

Immunoglobulins in Jamaicans and Nigerians with immunogenetic typing of myeloma and lymphoma in Jamaicans

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SYNOPSIS Serum IgG concentration was lower in Jamaicans than in Nigerians. The maternal-foetal IgG ratio was also lower in Jamaican sera than in Nigerian sera. It is suggested that endemic malaria in Nigeria may be responsible for these differences. The higher IgM concentration in the Nigerian cord sera may be further evidence of this. Eighteen new cases of myeloma were detected in Jamaicans between August 1966 and May 1967. Based on Gm typing, only two of these showed evidence of mixed white ancestry. All the others had the typical Gm groups of Negroes. Similarly, only two patients out of a total of 17 with malignant lymphoma showed evidence of mixed white ancestry. Twelve of the patients with myeloma showed serum proteins of the IgG type, five were IgA, and one had only light chains in the serum. The majority of the patients had myeloma protein of the kappa type. The Gm typing suggested that six patients had myeloma protein of the $\gamma 1$ heavy chain subclass, and one patient had a $\gamma 3$ subclass heavy chain, the remainder belonging most likely to the $\gamma 2$ heavy chain subclass since $\gamma 2$ occurs about four times as frequently as $\gamma 4$.

The last five years have seen great advances in the study of the immunoglobulins in health and disease and one of the first diseases in which they were studied was multiple myeloma. This disease is very uncommon in those parts of Africa populated by Negroes (Camain and Lambert, 1964; Davies, 1964; Edington and MacLean, 1964) while in the American Negro its incidence is much higher than in white Americans (MacMahon and Clark, 1956). The incidence of multiple myeloma is also high in Jamaicans (McFarlane, 1966; Talerman, 1968). Various reasons have been advanced for the higher levels of gamma globulin in Africans than in Caucasians (Mohun, 1946; Edozien, 1957).

Materials and Methods

Blood was obtained from 150 Jamaican and

65 Nigerian blood donors; from 35 Nigerian and 30 Jamaican paired maternal cord blood samples (postpartum); from 18 patients with multiple myeloma; and from 17 patients with malignant lymphoma from Jamaica. The diagnosis of multiple myeloma was made on bone marrow biopsy and confirmed biochemically and radiologically. The patients with malignant lymphoma were diagnosed by lymph node biopsy.

The myeloma patients were diagnosed between August 1966 and May 1967. The diagnosis was confirmed both radiologically and by bone marrow biopsy. The myeloma group consisted of eight women and 10 men and the ages ranged between 35 and 68 years.

Total protein, albumin, and globulin were estimated by the biuret method and immunoglobulins by the single radial immunodiffusion method of Mancini, Vaerman, Garbonara, and Heremans (1964) using both Beringwerke and Hyland immunoplates.

Immunoelectrophoresis was determined by the method of Scheidegger (1955) and Gm and Inv groups by the method of Steinberg (1962).

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The following reagents were used to determine the Gm and Inv antigens.

Antigen	Antibody	Anti-Immunoglobulin		Incomplete Anti-D Dilution
		Dilution	Anti-D	
Gm 1	Wils	1/4	251	1/3
Gm 3	Ew	1/4	Jack	1/3
Gm 5	Dr	1/8	3419	1/10
Gm 6	Wms	1/4	Warren	1/3
Inv 1	Math	1/4	Roehm	9/10

The samples from patients with multiple myeloma were tested for Gm 1, Gm 2, Gm 3, Gm 5, and Gm 6, and for Inv 1. To conserve reagents and the patients' sera, of which only small samples were available, sera from the myeloma patients were initially tested at 1/32 dilution.

The samples from the lymphoma patients were tested only for Gm 1, Gm 3, Gm 5, and Gm 6 at 1/16 dilution. None of these samples was titrated.

Results

The results of immunoglobulin levels are summarized in Table I. The values for IgA were similar in various groups except in cord blood. The levels of IgG were significantly lower in all the Jamaican sera than in the corresponding Nigerian sera. The ratio of maternal to foetal IgG was 0.77 in the Jamaican but 1.09 in the Nigerians. Blood donor IgM in both groups was significantly lower than maternal IgM. Jamaican cord sera contained significantly less IgM than Nigerian cord sera.

