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Carrier Testing and Prenatal Diagnosis for Hemophilia: Experiences and Attitudes of 549 Potential and Obligate Carriers

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Experiences with and attitudes toward carrier testing and prenatal diagnosis were evaluated among 549 potential and obligate carriers of hemophilia. Almost everybody considered carrier testing to be useful. Forty-nine percent had been tested for carriership, 10% had only received limited information, and 41% had not been tested and had never received information about the heredity of hemophilia. More married women, women with severe hemophilia in their family, and women closely related to a patient with hemophilia had been tested for carriership than others. Lack of information about the probability of carriership for female relatives and a similar ignorance of the possibility of carrier testing were important reasons for not having been tested. Eleven percent of the women with one or more children had undergone prenatal diagnosis in the past. Thirty-one percent of the study population would favour prenatal diagnosis with the implication of a potential abortion in early pregnancy and half of them would choose this option even in late pregnancy. Most of the women who objected to prenatal diagnosis did so because they did not consider hemophilia to be a sufficiently serious disorder to justify an abortion.

KEY WORDS: genetic counseling, reproductive behavior, termination of pregnancy

INTRODUCTION

Improvements in the treatment of hemophilia over the past 20 years have changed the life of hemophiliacs

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considerably. Hemorrhages are treated with concentrated blood products and home treatment and prophylactic treatment have been introduced. As a consequence life expectancy has increased to 66 years and future generations are expected to suffer less disability [Smit et al., 1989; Rosendaal et al., 1989]. However, for many patients hemophilia is still a serious disease because of arthropathy and complications of treatment like viral infections (hepatitis, human immunodeficiency virus) and inhibitor development. Seventeen percent of Dutch hemophiliacs became HIV-seropositive in the years prior to 1985 [Rosendaal et al., 1988]. In 1985, donors belonging to a risk group for AIDS were requested to withdraw. Furthermore, screening of blood donations and heat treatment of blood products were introduced in 1985. These measures substantially reduced the risk of infection.

During the same period, developments in clinical genetics have offered the female relatives of hemophiliacs the opportunity of attaining more certainty about their progeny. In the Seventies a more reliable method based on pedigree analysis and clotting factor VIII or IX assays became available by which 70 to 80% of potential carriers could be informed of a probability of carriership lower than 5% or higher than 95% [Akhmeteli et al., 1977; Green et al., 1986]. In 1984 it became possible to ascertain the carrier status by means of DNA analysis [Giannelli et al., 1984; Harper et al., 1984; Bröcker-Vriends et al., 1985, 1987]. At present restriction fragment length polymorphism analysis is informative for most of the potential carriers. In combination with coagulation assays, DNA analysis now offers more certainty to more of the women at risk [Bröcker-Vriends et al., 1987].

Prenatal diagnosis for hemophilia has been available since 1970 and was at first restricted to amniocentesis in the 16-18th gestational week to determine the sex of the fetus. In 1979 it became possible to sample fetal blood and to measure fetal clotting factors. This procedure can only be performed in the 18-20th week of pregnancy in specialized centers. Since 1985 prenatal diagnosis in the 8-10th week has become possible by chromosome analysis and, if the fetus appears to be male, DNA analysis of chorion villi [Bröcker-Vriends et

al., 1988] is available. Prenatal diagnosis in the first trimester of pregnancy implies a shorter period of uncertainty for the couple. Also, termination of pregnancy in the case of an affected fetus may be physically and emotionally less demanding at this stage.

Several studies have been conducted on the experience of female relatives of hemophiliacs with genetic counseling, carrier testing or prenatal diagnosis [Markova et al., 1984, 1986; Evans and Shaw, 1979; Barrow et al., 1982; Miller et al., 1987; Kraus and Brettler, 1988; Ljung et al., 1987; Beeson and Golbus, 1985; Francis and Kasper, 1983; Lubs and Falk, 1977]. Most of these studies focused on reproductive behaviour and attitudes toward prenatal diagnosis. They show varying results regarding attitudes toward prenatal diagnosis, although generally the majority of respondents were opposed to it. Lubs and Falk [1977], in addition, examined the use of genetic counseling and carrier testing. They contacted the female relatives of hemophiliacs through patients and patients' associations and found that less than half of the female relatives had received genetic counseling, with the exception of mothers of patients. A disadvantage of many of the above-mentioned studies is that they have been conducted on women who were registered at hemophilia treatment centers [Markova et al., 1984, 1986; Evans and Shaw, 1979; Barrow et al., 1982; Miller et al., 1987; Kraus and Brettler, 1988], a coagulation laboratory [Ljung et al., 1987], or a department of obstetrics [Beeson and Golbus, 1985]. The samples in these studies were often small and the fact that many of the respondents in these studies were mothers of a hemophilic son implies a bias.

