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REVIEW ARTICLE

Changing Public Demand in the Genetic Counseling during the Past Decades

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ABSTRACT

Before discovering genetic rules, genetic counseling was based on empirical observations. In this process, it was important to recognize that certain diagnoses were more frequent in certain couples' descendants. The 20th century witnessed revolutionary progress in the science of genetics that coincided with increasing societal demands and therefore became an integral part of modern genetic counseling.

Genetic screening is changing from Mendelian disease ascertainment to predictive testing. We are also learning that the phenotypes of even simple Mendelian disorders are influenced by complex genetic and environmental factors. Moreover, developing knowledge about genotype/phenotype associations and many other aspects of genetic epidemiology will increasingly require referral to clinical geneticists.

Keywords: Fetal anomalies, Genetic counseling, Genetic diseases, Predictive genetic testing, Prenatal diagnosis.

INTRODUCTION

Genetic counseling is a field of professional expertise that involves diagnosis, provision of information and consultation with individuals about their genetic make-up and changes of bearing a child with a severe birth defect. Genetic counseling units are usually headed by medical geneticists and are located in large university hospitals or medical centers.

Genetic counselors typically consult with couple who have previously borne a child with a defect, have one or more relatives suffering from a disease, or have a pregnancy in which they are afraid of preconception or prenatal damage to the embryo or fetus. Most clients are referred by other physicians, though increasing numbers are self-referred. Couples who just want to obtain information about their genetic make-up are also considered legitimate clients.

Genetic counseling developed from two different occupational groups[1]: The early pioneers, the biologists and geneticists belonging to profession of natural science, and the medical doctors mainly pediatricians and obstetricians, who later assumed control over the field, belonging to the old established professions.

The pioneers in human genetics were mainly self-trained biologists and geneticists. Their high status, as scientists, was derived from working in areas involving mysteries, elements considered sacred by society. They worked within academic departments isolated from the fields of psychology and medicine. Geneticists dealt with population genetics and often were more interested in the effects on human evolution than on the individual.[2]

During the first third of the 20th century, genetic counseling services offered premarital, preconception and postconception heredity counseling. The counselor proffered highly directive advice as to whether or not to marry or reproduce.[3] The typical genetic counseling process consisted of a sole interview in which a pedigree was taken and a recurrence risk estimate presented. This approach fitted with the eugenics movement's interest in bringing about a decrease in harmful genes and an increase in desirable genes.[4,5] Even as late as 1960, Curt Stern in his textbook[6] used the term genetic counseling interchangeably with eugenics counseling.

By the 1950s, important breakthroughs in the study of hereditary diseases involving enzyme deficiencies and the study of cytological and chromosomal genetics broadened the clinical applications of human genetics and medicine.[7] The entrance of medicine as a discipline substituted concern about the future of the gene pool for an emphasis on the prevention of the birth of individuals who might have a severe birth defect. The service orientation of the doctor aimed at helping the individual patient/client, overrode the social implications in many physicians' minds as well as in the public's mind.

OBSTETRIC GENETICS

The neonate is no longer our youngest patient. Fetal medicine has emerged as a scientific discipline and the fetus, its chromosomes, enzymes and individual genes can be examined *in utero*. Currently employed prenatal tests include amniocentesis, chorionic villus sampling, cordocentesis and ultrasound, the latter enabling us to recognize major anatomical defects in the fetus.[8]

With the wider availability of genetic counseling, there are four main roads to the prevention of genetic disease:[8]

1. Individuals can be identified as being at high risk transmitting harmful mutant genes, and may be informed of this (classical genetic counseling). Their options may include various forms of contraception, sterilization,

adoption, artificial insemination by donor, *in vitro* fertilization (egg donation), preimplantation diagnosis (preferential selection of unaffected pre-embryos for transfer) and taking the risk of a normally conceived pregnancy, with or without prenatal diagnosis.

2. Preconceptual damage to the gametes (mutagens, clastogens) can be avoided by improvements in public health and hygiene, by more intensive programs of immunization (rubella), by reduced exposure to viruses, ionizing radiation, unnecessary medication and other potentially harmful factors, by provision where appropriate of some vitamins and by generally raising the standards of antenatal care.
3. The increased use of prenatal or neonatal screening, or prenatal diagnosis to allow measures to be taken earlier which are specially designed to support the genetically or environmentally damaged fetus or neonate (fetal/neonatal therapy).
4. Where there are no real prospects for treatment, and for major malformations or highly damaging or deleterious genetic disease, interruption of pregnancy may be offered by means of induced abortion or premature induction of labor.

