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RACIAL PATTERNS IN PERNICIOUS ANEMIA

Early Age at Onset and Increased Frequency of Intrinsic-Factor Antibody in Black Women

RALPH CARMEL, M.D., AND CAGE S. JOHNSON, M.D.

Abstract Pernicious anemia affects primarily elderly northern Europeans, but may affect others more often than previously thought. Therefore, we analyzed the data from 156 documented cases: there were 73 patients of "European" origin, 52 black patients and 31 Latin-American patients. The mean age (±1 S.D.) at presentation among black women, 53±16 years, was lower than that of all the others (P<0.001 in most comparisons), and seven of the 33 black women were less than 40 years old. In addition, 23 of the 24 black women tested had circulating antibody to intrinsic factor. A similar though less striking antibody prevalence (85 per cent) and age pattern (60±13 years) in Latin-American women did not reach statistical significance. No other group exceeded the usual 55 to 70 per cent prevalence of antibody. These findings suggest a different form of or a different response to the disease in black women and perhaps in Latin-American women. (N Engl J Med 298:647-650, 1978)

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Pernicious anemia predominates in people of northern European origin.1 Yet surveys in racial groups in whom this disease was widely regarded as rare, such as American blacks and American Indians, suggest an incidence in them higher than has been assumed.2-5 We were impressed not only by the relative frequency of the disease in our non-European patients but also by its early age at onset in many blacks. In fact, preconceptions about age and race in many such cases may have unduly delayed the recognition of pernicious anemia. We therefore surveyed all available patients with pernicious anemia, and pre-sent our findings here with special emphasis on the unusual age at presentation and autoantibody incidence in black women.

Methods and Materials

We compiled a list of 257 patients with the diagnosis of pernicious anemia from hospital and laboratory records at Los Angeles County—University of Southern California Medical Center from 1961 to the present. We reviewed charts to assess the validity of diagnosis. At least one of the following criteria was required for acceptance of a valid diagnosis of pernicious anemia and inclusion in our series: an abnormal Schilling test corrected on repetition with an oral dose of intrinsic factor; absence of intrinsic factor on assay of betazole-stimulated or pentagastrin-stimulated gastric juice; and positive blocking (Type I) antibody to intrinsic factor in serum, free of vitamin B12 artifact (see below). When possible, patients were seen for further evaluation, especially for testing for antibody to intrinsic factor. We excluded 116 patients from our series: eight who turned out not to have pernicious anemia on re-evaluation and 108 in whom data were insufficient for diagnosis. To the remaining 141 patients in whom the diagnosis could be made with confidence were added 15 such patients seen at Grace Hospital, Detroit, Michigan, from 1972 to 1975. The diagnosis was established primarily by classic Schilling-test results in 111 cases, by absence of intrinsic factor
in gastric juice in another 22 cases and by antibody to intrinsic factor in serum in the 23 remaining patients. In these 23 patients evidence of vitamin B₁₂ deficiency was also present, thus excluding the apparently "false-positive" antibody described in rare patients with thyroid disease and diabetes without pernicious anemia.⁷,⁸ Black and Latin-American women did not predominate in this group of 23 patients.

The assay for antibody to intrinsic factor was done by the method of Gottlieb et al.⁴ All serum specimens were first screened for presence of excess vitamin B₁₂, such as commonly follows vitamin B₁₂ injection and has been observed by us and others⁴,⁹ to cause falsely positive blocking-antibody results. Such serum samples were not used, nor did we rely on results of assays done outside our laboratory. Since the antibody assay was not generally available until the last few years, only 18 of the 72 patients whose diagnoses were made before 1970 were available for testing for antibody, as compared with 59 of the 84 with diagnoses after 1970.

The age at which the diagnosis of pernicious anemia was first established was taken as the age at presentation. In the cases in which the patient presented with pernicious anemia but the diagnosis was not adequately established until later, the earlier date was taken. Age at relapse was not used. Race was determined from the information given to the hospital records office by the patient.

