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ORIGINAL ARTICLES

# What young people think and do when the option for cystic fibrosis carrier testing is available

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**Abstract**

**We report findings in phase II of a pilot study of cystic fibrosis (CF) carrier screening/testing by mutation analysis. Phase I has been reported elsewhere. Eligible participants in phase II (n = 815) were students (15 to 17 years of age) in public high schools. An educational component (exchange of information and discussion about common genetic disorders including CF) preceded, by one week or more, voluntary participation in the screening component which required a blood sample.**

**The uptake rate for screening was 42%. Nine carriers (2pq = 0·0260) were identified, all with the ΔF508 mutation; students were also tested for G551D, G542X, W1282X, and -549- mutations, but no carriers of these alleles were found. Carriers had positive views of the education and testing experiences. Persons identified as 'non-carriers' were also surveyed (n = 135, response rate 41%). As in phase I, the majority (83%) again understood that a negative DNA test had not excluded them from possible carrier status. Students who participated in the informational component but were not screened served here as controls in the follow up survey (n = 208, response rate 53%). Their views were similar to those of the screened non-carriers, and similar also to those held by students, adults, pregnant women, couples, and CF relatives in other communities.**

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Cystic fibrosis (CF) is one of the most common of the severe autosomal recessive diseases affecting Caucasians.[1] The carrier frequency is about 1 in 25 among Europeans. Identification and characterisation of the cystic fibrosis transmembrane regulator (CFTR) gene,[2 3] and of the most prevalent mutation associated with CF,[4] has made carrier screening both a possibility and a subject of controversy.

There are reasons for and against CF carrier screening or testing at the present time.[5–7] We distinguish here between genetic screening and testing.[7] The former refers to a test applied to a population, group, or individual person to distinguish between persons carrying a CF mutation and those who do not. Testing implies the use of specific methods to identify the genetic status of consultands known to be at high risk because of a family history. Among the reasons for proceeding with caution is the imperfect sensitivity of a test based on DNA analysis that does not identify all possible CF mutations. For the purposes of reproductive counselling of couples with one known carrier, one can only provide an accurate screening test when the risk falls below the population risk for the disorder. In the case of CF, where carrier frequency (q) = 1/25, this can only be achieved when the proportion of carriers that can be detected exceeds 96%.[8 9] So far, this condition has been met in only two populations.[10 11]

In the meantime, in keeping with recommendations that pilot studies should be done for genetic screening/testing procedures in general,[12] and for CF carrier screening in particular,[7 13 14] we have been conducting a pilot study in Montreal. We report here results from phase II of the project. Our objectives are the same as those that informed phase I,[15] namely (1) to obtain information on unconditional allele frequencies in the population; (2) to evaluate how well participants understand the limitations in sensitivity of mutation detection for purposes of genetic screening/testing; and (3) to ascertain their views on genetic screening/testing in general and for carriers of cystic fibrosis alleles in particular.

## Methods

Phase II of the project was conducted in four public high schools during 1991. The schools are the same as those in which pre-pregnancy screening for carriers of Tay-Sachs and β thalassaemia alleles has been in progress for the past two decades.[16 17]

### SUBJECTS

Persons of Italian descent were heavily represented in phase II (54% of participants). Students aged 15 or over attending high school were eligible for the project. Those who participated in an information seminar, but did not take the screening test, served as controls. Participation at all stages was voluntary, with

consent of parents, the school board, and the teachers.

UPTAKE

Students first attended an information session which covered basic genetic principles and relevant information about CF. Pamphlets describing CF, the project, and issues associated with carrier screening were given to each student. Participants in the screening component identified their ancestral origins (ethnic and geographical).

SAMPLE

Heparinised venous blood was drawn from the antecubital vein and, on the same day, DNA was phenol extracted from leucocytes. Screening took place at least one week after the information session; it was organised within curriculum time on school premises.

TEST RESULTS

A personal letter explaining the result of mutation analysis was sent to each participant. One or two weeks after the results were sent, carriers were called, counselled further if the letter explaining the significance of carrier status needed clarification, and asked questions relevant to the project (see below). Counselling, with mutation analysis if desired, was offered to family members.

ANALYTICAL METHODS

DNA was amplified by the polymerase chain reaction (PCR), and analysed for the mutations ΔF508, G551D, G542X, W1282X, and -549-.

EVALUATION

This component was carried out after the results of the test had been returned to the participants. We distributed a questionnaire to all participants, both carriers and non-carriers. A separate questionnaire was also distributed to persons who had not participated in the screening phase (controls) to evaluate their attitudes and reasons for non-participation. Controls were selected to match the participants according to school attended, gender, and age.