In our article results will be presented on a survey among a large group of female relatives of hemophiliacs in The Netherlands. These potential and obligate carriers were contacted through patients. The aim of the study was to assess knowledge of, attitudes toward, and the use of carrier testing and prenatal diagnosis. We also assessed the influence on these parameters of marital status, parenthood, severity of hemophilia in the family, and family relation to the nearest patient in the family.

PATIENTS AND METHODS

Subjects

The number of hemophilia patients in The Netherlands is estimated to be between 1,200 and 1,300 [Rosendaal et al., 1989]. Eleven hundred and sixty-two registered patients were requested to supply us with the addresses of their mothers, daughters, sisters, and maternal aunts. Half of the patients sent us the addresses of some or all of these female relatives. Elder sisters and aunts were asked to give us the addresses of their daughters. In this way we acquired a list of addresses of mothers, sisters, daughters, aunts, cousins, and nieces. Women in the age group from 18 to 38 years were selected in order to include most of the women for whom carrier testing and prenatal diagnosis may be relevant or may have been relevant in recent years. In 1987, the women selected ($n = 654$) were sent a letter of introduction which explained the purpose of the survey. Two weeks later they received a standardized mail question-

naire. This procedure was approved by the Medical Ethics Committee of the University Hospital, Leiden.

At the time of the survey we also performed another study among 114 possible carriers of hemophilia. The purpose of that study was to evaluate the contents and effects of genetic counseling and carrier testing given at the University Hospital of Leiden. Thirty-one of these 114 women were also on the list of addresses we gathered via the hemophiliacs. For reasons of representativeness, the data on these 31 women have been included in this study. This was possible because the studies were to a large extent overlapping. However, some detailed questions were not asked to these 31 women.

Five hundred and seventy-nine questionnaires were returned. Thirty were excluded from analysis because the respondents did not meet the age-limit criterion (14), questionnaires were not filled in (4) or not completed (9), or for other reasons (3). Disregarding the respondents who were too young or too old, the response rate was 86%.

Two methods were used to estimate how many of the female relatives of hemophiliacs in The Netherlands participated. The evaluative study mentioned above comprised 97 women in the age group 18 to 38 years. If we had reached 100% of the potential and obligate carriers in The Netherlands, these 97 women would have been listed in our file of addresses. The overlap was 31 addresses which means that, at most, one third of all potential and obligate carriers were on our mailing list.

The other method is based on a demographic assumption on the number of female relatives of hemophiliacs. Here we restrict ourselves to one subgroup of female relatives, the sisters, and take the group of hemophiliacs aged 18-38 years as a starting point. Four hundred and twenty-eight hemophiliacs in this age group participated in a Dutch survey that was estimated to cover ± 75 percent of the Dutch hemophiliacs [Rosendaal et al., 1989]. Thus, there were ± 571 hemophiliacs aged 18-38 years in The Netherlands. Based on the assumption of 1.5 sisters in a sibship for this age-group (Central Bureau of Statistics, Department of Population Statistics, unpublished figure), the number of sisters aged 18-38 years was expected to be ± 857 . In our survey 235 sisters participated which means that ± 27 percent of this subgroup was covered. Assuming a coverage that is about the same for the other subgroups, we estimated that about a quarter of the total group of potential and obligate carriers was covered by our survey.

Concepts and Measurement Instruments

It is important to distinguish between the concepts of genetic counseling, information about hereditary diseases, and carrier testing. Methodological considerations dissuaded us from paying attention to the question of whether or not the respondents had received genetic counseling; neither did we try to evaluate genetic counseling as provided to the respondent. Genetic counseling has developed over the past decades from an incidental activity of physicians to a medical specialty with specified subject matters, procedures, and objectives. Given this professional development, and given the way we

contacted female relatives, through patients and not through departments of clinical genetics or hemophilia centers, answers on the question of whether or not genetic counseling was received were considered difficult to interpret. The respondents were classified into three groups: 1) women who had been tested for carriership, 2) women who had not been tested, but who were informed by a physician about the heredity of hemophilia, and 3) women who had not been tested and who never were informed about the heredity of hemophilia.

