

# The Truth About Multiples

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**Over the past 30 years, treatment of infertility has permitted millions of couples to have their own children, but of all babies born following in vitro fertilization, more than half are part of a multiple pregnancy.<sup>1</sup> Twins, commonly quoted for decades to account for 1 in 90 births, have more than doubled; about 65% of twins in the United States emanate from infertility treatments. Incidence of monozygotic (MZ) twins, per se and as part of higher-order multiples, has continued to rise, with associated dramatically increased risks for anomalies, loss, and prematurity.<sup>2</sup>**

## RISKS FOR ANOMALIES

For dizygotic (DZ) twins, there are independent probabilities of anomalies. The chance of 1 of 2 DZ twins having aneuploidy is nearly double. For Mendelian recessives, the chance of one twin being affected is 44%. However, some structural abnormalities, such as cardiac and neural tube defects, are actually considerably more common in twin gestations than singletons. MZ twins are identical in chromosomes and Mendelian genetics, but MZ twins are especially prone to defects of laterality, such as situs inversus. Overall, the risks of twins are not twice those of singletons; they are about 4 times. For cerebral palsy, the risk in a singleton is about 1 in 700, while 1 in 100 for a twin baby—such that for a given pregnancy there is a 1 in 50 risk of at least 1 twin being affected.<sup>3</sup>

Genetic counseling should include appreciation of the differences between screening and diagnosis and the risks and benefits of each. The majority of multiples are now conceived

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after infertility treatment, and patients are understandably scared of both the inherent risks and the complications in testing. Furthermore, because of the increasing percentage of patients using eggs from much younger donors, the difference between the numerical, genetic risk based upon egg age and the patient's "tolerance" for risk are often discordant. Very often patients in their 40s and 50s specifically state they would rather take the risk of diagnostic procedures, even with a low abnormality incidence, to avoid the chance of being in their 70s and having a child with special needs.<sup>4-6</sup>

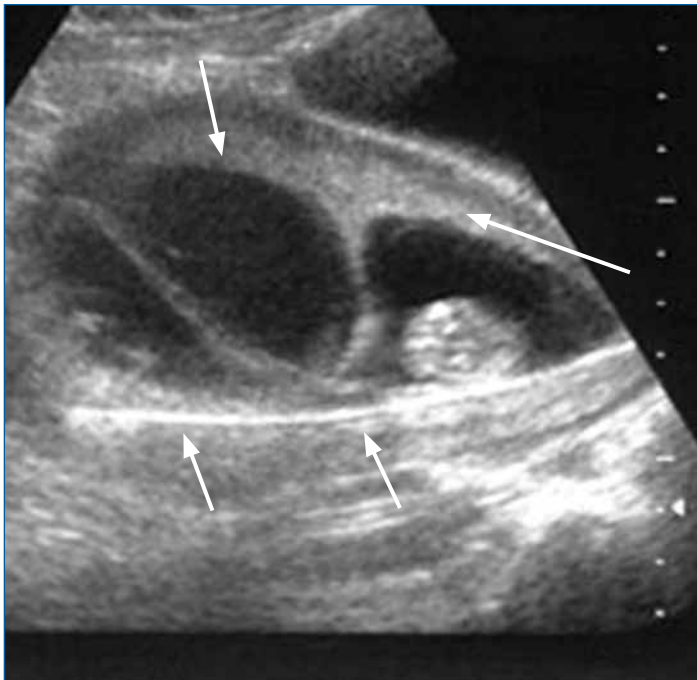
First-trimester nuchal translucency (NT) measurements comprise the most reliable screening method for aneuploidy in twins. Serum screenings (for free  $\beta$  human chorionic gonadotropin and pregnancy-associated plasma protein A) are interpretable, but the detection rate is about 10% lower than in singletons. Second-trimester serum screenings are worse, and they are useless with triplets.<sup>7</sup>

For a definitive diagnosis, in the most experienced hands, chorionic villus sampling (CVS) is as safe as amniocentesis and has many advantages, particularly in multiples; eg, determination of zygosity is much better in the first trimester, and multifetal pregnancy reduction (MFPR), if chosen by the patient, has much better outcomes in the first trimester as well.