As a result of the many recent fundamental advances in medicine and science, there are now these four modes of prevention (genetic counseling, pre- and periconceptual care, fetal therapy and abortion), but they cannot be put into practice without the goodwill and collaboration of the parents. Often, they also require the assistance or intervention of an obstetrician. In this respect, we should not expect geneticists to become obstetricians, but rather that obstetricians master fetal diagnosis and understand basic genetics in theory and practice.

Obstetrics must not only be concerned with preserving what has already been achieved—the ability to ensure that a healthy fetus be born healthy and not die or suffer permanent damage as a result of obstetric complications—but must also strive to bring children into the world who are well endowed mentally and physically like their parents. Many embryos, carriers of mutant and/or defective genes or badly damaged by malformation, will inevitably die *in utero*, as a result of biological selection. However, where they survive to born alive despite the natural screening process, families and individuals may experience many years of suffering.

PRENATAL GENETIC COUNSELING

I received my basic knowledge in genetics from my university professor of biology and genetics when I was a medical student in 1960. In 1964, I decided to become an obstetrician who was capable of understanding basic genetics and of serving the interest of seeing fetus unaffected by any disease.[9] I graduated in 1966 and started my career at the University Department of Obstetrics and Gynecology in Debrecen. With my director's support, I established a genetic counseling service within the obstetric department. During the first 10 years, I worked to introduce new techniques applicable in pregnancy, such as amniocentesis, chromosome analysis from amniotic fluid cells, postmortem cord blood lymphocytes, etc.[10-13] The program was officially confirmed in 1976.

I also have experience in classical genetic counseling and, in 1976, I combined this with the prenatal diagnosis and screening. This approach is called 'obstetric genetics'.[8] The main components of a prenatal genetic counseling service are given below.[8]

Consultation (Interview) with the Couple

The counselor must answer four questions for the couple:

1. What is the disease in question?
2. How severe is it and what can be done to treat the affected child?
3. How is it caused/inherited?
4. What can be done to avoid or prevent the disease in the future?

It is essential to present a clear and full description of the relevant disorder and to answer all questions honestly and promptly. A good and harmonious relationship should develop or be developed between the counselor and the couple. The physician-patient relationship always important in medicine, is thus replaced by physician/counselor-family relationship, which deepens through the course of counseling. This sort of relationship is necessary for the proper help and management of high-risk couples receiving counseling. A great deal depends on the character of the individual physician.

The physician/counselor gives information, and the parents, in the light of their own individual circumstances and attitudes, make the decision. We call our practice nondirective prenatal genetic counseling.[14]

Cytogenetic, Enzyme and Molecular Genetic Laboratories

The diagnosis in an affected child or adult or in the fetus *in utero* must be made with the most up-to-date methods available. Obtaining old or recent medical records, special laboratory tests and other investigations (may be involving referral to other specialist departments) can all be relevant or necessary procedures. All units including the genetic laboratory should be in the same building, which makes communication between the units and the transportation of patients and various tissue samples from the operating room to the laboratories easier.

Ultrasound Laboratory with Techniques for Sampling

Fetal ultrasound has a fundamental role in prenatal diagnosis. Unlike radiography, ultrasound diagnosis is risk-free for the mother, fetus and person performing the examination. It is atraumatic, noninvasive and does not produce discomfort. Prolonged examinations may be performed, and may be repeated as often as necessary. Ultrasound examination provides an emotional experience for both parents, who see the fetus for the first time as it moves *in utero*, and the parental relationship gains in strength, as does the "bonding" between parents and unborn child. Invasive procedures, such as amniocentesis,

chorionic villus sampling and cordocentesis, start with and are guided by ultrasound examination.

Screening of Fetal Anomalies

After showing that in pregnancies with a high risk of neural tube defects, the previously recommended amniocentesis may be omitted if the sonogram is performed by experienced personnel[15] and following our positive experiences in ultrasound screening[16-17] on January 1, 1988, in Eastern Hungary, we introduced nonselected, second-trimester ultrasound screening for fetal anomalies in low-risk women. Since I became the head of the first Department of Obstetrics and Gynecology at Semmelweis University in Budapest in 1990, we have been able to introduce this screening protocol throughout the whole of Hungary. The Hungarian Society of Ultrasound in Obstetrics and Gynecology founded in 1992, oversees quality assurance and carries out annual testing of obstetricians, gynecologists and sonographers working in the field of ultrasound.[18-19] In Hungary, four screening ultrasounds are offered for low-risk pregnant women (in the 8th, 18th, 28th and 38th week of gestation).

