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Prenatal Screening and Diagnosis: Time for a Paradigm Shift

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Abstract

Recent advances in genetics and imaging have ushered substantial breakthroughs in screening and diagnosis for chromosomal and structural abnormalities. Thus, it is imperative that health care providers caring for pregnant individuals should reexamine established practices in prenatal screening and diagnosis. In the past, screening for chromosomal abnormalities was based almost entirely on Down syndrome. Pregnant individuals aged > 35 years were considered at "high risk" or of "advanced maternal age" based on age alone; however, the advent of tests with high sensitivity for prenatal detection of chromosomal abnormalities should lead to abandoning that concept, at least from the perspective of chromosomal abnormalities. Given that first-trimester and second-trimester screenings will fail to detect between 5 and 20% of Down syndrome, in most situations, noninvasive testing with cell-free DNA should be the first-line screen for Down syndrome. The fact that over 99% of fetuses with Down syndrome will be detected prenatally with cell-free DNA gives other fetal chromosomal and structural abnormalities increasing prominence. Chromosomal microarray analysis (CMA) permits prenatal detection of several clinically important chromosomal aberrations that cannot be detected by karyotype and may exist in structurally normal fetuses with low-risk cell-free DNA screening. As such, CMA should be more readily conducted when invasive testing is performed, regardless of the presence of a structural abnormality. Isolated sonographic "soft markers" have no clinical significance in patients who have normal cell-free DNA screening, can cause unwarranted anxiety and a negative impact on pregnancy, and perhaps it is time to stop discussing them. Detailed first-trimester ultrasound allows early detection of several severe fetal anomalies and, therefore, in settings with adequately trained personnel and resources, should be used more frequently. This opinion traces the evolution of prenatal screening and diagnosis and advocates for a paradigm shift that aligns with recent developments in prenatal screening and diagnostic capabilities.

Keywords

- prenatal screening
- prenatal diagnosis
- chromosomal aberrations
- chromosomal microarray
- noninvasive prenatal screening
- karyotype

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Key Points

- Noninvasive prenatal testing with cell-free DNA should be available to all pregnant individuals.
- Chromosomal microarray should be available to all pregnant individuals undergoing amniocentesis.
- Patients >35 years with low-risk screening are not at "high risk" for chromosomal abnormalities.

In the past 30 years, rapid advances in genetics and ultrasound have led to the recognition of countless fetal chromosomal, genetic, and structural malformations that can be detected prenatally with a high degree of accuracy. Ultimately, the purpose of prenatal screening is to detect fetuses that may have abnormalities, especially those associated with lethality, neurodevelopmental impairment, severe medical debility, and reduced quality of life. This gives the prospective parents the full option of reproductive choices including termination of pregnancy, but even when patients opt to carry on with the pregnancy, this helps prepare the potential parents and the health care team to provide appropriate prenatal care to achieve the best outcomes. However, we, as maternal–fetal medicine specialists, geneticists, and genetic counselors, have observed in our daily practice that several concepts regarding prenatal screening and diagnosis for chromosomal and genetic conditions that were introduced over 30 years ago remain prevalent among practitioners who care for pregnant persons, individuals who are pregnant or contemplating pregnancy, and insurance companies who pay for health care in pregnant individuals. This clinical opinion aims at correcting some common misconceptions and gives some guidance for prenatal and preconception screening and diagnosis in the 21st century.

