

'Neutropenia' in Black West Indians

A.V. Zezulka, J.S. Gill and D.G. Beevers

University Department of Medicine, Dudley Road Hospital, Birmingham B18 8QH, UK.

Summary: A prospective case control study of routine haematological parameters was conducted in 294 healthy Black and White age/sex-matched subjects. The most important finding relevant to clinical practice was a reduction of total white cell count in Blacks due mainly to reduced neutrophil numbers. Twenty-one percent of sickle negative Blacks had white cell counts below the lowest value seen in Whites. The haemoglobin concentration, erythrocyte mean cell volume and monocyte count were also significantly lower amongst Blacks though lymphocyte counts were higher. The racial differences in haemoglobin and white count were not accounted for by differences in smoking and drinking habits. They were also found when Blacks with sickle cell trait were compared to age/sex-matched Whites and in others taking the oral contraceptive pill. Awareness of racial group should aid interpretation of routine tests and avoid unnecessary investigation of normal 'neutropenic' Blacks.

Introduction

Awareness of racial differences in health and disease is important to clinical practice in both the developed and emerging nations. Medical contact with different ethnic groups is particularly frequent in British inner city areas. We noted that 19 of 105 (18%) Black patients attending our blood pressure clinic had total white cell counts below the local White reference range. This did not appear to be attributable to drug therapy or obvious clinical disease. Possible ethnic differences in white cell numbers are not routinely taken into account in haematological reporting in most centres. We therefore prospectively studied routine haematological measurements in healthy age- and sex-matched Black and White people.

Methods

Healthy Afro-Caribbean Black and age/sex-matched White volunteers were recruited from the hospital out-patient area. Subjects were either patients with minor conditions such as lipomas and ganglions or accompanying friends and relatives. Only one member of any family was studied. All subjects were seen between 0930 and 1300 hours. A detailed questionnaire of current symptoms, past medical history, family history, drugs, alcohol intake and smoking was completed. Blood pressure, height and weight were measured. Peripheral venous blood samples were

taken for routine full blood count and indices, differential white cell and platelet counts. Full blood count was measured on a potassium EDTA sample by a standard automated method using the Coulter Counter S Senior. A manual differential white count was made on longitudinal bands of 100 cells using a modified Wright's stain (polychrome methyl blue and eosin in methanol). Platelets were counted with a Coulter Counter P260. Blood from Black people was screened for sickle cell haemoglobin using a modified Itano's Solubility test. Positive samples then underwent cellulose acetate haemoglobin electrophoresis at alkaline pH.

Subjects with symptoms, current illness (including minor ailments such as upper respiratory tract infection) and past medical history of serious or allergic illnesses were excluded as were those currently pregnant or taking any medications. People taking the oral contraceptive and those with sickle cell trait (haemoglobin A/S) were analysed separately. Only those whose parents were known to be of the same racial group were analysed. White western Europeans were sex- and age-matched to \pm one year with the Black West Indians.

Since many parameters are not normally distributed, medians were calculated for continuous variables and the significance of any differences tested by non-parametric statistics (Wilcoxon's two group test). Differences in frequencies of discontinuous variables were analysed by the Chi squared test with Yates correction. Correlation coefficients were calculated using rank order data.

Correspondence: A.V. Zezulka, B.Sc., M.R.C.P.
Accepted: 29 September 1986

Results

The data from 294 unrelated healthy volunteers were analysed (147 Blacks and 147 age/sex-matched Whites). One hundred and nine Blacks were sickle negative and 38 had sickle trait. Nine of the sickle negative Blacks were taking an oral contraceptive pill and these were matched with nine White oral contraceptive users. All the Whites were United Kingdom born, the majority being English (81%) and the remainder Irish, Scottish or Welsh. Amongst the Black West Indians 87% were of Jamaican background and 53% were born in England.

The findings from full blood counts, differential white cell and platelet counts of sickle negative Blacks and matched Whites are shown in Table I. Total white cell count was significantly lower amongst Blacks and did not differ between sexes within each racial group (Figure 1). Fourteen Black women (20.9%) and 7 Black men (21.2%) had total white counts below the lowest value of the matched Whites. The lower total white cell count in Blacks was attributable to reduction in the absolute neutrophil count (Figure 2) though the absolute monocyte count was also significantly lower. The lymphocyte count was significantly higher amongst Black men and women who showed similar absolute values. No significant differences between the races were found in absolute eosinophil and basophil counts and there were no sex differences.