Many respondents were related to more than one patient. To establish the family relation to the nearest patient we employed the following order of proximity: mother, sister, daughter, aunt, niece (daughter of sister), and cousin (daughter of aunt).

Twenty-three statements were phrased about hemophilia, the heredity of hemophilia, and about the present facilities of carrier testing and prenatal diagnosis, to test the knowledge of the respondents. They were asked whether they agreed or disagreed with the statements, half of which were formulated incorrectly. For every right answer a score of 1 was assigned, after which the total score was calculated.

The respondents were asked whether or not they considered a termination of pregnancy acceptable in a series of different circumstances. The answers were analysed by Mokken scale analysis [Mokken, 1971], the purpose of which was to analyse whether it was possible to arrange the circumstances from more to less acceptable; this means that a positive answer for a "less acceptable" circumstance implies a positive answer for a "more acceptable" circumstance. The scalability coefficient *H* was .54, which means that the items, as formulated in Table VIII, form a "strong" hierarchical scale; the reliability coefficient *r* was .77.

RESULTS

General Characteristics

Table I shows the general characteristics of the surveyed population. The distribution according to the severity of hemophilia in the family is nearly the same as the distribution according to the severity found in the population of hemophiliacs who formed the basis of the survey population. Two thirds of the women were familiar with hemophilia because they had a close relative (a father, a brother, or a son) with hemophilia. The others had a further removed relative (an uncle, a cousin, or a nephew) with hemophilia. More than half of the respondents were married but less than half had children.

Carrier Testing and Knowledge

Forty-nine percent of the respondents had been tested for carriership. Another 10% were not tested but were informed by a physician about the heredity of hemophilia, and 41% had not been tested and were never informed. However, more than 95% of the respondents considered carrier testing useful.

Information about the heredity of hemophilia, whether or not in combination with carrier testing, was given in more than half of the cases by the hematologist or pediatrician at the hemophilia center. One third were

TABLE I. General Characteristics of the Survey Population (n = 549)

	%
Severity of hemophilia in the family,	
Severe	40
Moderately severe	21
Mild	39
Family relation to nearest patient,	
Mother	12
Sister	39
Daughter	14
Aunt	8
Niece	11
Cousin	17
Marital status,	
Unmarried	46
Married/divorced/widowed	54
Children,	
Yes	41
No	59

informed by clinical geneticists and a small minority by general practitioners.

The age at which women were tested for carriership varied from 2 to 37 years and was 20 years on average. Twenty-three percent were tested before age 15 years. A relatively large group of these women, about 45%, stated that, notwithstanding the carrier detection test, they had not received information about the heredity of hemophilia. Half of the women tested had been tested more than 10 years before this survey.

The knowledge of the respondents about hemophilia, the heredity of hemophilia, and the present facilities for carrier testing and prenatal diagnosis was assessed for women who had been tested and women who had not been tested (Table II). The minimum scores for the scales were zero, but we have to bear in mind that a score halfway through the range could easily be obtained by a respondent who knew nothing about the subject. Table II shows small but statistically significant differences between the two groups. Some misconceptions were

TABLE II. Knowledge About Hemophilia, the Heredity of Hemophilia, and Carrier Testing and Prenatal Diagnosis for Women Who Were Tested for Carriership and Women Who Were Not Tested (One-Tailed Test)

	Mean score		T-Test	
	Carrier test (n = 240)	No carrier test (n = 277)	T	P
Knowledge of Hemophilia (range 0-8)	6.3	5.4	7.7	<.0005
Heredity of hemophilia (range 0-8)	6.6	6.1	4.3	<.0005
Present facilities of carrier testing and prenatal diagnosis (range 0-7)	6.0	5.6	3.5	<.0005

found to be widespread, even among the women who had been tested. Many women *believed* that:

- A small cut on a finger is dangerous for a hemophiliac.
- The severity of hemophilia within a family may vary from one patient to another.
- The likelihood of carriership for a niece or cousin of a hemophiliac is less than 1 in 100.
- The daughter of a hemophiliac is not necessarily a carrier.