When an abnormal or suspicious prenatal ultrasound finding is obtained, most cases are referred to university centers. In this way, we are able to gather extensive experience in the prenatal diagnosis and fetopathological evaluation of congenital anomalies.[20]

Termination Ward

Ideally, induction of abortion should be effective without causing danger to the mother or damage to the fetus, and should allow confirmation of the pretermination diagnosis, full histopathological examination and further investigations where appropriate.[21-22] Cervical ripening in first-trimester abortion can be achieved with medical management using laminaria, prostaglandins, progesterone agonists and/or prostaglandin analogs, such as sulprostone, gemeprost, misoprostol and methotrexate.[23] These methods of pregnancy termination cannot be used after the 12th week, when labor must be induced. Although the fetus is usually expelled completely, instrumental emptying of the uterus is often required because of incomplete expulsion of placenta and membranes. In second-trimester terminations, prostaglandins are widely used. We have also had good experience with transcervical extra-amniotic instillation of ethacridine lactate (a myometrium-stimulating acridine dye).[21]

Fetopathological Unit

Fetopathology has been, and continues to be, an important issue and an integral part of the genetic counseling process. Post-termination pathological and special laboratory examinations can confirm the prenatal diagnosis. Diagnosis is not simply question of terminology, because the diagnosis and the estimated risk of recurrence depend on the final opinion presented by the fetopathologists. Only fetopathology can answer all the questions of differential diagnosis.

Currently, fetal pathology, the publicity of fetal pathology and the retaining of fetal organs raise sensible medicolegal issues in terms of informed consent and human rights. We are still convinced, however, that within certain limits fetopathological examination must be a part of the graduate, postgraduate and the specialist's education. This can be achieved by participating in autopsies or demonstrations of typical or rare developmental abnormalities. We believe that this speciality must be a part of the specialist and sonographer's training. Nothing can compare with *in situ* fetal demonstration in terms of effectiveness. It serves to better the specialist's education for the benefit of society.

Post-termination (Bereavement) Counseling with Availability of a Psychologist

Pregnant women, even those not burdened by genetic problems, often become anxious when thinking of their unborn child. Women at high risk of having a malformed fetus may feel shame and remorse in addition to anxiety. The genetic counselor must understand and attempt to satisfy the psychological needs and demands of the couple.

It is very important to provide follow-up for women who have had a termination for fetal reasons. These women may become very depressed immediately after termination and require support that is difficult to get from their own general practitioners. A clinical psychologist and a social worker have always been available in our department to help patients deal with their loss in complicated cases of abortion and to provide counseling or care following unsuccessful pregnancies. They also need a change to discuss the genetics again at a later time. This includes discussing the recent termination and the specific fetal malformations/aneuploidy and also the prospects for future pregnancies and how the next pregnancy might be managed.[24]

Assisted Reproduction Unit with Capability of Blastomere Biopsy, Nuclear Transfer and Cytoplasmic Transfer

In the past few decades, scientifically based procedures have been developed which enable children to be born independently of sexul intercourse and, as a result, thousands of people are alive today who were conceived with the help of such techniques. At the beginning, assisted reproductive technologies gained ground all over the world as a treatment for sterility and infertility. Later, they acquired a role in the prevention of certain genetic diseases.

Blastomere biopsy is an important part of the preimplantation genetic diagnostic procedure for monogenically inherited diseases, such as cystic fibrosis. At this time, nuclear transfer and cytoplasmic transfer are the most promising methods in the prevention of mitochondrially determined disorders. Mitochondrial genetics is quite different from Mendelian

genetics, and it is important to recognize this when attempting diagnosis and counseling for this group of disorders.[25]

Ethical and Legal Background

The couple may choose to attempt or continue a pregnancy or they may choose to terminate. A free decision is made by the parents and actions taken are within the law. Society creates the laws that regulate the termination of pregnancy. The legal rules and the professional codes and regulations provide a framework by which each case must be individually evaluated.

In Hungary, there is a legal framework for abortion, based on genetic indications. We have also contributed to the development of this system.[26-27] Legally, pregnancies with a prenatal diagnosis of genetic or anatomical defects that are compatible with postnatal life (such as trisomy 21 and spina bifida) can be terminated until the 24th week of gestation at the request of the couple. If the defects are incompatible with postnatal life (such as anencephaly and bilateral renal agenesis), pregnancies may be terminated in any subsequent week of gestation. In Hungary, following the prenatal diagnosis of severe conditions 99% of married couples request termination of pregnancy or the induction of premature delivery, and opt for reproductive compensation.[8-28]

Computer Database and Follow-up

All cases from our genetic counseling service have been recorded in our computer since 1976.[29] We implemented non-directive counseling from the start of this service, so we have over 100,000 counseling situations from which to study patients' views and reproductive decisions. We also obtain follow-up information on children born following a pathological prenatal diagnosis.

