

Towards DNA: Issues and Implications of Non-invasive Prenatal Genetic Testing

ADN : Enjeux et conséquences du dépistage génétique prénatal non effractif

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ABSTRACT

Non-invasive prenatal diagnosis (NIPD) will soon become the standard of care for prenatal genetic testing. NIPD uses DNA and has the potential to sequence the entire fetal genome and detect many diverse traits. Although both the public and midwives support the implementation of NIPD, concerns arise owing to the lack of agreement about what constitutes severe disabling traits. Further, there is limited understanding of the implications of such testing at both the individual and population levels. Midwives and other maternity care providers need to be better educated on all aspects of prenatal genetic testing - the limitations and implications of NIPD, as well as disability traits and living with them - in order to help their clients make truly informed choices.

KEYWORDS

prenatal diagnosis, genetic testing, best practices, future

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RÉSUMÉ

Le diagnostic prénatal non effractif (DPNE) deviendra bientôt la norme de soins en ce qui a trait au dépistage génétique prénatal. Le DPNE utilise l'ADN, ce qui pourrait lui permettre d'établir la séquence complète du génome du fœtus et de détecter bon nombre de caractères variés. Malgré le fait que le public et les fournisseurs de soins appuient la mise en œuvre du DPNE, celui-ci suscite l'inquiétude en raison de l'absence de consensus relativement à ce que constitue un caractère invalidant grave. Qui plus est, on comprend peu les conséquences de ce type de dépistage aux niveaux personnel et populationnel. Les fournisseurs de soins doivent améliorer leurs connaissances au sujet de tous les aspects du dépistage génétique prénatal (les limites et les conséquences du DPNE), de même qu'au sujet des caractères invalidants et des adaptations qu'ils nécessitent, afin d'aider leurs clients à prendre des décisions vraiment éclairées.

MOTS-CLÉS :

diagnostic anténatal, les tests génétiques, les meilleures pratiques, l'avenir

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In the next two to five years, it is expected that NIPD [non-invasive prenatal diagnosis] performed on cell-free fetal DNA (cffDNA) and cffRNA in maternal blood will be introduced as a routine screening test for aneuploidies.¹ Attempts to find a non-invasive method of diagnosing a fetus with a genetic abnormality have been underway for more than a decade. In 1997, Lo and colleagues isolated cell-free fetal deoxyribonucleic acid (DNA) in maternal blood, heralding the next generation of prenatal genetic testing.² Noninvasive prenatal diagnosis (NIPD) has two major advantages over current methods: there is no risk of miscarriage, and it can be performed much earlier in pregnancy.³ NIPD has advanced since its discovery and has known benefits over current methods. However, there is still much to be done before NIPD can be safely and ethically integrated into Canadian prenatal care.

Every pregnant woman in Canada is eligible for prenatal screening. The current screen gives an estimate of the chance that the fetus has spina bifida, trisomy 18, or trisomy 21. Only women whose chance of having one of these three abnormalities is above one in 200 (the generally agreed-upon maximum risk for spontaneous miscarriage from amniocentesis) are given the option of invasive diagnostic testing. Although all Canadian women are eligible for prenatal screening, such screening is not accessible to all women. The current “gold standard,” integrated prenatal screening (IPS), involves two separate venipunctures and ultrasonography. Many Canadian women live in isolated areas with no access to ultrasound equipment. In contrast, NIPD requires only one venipuncture. The test isolates cell-free fetal DNA in maternal blood; this DNA can be detected reliably as early as seven weeks’ gestation.⁴ The major barrier to offering NIPD at the population level is the cost of setting up laboratories and training personnel.⁴ At the individual level, NIPD would represent a cost saving by reducing the number of invasive diagnostic tests (currently used in about 5% of all pregnancies) and early ultrasound examinations for IPS; however, this would not be enough to offset the projected number of women requesting NIPD (expected to be 80%–90% or more of all pregnant

women),⁴ and depending on laboratory availability, many women may still have difficulty accessing this service.

Whereas current screening methods use ultrasonography and chemical levels in maternal blood to assess risk, NIPD uses DNA analysis and is diagnostic. DNA analysis has the potential to sequence the entire fetal genome; thus, many conditions could be detected.⁵ NIPD also has implications for sex determination, paternity testing, and Rh compatibility.⁴ Whereas NIPD for determining sex and paternity has the potential to lead to ethical debates similar to those around the use of NIPD for disability prediction, using NIPD to determine Rh compatibility is relatively free from the ethical quagmire that surrounds its other uses. Eliminating the prophylactic use of anti-D antibody in Rh-negative women is a clinical advancement that appears to have no down side. This may be the starting point for the everyday clinical use of NIPD and a stepping stone to further NIPD tests.

Hathaway, Burns, and Ostrer found that over half of their sample population (n = 999) would have liked prenatal testing for blindness, deafness, dwarfism, heart disease, and cancer.⁶ Arguably, individuals with a predisposition to heart disease and cancer can lead long, functional lives, possibly suffering from these conditions only in the later stages of life. Is this information useful prenatally? This gets at the heart of the clinical and ethical controversy over what conditions and traits should be identified by prenatal genetic diagnostic testing. The implications of NIPD must be considered at both the individual and the population level. This article: 1) explores how the public, midwives, and other maternity care providers perceive NIPD, 2) analyzes the implications of NIPD, and 3) puts forward recommendations to help midwives guide their clients.

