Prenatal testing in Poland

The Very First Diagnosis

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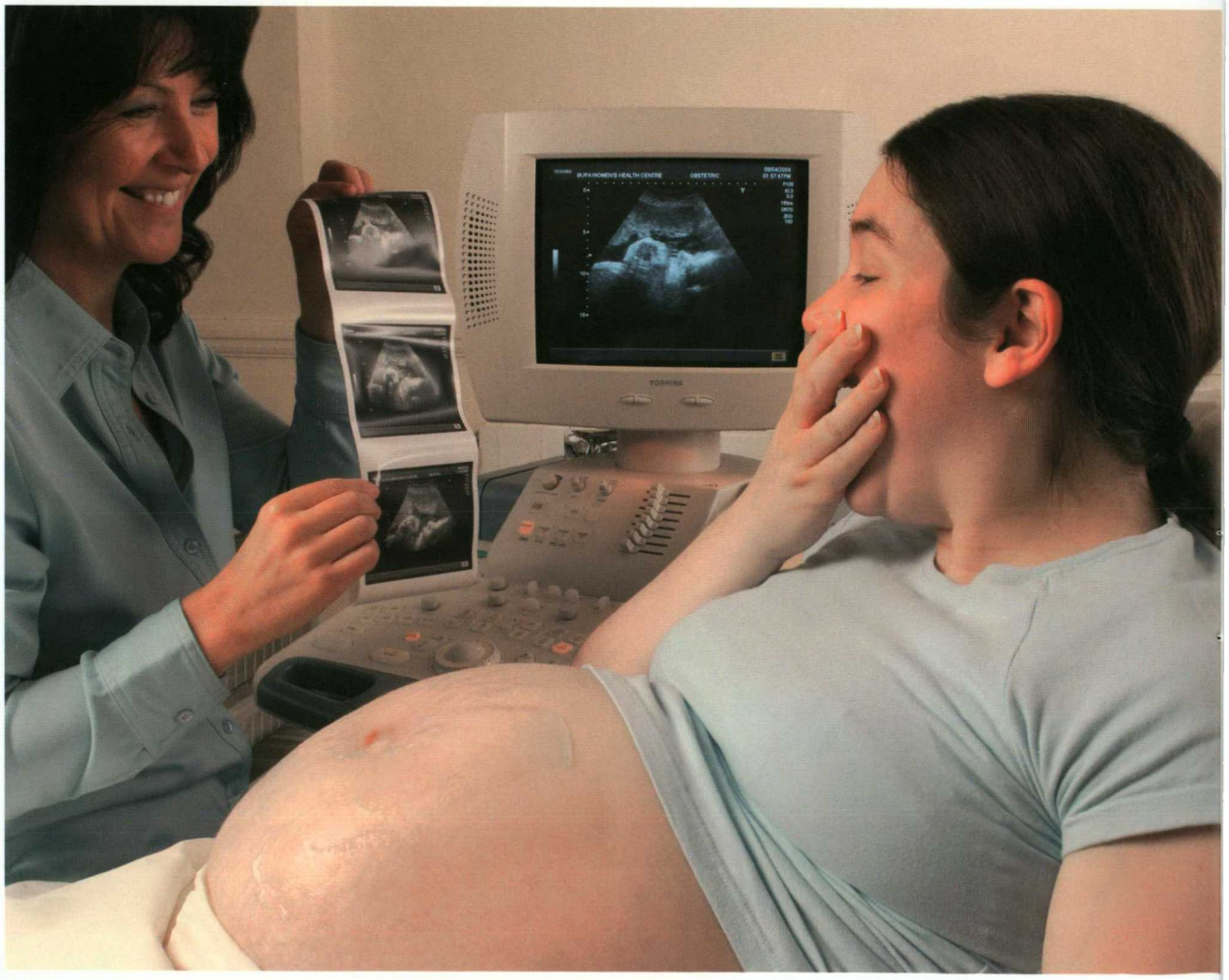
Prenatal diagnosis makes it possible to begin treating a fetus with a medical condition as early as possible – perhaps even while still inside the mother's womb. In the case of untreatable defects and illnesses, it can enable parents to make a conscious decision about the further course of pregnancy