Historical Background

For the most part, the concepts of prenatal screening and diagnosis came about in the 20th century. The first reported prenatal diagnosis of a fetal condition was the detection of fetal anencephaly in 1917 by James T. Case using X-ray.[1] Until approximately 30 years ago, the main focuses of prenatal screening for chromosomal abnormalities were Down syndrome and, to a lesser extent, trisomies 18 and 13.[2] Other frequent indications for screening for genetic conditions included hemoglobinopathies and cystic fibrosis. Amniocentesis was first introduced in the 1930s and was subsequently used in the 1950s as means of diagnosing and treating Rh disease.[3] Genetic amniocentesis for prenatal detection of chromosomal abnormalities was until recently performed mainly for the detection of Down syndrome, with the earliest reports published around 1971.[4] More rarely, amniocentesis was performed for the detection of the inherited conditions Pompe's disease, cystic fibrosis, and mucopolysaccharidosis.[5] In 1956, Tjio first reported that human cells had 46 chromosomes,[6] and subsequently, Lejeune and Turpin first showed that Down syndrome was associated with an extra copy of chromosome 21.[7] It was the observation in the 1960s that amniotic fluid contained cells that could be cultured that made prenatal diagnosis of chromosomal abnormalities possible.[8]

The Concept of Advanced Maternal Age

The recognition that the incidence of Down syndrome increased with maternal age led to the concept of categorizing women of age greater than 35 years as being of "advanced maternal age" or being at "high risk" and routinely offering such women amniocentesis, while those below 35 were considered "low risk" and not routinely offered amniocentesis.[9,10] Several different explanations have been proffered for having selected this age cut-off.[3] The most common reason given was that the prevalence of Down syndrome at the age of 35 years at the time was where the risk of having a baby with Down syndrome approximately equaled that of pregnancy loss from amniocentesis.[11] Another was based on the maternal age distribution of the pregnant women between the 1960s and 1970s when 5% were 35 years old or older at the time of delivery; since genetic amniocentesis was associated with some risk of pregnancy loss, a 5% "false-positive rate" was accepted as a reasonable cutoff. However, Resta challenges these views and argued that the cut-off age of 35 years was selected based on economic cost-benefit analysis rather than objective medical criteria.[3] Regardless of the reason, this age was chosen as a cut-off; clearly, maternal age >35 years alone was not an ideal screen for Down syndrome. However, at the time, there were no effective screening tests for Down syndrome. This strategy of offering amniocentesis based on maternal age alone had major limitations: only one-third of babies with Down syndrome were born to women aged 35 years or older. As a consequence, this approach not only missed two-thirds of fetuses with Down syndrome but also inappropriately worried women aged 35 or older, while falsely reassuring those aged less than 35 years.[12,13] Furthermore, the risk of Down syndrome at term in women aged 30 years is approximately 1:900, while the risk for women aged 40 years at delivery is approximately 1:90.[14,15] In both these age-based situations, greater than 98.5% of women do not have fetuses with Down syndrome.[15] Importantly, the American College of Obstetricians and Gynecologists now recommends that all pregnant individuals, regardless of age, should be offered invasive testing.[13] However, the idea that women aged 35 years or older are at "high risk" for chromosomal abnormalities remains pervasive.

The Advent of Serum Screening

While advanced maternal age initially served as the primary screen for Down syndrome, the advent of serum screening allowed patients to be assigned an individualized risk that took into consideration factors beyond maternal age alone.[13] The first analyte widely used for serum screening was

maternal serum α-fetoprotein (MSAFP), which was determined to be elevated in fetal spina bifida and anencephaly.[16,17] Prior to that α-fetoprotein had been shown in the early 1970s to be elevated in amniotic fluid of fetuses with neural tube defects.[18] The subsequent observation that pregnancies affected by fetal Down syndrome had low levels of MSAFP led to the introduction of this marker in combination with maternal age, as a screen for Down syndrome.[19,20] Shortly thereafter, it was found that pregnancies in which the fetus had Down syndrome had lower levels of maternal serum estriol.[21] Over time, maternal serum human chorionic gonadotropin and inhibin were added to the second-trimester analytes (the "quadruple" or "penta" tests), with increasing, but still not ideal, detection rates for Down syndrome (only 69 and 80% for the triple and quad tests, respectively) and a 5% false-positive rate.[11,13,22–24]

