Ethical aspects arising from non-invasive fetal diagnosis

Ainsley J. Newson, 2008

Summary

Non-invasive prenatal diagnosis (NIPD) could significantly change the framework for testing and screening in pregnancy. This chapter reviews the ethical implications of this technology, including current issues in prenatal diagnosis, implications for informed consent, possible non-medical uses and options for regulation. The prospect of NIPD normalising screening and termination in pregnancy is raised as a concern. NIPD will also require monitoring to ensure women are making well-informed decisions, given that a risk to the pregnancy is absent. The question of whether NIPD will reduce anxiety needs to be established and the prospect that it will increase terminations on the grounds of disability should be recognised. The offer of NIPD external to any clinical oversight might give rise to wider social sex selection, paternity testing or testing 'for information'. The value assumptions of these uses of NIPD need to be addressed.

Keywords: Ethical issues; Genetic counselling; Informed consent; Mass screening; Prenatal diagnosis; Sex selection

Introduction

Testing or screening for fetal abnormality has fundamentally changed women's experiences of pregnancy. The advent of ultrasound, amniocentesis, chorionic villus sampling (CVS) and maternal serum screening (MSS) have enabled health professionals to offer women several sources of potentially significant information about the health of their fetus. Yet although these technologies do allow women to make informed choices in pregnancy, each is subject to limitations. Ultrasound can only detect physical abnormality, amniocentesis and CVS carry a small risk of pregnancy loss and MSS provides only a probability of harm, which can be difficult to interpret.

In the past decade, the isolation and analysis of free fetal DNA (ffDNA) or whole fetal cells in maternal blood has emerged as another method for testing during pregnancy. These technologies, explained in more detail elsewhere in this special issue, aim to offer non-invasive prenatal diagnosis (NIPD) to provide definitive molecular or chromosomal information about the health of a fetus without posing a risk to the pregnancy.1 NIPD is now beginning to change the landscape of prenatal testing: tests on ffDNA are already proven for fetal gender, rhesus D blood type and some Mendelian conditions such as achondroplasia. More tests are under development, including aneuploidy detection and Down syndrome.2 For the purposes of this chapter, NIPD is assumed to be clinically valid, with a predictive value commensurate to invasive methods.

The impact of NIPD on fetal medicine and pregnant women is predicted to be significant and ethical issues will arise.3 In contemplating the implementation of this technology, we can ask whether aspects of NIPD give rise to new ethical questions, or whether we are instead required to revisit existing dilemmas in prenatal diagnosis. NIPD is not the only non-invasive procedure available to women during pregnancy; ultrasound and MSS are also non-invasive. But unlike these existing methods, NIPD can offer definitive information about the health of a fetus at an early stage of pregnancy without putting the pregnancy at risk. Arguably, this gives rise to new nuances in ethical debates over prenatal diagnosis, perhaps most importantly the implications for informed consent. Yet existing issues in prenatal diagnosis will continue to be relevant, and for this reason these debates are briefly rehearsed in the following section.

Ethical issues in prenatal diagnosis

As a source of information about the health of a fetus during pregnancy, NIPD raises ethical issues familiar to anyone with experience of prenatal diagnosis (PND). Several existing issues in PND remain unresolved and, as the molecular bases of more and more conditions affecting health are identified, the dilemma of what constitutes a permissible test remains acute. The development and implementation of NIPD will raise new ethical concerns but these should also be assessed against existing debates over PND.4

With any offer of PND to a pregnant woman, there is an implicit value assumption that some inherited or congenital conditions give rise to a lower quality of life for those who have them. At the level of screening, there is an accepted yet unarticulated expectation that the availability of a screening programme will reduce the incidence of the condition of interest in the population, although programmes do emphasise that women should be assisted to make an informed choice. These factors are naturally sensitive and have given rise to myriad debates in the clinical and ethical literature. These debates tend to focus on two interrelated problems: whether PND is eugenic and whether it discriminates against people living with the condition (the ‘disability rights critique’).

