Second Quarter 2017 • Vol. XXX • Number 2

PLUS Journal *Reprint*
5353 Wayzata Blvd., Suite 600
Minneapolis, MN 55416-4758
phone 800.845.0778 or 952.746.2580

The mission of the Professional Liability Underwriting Society is to be the global community for the professional liability insurance industry by providing essential knowledge, thought leadership and career development opportunities.

PLUS
PROFESSIONAL LIABILITY UNDERWRITING SOCIETY
Journal
YOUR SOURCE FOR PROFESSIONAL LIABILITY EDUCATION AND NETWORKING

Noninvasive Prenatal Genetic Testing: Cutting Edge Technology Portends New Wrongful Life/Birth Theories of Liability Against Healthcare Providers, Labs & Diagnostic Companies

by Alicia Bromfield, Esq. and Donald B. Lenderman

Alicia Bromfield, Esq. *manages complex claims, including life sciences and managed care matters, and counsels on coverage issues at IronHealth, a division of Ironshore Insurance Company. Alicia's role includes the comprehensive management of high exposure claims in the life sciences and managed care arenas, including matters involving coverage litigation. She can be reached at Alicia.Bromfield@ironshore.com.*

Donald B. Lenderman *is a principal and leader of the Kitch Firm's highly-regarded birth trauma and catastrophic damages defense practice in Detroit, MI and Chicago, IL. With more than 25 years of litigation experience, he primarily represents healthcare providers and hospitals across the country in the defense of obstetrical, gynecologic, and neonatal malpractice claims. He can be reached at don.lenderman@kitch.com*

Noninvasive prenatal testing ("NIPT") is a popular option for high risk pregnancy patients desiring to screen for chromosomal abnormalities.[1] By analyzing fetal DNA circulating within the maternal blood, NIPT does not require an invasive procedure that involves extraction of fetal cells for chromosomal analysis; rather, it involves a simple blood test. The patient who elects NIPT can avoid the procedure-related risk–albeit small–of miscarriage that accompanies amniocentesis and chorionic villous sampling. Through direct-to-consumer advertising, manufacturers of NIPT kits are dominating the market for prenatal screening. NIPT use has quickly penetrated clinical practice, and it has become the screening test of choice for fetal aneuploidy.[2]

We anticipate that clinical healthcare providers, laboratories and the NIPT developers will face significant liability exposure in connection with NIPT technology. The number of wrongful life and/or birth suits alleging failure to diagnose chromosomal abnormalities utilizing conventional biochemical serum testing and diagnostic testing has resulted in staggering verdicts and settlements (see chart on pg. 15). We anticipate similar wrongful life/birth claims will be pursued in connection with the more widespread use of the NIPT. In this article, we explore some of the anticipated theories that will be advanced by the plaintiffs' bar. Given the potential for an increase in wrongful life/birth claims, healthcare providers, laboratories and NIPT developers should ensure their insurance, including professional liability and/or products liability coverage, protects them from the liability exposures emanating from this newer technology.

Understanding Noninvasive Prenatal Testing

NIPT analyzes fragments of cell free DNA circulating within the maternal blood stream.[3] NIPT is a screening test that determines the probability of a limited number of common chromosome abnormalities (e.g., Trisomy 13, Trisomy 18 [Edward Syndrome], Trisomy 21 [Down Syndrome], and sex chromosome abnormalities). It does not provide screening for a broader range of genetic abnormalities such as neural tube defects or ventral wall defects.[4]

As a screening test, NIPT is designed to assess the risk for a potential genetic problem rather than to make the diagnosis of an actual genetic condition. A "positive" result on NIPT does not necessarily mean that the fetus in fact has a chromosomal abnormality. False positive and false negative results do occur, implicating the need for counseling from a qualified maternal fetal medicine specialist, geneticist, or genetic counselor to guide management decisions in light of positive results.

Understanding NIPT Results

The healthcare provider must set expectations with respect to the limitation of NIPT as a screening test. A patient looks to the provider as a learned intermediary to interpret results and to tailor management options. Individualized assessment of the risk of a genetic abnormality is vital if the patient is to make an informed management decision that may result in termination of a pregnancy.

One of the advantages of NIPT is that more affected fetuses will be discovered when compared to conventional biochemical screening (i.e., triple screen or quad screen testing). Studies have shown that NIPT is generally highly sensitive (>90%), meaning that the test is quite capable of detecting positive cases of chromosomal abnormalities. Sensitivity is an

indication of the proportion of positive subjects in a population correctly identified by the test. The specificity of NIPT is also high (greater than 99%), meaning that the non-affected subjects in the population are identified as negative by the test. Despite the high sensitivity and specificity of NIPT, false-positive and false-negative results may still occur. The challenge to healthcare providers is to identify whether a positive screening result actually represents an affected fetus or whether the result is a false-positive.

