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Old Questions, New Paradigms: Ethical, Legal, and Social Complications of Noninvasive Prenatal Testing

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Recent rapid changes in prenatal care have resulted from the discovery that cell-free fetal DNA (cffDNA) circulates in the maternal bloodstream during pregnancy (Lo et al. 1997). The discovery of cffDNA in maternal serum, combined with sequencing and bioinformatic techniques, has allowed the detection of an anomalous number of chromosomes in a developing fetus (Chiu et al. 2008; Fan et al. 2008). For the first time, clinicians can offer genetic testing in the prenatal period without using invasive procedures, such as amniocentesis, that carry a slight risk of miscarriage.

Noninvasive prenatal testing (NIPT) is recognized by professional societies as a highly sensitive, non-diagnostic screening test (American College of Obstetricians and Gynecologists [ACOG] 2012; Benn et al. 2013). For some chromosomal aneuploidies, especially trisomies 13, 18, and 21, NIPT has a sensitivity and specificity in excess of 95% (Bianchi et al. 2014). Microdeletions and single-gene disorders may also be detected with NIPT through microarray, whole genome sequencing, or targeted single-nucleotide polymorphism (SNP) analysis (Fan et al. 2012; Juneau et al. 2014; Kitzman et al. 2012; Rabinowitz et al. 2014). While these techniques allow for a more detailed examination of the fetal genome, they also bring into the prenatal period many of the debates and ethical concerns previously associated with pediatric and adult sequencing (Donley, Hull, and Berkman 2012; Tabor et al. 2012).

Intimately bound up with technological questions regarding NIPT are many ethical questions, and this special issue of *AJOB Empirical Bioethics* addresses a wide range of these issues. The articles that follow represent emerging empirical work on the ethical issues that are raised by NIPT, heightened by its rapid clinical implementation, and contextualized

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within the larger landscape of prenatal testing. Here, we summarize a few of these concerns and provide an overview of the articles in this issue.

BLURRING OF SCREENING AND TESTING

The simplicity of the NIPT test procedure—a blood draw during a time when pregnant women already undergo numerous blood draws—belies the complexity of the information it may yield (Farrell et al. 2014). Genetic information obtained by NIPT is complex both in a technological sense and in the ways it raises ethical issues at the social, familial, and personal levels (Benn and Chapman 2010; de Jong et al. 2011; Skirton, Goldsmith, and Chitty 2014; Van Riper 2012). By combining the procedural ease of screening tests with a volume of information previously limited to invasive diagnostic testing, NIPT blurs a once-bright line between screening and diagnosis in prenatal testing.

Allyse et al. (2015), for instance, surveyed members of the general public, asking them to respond to a scenario describing choices between prenatal testing modalities that many women are now asked to make: low-cost serum screening with a moderate sensitivity versus high-cost NIPT with a higher sensitivity, with both tests potentially followed by invasive testing. Participants were predictably concerned with accuracy, but were divided on issues of cost: some felt that no cost was too high to assure peace of mind, while others thought that NIPT was too expensive and unnecessary. Furthermore, some participants questioned the desirability of any prenatal testing, and some expressed suspicion that NIPT reflected yet another extension of a medico-technical realm that was more concerned with innovation and profit than patient care.

INFORMED DECISION MAKING

NIPT's rapid translation and expansion can cause confusion for women who are offered the test. Because the procedure is "low-risk," some providers may not encourage patients to consider an informed decision in the same careful way they would for an invasive and more "risky" amniocentesis (van den Heuvel et al. 2010). Some scholars and clinicians have expressed concerns that the apparent simplicity of NIPT will accelerate the routinization of prenatal testing and erode informed decision making (Deans and Newson 2012; Hill et al. 2013). Yet even with extensive genetic counseling, women are still faced with difficult decisions about the justification and consequences of genetic testing during pregnancy, decisions that NIPT eases in some ways and intensifies in others (Farrell et al. 2014; Kellogg et al. 2014).

As Leach (2015) points out in his analysis, this decision-making process is inhibited by the imbalance in resources devoted to the technical accomplishments of new prenatal tests versus the education and context needed to implement them successfully. While considerable time and physician resources are employed in the development and distribution of NIPT tests, and in convincing other providers of their value, there is little attention to educating providers on the very real psychosocial problems that NIPT's technical advancements do nothing to allay.