RESULTS

Our series consisted of 92 women and 64 men, ranging in age from 10 to 90 years. Seventy-three (47 per cent) were of "European" origin, 52 (33 per cent) were blacks and 31 (20 per cent) were Latin-American (Fig. 1). These numbers may be compared in part to our hospital's inpatient distribution of 30 to 35 per cent "white," 20 to 25 per cent black and 40 to 45 per cent Spanish-surnamed patients over the past five years. The disease appeared in 26 of the blacks before 1970 and 26 after 1970. In "Europeans" the respective numbers were 47 and 26, and in Latin-Americans, they were 14 and 17. Most of the "Europeans" in our series were of Scandinavian or British origin as far as could be determined. Also included were several of Irish, Italian, Jewish, German, Polish, Dutch, Austrian, Russian and Basque origin, in approximately descending order of frequency. Grouped among the "Europeans" were also one Assyrian and one Lebanese. The Latin-American patients were predominantly of Mexican origin but included four from Cuba and two each from El Salvador and Ecuador.

All blacks (P<0.001 by Student's t-test) and all Latin-Americans (P<0.05) were younger than all "Europeans." However, the significant age differences were confined to the women; the three male groups did not differ significantly from each other. The black women were significantly younger than all the other groups of patients (P<0.001) except the Latin-American women and the black men, in whom the age difference did not reach statistical significance. Furthermore, a smaller proportion of the black women were 70 years or older, and a larger proportion were 40 years or younger than in all the other groups (Table 1). In fact, the age distribution among the black women may be a bimodal one, with one cluster about a median age of 62 and the other about a median age of 31 (Fig. 1). The Latin-American women were not significantly younger than any other group except the "European" men (P<0.05). Within each racial category, the women tended to be younger than the men, but the differences never reached statistical significance.

The prevalence of serum antibody to intrinsic factor in the subgroups was similar to the usually reported rate of about 55 to 70 per cent¹¹,¹² with only two exceptions (Table 1). The first was that antibody was found in 96 per cent of the 24 black women tested, the figure being significantly different from that in each of the other groups (the differences being 2.0 to 2.9 times Standard Error) except the Latin-American women. Secondly, antibody was found in 85 per cent of these Latin-American women, but possibly because only 13 were tested, statistically significant difference was not achieved as compared to any of the other groups.

DISCUSSION

Originally thought to be extremely rare in blacks,¹³ pernicious anemia has seemed to become more common in them with each survey.²,⁴,¹⁴,¹⁵ Whether the progressive increase is real is unclear because the early studies used diagnostic criteria that are inadequate by today's standards, but our data suggest the increase may be real, at least at our hospital. A comparable decrease in both black and white census has been accompanied by a striking fall in new cases among "Europeans" since 1970 but no change in the number of new cases among blacks. We cannot draw firm conclusions about relative incidence in racial groups from our data; among other things, most patients excluded from our series because of inadequate documentation of diagnosis were white. However, though pernicious anemia clearly remains most common in whites of northern European origin, its in-
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Table 1. Age at Presentation and Data on Antibody to Intrinsic Factor in the Different Racial and Sex Groups.

<table>
<thead>
<tr>
<th>Datum</th>
<th>Europeans</th>
<th>Blacks</th>
<th>Latin-Americans</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>42 women</td>
<td>33 women</td>
<td>17 women</td>
</tr>
<tr>
<td>Mean age ± 1 SD (yr)</td>
<td>67 ± 13</td>
<td>53 ± 16</td>
<td>60 ± 13</td>
</tr>
<tr>
<td>Median age (yr)</td>
<td>69</td>
<td>56</td>
<td>62</td>
</tr>
<tr>
<td>Patients &gt; 70 yr</td>
<td>20 (48%)</td>
<td>5 (15%)</td>
<td>4 (24%)</td>
</tr>
<tr>
<td>Patients ≤ 40 yr</td>
<td>1 (2%)</td>
<td>7 (21%)</td>
<td>1 (6%)</td>
</tr>
<tr>
<td>Patients with antibody</td>
<td>9/15 (60%)</td>
<td>23/24 (96%)</td>
<td>11/13 (85%)</td>
</tr>
</tbody>
</table>

