First- and Second-trimester Down Syndrome Screening: Current Strategies and Clinical Guidelines

To the Editor:

I read the review article "First- and Second-trimester Down Syndrome Screening: Current Strategies and Clinical Guidelines" with great pleasure [1]. The first sentence started with "Down syndrome is the most common human disease caused by a structural chromosome defect." It raised a major question, and I quote a sentence from Wikipedia for comparison, "Named after John Langdon Down, the first physician to identify the syndrome, Down syndrome is the most frequent genetic cause of mild to moderate mental retardation and associated medical problems and occurs in one out of 800 live births, in all races and economic groups."

Down syndrome is a well known chromosomal disorder caused by an error in cell division that results in the presence of an additional third chromosome 21 or "trisomy 21" (in approximately 92% of all cases of Down syndrome) [2]. A genetic disorder is caused by an altered or faulty gene or set of genes. Over 1,000 known disorders are caused by chromosomal abnormalities. Chromosomal abnormalities can include changes in number, changes in structure, uniparental disomy, and mosaicism. Down syndrome, or trisomy 21, is an example of a condition caused by numerical abnormalities (three copies of chromosome 21). Turner syndrome is an example of monosomy, where the individual (in this case a female) is born with only one sex chromosome, an X. Structural abnormalities include deletions, duplications, translocations, inversions, and rings. Approximately 2–4% of Down syndrome cases are due to mosaic trisomy 21 and approximately 3–4% are due to translocation trisomy 21. Therefore, most cases of Down syndrome are not caused by structural abnormalities. In 88% of cases, the extra copy of chromosome 21 is derived from the mother, in 8% of the cases, the extra copy comes from the father, and in the remaining 2% of cases, Down syndrome is due to mitotic errors [2]. The rising incidence of Down syndrome with increasing maternal age is well known. The likelihood that a woman under 30 who becomes pregnant will have a baby with Down syndrome is less than 1 in 1,000, but the chance of having a baby with Down syndrome increases to 1 in 400 for women who become pregnant at age 35.

Approximately 98% of all fetuses with Turner syndrome result in miscarriage. Turner syndrome accounts for about 10% of the total number of spontaneous abortions in the United States. The incidence of Turner syndrome in live female births is believed to be 1 in 2,500. Turner syndrome is a genetic disorder associated with abnormalities of the X chromosome, occurring in about 50 per 100,000 liveborn girls. The leading cause of Down syndrome is nondisjunction of chromosome 21 occurring during the formation of gametes. The two risk factors for maternal nondisjunction of chromosome 21 are increased maternal age and altered recombination. Regarding sex chromosomes, XXY aneuploidy is the most common disorder of sex chromosomes in humans, with prevalence of 1 in 500 males.

When we talk about the incidence or prevalence of a specific disease or syndrome, we should be very careful not to mislead. There has been no overall change in the prevalence of live infants born with Down syndrome. Based on a malformation registry, Down syndrome affected 1,188 pregnancies among 690,215 live births in the United Kingdom (1.72 per 1,000 total births) between 1985 and 2004 [3]. Therefore, Down syndrome is not the most common human disease caused by a structural chromosome defect, but one of the most common human diseases caused by a numerical chromosome defect. Or, Down syndrome is the most commonly identified genetic form of mental retardation and the leading cause of specific birth defects and medical conditions [4].

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References

1. Shaw SW, Hsu JJ, Lee CN, Hsiao CH, Chen CP, Hsieh TT, Cheng PJ. First- and second-trimester Down syndrome

screening: current strategies and clinical guidelines. *Taiwan J Obstet Gynecol* 2008;47:157–62.
2. National Institute of Child Health and Human Development. Down syndrome rates. Available at: http://web.archive.org/web/20060901004316/http://www.nichd.nih.gov/publications/pubs/downsyndrome/down.htm
3. Irving C, Basu A, Richmond S, Burn J, Wren C. Twenty-year trends in prevalence and survival of Down syndrome. *Eur J Hum Genet* 2008;16:1336–40.
4. Sherman SL, Allen EG, Bean LH, Freeman SB. Epidemiology of Down syndrome. *Ment Retard Dev Disabil Res Rev* 2007; 13:221–7.