The term "prenatal diagnosis" describes tests that are performed in the first and second trimesters of pregnancy in order to detect and identify fetal disease and defects, mostly genetically determined. Invasive prenatal testing was first performed 37 years ago, arriving in Poland 31 years ago. The techniques used in such tests reflect the progress that has been made in the medical sciences in general, and human genetics in particular. Since 1966 it has been possible to test the fetal chromosomes present in amniocytes (cells of fetal origin contained in the amniotic fluid). Several years later,



Ultrasonographic images are far more than just a precious gift for future mothers. Ultrasonograms constitute an integral part of prenatal testing, enabling doctors to detect many fetal developmental defects

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owing to progress in biochemical research, it also became possible to detect genetically determined metabolic defects in fetuses, such as mucopolysaccharidoses (e.g. Hunter's disease) and lipidoses (e.g. Tay-Sachs disease).

Great progress in the prenatal detection of fetal disease has been made owing to the development of molecular investigations. DNA analysis has enabled the genes involved in many genetic diseases - such as cystic fibrosis, spinal muscular atrophy, Duchenne's muscular dystrophy and fragile X syndrome - to be mapped and cloned. Prenatal diagnosis also became available in the early 1970s for what are called open neural tube defects, by determining the level of alphafetoprotein (AFP) and acetylcholinesterase in the amniotic fluid and by ultrasound scanning of the fetus.

Sources of information

Improved ultrasonography now makes it possible to detect many fetal developmental defects, such as congenital heart disease, defects of the central nervous system, and others. Ultrasonogram images can indicate that a fetus is highly likely to be afflicted by chromosome aberration. For example the presence of an extra chromosome 21, known as a cause of Down's syndrome, may be suspected on the basis of increased thickness of fetal nuchal translucency at 11th-13th week of gestation and the absence or hypoplasia (partial absence) of the nasal bone (at 15th--24th week of gestation). Ultrasonograms constitute an integral part of prenatal testing, because they are used to monitor the performance of amniocentesis, an invasive procedure for extracting a sample of amniotic fluid from the amniotic sac. Such fluid and the fetal cells it contains were initially the only material available for carrying out prenatal tests. A new technique began to be used in the 1980s, involving cells obtained by a chorion villus sampling during the first trimester of pregnancy - such cells represent excellent material for cytogenetic, biochemical, and DNA tests. Another useful procedure involves extracting fetal blood cells from the umbilical vein, usually performed after the 18th week of gestation.

Noninvasive methods of obtaining fetal material will most likely be growing more prevalent in prenatal diagnosis. It was demonstrated back in the 1970s that nuclear

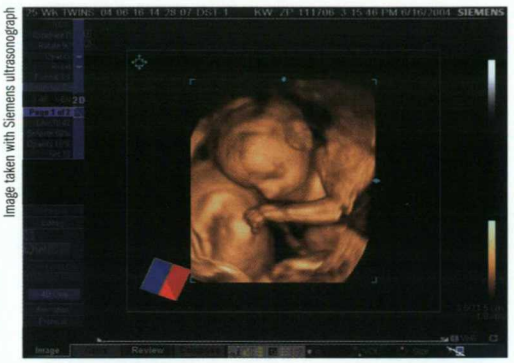


Image taken with Siemens ultrasonograph

Three-dimentional ultrasonography serves as a powerful tool in prenatal diagnostics

cells of fetal origin (such as erythroblasts and leukocytes) are present in the blood of pregnant women. More than 100 nuclear cells of fetal origin can be obtained from 10 ml of mother's blood during the 8th-12th week of pregnancy. Such cells can be used in molecular and cytogenetic diagnostics. An important obstacle to the more widespread use of this method (also as yet unavailable in Poland) is posed by the complicated technique of separating cells of fetal origin from the mother's own cells.