Serum Immunoglobulin Values (mg/ml)				
	Jamaican		Nigerian ¹	
<i>IgA</i> (mg/ml)				
Blood donors	2.66 ± 0.18	} P > 0.5	2.37 ± 0.4	} P > 0.5
Maternal	2.40 ± 0.14		2.44 ± 0.68	
Foetal	68% = Nil 32% = Trace		80% = Trace 20% = Nil	
<i>IgG</i> (mg/ml)				
Blood donors	13.18 ± 6.54	} P = 0.005	36.57 ± 2.80	} P = 0.001
Maternal	10.29 ± 5.85		27.00 ± 5.50	
Foetal	13.13 ± 7.08	} P = 0.005	24.96 ± 7.70	} P < 0.01
<i>IgM</i> (mg/ml)				
Blood donors	1.02 ± 0.58	} P = 0.002	1.21 ± 0.56	} P = 0.001
Maternal	2.08 ± 2.71		2.90 ± 1.05	
Foetal	75% = Trace 25% = Nil		0.091 ± 0.03	} P = 0.001

Table I Summary of serum immunoglobulin values¹

¹Modified from data given by McFarlane and Udeozo (McFarlane, H., and Udeozo, I. O. K. (1968). *Arch. Dis. Childh.*, 43, 42).

Table II summarizes the findings in multiple myelomatosis. Here it can be seen that the age range was between 35 and 68 years. There was no difference in the sex distribution. Twelve of these patients were of IgG type myeloma, five were of IgA type, and in one patient (case 16) the serum protein was of Bence-Jones type. Table II also shows that six of these patients had myeloma protein of the lambda type light chain, whereas in 12 patients the myeloma protein was of the kappa type light chain. One patient (case 16, Table II) may belong to that rare group of myelomatoses with a unique type of lambda Bence-Jones proteinaemia of the disulphide dimer type recently referred to by Grey and Kohler (1968). Eight of the 17 patients whose urines were tested gave a positive reaction for Bence-Jones proteins.

Antisera to determine the heavy chain subtypes of the G myeloma protein were not available, and the results of the Gm determinations were used to estimate the γ chain subclass. Four of the IgG myeloma samples (nos. 3, 4, 10, and 12) have a raised concentration of the Gm 1 antigen. It is highly probable that this antigen is carried by the myeloma protein. One sample (no. 14) has a high titre of Gm 5 and Gm 6. These antigens are probably carried by the myeloma protein. Kunkel, Allen, Grey, and Martenson (1964) and Terry, Fahey, and Steinberg (1965) have shown that Gm 1 and Gm 3 are carried by the γ_1 chain and that Gm 5 and Gm 6 are carried by the γ_3 chain. The Gm typing suggests that the myeloma protein in samples 3, 4, 10, 11, 12, and 13 has a γ_1 heavy chain, and that the heavy chain in sample 14 is γ_3 . The heavy chain in the remaining samples may be either γ_2 or γ_3 .

The Inv 1 titre of the sera is also shown in Table II. One sample (no. 14) had a high titre of Inv 1 but none of the others did.

Two of the myeloma patients (cases 3 and 16) showed the presence of Gm 3 in their non-myeloma IgG protein, and this is evidence of white ancestry. No evidence of white ancestry was evident in any of the other samples. Similarly in the group of 17 lymphoma patients, only two were observed with the Gm phenotype of mixed white ancestry.

Discussion

Endemic malaria in Nigeria may be responsible for the higher concentrations of serum IgG in Nigerians than in Jamaicans and for the lower maternal-foetal IgG ratio in the Jamaicans. The higher IgM level in the Nigerian foetal sera appears to support this hypothesis. The cause of the higher IgM level in maternal blood than in donor blood is not known but similar results have been reported by Rowe, McGregor, Smith, Hall, and Williams (1968).