Although an in-depth analysis of these debates is beyond the scope of this chapter, they should not go unnoticed. One concern with PND is whether it exemplifies eugenics—the improvement of the gene pool for the next generation through eradicating genetic disease. Although modern practice in fetal medicine and clinical genetics is nothing like the state-imposed ideals of population perfection that occurred in the early twentieth century, considerations of social justice cannot be ignored.5 Likewise, women require access to high-quality and unbiased information on the condition they are being tested for and they must be free to make informed choices about PND, including refusing testing.

A related concern with PND is that it devalues the lives of, or otherwise discriminates against, people living with the condition being tested for. Activists in this debate query the impact of a test on our attitudes to the condition (for example, Down syndrome) and claim that the availability of tests systematically stigmatises these groups, even if no overtly discriminatory statements are made. One response to the disability critique is that women choosing to terminate an affected pregnancy are not discriminating against or stigmatising existing people with the same condition, but that having been given a choice they are deciding they would rather have a child without the condition. They are also choosing to select against a condition and not against a person.6 But as Asch recognises, choosing against a trait is difficult without also choosing against a fetus.7

NIPD does give rise to a small but insidious risk that screening in pregnancy and termination of affected fetuses could become normalised. Press coverage of NIPD to date has, however, concentrated on the prevention of miscarriage.8 There is little mention that, if offered widely, NIPD could increase the detection of abnormalities in pregnancy, potentially leading to increased terminations. Women should have access to sound and unbiased information and appropriate time

to reflect before making a decision about NIPD. We should also ensure it does not lead to a perpetuation of negative conceptions of illness and disease.

Other ethical considerations arising in PND will, by implication, need to be assessed in the context of NIPD:

- In comparison with previous generations, women now experience a so-called medicalised or 'tentative pregnancy', in which they might be unable to bond with their fetus until it is known that 'all is well'. In some cases this can be quite late in the pregnancy.9, 10 and 11
- Is there a right 'not to know' or a right to remain in ignorance about the health of a fetus during pregnancy?12
- Should only 'serious' conditions be subject to PND? Or, should it be up to women and couples to autonomously decide what is 'serious' for them (and which might be 'minor' to others), based on their 'lived experience' of the condition?13*, 14, 15* and 16
- As a matter of professional ethics, deciding what to do when a woman or couple makes a seemingly unjustifiable request for PND.17 and 18
- Whether and how unexpected information should be passed on to women, particularly in a context of 'targeted testing', where women are informed about only a few conditions before PND takes place.19

Advantages of NIPD

Despite the ethical issues arising in the provision of PND, NIPD might offer some practical (and therefore ethical) advantages. Primarily, NIPD could reduce the number of miscarriages caused by PND, as amniocentesis and CVS carry a small risk of pregnancy loss. A 'normal' result from NIPD—a test that poses no risk to the pregnancy—could mean that fewer women undergo further invasive testing. However, not all women might be reassured by a normal NIPD result. One North American study examining attitudes to NIPD of fetal cells suggests that nearly half of the women receiving a 'normal' result would still opt for invasive diagnosis, just to be sure.20 In a resource-constrained environment like the National Health Service this is a point to consider—is there value in offering NIPD when it might not prevent women from seeking PND? However, with careful pretest information, this consequence is not a certainty.

Another benefit of NIPD is that as the test can be performed and results reported earlier in pregnancy than for CVS or amniocentesis, anxiety might be reduced. Women will be able to make decisions earlier and will therefore have better opportunities for prenatal bonding. They are also sure to appreciate the reduced pain and discomfort offered by NIPD. However women must also be informed that the earlier NIPD is performed in pregnancy, the less accurate it might be. Another potential concern is that those women receiving 'abnormal' results will then have to decide whether to proceed to invasive diagnosis before making a decision about termination, which might necessitate waiting until the appropriate week of gestation. This intervening period could raise anxiety levels, counteracting any benefit of NIPD.

Informed consent and informed choice to NIPD

A decision about testing or screening in pregnancy carries significant weight and can have far-reaching implications for women. To this end, any decision about NIPD should be made in accordance with a suitable model of informed choice or informed consent.