The coming integration of NIPD into standard prenatal care has spurred many researchers to investigate public perception and potential demand for prenatal genetic testing. There are discrepancies between the results of survey studies and the actual current use of prenatal testing. One study found that 80% of the surveyed population wanted prenatal

testing for conditions involving “mental retardation,” yet 100% of the women surveyed were at a genetic counselling clinic for Down syndrome, a condition defined by “mental retardation.”⁶ Similar discrepancies were reported between the current relatively high uptake of prenatal genetic testing for conditions such as cystic fibrosis (and other conditions causing a decreased life expectancy) and survey results for conditions resulting in death by the ages of five years and 20 years. Of individuals who presented at a genetic clinic for counselling for cystic fibrosis and other early lethal conditions, only 49% indicated that they would like prenatal testing for conditions resulting in death by the age of five years, and 41% said they would like testing for conditions resulting in death by the age of 20 years.⁶ These discrepancies could result from a lack of knowledge about genetic conditions and testing, uncertainties regarding what is “best,” and a lack of public agreement as to what conditions are best suited for genetic testing.⁶ This may stem from varied individual perceptions about adult-onset conditions versus child-onset conditions.⁶

Similar discrepancies are seen with termination rates. According to survey research, about 75% of women would choose to terminate a pregnancy in the event of a developmental disorder such as Down syndrome.^{6,7} The number of actual terminations based on positive test results is significantly higher (92%).⁸ A meta-analysis shows that termination rates have remained stable throughout the 18-year period investigated.⁸ This suggests that increased testing has not resulted in higher termination rates, negating fears that increased testing would lead to a lower tolerance of disability.⁸ The discrepancy between the survey results and the actual termination rates could be due to the contentious nature of the topic: women may overstate their acceptance of disability in order to be “politically correct,” but when faced with a personal choice, their opinions change, which implies a deep intolerance towards raising a child with a disability.

Hathaway and colleagues state, “the medical community will need to decide whether the degree of disability should be taken into account when making prenatal decisions and that guidelines should be established to aid practitioners in caring for their patients.”⁶ Although it may appear logical for the medical

community to determine the necessity of various tests, “the severity of different diseases is perceived differently among both health care professionals and pregnant women.”¹ Further, midwives and other maternity care providers do not agree as to what constitutes a “serious” trait. As Wertz found in a 1998 survey of genetic counsellors, “Cleft lip and palate, hereditary deafness, insulin-dependent diabetes, Huntington disease, cystic fibrosis, sickle cell anemia, Down syndrome, and manic depression were deemed serious by some professionals and not serious by others.”⁹ This variability is not surprising; several researchers have commented on medical students’ lack of clinical training in interaction with people who have disabilities.¹⁰ Eighty-one percent of surveyed medical students reported no clinical training regarding intellectual disabilities, and 58% of school deans stated that it is not a high priority.¹¹ Given this lack of training, the medical community is poorly prepared to discuss the necessity and feasibility of various prenatal tests based on severity of condition. Furthermore, medical consensus on the topic will be as difficult to achieve as will public consensus.

NIPD has several implications at the population level. Termination rates were stable throughout the 1980s and 1990s;⁸ however, the methods of NIPD were not discovered until 1997.³ Eliminating the risk of miscarriage associated with NIPD will likely lead to an increase in prenatal genetic testing.¹² In fact, one study found that owing to the decrease in risk, some women would feel increased pressure to have prenatal testing.¹³ Increased testing will result in more pregnancies diagnosed with abnormalities, which will potentially increase the number of terminations.^{10,14} Terminations may also increase because NIPD will provide a diagnosis during the first trimester, before women begin showing physical signs of pregnancy; women can choose to terminate before family and friends know of the pregnancy, thus keeping their choice private.¹¹ Some researchers feel that NIPD’s removal of the “gatekeeper” effect (the risk of miscarriage with amniocentesis and chorionic villus sampling) may allow prenatal genetic testing to go too far and could “contribute to testing for minor abnormalities or non-health related conditions and to a corresponding ‘trivialization’ of abortion.”¹ Ethicist C. B. Mitchel (1997) suggests that a shadow of suspicion would be cast over every unborn baby

and that every pregnancy is “tentative,” awaiting the results of prenatal testing.¹⁰ Although this may be true for many women, NIPD is able to resolve this sooner than current prenatal screening tools because it can be performed earlier in the pregnancy.