PRENATAL GENETIC COUNSELING SERVICE DATA

The genetic counseling service founded in Debrecen, was accepted and supported officially by the government in 1976. Since then, all cases have been registered and stored in the computer database system. Data from the first 15 years (1976-1990) were collected in Debrecen. In 1990, I organized a genetic counseling unit in Budapest as well. I also collected data from the first decade of the period 1991 to 2000.

When registering cases in addition to personal identification data, we always note the main reasons for genetic counseling (at least three in every case), the established specific risk, the attitude of the couple, the examinations performed, including prenatal diagnosis, and the outcome of the pregnancy. Possible attitudes of the couples involved are presented in Table 1.

In the present study, I collected experiences from the past 25 years (1976-2000) and, in order to demonstrate the changing demands, differentiated 5-year subgroups (1976-1980, 1981-1985, 1986-1990, 1991-1995 and 1996-2000). During these 25 years, 51,385 couples were counseled regarding 54,018 pregnancies or before planned pregnancies in 65,934 situations (requests to be answered) (Table 2).

Table 3 shows the distribution of the various genetic situations addressed during genetic counseling. The couples' decisions in cases where the Mendelian inherited disease or condition was the main reason for genetic counseling and where the risk was $\geq$ 25%, are shown in Table 4. In Tables 5 and 6, the maternal age distribution at time of counseling and the number of genetic amniocenteses performed because of advanced maternal age can be seen.

COUNSELING TOPICS

The number of couples requesting genetic counseling has continuously increased since the establishment of our genetic counseling service (Table 2). This increase had a transient decrease in the beginning of the 1990s because of the transfer of staff from Debrecen to Budapest. Independent of this slight decrease, more and more couples (mainly pregnant women) demand genetic counseling. The distribution of genetic diseases or congenital anomalies as indicators for counseling is influenced mainly by the continuous improvement of pre- and postnatal imaging, ultrasound techniques and the availability of molecular genetic methods (Table 3). Therefore, the detected cases of corpus callosum agenesis, Dandy-Walker anomaly, thoracic malformations (such as Ivemark syndrome), congenital heart defects and some monogenically inherited disorders with known gene localization, such as adult polycystic kidney disease, Huntington disease, neurofibromatosis and intestinal polyposis are increasing. The detected cases of some conditions, such as metachromatic leukodystrophy and Sanfilippo syndrome, are decreasing because of the difficulties in diagnosing enzyme disorders in pediatric practice in Hungary.

The demand for counseling from couples at high risk for cystic fibrosis, Duchenne muscular dystrophy, hemophilia, osteogenesis imperfecta and Werdnig-Hoffmann disease been extensive during the past 25 years. Despite improving prospects, these are still crippling disorders with a relatively high prevalence, and many parents of affected children seek prenatal diagnosis for subsequent pregnancies. When prenatal diagnosis was not available, the reproductive decision was strongly influenced by the 25 to 50% genetic risk of disease in future offspring. A considerable proportion of parents with an affected child changed their intended family size or abstained from further childbearing. The availability of prenatal diagnosis induced a change in reproductive planning in a majority of parents with one or more children affected by such diseases.[30] Our experiences confirm that the availability and reliability of prenatal diagnosis are the most decisive factors in the reproductive planning of couples at high risk for such diseases.[28] The strength of desire to have children can be inferred from the number of affected and healthy children the couples had during the decision-making period.[30]

The desire to have children is also reflected by the position of the affected child holds in the birth order. Our experience

Table 1: Possible attitudes of married couples regarding genetic counseling

Genetic counseling	*Attitude*
Pregnancy can be attempted or carried to term (genetic risk <10%, no prenatal diagnosis)	Genetic counseling was followed
Pregnancy can be attempted or carried to term (genetic risk <10%, no prenatal diagnosis)	Genetic counseling was not followed (no pregnancy was attempted or termination of pregnancy was requested based on other reasons)
Pregnancy can be attempted or carried to term (genetic risk <10%, prenatal diagnosis available)	Genetic counseling was followed, and prenatal diagnosis was performed
Pregnancy can be attempted or carried to term (genetic risk <10%, prenatal diagnosis available)	Genetic counseling was followed partially (the pregnancy was achieved, but no prenatal diagnosis was performed)
Pregnancy can be attempted or carried to term (genetic risk <10%, prenatal diagnosis available)	Genetic counseling was not followed (no pregnancy was attempted, or termination of pregnancy was requested based on other reasons)
Pregnancy can be attempted or carried to term under the protection of prenatal diagnosis (genetic risk 10-99%)	Genetic counseling was followed and prenatal diagnosis was performed
Pregnancy can be attempted or carried to term under the protection of prenatal diagnosis (genetic risk 10-99%)	Genetic counseling was followed partially (pregnancy was achieved, but no prenatal diagnosis was performed)
Pregnancy can be attempted or carried to term under the protection of prenatal diagnosis (genetic risk 10-99%)	Genetic counseling was not followed (no pregnancy was attempted or termination of pregnancy was requested based on other reasons)
It is not advisable to attempt pregnancy or to carry the pregnancy to term (genetic risk ≥ 25%, no prenatal diagnosis)	Genetic counseling was followed (no pregnancy was attempted or termination of pregnancy was requested)
It is not advisable to attempt pregnancy or to carry the pregnancy to term (genetic risk ≥ 25%, no prenatal diagnosis)	Genetic counseling was not followed (pregnancy was attempted or termination of pregnancy was not requested)
The decision of the married couple will be based on the knowledge of the genetic risk of medium value (≥ 10 and < 25%)	
Genetic counseling because of sterility	
Other cases of genetic counseling	

