Population Genetic Studies in the Congo

IV. Haptoglobin and Transferrin Serum Groups in the Congo and in Other African Populations

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GENETIC HETEROGENEITY among the various Negroid populations of Africa is amply demonstrated by the gene distributions within the blood groups, the abnormal hemoglobins, and the locus determining glucose-6-phosphate dehydrogenase (G6PD) production. This variation in Congolese populations is described in three companion papers (Motulsky *et al.*, 1966; Fraser, 1966; Fraser *et al.*, 1966). Numerous investigators have reported the haptoglobin and, to a lesser extent, transferrin phenotypes among various tribal groups. This paper will summarize those findings and will present hitherto unpublished data on Congolese natives as well as two Bantu tribes in South Africa.

MATERIALS AND METHODS

In 1959, specimens of blood were collected from Pygmies in the Ituri Forest and from various inhabitants of rural and urban areas in the Congo region. Serum was shipped by air to Seattle in ice-containing thermos jugs, arriving in good condition. During a similar period, serum specimens obtained from South African native blood donors by Dr. A. Zoutendyk were also sent by air, and most of these were in satisfactory condition for electrophoretic analysis.

Starch gel electrophoresis was performed by the horizontal method of Smithies (1955), although occasional samples were repeated by the vertical method (Smithies, 1959). A discontinuous buffer system (Poulik, 1957) was employed for both kinds of gels. Control sera of known haptoglobin and transferrin types were routinely included for comparison. Gels were sliced and stained with benzidine and amido black as previously described (Giblett, 1959).

Table 1 lists the geographic origin, tribe, sex, relative age, per cent with hemoglobin AS, frequency of G6PD deficiency, regional incidence of malaria, and any additional known data pertaining to the subjects tested. Most individuals were in apparently good health, and 25 of the Yaka women were pregnant. A number of people tested in series Stan, Ya, and Leo were hospital patients.

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TABLE 1. SOURCE OF SPECIMENS AND DETAILS OF INDIVIDUALS SURVEYED IN THIS PAPER.

Geographical source and series designation		Tribe	No.	Sex	Age	Hb AS %	G6PD deficiency (males) %	Malaria	Additional
Leopoldville	Leo	Mixed Bantu	99	78♂ 21♀	Adult	20.4	13.9	Low	A few were hospital patients
Stanleyville	Stan	Mixed Bantu	98	♂	Adult	29.2	14.3	Low	Hospital patients
Bukavu	Shi	Shi	116	♂	10–20 yrs.	6.5	13.8	Low	School children
Astrida	Tu	Tutsi	90	♂	10–20 yrs.	none	2.2	Low	School children
Nyanza	Hu	Hutu	99	♂	10–20 yrs.	5.1	6.1	Low	School children
Popokabaka	Ya	Yaka	101	41♂ 60♀	Adults	28.0	22.0	Prevalent	Hospital patients (25 women pregnant)
Gemena	Wa	Ngbaka	57	♂	Adults	10.5	6.1	Prevalent	Mostly hospital patients
Ituri Forest	Pyg	Pygmies	126	♂	Adults	31.0	4.0	Prevalent	
Johannesburg		Xhosa	265	♂	Adults	—	—	Low	Blood donors
Johannesburg		Msutu	218	♂	Adults	—	—	Low	Blood donors

TABLE 2. HAPTOGLOBIN AND TRANSFERRIN TYPES OF CENTRAL AND SOUTH AFRICANS OF THIS PAPER.

		HAPTOGLOBINS										TRANSFERRINS			
		1-1		2-2		2-1		2-1(mod)		0		CD_1		C	
Population	No.	No.	Frequency	No.	Frequency	No.	Frequency	No.	Frequency	No.	Frequency	No.	Frequency	No.	Frequency
CONGO															
Pyg	121	8	.066	25	.206	49	.405	1	.009	38	.314	8	.067	113	.933
Leo	93	34	.366	14	.150	34	.366	8	.086	3	.032	3	.032	90	.968
Stan	93	28	.301	13	.140	46	.495	0	0	6	.064	5	.054	88	.946
Ya	98	34	.347	4	.041	25	.255	5	.051	30	.306	10	.102	88	.898
Wa	57	15	.263	10	.175	21	.368	2	.035	9	.158	6	.105	51	.895
Shi	110	19	.173	14	.127	48	.436	5	.045	24	.218	8	.073	102	.927
Hu	91	28	.308	18	.197	27	.297	2	.022	16	.175	2	.022	89	.978
Tu	90	25	.277	24	.266	23	.255	2	.022	16	.177	4	.044	86	.956
SOUTH AFRICA															
Xhosa	265	75	.283	57	.215	96	.362	28	.106	9	.034	6	.023	259	.977
Msutu	218	63	.289	46	.211	83	.381	15	.069	11	.050	20	.091	198	.909

RESULTS AND DISCUSSION

Table 2 presents the observed haptoglobin and transferrin phenotype frequencies. These results may be compared with the data in Table 3, which summarizes the reports of other workers and includes a large sample of random American Negro adults studied in this laboratory.