Screening tests aimed at detecting open neural tube defects were already being performed in the 1970s. They involved determining the level of AFP in the blood serum of women in the 16th-18th week of pregnancy. When a fetus has such a defect, the level of AFP in the mother's blood serum is significantly elevated. Women with raised AFP levels were given thorough ultrasonography and amniocentesis tests, thus significantly reducing the number of births with open neural tube defects.

It soon turned out that determining the level of AFP in the mother's blood serum may also indicate some chromosome aberrations, such as Down's syndrome. In this latter case, a lower concentration of AFP is seen in the blood, together with a lower concentration of unconjugated estriol (uE3) and a higher level of human chorionic gonadotrophin (hCG). All of these markers, as well as the maternal age, are currently used in second trimester screening for Down's syndrome and trisomy of chromosome 13 (Patau syndrome) or chromosome 18 (Edward's syndrome).

Who should be tested?

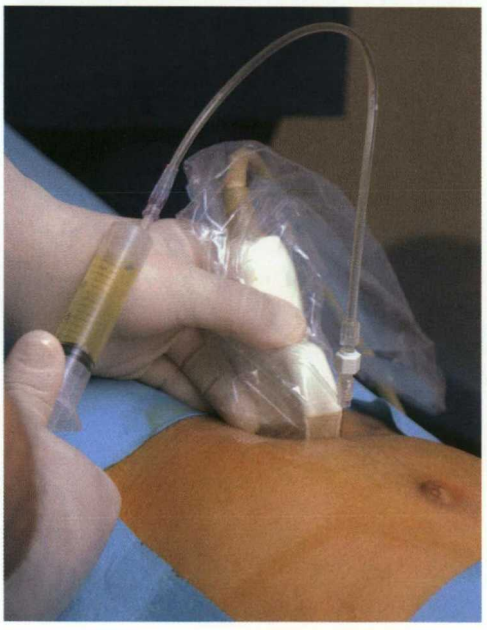
The first trimester screening is considered the most effective: testing the mother's blood serum for concentrations of pregnancy asso-

ciated plasma protein A (PAPP-A), free beta human chorionic gonadotrophin (βhCG), and ultrasonographic testing of the fetal nuchal translucency. Screening tests also take the mother's age into account when assesing the risk. An invasive procedure is offered to women if the risk of the fetal abnormality - based upon the result of the screening - is 1:300 or greater. The risk of miscarriages following invasive procedures is 0.5%-1%. Screening tests reduce the number of such miscarriages by avoiding the need for amniocentesis in many women over 35.

The group at increased risk can be identified by offering the first trimester screening (including the nuchal translucency test) in the 11th-13th week, or the second trimester screening. Fetal defects discovered by ultrasound between the 16th and 22nd week of pregnancy may also be considered as an indication for amniotic fluid tests, since such defects are not infrequently caused by chromosome aberrations.

We are currently aware of more than 1,500 inherited disorders that can be recognized prenatally. In Poland, prenatal tests are available for about 60 monogenic disorders, some developmental defects, and chromosome aberrations.

An important argument in favor of prenatal testing is the fact that the result they show is normal in 95% of cases (when overall indications are considered together). Most frequently such exams are performed so as to make sure that a fetus is unaffected. Only in 4-5% of cases do the results indicate that a fetus is affected. Moreover, only in some of these cases does the mother/couple decide to terminate the pregnancy. For example, 4,231 invasive tests were performed over the past 6 years at the Department of Genetics of the Institute of Psychiatry and Neurology. In 4,012 cases (94.8%) the result of the test was normal. Fetal pathology was detected in 219 cases (5.2%). Nevertheless, only 99 patients (2.3%) opted for a legal termination of pregnancy. Seven of the 65 women who were found to be carrying a fetus with Down's syndrome decided to continue the pregnancy, while as many as eight of 11 women showing Klinefelter's syndrome (karyotype 47, XXY) decided to continue their pregnancy.



