THE DISTRIBUTION OF BLOOD GENETIC MARKERS IN THE MALAY POPULATIONS OF THE MALAY PENINSULA RUNNING TITLE: GENETIC MARKERS IN MALAYS

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INTRODUCTION

West Malaysia occupies the greater part of the area of the Malay Peninsula and has a population of 9·36 million, whilst the island Republic of Singapore at the southern extremity of the Peninsula has a total area of approximately 226 square miles populated by 2·07 million people (Department of Statistics, Malaysia, 1972; Chief Statistician, Singapore, 1972). The population of the Peninsula is of diverse ethnic background, but consists predominantly of Malays, Chinese and Indians. In addition to these three ethnic groups, West Malaysia has a small aboriginal population which totalled approximately 41,000 in the 1957 Population Census for the Federation of Malaya, (Department of Statistics, Federation of Malaya, 1957). The Malay term *Orang Asli* meaning 'aborigines' is now generally used to make reference to this small group of the population and replaces the term *Sakai* meaning 'dependant' or 'subject' which has often been used in the past. The aboriginal population is quite heterogeneous and encompasses a number of groups with varying degrees of admixture. Ethnological classification of these groups is, therefore, difficult, but three broad classifications are generally acceptable: Negritos, Senoi, and Proto-Malays.

The Negritos (or Semang) are a small band of pygmy blacks who now occupy parts of the north and central areas of Peninsular Malaysia. This group is thought to have been the earliest inhabitants of the Peninsula. The 1957 Census enumerated only 841 Negritos compared with 2,931 in 1947, but no explanation for the substantial reduction in numbers was offered.

The Senoi, now found in the central parts of the Peninsula consist of a number of subgroups of which Semai, Semelai, and Temiar are typical examples. These three groups numbered 12,451, 2,821 and 9,408 respectively in the 1957 Census (the most recent for which the aboriginal groups have been separately classified).

The south of the Peninsula contains remnant bands of the earliest forerunners of the present day Malays known as Proto-Malays, Jakun, Orang Laut, and, most frequently, aboriginal Malays. The term 'Orang Laut', however, meaning 'People of the Sea' is quite appropriate since this group is thought to have reached the Peninsula in a massive sea migration which populated South East Asia with closely related groups of people. Hence, the Bataks of North Sumatra, and the Orang Laut of Borneo share close similarities with the Proto-Malays of the Malay Peninsula.

The present day Malays are undoubtedly related to some extent to these early settlers, but their origin is predominantly in the early communities of Sumatra who began large scale migration to the Peninsula during the early 19th century.

BLOOD GROUP STUDIES

In 1954, Mourant surveyed the world literature on the distribution of human blood groups, and Mourant, Kopec and Domaniewska-Sobzak (1958) compiled extensive tables of the distribution of the ABO groups throughout the world. These surveys revealed that the people of Malaya formed only about 0·1% of over six million individuals upon whose blood groups the literature was based. The period since these surveys were published has seen a considerable increase in the knowledge on the human blood groups (reviewed by Race and Sanger, 1968), but even more outstanding is the number of red cell enzymes and serum protein systems which have been found to be polymorphic in human populations. A detailed account of these markers is given by Giblett (1969). For the Malay populations of the Malaysia Peninsula however, the literature on genetic markers has remained sparse. The purpose of this survey is to collate the data presently available on the distribution of some of these marker systems in aboriginal and non-aboriginal Malays as a basis for future comparative studies.

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The ABO Groups

The ABO blood groups remain the most widely studied marker system in Malays. The results of a number of reports on the ABO blood group distribution in non-aboriginal Malays are summarised in Table I. The surveys of Schebesta (1952) and Gibson-Hill (1953) have not been included in view of the very small number of subjects studied. The aboriginal populations in Peninsular Malaysia have been studied by Green (1949), Simmons *et al* (1950) and by Polunin and Sneath (1953). The Negritos were studied in some detail by Schebesta (1952), but this report is written in German and is rarely quoted. The results of the surveys of ABO blood group distribution in the aboriginal populations are summarised without further comment in Table II. To maintain uniformity, Tables I and II include maximum likelihood estimates of the *A*, *B*, and *O* gene frequencies obtained from the phenotype data given in the original reports. Each estimate is followed by its standard error. These estimates and those for the other genetic marker systems quoted in this paper were obtained using a maximum likelihood program written by Dr. W.J. Schull for the IBM 360 at the Australian National University.