Haemoglobin level, mean cell volume and mean corpuscular haemoglobin concentration were significantly higher amongst Whites. With the exception of the mean cell volume differences these are also significantly greater in men than women irrespective

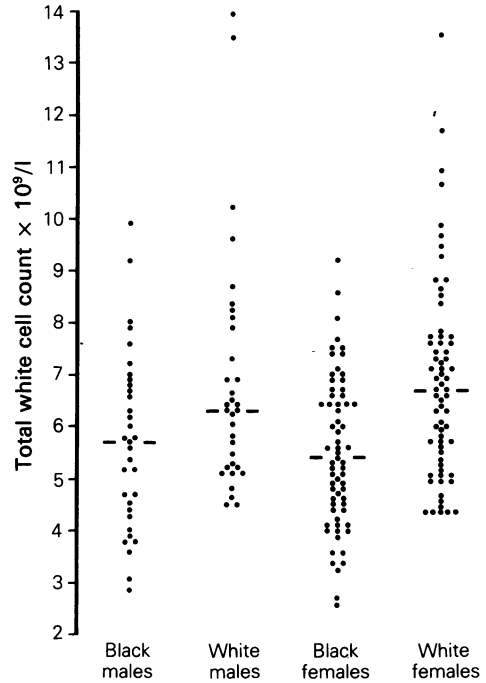


Figure 1 Total white cell count ($\times 10^9/l$) of Black and White men and women. Bars show the median.

of ethnic group. Twenty-four per cent of Black men and 17.9% of Black women had haemoglobin levels below the lowest value found amongst matched Whites (13.5 g/dl for men and 11.7 for women) (Figure

Table I Race and sex differences in routine haematological measurements; all values are medians.

	Male		Female		<i>P</i> values for sex differences	
	White	Black	White	Black	Whites	Blacks
Number	33	33	67	67		
Age (years)	23	23	25	25		
Haemoglobin (g/dl)	15.6†	14.5	13.7*	12.7	<i>P</i> < 0.0001	<i>P</i> < 0.0001
Red blood cells ($\times 10^{12}/l$)	5.04	4.92	4.41	4.4	<i>P</i> < 0.0001	<i>P</i> < 0.0001
Mean cell volume (fl)	89‡	87	91*	84	<i>P</i> < 0.03	
Mean corpuscular haemoglobin concentration (g/dl)	35.4 *	33.9	34.4*	33.6	<i>P</i> < 0.0001	<i>P</i> < 0.03
White blood cell count ($\times 10^9/l$)	6.3‡	5.7	6.7*	5.4		
Neutrophils	3.86†	2.8	4.28*	2.76		
Lymphocytes	1.84‡	2.09	1.85‡	2.13		
Monocytes	0.27‡	0.21	0.3‡	0.21		
Eosinophils	0.07	0.09	0.07	0.07		
Basophils	0.01	0.015	0.01	0.016		
Platelet count ($\times 10^9/l$)	265	260	288§	269	<i>P</i> < 0.03	

Symbols show significance of differences between races: * = *P* < 0.0001 † = *P* < 0.001 ‡ = *P* < 0.03 § = *P* < 0.05

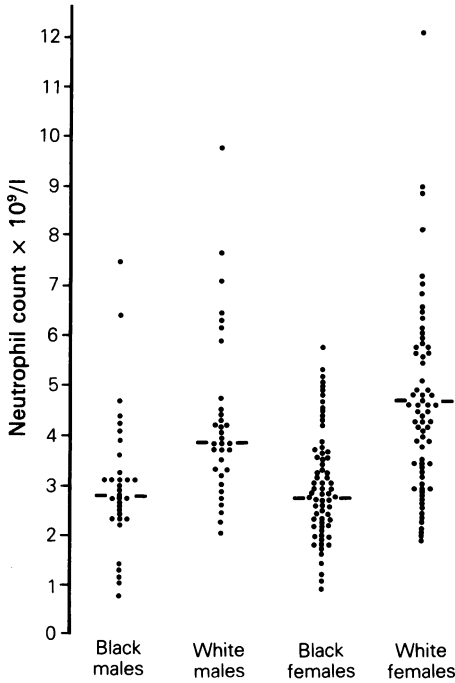


Figure 2 Absolute neutrophil count ($\times 10^9/l$) of Black and White men and women. Bars show the median.

