GENETIC MARKERS IN LIVER DISEASE*

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As part of a programme of research into the ecology of hypertension in Cape Town's racial groups, an attempt is being made to characterize these racial groups in terms of their gene frequencies. For this purpose a number of 'genetic markers' are being studied in members of the 4 main ethnic groups: White, African, Cape Coloured and Cape Malay. The genetic markers which are under investigation include several blood group systems, certain serum-protein components and enzymes and a number of physical traits (PTC tasting, colour vision, etc.). A variety of other constitutional characteristics are also being examined.

To start with, blood samples were collected from adult patients in Groote Schuur Hospital. Patients who had recently received blood transfusions, those with haemoglobin levels of less than 11·0 G per 100 ml. and those known to have liver disease were excluded. The material included 100 patients from each of the 4 racial groups and they were drawn from all the wards of the hospital ('hospital series').

In addition, blood samples were collected from 50 patients—irrespective of race—with diffuse hepato-cellular disease. This 'liver disease' series included 16 Whites, 16 Africans, 16 Cape Coloureds and 2 Cape Malays. The causes of the liver disease included alcoholic cirrhosis (28 cases), cryptogenic cirrhosis (9 cases), cardiac cirrhosis (4 cases), biliary cirrhosis (2 cases) and viral hepatitis (7 cases).

The 'liver disease' series was analysed separately in order to determine whether the presence of liver disease interfered with the expression of the genotype particularly with respect to the serum-protein components (haptoglobins, transferrins and haemoglobins) and the enzymes (glucose-6-phosphate dehydrogenase and serum cholinesterase). This was relevant to our general survey of genetic markers because it has frequently been reported that absence of haptoglobins is common in African populations. While this phenomenon is widely regarded as an African 'genetic' trait, we suspected that sometimes it may be an acquired characteristic secondary to liver disease.

Results

Some of the findings in this preliminary survey are summarized in this paper.

1. *Serum haptoglobin phenotypes* were assayed by starch-gel electrophoresis. The results are shown in Table I. No conclusions about racial affinities and differences should be drawn from this series of hospital patients, but it may be noted that in general the Hp^1 and Hp^2 gene frequencies in Africans and Whites follow the pattern reported from other parts of the world, i.e. a relative deficiency of Hp^2 in Africans compared with Whites. In Table II the percentage distribution of the haptoglobin phenotypes is shown for the general hospital series and for the liver-disease group. In the hospital series, only one patient in 400 (an African) was found with absent haptoglobins (0·25%). In the liver series, 17 patients had absent haptoglobins (34%). It will be seen from Table III that in the liver series, *haptoglobins were absent in members of all 4 racial groups.*

TABLE I. HAPTOGLOBIN GENE FREQUENCIES

Hospital series	Hp^1	Hp^2	*Absent haptoglobin (%)*
White	·39	·61	—
Malay	·33	·67	—
Cape Coloured	·39	·61	—
African	·56	·44	1

TABLE II. HAPTOGLOBIN PHENOTYPES (PERCENTAGE DISTRIBUTION)

	Hospital series				
	White	*Malay*	*Coloured*	*African*	*Liver disease*
Number	100	100	100	100	50
1–1	18	13	16	34	18
1–2	43	41	46	43	26
2–2	39	46	38	22	22
Absent	0	0	0	1	34

In a few of the liver patients, it was possible to do repeated examinations of the haptoglobin pattern. There were 2 Coloured patients with severe viral hepatitis in whom the haptoglobins were initially absent. As the disease subsided, a 2:2 and a 2:1 haptoglobin pattern appeared in their sera. A White patient with alcoholic cirrhosis of the liver was found to have a 2:2 pattern when he first came to hospital; when his condition deteriorated, his haptoglobins disappeared.

TABLE III. HAPTOGLOBIN PHENOTYPES: LIVER DISEASE

	White	*Malay*	*Coloured*	*African*	*Total*
Number	16	2	16	16	50
1–1	2	0	2	5	9 (18%)
1–2	5	0	5	3	13 (26%)
2–2	5	0	4	2	11 (22%)
Absent	4	2	5	6	17 (34%)

There seems little doubt that, in many cases, absent haptoglobin is an acquired characteristic and that liver disease is one of the causes of absent haptoglobin bands on starch-gel electrophoresis. Particularly when studying African populations, in whom liver disease is quite common, this fact must be taken into account before absent haptoglobins can be assumed to be a genetic trait.

2. *Transferrin phenotypes* were also determined by starch-gel electrophoresis. The findings are shown in Table IV. In this investigation there was nothing unusual about the distribution of transferrin phenotypes in patients with liver disease.

3. *Haemoglobin phenotypes* were characterized by electrophoresis on cellulose acetate. In this investigation only 3 patients with abnormal haemoglobins were detected (2 Whites and 1 Malay). There were no abnormal haemoglobins in the liver series.

4. *Glucose-6-phosphate dehydrogenase activity* was determined by the method of Motulsky and Campbell. There were only 2 patients (a Coloured and an African) with deficiency of this enzyme; neither of them had liver disease.

*Abstract of a paper presented at a meeting of Research Forum, University of Cape Town, held on 2 April 1964.

TABLE IV. TRANSFERRIN PHENOTYPES (PERCENTAGE DISTRIBUTION)

	Hospital series				Liver disease
	White	Malay	Coloured	African	
Number	100	100	100	100	50
CD_1	1	2	3	6	4
C	98	98	97	94	96
B_2C	1	0	0	0	0

TABLE V. SERUM CHOLINESTERASE PHENOTYPES (PERCENTAGE DISTRIBUTION)

	Hospital series				Liver disease
	White	Malay	Coloured	African	
Number	100	100	100	100	50
Usual	94	99	98	99	84
Unusual	6	1	2	1	16

5. *Serum cholinesterase phenotypes.* The method of Harris and Robson was used. The findings are set out in Table V. The relatively low frequency of the 'unusual' variants in the non-White members of the hospital series is noteworthy but the significance of this finding in a selected sample is doubtful. The relatively high incidence (16%) of 'unusual' variants in the liver series compared with the hospital series (2·5%) is significant. It may indicate that there is abnormal serum cholinesterase production in patients with liver disease or that liver disease is more common in people who have inherited unusual cholinesterases.

These studies are being extended to include other genetic markers and the tests are being applied to unselected members of these 4 racial groups in the general population

This investigation was supported by a generous grant (HE-06267) from the National Institutes of Health of the Public Health Service of the USA.