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Evaluation of information-guidance genetic counselling

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SUMMARY The impact of information-guidance type of genetic counselling was evaluated for the family planning of 2082 consultands. The understanding of the risks, parental decision, and the number of induced and spontaneous abortions were evaluated by the use of questionnaires. The stillbirths, livebirths, infant deaths, and babies with inherited or congenital anomalies were checked by experts. When pregnancy was recommended the rate deterred was 4·7% while this rate was 61·7% and 60·7% when pregnancy was not recommended or pregnancy required consideration. When pregnancy was not recommended, 43·5% of offspring had congenital anomalies, while this value fitted with random risk (4%) in offspring born after recommended pregnancies.

Recently Evers-Kiebooms and van den Berghe[1] reviewed the retrospective follow-up studies on the impact of genetic counselling. Nine samples involving 2922 cases included many different disease groups. Our genetic counselling clinic was established in 1973 and consisted of 2654 counsellees until the end of 1977. The impact of genetic counselling was evaluated for the family planning of 2082 consultands in the first quarter of 1979. Particular attention was given to the decisions concerning further pregnancies and their outcome after genetic counselling, because of differences in the methods of genetic counselling in Hungary compared to the usual non-directive practice.

The usual English practice is to give only information without any advice. ("It is no part of the task to advise patients whether or not they should have children".[2]) This practice was further developed by Carter *et al*,[3] who, after the recognition of the relatively high percentage of consultands deterred from pregnancy in the category of moderate risk, introduced the practice of saying to these couples: "In your place I would not take a risk of this kind too seriously". This constitutes a balance between being purely informative and being directive. Our counsellees said they needed "more help", and asked for our advice too. Thus in our practice the so-called 'information-guidance' method was adopted. We explain to the parents the biological-medical perspectives of planning a child or further children. This involves: (1) the burden of expected disorders; (2) the possibilities of treatment; (3) the possibility of prenatal diagnosis; (4) the specific genetic or teratogenic risk; (5) the sociomedical situation of the family in relation to the postnatal development of children, for example, serious disease in the parents, the socioeconomic conditions of the family, the number of affected and healthy children already born; and (6) the maternal risk during pregnancy. This advice can be roughly classified into five categories as in table 1. Advice I means that the couple are told that there is no essential problem and pregnancy is recommended. Advice II means that the pregnancy is recommended after some preparation, for example, treatment, special investigations, waiting for the optimal time of conception, and also when the risk involves only fetal death such as in habitual abortions. Advice III means that pregnancy is recommended with prenatal diagnosis. Advice IV

TABLE 1 *Distribution of consultands who wanted further children by five categories of 'advice'*

Category and meaning of advice		*Consultands*	
		No	*%*
Advice I	No essential problem, pregnancy is recommended	1072	58·2
Advice II	Pregnancy is recommended after some preparations	444	24·1
Advice III	Pregnancy is recommended with prenatal examination	177	9·6
Advice IV	There is some problem, pregnancy requires consideration	88	4·8
Advice V	Pregnancy is not recommended	60	3·3
Total		1841	100·0

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means there is some problem and pregnancy requires serious consideration, that is, some caution is advised on account of a risk of between 5 and 19% of severe, untreatable disease where prenatal diagnosis is not available, or a higher risk of probably treatable, preventable, or not too serious disease. Finally, advice V means pregnancy is not recommended because the expected disorder is severe, untreatable, prenatal diagnosis is not available, and the risk exceeds 20%. Of course, it is only a recommendation and the right and responsibility of decision is left to the consultands and we honour their decision. Table 1 shows the percentage distribution of the advice.

We are aware that some experts prefer the non-directive approach of counselling,[4] in which the physician-counsellor strives to help the counsellees help themselves. In our opinion the strategy of counselling may depend on (1) the general needs of counsellees/consultands; (2) the couple's education, sex, age, behaviour, etc; (3) the actual possibilities (for example, the time and atmosphere for counselling are limited in the usual outpatient clinics); (4) the legal protection of the counsellor; and last but not least (5) the efficiency of counselling. This paper summarises the results of an 'information-guidance' type of counselling.

Methods and materials

A total of 2654 counsellees was divided into 15 different categories according to reasons for seeking genetic counselling.[5] We excluded 142 counsellees because the probands or consultands were not their first degree relatives. In the first phase of the study a questionnaire was sent to the address of the remaining 2512 counsellees. In 186 cases the address was wrong or had changed. Counsellees who did not reply were asked again to fill in the questionnaire. Finally the data of 2082 counsellees (89·5%) were evaluated from the 2326 cases whose addresses were known.