The scattergrams show that a few individuals have white counts and haemoglobin levels that would clinically be considered abnormal. These subjects all met our screening criteria for 'health' and they cannot therefore be retrospectively excluded. However, re-analysis without these data confirms that they do not influence the results. Also, the results did not differ when West Indian and United Kingdom born Blacks were analysed separately.

White men and women were found to have significantly higher alcohol and cigarette consumption than Blacks. White and Black non-smokers and also non-smoking non-drinkers were age- and sex-matched. Healthy Blacks with sickle trait and oral contraceptive users not included in the initial analysis were age- and sex-matched with healthy White oral contraceptive non-users and users. Smoking and drinking habits, sickle trait and the oral contraceptive pill did not affect the racial differences in white count and haemoglobin (Table II). Total white cell counts were higher in both Black and White women taking the oral contraceptive. No differences were found in total or differential white cell counts in 36 sickle trait Blacks compared with age- and sex-matched sickle negative Blacks.

Discussion

This study shows several differences in the routine blood counts of Whites and Blacks. Clinically, the

3). The distributions of mean cell volume (Figure 4) were similar to those of haemoglobin and these parameters correlated in Blacks ($r = 0.42, P < 0.001$) but not Whites ($r = 0.04$). Platelet counts in Blacks and Whites were similar.

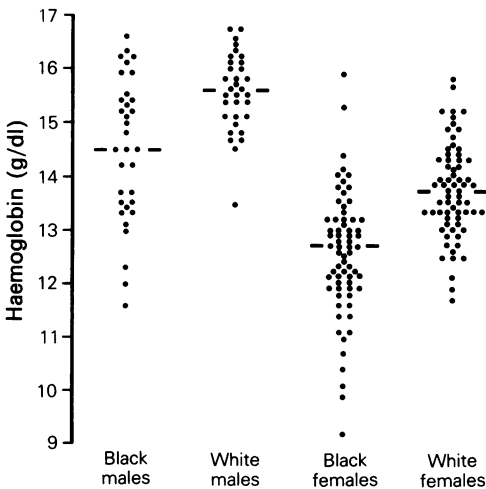


Figure 3 Haemoglobin level (g/dl) of Black and White men and women. Bars show the median.

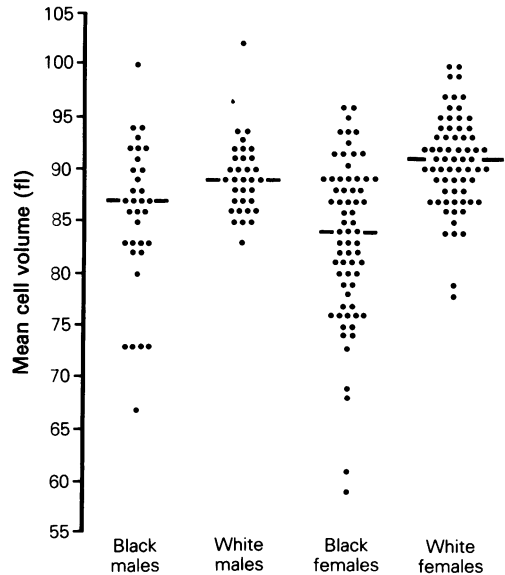


Figure 4 Erythrocyte mean cell volume (fl) of Black and White men and women. Bars show the median.

Table II Total white cell count and haemoglobin of healthy Blacks (B) and Whites (W), matched for age, sex and other characteristics.