The observation that most fetuses with Down syndrome had increased first-trimester nuchal translucency measurements brought a realistic prospect of first-trimester screening for Down syndrome.[25] This had the benefit of earlier diagnosis in the first trimester, which, with the emergence of chorionic villus sampling, allowed earlier decision-making.[25] The introduction of first-trimester screening with nuchal translucency, nasal bone, and serum analytes led to the ability to detect common aneuploidies earlier, in the first trimester with higher detection rates, and relatively low false positives.[26,27] High-resolution ultrasound further improved the detection rate and reduced false positives, but still had a relatively high false-positive rate. At best, second-trimester serum screening would detect approximately 80% of fetuses with Down syndrome, with a 5% false-positive rate, while first-trimester combined screening (including nasal bone assessment) would potentially detect between 90 and 95% of fetuses with Down syndrome.[26] As such, both these modalities for screening would miss between 5 and 20 percent of fetuses with Down syndrome, while screening 5% of patients positive.[26]

Ultrasound

The observation that fetuses with Down syndrome and trisomy 18 often had sonographically detected findings (called "soft markers") which occurred with some frequency in chromosomally normal fetuses but occurred more frequently in fetuses affected by trisomies 21 and 18 led to the incorporation of these "soft markers" into screening for chromosomal abnormalities.[28] The concept of "genetic ultrasound" was introduced and used to modify the prior second-trimester serum screen risk for trisomies.[29–31] So, if a thorough sonographic examination failed to show any "soft markers," it was considered to further reduce the risk for chromosomal abnormalities, while the presence of "soft markers" increased the prior risk.[30–36] Soft markers include intracardiac echogenic focus (which occurs in approximately 2–5% of normal fetuses and up to 30% of fetuses of women of Asian descent), choroid plexus cysts (2% of normal fetuses), single umbilical artery (1–2% of normal fetuses), short femur or humerus <5th centile (found in 5% of normal fetuses), echogenic bowel (found in 2% of normal fetuses), and urinary tract dilation (found in 4% of normal fetuses).[30,31,35,36] Other proposed "soft markers" included clinodactyly and sandal-gap toes.[29,37] Detection of these common findings on routine prenatal ultrasound often led to great anxiety and worry, as well as to the patients being offered amniocentesis.[38] Other sonographic markers for Down syndrome include absent or hypoplastic nasal bone and increased nuchal fold thickness.[33] However, these two markers greatly increase the risk of Down syndrome and should not be considered "soft markers."[33] Importantly, these "soft markers" differ from major fetal structural abnormalities, which greatly increase the risk of chromosomal abnormalities and genetic syndromes. For instance, the finding of a fetal cardiac defect, cleft lip/palate, or other major structural abnormality should always lead to genetic counseling and invasive testing being offered.[11,13]

Recent guidelines in the era of NIPT have recommended that most "soft markers," when they occur in isolation, be considered normal variants and that patients should be informed that these findings have no clinical significance, and no further testing is recommended.[28] Given, as the guidelines state, these findings are "normal variants" of "no clinical significance," there are those that argue that their presence should not be mentioned at all.[38] However, others have argued, albeit before the widespread usage of noninvasive testing with cell-free DNA, that the physician has an obligation to inform the patient of these findings.[39] Thus, there remains great confusion among practitioners as to whether or not to report these findings or to mention them to patients; unfortunately, guidelines have not addressed these issues. Consequently, the findings of soft markers on routine ultrasound continue to elicit tremendous anxiety for patients and some still opt for amniocentesis based on these findings alone. The detrimental psychological impact of informing a pregnant individual of the finding of a soft marker may not be adequately appreciated by the physician.[40,41] A negative impact on maternal–infant interaction has been found in one study.[41] Another study found higher rates of depression and anxiety among women who had been informed that they had soft markers detected on prenatal ultrasound, even in the presence of a normal serum screen.[42]