In the second phase of study the outcome of pregnancies of consultands was evaluated.

(1) Sixty-four spontaneous and 197 induced abortions, as well as eight extrauterine pregnancies, were accepted on the basis of questionnaires.

(2) A detailed necropsy record was requested from the pathology department in the cases of 24 stillborns. Thirteen suitable replies arrived without mentioning anomalies.

(3) A total of 957 children were described as being healthy by parents. Their paediatricians were asked to confirm this and information was received about 856 children (89·4%). Six children (0·6%) had congenital abnormalities.

(4) The parents of 74 children with birth defects or who died after birth were requested to come again to our genetic counselling clinic with their children or medical documentation. Three of them did not come but were visited at home. The affected children or the documentation of their necropsies were checked thoroughly with the help of experts. Some minor anomalies, for example, umbilical hernia, and unrelated conditions, for example, bronchial asthma, were not taken into consideration.

Results and discussion

The couples' understanding and recollection of risks involved were evaluated in three different ways. Only 24·7% were able to state correctly the exact figures of specific risks. Of the consultands, 74·5% knew the order of magnitude of risk: minimal, <2%; low, 2 to 5%; moderate, 5 to 9%; high I, 10 to 19%; high II, 20 to 50%; and high III, >50%. Finally, 91·5% of consultands understood the final advice of the genetic counsellor.

Table 2 shows the number and percentage of counsellees evaluated (in general consultands) as well as the parental decisions about family planning and the number of pregnancies after genetic counselling in 15 nosological categories. Some 11·6% of consultands did not want another child when they came to our genetic counselling clinic. Their purpose was to enquire about diagnosis, treatment, prognosis of probands, etc. Of 1841 counsellees who wanted a child, 1253 consultands had 1416 pregnancies. Ninety-four of them were pregnant in the first quarter of 1979. The relatively high percentage of pregnancies in the sterility category is worth mentioning.

The parental decisions concerning further pregnancies are summarised in table 3. After advice I or II 95·3% of consultands wanted to have further children. This value exceeds the data of Carter *et al.*[3] It is difficult to say whether this is connected with the different method of counselling or with the difference of population. Following advice III 90·4% of consultands planned pregnancies. Within this group there is an interesting trend of deciding against further pregnancies according to the indications for prenatal diagnosis: amniotic α-fetoprotein because of a higher risk of neural tube defects, 4·5%; chromosome analysis because of a risk of chromosome aberrations, 12·1%; X linked disorders, 28·6%. After advice IV, 53 of 88 consultands (60·2%) did not want further pregnancies. Advice V was given to 60 counsellees and 37 consultands (61·7%) did not plan further pregnancies after genetic counselling. There is no significant difference in the rate deterred between advice IV and

TABLE 2 *Number of registered and evaluated counsellees and number of pregnancies after genetic counselling*

Nosological categories	*Registered No of cases*	*Evaluated No of cases*		*Counsellees who did not want more children*		*Counsellees/consultands who wanted further children*				*No of pregnancies after counselling*					*Pregnancy at the time of study*	*Evaluated No of pregnancies*
		No	*%*	*No*	*%*	*Pregnancy occurred*		*Pregnancy did not occur*		*1*	*2*	*3*	*4*	*Total*		
						No	*%*	*No*	*%*							
Mendelian conditions	414	327	79·1	71	21·7	49	15·0	207	63·3	188	18	0	1	228	11	217
Chromosomal aberrations	177	120	67·8	28	23·3	34	28·3	58	48·3	46	11	1	0	71	3	68
Multifactorial threshold model																
Congenital abnormalities	328	238	78·7	17	6·6	65	25·2	176	68·2	154	20	2	0	200	13	187
Common diseases	107	107	85·0	5	4·7	49	45·8	53	49·5	49	4	1	0	60	4	56
Mutagenic noxae	34	26	76·5	0	0·0	15	57·7	11	42·3	10	1	0	0	12	0	12
Consanguinity	33	27	81·8	0	0·0	14	51·9	13	48·1	10	2	1	0	17	4	13
Exogenic noxae during pregnancy	78	62	79·5	11	17·7	8	12·9	43	68·4	36	6	1	0	51	2	49
Congenital abnormalities caused by teratogenic and maternal noxae	186	149	80·1	0	0·0	0	0·0	149	100·0	149	0	0	0	149	0	149
Sterility	507	364	71·8	0	0·0	260	71·4	104	28·6	92	10	2	0	118	14	104
Fetal death	365	321	87·9	34	10·6	31	9·7	256	79·7	214	36	4	2	306	28	278
Early death	140	104	74·3	26	25·0	26	25·0	52	50·0	46	3	3	0	61	7	54
Defect (mental subnormality, etc)	69	51	73·9	16	31·4	7	13·7	28	54·9	23	5	0	0	33	1	32
Congenital abnormalities of unknown origin	116	87	75·0	20	23·0	8	9·2	59	67·8	54	5	0	0	64	6	58
Diseases without genetic origin	50	37	74·0	11	29·7	2	5·4	24	64·9	22	2	0	0	26	0	26
General information	50	42	84·0	2	4·8	20	47·6	20	47·6	20	0	0	0	20	1	19
Total	2654	2082	78·4	241	11·6	588	28·2	1253	60·2	1113	123	15	3	1416	94	1322