Table 2: Genetic counseling data

	1976-1980	*1981-1985*	*1986-1990*	*1991-1995**	*1996-2000*	*Total*
Number of couples	2,088	9,226	10,877	10,214	18,980	51,385
Number of preconceptional or prenatal counseling sessions	2,498	9,721	11,761	10,480	19,558	54,018
Number of requests to be answered	3,166	11,970	14,474	11,881	24,443	65,934

*The Budapest genetic counseling service was established in 1990. This is the reason for the decline in numbers

shows that couples were more likely to plan a subsequent pregnancy when the affected child was the first-born.[28]

When a Mendelian inherited disease or condition was the main reason for genetic diagnosis, only 15% of the couples requested termination or did not attempt a pregnancy (Table 4). The majority of women (85%) decided to attempt or continue a pregnancy and nearly 70% of them requested prenatal diagnosis. This distribution of decision-making behavior was consistent throughout the examined 25 years and was mainly influenced by the psychological and emotional attitudes of the couples. Maternal serum α-fetoprotein (AFP) screening for the detection of neural tube defects has been a routine practice in Hungary for many years. Similarly, ultrasound screening for fetal anomalies is another option which has been accepted by the majority of pregnant women. The biochemical screening for trisomy 21 was not widely used in our country, but, because of the anxiety and concern caused by low maternal serum AFP level many pregnant women are referred to our center (Table 3). Consequently, there are a great number of unnecessary genetic amniocentesis and prenatal chromosome analyses. Conversely, most abnormal sonographic findings in women referred to our department are confirmed, resulting in many prenatally

Table 3: Distribution of the indications for counseling from 1976 to 2000

Indication	*1976-1980*	*1981-1985*	*1986-1990*	*1991-1995*	*1996-2000*	*Total*
Mendelian inherited disease or condition	132	415	668	412	584	2,211
Autosomal dominant trait	22	81	108	103	159	473
Autosomal recessive trait	88	227	420	220	290	1,245
X-linked recessive trait	22	104	136	87	131	480
X-linked dominant trait	0	3	4	2	4	13
Consanguinity	29	70	77	38	71	285
Chromosome aberrations	101	178	279	294	678	1,530
Multifactorially determined common chronic diseases	210	1,002	1,001	342	720	3,275
Congenital anomalies	602	1,793	1,959	843	1,727	6,924
Pathology of placenta and membranes	4	33	47	21	10	115
Multiple malformation syndrome	126	338	302	154	316	1,236
Thoracic malformation	94	341	403	196	468	1,502
Abdominal malformation	38	130	128	48	72	416
Cystic kidney disease	10	52	65	50	78	255
Obstructive uropathy	3	17	31	13	16	80
Skeletal malformation	39	125	119	69	106	458
Craniospinal malformation	279	709	774	246	568	2,576
Immune and nonimmune hydrops	8	38	71	44	44	205
Pathology of multiple pregnancy	1	10	19	2	49	81
Maternal serum AFP screening	14	1,493	1,255	1,193	4,805	8,760
High AFP level	1	33	137	591	2,013	2,775
Low AFP level	0	0	18	585	2,682	3,285
MSAFP + ultrasound screening organized by the service	13	1,460	1,100	17	110	2,700
Abnormal sonographic finding	16	227	489	1,721	3,245	5,698
Fetal anatomy	5	200	443	1,704	2,806	5,158
Amniotic fluid volume (poly- and oligohydramnios)	11	27	46	17	439	540
Unsuccessful previous pregnancies	422	1,371	1,230	508	1,042	4,573
Recurrent abortion and/or perinatal death (still birth or infant death)	412	1,356	1,217	507	1,032	4,524
Hydatidiform mole	10	15	13	1	10	49
Perinatal damage, mental handicap (not classified)	126	302	282	139	239	1,088
Teratogenic exposition during pregnancy	1,065	3,426	3,747	1,539	3,150	1,2927
Drug (medicine) and/or chemical	559	2,185	2,466	1,047	2,092	8,349
Bacterial, viral, protozoon	333	836	797	273	550	2,789
Others	173	405	484	219	508	1,789
Advanced maternal age (as a main request)	86	777	2,598	4,338	6,710	14,509
Infertility	298	547	536	210	701	2,292
Sterility	126	306	296	70	83	881
Pregnancy conceived by assisted reproduction technology	1	5	3	35	444	488
Amenorrhea, intersexuality	171	236	237	105	174	923
Trivial complaint	65	369	353	304	771	1,862
Total	3,166	11,970	14,474	11,881	24,443	65,934