*Table 1 Comparison of attitudes of non-carriers in phase I and phase II (% yes).*

| | Phase I (n=78) | Phase II (n=135) |
|---|---|---|
| Does a negative test for ΔF508 mean that you can still be carrying a CF mutation? | 95 | 83 |
| If you were a carrier would it lower your self image? | 21 | 24 |
| Did you learn something useful about CF? | 85 | 78 |
| Did you learn something new about genetic disease in humans? | 84 | 79 |
| Are you satisfied that you were tested? | 84 | 94 |
| Do you approve of carrier screening in high schools as a form of pre-pregnancy screening? | 96 | 90 |
| Would you recommend that your friends take the test as it was offered to you? | 93 | 89 |
| Would you want your future partner tested for cystic fibrosis carrier status? | 65 | 89 |
| If your partner were a carrier, would it affect your relationship? | 12 | 17 |

## Results

PARTICIPATION RATES

There were 815 eligible students in phase II of the project; of these, 341 (42%) participated in both the education and the screening component. Participation rates in the follow up components were 41% for non-carriers and 78% for carriers. The response rate was 53% (n=208) in the control group (students who attended the education component but were not screened).

MUTATION ANALYSIS

Nine carriers were identified, all with the ΔF508 mutation. There were no carriers of the G551D, G542X, W1282X, and -549- alleles. The observed carrier frequency was 0·0260 in phase II. There were 386 chromosomes of Italian descent, four of which carried the ΔF508 alleles. Accordingly, the unconditional frequency of ΔF508 carriers in this sample of Italians in Montreal is 0·0208.

PERCEPTIONS OF CARRIERS

All carriers believed that their CF carrier status had not harmed their own health. Three had experienced what they considered to be modest anxiety and one had great anxiety on receiving the test result. Anxiety had dissipated in all respondents by the time of the follow up interview. The newly identified carrier status did not affect self-image. Seven carriers expressed interest in having family members tested. They also indicated they would seek further counselling before pregnancy or planning a family. These findings show that carriers in phases I and II of the study held similar views.

PERCEPTIONS OF NON-CARRIERS IN PHASES I AND II

We compared attitudes among the non-carrier participants in phases I and II (table 1). The great majority (>83%) of students in both phases understood that testing only for ΔF508 did not rule out carrier status. The majority (>90%) approved of genetic screening in high schools, were satisfied (>84%) that they had been tested, would recommend the test to their friends (>89%), would want their future partner to be tested (>65%), and did not think that this would affect their self-image (>76%) or future relationships (>83%). The majority (>78%) learned something new about genetic disease in general and something useful about CF in particular.

PERCEPTIONS OF CONTROLS (NON-SCREENED STUDENTS)

Knowledge and attitudes among the non-screened controls (n=208) were compared with screened non-carriers (n=135) (table 2). Attitudes in the two groups were very similar. Among the screened non-carrier respondents, only one expressed disapproval of pre-pregnancy carrier testing, and among the controls

*Table 2 Comparison of knowledge in screened non-carriers and non-screened controls.*

| | Screened non-carriers (n = 135) Yes (%) | Non-screened controls (n = 208) Yes (%) |
|---|---|---|
| Did you learn something useful about CF? | 79 | 74 |
| Does CF affect the lungs? | 72 | 70 |
| Does CF affect the pancreas? | 24 | 29 |
| Does CF affect the digestive tract? | 35 | 34 |
| Does CF affect the brain? | 7 | 35 |
| Did you learn something about genetic disease in humans? | 79 | 76 |
| At the present time, does CF shorten life span? | 60 | 63 |
| Is CF carrier frequency higher in Caucasians when compared to other ethnic groups? | 63 | 69 |
| Do you approve of genetic screening in high schools? | 90 | 83 |

*Table 3 Comparison of studies surveying attitudes towards CF carrier screening (% yes).*

| Source, population, and respondents to survey (n) | Are you interested in carrier screening? | Do you understand limitations of DNA test? | Will carrier status influence your choice of partner? | Is PND relevant if both partners are carriers? | Do you accept preconceptual screening? |
|---|---|---|---|---|---|
| This study | | | | | |
| High school students, Montreal | | | | | |
| Carriers (n = 7) | 100 | — | 28 | 86 | — |
| Non-carriers (n = 135) | 90 | 83 | 17 | — | 87 |
| Controls (n = 208*) | 83 | — | — | — | 77 |
| Cobb *et al*[18] | | | | | |
| Age 14–16, Scotland (n = 216) | 86 | — | — | 88 | — |
| Botkin and Alemagno[19] | | | | | |
| Pregnant women, USA (n = 214) | — | — | 9 | 67 | 98 |
| Green[20] | | | | | |
| Couples with children, England (n = 175) | 83 | — | 11 | 85 | 47† |
| Decruyenaere *et al*[21] | | | | | |
| Adults, Belgium (n = 385) | 76 | — | — | 75 | 86 |
| Denayer *et al*[22] | | | | | |
| Adult CF relatives, Belgium (n = 109) | 74 | — | 6 | 73 | — |
| Watson *et al*[23] | | | | | |
| Adults, UK | | | | | |
| Carriers (n = 88) | — | 46‡ | — | 78§ | — |
| Non-carriers (n = 111) | — | 57‡ | 16 | — | — |

* Non-screened subjects were matched to screened carriers and non-carriers.
† Indicates the sum of two choices in a multiple choice question. The most popular single choice was school leavers at 34%.
‡ Respondents for this question: carriers n = 26, non-carriers n = 133.
§ Answer given after counselling.

only two students held this opinion. The two groups did not differ in their knowledge of CF gained at the education session; in both, the majority (>74%) felt they had learned something useful about the significance of genetic disease in humans. The majority (>60%) understood that CF was associated with a shortened life span at present and had the highest prevalence among Caucasians. Reasons for non-participation among the controls included (1) lack of interest (27%), (2) fear of a blood test (27%), and (3) failure to complete or return the consent form (29%).