TABLE 3 *Parental decision after genetic counselling*

Advice	*No of consultands*	*Deterred (%)*	*Undeterred (%)*
Pregnancy was recommended (advice I–II)	1516	4·7	95·3
Pregnancy was recommended with prenatal diagnosis	177	9·6	90·4
Pregnancy required consideration	88	60·2	39·8
Pregnancy was not recommended	60	61·7	38·3

V. These deterred rates fit well with the data of Carter *et al.*[3] Another point is that from the 90 consultand females deterred 33 (36·7%) conceived as a result of failure of contraception or were pregnant when seeking genetic counselling. Within this group, however, in 28 cases (84·8%) the pregnancies were terminated.

The outcome of pregnancies after genetic counselling was evaluated in detail. In table 4 only those categories which showed a significant increase in different types of mortality are included. The normal rate of spontaneous abortions was raised in the categories of sterility and fetal death involving mainly habitual abortions. The 4·8% of extrauterine pregnancies is very high in the sterility category. The stillbirth rate increased significantly in the categories of fetal death (3·9%) and, particularly, early mortality (15·2%). After a previous 'early death' the rate of infant deaths was extremely high. 'Habitual' infant mortality seems to be a valid concept.

The evaluation of livebirths seems to be most important. The data regarding affected offspring (with birth defects, table 5) or infant death are summarised in the appendix. The main conclusions are as follows.

(1) After advice I, II, and III 4% of babies had congenital anomalies. Two of these were recurrences. Both consultands had a higher risk of neural tube defects, but the amniotic α-fetoprotein gave false negative or intermediate values. The remaining 37 congenital abnormalities (3·8%) do not seem to have a causal relationship with the previous disorders. They may be the manifestation of 'random' risk. In Hungary the registered prevalence of total congenital abnormalities is about 4%.

(2) After advice IV 19·4% of liveborn babies had inherited or congenital anomalies. These were a recurrence of coproporphyria (expected risk was 30%), a recurrence of lethal hydrops fetalis, a lethal valvular heart defect in the offspring of a diabetic female, unilateral cryptorchidism, and a sacrococcygeal tail-like appendage (the latter two are not considered as severe anomalies), as well as a case of microcephaly. The last case was an error. The aetiology of microcephaly was not identified in the proband and owing to the 6% recurrence risk of microcephaly with unknown aetiology advice IV was given. A second baby with microcephaly was delivered and thus these were cases of true microcephaly with autosomal recessive inheritance.

(3) After advice V 22 consultands had 23 livebirths, 19 of which were planned and three were not. Ten anomalies were found among these newborns, a 43·5% affected rate (table 6). Taking only those

TABLE 4 *Percentage values of pre- and postnatal mortality after genetic counselling*

Mortality	*Spontaneous abortions**		*Extrauterine pregnancies**		*Stillbirths†*		*Infant deaths‡*	
	No	*%*	*No*	*%*	*No*	*%*	*No*	*%*
Sterility	26	23·1	3	4·8	1	1·3	1	1·4
Fetal death	71	25·9	0	—	8	3·9	5	2·6
Early death	7	13·2	0	—	7	15·2	8	20·5
National value	—	12–14	–	0·4	–	0·8–0·9	–	3·0

*Percentage was calculated on all unterminated pregnancies.
†Percentage was calculated on total births.
‡Percentage was calculated on livebirths.