Factors Influencing the Use of Carrier Detection Tests

Table III shows the association between carrier testing and four independent variables. Married women, women with children, and women related to patients with severe hemophilia had been tested more often than others. When the patient was a relative in the first degree or the son of a sister, at least half of the women had been tested. When the nearest patient was an uncle or a cousin, only 27 and 19% had been tested, respectively. Table III shows the situation concerning marital status, parenthood, and family relation at the time of the study. It is possible that at the time of carrier testing, some women were not yet married or had no children, whereas their situation has changed in the meantime. Also, it is possible that the "nearest" patient was "more distant" and that a hemophilic son or nephew was born afterwards. This means a slight overestimation of the percentage who had carrier testing in the group of married women and mothers and a slight underestimation for the group of cousins and nieces and either is possible for the group of aunts.

Half of the women were not tested for carriership. Forty percent of them planned to be tested in the future, 35% thought they might have the test later, and 26% did

not intend to apply for testing. About a quarter of these untested women stated that they had not known about the possibility of carrier detection tests until they received our questionnaire. Ignorance of the facilities for carrier testing was associated with family relation to the nearest patient: the "more distant" relatives were less often acquainted with it (Table IV). The respondents who were acquainted with the possibility of carrier detection tests were asked to mark one or more reasons why they had not been tested. The following reasons were given most often:

- I intend to have the test, but I haven't got to it yet (68).
- I will apply for testing when I am older (39).
- I will apply for testing when I start a family (16).
- I think that I am not a carrier (18).
- I am an obligate carrier (16).
- I do not know where I can have a carrier detection test (15).

It appeared that for 18 women the reason for not having a carrier detection test was the conviction that they were not a carrier. For others the idea that carriership was unlikely could have been a factor. Table V shows the assessments of the probability of carriership made by the women who had not been tested. About 40% of this group did not give an estimation of their probability of carriership in percentages. If they did, it appeared that they often under- or overestimated their prior probability of being a carrier. For instance about 40% of the daughters of hemophiliacs in this group did not know that they were obligate carriers and almost 40% of the untested cousins estimated their probability of being a carrier to be less than 5% or even less than 1%.

Prenatal Diagnosis

The women who had no experience with prenatal diagnosis for hemophilia were asked their opinion on termination of pregnancy because of hemophilia. Half of the women were found to be opposed to abortion. When hemophilia in the family was more severe, fewer women were opposed to abortion (Table VI). We also analysed whether or not there was an association between the attitude toward abortion and the probability of being a carrier. The analysis was restricted to women tested for carriership; they were divided into three categories: probably/sure a carrier, perhaps a carrier, and probably/

TABLE III. The Use of Carrier Detection Tests Associated With Marital Status, Parenthood, Severity of Hemophilia, and Family Relation to the Nearest Patient*

	Carrier detection test		
	Yes, %	No, %	Total (n)
Marital status			
Unmarried	39	61	(255)
Married/divorced/widowed	58	42	(293)
Children			
No children	41	59	(323)
Children	62	38	(222)
Severity of hemophilia			
Severe	59	41	(211)
Moderately severe	54	46	(113)
Mild	40	60	(203)
Family relation to nearest patient			
Mother	70	30	(64)
Sister	62	38	(210)
Daughter	50	50	(74)
Aunt	53	47	(43)
Niece	27	73	(62)
Cousin	19	81	(93)

*The family relation is the relation at the time of the study.

TABLE IV. Ignorance of the Possibility of Carrier Testing

Family relation to nearest patient	Ignorance of carrier testing		
	Yes, %	No, %	Total (n)
Mother	6	94	(64)
Sister	6	94	(210)
Daughter	12	88	(74)
Aunt	14	86	(43)
Niece	19	81	(62)
Cousin	30	70	(92)
Total	13	87	(545)

TABLE V. Estimation of the Probability of Carriership by the Untested Women

Estimation of probability of carriership	Family relation to nearest patient, %					
	Mother (n = 19)	Sister (n = 80)	Daughter (n = 37)	Aunt (n = 20)	Niece (n = 45)	Cousin (n = 75)
Too low	5	14	35	25	9	38
Correct	63	28	54	20	16	11
Too high	—	9	—	15	26	6
No percentage/do not know	32	50	11	40	49	44