Cell-Free DNA and Microarray

Two major advances in prenatal diagnosis have changed the paradigm for prenatal screening. The first was the advent of cell-free DNA (cfDNA) which allows a simple noninvasive prenatal screening test (NIPT) with an extremely high detection rate (greater than 99% for Down syndrome) and a low false-positive rate (generally less than 1% for Down syndrome).[43–47]

Given that both first-trimester and second-trimester screening for chromosomal abnormalities (based on nuchal translucency and various permutations of serum screening) will fail to detect between 5 and 20% of fetuses with Down syndrome while screening 5% of patients positive, and that

an easily accessible test is now available that detects > 99% of fetuses with Down syndrome with a false positive of <1%, we feel it is unethical at this time to not have NIPT with cfDNA available to all patients as a first line screen test for aneuploidy. Additionally, universal NIPT with cfDNA is a cost-effective alternative to first- or second-trimester screening, particularly when viewed from a societal perspective and considering the lifetime costs associated with live births affected by genetic conditions.[48] While, in the past, NIPT was prohibitively expensive, over time, the cost has dropped such that costs for NIPT and first-trimester screening with nuchal translucency and serum analytes are similar, making NIPT a more cost-effective option. As of now, nine leading U.S. insurance providers offer coverage for NIPT for all singleton pregnancies. Among these, four companies do not require preauthorization, while the other five do. TriCare, the military insurer, and Molina Healthcare provide coverage for NIPT in only "high-risk" pregnancies. Presently, Medicaid extends NIPT coverage to all singleton pregnancies in 34 states but limits coverage to only "high-risk pregnancies" in 14 states. In Nebraska, Nevada, and Utah, all pregnant individuals are denied coverage for NIPT, regardless of their risk levels. The out-of-pocket cost for those patients for whom NIPT is not covered by insurance is about $250. To paraphrase Sharma et al, "Based on the ethical principles of respect for autonomy, beneficence, and justice, we argue that routinely offering NIPT with cfDNA is ethically obligatory and denying pregnant individuals access to this test is ethically unjustified."[49] More recently, some laboratories have included microdeletion assessment in their cfDNA testing; however, the sensitivity and specificity of cfDNA for these abnormalities are suboptimal, and at present, these tests are not recommended for general use. A discussion of these tests is beyond the scope of this opinion.

The other advance is chromosomal microarray analysis (CMA) which detects chromosomal aberrations such as copy number variations (CNV; microdeletions and duplications) that would not be detected by conventional karyotyping.[13,50] The prior phenotype-based categorization of fetal congenital malformations and genetic syndromes was totally upended by the advent of CMA. It soon became apparent that many genetic syndromes that were previously described based on phenotype had an underlying chromosomal abnormality that would not be detected by traditional karyotyping. In a large study of over 4,000 pregnancies, CMA revealed a clinically significant CNV in 6% of patients with a single structural anomaly and a normal karyotype.[50,51] In addition, 1.7% of pregnancies without a sonographically detected fetal structural abnormality with a normal karyotype on invasive testing (due to advanced maternal age or positive screen) had a clinically relevant CNV.[50] Studies consistently show that pathogenic CNVs can be identified in 0.4 to 2.5% of structurally normal fetuses.[52,53] While CNVs may be associated with a wide variety of outcomes and varying penetrance and expressivity, a substantial proportion are associated with major neurodevelopmental impairment or physical/medical debility. However, the detection of variants of uncertain significance presents some challenges for the use of CMA, and it is essential that genetic counseling addresses this prospect before invasive testing.[51] Importantly, the incidence of these CNVs does not increase with advancing maternal age.[13] Furthermore, the overall incidence of CNVs that are clinically significant and may be associated with neurodevelopmental impairment is higher than the background risk for Down syndrome. Thus, in the era of tests that detect conditions associated with severe disability for the offspring, it is not appropriate to continue making Down syndrome screening alone the primary focus of prenatal screening, especially given that almost all cases of Down syndrome will be detected by NIPT with cfDNA.[13] Currently, insurance companies will cover CMA when medically indicated (defined as in patients of age 35 years or older, pregnancies in which fetal structural abnormalities have been identified on prenatal imaging), when NIPT shows an abnormal screen, when fetal growth restriction is identified, and when there is a parental history of CNVs.