AFP – α-fetoprotein; MASAFP – maternal serum AFP

Table 4: Decisions made by couples in cases where a Mendelian inherited disease or condition was the main indicator for genetic counseling (risk ≥ 25%)

	Prenatal diagnosis available		*Prenatal diagnosis not available*		
Inheritance	*Prenatal diagnosis performed*	*Prenatal diagnosis not requested*	*Terminated without prenatal diagnosis*	*Termination requested*	*Pregnancy continued*
Autosomal dominant	12	23	12	69	90
Autosomal recessive	265	102	55	64	131
X-linked recessive	124	59	38	10	17
X-linked dominant	2	2	0	3	0
Total	403	186	105	146	238

Table 5: Maternal age distribution at time of counseling

Maternal age (years)	*1976-1980*		*1981-1985*		*1986-1990*		*1991-1995*		*1996-2000*		*Total*	
	No.	*%*	*No.*	*%*	*No.*	*%*	*No.*	*%*	*No.*	*%*	*No.*	*%*
< 35	2,295	92.0	8,406	86.5	8,755	74.4	6,117	58.4	13,595	69.5	39,168	72.5
35-37	96	3.8	568	5.8	1,277	10.9	1,838	17.5	2,890	14.8	6,669	12.3
38-40	66	2.6	405	4.2	1,104	9.4	1,678	16.0	2,035	10.4	5,288	9.8
41-43	30	1.2	250	2.6	517	4.4	709	6.8	864	4.4	2,370	4.4
> 43	11	0.4	92	0.9	108	0.9	138	1.3	174	0.9	523	1.0
Total	2,498	100.0	9,721	100.0	11,761	100.0	10,480	100.0	19,558	100.0	54,018	100.0

Table 6: Number of prenatal chromosome analysis requested and performed. Values in parentheses are the numbers of patients of advanced maternal age (≥ 35 years)

1976-1980		*1981-1985*		*1986-1990*		*1991-1995*		*1996-2000*	
Year	*No.*	*Year*	*No.*	*Year*	*No.*	*Year*	*No.*	*Year*	*No.*
1976	5	1981	59	1986	120	1991	288	1996	1,033
1977	6	1982	84	1987	149	1992	471	1997	1,313
1978	5	1983	101	1988	209	1993	755	1998	1,339
1979	11	1984	104	1989	304	1994	823	1999	1,564
1980	27	1985	118	1990	146	1995	867	2000	1,769
Total	54 (48)		466 (428)		928 (903)		3,204 (2050)		7,018 (3011)

diagnosed cases of fetal anomalies and pathological pregnancy cases. The number of patients seeking advice because of unsuccessful previous pregnancies is decreasing slightly, because most recurrent miscarriages are not genetic in origin. Since 2000, the combined and integrated tests for screening of fetal aneuploidies have been introduced and widely used in Hungary.

Anxiety because of teratogenic exposure during pregnancy is still a frequent counseling issue, because the administration of drugs during pregnancy is still unnecessarily high, even though a large proportion of drugs have no real clinical indication during pregnancy. By analyzing the outcome of pregnancies with drug exposure during early gestation, it is relevant that no significant increase in congenital anomalies can be observed in these cases. In this respect, the large number of pregnant women afraid of the consequences of teratogenic exposure is not justified and public health education is required.

The age distribution of women receiving counseling has changed during the period. The number of women 35 to 43 years of age and their requests for prenatal chromosome analysis are continuously increasing (Tables 5 and 6). Between 1976 and 1980, 25% of women over 34 years of age requested genetic amniocentesis. Later on, this proportion has risen to nearly 50%. The indication for prenatal chromosome analysis has justifiably changed in favor of abnormal ultrasound finding and the large number of positive biochemical screening test results.

