Hemoglobinopathies: how big a problem?

Over the last few centuries, but especially since World War II, there has been continuing emigration from Africa, Asia and Europe to North America. As a result hemoglobinopathies are now recognized as the most important group of genetic diseases in the United States. Few can doubt that hemoglobinopathies present a health-care problem in Canada also, but the size of the problem is much more difficult to estimate. With a knowledge of the countries where the abnormal hemoglobins and thalassemia originate and a copy of the Canadian census and immigration figures, one would expect to be able to predict the impact of hemoglobinopathies on present-day Canada. There are a number of drawbacks to this "armchair" approach but, because it may be followed by the planners of health-care delivery, it is at least worthy of exploration.

The geographic areas where the common abnormal hemoglobins (sickle cell, C, D Punjab [or Los Angeles] and E) are endemic are well recognized.[1,2] Hemoglobin C is localized to persons of West African origin. In contrast, sickle cell hemoglobin is more widespread; it is found predominately in African blacks, but also to a lesser extent in persons from Greece and the Middle East and among aboriginal tribes in India. Hemoglobin D Punjab and E are likely to be seen in persons of Asiatic origin; the former is found mainly in the Punjab and the latter in Thailand, among the native Indo-Chinese rather than the more recently arrived Chinese.

Beta-thalassemia, although first recognized by Cooley and Lee[3] in Italian immigrants in the United States and therefore named Mediterranean anemia, exists widely across the Mediterranean and the Middle and Far East. Despite the claim that there is a higher frequency of thalassemia in the Chinese than in the total Mediterranean populaton,[4] it is interesting that the 966 persons with thalassemia variants found in the Vancouver survey of Gray and Marion (see page 701 for their report) were reasonably evenly divided between Mediterranean and Asian origin.

It is convenient to consider that α- and β-thalassemia have roughly the same geographic distribution.[5] However, the carrier state of α-thalassemia is symptomless and is therefore difficult to categorically detect without support from a direct, but somewhat complicated, measurement of α-chain production in the erythrocytes. Carriers of α-thalassemia$_1$ are the exception to the rule in that their condition may be suspected when an unusually low mean corpuscular volume is recorded on an electronic cell counter.[6] A more severe form of α-thalassemia, hemoglobin H disease, presents with moderately severe anemia and splenomegaly, and again appears to have roughly the same distribution as β-thalassemia. Alpha-thalassemia major, which is incompatible with life, is especially prevalent in Asia; it is the most frequent cause of hydrops fetalis in Malaysia.[7]

Among the hemoglobinopathies, sickle cell anemia and β-thalassemia major, because of their frequency and clinical severity, are the most important in Canada. With a carrier rate of about 8% for the sickle cell trait among blacks in the United States one could expect about 1 in 500 blacks in Canada to be born with this potentially lethal disease. Sickle cell anemia (homozygous sickle cell disease) presents clinically with either the classic painful infarctive crisis or a catastrophic decrease in the steady state concentration of hemoglobin.

Beta-thalassemia minor (the carrier state of β-thalassemia) may be found in 5% to 10% of many of the affected populations. It presents classically as iron-resistant hypochromic anemia, with a hemoglobin concentration of 10 to 12 g/dL. Because of the superfluity of erythrocytes, an automated counter gives lower values for the mean corpuscular hemoglobin and the mean corpuscular volume than one would expect in pure iron deficiency. The patient with β-thalassemia minor commonly has normal or increased stores of iron. Despite the fact that the coexistence of β-thalassemia and iron deficiency is perhaps more common than previously realized, iron therapy should not be given unless a decrease in the serum concentration of iron is first demonstrated. Beta-thalassemia major, with its severe anemia and massive hepatosplenomegaly, presents a heavy therapeutic challenge but is seldom a diagnostic problem; even if the physician is uncertain about the diagnosis, the disease is all too often recognized by the relatives of the afflicted child.

The Canadian population can be divided relatively easily into three categories with the use of the census and immigration figures.[8]

1. *Native:* By sheer weight of numbers Canada has an immigrant population. The native population (about 300 000) do not have hemoglobinopathies to add to what many consider an already heavy burden of disadvantage.