CVS operators should be skilled in both transcervical and transabdominal approaches, as both are commonly required even in the same patient (Figure 1).<sup>8</sup> Transcervical procedures require considerably more skill and experience for the operator to become competent, but for optimal outcomes, both procedures need to be in the armamentarium of the prenatal diagnostic center. Papers suggesting that amniocentesis is safer than CVS are not supported by rigorous analysis of the data.<sup>8,9</sup>

## FOCUSPOINT

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**FIGURE 1.** Triplet Chorionic Villus Sampling Technique. Arrows at bottom shows catheter in posterior fundal placenta. Arrow at right shows path for catheter into low anterior placenta. Arrow at top shows path for needle to anterior fundal placenta. Image courtesy of Mark I. Evans, MD.

### MULTIFETAL PREGNANCY REDUCTION

MFPR has improved the clinical outcome of high-order multiple pregnancies for thousands of high-risk pregnancies.<sup>4</sup> If success is defined as a healthy mother and family, clearly fewer are better. Furthermore, recent data suggest that for women who start with twins, it is safer to reduce to a singleton than to keep the twins.<sup>10</sup> The specifics depend upon actual starting and finishing numbers (Figure 2).<sup>4,10</sup>

### CVS AND MFPR

In inexperienced hands, the selection process for MFPR is essentially empirical (such as fetal location). In experienced hands, it is hierarchical, using both ultrasound and, preferably, CVS test results. My program's approach is to offer CVS prior to reduction in most cases. In our experience, CVS prior to MFPR does not increase the risk for miscarriage or early delivery and lowers the chance of inadvertently keeping a fetus with serious abnormalities. Typically, we sample one more fetus than we are planning on continuing; ie, if we are planning on twins, we will sample all 3 triplets or 3 of 4 quadruplets. We then run a fluorescence in situ hybridization analysis overnight and use that data in the overall evaluation of which fetuses to preserve for MFPR performed the next afternoon.

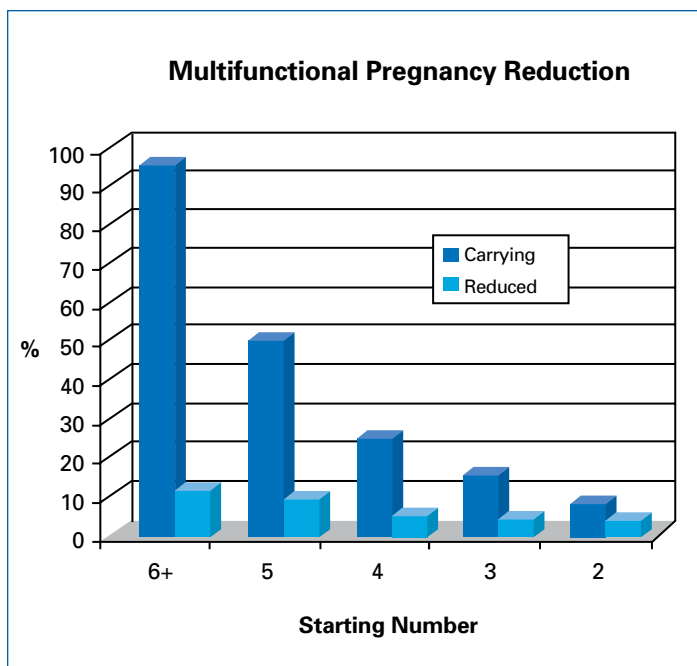
We use the following hierarchy:

1. A documented abnormality
2. Suspicion and concern, such as smaller crown-rump length or larger NT or MZ twins
3. Other technical factors of serious concern
4. If nothing else matters, then we can consider gender differences.

The last criteria is new and was added only in the past several years, as there is now balance in gender preferences rather than the previously seen male dominance. For couples reducing to twins, the most common preference is for one of each gender, and for those going to a singleton, more than half want a girl.<sup>4</sup>

### CONCLUSION

The risks in multiple pregnancies are disproportionately larger than in singleton pregnancies—a fact commonly lost in the public's perception. In the management of twin pregnancies, the choice of screening or diagnostic procedures depends on several factors but ultimately comes down to a personal choice of



**FIGURE 2.** Improvements in Pregnancy Outcomes With MFPR. Dark Blue: Loss rates carrying starting number. Light Blue: Loss rates after reduction to twins (3+) and twins to singleton.

where the patient wishes to put her risk, ie, taking a small risk of having a baby with a serious disorder versus a small risk of having a complication because she wishes to avoid that. The advantages of early diagnosis are clear.<sup>8</sup> How patients process information (framing) involves many factors, and there is no clear answer that applies to every patient.<sup>5</sup>

On balance, it seems that the limitations of screening efficacy in multiples tilt the equation toward definitive answers with CVS. Having results as opposed to odds then allows for early reassurance in most cases and optimizes the statistics for MFPR when chosen by patients.

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