TABLE VI. Attitude Toward Termination of Pregnancy Because of Hemophilia and Severity of Hemophilia*

Attitude	Severity of hemophilia, %			
	Severe (n = 184)	Moderate (n = 103)	Mild (n = 191)	Total (n = 495)
Not opposed	38	30	25	31
No opinion	20	20	16	19
Opposed	42	51	59	51

* $\chi^2 = 10.8$, $df = 4$, $P = .03$, Cramér's $V = .10$.

sure not a carrier. It turned out that there was no such association between the attitude toward termination of pregnancy and the probability of being a carrier among the women tested for carriership ($\chi^2 = 2.2$, $P = .70$). However, as a group the tested women were less often opposed to abortion than the not-tested women: 41% v. 58% was opposed ($\chi^2 = 21.8$, $df = 2$, $P < .0001$, Cramér's $V = .21$).

We also asked all the women whether or not they thought termination of pregnancy was acceptable in various circumstances, including hemophilia. As has been explained in the section on Methods these circumstances form a strong hierarchical scale. Table VII shows the hierarchy of these circumstances. Hemophilia as a reason for abortion appeared to be hardly more acceptable than an abortion on social grounds. This corroborates the findings of Table VI.

In addition to the large group of women who opposed termination of pregnancy because of hemophilia, it appeared that a minority had no clear opinion (Table VI) or was unsure (Table VII).

Only 24 respondents, 11% of the women with children, had undergone prenatal diagnosis. All the women were

asked whether or not they would make use of prenatal diagnosis in the future if it meant that they might have to undergo an abortion in the 8–10th week or the 18–20th week of pregnancy. The only possible answers were yes and no. Fifteen percent answered yes if prenatal diagnosis and termination could only take place in the 18–20th gestational week, while 31% answered yes to prenatal diagnosis and termination in the 8–10th week.

The following reasons for not making use of prenatal diagnosis in the past or not intending to do so in the future scored high (more than one answer could be mentioned):

- I accept the possibility that the child will have hemophilia (184).
- The hemophilia in my family is not serious enough for that (108).
- I think the risk of having a hemophilic child is rather small (103).
- I am against abortion (97).
- I can't bear the thought of having an abortion after I have felt that the baby is living (72).
- I did not know that prenatal diagnosis was possible (61).
- I am afraid for injury to the baby because of the examination (29).
- I am afraid of having a miscarriage caused by the examination (26).

The Relation Between Carrier Detection Tests, Prenatal Diagnosis, and Reproductive Behaviour

Almost all the respondents agreed that carrier testing is useful. Nevertheless, only a minority would opt for prenatal diagnosis. This raises the question as to the consequences of carrier testing for reproductive choices. In Table VIII the survey population is broken down into

TABLE VII. Attitude Towards Abortion in Different Circumstances

I think abortion is acceptable if:	%		
	Agreed	Unsure	Disagreed
My health is in danger because of the pregnancy	80	14	6
The health of the baby is in danger because of the pregnancy	72	20	8
Prenatal diagnosis shows a serious disease	57	34	9
Prenatal diagnosis shows Down syndrome	46	31	23
Prenatal diagnosis shows hemophilia	22	25	53
The baby is unwanted (for other than medical reasons)	21	24	56

TABLE VIII. Cross-tabulation of Attitude Towards Prenatal Diagnosis and Reproductive Behavior (n = 312)

The No. of children will be/has been restricted because of hemophilia	Attitude towards prenatal diagnosis and potential abortion, n		
	Acceptance	No acceptance	Total
Yes/possibly	75	61	136
No	47	129	176
Total	122	190	312

*Excluded from this analysis are: the mothers of a hemophilic son, the untested women who do not intend to be tested in the future, and the women who have been tested and are probably not a carrier or have a probability of carriership lower than 26%.

a group of those who stated that hemophilia will (possibly) implicate a restriction in the number of children born in the future, or already has resulted in restriction in the number of children, and a group of those who stated that hemophilia did or does not have these implications. In addition, the survey population is broken down into a group with an accepting attitude toward prenatal diagnosis and a group of those who do not have an accepting attitude toward it. Tested respondents with a low probability of carriership were excluded, because we assumed that the reproductive behaviour of many of them would be influenced by the assumption that they were not a carrier. Also, mothers of a hemophilic son were excluded because we felt that they might restrict the number of children, not out of fear of having another hemophilic child, but because the first one needed extra care. Women who were not intending to have a carrier test in the future were excluded as well.