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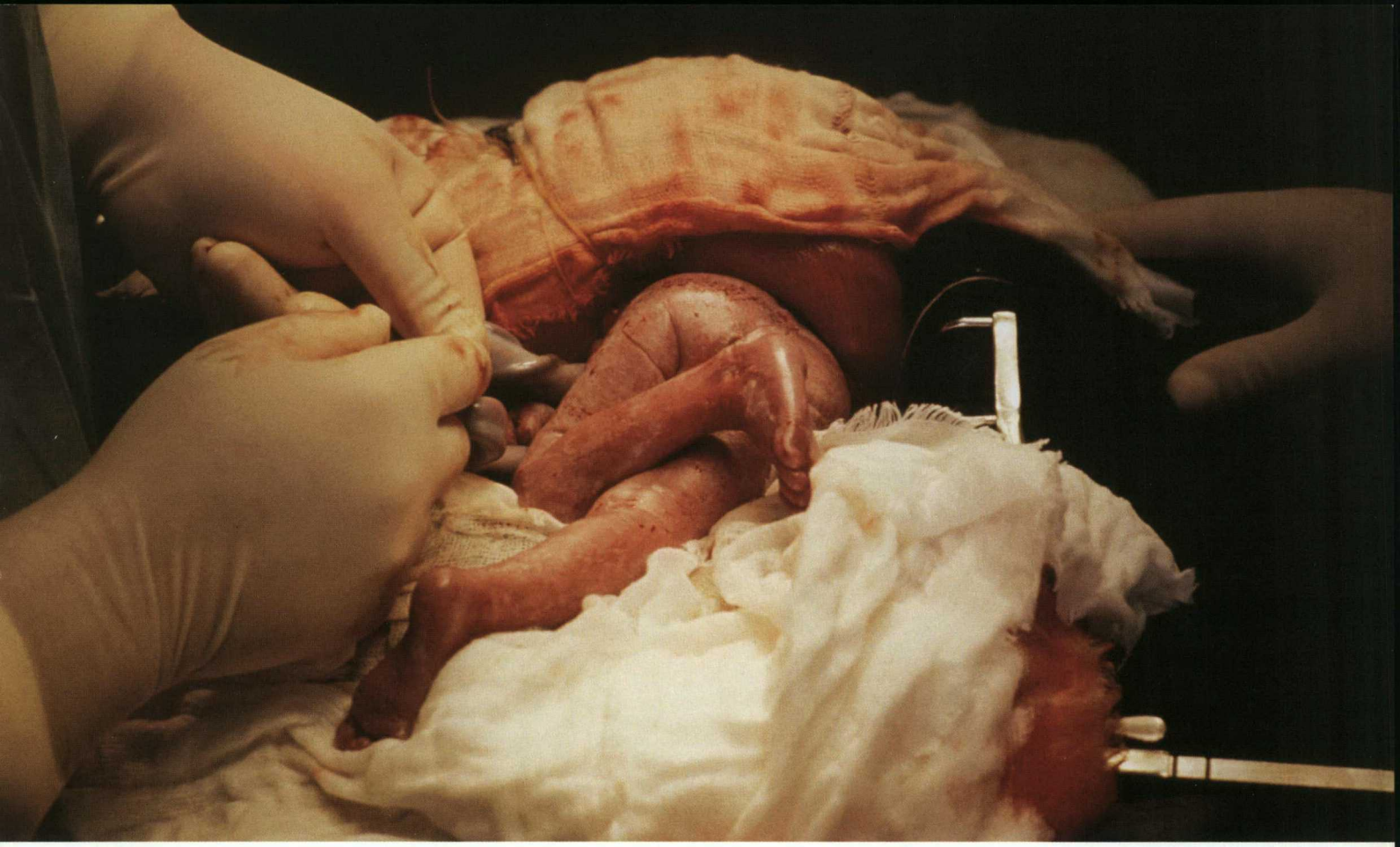
Amniocentesis is an invasive procedure for extracting a sample of fluid from the amniotic sac. Such fluid and the fetal-origin cells it contains were initially the only material available for carrying out prenatal tests