### PERCEPTIONS IDENTIFIED IN OTHER SURVEYS

We compared findings in our study with those reported in other recent surveys (table 3). The actual wording of questions, which were common in content in the various studies, required modification for the sake of clarity in table 3. Our actual questions are listed in the appendix. Views about carrier screening and testing are strikingly similar among several contemporary populations.

## Discussion

Since the discovery of the CF gene in 1989, and identification of the prevalent ΔF508 mutation, there has been discussion among geneticists about the potential merits of genetic testing or screening for CF carriers.[5–7 13 14] Meanwhile, we and others (table 3) have gone instead to the community to ascertain the opinions of potential participants. In our pilot study, phase I of which has been previously reported,[15] we are also obtaining data on unconditional allele frequencies in Quebec populations.

Understanding and attitudes of participants in the second phase of our study did not differ significantly from those observed in the first phase of our project[15] (table 1). Phases I and II embraced private and public schools respectively with implications about social advantage and other factors that might influence attitudes and understanding. High school students in Scotland[18] and in Montreal (this study) are indeed interested in the possibility of CF carrier screening for purposes of reproductive counselling. When high school students are

given the chance to learn and participate, the majority understand and accept the imperfect sensitivity of the DNA test, only a small minority state that carrier status might influence choice of partner, and the majority express familiar views[16 24] about future reproductive decisions. In other studies of opportunistic testing in an antenatal clinic,[25] general practice,[23 26 27] and a family planning clinic[23 26] virtually all participants regarded the process as a positive learning experience and accepted the newly gained information. The hypothetical[18–22] and opportunistic[23 25–27] studies all indicated similar positive attitudes toward carrier screening in various populations.

Less clear is to what extent the information that can be gained by CF carrier testing with current methods will help family members to deal with the possibility of having an affected offspring. The issue here involves sensitivity of the test, a problem not new to CF carrier testing, and one that we, among others, have examined in other genetic screening programmes in Montreal.[28 29] Follow up studies, similar to those performed in Tay-Sachs and β thalassaemia carrier screening programmes,[16 30] will be necessary to show the effectiveness and impact of information gained from current modes of CF carrier testing.

Attitudes of participants towards CF carrier screening are very similar in several different populations; they are not apparently influenced by age, social class, level of education (high school and beyond), or country of origin (table 3). In communities where opinions were sought, the majority of persons surveyed indicated the 'ideal time' for testing was preconceptual.[19–21] Such testing can take place in an opportunistic setting, such as a family medical practice or in groups with common ground, such as the high school classroom. Testing in high schools, in our experience,[16 17] has the advantage of efficiency and it can be coupled with a formal educational component. We are aware that the positive findings in Montreal[16 17 24] may not be representative of other communities.

Participation rates in the screening components of phases I and II in the project were low (<43%) compared to about 70% in the corresponding Tay-Sachs and β thalassaemia screening programmes in Montreal. The reasons given for non-participation here were objection to a blood test and possible AIDS infection, failure to bring the signed permission form (a requisite for the pilot study), and lack of interest. Nevertheless these factors clearly did not imply disapproval of screening (table 2). When the blood test was replaced by a buccal rinse in phase III, the participation rose to 70%.[31]

The frequency of detectable CF mutation has reached an 'acceptable' level in two populations[10 11] and is near the desired level in three others.[32–34] Enhanced public education about CF, development of a more efficient DNA or phenotype test, ability to offer informed counselling to client populations, and maintenance of personal choice when options exist will propel communities to consider what is to be done. The findings described here suggest that young citizens have calm views about CF carrier screening.

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*Appendix Questions referred to in table 3 and used in the follow up survey of phase II in the CF carrier testing project.*

(1) Do you approve of genetic screening, in principle, in high schools to detect the silent carriers of recessive mutations causing diseases such as Tay-Sachs disease, thalassaemia, sickle cell anaemia, and cystic fibrosis?
(2) Does the negative test result mean that you cannot be carrying any cystic fibrosis mutation at all?
(3) If your partner were a carrier, would it affect your relationship?
(4) If you and your partner were both carriers of a cystic fibrosis mutation would you:
  (a) not have children?
  (b) take your chances and have children?
  (c) have children but take steps to have children unaffected by cystic fibrosis; options that would allow a family to have a child without cystic fibrosis include adoption, artificial insemination by a donor, and prenatal diagnosis with selective abortion?
  (d) don't know.
(5) Do you think carrier screening should take place:
  (a) in senior high school?
  (b) when couples are planning to get married?
  (c) when couples are planning to have a baby?
  (d) don't know.
  (e) should not be done at all.