A notable feature is the variable frequency of apparent ahaptoglobinemia. This phenomenon is known to be associated with increased red cell destruction and is also subject to hormonal influence. Barnicot *et al.* (1960) noted a higher frequency among women in Nigeria, and this finding was confirmed in Liberian subjects by Neel *et al.* (1961), who also found that pregnancy was a contributing factor. Among the 25 pregnant women in the Yaka sample tested, 14 had no demonstrable haptoglobin, as compared with only six of the 35 nonpregnant women. Among the 39 males tested, however, ten were haptoglobin deficient, so that, if sex alone is a determinant of haptoglobin level, its effect is apparently masked by other factors in this population.

Attempts to correlate the frequency of ahaptoglobinemia with the distribution of malaria, sickle hemoglobin, and G6PD deficiency were largely unrewarding, in accordance with the findings of Barnicot *et al.* (1960). For example, although those tribes having a high incidence of malaria, such as the Ngbaka, Yaka, and Pygmy, also had high levels of ahaptoglobinemia (15 to 31%), other tribes with little or no malaria, such as the Shi and Tutsi, also had high levels of ahaptoglobinemia. No correlation was found with sickle trait; several tribes with a relatively low frequency of hemoglobin S had large numbers of ahaptoglobinemics, and no difference in the frequency of ahaptoglobinemia was found between sicklers and nonsicklers as a whole. Similarly, G6PD deficiency could not be shown to occur more commonly in those groups with absent haptoglobin. Nevertheless four of the 12 individuals who were both sicklers and enzyme deficient were ahaptoglobinemic. Although these numbers are small, this finding might indicate that possession of both these genes may have caused the depression of serum haptoglobin levels that neither can do alone. It may be significant that the population samples obtained in two urban areas, Leopoldville and Stanleyville, had the smallest number of individuals without demonstrable haptoglobin. This might be a reflection of the lower prevalence of a variety of diseases associated with red cell parasitism and/or liver damage as compared to rural populations.

Calculation of haptoglobin gene frequencies is necessarily based on the assumption that genetic, physiological, and environmental agents tending to depress the amount of serum haptoglobin affect all phenotypes equally. This assumption is unlikely to be correct for two reasons: (1) Individuals of type 1–1 ordinarily have higher haptoglobin levels than those of type 2–2 (Nyman, 1959), and therefore one might reasonably expect that individuals of the latter phenotype would be more susceptible to "suppressive" influences. (2) Studies of American Negro families (Giblett and Steinberg, 1960) indicate a higher incidence of ahaptoglobinemia among individuals who carry a gene associated with the Hp 2–1(mod) phenotype. Parker and Bearn (1963) consider this to be an operator rather than structural gene mutant, but the argument is un-

TABLE 3. HAPTOGLOBIN AND TRANSFERRIN PHENOTYPES IN NEGRO SUBJECTS PREVIOUSLY REPORTED FROM THIS AND OTHER LABORATORIES.