TABLE 5 *Proportion of malformed children born after genetic counselling*

Advice	*No of livebirths*	*Inherited or congenital anomalies*	
		No	*%*
Pregnancy was recommended (advice I, II, III)	975	39	4·0
Pregnancy required consideration	31	6	19·4
Pregnancy was not recommended	23	10	43·5

TABLE 6 *Disease of proband and recurrence after genetic counselling when family planning was not suggested*

Proband	*Diagnosis*	*Aetiology*	*Risk (%)*	*Recurrence*
Sib	Cystic fibrosis	AR	25	Cystic fibrosis*
Sib (3)	Cirrhosis, hepatis	AR	25	Cirrhosis, hepatis*
Sib	Erythroblastosis fetalis	AD	100	Erythroblastosis fetalis*
Sib	Cystic fibrosis	AR	25	Cystic fibrosis
Sib	Werdnig-Hoffmann disease	AR	25	Werdnig-Hoffmann disease*
Mother	Osteogenesis imperpecta, type I	AD	50	Osteogenesis imperfecta
Sib (2)	Werdnig-Hoffmann disease	AR	25	Werdnig-Hoffman disease (not planned)*
Sib (3)	Ellis-van Creveld disease	AR	25	Renal agenesis*
Sib	Polycystic kidney, infantile type I	AR	25	Dextrocardia,* hip dislocation
Mother	Heart defect, thrombophlebitis with oral coagulant and other drugs	Ter+Mat	20	Complex heart defect, anal atresia*

*Death
Ter=teratogenic noxa
Mat=maternal noxa
AR=autosomal recessive
AD=autosomal dominant

with risks of Mendelian disorders, 17 consultands had 18 livebirths (15 planned and three accidental) and nine of them (50%) were affected seriously (six died). Two of them, however, were not aetiologically related to the previous disorders. The tenth pregnant woman had an approximately 20% risk from her disease and treatment. The remaining four consultands from three categories (Mendelian conditions, 2; mutagenic noxae, 1; exogenic noxae during pregnancy, 1) had healthy babies. The affected rate was significantly higher after advice V than after advice IV.

(4) Forty infant deaths occurred. The general occurrence (3·9%) does not considerably exceed the Hungarian average (about 3% in the 1970s). The backgrounds of 14 and seven infant deaths are shown in tables 4 and 6, respectively. Excluding four single cases, a further seven, four, two, and two infant deaths were registered in the categories of multifactorial congenital abnormalities, Mendelian conditions, chromosomal aberrations and exogenic noxae during pregnancy, respectively. The majority of these babies died in the first week (65%), and 37·5% in the first day. The presence of 15 instances of congenital abnormality in association with infant death, however, was twice as high (37·5%) as in the national statistics (17 to 21%).

(5) Prenatal diagnosis can be of value in supplementing genetic counselling. Two neural tube defects and two chromosome aberrations were diagnosed in utero. They probably lowered the total birth prevalence of congenital abnormalities by 7%. Of 111 consultands with a recurrence risk of neural tube defects four had anencephaly or spina bifida cystica (3·6%).

(6) Uncertainty in diagnosis may considerably influence the reliability of genetic counselling. In the Mendelian category the recurrence was 1·9% after advice I, II, and III. The recurrence of congenital abnormalities with unknown aetiology, however, was found to be 8·9%. The difference is nearly five-fold. Unknown aetiology caused several problems in fetal and early death categories too. Three healthy newborns of healthy parents without any electrocardiographic anomalies, after a normal pregnancy, delivery and early development, unexpectedly died in the fourth month of age. The diagnosis was cardiac insufficiency. The possibility of inborn errors of metabolism was excluded. Finally idiopathic familial cardiomyopathy was suggested. This has an autosomal dominant inheritance and these cases obviously suggest recessive inheritance.

(7) The empirical risk figures for congenital anomalies in the categories of sterility, fetal death, and infant death were 5·4% (4/54), 3·1% (6/195), and 10·3% (4/39), respectively. The registered prevalence of total congenital anomalies is about 4% in Hungary. The final evaluation of common diseases with multifactorial aetiology is not yet possible owing to their late onset.

Our experience confirms the importance and efficacy of genetic counselling in general. Furthermore, the significantly higher rate undeterred after counselling of low risk and the same rate deterred after counselling of moderate and high risk seem to prove some advantage of the information-guidance type of genetic counselling in our community.