Skotko argues that by supporting prenatal screening for Down syndrome, the American College of Obstetricians and Gynecologists has “endorsed a climate in which disability discrimination could more easily flourish.”¹¹ The implementation of NIPD and the corresponding expected decrease in the number of affected infants born could further promote such a climate and possibly result in less social support for people with disabilities. The Ontario government currently provides a number of supports for families of children with disabilities. These supports include a financial component: the Child Disability Benefit, which pays a maximum of just over \$200 per month for each of up to three disabled children.¹⁵ In addition, caregivers can apply for help with costs, including the costs of travel to doctors’ offices and hospitals, assistive devices, medications, and parental relief.¹⁶ Other publicly funded support includes respite care, specialized community supports, and residential services.¹⁶ Although an analysis of just how beneficial this amount of support is to any individual family is beyond the scope of this article, it is obvious that if one parent chooses to stay home with a disabled child, the loss of income is not offset by the Child Disability Benefit of \$2,500 per year. Decreased governmental support could have a spiraling effect: increased difficulty for families supporting disabled children, potentially making having a disabled child less desirable, thus increasing the rate of testing and termination, which further feeds the climate of discrimination against those with disabilities. This also has implications for those who choose not to be tested or for those who are tested but choose not to terminate. As NIPD is so simple and low in risk, will families who have a child with a disability be told they have put a “burden on society” for something that could have been “easily prevented”?

NIPD is debated within the disability community because it is widely accepted as a precursor to selective abortion for disability traits. The disability critique finds this morally problematic on two fronts: “First,

it expresses negative or discriminatory attitudes not merely about a disabling trait, but about those who carry it. Second, it signals an intolerance of diversity not merely in the society but in the family, and ultimately it could harm parental attitudes toward all children.”⁹

These attitudes are seen in research showing that women can suffer from pregnancy anxiety (as distinct from general anxiety) due in part to “fear of bearing a physically or mentally handicapped child.”¹⁷ Also, women who are committed to genetic screening tend to delay forming an emotional attachment with the fetus until after test results are known.¹⁸ This implies that if the test results were abnormal, women would choose to terminate. The single “abnormal” trait represents and obliterates the whole individual; there is no need to find out about the rest.⁹ Fears of negative attitudes towards disability and diversity, both those who carry it within themselves and their families, are supported by research.

DISCUSSION

The trend towards NIPD⁴ is supported by public intention to increase testing due to: 1) its removal of the risk of miscarriage resulting from amniocentesis, 2) earlier diagnosis, and 3) a desire for more options in prenatal testing.⁶ Many researchers have written of the importance of providing potential NIPD users with information to help them make informed choices.^{9,12,19} There are concerns that the ability to perform NIPD so easily with few risks may render the procedure routine, a phenomenon already seen with current screening methods.^{6,20} Practitioners view the consent process for NIPD differently from that needed for invasive prenatal diagnosis.¹⁹ This is problematic because although the risks are different, the implications for outcomes are the same.

Although there is no real consensus on what constitutes an informed choice,²¹ at minimum it should include the acquisition of knowledge and the freedom to choose what to do with that knowledge.²⁰ Thus, midwives should impart information about the NIPD testing process, including information about the details of the procedure, the reliability of the results, the benefits, risks, and alternatives, community standards, research evidence, recommendations, and the implications of the client’s potential choices.²²

Parens and Asch argued that more information is also necessary; women need information about what life is like for families with children who have disabilities, and providers must have access to good information on this topic and must impart it as a routine aspect of discussions about NIPD.⁹ Midwives must listen to their clients, understand their cultural framework and subjective moral sense, then frame the information so that clients can interpret it within their own moral understanding and patterns of ethical reasoning.²³ By doing this, midwives will help women make autonomous decisions about prenatal genetic tests.²³ Midwives have an advantage in this instance because the practice of spending time with clients, getting to know them, and learning their individual perspectives is widespread.

NIPD has clinical implications for the scope of practice of all midwives. Currently, midwives and family doctors order the prenatal screening; a woman with a positive screen result is referred to genetic counsellors, who offer her information and further testing. NIPD negates the need for further testing. With NIPD, would it then become the responsibility of the ordering midwife to discuss the implications of a positive result and make any further arrangements, or would women still be referred to genetic counsellors for information and follow-up? These logistical questions need to be answered in the scope of practice of all involved and incorporated into midwifery education.

As NIPD is slated to become the standard of care, it behooves all medical education programs and professional associations to educate current and future midwives and other maternity care providers about the testing process, its implications, approaches to informed-choice discussions, and what NIPD means for families that live with disabilities. All midwives need to fully grasp all the implications of this test so that it does not get brushed aside as “routine” prenatal care. In doing so, midwives can enhance their clients’ understanding of NIPD and help them make the best decisions for themselves and their families.

SUMMARY

NIPD is the immediate future for prenatal genetic testing. Any new technology is often assumed to be an improvement, and as such, medical science is rushing

towards the general implementation and acceptance of NIPD. Although its benefits over current methods are indisputable, many contentious questions must still be considered and answered. Given our potential ability to sequence the entire fetal genome and acquire untold information about the unborn fetus, who decides what we should know? Information has consequences not just at the individual level but at the population level as well. More research is needed to fully interpret the needs and the wants of women, their families, and their care providers. Most important, midwives and other maternity care providers must have a full understanding and respect for the scope and implications of NIPD as it pertains to their individual clients. Only when this is fully understood can midwives help women make informed choices for themselves and their families.

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