The operation of informed consent and informed choice are subtly different. Informed consent tends to be applied in situations where a woman is facing a designated diagnostic test. Three

elements need to be satisfied: the provision of appropriate information, the recipient's capacity to make a decision and an absence of undue force (including adequate time to decide). Informed choice, on the other hand, tends to be used in screening programmes where a test might be for susceptibility rather than diagnosis. Informed choice requires that a decision be based on relevant knowledge, consistency with the values of the decision-maker and behavioural implementation.21 The process of making a decision might be less active than with informed consent and might not require sustained discussions with a health professional.22

Before women are offered NIPD on a wider scale, we should ask what model(s) of pretest decision making are appropriate. Should women be offered testing and be provided with information some time before having the test? Or, should it instead form a routine part of antenatal care, requiring less information, formality of consent and time for reflection? This will likely depend on whether NIPD is being used to ascertain a woman's risk in light of a positive family history, or whether it forms part of a risk assessment offered to all pregnant women. Whilst in its early implementation a woman is unlikely to base a termination decision on NIPD alone, results could establish women on a path towards a decision about termination; something they may not have contemplated when electing to have NIPD. Additionally, women can experience a burden from choice and this should be taken into account.23

NIPD circumvents the initial risk-based result obtained with MSS and removes the risk to pregnancy as a reason for declining testing. These parameters can act as powerful regulators of the uptake of definitive testing in pregnancy; having time to reflect and refine one's attitudes towards disability or impairment can be valuable before receiving definitive information. We need to plan for how their possible removal might affect women's experience of prenatal testing and screening; if a barrier to testing is removed, will women feel less justified in declining or be more open to persuasion? The similarity of these tests with other blood draws during pregnancy might mask the implications. Professionals providing NIPD should ensure that, before definitive testing, all the facts are presented with adequate time for reflection, including the voluntary nature of testing and where to obtain further support if required.

Current debates on prenatal diagnosis and screening should also be taken into account. Researchers have questioned whether women are providing informed consent or making informed choices, or whether they are having testing in reaction to external pressures. Information provided to women varies across Europe24 and the routinisation of antenatal screening has also led some to ask whether women are making considered decisions.25 A recent French study, for example, concluded that the majority of women do not currently provide fully informed consent for maternal serum screening.26 However, two Dutch studies examining prenatal screening offer a more optimistic assessment of whether informed choice is being achieved.27 and 28 Yet one of these also found that those who accepted testing made less informed decisions than those who declined27 and the other contended that insufficient knowledge remains a problem.28

A North American study has also examined informed consent to NIPD and found a similar pattern.20 Researchers asked whether women would feel pressured to have a non-invasive diagnostic maternal blood test, and found that a substantial minority (28.5%) would perceive no choice but to have the test. Another minor but substantial proportion would have the test on a doctor's recommendation (28.8%). As a new technology, NIPD will be accompanied by sound pre-test counselling, including descriptions of any limitations to the technology. But as it becomes more integrated into clinical practice, the choices being offered to women and the models of informed consent or informed choice being used should be re-evaluated. Psychosocial studies should be carried out during the early stages of NIPD to help inform an appropriate model for pre-test information and counselling.

NIPD and fetal sexing

The first application of NIPD was to determine fetal sex, as the detection of Y-chromosome DNA in a pregnant woman offers a robust prediction of a male fetus. This might be more predictive than ultrasound and easier to provide than other invasive molecular methods of determining sex that necessitate access to clinical services. Indeed, commercial providers of NIPD for fetal sex are already operating.29, 30 and 31* The ethical implications of prenatal sex determination are well-addressed in the literature but, given their importance to NIPD, they are addressed briefly here.