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APPENDIX *Affected or dead offspring born after genetic counselling*

Ref No	*Proband*	*Advice (specific risk)*	*Outcome of pregnancies after genetic counselling*
MENDELIAN DISORDERS			
110/974	Son 11.7.1973 (19.11) cystic fibrosis	V (25%)	Son 23.12.1975 (14.6.1979) *cystic fibrosis*
143/975	Consultand female, 2.2.1953, coproporphyria. (Sister, mother, grandmother also had coproporphyria)	IV (30%)	Son 4.7.1975, *coproporphyria* Son 26.7.1977, not affected
635/975	Daughter 13.4.1969 (5.5) Son 16.9.1970 (26.9) Son 7.7.1973 (14.9), cirrhosis of liver occurred in all probands	V (25%)	Son 15.6.1977 (5.9) *cirrhosis of liver*
825/975	Daughter 21.3.1974, Willebrand (parents not affected)	I (0%)	Daughter 31.3.1976 (31.3), immaturity (1800g), haemorrhagic diathesis (?)
848/975	Son 12.4.1973 (16.4) Daughter 12.11.1974 (12.11), erythroblastosis fetalis caused by Rh blood group incompatibility in mother-fetus (occurred in both probands)	V (100%)	Daughter 24.4.1976 (24.4), *erythroblastosis fetalis*
67/976	Son 25.7.1974 (8.7), cystic fibrosis	V (25%)	Son 29.6.1978, *cystic fibrosis*
429/976	Son 30.1.1975, icterus gravis caused by Rh blood group incompatibility in mother-fetus (father heterozygote) Th: plasmapheresis	IV (50%)	Daughter 7.8.1977 (9.8), immaturity (1650g)
463/976	Son 29.11.1975 (29.6.1976), Werdnig-Hoffmann	V (25%)	Son 26.1.1978 (24.11), *Werdnig-Hoffmann*
622/976	Son 1.1.1976 (25.6), polycystic kidney, infantile type I	V (25%)	Daughter 27.6.1977, dextrocardia + congenital dislocation of hip
634/976	Mother 2.9.1950, osteogenesis imperfecta type I	V (50%)	Son 29.9.1976, *osteogenesis imperfecta type I*
1062/976	Daughter 15.3.1972, retinoblastoma 1d (parents not affected)	I (<3%)	Daughter 31.3.1977 (1.4), immaturity (1120g), RDS
1116/976	Son 12.8.1976 (12.8), hyperbilirubinaemia (1850g), presumed Rh incompatibility was excluded	I (0%)	Son 9.4.1977 (13.4), immaturity (850g) Daughter 17.11.1978 (19.11), oesophageal atresia
1212/976	Daughter 17.8.1971 (28.8) Son 3.7.1972 (3.7) Son 6.11.1975 (25.1.1976), new 'cardiodigital' or Ellis-van Creveld syndrome (parents not affected) in all probands	V (25%)	Son 5.4.1978 (5.4), renal agenesis lu Son 14.4.1979, not affected
65/1977	Daughter 8.12.1974, hypothyroidism	IV (25%)	Son 26.1.1978, cryptorchidism ld
881/977	Son 29.1.1976 (21.3) Son 13.4.1977 (26.5), Werdnig-Hoffmann in both probands	V (25%)	Daughter 29.9.1978 (6.3.1979), *Werdnig-Hoffmann* (unplanned pregnancy with IUD: decision for adoption)