Unfortunately, both physicians and patients often are stuck in the old paradigm, where the screening and quantification of risks are entirely Down syndrome derived. In patients over 35 years who have low-risk cfDNA screening, the risk for Down syndrome or trisomies 18 or 13 is extremely low.[13] However, often, when we, the authors, have a patient without a finding of fetal structural abnormalities referred to us for amniocentesis, one of the most common reasons given is maternal age, even when the NIPT has been low risk. The risk of a clinically significant CNV will by far exceed that of Down syndrome in such a patient who has had low-risk screening for common aneuploidies. As such, it does not make sense that a patient who is 40 years old who has a low-risk cfDNA screen yet opts to have an amniocentesis has only a karyotype (which is likely to be normal) but is not offered CMA testing. A CMA is much more likely to yield an abnormal result than for Down syndrome to be detected in this scenario. Similarly, in a fetus with structural abnormalities that do not follow any characteristic aneuploidy pattern in a patient who has had low-risk cfDNA screening, CMA is generally a much more appropriate and reasonable test.

However, genetic counseling and testing are both frequently based on the old paradigm. Often patients are counseled to have amniocenteses without CMA being routinely mentioned or offered. Our experience is that this approach is pervasive. It has also been our experience that insurance companies will frequently deny authorizations for CMA for a patient younger than 35 years and undergoing amniocentesis, despite the presence of a pertinent family history or structural abnormality, often citing that the criteria of advanced maternal age have not been met, and thus, CMA is not medically necessary. This creates inequity for patients who desire CMA but do not meet certain insurance criteria and cannot cover the large out-of-pocket costs of CMA without insurance coverage. In our view, this is both unacceptable and unethical. Importantly, as awareness of available genetic testing options has increased, so has patient desire for CMA, emphasizing the need for CMA to be routinely offered when invasive testing is performed.

Whole Exome and Genome Sequencing

Improvements in the understanding of the molecular basis of inherited conditions have led to the development of advanced sequencing technologies such as whole-exome-sequencing (WES). WES involves sequencing only the exons, or protein coding regions of the genome, to identify an underlying etiology. As standard chromosomal analysis fails to establish a diagnosis in 20 to 30% of prenatal cases with ultrasound findings, WES should be offered when a specific genetic test for a phenotype (targeted panel testing) and routine cytogenetic testing is uninformative, and a genetic etiology is suspected. WES may identify a genetic abnormality in 15 to 19% of fetuses with multiple anomalies with a normal karyotype, microarray, or both.[54] The nuances of WES and secondary findings emphasize the need for detailed counseling completed by an individual trained in genetics. However, our experience has been that insurance companies will often not cover WES in patients who have major fetal structural abnormalities with normal CMA.

Whole genome sequencing (which involves sequencing an individual's entire genome, unlike WES which just sequences the exons) is emerging as a promising tool in pediatrics and has been proposed as an alternative to conventional newborn screening. Its use is currently not recommended in prenatal diagnosis outside of a research setting. However, this technology holds great promise and may in the future become a test with prenatal applications.