At the beginning, our genetic counseling service dealt with infertile couples and amenorrhea patients as well, but new assisted reproductive technology has changed the management of infertility and a modern endocrine laboratory has also been established. These couples now look to the genetic counseling service for prenatal chromosome analysis (Table 3).

NONDIRECTIVE OR DIRECTIVE GENETIC COUNSELING

The information to be given in the context of genetic counseling should include:

1. The purpose and nature of the intervention
2. The possible risks
3. The diagnosis and prognosis for the person concerned
4. The risk of disease for future children of other family members
5. The consequences and choices available for the person concerned.

There is widespread support among medical geneticists and genetic counselors for nondirectiveness and value neutrality in genetic counseling.[31,32] Such support arises from concern about early abuses in the eugenics movement recognition of the right to privacy and autonomy in reproductive decisions. Recently, discussions have focused on the desirability and practicality of nondirective and value-neutral counseling with a number of authors questioning whether it is ever possible to achieve.[33-35] Despite the ethos of nondirectiveness that has prevailed in genetic counseling, there have been few empirical studies of directiveness, and no method of measuring it has been suggested or tested.

Michie et al have presented a methodology for quantifying directiveness in a clinical genetics setting.[36] What can we learn from this study? First, as stated by the authors, the practice of genetic counseling "is not characterized… as uniformly nondirective". Kessler[34] has suggested that directive counseling that supports the client's decision direction is often helpful but requires "greater flexibility than dogmatism in genetic counseling practices".

Genetic counselors always have the power to influence clients by choosing to discuss one aspect of a situation while ignoring or downplaying another. Through interviews with genetic counselors and genetic-counseling students, Brunger and Lippman have shown how a genetic-counseling session is context dependent.[37] For example, the information on Down's syndrome that is included in a preamniocentesis counseling session differs greatly from that in a session concerning a neonate with Down's syndrome.[38]

A partnership model has evolved that incorporates high levels of both provider and patient participation in decision-making.[39] This model acknowledges that the patients' needs and desires to be considered and that patients play a role in decision making, but it does not go so far as to advocate that physicians abdicate their role in providing recommendations.[40]

A review of the literature provides no evidence that a non-directive approach benefits the clients.[41] On the contrary, there is an indication that genetic-counseling clients may welcome exactly the opposite. Shiloh and Saxe[42] have shown that genetic-counseling clients reported a higher perceived risk associated with more neutral counseling, perhaps stemming from client belief that the counselor must be concealing bad news. In another study, Furu and colleagues[43] have reported that among individuals with retinitis pigmentosa or choroideremia and their relatives, 80% would like to know the opinion of the genetic counselor with regard or undergo abortion after a positive prenatal diagnosis result.

One of the most significant contributions of the Michie study[36] relates to the lack of association of rated directiveness with client satisfaction, fulfilment of client expectation and self-reported client anxiety and concern. The study shows that, even when clients knew the counselor had an opinion as to what decision they should make, many clients did not feel steered by this opinion. The implication that provider directiveness may not really matter to clients forces us to consider whether focusing on nondirectiveness as the *sine qua non* of current genetic counseling practice diverts attention from other important goals, process measures or outcomes of genetic counseling. Such consideration is especially timely, given the need for outcome-based measures.[44] In the majority of agreement between the counselor and the client as to the agenda items that each wants to address. Without agreement between counselor and counselee as to what outcomes to expect, measurements will be meaningless.

Not all individuals at risk for transmitting a genetic defect wish to prevent its occurrence if it means relinquishing biological parenthood; some do not even agree with the counselor's view that a specific genetic disease ought to be prevented.

I think that the most important principle is to transmit the information in a nondirective manner and adapt it to the needs of each person. As Table 4 shows, we prefer the nondirective approach to genetic counseling. This approach is a logical consequence of the principle that consultants must be assisted in reaching an informed and autonomous decision that is appropriate to their life situation. The options of attempting a pregnancy and requesting prenatal diagnosis belong to the parents. That is the principle of nondirective prenatal genetic counseling. Nevertheless, supportive counseling by social workers and clinical psychologists affiliated with prenatal genetic counseling centers can be essential in helping consultants in their decision-making process. This principle has remained unchanged in our practice for the last decades.

Most discussions of nondirectiveness have focused on prenatal testing and reproductive decision-making, areas in which genetic counseling has been focused for at least 25 years. Genetic counseling will increasingly be provided in conjunction with the offering of presymptomatic or predisposition testing.

Because early treatment might be effective for some disorders for which predisposition testing is available, providers arguably should recommend that clients be tested. How likely is it that of nondirectiveness will or should be upheld in the era of predictive testing for common adult-onset disorders?