CHROMOSOME ABERRATIONS			
93/974	Son 6.2.1974, Down syndrome	I (1%)	Son 8.5.1978, hypospadias
115/975	Son 1.12.1965, Down syndrome	I (1%)	Son 9.6.1975 (6.12), pneumonia
454/975	Consultand female, 15.10.1941, carrier of balanced reciprocal translocation (46,XX,t (4p;10q), 4 miscarriages (1963, 1964, 1964, 1967)	III (15%)	Daughter 12.1.1977 (12.1), immaturity (800g)
COMMON ISOLATED CONGENITAL ABNORMALITIES WITH MULTIFACTORIAL AETIOLOGY			
1/974	Daughter 4.2.1966 (4.2), anencephaly	III (4%)	Son 5.6.1974 (5.6), immaturity (1200g), RDS Son 13.4.1975 (21.12), birth trauma + pneumonia
56/975	Son 12.10.1969, congenital dislocation of hip	II (12%)	Daughter 1.7.1975, heart defect (valvular) Son 24.5.1977, not affected
142/975	Son 14.10.1974 (16.10), spina bifida cystica (new marriage)	III (2%)	Son 26.6.1978 (4.9), perinatal brain hypoxia, pneumonia
350/975	Daughter 6.5.1974, coarctation of aorta	I (2%)	Daughter/daughter 7.10.1978, (A) not affected; (B) congenital inguinal hernia
377/975	Son 22.2.1970 (25.2), spina bifida cystica	III (4+5%)	Son 2.10.1975, not affected Daughter 28.4.1977 (29.4), immaturity (1100g)
479/975	Daughter 12.2.1970, stillborn, anencephaly	III (4%)	Son 8.6.1978, congenital dislocation of hip
14/976	Son 14.2.1973 (15.2), spina bifida cystica Daughter 15.11.1974, congenital dislocation of hip	III (4+13%)	Son 14.5.1976 (16.5), RDS (2350g), perinatal brain hypoxia, pneumonia
24/976	Son 10.10.1975, atrial septal defect type II	I (3%)	Daughter 22.7.1977, congenital dislocation of hip
114/976	Daughter 19.10.1975 (29.10), spina bifida cystica	III (4%)	Son 29.11.1976, cryptorchidism lu
196/976	Daughter 31.8.1973, stillborn with unknown aetiology Son 3.9.1974 (10.9), spina bifida cystica	III (6%)	Son 7.9.1976, not affected Son 20.6.1977 (20.6), RDS (1900g)
410/976	Daughter 10.6.1970 (13.6), spina bifida cystica, Son 27.8.1972, perinatal brain hypoxia with convulsions	III (4+5%)	Daughter 29.12.1976, low birthweight (1900g); she did not speak in July 1979
532/976	Consultand female, 9.11.1954, spina bifida occulta (sister died of spina bifida cystica)	III (2%)	Son 28.12.1976, *spina bifida cystica* [1. AFP value was 50μg/ml in blood contaminated amniotic fluid. 2. AFP value was 140μg/ml in blood contaminated amniotic fluid. Ultrasound did not show any alteration, the pregnancy was in the 22nd week, the consultands did not want to terminate pregnancy.]
670/976	Son 22.9.1974 (2.12), cleft lip and palate	II (5%)	Son 25.2.1978, Down syndrome with cleft lip and palate