First-Trimester Detailed Ultrasound

Ultrasound at 11 to 13 weeks of gestation was first introduced as a screen for Down syndrome, through the use of nuchal translucency measurement.[25] Because of the availability of cfDNA screening, which gives a high detection for Down syndrome, the first-trimester scan is no longer the optimal test for Down syndrome. However, several fetal structural and genetic abnormalities may be detected in the first trimester.[55–59] In an era where reproductive rights are being challenged and where in several states lower gestational age thresholds are being instituted for the option of termination of pregnancy, detection of fetal anomalies in the first trimester will play an increasing role in the management of pregnancies complicated by fetal anomalies.[59–61] However, the limitations of first-trimester detection of anomalies must be taken into consideration.[58,59] Some anomalies may not be detected in the first trimester, while there may be some false-positive diagnoses. In addition, first-trimester detailed sonography requires some skill and training.[58] Thus, it is essential to include comprehensive training in first-trimester detailed ultrasound for both sonographers and sonologists to ensure proficiency in accurately assessing early fetal development. Where such resources are available, we suggest expanded utilization of first-trimester detailed ultrasound.

Carrier Screening

Historically, carrier screening was targeted toward specific ethnic populations known to be at increased risk of particular disorders. Known as ethnic-based carrier screening, examples include screening those of Ashkenazi Jewish descent for Tay–Sachs disease and cystic fibrosis, those of African descent for sickle cell disease, and those of Mediterranean descent for thalassemia. Given the high incidence and awareness of these conditions in these populations, screening was often conducted preconceptions. At the time, only a few inherited conditions were screened for prenatally. Besides screening based on ethnic ancestry, some inherited conditions were only screened for when an affected individual brought the condition to attention, with most screening occurring prenatally, rather than preconception. However, the complexity of defining an individual's ancestry in today's multiracial society challenges these traditional assumptions, suggesting that pan-ethnic screening might be more effective and equitable.[62–64]

Because genetic testing technology has evolved rapidly over the past decade, it is now possible to screen for a large number (anywhere between 5 to several hundred) genetic conditions simultaneously.[63] The American College of Medical Genetics recommends that all pregnant patients and those planning pregnancy should be offered carrier screening for conditions with carrier frequency $>1/200$.[64] We agree with this recommendation.

Despite its benefits, expanded carrier screening often lacks routine insurance coverage, even though its cost may be comparable to or less than screening for a single condition.[63] Given the wide array of carrier screening tests and panels available, the genetic counselor is crucial in navigating patients through the selection process, providing tailored advice, considering the patient's medical history, personal circumstances, preferences, risk factors, and financial situation, to determine the most suitable test for each individual. It is essential that pretest counseling by a genetic counselor occur before conception or in early pregnancy to discuss possible results, their implications, and the inheritance patterns and natural history of potential conditions identified. Specifically, patients should be counseled on the possibility for an individual to be determined to be at risk themselves, as well as of the possibility for results with uncertain implications including likely pathogenic variants or variants of uncertain significance that may have varying health implications. Patients should be informed of the inheritance patterns and natural history of conditions included on the selected carrier screening panel to be performed. While there is an ongoing debate about reproductive rights and in particular abortion, there is agreement that identification of risk for a lethal or severe fetal abnormality prior to conception is preferable to that of termination of pregnancy. With the enhanced ability to predict genetic disorder risks before conception, expanding carrier screening to identify prospective parents at risk of transmitting genetic conditions is both a logical and scientific strategy.

Genetic Counseling

The field of prenatal screening and diagnosis has advanced in leaps and bounds. With these advances have come challenges

in counseling and decision-making. Some tests will lead to more anxiety and may have ambiguous results, creating more uncertainty than clarity. Patients should be aware of testing benefits and limitations, the nuances of testing methodologies at various performing laboratories, and the reporting of incidental findings prior to testing being performed.[11,13] Furthermore, results may have implications for the lives of the patients and their relatives as well as life and health care insurance consequences. There was a time when most obstetricians were comfortable in counseling patients about the limited range of genetic conditions and prenatal screening and diagnostic tests that were available. Today, countless conditions and testing options exist. As such, we suggest increased availability of genetic counseling and training to all involved in prenatal care to ensure proficient patient counseling and consent.