Manufacturers' claims that suggest near certainty of test results are based on the sensitivity of the testing. If a screening test yields a false-positive result, diagnostic testing is warranted to ascertain whether the fetus is truly affected. If the patient declines diagnostic testing, some patients may elect termination of the pregnancy based solely on the positive screening result. Without diagnostic confirmation, some of those patients may terminate normal pregnancies that were false-positives.

The limitations of NIPT are revealed in their positive predictive value. This statistical concept helps elucidate what role NIPT results will play in a woman's management decisions during the pregnancy. The positive predictive value is a measure of the likelihood that a patient with a positive test result is a true-positive and has the subject condition. It is defined as the number of true-positives divided by the sum of true-positives and false-positives. The concept is related to how frequently the condition occurs within a tested population.

Discussion of the positive predictive value can help the patient to place a positive screening result in a more meaningful context. For example, a comparison of the incidence of Down Syndrome in a low risk pregnant population (women under age 35) to a high risk population (women over age 35) illustrates the importance of context when interpreting a positive screening result. The prevalence of Down Syndrome increases with advancing age. The incidence of Down Syndrome at a maternal age of 25 is approximately 1 in 1000. By age 40, the incidence increases to approximately 1 in 75. The reported positive predictive value of NIPT for detecting Down Syndrome at age 25 is 33%. By age 40, the positive predictive value increases to 87%. The implication is that only 1 in 3 women with a positive screening result at age 25 will be a true-positive with an affected fetus whereas the chance of a true-positive is considerably greater at age 40.[5] When the prevalence of the condition is rare, the positive predictive value of the screening test decreases. Consequently, positive results are more likely to be false-positives in such low risk populations with a low prevalence of the condition.

Healthcare Providers–Potential Liabilities

The interval between development of a new technology and its implementation into clinical practice is a vulnerable time for providers. The potential for liability exists as providers learn about NIPT. During that period, standards of practice are coalescing as more and more providers become familiar with the technology and make it available to their patients.

To minimize the potential for liability, healthcare providers should consider the following:

1. As a screening test, how likely is NIPT to uncover an abnormal result? What interventions, if any, are available to address the result?
2. What are the patient's preferences about undergoing testing? What options are available to the patient in light of a positive result, a negative result, or no result?
3. What are the detection rates of false-positive and false-negative? What is the likelihood that a positive result is a true positive?

These above –referenced topics are a mere sampling of information that the provider should incorporate into the informed consent discussion prior to offering NIPT. Well-documented communications in the patient chart are valuable in the event of future litigation.

Noninvasive prenatal testing has rapidly emerged as a beneficial technology to identify certain fetal chromosomal abnormalities. As providers and patients navigate the NIPT learning curve, potential liabilities arise from knowledge gaps about the limitations of NIPT and its role in a broader prenatal care regimen. As providers incorporate NIPT into practice, they are well advised to provide pre- and post-test counseling and to consult genetics experts as appropriate.

Potential theories of tort liability relating to NIPT include:

Failure to Offer NIPT

The failure to offer prenatal testing, including NIPT, is a concern, particularly in areas underserved by genetics specialists. Plaintiffs' attorneys will exploit not only the failure to use NIPT technology appropriately but also the failure to offer it to patients as well. Plaintiffs' attorneys are already marketing to clients who had "inadequate prenatal screenings." Litigation experts will soon emerge on both sides of the issue of whether NIPT is an available option for prenatal screening or is mandated as a first-line screening test.

In 2007, the American College of Obstetricians & Gynecologists recommended fetal chromosomal screening to all pregnant patients regardless of age.[6] The organization also urged physicians to provide information on detection and false positive rates, limitations of screening testing and diagnostic procedures, and the risks of such testing. Reaffirmed in 2013, ACOG's recommendation is evidence of an established standard of practice for prenatal care.

Inadequate History Taking and Communication

A recent notable verdict sheds light on this potential area of liability. In December 2013, a jury in King County, Washington returned a $50 million verdict against a hospital and a laboratory for negligent performance of genetic testing.[7] The parents of the minor plaintiff sought prenatal genetic testing because the father was a carrier for a genetic condition known as an unbalanced chromosome translocation.[8] Plaintiff alleged that the parents sought the testing to decide whether to continue the pregnancy. Plaintiff's counsel persuaded the jury that understaffing in the hospital's genetics counseling clinic resulted in a failure to provide appropriate history and instructions to the laboratory that performed the testing. As a result, the laboratory failed to look specifically for the translocation and failed to detect the genetic abnormality. The child was born with profound cognitive and physical deficits.

Failure to Provide Informed Consent Regarding Risks

As NIPT is available for all pregnant patients rather than just high risk patients, providers must be cognizant of the limitations of NIPT in that population and effectively communicate them to their patients. NIPT is screening and not diagnostic. Although NIPT has higher sensitivity to detect Trisomy 18 and 21 when compared to conventional serum testing, false positives and negatives are still possible.