Population	No.	HAPTOGLOBINS 1-1 No.	1-1 Frequency	2-2 No.	2-2 Frequency	2-1 No.	2-1 Frequency	2-1(mod) No.	2-1(mod) Frequency	0 No.	0 Frequency	TRANSFERRINS CD_1 No.	CD_1 Frequency	C No.	C Frequency
NORTH AFRICA															
Liberia and Ivory Coast[1]	614	327	.532	55	.089	232	.378	—	—	—	—	—	—	—	—
Liberia[2]	356	149	.419	33	.093	67	.188	37	.104	70	.197	25	.069	308	.925
Nigeria															
Yoruba[3]	99	53	.535	3	.030	11	.111	—	—	32	.323	—	—	—	—
Fulani[4]	111	40	.360	3	.027	22	.198	5	.045	41	.369	7	.063	104	.937
Fulani[5]	84	24	.286	4	.048	14	.166	—	—	42	.500	10	.147	57	.838
Habe[4]	120	24	.200	7	.058	52	.433	4	.033	33	.275	18	.150	102	.850
Ibo[6]	70	13	.185	4	.057	12	.171	7	.100	34	.486	9	.128	61	.872
Senegal[7]	396	148	.374	47	.119	141	.356	44	.111	16	.040	—	—	—	—
Gambia[6]	157	48	.306	11	.070	23	.146	11	.070	64	.408	4	.025	153	.975
EAST AFRICA[8]															
Uganda Baganda	165	47	.285	14	.085	54	.327	10	.060	40	.242	5	.030	160	.970
Misc. Bantu	26	4	.154	2	.076	12	.462	4	.154	4	.154	0	0	26	1.0
Tanganyika Bondi	60	10	.167	14	.233	21	.350	3	.050	12	.200	5	.083	55	.917
Kenya Masai	50	10	.200	12	.240	22	.440	1	.020	5	.100	0	0	50	1.0
CENTRAL AFRICA															
Congo Leopoldville[9]	140	82	.59	5	.035	53	.375	—	—	0	0	—	—	—	—
Tutsi[10]	86	24	.279	19	.221	41	.477	—	—	2	.023	13	.075	100	.925
Hutu[10,11]	96	27	.282	19	.198	46	.479	—	—	4	.041				
Congo[11]	99	38	.384	13	.131	44	.444	2	.020	2	.020	6	.061	93	.939
SOUTH AFRICA[12]															
Zulu	116	36	.310	29	.250	45	.388	3	.026	3	.026	3	.026	113	.974
Hottentot	59	18	.305	16	.271	25	.424	0	0	0	0	4	.067	55	.933
Bushmen	113	12	.106	59	.523	40	.354	0	0	2	.017	14	.124	99	.876
Cape Colored	88	17	.193	22	.250	49	.557	0	0	0	0	2	.023	86	.977
NORTH AMERICA[13]															
Negroes	952	277	.291	170	.178	355	.373	115	.121	35	.037	78	.081	874	.919

[1]Sutton *et al.* (1959).
[2]Neel *et al.* (1961).
[3]Allison *et al.* (1958).
[4]Barnicot *et al.* (1960).
[5]Blumberg and Gentile (1961).
[6]Harris *et al.* (1959).
[7]Moullec *et al.* (1960).
[8]Allison and Barnicot (1960).
[9]Sonnet and Michaux (1960).
[10]Van Sande *et al.* (1963).
[11]Van Ros *et al.* (1963).
[12]Barnicot *et al.* (1959).
[13]Giblett (1962).

affected, regardless of the genetic mechanism. Thus, one might anticipate that mildly suppressive agents would be more effective in individuals with the Hp 2–2 phenotype, but this would not be observed in populations subject to highly active "suppressors," such as severe hemolytic disease, liver damage, or combinations of these and other factors with pregnancy. Furthermore, if one combines the Hp^2 and Hp^{2m} gene frequencies, those populations having the largest number of individuals with the Hp 2–1(mod) phenotype should show a deficiency of the (combined) Hp^2 gene, provided the effect of environmental factors is minimal.

In view of these difficulties, only approximate Hp gene frequencies can be obtained. Thus in the Congo, omitting the Pygmies and the Hp 2-1(mod) and Hp 0 phenotypes, 183 individuals were Hp 1-1, 224 Hp 2-1, and 97 Hp 2-2. This leads to an estimate of the gene frequencies as $Hp^1 = 0.585$ and $Hp^2 = 0.415$ ($\chi^2[1] = 3.65$). In South Africa, the Xhosa and Msutu have rather lower frequencies of the Hp 2-1(mod) and Hp 0 phenotypes. More realistic estimates of the frequencies may therefore be obtained as follows

Xhosa	$Hp^1 = 0.539,$	$Hp^2 = 0.461$	$(\chi^2[1] = 5.48)$
Msutu	$Hp^1 = 0.544,$	$Hp^2 = 0.456$	$(\chi^2[1] = 3.05)$

The data on transferrin has been summarized previously by Giblett (1962) and are presented here to indicate the range in frequency of the Tf CD_1 phenotype among the various tribes. In this and previous reports on transferrins in Africa, the slow-moving variant has been assumed to be Tf D_1 in the absence of adequate control sera. However, Parker and Bearn (1961) have described a variant, D_{Chi}, which can only be differentiated from D_1 by electrophoresis at higher than usual voltage at a cold temperature. However, since the phenotype of most Negro subjects with a slow moving Tf variant whose serum has been adequately tested has been designated Tf CD_1, it is probable that this variant is the most common of the variant phenotypes in Africa.

SUMMARY

The haptoglobin and transferrin phenotype frequencies of several Congolese populations and two South African tribes are presented. The high frequency of Hp^1 characteristic of most other areas of Africa was also found in these people, although there was considerable variability. Apparent ahaptoglobinemia, also characteristic of African populations, was particularly common in tribal peoples, and some factors influencing this phenomenon are discussed.

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