TAB OFFICE OF TECHNOLOGY ASSESSMENT AT THE GERMAN BUNDESTAG

Status quo and developments of prenatal diagnosis

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Summary

- In Germany, prenatal diagnostic procedures have been part of medical pregnancy care for 40 years. Since then, the number of available methods has increased significantly.
- By summer 2019, the German Federal Joint Committee (G-BA) will examine whether non-invasive prenatal tests (NIPTs) will become a benefit provided and reimbursed by the statutory health insurance scheme (GKV). NIPTs can detect certain genetic variations (e. g. trisomy 13, 18 or 21) of the foetus in the maternal blood.
- The availability of low-risk NIPTs might lead to genetic examinations of the foetus becoming the norm. Thus, fundamental questions about prenatal diagnosis are raised with a new urgency, e. g. how discrimination against people with disabilities can be avoided without calling into question the right to a self-determined desire to have children.
- The debate that seems to be necessary for society as a whole could be initiated and characterised by parliamentary activities.

What is involved

Prenatal diagnosis (PND) includes all prenatal examinations aimed at obtaining information about the unborn child. There is a number of examination methods, which are mostly divided into so-called invasive and non-invasive procedures (Fig. 2). Invasive procedures are associated with a puncture of the amnion or placenta and therefore involve higher procedural risks (e. g. of miscarriage) than non-invasive procedures. Non-invasive procedures such as ultrasound examinations, however, do not involve uterine interventions, but are not considered to be diagnostic. Consequently, they can only provide information on diagnoses that must be verified subsequently using other procedures.

Prenatal examinations make it possible to medically accompany pregnancy and childbirth – especially in case of abnormalities – in such a way that damage to the expectant mother and child can be averted (e. g. by means of medication, surgeries on the foetus in the mother's womb and immediate post-natal therapy). However, there are no causal therapies for many of the disabilities that are focused on in prenatal diagnosis (such as trisomies 13, 18 and 21; see Fig. 1). If such a disability is discovered prenatally, the expectant parents are often confronted with the question of whether to continue or terminate the pregnancy. In Germany, an abortion is possible during the entire pregnancy if there is a so-called medical indication. To do this, a doctor must attest the pregnant woman that abortion is the only way not to endanger her physical or mental health.

There are no uniformly collected national data with regard to the use and consequences of prenatal diagnostics. In various studies, it is unanimously pointed out that for most congenital disabilities, the abortion rate following a prenatal diagnosis is higher than 50 % (and higher than 85 % for trisomies 13, 18 and 21). The novel NIPTs allow a medically largely risk-free, very early prognosis regarding the presence of a foetal disability. Critics fear that, thus, the selection of unborn children with disabilities will continue to expand.

Non-invasive prenatal tests

A comparatively new prenatal diagnostic procedure in the field of non-invasive procedures aims at the examination of cell-free »foetal« (actually placental) DNA from the mother's blood. In these procedures – which are optionally referred to as non-invasive prenatal tests, non-invasive prenatal diagnostics, cell-free DNA tests or simply blood tests – taking a simple blood sample from the pregnant woman is the basis for making statements about the probability of genetically induced variations of the foetus. The

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tests can detect the trisomies 13, 18 and 21 as well as the foetal sex with high accuracy. They are not considered to be diagnostic, so that an abnormal finding should be verified using other, usually invasive procedures. NIPTs have been approved as a self-pay service for pregnant women in Germany since 2012.

In the field of prenatal diagnosis and in particular in the field of new genetic analysis methods such as NIPTs, efforts are being made by companies providing prenatal tests to develop and patent new, faster and diagnostically more comprehensive procedures. It is to be expected that many research institutions and research-based companies will extend prenatal diagnosis both in terms of its methodological diversity and its diagnostic scope. Thus, the volume of prenatally available genetic information about foetuses and embryos would increase drastically.

Fig. 1 Prenatally detectable abnormalities

Chromosome aberrations (trisomies, monosomies, translokations)

(mono)genetically conditioned diseases (e. g. cystic fibrosis)

physical malformations (central nervous system, organs, skeleton)

Legal basis

With regard to NIPTs, there is a method evaluation procedure that will run until summer 2019. In this procedure, the German Joint Federal Committee (G-BA) will decide whether non-invasive prenatal tests for trisomies 13, 18 and 21 should be offered free of charge to so-called women with high-risk pregnancies as part of the statutory health insurance scheme. In this context, there is no conclusive definition of a high-risk pregnancy with regard to a certain probability of developing a trisomy. So far, the method evaluation procedure for NIPTs has led to fierce controversies, particularly among parts of civil society. This debate focuses on the question of the extent to which prenatal diagnostic procedures that do not open up primary therapeutic options should be part of the statutory health insurance benefits. Critics of the tests argue that their primary purpose is to terminate pregnancies with disabled foetuses. They call for a broad societal debate on whether these tests are socially desirable and whether prenatal diagnosis is accompanied by an implicit value judgement about people with disabilities.

