

# The Australia antigen in Brazilian healthy persons and in leprosy and leukaemia patients

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**SYNOPSIS** The distribution of the Australia antigen was investigated in 633 white and negroid healthy persons, 218 white and negroid leprosy patients, and 50 white leukaemia patients. The subjects were living at the time of the investigation in two southern Brazilian cities. Two of the patients with leukaemia showed the antigen, as also did three out of 358 negro subjects, but no reactors were found among the healthy white subjects and leprosy patients.

Australia antigen, so called because it was first found in the serum of an Australian aborigine, is detected using antisera from patients who have received large numbers of transfusions. The studies on the antigen have been summarized recently (Blumberg, Sutnick, and London, 1968). Soon after its discovery, the association of the antigen with hepatitis virus was established (Blumberg, Gerstley, Hungerford, London, and Sutnick, 1967a). Although the antigen is rare in normal American populations, it is found fairly often in patients with acute viral hepatitis (both 'infectious' and 'post-transfusion'), but not in patients with a variety of other liver diseases. Also it is often found in sera from cases of chronic disease characterized by a prolonged and (usually) severely impaired immune mechanism (Blumberg *et al*, 1968; Sutnick, London, Gerstley,

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Cronlund, and Blumberg, 1968; London, Sutnick, and Blumberg, 1969). In these patients the presence of the antigen identifies chronic anicteric hepatitis. The sera from chronic diseases in which the antigen is found include Down's syndrome (mongolism), leukaemia, and chronic renal disease in patients undergoing haemodialysis. The antigen has been isolated from blood, and under the electron microscope is seen to be a particle of 200 Å diameter which has the appearance of a virus (Bayer, Blumberg, and Werner, 1968). In addition to these disease associations the antigen is common in apparently normal people living in parts of the tropics and tens of millions of people probably carry it. These apparently normal people do not have overt evidence of hepatitis but appear to be carriers of the disease. Their identification is useful in the screening tests to eliminate carriers of hepatitis.

In some of these tropical regions the antigen is more often found in patients with lepromatous leprosy (particularly young males) than in patients with tuberculoid leprosy or in non-leprosy controls from the same region (Blumberg, Melartin, Lechat, and Guinto, 1967b; Blumberg, Friedlaender, and Woodside, 1969a). Where Australia antigen is very rare in the general population, eg, Italy, the United States of America, the frequency of Australia antigen is not increased in lepromatous leprosy patients who have been tested. An interesting feature of the distribution of the disease in tropical populations is that the family segregation is consistent with simple autosomal recessive inheritance (Blumberg, Melartin, Guinto, and Werner, 1966; Blumberg, Melartin, Guinto, and Lechat, 1969b).

Sample	No. Studied	No. with Australia Antigen
<i>Healthy individuals</i>		
Whites, Florianópolis	109	0
Whites, Pôrto Alegre	120	0
Whites, relatives of leukaemia patients mainly from Pôrto Alegre	46	0
Light Mulattoes, Pôrto Alegre	120	0
Dark Mulattoes, Pôrto Alegre	120	1 (0.8%)
Negroes, Pôrto Alegre	118	2 (1.7%)
Total	633	3 (0.5%)
<i>Sick Persons</i>		
Leprosy { Whites, Florianópolis	200	0
Negroids, Florianópolis	18	0
Leukaemic Whites, mainly from Pôrto Alegre	50	2 (4.0%)
Total	268	2 (0.7%)
Grand total	901	5 (0.6%)

Table I *The distribution of Australia antigen in selected samples of southern Brazilian populations*

Sample	Sex		Age Group (yr)			
	M	F	0-29	30-59	Over 60	Unknown
<i>Healthy individuals</i>						
White, Florianópolis	33.9	66.1	63.3	34.9	1.8	—
White, Pôrto Alegre	44.2	55.8	47.5	43.3	9.2	—
White, relatives of leukaemia patients mainly from Pôrto Alegre	47.8	52.2	41.2	58.8	—	—
Light Mulattoes, Pôrto Alegre	25.8	74.2	55.1	42.8	2.5	—
Dark Mulattoes, Pôrto Alegre	30.4	69.2	51.7	43.3	5.0	—
Negroes, Pôrto Alegre	36.4	63.6	44.9	49.2	5.9	—
Total	35.2	64.8	51.5	43.9	4.6	—
<i>Sick persons</i>						
Leprosy, White, Florianópolis	51.5	48.5	23.5	62.5	12.0	2.0
Leprosy, Negroid, Florianópolis	66.7	33.3	5.6	61.1	22.2	11.1
Leukaemic Whites, mainly from Pôrto Alegre	52.0	48.0	50.0	40.0	10.0	—
Total	52.6	47.4	27.3	58.2	12.3	2.2
Grand total	40.4	59.6	44.3	48.1	6.9	0.7

Table II *Sex, age, and genetic group of individuals studied*

## Materials and Methods

Blood was collected from (1) healthy white and negro subjects between December 1961 and June 1965 for gene flow studies and other investigations (Salzano, Suñé, and Ferlauto, 1966; Salzano, Rocha, and Tondo, 1968); (2) healthy whites and leprosy patients between August 1963 and March 1964 for the study of the relationship between genetic polymorphisms and leprosy (Schwantes, Salzano, Castro, and Tondo, 1966; Salzano *et al*, 1967); (3) leukaemic patients and their relatives between June and November 1963 for the investigation of blood group changes in leukaemia (Ayres, Salzano, and Ludwig, 1966).