The intriguing question is why black women, and possibly Latin-American women, should have this unusual presentation. The increased propensity of women to most so-called "autoimmune" disorders is well established. Hippe and Jensen,29 in a study of Scandinavians, also found that women with pernicious anemia who had a family history of the disease and a higher incidence of other "autoimmune" disorders were younger and had antibody to intrinsic factor more frequently than those without such a history. Perhaps among blacks an added genetic or acquired factor potentiates the predisposition in women. Alternatively, the disease in black women, or at least in some of them, may arise by a mechanism different from that in other patients. Our findings further suggest that examining the incidence and pattern of other "autoimmune" disorders in black women, and perhaps Latin-American women, may also prove rewarding.

We are indebted to Diane Holdorf, R.N., for her help in locating and restudying patients and to Lynn Baril for technical assistance.

References


*In the study of Dudley and Colman the black patient was inadvertently listed as Caucasian (Colman CA Jr: personal communication).
SPECIAL ARTICLE

CONSUMER-CHOICE HEALTH PLAN (First of Two Parts)

Inflation and Inequity in Health Care Today: Alternatives for Cost Control and an Analysis of Proposals for National Health Insurance

Alain C. Enthoven, Ph.D.

Abstract The financing system for medical costs in this country suffers from severe inflation and inequity. The tax-supported system of fee for service for doctors, third-party intermediaries and cost reimbursement for hospitals produces inflation by rewarding cost-increasing behavior and failing to provide incentives for economy. The system is inequitable because the government pays more on behalf of those who choose more costly systems of care, because tax benefits subsidize the health insurance of the well-to-do, while not helping many low-income people, and because employment health insurance does not guarantee continuity of coverage and is regressive in its financing. Analysis of previous proposals for national health insurance shows none to be capable of solving most of these problems. Direct economic regulation by government will not improve the situation. Cost controls through incentives and regulated competition in the private sector are most likely to be effective. (N Engl J Med 298:650-658, 1978)

HEADLINES will soon appear proclaiming the latest round of health-care cost increases. The nation's health-care spending exceeded $160 billion in 1977 — four times the 1965 amount. Congress will consider cost-control measures with increasing urgency. The Carter Administration is working to develop a national-health-insurance (NHI) proposal that will satisfy key constituencies and still have a chance of passage. The problems are closely interrelated.

INFLATION AND INEQUITY TODAY

Main Problems

Real per capita spending on health care (i.e., net of general inflation) increased 79 per cent from 1965 to 1976; it increased 74 per cent on physicians' services and 110 per cent on hospital care. As a proportion of the Gross National Product, health care went from 5.9 to 8.6 per cent. Costs of medical care are straining public finances at every level of government, and are forcing cutbacks in services to the needy. Public-sector spending rose from $9.5 billion, or 25 per cent of the total, in 1965 to $59 billion, or 42 per cent of the total, in 1976. Most of this outlay is in open-ended, third-party reimbursement programs in which government spending is not controllable. For example, Medicare outlays are increasing from about $17.8 billion in (fiscal) 1976 to about $26 billion in 1978 (i.e., by nearly 50 per cent in two years). In 1975, the increase in medical costs forced Massachusetts to stop paying for the health care of the general-relief population, throwing the burden on local government. From 1968-69 to 1975-76, Medi-Cal costs in Los Angeles County increased from 24 to 42 per cent of property-tax revenue.

Meanwhile, President Carter has recommended a tax cut of some $25 billion. Such a cut is urgently needed to lower the tax burden on the productive sec-