As a consequence of these limitations, professional societies recommend a diagnostic test for any patient with a positive NIPT result. Moreover, they caution that "management decisions, including termination of the pregnancy, should not be based on the results of the cell-free DNA screening alone."[9] The informed consent discussion with the patient is likely to be longer given the addition of NIPT to the prenatal screening regimen. Providers may also have to clarify patients' misperceptions about the role of NIPT in prenatal diagnosis as the result of aggressive direct-to-consumer marketing efforts. Documentation of the informed consent discussion remains an integral part of reducing the risk of malpractice claims.

Failure to Warn Relatives and the Duty of Confidentiality

Inherent to genetic testing is the ability to learn information that may impact a patient's biologic family members. The limit of patient privacy in the field of genetics is evolving. The physician's duty of patient confidentiality may collide with the desire to counsel other family members about a familial genetic issue. Physicians often treat multiple members within the same family. The physician may be in the unenviable position of learning that one family member is a carrier of a genetic abnormality while the patient's sister does not know or would not want to know about any prenatal genetic information.

The prevailing legal stance is that physicians must protect the confidential information of patients. However, three states (FL, MN, and NJ) have recognized a duty that extends to family members who may be affected by the information.[10] The implications of genetic information can be significant. The question of whether to notify relatives of pertinent findings highlights the importance of pretest counseling regarding the impact of test results not only for the patient but also for her relatives and offspring. The law will need to address this very important arena as the popularity of NIPT surges.

Diagnostic Companies/Labs-Potential Liabilities

As the plaintiffs' bar continues to search for new deep pockets and new theories of liability in wrongful birth/wrongful life litigation, some attorneys have turned their attentions to the diagnostic companies. By targeting these companies instead of or in addition to typical healthcare providers, plaintiffs may be able to circumvent medical malpractice damages caps in certain states. In addition, the competition among NIPT companies is fierce and has resulted in several instances of patent litigation and litigation involving unfair competition. Such competition creates fodder for plaintiffs' bar to argue that diagnostic companies put profit over people; that NIPT kits have been rushed to market, and that the methodologies have not been scientifically vetted.

Failure to Warn–Representations made in advertising and Inadequate Disclaimers

Plaintiffs may allege that certain representations made in direct to consumer advertising of NIPTs amount to negligent misrepresentations and/or false advertising. Such statements, posted on diagnostic company websites and in promotional materials, could include "clear answers" and "results you can count on." Although such statements are more akin to "puffery," plaintiffs will allege that they relied on such statements as truth and were damaged when such statements proved to be false. Due to the intense competition among NIPT companies, tests are aggressively marketed and plaintiffs will claim that such advertisements fail to warn sufficiently of the limitations and potential errors in the test. Although NIPT results are typically delivered directly to physicians, a claim could also be made that the test results, themselves, do not contain adequate disclaimers and warnings regarding the accuracy of the screen.[11]

Defective Design

Plaintiffs will claim that in addition to tests being falsely advertised, the NIPTs themselves are defectively designed and/or manufactured. Any time parents receive a false positive or false negative, they can argue that the test is per se defective due to its yielding the wrong results. Such claims could be bolstered by allegations that the intense competition and pressure to rush the tests to market resulted in inadequate

trials and false confirmation that the test methodologies were sound.[12]

What's at stake? Wrongful Birth/Wrongful Life Verdicts and Settlements

Although not all states recognize causes of action for wrongful birth and/or wrongful life, where such lawsuits are allowed to proceed, the damages can be staggering. (See chart below, which provides a sampling of jury verdicts and settlements that highlight the high stakes of wrongful birth claims.)

With new technology comes new expectations and potential new liabilities. Given the potential for an increase in wrongful life/birth claims resulting from new techonolgies, all involved in prenatal care—from healthcare providers to laboratories to NIPT developers —should ensure their insurance provides the best protection from these new liability exposures.

