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Statement on Guidance for Genetic Counseling in Advanced Paternal Age

There is no clear accepted definition of advanced paternal age. A frequently used criterion is any male, age 40 years or older at the time of conception, as opposed to the current population mean paternal age of 27 years. The risk for genetic defects does not increase dramatically at age 40, but rather increases linearly with age. Some studies have suggested that the risk of genetic defects, specifically, sporadic dominant single-gene mutations, is 4-5 times greater for fathers aged 45 and above than for their 20-25 year old counterparts.

Advanced paternal age is associated with an increased risk of new mutations. All populations are at risk. The relative increased risk for these defects is related to advanced age of the father for autosomal dominant conditions and the maternal grandfather for X-linked conditions. Family histories will not provide clues as these types of mutations are sporadic. Examples of autosomal dominant conditions associated with advanced paternal age include achondroplasia, neurofibromatosis, Marfan syndrome, Treacher Collins syndrome, Waardenberg syndrome, thanatophoric dysplasia, osteogenesis imperfecta, and Apert syndrome. Examples of X-linked conditions associated with increased maternal grandfather's age include fragile X, hemophilia A (Factor VIII deficiency), Hemophilia B (Factor IX deficiency), Duchenne muscular dystrophy, incontinentia pigment), Hunter syndrome, Bruton agammaglobulinemia, and retinitis pigmentosa.

Given the wide range of genetic diseases which may be related to advanced paternal age, there is currently no single test available for prenatal screening or diagnosis. Unfortunately, prenatal ultrasound is not particularly useful in detecting many of these conditions. The detectable features may be nonspecific and could represent a variety of etiologies, not necessarily those related to advanced paternal age. For this reason, screening ultrasounds specifically for advanced paternal age are usually of little benefit. Prospective couples should receive individualized genetic counseling to address specific concerns.

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This guideline is designed primarily as an educational resource for medical geneticists and other health care providers to help them provide quality medical genetic services. Adherence to this guideline does not necessarily assure a successful medical outcome. This guideline should not be considered inclusive of all proper procedures and tests or exclusive of other procedures and tests that are reasonably directed to

obtaining the same results. In determining the propriety of any specific procedure or test, the geneticist should apply his or her own professional judgment to the specific clinical circumstances presented by the individual patient or specimen. It may be prudent, however, to document in the patient's record the rationale for any significant deviation from this guideline.

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