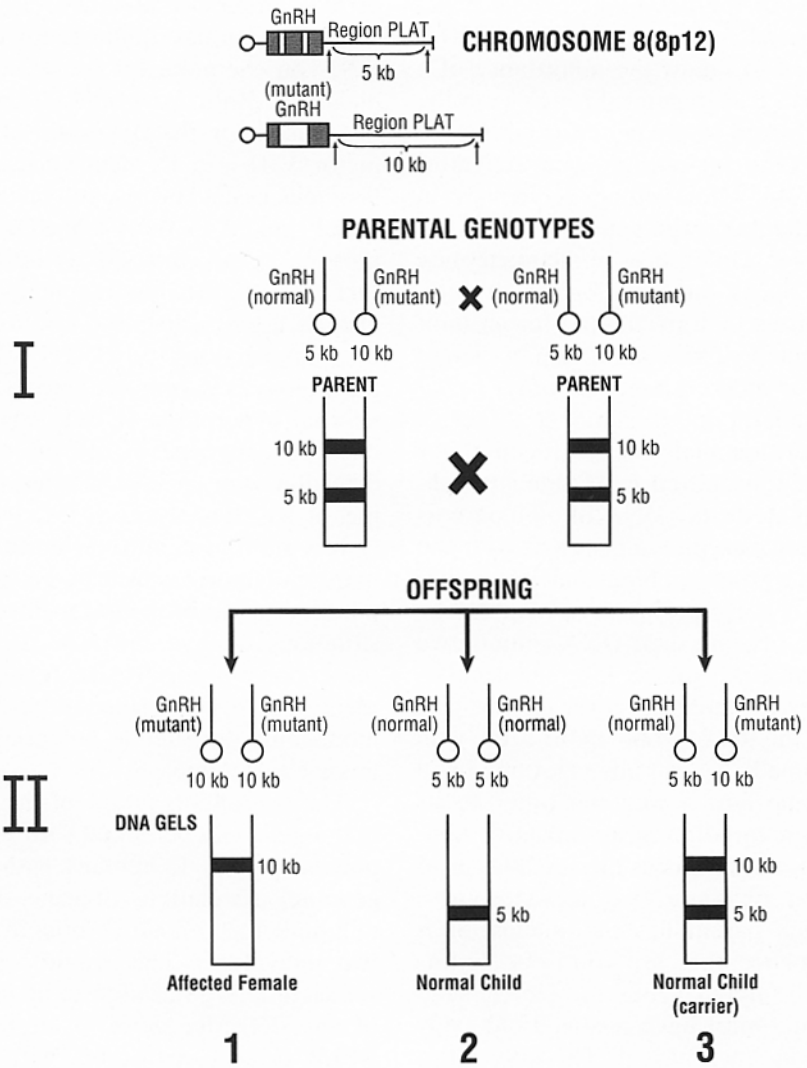

Fig. 5 Hypothetical illustration of the use of a restriction fragment length polymorphism to follow the segregation of a mutant allele. Pedigree of family with three female offspring. The eldest daughter (II-1) has hypogonadotropic hypogonadism due to a deficiency of GnRH. The parents request to know if their two prepubertal daughters (II-2, II-3) will be similarly affected. The gene for GnRH is mapped to 8p, but is not polymorphic. A closely linked gene for plasminogen activator, tissue (PLAT) is dimorphic demonstrating two different alleles, one 10 kb and the other 5 kb. Extracted DNAs from the parents probed with PLAT demonstrate they are heterozygous for these two different alleles. The affected daughter (II-1) is homozygous for the 10 kb band indicating that the mutant GnRH gene is segregating in this family with this PLAT allele. One younger daughter (II-2) is homozygous for the 5 kb band (normal) and the other child (II-3) is a heterozygous carrier demonstrating both bands similar to the parents. (ref. 39. Reprinted by permission from McDonough PG. Molecular Biology in Reproductive Endocrinology. In Yen SSC, Jaffe RB, eds: Reproductive Endocrinology, third edition. Philadelphia: WB Saunders 1991 p 59.)

tides, each carrying a different mutant for the GnRH gene. It is possible that the mutation producing GnRH absence in Kenya may be different from that of the rest of the world. This lack of knowledge concerning the molecular pathology of the gene under study limits the first two approaches for analysis of the mutant gene. The analysis of gene pathology by use of RFLP analysis does not require any presumptive information concern-