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Genetic Counseling for Hemoglobinopathies

A Model for Large Scale Application

Charles E. Jackson, M.D., Esly S. Caldwell, M.D., and Ellis J. Van Slyck, M.D.*

This report describes a project in a large urban, predominantly black, high school which combined a hemoglobinopathy survey with an educational and genetic counseling emphasis. The faculty and students received information on sickle cell disease explaining its genetic and personal implications. About 29% of the 2,700 students received parental permission and volunteered for blood tests in the initial year. Blood was examined by starch gel electrophoresis during the first year and by cellulose acetate electrophoresis during the second year. Of the 1300 total individuals studied, 7% were found to have sickle cell trait and 2% hemoglobin C trait. The cellulose acetate electrophoretic procedure was found to be as satisfactory as the starch gel procedure at less cost ($1.32 per person). Those with abnormalities were given counseling which simply emphasized the risk to their progeny should they marry another heterozygote. For adequate genetic counseling purposes, the seriousness of SC disease and the frequency of hemoglobin C trait preclude the use of any screening procedure which fails to detect C hemoglobin. The described program detects hemoglobinopathies common in the black population, is practical, is directed to youth for maximum effect of genetic counseling, and is adaptable to large scale application.

Sickle cell anemia represents a serious public health problem with respect to morbidity and mortality in the black population. Almost 10% of American Negroes carry the sickle cell trait and 1 in 400-500 Negro births result in homozygous sickle cell disease. Motulsky¹ has emphasized that even though sickle cell anemia has the highest frequency of any autosomal recessive disease in the United States, no public health agency has spread the information to those at risk. Scott’s recent communication² also emphasized the extent of the health problem produced by sickle cell hemoglobin as well as a surprising ignorance about its effects and mode of inheritance among even an educated black population. Other genetically determined abnormal hemoglobins, particularly hemoglobin C³ and thalassemia⁴, are also found in significant numbers among
Negroes and produce serious disease, especially when combined with hemoglobin S. 5,6,7

The need is evident for comprehensive surveys of black populations for all the common hemoglobin abnormalities. Young people in particular should be screened with the emphasis on education and genetic counseling. Even if only partially successful, this endeavor would be worthwhile and would contribute to a reduction of the disease.

This report describes an exploratory project undertaken during two consecutive years in an urban, predominantly black, high school. It might well serve as a model for mass screening for hemoglobinopathies and for other detectable recessive conditions.

Procedures

Permission to survey and counsel the students in one high school near Henry Ford Hospital was obtained from the school administration and from the Detroit Board of Education. The school faculty was oriented to the purposes and significance of the project by an educational program. Assemblies were held for each of the four high school classes and literature on sickle cell disease was distributed. Somewhat dramatic presentations were provided to emphasize the possible importance of the disease to the students as individuals. These included the participation of a mother whose son has sickle cell anemia and whose brother had died of the disease. Also, an affected college girl provided testimony of the personal impact of the disease. Question-and-answer sessions served to clarify points of misunderstanding and pointed up the lack of previous education about sickle cell disease.

During the initial year's trial, students who returned parental permission cards had venous blood drawn by vacutainers into ACD solution for starch gel electrophoresis. In the second year of this study, finger prick blood was obtained in heparinized capillary tubes for cellulose acetate electrophoresis. A full day session was scheduled at the school each year using teams which included doctors, nurses, and high school students from a medical careers club. Specimens were carefully and properly identified by previously numbered duplicate labels applied to the specimens and to the permission card. All participating students were notified of their results by letter and each was given a wallet-sized card for future identification. Those with abnormalities were given genetic counseling which reinforced the information provided in the assemblies. This counseling simply stated the risk to their progeny should they marry another heterozygote.

Laboratory Methods

In the first year hemoglobin electrophoresis was performed on vertical starch gel in tris-EDTA-boric acid buffer at pH 8.6 for 16 to 18 hours.8 With equipment described by Brewer,9 16 specimens were run per tray, or 80-96 per night with one power supply (See Figure 1). Processing time was shortened by using only 0.5 cc of packed cells with a single 10 cc saline wash, plus toluene extraction of red cell stroma. In the second year hemoglobin electrophoresis was performed on cellulose acetate in tris-EDTA-boric
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Figure I
Illustration of vertical starch gel electrophoresis apparatus.

acid buffer at pH 9.1 for 75 minutes.10 A freeze-thaw technique was used to hemolyze the blood in the capillary tubes. All hemoglobins migrating as S were subjected to solubility studies11 and acid agar12 electrophoresis to exclude hemoglobin D.