A considerable range in the estimates of the *A*, *B*, and *O* gene frequencies was observed from Table I. The phenotype data were therefore tested for heterogeneity by the log likelihood ratio test (the G-test) of Woolf (1957). A G value of 118·55 was obtained. On the assumption that G follows a X^2 distribution, this value corresponds to a level of significance of less than 0·1% for 27 degrees of freedom. This suggests that marked heterogeneity exists in the ten sets of phenotypes. Since the majority of the data relate to surveys of blood donors in Singapore, the surveys in Singapore were considered separately. No significant heterogeneity ($X^2_9=7·24$) was detected in the results of four of these surveys (Lai and Kwa, 1968; Yap *et al*, 1972; Shanmugaratnam, 1972; Hawkins and Simons, 1972). However, when these four surveys were combined and compared with the surveys of Allen and Scott-McGregor (1947) and Chan (1961), highly significant heterogeneity was observed ($X^2_8 = 20·46$, $0·001 < p < 0·005$). Similarly in the two surveys from West Malaysia, highly significant heterogeneity ($X^2_3 = 17·50$, $p<0·001$) was observed when the survey of forensic cases by Poon and Amarasingham (1968) was compared with the blood donor survey of Duraisamy and Amarasingham (1970). The reason for this heterogeneity is not clear. However, Shanmugaratnam (1972) has suggested that donors of certain blood groups may from time to time be preferentially recruited according to blood bank stock requirements. If this view is correct, it may help to explain the considerable heterogeneity observed in the distribution of ABO phenotypes in what is ostensibly the same population.

Only limited investigations for the presence of the A_2 subgroup of A in Malays have been undertaken. Polunin and Sneath (1953) did not detect the A_2 antigen in the aboriginal populations, but Van der Heide (1963) found four out of 106 group A and AB Malays in Indonesia to be of group A_2 and reported the frequency of the A_2 gene to be 0·008. Case and Lopez (1973) found the same frequency of A_2 amongst 437 Malay blood donors in Kuala Lumpur.

The Rhesus System

The unpublished records of hospital blood banks confirm that Rhesus negative individuals are rare amongst Malays. Duraisamy (1973), for example, found only 16 Rhesus negative subjects amongst 5,282 Malays consisting of blood donors and transfusion recipients in Kuala Lumpur. A relatively small number of Malay blood donors in Singapore and in Kuala Lumpur have been tested additionally for the Rhesus antigens C, E, c and e. The data of Shanmugaratnam (1972) and of Case and Lopez (1973) on the distribution of these antigens is currently in preparation for publication, but these workers have kindly made their gene frequency data available for comparison purposes. This data, together with a summary of the data on the distribution of the Rhesus groups in the aboriginal populations, is presented in Table III.

The only investigation for the presence of the C^W antigen of the Rhesus system in non-aboriginal Malays appears to be the 80 individuals in Singapore tested by Hawkins and Simons (1972). The antigen was not detected in this small series. Van der Heide (1963), however, found one example in only six 'Malayans' he tested for the antigen in Indonesia.

Two of the aboriginal Malays tested by Polunin and Sneath (1953) were thought to possess the C^W antigen. This observation is of interest since the C^W antigen has since been found in the Toba Batak population of North Sumatra who are thought to be related to the aboriginal population of the Malay Peninsula (Hawkins *et al*, 1973).

The MNSs System

Two surveys in Singapore and one in Kuala Lumpur have investigated the distribution of MNSs groups in Malay blood donors. As in the case of the Rhesus system, the results have not been published but they have been made available for comparison. They are summarised in Table IV from which no significant differences are apparent.

TABLE I

ABO GROUPS OF NON-ABORIGINAL MALAY POPULATIONS

Investigators	Malay Population	Number Studied	Observed Numbers of Phenotypes				Gene Frequencies		
			O	A	B	AB	A	B	O
Allen and Scott-McGregor (1947)	Blood donors Singapore	1963	794	521	504	144	·1864 ±·0065	·1811 ±·0065	·6324 ±·0082
Chan (1961)	Blood donors Singapore	5461	2098	1369	1596	398	·1775 ±·0038	·2032 ±·0041	·6194 ±·0045
Van der Heide (1963)	Indonesia	327	110	89	101	27	·1971 ±·0165	·2203 ±·0173	·5827 ±·0209
Poon and Amarasingham (1970)	Forensic Cases West Malaysia	616	227	155	197	37	·1712 ±·0112	·2136 ±·0124	·6152 ±·0149
Lai and Kwa (1968)	Blood donors Singapore	260	102	54	75	29	·1726 ±·0174	·2224 ±·0195	·6050 ±·0231
Duraisamy and Amarasingham (1970)	Blood donors Kuala Lumpur	14556	6450	3509	3696	901	·1648 ±·0023	·1725 ±·0023	·6627 ±·0029
Yap *et al* (1972)	Blood donors Singapore	444	204	90	118	32	·1475 ±·0124	·1851 ±·0137	·6674 ±·0168
Shanmugaratnam (1972)	Blood donors Singapore	200	81	44	57	18	·1681 ±·0196	·2078 ±·0215	·6241 ±·0260
Hawkins and Simons (1972)	Blood donors Singapore	152	58	38	43	13	·1841 ±·0234	·2045 ±·0245	·6114 ±·0201
Saha *et al* (1973)	Newborn Infants Singapore	535	212	119	169	135	·1562 ±·0116	·2135 ±·0133	·6303 ±·0158