In the material obtained in Brazil, if possible, the red cells and plasma were immediately separated after collection, the plasma being kept in the deep freeze at about  $-20^{\circ}\text{C}$  until they were sent by air to Philadelphia for the determination of Australia antigen. Otherwise plasma was frozen immediately and later with the other material sent to Philadelphia.

Australia antigen determinations were carried out in Philadelphia from June to August 1966, by precipitation in agar gel using the double diffusion micro-Ouchterlony technique described elsewhere (Blumberg and Riddell, 1963; Blumberg *et al*, 1966). The antiserum used was rabbit antiserum no. 6 (Melartin and Blumberg, 1966) and a human antiserum. The material tested, therefore, was stored between four and a half years or seven months. Since the Australia antigen was present in sera or plasma stored for up to seven years (Blumberg, Alter, and Visnich, 1965), the long storage of some of our material has probably not affected the results.

## Results and Discussion

Table I shows the distribution of Australia antigen in the samples tested and Tables II and III furnish additional clinical information.

Fewer than half of the individuals studied were males and about half were distributed in the age group 0 to 29 years. Some 80% of the leprosy patients had lepromatous leprosy which was generally of the mild type, and 20% of those with leukaemia showed the acute myeloblastic form. The Australia antigen was present in only three of the 633 healthy persons studied (0.5%), was completely absent among the 218 leprosy patients tested, but was present in two of the leukaemia patients. The individuals showing Australia antigen were a dark Mulatto, a woman, age 28; two Negroes, both male, were aged 67 and 67. All three came to the collecting post because they were receiving some kind of treatment but none presented abnormal haemoglobin (Table II). The following is an account

Genetic Group	Type of Leprosy				Severity of the Disease			
	Lepromatous	Tuberculoid	Indeterminate	Unknown	Mild	Moderate	Severe	Unknown
Whites, Florianópolis	79.0	9.5	11.0	0.5	90.5	8.5	0.5	0.5
Negros, Florianópolis	88.9	5.5	5.6	—	100.0	—	—	—
Total	79.8	9.2	10.5	0.5	91.3	7.8	0.5	0.4

Table IIIa Clinical summary of the leprosy patients

Genetic Group	Type of Leukaemia				
	Acute Lymphoblastic	Acute Myeloblastic	Chronic Lymphoid	Chronic Myeloid	Other
Whites, mainly from Pôrto Alegre	26.0	20.0	14.0	36.0	4.0

Table IIIb Clinical summary of leukaemic patients

of the main clinical findings observed in two patients who carried the antigen.

#### ILLUSTRATIVE CASES

##### Case 15704

A white woman, aged 68 (maternal and paternal grandparents of Portuguese ancestry), was living at the time of examination in the city of Rio Grande. She showed the first symptoms of disease in June 1959, and blood was tested on 18 November 1965. At the time of examination the only symptom she presented was splenomegaly and clinically she was considered to be in good health. No information is available about previous treatment and transfusions. Haematological tests performed in 1965 showed 82,000 leucocytes (0.5% leucoblasts), 413 m/cmm red blood cells, and a haemoglobin level of 80% of the normal. She was diagnosed as having chronic myeloid leukaemia. Blood group antigens did not show any abnormality but there appeared to be a depression in the  $\alpha$  and  $\beta$  agglutinins in the plasma (group O, titre of anti-A 1:2 against 1:32 in the control; anti-B: 1:1 against 1:32 in the control).

##### Case 157075

A white man, aged 57 (maternal grandparents of German ancestry, paternal grandparents of Spanish ancestry), was living at the time of investigation in the city of Pelotas. He showed the first symptoms of disease in May 1962, and blood was tested on 18 November 1965. At the time of examination he showed adenopathy, splenomegaly, and hepatomegaly; his clinical condition was considered to be fair. He had not been treated with corticoid and antimetabolite drugs since June 1965 and had received radiotherapy in 1963 but never any blood transfusion. Haematological tests performed in 1965 showed

41,000 leucocytes (44% leucoblasts) and 214 mc/mm red blood cells. The diagnosis was of chronic lymphoid leukaemia. He presented two abnormalities in blood group antigens, a depression in  $A_1$  (45% of agglutination against 96% in the control) and a rise in an H-like element (14% of agglutination against 3% in the control). Evidence that he was genetically of group A and not an intermediary was obtained through the testing of his daughter, who had a normal group A blood; his wife was group O. No changes in his  $\beta$  agglutinin were detected. The inhibition titre of saliva was A antigen, 1:8, and H antigen, 1:1; that of his daughter was A 1:64 and of H, 1:16.

The frequency of Australia antigen in the leukaemia patients appears to be somewhat less than that found in American populations, but since the numbers tested in Brazil are small these differences may not be significant.

As noted above, Australia antigen is not found in increased frequency in lepromatous leprosy in areas where the antigen is not common in the general population. However, it is significantly more common in lepromatous leprosy in areas where its frequency is high in the general population. Thus the frequency of Australia antigen in lepromatous leprosy in the Philippines and India is nearly twice as high as it is in the normal populations or in those patients with tuberculoid leprosy. From this we may surmise that lepromatous leprosy patients are more susceptible to chronic infection with hepatitis, but this would not become manifest unless the organism were relatively common in the general population.

The antigen seems to be rare in healthy white and negro Brazilian populations (no reactors among 275 white and two among 358 negro subjects; see Table I). This is a finding which is not much at variance with previous results. Thus, Blumberg *et al* (1966) did not find the antigen among 607 US Negroes or 101 Italians, and only one out of 44 Portuguese living in Hawaii showed it.

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