Medically indicated fetal sexing

Not all prenatal sex determination is ethically contentious. When a diagnostic test for an X-linked condition is not available, fetal sexing can be used even though it might mean that a healthy male pregnancy is terminated. More frequently, it is used as a first-line investigation before a more involved (and therefore expensive) molecular test. NIPD might serve as a substitute for PND in both of these situations. It will also help avoid invasive testing for some X-linked conditions as no invasive PND will be required if NIPD indicates a female fetus.32

NIPD does give rise to two new ethical concerns over medically indicated fetal sexing. A recent audit of NIPD indicates that 23% of 160 women obtaining NIPD have done so for haemophilia (L Chitty, personal communication). This condition is usually treatable and is not a common indication for requesting invasive diagnostic prenatal diagnosis, at least in the UK. Knowing whether a fetus is at risk will change arrangements for delivery, but sex can be determined at the 20-week scan for no extra cost. It therefore appears that some women might be accessing NIPD to establish fetal sex earlier in the pregnancy. Although there is no suggestion that women are seeking terminations based on fetal sex in these circumstances (which would constitute sex selection via the ‘back door’), providing a test that could be achieved via other means has resource implications.

Women could also use NIPD to sidestep the need for preimplantation genetic diagnosis (PGD) for X-linked conditions. Given the expense and low success rate associated with PGD, women could become pregnant naturally, use NIPD to establish fetal sex and then procure a termination for male fetuses early in pregnancy using the safe medical methods now available. This could lead to the establishment of a pregnancy that is not at risk more quickly than undergoing PGD. This raises implications for policy makers. In response to these developments, the criteria for reporting fetal sex should be carefully monitored.

Fetal sexing for non-medical reasons

Whereas finding out a baby's gender might be a benign diversion for a couple impatient to bond with their baby, it also raises concerns over the potential for terminating a pregnancy deemed to be of the ‘wrong’ sex for personal, cultural or economic reasons. The clinical consensus regarding sex selection in established pregnancies is that this should not be permitted. Support exists for restricting information about sex given to women within legal abortion limits, unless the information is medically relevant.33 The predominant arguments against non-medical sex selection are that it:

- will cause harm to the child born as a result of stereotyped expectations
- demonstrates sex discrimination
- is not part of a parent's prerogative34
- makes professionals morally complicit in an unethical activity
- could upset sex ratios
- will lead us down a ‘slippery slope’ to ‘designer children’35

Those adopting a permissive stance towards sex selection instead highlight the importance of procreative liberty or autonomy, in which parents should be able to make considered choices consistent with their values.35 Also raised are claims about the dearth of empirical literature proving harm, the unlikely skewing of sex ratios in most cultures and the acceptability of 'family balancing'.36

The non-invasive nature of NIPD could add to these debates. It has become possible to detect fetal sex without leaving one's home; using mail-order test kits to exploit finger-prick blood samples. In one instance, wide use of such a kit has led to a class action following inaccurate results.37 At present, NIPD explicitly for the purpose of gender selection is unlikely to be offered by any professional in fetal medicine, and women are not indicating they would desire it.20 And any termination of pregnancy that might result following from this test will have to be lawful within the relevant jurisdiction. However, technically there is no barrier to a couple determining sex and then seeking a 'social termination' from a separate provider.

The issue of non-medical sex selection is of concern to those working in NIPD, and some have called for international guidelines to regulate its application.38 Moreover, if a woman is suffering oppression or pressure from her family or wider culture to have a child of a chosen sex, the prospect of her being subjected to this test against her will is a possibility. In response to this, the burden of proof for consent to testing should be made the responsibility of the test provider and educational materials should take this into account. Should NIPD for gender testing become widespread, women seeking social terminations could also be asked to sign a declaration about NIPD for gender.

Other non-medical uses of NIPD

Fetal sex might not be the only non-medical application for which NIPD is sought. Women or couples might also be interested in using the technology 'for information only', or to undertake a prenatal paternity test.