APPENDIX—*continued*

Ref No	*Proband*	*Advice (specific risk)*	*Outcome of pregnancies after genetic counselling*
425/977	Daughter 7.2.1975 (18.10), spina bifida cystica	III (4%)	Son 29.10.1977, not affected Daughter 2.12.1978, congenital dislocation of hip
453/977	Son 20.10.1976 (19.4.1978), spina bifida cystica	III (4%)	Daughter 18.11.1977, not affected Son 24.11.1978, posterior cleft palate
924/977	Son 2.12.1976, spina bifida cystica	III (4%)	Son 26.11.1978 (29.11), *spina bifida cystica* (amniotic AFP value was 21μg/ml, ie normal)
COMMON DISEASES WITH PRESUMABLY MULTIFACTORIAL AETIOLOGY			
359/976	Consultand female 8.6.1948, polyarthritis rheumatica (Th: indomethacin, gold, prednisolone, Rheosolon, Chlorferit)	II (5%)	Son 9.6.1977, congenital inguinal hernia
390/976	Consultand female 28.3.1953, diabetes mellitus	IV (8%)	Son 23.1.1976 (23.1), heart defect (valvular)
ENVIRONMENTAL NOXAE DURING PREGNANCY			
87/975	Pregnant. Contraceptive pills in first 4 weeks of pregnancy	I (1%)	Daughter 14.8.1976, congenital dislocation of hip
111/975	Pregnant. Rubella virus infection (previous infection was proved)	II (0%)	Son 4.8.1975 (1.5.1976), Down syndrome
34/976	Pregnant, had acquired heart (bicuspidal) defect and had oral anticoagulant and cardial drug treatment	V (20%)	Daughter 14.3.1978 (12.12), complex heart defect with anal atresia
715/976	Pregnant. Rubella virus infection (previous infection was proved)	II (0%)	Son 22.2.1977, perinatal brain damage, hypotonic paresis in lower limbs
806/976	Pregnant. Diagnostic chest and abdominal *x*-ray examination on 12th day of pregnancy	I (<1%)	Son 16.3.1977, spina bifida cystica
31/977	Pregnant. Contraceptive pills in first 8 weeks of pregnancy	I (1%)	Daughter 11.5.1977, low birthweight (2400g), somatic retardation
190/977	Pregnant. Herpes simplex type II (caesarean section was suggested and performed)	II (0%)	Son 8.8.1977, aortic stenosis
CONGENITAL ABNORMALITIES CAUSED BY ENVIRONMENTAL FACTORS			
118/974	Daughter 11.5.1974 (13.5), connatal toxoplasmosis	I (0%)	Son 20.8.1976, not affected Daughter 15.7.1977 (16.7), immaturity (1400g), RDS
283/976	Daughter 3.4.1974 (3.4), transverse lower limb reduction ld and immaturity (1400g).	II (0%)	Son-son 6.2.1977, (A) not affected, (B) immaturity (1300g)
STERILITY			
416/976	Consultand female 14.8.1952. Type I. Anovulation. Th: ovulation induction	II (<5%)	Miscarriage (10th week), 23.4.1977 Son 29.7.1978, aortic stenosis
318/977	Consultand male 7.11.1949. Type I. Hypospermia. Th: hormone stimulation	II (<5%)	Son 15.12.1977, structural talipes equinovarus ld
404/977	Consultand male 31.8.1947. Type I. Aspermia. AID	II (0%)	Son 5.9.1978, postural deformity of lower limb ld
779/977	Consultand female 5.1.1955. Type II. Salpingitis. Th: antibiotics and perhydration	II (<5%)	Daughter 15.6.1978 (15.6), immaturity (500g)
893/977	Consultand female 7.2.1953. Type I. Anovulation. Th: ovulation induction	II (<5%)	Son 25.12.1978 (15.4.1979), transverse upper limb reduction ls and anal atresia
PREVIOUS FETAL DEATH			
95/974	Consultand female, 2 (2nd month) miscarriages in 1973 and 1974. Parents had normal karyotypes	II (26%)	Daughter 25.9.1975 (27.9), complex heart defect Miscarriage (1st–2nd month), 3.6.1977 Miscarriage (1st–2nd month), 11.11.1977 Miscarriage (1st–2nd month), 14.5.1978
99/975	Consultand female, 3 (4th–5th month) miscarriages in 1970, 1972, and 1974, as well as an unaffected son on 23.3.1973. Parents' karyotypes are normal. Owing to suspected cervical incompetency cerclage operation was performed	II (<5%)	Daughter 28.9.1978 (29.9), immaturity (900g)
114/975	Consultand female, 4 (2nd–4th month) miscarriages in 1970, 1971, 1972, and 1974. Parents had normal karyotypes	II (40%)	Son 14.5.1977 (14.5), multiple abnormalities (polycystic kidney ls, exomphalos, agenesis ani and coli transversi, spina bifida cystica = extrophia cloacae (?))
117/975	Consultand female, 3 (4th–6th month) miscarriages in 1971, 1972, and 1974. Parents are healthy, their karyotypes are normal	II (32%)	Son 30.3.1970, multiple abnormalities (chorioretinitis ld, congenital inguinal hernia ld)
17/976	Consultand female, 4 (3rd–4th month) miscarriages in 1972, 1972, 1973, and 1975; furthermore she delivered a son with Little disease on 20.12.1967 (7.11.1974). Parents are healthy with normal karyotypes	II (40%)	Son 30.5.1976, Little disease (2900g) with unknown aetiology
215/976	Consultand female, 3 (2nd month) miscarriages in 1973, 1974, and 1975 owing to corpus luteal insufficiency. Th: hormone substitution	II (<5%)	Daughter 28.4.1978, congenital dislocation of hip
218/976	Consultand female, 3 (1st–2nd month) miscarriages in 1971, 1973, and 1976. Father had severe occupational lead exposure presumably causing pathospermia: changing of job was suggested	II (<5%)	Son 9.12.1976, congenital inguinal hernia ls
650/976	Consultand female, one miscarriage (3rd month) owing to hypoplasia uteri. Th: hormone substitution	II (<5%)	Daughter 20.7.1978 (22.7), low birthweight (2140g), RDS (Miscarriage (3rd–4th month) 15.5.1979)