Results
Of the 2,700 member student body, 770 (29%) obtained parental permission and allowed blood to be drawn during the initial year. Blood was obtained from an additional 533 students during the second year of the study. The number of S and C heterozygotes found (Table I) is consistent with previously reported prevalences.3,13 The student with homozygous S had known of this prior to the study but the SC student was unaware of her condition. No thalassemia was noted but one instance of persistent high fetal hemoglobin was detected.

Using two electrophoretic techniques in the two separate years has allowed a comparison of the relative costs of each. The starch gel electrophoretic procedure cost $2.25 in technician time and $.30 in consumable supplies.* The cellulose acetate electrophoretic procedure cost $1.11 in technician time and $.21 in consumable supplies.*

Discussion
Since no effective treatment has

*To these figures would have to be added the proportionate share of professional fees and laboratory overhead.
been established for patients with clinically significant hemoglobinopathy, the application of preventative measures is all the more vital. Genetic counseling offers the best prospect for prevention. Before initiating a large scale genetic counseling program for hemoglobin abnormalities, we considered the following criteria important: 1) that all hemoglobinopathies of significant prevalence in the population be detected by the laboratory procedures, 2) that the procedures be practicable and relatively inexpensive, 3) that the program be directed to the segment of population in which the genetic counseling would have the maximum impact, and 4) that the program have an effective educational emphasis. The survey described here fulfills these criteria and is readily adaptable for larger programs.

For adequate genetic counseling purposes, the seriousness of SC disease and the frequency of hemoglobin C trait preclude any screening procedure which fails to detect C hemoglobin. Starch gel electrophoresis was chosen initially in this study because it is capable of detecting hemoglobin S, C, Aα, and F as well as other less common hemoglobins. During the second year the use of cellulose acetate electrophoresis provided the same quality of information at less cost ($1.32 vs $2.55 per sample). It should be noted that the sodium metabisulfite test and variations of Itano’s solubility test allow detection of only hemoglobins which sickle and not some of the other common abnormal hemoglobins. The modifications of the electrophoretic procedure can make the cost reasonable and bring it into a range near to that of these less satisfactory screening methods. Furthermore, the electrophoretic studies have the advantage of being able to detect previously undescribed abnormal hemoglobins which would be overlooked by simpler techniques. We feel the additional effort required to perform electrophoretic screening procedures is justified by the vital information provided.

To be most effective for genetic counseling, the major effort should be directed to young people prior to reproductive activity. Although premarital testing provides information important to a couple, a better time for genetic counseling of this sort would be before they even considered marriage. Our results suggested that students in the upper grades are more likely to volunteer for this type of study (see Table II).
TABLE II
PROPORTION OF VARIOUS CLASSES ALLOWING BLOOD TESTS

<table>
<thead>
<tr>
<th>GRADE</th>
<th>BOYS</th>
<th>GIRLS</th>
<th>TOTAL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ninth</td>
<td>10%</td>
<td>11%</td>
<td>11%</td>
</tr>
<tr>
<td>Tenth</td>
<td>14%</td>
<td>27%</td>
<td>21%</td>
</tr>
<tr>
<td>Eleventh</td>
<td>16%</td>
<td>35%</td>
<td>24%</td>
</tr>
<tr>
<td>Twelfth</td>
<td>27%</td>
<td>49%</td>
<td>43%</td>
</tr>
</tbody>
</table>

(770)
TOTAL 21% 37% 29%

Male students seemed more cooperative, it is obvious that a testing program involving only females would be inadequate for genetic purposes. We believe a program in the elementary grades would have several advantages: Information would be available before mating practices were established, knowledge of the disease could be reinforced yearly within the educational system, and parental persuasion to participate might be more effective. (In a preliminary effort in a grade school, we had 96% of 300 students returning permission cards and allowing finger prick blood specimens to be obtained).

The ultimate goal of an effective educational program would be to make information about the hemoglobinopathies common knowledge within the population at risk. Genetic counseling would be automatic with the increased understanding. In conducting a successful voluntary screening program, it is inherent that students and their parents receive information about genetic conditions in order to secure their cooperation. An additional advantage of a non-compulsory program is that volunteers are more likely to consider the personal implications of the findings.

The success of such a program will require many years, perhaps even generations, to evaluate properly. Nevertheless, the practical application of current knowledge of hemoglobinopathies in this major public health problem is overdue. It should not be delayed further. The technological procedures and educational promotion outlined in this paper can provide a method of approaching the problem on a large scale.

Acknowledgements

The study was supported in part by U.S. Public Health Service Grant AM 14876. The authors are grateful to the administration and faculty of the high school and to the Detroit Board of Education for their cooperation, to Charlotte McCollum, Larry Magid, and Nahla Ayoub for their technical help and to the many others who provided assistance in this project.

REFERENCES

2. Scott, RB: Health care priority and sickle cell anemia, JAMA 214:731-4, 26 Oct 1970


10. Rucknagel, DL: Personal communication, 1972