Use of NIPD for 'information'

The fact that NIPD removes the risk of pregnancy loss could have another interesting outcome. Presently, couples tend not to proceed with an invasive test in pregnancy if they have no intention to terminate in light of a gene-positive result. However, if NIPD were to become widely available then couples could obtain information on a range of conditions (medically significant or otherwise), which they might be interested to know about but would not want to risk the pregnancy to find out. Indeed, NIPD has already been used for achondroplasia.39

In questioning the acceptability of such testing, several factors should be considered, including: Does the test represent a good use of scarce resources? Will the management of the pregnancy change as a result of the test? What expectations might the couple have for the pregnancy and the child who will be born? Would a similar test be offered if the child was already born?40 and 41 One group of clinicians has already suggested that the precedent of whether PND is available for a chosen condition should be used to indicate the acceptability of NIPD.3

Prenatal paternity testing

A potentially more worrying application of NIPD is in prenatal paternity testing. Although this is not yet in the literature, experts in NIPD have already raised the issue.3 Prenatal paternity testing is currently rare, as placing a pregnancy at risk merely to determine who the genetic father will be is problematic. However, once the risk of pregnancy loss is removed, would NIPD to determine paternity be acceptable?

On the one hand, we can imagine a pregnant woman who is conscious that her child's genetic parentage might be uncertain. If she is able to determine this definitively early in pregnancy she can inform the biological progenitor (and potentially the other interested party). This will remove any prospect of a man harbouring incorrect assumptions about pending biological parenthood.

However, we can also imagine a pregnant women intent on testing to determine whether she will continue the pregnancy. This is more difficult to justify (perhaps with some exceptions, such as pregnancy as a result of rape) as it would seem that the woman is prepared only to carry a pregnancy to term based on a particular biological father.

Detailed consideration of these issues is beyond the scope of this chapter but should be borne in mind by policy makers, as should the possibility that inadvertent paternity testing could occur when performing some non-invasive tests, such as early fetal rhesus typing. Additionally, as with any paternity test, a woman commissioning NIPD for paternity should be counselled about the legal and financial implications of testing, the potential for psychological harm and the significance of biological over social kinship.

Regulatory issues in the provision of NIPD

The simplicity of obtaining samples for NIPD gives rise to the prospect that this technology will be made available on a commercial basis, perhaps circumventing clinical professionals altogether. This property of NIPD means that policy and regulatory issues regarding the availability of this testing need to be addressed soon. Annas recognised this potential problem over a decade ago.42 He proposed three alternative models for control of NIPD: the medical, market and regulatory models.

Under the medical model, health professionals would act as gatekeepers to NIPD. This would respect the current status quo, whereby there is professional discretion to determine whether a test is indicated. Professional colleges and associations can also develop policy to provide overarching guidance.

The market model reflects some of the developments in modern genetics, particularly in North America. That is, commercial entities are permitted to offer NIPD in response to consumer demand, based on personal values. Services can be provided in person, by mail-order or online. Those providing NIPD on a commercial basis should be largely left alone to get on with business, albeit one in which they are not permitted to miss-sell their product or otherwise mislead consumers. Women might be convinced they ‘need’ NIPD through targeted advertising. This model is already visible in over-the-counter genetic testing and will be difficult to control in a global marketplace.43

A strict regulatory model is, if broadly applied, likely to lead to claims of government intrusion in private decision-making. In countries like the UK, great value is placed on individual freedom and society is generally suspicious of attempts of overarching regulation. That said, the Human Fertilization and Embryology Authority has successfully regulated assisted reproduction for over 15 years and, despite some criticism, is generally considered a responsible body for overseeing this complex area. Although regulations demanding mandatory screening are unlikely, a ‘lighter-touch’ regime from governments making general recommendations about NIPD is likely to be welcomed by most.

Conclusion

Non-invasive prenatal diagnosis is a promising technology. It will simplify many aspects of testing and screening in pregnancy, but will also introduce some new complexities. NIPD also forces us to revisit existing debates in prenatal diagnosis, to determine how they might change and what safeguards might be required.

At the very least, some of the questions that should be applied to NIPD are: Why is this test being considered at this stage in pregnancy? What benefits and concerns might it give rise to and what does existing practice tell us? These will serve as useful guides to the acceptability of NIPD, whether for prenatal diagnosis, antenatal screening, sex identification, paternity testing or 'information'. The psychosocial issues raised by this technology should also be investigated before it is widely introduced.20

Practice points

- Non-invasive prenatal diagnosis will allow women to obtain information about the health of their fetus without the risk of pregnancy loss.
- It is important to bear in mind existing issues in prenatal diagnosis and to recognise that NIPD will not circumvent these.
- Careful attention should be paid to mechanisms of informed consent and informed choice for NIPD.
- Policy makers and clinicians should be ready to respond to possible non-medical uses of NIPD, such as social sex selection and paternity testing.