Adapting Prenatal Screening and Diagnosis for the Post-Roe Legal Landscape

The U.S. Supreme Court's decision on June 24, 2021, in Dobbs v. Jackson Women's Health Organization, which effectively overturned Roe v. Wade, has profoundly transformed the landscape of reproductive rights and abortion access in the United States. In the aftermath, a diverse array of abortion regulations has emerged: some states have enacted comprehensive bans, while others have implemented stricter gestational age limits for the procedure.[59,65] These shifts carry tremendous implications for prenatal screening and diagnostic practices.[59,65] The imperative for early detection of genetic and structural anomalies has intensified, necessitating that such screenings are both widely available and achieve a high level of precision. Early accurate diagnosis will permit more parental control in appropriate pregnancy decision-making.[60] Concurrently, the evolving legal environment, coupled with technological advancements, presents a complex array of challenges that health care providers must adeptly navigate.

Proposals

We wish to propose the following:

1. The concept of pregnant individuals greater than 35 years of age being categorized as being at "high risk" or of "advanced maternal age" solely for the purpose of assessing risk for chromosomal abnormalities should be abandoned. After screening with cfDNA, the patient aged 35 years or older is no longer at increased risk for common aneuploidies. In addition, the incidence of CNV does not increase with maternal age.[13]
2. All pregnant individuals should be offered NIPT with cfDNA. We feel that, in most situations, it is inappropriate to continue using traditional first- or second-trimester screens that will fail to detect between 5 and 20% of fetuses with Down syndrome when there is a widely available test that will detect $>99\%$ of cases with an extremely low false-positive rate.[11,13] Furthermore, cfDNA remains, at this time, the only screening test for fetal sex chromosome abnormalities.[13]
3. Given that isolated soft markers in low-risk patients are considered normal variants and do not appreciably increase the risk for chromosomal abnormalities in low-risk screen negative pregnancies, we advocate refraining from informing patients about these findings. The considerable anxiety that these findings evoke suggests that it is time to stop mentioning them to patients unless the soft markers are found in combination with a positive screen or more than a single soft marker is present.
4. In cases where patient autonomy necessitates the disclosure of the presence of isolated soft markers, health care clinicians should be trained to effectively communicate the limited clinical significance of these findings, to minimize undue patient anxiety.
5. When patients undergo amniocentesis for a suspected genetic etiology or fetal structural abnormalities, CMA should be routinely available to all of them. Recommending CMA becomes especially important when patients undergo amniocentesis for structural abnormalities. CMA should not be limited to just women over the age of 35 years. When fetal structural abnormalities are found with a normal karyotype or CMA, we recommend offering the patient whole exome sequencing.
6. We recommend that, where skilled sonographers are available, detailed first-trimester ultrasound be performed more frequently.
7. Health care providers, hospitals, insurance companies, and all other stakeholders should be aware of new developments in prenatal screening and diagnosis and make the most appropriate tests available to patients. In addition, insurance companies should expand coverage for tests that best serve patient and societal needs.
8. We suggest that appropriate preconception and prenatal carrier screening should be made more widely available and accessible.
9. Finally, the essential role of skilled credentialed genetic counselors cannot be overstated.

Conclusion

In summary, significant advances over the past 30 years have greatly enhanced our ability to screen and diagnose fetal chromosomal, genetic, and structural abnormalities. We now have the capacity to detect countless problems that have potentially devastating life-long consequences for the offspring. While in the past, criteria such as maternal age and a positive first- or second-trimester screen provided the basis for diagnostic testing for fetal chromosomal abnormalities, the availability of tests with much-improved detection and lower false positives should lead to the adoption of these improved tests. Furthermore, the time has come to stop creating unnecessary alarms in patients who are over the age of 35 years. It is time to abandon old paradigms and move to a more contemporary evidence-based approach to prenatal screening and diagnosis.

Summary

Recent advances in genetics and imaging require that health care providers involved in pregnancy care reevaluate current prenatal screening practices and adopt a paradigm shift.

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Conflict of Interest

None declared.

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