	<i>Non-smokers</i>		<i>Non-smokers non-drinkers</i>		<i>Sickle trait Blacks</i>	<i>Matched Whites</i>	<i>Oral contraceptive users</i>	
	<i>B</i>	<i>W</i>	<i>B</i>	<i>W</i>			<i>B</i>	<i>W</i>
Number	67	67	16	16	38	38	9	9
Median white cell count ($\times 10^9/l$)	5.3	6.3*	5.3	6.4†	5.2	6.9*	6	7.5†
Median haemoglobin (g/dl)	12.9	13.9*	13	13.8†	13.3	14†	13	13.7‡

* = $P < 0.001$; † = $P < 0.03$; ‡ = $P < 0.05$

most important observation is the lower white cell count in Blacks and total counts were below the lowest value for matched Whites in 21% of cases. This was mainly due to reduced absolute neutrophil counts. Neutrophil counts of less than $2.5 \times 10^9/l$ are often considered in need of further investigation.¹ By this criteria 37% of Blacks and 10% of Whites in our healthy sample would be candidates for further investigation. Despite the large ethnic communities served by our hospital, our own experience is that such Black patients are subjected to many unnecessary investigations including bone marrow examination.

Lower leucocyte and neutrophil counts have been reported in young and old Blacks in Africa and the United States.²⁻⁷ Data on United Kingdom Blacks are limited.⁷⁻⁹ These studies have problems including the analysis of West Indian and African Blacks together, limitation to single sex, failure to exclude current illness, drug usage and haemoglobinopathy or lack of satisfactory controls. Further, parametric statistical methods have been applied to non-normally distributed data. The time of venepuncture was not standardized to take account of diurnal variation in white count and confounding effects of smoking and alcohol consumption were not examined. Our data show that lower white cell counts occur in both Black West Indian men and women which persist even when these confounding factors are taken into account. The differences in white count were found both in those who were either West Indian or United Kingdom born. White women are reported to have higher white counts than White males.¹ However, no statistically significant difference between the sexes in either racial group was found in this study.

Absolute lymphocyte counts were higher in both Black men and women when compared to Whites. Previous observations on the lymphocyte count are conflicting though the majority do not show ethnic variation. Increased lymphocyte count and raised immunoglobins have been described in Black

Africans.³ No difference was found in the absolute eosinophil counts in our study and Black women in London had similar eosinophil counts to Whites.⁹ Eosinophilia is frequently encountered in Black Africans and has been attributed to parasitic infestation.³ We have specifically excluded subjects with allergic histories to avoid the confounding effect of ethnic differences in allergic disease. Low monocyte counts have been noted in Black Africans but not always in Black Americans.¹⁰ Since neutrophil granulocytopenia and monocytopenia are closely related,¹¹ this suggests that a precursor cell common to both cell lines may be the primary ethnic difference. However, a study of Black and White American infants showed racial differences in peripheral blood leucocyte counts with no difference in bone marrow myeloid or small lymphocyte cells.⁶ Thus, racial differences probably exist in the marginal leucocyte pool or in the blood volume to haemopoietic marrow volume ratio.

The explanation for differences in white cell count is not known but both genetic and environmental causes have been suggested. Arguments to support the genetic hypothesis include the observation that neutropenia may be found in Blacks in Africa, America and the United Kingdom whether or not they were born in those countries. Relatives of 'neutropenic' Gambians did not have different total white counts compared with relatives of families with 'neutrophilic' propositi suggesting that this is not simple Mendelian inheritance.¹² Environmental factors are suggested by an apparent lessening of differences between the ethnic groups in Zambia perhaps due to improving socio-economic conditions.¹³ Dietary factors have been implicated because Blacks eating 'European' diets show less differences from Whites than those taking 'African' diets.⁵ Most of the Blacks studied here were Jamaican and many continue to eat some Caribbean foods together with English foods. Other factors such as endemic infection including

malaria and reduced adrenocortical activity amongst Blacks in Africa have also been proposed as explanations.³

Haemoglobin levels were lower in women as expected. However, haemoglobin was lower by 1 g/dl amongst Blacks of both sexes so this cannot be attributed to menorrhagia. We found that 28.4% of Black women and 3% of Whites had haemoglobins below our laboratory lower limit of 12.0 g/dl. No White men and only 3% of Black men fell below this criterion. We did not find significant correlations between white cell count and haemoglobin concentrations for either race or sex. In the American Ten-state national nutrition survey of 1968 to 1970 Blacks had similarly lower haemoglobin levels than Whites.¹⁴ This difference remained after matching for age, sex, socio-economic status and iron intake and has also been found in highly trained Black and White athletes.¹⁵ Similarly in England there was no difference in the iron intake of Black and White women.⁹ A genetic rather than environmental explanation is supported by the finding of relative erythroid hyperplasia in normal young Black Americans compared with Whites.⁶ Approximately one quarter of Black Americans are reported

to have the single alpha gene deletion type of alpha thalassaemia (heterozygous α -thalassaemia 2/silent carrier).¹⁶ Haematological indices are often in the lower normal range^{17,18} so this might explain the racial differences found in haemoglobin level and erythrocyte mean cell volume. Haemoglobin levels in women should be interpreted taking into account ethnic origin.