Acknowledgements

The author acknowledges Dr Lyn Chitty, Professor Angus Clarke, Dr Elizabeth Dormandy, Professor Theresa Marteau and Ms Ananda van den Heuvel for helpful and thought-provoking discussions. This chapter will inform a larger analysis to be undertaken by the author in 2008, funded by the SAFE Network (http://www.safenoe.org).

Conflict of interest

The sponsors of this study had no involvement in the writing of this chapter. The author declares no conflict of interest.

References

1. Maron JL, Bianchi DW. Prenatal diagnosis using cell-free nucleic acids in maternal body fluids: a decade of progress. Am J Med Genet C Semin Med Genet2007;145:5e17.
2. Lo YM, Tsui NB, Chiu RW, et al. Plasma placental RNA allelic ratio permits noninvasive prenatal chromosomal aneuploidy detection. Nat Med2007;13:218e23.
3. Smith RP, Lombaard H, Soothill PW. The obstetrician's view: ethical and societal implications of non-invasive prenatal diagnosis. Prenat Diagn2006;26:631e34.
4. Wertz DC, Fletcher JC. Ethical issues in prenatal diagnosis. Pediatr Ann1989;18:739e49.
5. Wikler D. Can we learn from eugenics? J Med Ethics1999;25: 183e94.
6. Mahowald MB. Prenatal testing for selection against disabilities. Camb Q Healthc Ethics2007;16:457e62.
7. Asch A. Prenatal diagnosis and selective abortion: a challenge to practice and policy. Am J Public Health1999;89:1649e57.

8. Highfield R. Scientists close to safer testing of unborn babies. The Daily Telegraph; 4 October 2005;14.
9. Katz Rothman B.The tentative pregnancy: how amniocentesis changes the experience of motherhood. New York: WW Norton; 1993.
10. Tymstra T. Prenatal diagnosis, prenatal screening, and the rise of the tentative pregnancy. Int J Technol Assess Health Care 1991;7:509e16.
11. Lippman A. Prenatal genetic testing and screening: constructing needs and reinforcing inequities. Am J Law Med1991;17:15e50.
12. Bennett R. Antenatal genetic testing and the right to remain in ignorance. Theor Med Bioeth2001;22:461e71.
13. Wertz DC, Knoppers BM. Serous genetic disorders: can or should they be defined? Am J Med Genet2002;108:29e35.
14. Boyle RJ, Savulescu J. Prenatal diagnosis for 'minor' genetic abnormalities is ethical.Am J Bioeth2003;3(1):W-IF 3.
15. Strong C. Tomorrow's prenatal genetic testing. Should we test for 'minor' diseases? Arch Fam Med1993;2:1187e93.
16. Atkins K. Autonomy and the subjective character of experience.J Appl Philos2000;17:71e9. 17. Wertz DC, Fletcher JC, Nippert I, Wolff G, Ayme S. Has patient autonomy gone too far? Geneticists' views in 36 nations.Am J Bioeth2002;2(4):W21.
17. Duncan RE, Foddy B, Delatycki MB. Refusing to provide a prenatal test: can it ever be ethical?BMJ2006;333:1066e8.
18. Van Zwieten MC, Willems DL, Litjens LL, Schuring-Blom HG, Leschot N. How unexpected are unexpected findings in prenatal cytogenetic diagnosis? A literature review. Eur J Obstet Gynecol Reprod Biol2005;120:15e21.
19. Zamerowski ST, Lumley MA, Arreola RA, Dukes K, Sullivan L. Favorable attitudes toward testing for chromosomal abnormalities via analysis of fetal cells in maternal blood. Genet Med2001;3:301e9.
20. Marteau TM, Dormandy E, Michie S. A measure of informed choice. Health Expect2001;4:99e108.
21. Jepson RG, Hewison J, Thompson AG, Weller D. How should we measure informed choice? The case of cancer screening. J Med Ethics2005;31:192e6.
22. van Berkel D, van der Weele C. Norms and prenorms on prenatal diagnosis: new ways to deal with morality in counselling. Patient Educ Couns1999;37:153e63.
23. Hall S, Chitty L, Dormandy E, et al. Undergoing prenatal screening for Down's syndrome: presentation of choice and information in Europe and Asia. Eur J Hum Genet2007;15:563e9.
24. Clarke A. Genetic counselling. In: Ashcroft RE, Dawson A, Draper H, McMillan JR, editors. Principles of health care ethics. 2nd ed. Chichester: John Wiley & Sons Ltd; 1997. p. 427e34.
25. Favre R, Duchange N, VayssiereC, et al. How important is consent in maternal serum screening for Down syndrome in France? Information and consent evaluation in maternal serum screening for Down syndrome: a French study. Prenat Diagn 2007;27:197e205.
26. van den Berg M, Timmermans DR, ten Kate LP, van Vugt JM, van der Wal G. Informed decision making in the context of prenatal screening. Patient Educ Couns2006;63:110e7.