APPENDIX—*continued*

Ref No	*Proband*	*Advice (specific risk)*	*Outcome of pregnancies after genetic counselling*
856/977	Consultand female, 3 (5th month) miscarriages from two marriages in 1968, 1975, and 1976. Owing to cervix incompetency cerclage operation was performed	II (<5%)	Son 1.2.1978 (7.2), *immaturity* (1800g), RDS, pneumonia,
PREVIOUS EARLY DEATH			
439/975	Son 4.2.1973 (12.3.1975), repeated infections (otitis, meningoencephalitis, sepsis)	II (<5%)	Son 22.12.1975 (9.2.1977), repeated infections, finally *sepsis*. (Immunodeficiency?)
452/975	Son 20.8.1973 (22.8), immaturity (600g) Daughter 12.1.1975 (stillborn) (500g). Owing to cervix incompetency cerclage operation was performed	II (<5%)	Son 11.5.1977 (12.5), *immaturity* (1250g), RDS
617/975	Son 30.9.1972 (12.2.1973), pneumonia Son 3.1.1974 (7.5), pneumonia, heart defect (?)	I (3%)	Daughter 25.2.1978 (22.6), after uncomplicated pregnancy healthy baby of 3000g birthweight was born. After normal development the infant died in the 4th month with signs of *cardiac insufficiency*. (Autosomal recessive syndrome?)
654/975	Son 25.5.1972 (26.5), placenta praevia (1850g), perinatal brain damage. Consultand female had 2 miscarriages (2nd–3rd month) in 1972 and 1975; healthy parents with normal karyotype	II (26%)	Son 18.7.1976, congenital inguinal hernia ld Son 10.11.1977, not affected
658/975	Son 29.4.1968 (stillborn) (1500g), hydrops fetalis Daughter 21.8.1969 (21.8) (2800g), hydrops fetalis. Blood group of mother is B, Rh+. Parents are healthy. Hyperemesis gravidarum.	IV (25%)	Son 29.12.1978 (29.12) after hyperemesis gravidarum *hydrops fetalis* (1850g)
798/975	Daughter 3.8.1974 (6.8), placenta praevia, immaturity (900g), RDS Miscarriage(boy) (4th month) in 1975 Parents had normal karyotypes	II (26%)	Miscarriage (4th month), 21.10.1976 Daughter 17.9.1978 (20.9), immaturity (800g)
202/1976	Daughter 26.9.1968 (2.10), immaturity (900g) Daughter 29.7.1969 (30.7), immaturity (1100g) Son 20.4.1973 (stillborn 1979) Miscarriage (1971), cervix incompetency, cerclage	II (<5%)	Son 15.3.1978 (7.10), not affected, later ileus and peritonitis
661/976	Daughter 19.6.1975 (19.6), immaturity, (900g); the consultand female had 3 miscarriages (4th–5th month) in 1971, 1972, and 1975 owing to cervix incompetency. Cerclage	II (<5%)	Daughter 5.6.1978 (5.6), immaturity (1050g), RDS
922/976	Son 13.5.1973 (16.5), 3500g, perinatal brain damage Son 27.3.1975 (30.3), 3050g, RDS	II (5%)	Daughter 6.2.1978 (9.2), healthy newborn (3140g) died on 3rd day of life owing to RDS (?). (Coagulopathia?)
125/977	Son 29.10.1976 (12.11), perinatal brain damage	I (<1%)	Daughter 21.9.1977, ventricular septal defect (spontaneous closure)
HANDICAPPED PERSONS			
277/976	Consultand male 5.8.1948, Little disease	I (0%)	Son 30.12.1976, anal atresia
778/976	Daughter 1.12.1974, Little disease	I (0%)	Son 15.12.1978 (1.4.1979), cleft lip with cleft palate and complex heart defect
CONGENITAL ABNORMALITY WITH UNKNOWN AETIOLOGY			
411/1975	Daughter 29.4.1973 (29.4), multiple abnormalities (atrial septal defect type I, stenosis urethrae)	I (5%)	Daughter 1.12.1975, congenital dislocation of hip Daughter 15.6.1977, postural deformity of lower limb ld
728/976	Son 6.4.1975, microcephaly (46,XY)	IV (6%)	Son 26.3.1977, *microcephaly*
104/977	Son 25.3.1977 (26.3), diaphragmatic hernia	IV (10%)	Daughter 6.2.1979, sacrococcygeal tail-like appendage
GENERAL			
423/976	The proof of maternity since the baby of consultand couple may have been exchanged by mistake for another one in hospital	I (0%)	Son 10.3.1979 (5.5), multiple abnormalities (complex heart defect and biliary atresia)
916/977	No problem	I (0%)	Daughter 21.11.1978, perinatal brain damage, RDS

(The date of death is written in brackets. Specific recurrence is marked by being italicised. The possible specific recurrence is shown by dotted line. Th=therapy, RDS=respiratory distress syndrome.)