2. *British and French:* Between 1871 and 1971 the Canadian population increased from 3 689 000 to 21 568 000. The most pronounced changes during this period were the decrease in the proportion of British origin (from more than 60% in 1871 to 45% by 1971) and the increase in the proportion of those of all

origins other than French (from less than 10% in 1871 to more than 25% by 1971). The proportion of French origin remained relatively constant (at about 30%).

Although not major carriers of hemoglobinopathies, the native British population may be expected to carry hemoglobin D Punjab with a frequency of about 0.1% — a legacy of the substantial presence of the British military in the Indian subcontinent for 200 years.[9] Again, as Desjardins and colleagues point out in this issue of the Journal (page 709), one is not surprised to find that Mediterranean anemia occurs to a greater or lesser extent in a Canadian population of French origin.

3. *All others:* It is unfortunate, from the point of view of this review, that inexactness within the census figures is likely to arise at the subdivision of this heterogeneous label. For example, the rapid increase in the last decade in the "British" population (perhaps at the expense of "all others") may be in part due to the fact that "English" was the first choice as an answer to question 15 of the 1971 Census of Canada — "To what ethnic or cultural group did you or your ancestor (on the male side) belong on coming to this continent?" With such reservations in mind, one learns that there was an increase in Canada from 1961 to 1971 of 60 600 in the number of Chinese and 61 200 in the number of East Indians; the total number of "Asians" in 1971 was 285 500. The increase in the number of blacks in the same period, 2300, might appear modest to those living in the larger cities of Canada. Kralt believes that the estimate of 34 400 blacks in Canada in 1971 is probably conservative (personal communication, 1978). However, one might expect a considerable number of West Indians (whose total number was 28 000 in 1971) to fall into this category.

Canadian immigration figures based on the country of last permanent residence (i.e., of 1 year or more) give more recent data.[10,11] For example, the annual number of persons from the West Indies immigrating to Canada increased steadily from 1941 (118) to 1974 (23 670), then declined in 1975 (17 800), 1976 (14-700) and the first quarter of 1977 (2554). The figures from Asia have followed the same trend, increasing from 1941 (307) to 1974 (50 566), then declining in 1975 (47 382), 1976 (44 328) and the first quarter of 1977 (7027).

Most of the carriers of β-thalassemia of "Mediterranean" origin detected in the survey of Gray and Marion were Italians and Greeks. The pattern of immigration of these groups since World War II has been the same as that of the West Indians and Asians. However, the peak years were 1966 for the Italians (31 625) and 1967 for Greeks (10 650).

Figures such as these have to be interpreted with caution. For example, on the sole basis of country of last permanent residence, it must follow that not all "British" persons are native Britons. Indeed, the difficulties in compiling these data may be illustrated by my experience. Although I was born in Asia, my family and I were the only Caucasians among the band of hopeful "British" undergoing immigration screening one morning at the Canadian Consulate in Birmingham, England.

Assuming reasonable accuracy of the total immigration figures, a further problem in assessing health care needs arises because of the provincial disparity in the settlement pattern of different ethnic groups. As well as recognized historical patterns, such as the early black settlements in Nova Scotia,[12,13] there are more recent inequalities based on the general preference of many newly arrived immigrants to live in an urban area rather than a rural area. Because of such patterns a screening program for the detection of hemoglobinopathies in an urban area of British Columbia would have little relevance in a rural area of Newfoundland.

By now it must be apparent that the available population data are unlikely to be particularly helpful in the planning of Canadian health care programs directed at detection and treatment of hemoglobinopathies. Unfortunately, there appears to be no substitute for studies such as those reported in this issue of the Journal and those conducted by Ali[14] in Ontario and Vella[15] in Saskatchewan. With such studies the demand for therapy (mainly for sickle cell disease and β-thalassemia major) can be logically assessed on both a national and a provincial basis. In addition, one can be prepared, when requested,

to offer the carriers of sickle cell hemoglobin and β-thalassemia minor the necessary facilities for genetic counselling.

The Canadian Sickle Cell Society is seeking support for a large-scale screening program among the black population of Canada. Many of the errors made in the massive sickle cell program in the United States, when enthusiasm appeared at times to overtake wisdom, should be preventable in Canada. Nevertheless, despite the advantages offered by a late start and a slower pace, it would be something of a miracle if this country succeeded in travelling such a pot-holed road unscathed.

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BOOKS

This list is an acknowledgement of books received. It does not preclude review at a later date.

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continued on page 704