27. van den Berg M, Timmermans DR, Ten Kate LP, van Vugt JM, van der Wal G. Are pregnant women making informed choices about prenatal screening? Genet Med2005;7:332e8.
28. 29.http://www.babygendermentor.com/default.php [accessed 30 October 2007].
29. Bianchi DW. At-home fetal DNA gender testing: Caveat emptor. Obstet Gynecol2006;107:216e8.
30. Marteau TM, Chitty L, editors. Special issued Fetal sexing: global perspectives on practices, Ethics and Policy. Prenat Diagn2006;26. p. 597e653.
31. Hyett JA, Gardiner G, Stojilkovic-Mikic T, et al. Reduction in diagnostic and therapeutic interventions by non-invasive determination of fetal sex in early pregnancy. Prenat Diagn 2005;25:1111e6.
32. Human Fertilization and Embryology Authority. Sex selection: options for regulation. Available from:http://www.hfea.gov.uk/docs/Final_sex_selection_main_report.pdf ; 2003 (para 27) [accessed 30 October 2007].
33. McDougall R. Acting parentally: an argument against sex selection.J Med Ethics2005;31:601e5.
34. Human Fertilization and Embryology Authority.Sex selection: choice and responsibility in human reproduction; 2002. Available from: http://www.hfea.gov.uk/docs/Sex_Selection_choice_and_responsibility.pdf . Part Five [accessed 30 October 2007].
35. Steinbock B. Sex selection: not obviously wrong. Hast Cen Rep 2002;32:23e8.
36. Goldenberg S. Mothers sue over gender test that promised 99.9% accuracy. The Guardian; 18 March 2006;17.
37. Guetta E. Noninvasive detection of fetal sex: the laboratory diagnostician's view. Prenat Diagn2006;26:635e6.
38. Li Y, Page-Christiaens G CML, Gille JJP, Holzgreve W, Hahn S. Non-invasive prenatal detection of achondroplasia in size fractionated cell-free DNA by MALDI-TOF MS assay. Prenat Diagn2007;27:11e7.
39. Clarke A. The genetic testing of children. Working Party of the Clinical Genetics Society (UK). J Med Genet 1994;31: 785e97.
40. Duncan RE. Predictive testing in young people: when is it appropriate? J Paediatr Child Health2004;40:593e8.
41. Annas GJ. Ethical aspects of non-invasive prenatal diagnosis: medical, market, or regulatory model?Early Hum Dev1996; 47(Suppl):S5e11.
42. Human Genetics Commission.Genes direct: ensuring the effective oversight of genetic tests supplied directly to the public; 2003. Available from: http://www.hgc.gov.uk/UploadDocs/DocPub/ Document/genesdirect_full.pdf [accessed 30 October 2007]