Less than half of the women (136/312) stated that they (possibly) would restrict or had restricted the number of children because of hemophilia; the others stated that the number of children was not or would not be restricted because of hemophilia. It appeared that 183 women felt that hemophilia might have consequences on their reproductive behavior: they would make use of prenatal diagnosis and, if necessary, have an abortion, or they would (possibly) restrict the number of children. For 129 women (41%), the grounds for undergoing a carrier detection test did not necessarily lie in the prevention of the birth of a hemophilic son.

DISCUSSION

Figures on counseling at the clinical genetics centers in The Netherlands suggest that many prospective parents who are eligible for genetic counseling do not make use of these genetic counseling facilities [Ter Haar and Niermeijer, 1982; Frets et al., 1988].

This study gives an overview of the experiences of and attitudes toward carrier testing and prenatal diagnosis among 549 potential and obligate carriers of hemophilia in The Netherlands. We estimate we have covered roughly one quarter of the possible and obligate carriers in The Netherlands.

Hemophiliacs are less likely to have given us the addresses of female relatives they rarely meet and, on the whole, female relatives who do not keep in touch with the patient will be less well-informed about the

heredity of hemophilia, carrier testing, and prenatal diagnosis. This means that the results of our study will overestimate the use of carrier testing and knowledge about the heredity of hemophilia and the possibility of carrier testing and prenatal diagnosis. With this restriction in mind we think that, given the high response rate, we can give a reliable overview of carrier testing and prenatal diagnosis for hemophilia in The Netherlands.

Seven out of eight potential and obligate carriers were acquainted with carrier testing. The majority of the group who had been tested for carriership had not yet had an affected child. This reflects a general trend in genetic counseling: parents of affected children used to be the largest group of clients for genetic advice in the past but presently they are outnumbered by prospective parents with affected relatives [Ter Haar and Niermeijer, 1982].

Half of the potential carriers had not (yet) been tested. Most of these women argued that they considered being tested but had not come to it yet, or that they intended to be tested later on when they would start a family. This corresponds with the higher percentage of tested women among those who were married or who had children. However, whether or not carrier testing has been carried out appears also strongly associated with the family relation to the nearest patient. This suggests also other causal factors. One factor is the ignorance of the possibility of carrier testing, which is higher among the "more distant" relatives. Given the widespread misconception we found in our survey that cousins and nieces have a chance of less than 1% of being a carrier, an additional explanation appears to be that cousins and nieces are less well-informed about the heredity of hemophilia. Furthermore, cousins and nieces, not being part of the nuclear family of the hemophiliac, often are socially and psychologically less involved with the patient and the problems of the disease, which may add to this lack of information in these more distant relatives. As a result they may feel themselves less inclined to be tested. These factors make the statements of most of the respondents about future testing somewhat unreliable: if a woman intends to undergo testing in the future, but thinks at the same time that she is not a carrier, then tomorrow never comes.

Eleven percent of the respondents with children made use of prenatal diagnosis. This rather low percentage can partly be explained by the limited availability of adequate techniques at that time. A few years ago chorionic villus biopsy and DNA analysis were introduced which offered the advantage of prenatal diagnosis earlier in pregnancy. About 30% of our respondents stated that they will apply for prenatal diagnosis and potential abortion in the future if this is done early in pregnancy. This is twice the number of women that will apply for this technique if it is only possible in the 18-20th gestational week. Lubs and Falk [1977] also found a redoubling of the number of persons who opted for prenatal diagnosis for hemophilia when diagnostic techniques improved: only 14% opted for an abortion when prenatal diagnosis was restricted to sex determination; 27% opted for an abortion when prenatal diagnosis also included fetal blood sampling, which implied that only

hemophilic boys would be aborted [Lubs and Falk, 1977].