More and better

Prenatal diagnostics is constantly progressing and improving in highly developed countries. In Poland, however, prenatal tests are still not performed commonly enough (although their number is indeed constantly on the rise). Some 3,000 invasive exams were carried out in 2003, about 3,500 in 2004, and probably over 4,000 in 2005. They are performed by 13 centers throughout the country, although with uneven distribution. Half of all invasive prenatal tests are performed in Warsaw, while half of the country's 16 provinces lack any center offering such diagnostics. A rising proportion of invasive tests are being performed as the outcome of a screening and/or USG identification of fetal abnormalities - with such cases now representing 25% of the indications. In 2003, the Polish Ministry of Health appointed a Prenatal Testing Program Task Force in Poland, with the aim of improving access to prenatal diagnosis. Additional funding was allocated for screening tests, ultrasound diagnostics, and invasive diagnostics. Gradually increasing (albeit still too slowly) numbers of women are being offered invasive prenatal tests, preceded by screening and ultrasound scans.

Many Polish families from the high genetic risk group consider prenatal diagnostics to be a great blessing, and make their procreation decisions contingent upon access to such diagnostics. The moral dilemmas that frequently accompany this method should be resolved, as far as possible, by bioethics com-



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mittees on various levels - taking account of the principles of correct behavior set forth *inter alia* by the guidelines of the World Health Organization. In terms of prenatal diagnosis, these principles involve three ethical norms that are in force in medicine: respecting the patient's autonomy, abiding by the principle of justice, and avoiding solutions that might be harmful to a patient (*primum non nocere*).

Diagnostics and ethics

Of the many principles that should be observed, we will mention two particularly important ones here. Firstly, prenatal exams are performed exclusively for the purpose of identifying a fetus's state of health. Not acceptable is the use of prenatal diagnosis for paternity testing, except in cases of rape or incest, or for gender selection, apart from sex-linked diseases. Secondly, if a fetus turns out to be affected by a serious disease, the mother or couple's freedom of choice must be respected and protected, in line with the legal regulations in force in the given country. The choice is up to the couple in question, not to the doctor providing consultation.

In cases involving profound and untreatable defects and disease, parents have a right to make a decision about the further course of pregnancy. The law in most countries, including Poland, provides for the possibility of terminating a pregnancy in the event that prenatal exams detect a serious and untreatable disorder or defect in a fetus. Nevertheless, such a move is permitted only "until the point when the fetus gains the ability to survive on its own, outside the body of the pregnant woman," which in practice means until the 22nd-24th week of gestation. An exception to this may arise in the case of certain defects rendering the fetus incapable of surviving outside the mother's body.

It should be borne in mind, however, that the results of prenatal tests only rarely serve as an argument in favor of opting to terminate a pregnancy. This is evident, for example, in the experience of the Department directed by the present author, as cited above. Such results do, on the other hand, offer an opportunity for a better life for the child and its family. In cases where certain diseases or defects are identified in a fetus, for which effective treatment can be proposed, early detection and identification of the medical problem can facilitate the optimal handling of the pregnancy and birth. ■

State-of-the-art medical achievements can make it possible to provide therapeutic intervention to a child even prior to birth

Further reading:

Nicolaides K.H., Węgrzyn P. (2004). *Ultrasonography between 11-13 week of gestation*. Fetal Medicine Foundation, London.

A position statement from the Scientific Committee of the International Down Syndrome Screening Group http://www.leeds.ac.uk/idssg/position%20statement.htm

Proposed international guidelines on ethical issues in medical genetics and genetic services. Proposed ethical guidelines for prenatal diagnosis. (1998) WHO, Human Genetics Programme, 10-12.