Case No.	Age (years)	Sex	Type of Myeloma				Gm Titre of Whole Serum				Inv 1		
			Immuno-globulin	Light Chain	Heavy Chain	Gm	Inv	1	3	5		6	
1	67	F	G	l					<32	<32	<32	<32	<32
2	57	M	A	l					>32	<32	>32	<32	<32
3	62	F	G	k		1	1		>4096	128	64	<32	<32
4	47	M	G	l		1	1		2048	<32	32	<32	128
5	35	M	A	k				1	256	<32	<32	<32	64
6	62	M	A	k					>32	<32	>32	<32	<32
7	56	M	A	k					256	<32	<32	<32	64
8	48	M	G	k					<32	<32	<32	<32	<32
9	53	M	G	k					64	<32	<32	<32	<32
10	39	F	G	k		1	1		>4096	<32	<32	<32	<32
11	46	F	G	k		1	1	1	512	<32	<32	<32	512
12	62	M	G	k		1	1		>4096	<32	<32	<32	<32
13	59	M	G	k		1	1	1	512	<32	64	<32	256
14	52	F	G	k		3	5, 6	1	<32	<32	>4096	>4096	1024
15	54	F	A	l					64	<32	<32	<32	<32
16	53	F	B. J.	l					>32	>32	>32	<32	<32
17	68	M	G	k					Not done	Not done	Not done	Not done	Not done
18	53	F	G	l					Not done	Not done	Not done	Not done	Not done

Table II Summary of findings in myeloma in Jamaicans

It is clear that ideal conditions for studying the incidence of multiple myeloma could best be achieved if the study were carried out over a longer period and/or if a large population survey in the island could be undertaken.

The types of myeloma in Jamaica are similar to those reported elsewhere. The proportion of kappa light chain type to lambda light chain type is similar to the proportion of these light chain types reported in other series of myeloma. The Gm titre of the sera showed that the majority of both the myeloma and lymphoma patients are of Negroid stock, and this suggests that the incidence of myeloma in Jamaica may not be due to mixed racial ancestry.

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References

- Camain, R., and Lambert, D. (1964). Les hématosarcomes en Afrique noire Occidentale et Centrale francophone. In *The Lymphoreticular Tumours in Africa; A Symposium*, edited by F. C. Roulet, pp. 42-53. Karger, Basle.
- Davies, J. N. P. (1964). Lymphomas and leukaemias in Uganda Africans. *Ibid.*, pp. 67-79.
- Edington, G. M., and McLean, C. M. U. (1964). The relative incidence of tumours of the reticulo-endothelial system in Ibadan, Nigeria. *Ibid.*, pp. 54-66.
- Edozien, J. C. (1957). The serum proteins of healthy adult Nigerians. *J. clin. Path.*, 10, 276-279.
- Grey, H. M., and Kohler, P. F. (1968). A case of tetramer Bence-Jones proteinemia. *Clin. exp. Immunol.*, 3, 277-285.
- Kunkel, H. G., Allen, J. C., Grey, H. M., Martensson, L., and Grubb, R. (1964). A relationship between the H chain groups of 7S γ -Globulin and the Gm system. *Nature (Lond.)*, 203, 413-414.
- MacMahon, B., and Clark, D. W. (1956). The incidence of multiple myeloma. *J. chron. Dis.*, 4, 508-515.
- McFarlane, H. (1966). Multiple myeloma in Jamaica: a study of 40 cases with special reference to the incidence and laboratory diagnosis. *J. clin. Path.*, 19, 268-271.
- Mancini, G., Vaerman, G. P., Garbonara, A. O., and Heremans, J. F. (1964). A single-radial-diffusion method for the immunological quantitation of proteins. *Protides Biol. Fluids*, 11, 370-373.
- Mohun, A. F. (1946). Serum albumin and globulin levels in Africans as compared with Europeans, with note on technique. *Ann. trop. Med. Parasit.*, 40, 29-33.
- Rowe, D. S., McGregor, I. A., Smith, S. J., Hall, P., and Williams, K. (1968). Plasma immunoglobulin concentrations in a West African (Gambian) community and in a group of healthy British adults. *Clin. exp. Immunol.*, 3, 63-79.
- Scheidegger, J. J. (1955). Une micro-méthode de l'immuno-électrophorèse. *Int. Arch. Allergy*, 7, 103-110.
- Steinberg, A. G. (1962). Evidence for a Gm allele negative for both Gm (a) and Gm (b). *Vox Sang. (Basel)*, 7, 89-92.
- Talerman, A. (1968). Unpublished.
- Terry, W. D., Fahey, S. L., and Steinberg, A. G. (1965). Gm and Inv factors in subclasses of human IgG. *J. exp. Med.*, 122, 1087-1099.