However, for the majority of female relatives, prenatal diagnosis and potential termination of pregnancy still do not form an option. This corroborates the findings of Lubs and Falk [1977], Francis and Kasper [1983], and Kraus and Brettler [1988] in the United States and the findings of Markova et al. [1984] in Scotland and Canada. Evans and Shaw [1979] found a slightly higher acceptance in the United Kingdom, but still half of the respondents were opposed to prenatal diagnosis, notably because of the late time of abortion. Barrow et al. [1982] and Miller et al. [1987] found a higher acceptance in the United States than the studies mentioned before but their survey populations consisted largely of women seen at the hemophilia center because they were pregnant, and this will have caused a bias toward a more favorable attitude. Contrary to these findings, which are restricted to Western Europe and the United States, are the results of a Hungarian study on a group of obligate carriers [Lajos and Czeisel, 1987]. Forty-seven out of the 57 carriers favored prenatal diagnosis and 43 would have the pregnancy terminated in the case of a male fetus.

However, attitudes toward prenatal diagnosis are not only determined by the possibility of diagnostic techniques but also by the perceived burden of the disease. Since the introduction of modern substitution therapy for hemophilia, hemorrhages have fewer consequences and this is reflected in improvements in the medical and social situation of patients [Smit et al., 1989]. The result is that many prospective parents nowadays class hemophilia among the less serious diseases for which an abortion is not justified or for which the emotional, psychological, and physical consequences of an abortion are too profound. Thus, modern hemophilia treatment renders the disease less serious, as a result of which fewer parents feel obliged to prevent the birth of a hemophiliac. At the same time, for those parents who wish to prevent the birth of an affected child diagnostic procedures have been improved. At first sight this would appear to mean fewer problems for fewer people. Nevertheless a considerable group of (prospective) parents do not have a clear opinion on termination of pregnancy because of hemophilia. Maybe they have never considered the problem, but it is more likely that conflicting values make it difficult for them to form a clear opinion. The less serious nature of hemophilia combined with improved prenatal diagnosis techniques may leave the same group of prospective parents in doubt.

It has been pointed out that, given the increasing possibilities for diagnosis of genetic diseases and the great amount of publicity they receive, people feel obliged to make use of diagnostic procedures to preclude feelings of uncertainty and regret [Tijmstra, 1987]. Providing information about the heredity of a disease, carrier testing, and reproductive choices to prospective parents means that these parents may feel themselves obliged and, therefore, are forced to make a well-considered decision regarding their reproductive behavior, contrary to prospective parents who are ignorant of hereditary diseases in their family. This need to make a

decision is often experienced as a burden, the more so because one of the considerations is how others will view the parents as decision makers [Lippman-Hand and Fraser, 1979]. Little is known about the influence of perceived consequences, e.g., the influence of perceived social reactions to parents' decisions regarding their reproductive behavior. Certainly many clients will feel that they have to justify their actions, or that they have to be able to justify their actions afterwards. We may conclude that the possibility of prenatal diagnosis confronts parents with many puzzles in the short-term, but with some reservation we may say that it leads to fewer problems for some of them in the long-term.

In addition to this discussion on the value of prenatal diagnosis we would like to comment on the value of carrier testing. For some of the respondents, and probably for the financiers, the function of carrier testing lies in the prevention of the birth of affected children. For more than 40% of our respondents carrier testing does not explicitly have this function: they do not intend to make use of prenatal diagnosis; neither will they restrict the number of offspring. Moreover few respondents feel that carrier testing is useless. This gives rise to the question of what the function of carrier testing is for the latter group. Perhaps many people feel obliged, as has been discussed before, to make use of diagnostic procedures, at least when these do not yet have reproductive implications. Opinions about the usefulness of carrier testing may be for this group a rather automatic consequence of a generally optimistic view on new medical diagnostic techniques, instead of a well-considered opinion. However, for others a major function of carrier testing is that, being part of the procedure of genetic counseling, it supplies information about risk rates and aspects of the hereditary disease. This offers potential carriers the possibility of familiarizing themselves with their situation and it answers the question of whether or not they should start the difficult process of decision making regarding their reproductive behavior in the case of carriership. Furthermore, information dispels misconceptions and unjustified anxiety. Many women with a family history of mild hemophilia, for instance, are relieved to hear that they cannot be carriers of severe hemophilia. From our results it appears that women at risk are not optimally informed and that decisions concerning family planning and use of prenatal diagnosis are sometimes reached with difficulty. In giving information and helping prospective parents to come to a decision regarding reproduction lies the usefulness of genetic counseling centers.

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