Year Resolved	State	County	Amount	Defendants	Description
2015	New Jersey	Bergen County	$8,250,000 (settlement)	Healthcare providers, including u/s technician	Doctor and technician failed to interpret nuchal measurement abnormalities. Child born with numerous birth defects.
2013	New Jersey	Monmouth County	$7,100,000 (settlement)	Physicians, technicians, employer -hospital	Mother underwent an amniocentesis done so that prenatal cytogenetic testing could be performed to determine if the fetus was afflicted with any genetic disorders. The plaintiff maintained that the history of the mother giving birth to a special needs child and advanced maternal age placed her at higher risk, and that if the parents were advised of the abnormality, the pregnancy would have been terminated. The child was born with Wolf-Hirschhorn syndrome, a debilitating disease characterized by an abnormal facial appearance, delayed growth and development, intellectual disability, and seizures.
2013	Washington	King County	$50,000,000 (verdict)	Hospital and lab	Wrongful-birth claim brought by the parents of male infant who was born with an unbalanced translocation, resulting in myotubular myopathy with profound physical and cognitive disabilities. Allegations that defendants Lab and Medical Center failed to perform and secure genetic testing when it was known that the father had a chromosome abnormality that might produce a disabled child
2012	Oregon	Multnomah County	$2,943,505 (verdict)	Healthcare providers	Parents sought prenatal testing. CVS testing wrongly interpreted as showing no sign of Down Syndrome. Allegations that non-standard small tissue sample used. Child subsequently born with Down Syndrome.
2012	Massachusetts	Unknown	$2,900,000	Healthcare providers	Parents sought assurance that their 13 week fetus did not have any chromosomal issues. Child was born with Down Syndrome.
2011	Massachusetts	Worcester County	$7,611,806 (settlement)	Doctors	Mother, who at age 37, was a high risk pregnancy, received intermittent Cantonese interpreters during her prenatal care but, she was not provided with sufficient information necessary to make an informed decision regarding whether or not to undergo amniocentesis to determine if the fetus had an abnormality. Child born with Cri-du-Chat Syndrome
2011	Florida	West Palm Beach	$4,500,000 (verdict)	Healthcare providers (hospital settled pre-trial)	Mother had several ultrasounds where tech failed to confirm presence of legs or arms, part of minimal elements of standard examination of fetal anatomy. Child was born with aplasia and hypoplasia, with both arms absent, absent leg and other deformities.
2011	North Carolina	Mecklenburg County	$2,026,381 (arbitration)	Physician, reproductive clinic	IVF technician failed to recognize parents were carriers of cystic fibrosis gene. Child was born with cystic fibrosis.
2010	California	Los Angeles	$3,325,000 (settlement)	Healthcare providers	Physicians failed to diagnose chicken pox virus in utero. Child was born with multiple congenital abnormalities.

Year Resolved	State	County	Amount	Defendants	Description
2007	Florida	Unknown	$23,553,000 (verdict)	Hospital	Parents of one son diagnosed with Smith-Lemli Opitz Syndrome consulted geneticists during pregnancy with second child to confirm child did not have the same condition. They were told child was normal; however, child had same condition.
2007	New Jersey	Passaic County	$28,000,000 (verdict)	Physicians, laboratory	Child born with myotubular myopathy. His mother was a carrier, and two of her nephews died of the disease shortly after birth. Mother claimed that child's defect was never detected by medical professionals, despite her requests to test for MTM.
2006	New Jersey	Unknown	$14,000,000 (settlement)	Healthcare providers	Child born with thalassemia major. Early blood test showed abnormal hemoglobin marker. Incorrect diagnosis of anemia. Failed to run additional tests.
2002	New Jersey	Union County	$4,200,000 (settlement and verdict)	Hospital, doctors (including OB/GYN and radiologist, clinic	U/S technician reported possible heart defect. Radiologist did not order follow up. Child was born with deformed left ventricle.

Endnotes

1 This noninvasive approach differs from conventional biochemical serum screening (maternal serum alpha-fetoprotein, human chorionic gonadotropin, and unconjugated estriol), and diagnostic testing such as amniocentesis and chorionic villous sampling.

2 *American Journal of Obstetrics & Gynecology,* "Uptake of noninvasive prenatal testing at a large academic referral center," 211:651.e1-7 (Dec. 2014).

3 Society of Maternal Fetal Medicine, "Patient handout: Prenatal screening using cell-free DNA," contemporaryobgyn.modernmedicine.com (June 5, 2015).

4 ACOG Committee Opinion, "Cell-free DNA Screening for Fetal Aneuploidy," no. 640 (Sep. 2015).

5 ACOG Committee Opinion, "Cell-free DNA Screening for Fetal Aneuploidy," no. 640 (Sep. 2015).

6 ACOG Practice Bulletin, "Screening for Fetal Chromosomal Abnormalities," no. 77 (Jan. 2007).

7 *Wuth v Valley Medical Center, et al.,* Superior Court of King County, Washington (2013). The Court of Appeals upheld the verdict on August 24, 2015.

8 "$50M awarded over birth defect; test said baby would be OK," seattletimes.com, (Dec. 10, 2013).

9 ACOG Committee Opinion, "Cell-free DNA Screening for Fetal Aneuploidy," no. 640 (Sep. 2015).

10 ACOG Committee Opinion, "Ethical Issues in Genetic Testing," no. 410 (June 2008).

11 See, e.g. allegations set forth in Kivett v. Ariosa Diagnostics, Inc. et al., Superior Court of the State of California, County of San Mateo, Case No. CIV524508.

12 *Id.*.