Mozersky's (2015) in-depth account of patient experiences highlights the fact that the very ease of NIPT can elide the emotional preparation that patients need to make truly informed decisions. The women whose narratives she presents deferred the contemplation of personal values about disability and possible termination until they received results that forced them to confront these issues, raising questions about the quality of informed consent processes about a "no-risk" test.

Meanwhile, the findings of the Farrell et al. (2015) focus groups with pregnant women emphasize that the assurances of clinicians and testing providers may not always align with the perceptions and values of pregnant women. Despite clinical data on the actual risks of miscarriage from invasive procedures, and promises by testing companies that the rates of false positives and false negatives from NIPT are very low, some women in this study still considered the possibility of incorrect results a significant factor in their considerations surrounding testing decisions.

COMMERCIALIZATION AND MARKETING

One aspect of NIPT that sets it apart from previously available prenatal testing is that its patented technologies have been made available almost exclusively through private, for-profit laboratories. For some clinicians and other scholars, the commercialization of NIPT has heightened concerns about particular aspects of the testing, including the rapid push to offer it to a broader patient base for more conditions, and the ways in which it is vigorously marketed to doctors and patients (Dickens 2014; Norton, Rose, and Benn 2013).

As Vanstone et al. (2015) found, this commercial push has resulted in two increasingly divergent conceptualizations of NIPT's definition and ultimate function. In the one promoted by testing companies, NIPT is framed as an expansive testing regime encompassing all pregnancies and a potentially infinite number of genetic conditions. In the other, espoused by professional organizations, NIPT is a narrower, second-tier screen for patients who have elevated risks of specific trisomies. In some ways, these divergent views of NIPT reflect broader visions of alternative futures for genetics in the prenatal period.

In this highly commercialized landscape, information sources about NIPT, apart from test providers, are especially valuable. Unfortunately, as Truitt and Nguyen's (2015) analysis reveals, newspaper representations of NIPT frequently lack important information for potential consumers, including lay explanations of test statistics and cost, the current recommended scope of NIPT, and the experiences of people with disabilities and their families. These factors suggest that mass media provide an inadequate counternarrative to the aggressive marketing of NIPT vendors, and that clinicians should be aware that patients might have absorbed misinformation about NIPT prior to the clinical encounter.

ACCESS AND INTERNATIONAL IMPLEMENTATION

Finally, the benefits and challenges of NIPT must be considered in the varied social, economic, religious, and political contexts in which it is entering prenatal health care. We recognize that while most research on the clinical implementation of NIPT has focused on North America and Western Europe, this technology must be responsive to local concerns as

it spreads worldwide (Chandrasekharan et al. 2014). In the final section of this special issue on NIPT, we have highlighted non-Western perspectives.

In Hong Kong, the birthplace of NIPT, Yi et al. (2015) analyzed the perspectives of clinical providers offering NIPT. Their results suggest that providers in Hong Kong emphasize technical and economic elements of NIPT over ethical concerns surrounding broader social issues. This finding forms an interesting contrast with previous work by some of these researchers, in which patients describing their experiences with NIPT raised considerable ethical concerns surrounding the testing process (Yi et al. 2013). This disparity suggests a need for greater attention to patients' needs and values in prenatal testing by physicians and other stakeholders.

Religious perspectives are inextricably linked to social values about prenatal testing. Though nearly a quarter of the world's population is Muslim, little empirical research has been done on NIPT in Muslim communities. Focusing in detail on social and legal contexts in Iran and Saudi Arabia, Haidar and colleagues (2015) explore the impact NIPT may have in the Islamic world, with particular attention to the legal and religious status of abortion. Haider and colleagues suggest that empirical attention to the perspectives of Muslim religious scholars on NIPT will be especially useful in illuminating both public policy and individual decisions about NIPT in these contexts.

Finally, we commissioned two brief commentaries about the implementation of NIPT from clinicians operating on the ground in diverse geographic and socioeconomic contexts. From Hong Kong, Sahota (2015) reports on the uneven match between NIPT's relatively high cost and the public health system's need for cost-effectiveness in offering universal screening. From Argentina, Otanō and Igarzábal (2015) also note issues with NIPT's cost, which may compound existing health care inequities. The illegal status of elective pregnancy termination also complicates the local context for NIPT and prenatal care more generally in Argentina.

In this collection of qualitative and mixed methods bioethical research on NIPT, our fellow authors point to the many directions left to explore around this paradigm-changing technology. These articles also remind us that every family facing questions about prenatal testing and its possible outcomes experiences them as new.

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