The German Genetic Diagnosis Act, the German Act on Assistance to Avoid and Cope with Conflict in Pregnancy and the German Criminal Code are the central foundations with regard to the regulation of prenatal genetic analyses, the counselling of pregnant women and abortion. These laws aim at ensuring informed consent to prenatal genetic testing, strengthening the provision of psychosocial counselling during pregnancy, regulating how to cope with pregnancy conflicts and restricting abortions after the 12th week of pregnancy to particular cases of conflict.

In European neighbouring states, very different offers, uses and regulations for prenatal diagnostic examinations and possible subsequent abortions exist. Moreover, the accompanying societal debates also vary in intensity and focus on different aspects.

The situation of pregnant women

In Germany, surveys of (pregnant) women and doctors show that most pregnant women use prenatal diagnostic services that go far beyond the three ultrasound screenings provided for in the maternity guidelines (Fig. 2). And they are willing to pay for this. At the same time, the majority of pregnant women do not have a precise understanding of prenatal diagnosis and consider it to be a standard option in prenatal care. They often hope that prenatal diagnostic procedures will confirm the health of their unborn child. In the majority of cases, however, it is prenatal diagnosis that only raises the fear that the unborn child could be disabled. First and foremost, the vast majority of pregnant women associate the possibility of having a disabled child with fears regarding their own autonomy in terms of time and money and regarding their life as a couple.

In their decisions on prenatal diagnosis, pregnant women rely primarily on the information provided by their attending doctor. For this reason, the task of the doctors is to inform patients with only little prior knowledge about prenatal diagnosis within the framework of their liability-related obligations to act and to advise them comprehensively and neutrally.

Societal and ethical issues

Prenatal diagnostic examinations and the handling of resulting potentially serious diagnoses combine questions re-

garding one's personal life and individual decision-making in serious conflict situations with fundamental ethical and societal issues. On the one hand, this is due to the fact that the sum of individual decisions can have consequences for society as a whole, for example when fewer and fewer children are born with prenatally recognisable, congenital disabilities. On the other hand, it seems imaginable that options for action opening up (e. g. due to new, low-risk test procedures) could involve a change in social values. If, for example, it is possible to prenatally diagnose a foetus with Down's syndrome (trisomy 21) without any risk of intervention, will parents of a child with Down's syndrome in future be under even higher pressure to justify their decision to continue or terminate the pregnancy?

Critics fear this scenario and point out that Down's syndrome is by no means associated with suffering. In surveys, people with Down's syndrome indicate a high level of satisfaction with their lives and the vast majority of families with children with Down's syndrome do not »suffer« from the disability of their child or sibling – rather the opposite is true. Nevertheless, prenatal diagnosis particularly focuses on trisomy 21 and many prenatal diagnostic procedures show a particular sensitivity to the detection of this syndrome (e. g. NIPTs). The question of whether the offer to prenatally recognise certain disabilities represents a value judgement about this disability is only one of many social and ethical questions regarding prenatal diagnosis. There are further questions with regard to the following aspects:

