Screening for 22q11.2 Deletion with Ultrasound and Non-Invasive Prenatal Testing

22q11.2 microdeletion, or 22q, is present in 1 in 1000 pregnancies,[1] but prenatal signs can be elusive. Strategic use of targeted cell-free DNA (cfDNA) analysis and detailed ultrasound exams can enable early identification of fetuses at risk and allow for informed management to help improve outcomes.

22q11.2 deletion syndrome (22qDS), caused by the absence of segment of chromosome 22, typically occurs without any family history of the condition.[2,3] It is a significant cause of morbidity and mortality across the lifespan, but the extreme variability in clinical presentation can delay diagnosis for years after features manifest.[4] Clinical expressions are widely variable but often include congenital heart problems, frequent infections, developmental delay, learning problems and cleft palate.[2,5] (Table 1)

TABLE 1[2,3,10]

Finding	Estimated Prevalence in Individuals with 22qDS
Growth and developmental delays	>90%
Musculoskeletal (club foot, rib anomalies, vertebral differences, scoliosis)	>90%
Immune deficiency	77%
Palatal anomaly	67%
Gastrointestinal	65%
Congenital heart defect	64%
Neuropsychiatric disorders (autism, schizophrenia)	60%
Endocrine	55%
Genitourinary (typically renal)	16%

Standard karyotyping is not reliable in detecting the microdeletion and no standardized prenatal screening program for 22qDS exists.[6,7] Consequently, most individuals with 22qDS go undiagnosed for months to years after birth.[4] The missed opportunities for early interventions, anticipatory care and access to services can increase the likelihood of premature mortality as early as the neonatal period.[8,9]

Advances in ultrasound technology and maternal blood analysis have allowed for detailed first trimester evaluations for serious anomalies and more accurate screening for chromosomal conditions. The complementary technology of Harmony cell-free DNA testing and Voluson™ ultrasound systems can help deliver proven, clinically relevant information so clinicians and patients have answers sooner.

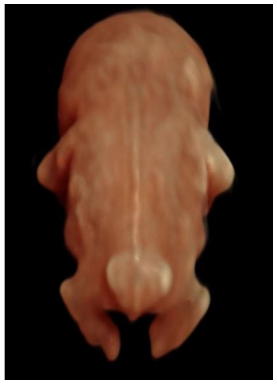

Image 1: 9W Spina Bifida highlighted with HD*live*™

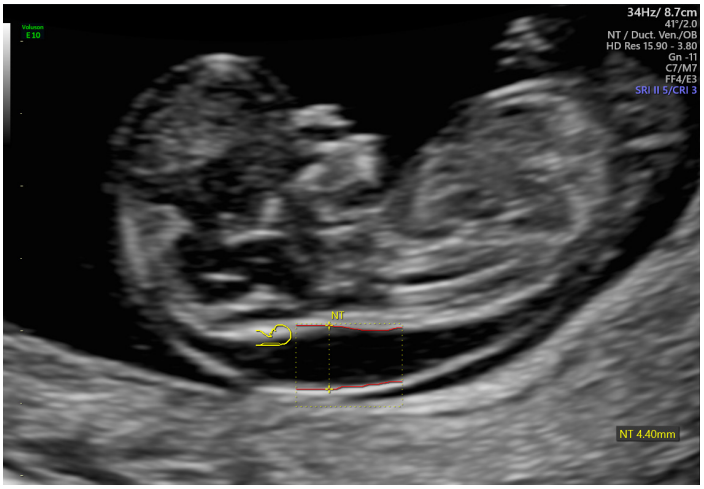

Image 2: 11 week increased Nuchal Translucency (NT)

First trimester ultrasound can help identify anomalies associated with 22qDS, including increased nuchal translucency, neural tube defects and cardiac defects, alerting clinicians to the need for chromosomal diagnostic testing.

However, many manifestations of 22qDS are best visualized during the second trimester when the window of opportunity for confirmatory prenatal testing has narrowed or passed.

TABLE 2[5,10]

Ultrasound Feature	Estimated prevalence in prenatally diagnosed 22q11.2 deletion
Cardiac	
Ventricular septal defect (VSD)	23
Tetralogy of Fallot	18
Aortic arch anomalies + Interrupted aortic arch	25
ASD	10
Thymus hypo/aplasia	>26%
Central Nervous System (neural tube, brain structures)	38%
Skeletal (vertebral, club foot)	19%
Genitourinary	16%
Facial differences	21%
Increased nuchal translucency	8-20%
Polyhydramnios	30%

As the second most common genetic cause of congenital heart defects (CHD), 22qDS is strongly associated with conotruncal malformations such as tetralogy of Fallot, Ventricular Septal Defect (VSD), interrupted aortic arch and truncus arteriosus.[10] Ultrasound can help detect and identify the fetal heart defect.

cfDNA analysis of maternal plasma, or non-invasive prenatal testing (NIPT) provides an opportunity to screen for 22qDS as early as 10 weeks gestation. Results can promote timely confirmatory testing and direct pregnancy management toward detailed ultrasound evaluations including fetal echocardiogram.

The Harmony prenatal test, a targeted cfDNA analysis, can identify pregnancies at-risk for 22qDS without significantly increasing the rate of unnecessary invasive procedures.[11] This was demonstrated in a clinical study of 735 pregnancies with confirmatory genetic outcomes – including 46 with a 22q deletion.

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TABLE 3[11]

Performance of Harmony test for 22q11.2 deletions in a large clinical cohort

Sensitivity	Specificity
70% (32/46)	100% (689/689)

Routine screening for 22qDS using the Harmony prenatal test can enable identification of pregnancies at increased risk without significantly increasing the likelihood of false positive results. With complementary technology available with the Harmony test and Voluson Ultrasound Systems, clinicians can use the screening results to adjust pregnancy management to include diagnostic testing and detailed ultrasound imaging in effort to improve clinical outcomes.[2,3,7]

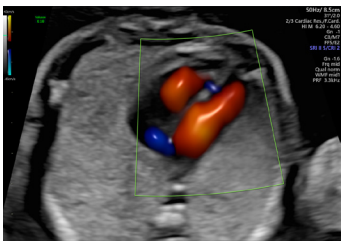

Image 3: VSD highlighted with Radiant*flow*™

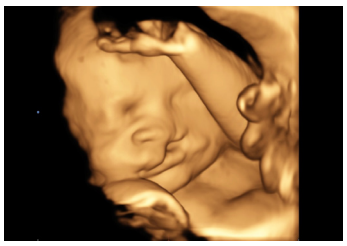

Image 4: Cleft Lip/Palate

References

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