For several reasons, it is likely that most clients seeking genetic counseling in conjunction with predictive testing will be given directive counseling. Genetic counseling and testing will increasingly move into the primary care arena and be provided by nongeneticists. There is a perception on the part of nongeneticist physicians that patients want direction. Many physicians believe that opinion seeking on the part of patients is a sign of trust and that not rendering an opinion is irresponsible.[45] The ethicist Caplan believes that primary-care physicians are unlikely to warm to suggestions that conversations become nondirective when the subject turns to heredity. Moreover, he suggests that their patients are unlikely to accept nondirectiveness with regard to genetic discussions when the said ethos does not prevail in other aspects of their relationships with providers.[46]

PREDICTIVE GENETIC TESTING

Predictive genetic testing is the use of a genetic test in an asymptomatic person to predict future risk of mainly multifactorially determined disease. The presymptomatic test is a predictive test with a high risk (almost 100%) for the development of the tested mainly dominantly inherited disease. These tests represent a new and growing class of medical tests, differing in fundamental ways from conventional medical diagnostic tests. The hope underlying such testing is that early identification of individuals at risk of a specific condition will lead to reduced morbidity and mortality through targeted screening, surveillance and prevention. Yet the clinical utility of predictive genetic testing for different diseases varies considerably.

A predictive genetic test informs us only about a future condition that may (or may not) develop. The indentified risk is sometimes high, but always contains a substantial component of uncertainty, not only regarding whether a specific condition will develop but also when it may appear and how severe it will be. Predictive genetic tests often carry a further element of uncertainty; the interventions available for individuals at risk are often untested and recommendations may be based on presumed benefit rather than observations of outcomes.

These uncertainties contrast with the presentation of predictive genetic testing in the popular media, which often fosters an illusion that genetic risk is highly predictable and determinative. In fact inherent uncertainties in most genetic tests represent a major limitation to their clinical utility.

Whereas conventional diagnostic testing rarely has medical importance for anyone other than the person tested (except in the case of communicable diseases), predictive genetic testing typically has direct implications for family members. Concern for relatives may be an important motivating factor for a patient's desire to undergo such testing. Some family members, however, may resist participating in the testing because they would rather not have information about their genetic risk. The utility of a predictive genetic test will, therefore, depend on whose point of view is considered.

Some of breast and ovarian cancers result from the inheritance of mutations in the BRCA1 or BRCA2 gene. Predictive genetic testing for breast and ovarian cancer, as for hereditary nonpolyposis colon cancer, can be useful to identify those at increased risk. In both breast and ovarian cancer, however, utility is limited because of considerable uncertainty about the predictive value of the test.

A woman carrying a mutation in the BRCA1 or BRCA2 gene may develop breast cancer, ovarian cancer, breast and ovarian cancers or no cancer at all. Penetrance estimates range from 36 to 85% for breast cancer and 10 to 44% for ovarian cancer. Moreover, the age at which cancer occurs is widely variable. These uncertainties probably reflect a combination of factors including the environment, modifying genes, the nature of a woman's specific mutation and purely stochastic processes.

Predictive genetic testing should be accompanied by genetic counseling. In the study by Holtzman and colleagues[47] which explored women's decision-making preferences with regard to genetic testing for susceptibility to breast cancer, they found that most women wanted to hear their providers' recommendation about testing. Women still wanted to make their own decisions, either by choosing to follow their provider's recommendation or by choosing to veto it. If a provider did not give a recommendation based on her expertise, women believed either that the provider was not fulfilling her duty or that they were not getting their money's worth. It has been suggested that concerns about autonomy should shift from focusing on whether the decision was made voluntarily or the decision-making process was entered voluntarily. Such a shift would preserve autonomy and empower patients, as they are able to play their preferred role in decision making.

Genetic screening is changing from Mendelian disease ascertainment to predictive testing. We are also learning that the phenotypes of even simple Mendelian disorders are influenced by complex genetic and environmental factors.[48-51] The observations that genotypes rarely predict phenotypes absolutely have significant ramifications for counseling. We must recognize that for single-gene disorders with high penetrance, the information derived from such testing may be relatively easy to interpret and apply. For complex diseases, however, the populations studied and their demographic characteristics are extremely important for extrapolation to counseling of individual patients.[52]

It is likely that the goals of genetic counseling vary according to individual client needs and should established or reestablished as each session begins. From the client's point of view, the goal might involve soliciting the counselor's expert opinion.

We need to accept that there are times when the recent challenges of genetics make directiveness permissible or even positive, and elucidate better ways to make our services more responsive to the needs of our clients and their families.[53-55]

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