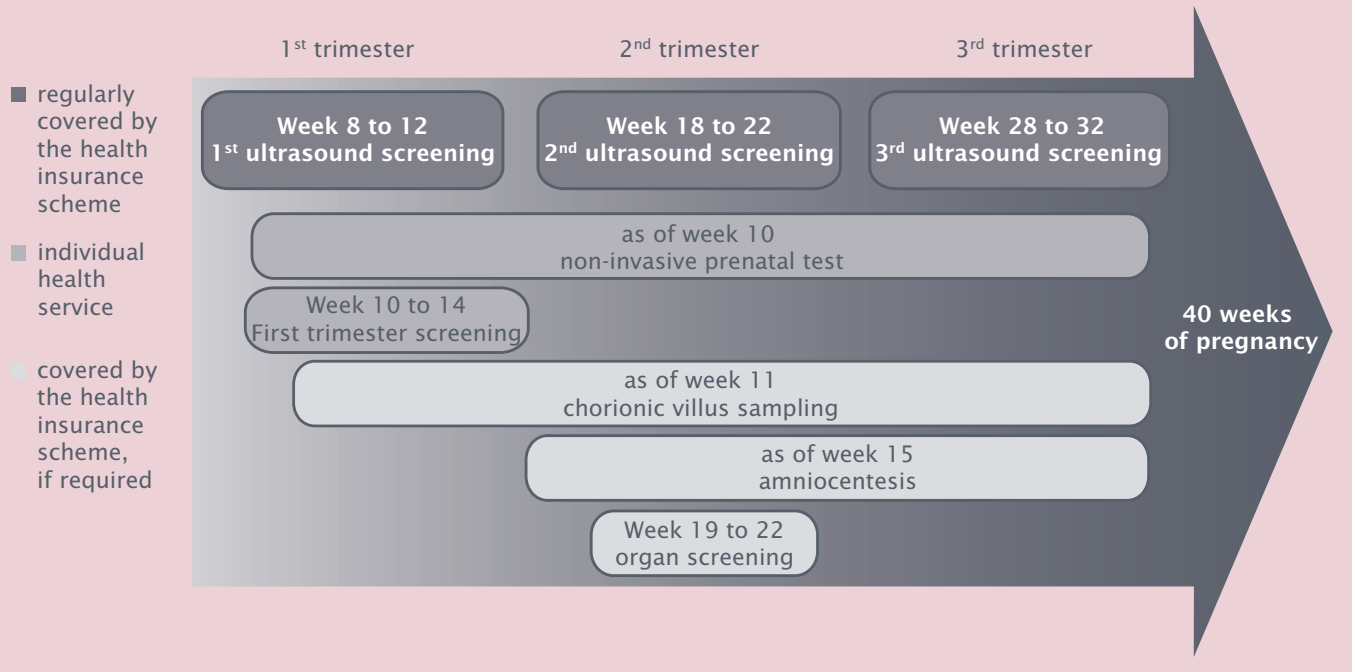
- Does prenatal diagnosis change the perception of pregnancy and parenthood? Do pregnant women only bond with their unborn child with reservations if the baby's health has not yet been »confirmed« by prenatal diagnosis? Or is it simply a decision-making aid for expectant parents?
- To what extent can NIPTs promote self-determined reproductive decisions? Does it represent a discrimination against socially disadvantaged pregnant women if they may use invasive prenatal diagnostic procedures free of charge, but not NIPTs, which have no increased risk of miscarriage?
- What challenges can result from gaining knowledge about the respective genetic findings for expectant parents, the concerned child and attending doctors? How much and what kind of genetic information of their unborn child should expectant parents be allowed to receive? How should findings with unclear clinical significance be dealt with?

Options for action

In summary, three central challenges can be identified with regard to the social use of prenatal diagnosis:

Gaps in knowledge regarding the current practice of prenatal diagnosis: The use of prenatal diagnosis and the consequences resulting from this use take place at decisive interfaces, as it were, in a »black box«. For example, there are no nationwide surveys covering all health insurance companies and institutions to determine which prenatal diagnostic procedures are used by pregnant women with which intentions, what prior knowledge the pregnant women have, how they

Fig. 2 Prenatal diagnostic examinations in the course of pregnancy



retrospectively assess the use of prenatal diagnosis and how often they get into conflict situations as a result of knowledge acquired by means of prenatal diagnosis.

The way individuals and society are dealing with the growing opportunities of genome analysis: The increased number of recognisable genetic peculiarities requires differentiated human genetic counselling in order to ensure an informed consent to genetic analyses. Due to the constantly increasing number of recognisable genetic peculiarities, the demands on counselling are increasing as well.

Difficult framework conditions for an informed decision by pregnant women: The current counselling and information landscape is influenced by company interests, which also play a central role in communicating information on NIPTs to both pregnant women and doctors. Most pregnant women have limited knowledge of prenatal diagnosis. For them, their attending doctor is the most important source of information. For their part, doctors report on time pressure during counselling and treatment, a lack of resources for further training and concern about liability claims if they do not provide sufficiently clear information about prenatal diagnostic examinations and the resulting findings.

To respond to these challenges, there are options for action in the fields of research and data acquisition, dialogue, counselling and participation as well as regulation. Research projects should examine the information needs of pregnant women, the social consequences of PND and the decision-making process in case of abnormal findings. With regard to an improvement of the counselling landscape, it would make sense to promote cooperation between doctors' practices, hospitals and counselling centres, to expand the range of further training on offer and to continuously improve information material. In addition, assistance for families with disabled or chronically ill children could be centralised and unbureaucratic support services could be expanded to ease the situation of these families. Finally, in parallel to the method evaluation procedure for NIPTs of the German Federal Joint Committee (G-BA), it seems desirable to initiate a broad social exchange on the opportunities and limitations of prenatal diagnosis and genetic knowledge and on how to deal with disabilities prior to birth. Stakeholders of central groups in society as well as the general public shall be invited to participate in this exchange.

In view of the decision regarding the method evaluation procedure of the G-BA due in summer 2019, it is obvious that the German Bundestag – in its legislative function – will take up and actively shape the debate on the previous and future role of prenatal diagnosis. An essential question with regard to future regulation is whether German politics – as requested by numerous organisations from the churches and civil society – would like to prevent a further expansion of prenatal diagnosis and restrict access to PND or whether the objective should be to improve the detection of foetal malformations at the earliest possible stage in pregnancy. Both objectives are based on diverging concepts for action.

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Aktueller Stand und Entwicklungen der Pränataldiagnostik
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www.tab-beim-bundestag.de/de/untersuchungen/u20810.html

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