We conclude that, when compared to Whites, lower haemoglobin concentrations, total white cell, neutrophil and monocyte counts are a normal feature of apparently healthy Blacks. Awareness of racial differences should aid interpretation of reduced white cell count, avoid false diagnosis of drug-induced neutropenia in patients taking drugs known to cause this problem¹⁹ and prevent unnecessary investigation of healthy 'neutropenic' Blacks.

Acknowledgements

We would like to thank the Haematology Laboratory staff of Dudley Road Hospital, Mrs Dilys Thomas for preparing the figures and Mrs Verdelle Stewart for her secretarial assistance.

References

- Bain, B.J. & England, J.M. Normal haematological values: sex differences in neutrophil count. *Br Med J* 1975, 1: 306-309.
- Broun, G.O., Herbig, F.K. & Hamilton, J.R. Leucopenia in negroes. *N Engl J Med* 1966, 275: 1410-1413.
- Wassermann, H.P. Leucocytes and melanin pigmentation. *SA Med J* 1966, 40 (suppl 21): 3-24.
- Shaper, A.G. & Lewis, P. Genetic neutropenia in people of African origin. *Lancet* 1971, ii: 1021-1023.
- Karayalcin, G., Rosner, F. & Sawitsky, A. Pseudo-neutropenia in American Negroes (letter). *Lancet* 1972, i: 387.
- Kraemer, M.J., Hunter, R., Rosse, C. & Smith, N.J. Race-related differences in peripheral blood and in bone marrow cell populations of American Black and American White infants. *J Natl Med Assoc* 1977, 69: 327-331.
- Ezeilo, G. Non-genetic neutropenia in Africans. *Lancet* 1972, ii: 1003-1004.
- Rippey, J.J. Leucopenia in West Indians and Africans (letter). *Lancet* 1967, ii: 44.
- Bain, B., Seed, M. & Godsland, I. Normal values for peripheral blood white cell counts in women of four different ethnic origins. *J Clin Path* 1984, 37: 188-193.
- Orfanakis, N.G., Ostlund, R.E., Bishop, C.R. & Athens, J.W. Normal blood leucocyte concentration values. *Am J Clin Path* 1970, 53: 647-651.
- Bain, B.J. & Wickramasinghe, S.N. Relationship between the concentration of neutrophils and monocytes in venous blood. *Acta Haemat* 1976, 55: 89-94.
- Howells, D.P.M. Neutropenia in people of African origin (letter). *Lancet* 1971, ii: 1318-1319.
- Shija, A.K., Wosornu, L. & Kasobe, L. Haematological norms in Zambians with special reference to chemotherapy. *Med J Zambia* 1978, 12: 90-92.
- Garn, S.M., Smith, N.J. & Clark, D.C. Lifelong differences in hemoglobin levels between Blacks and Whites. *J Natl Med Assoc* 1975, 67: 91-96.
- Kraemer, M.J., McFarland, R.M., Dillon, T.L. & Smith, N.J. The magnitude and implications of apparent race differences in hemoglobin values (letter). *Am J Clin Nutr* 1975, 28: 566.
- Dozy, A.M., Kan, Y.W., Embury SH *et al.* α -Globin gene organisation in blacks precludes the severe form of α -thalassaemia. *Nature* 1979, 280: 605-607.
- Higgs, D.R., Old, J.M., Clegg, J.B. *et al.* Negro α -thalassaemia is caused by deletion of a single α -globin gene. *Lancet* 1979, ii: 272-276.
- Higgs, D.R., Pressley, L., Serjeant, G.R., Clegg, J.B. & Weatherall, D.J. The genetics and molecular basis of alpha thalassaemia in association with HbS in Jamaican negroes. *Br J Haematol* 1981, 47: 43-56.
- Gavras, I. & Gavras, H. Leukopenia: idiopathic or drug-induced? (letter). *N Engl J Med* 1982, 306: 484.