TABLE II

ABO GROUPS OF ABORIGINAL MALAY POPULATIONS

Investigators	Aboriginal Population	Number Studied	Observed Numbers of Phenotypes				Gene Frequencies		
			O	A	B	AB	A	B	O
Green (1949)	Aboriginal Malays	66	31	12	19	4	·1291 ±·0302	·1921 ±·0362	·6788 ±·0431
	Senoi (Semai)	117	62	12	36	7	·0841 ±·0185	·2029 ±·0279	·7130 ±·0312
Simmons *et al* (1950)	'Sakai'	165	89	17	51	8	·0784 ±·0151	·1973 ±·0232	·7243 ±·0259
Schebesta (1952)	Semang (Jahay-Lanoh)	119	82	19	17	1	·0880 ±·0188	·0789 ±·0178	·8331 ±·0248
	(Kenta'—Kensiu)	105	49	21	28	7	·1429 ±·0251	·1826 ±·0281	·6745 ±·0343
Polunin and Sneath (1953)	Negritos	269	159	66	39	5	·1423 ±·0157	·0856 ±·0123	·7721 ±·0188
	Aboriginal Malays	193	91	35	60	7	·1158 ±·0168	·1926 ±·0212	·6916 ±·0249
	Senoi Ulu Jelai	135	76	2	53	4	·0223 ±·0090	·2384 ±·0279	·7393 ±·0286
	Senoi (Semai)	101	40	12	44	5	·0880 ±·0204	·2825 ±·0346	·6295 ±·0370
	Senoi (Temer)	104	50	7	47	0	·0345 ±·0128	·2613 ±·0330	·7042 ±·0342

TABLE III

RHESUS GENE FREQUENCIES IN MALAY POPULATIONS

Investigators	Malay Population	Number Studied	Gene Frequencies			
			CDe + Cde	cDE + cdE	cDe + cde	CDE + CdE
Polunin and Sneath (1953)	Senoi	101	·926	·069	·005	0
	Aboriginal Malays	107	·94	·04	·01	·01
	Negritos	104	·63	·10	·27	0
Shanmugaratnam (1972)	Blood Donors Singapore	200	·800	·125	·062	·015
Hawkins and Simons (1972)	Blood Donors Singapore	83	·734	·186	·067	·013
Case and Lopez (1973)	Blood Donors Kuala Lumpur	437	·7628	·1461	·0827	·0084

The frequency of the *S* gene appears from the data to be somewhat higher than in other mongoloid populations. Gordon (1965) reports the frequency of the *S* gene to be 0·25 in Malays in South Africa. The gene frequencies obtained by Polunin and Sneath (1953) are also included in Table IV.

Kell (K)

Polunin and Sneath (1953) did not detect the Kell antigen in blood samples from 42 Negritos, 51 Senoi and 27 Aboriginal Malays. Gordon (1965) reported the frequency of the *K* gene to be 1% amongst Malays in South Africa, but Shanmugaratnam (1972) and Hawkins and Simons (1972) found no examples of the Kell antigen in 271 Malays in two separate surveys in Singapore. In Kuala Lumpur, however, Case and Lopez (1973) found two out of 437 Malay blood donors to possess the antigen. The limited investigations to date, therefore, are in agreement that the *K* gene is rare amongst Malays. This appears to be a characteristic of Mongoloid populations.

Duffy (Fy^a)

Blood samples from all except one of the 200 Malay blood donors in Singapore tested by Shanmugaratnam (1972) and all of 71 Malay blood donors from Singapore tested by Hawkins and Simons (1972) gave positive results with anti-Fy^a serum. This high frequency of the Fy^a gene is not uncommon in Asian populations. Gordon (1965), however, has reported a somewhat lower frequency (52%) of the Fy^a gene in Malays in South Africa. The survey by Polunin and Sneath (1953) found 28 out of 35 Negritos and 28 out of 31 Aboriginal Malays to possess the Fy^a antigen.

TABLE IV

MNSs SYSTEM GENE FREQUENCIES IN MALAY POPULATIONS

Investigators	Malay Population	Number Studied	Gene Frequencies			
			MS	Ms	NS	Ns
Polunin and Sneath (1953)	Senoi	69		·72		·28
	Aboriginal Malays	107	·03	·77	0	·21
	Negritos	102	·09	·64	·05	·22
Shanmugaratnam (1972)	Blood Donors Singapore	200	·0516	·4959	·0511	·4014
Hawkins and Simons (1972)	Blood Donors Singapore	75	·101	·492	·032	·374
Case and Lopez (1973)	Blood Donors Kuala Lumpur	437	·0676	·5526	·0365	·3433

Other Blood Groups

Polunin and Sneath (1953) did not detect the Lutheran (Lu^a) antigen in blood samples from 105 Negritos and 46 Aboriginal Malays, but found one out of 101 Senoi to possess the antigen. No investigations for this marker in non-aboriginal Malay populations have been reported. The distribution of the antigen P was also investigated by Polunin and Sneath (1953) at a time when the genetic complexity of the P blood group system was not fully realised. The gene frequencies of *P* were reported to be 54% in the Senoi and 50% in the Aboriginal Malays. In the non-aboriginal population, Case and Lopez (1973) found 44% of 437 Malay blood donors to possess the P_1 antigen.

Vos and Kirk (1961) demonstrated a single subject with the Diego (Di^a) antigen amongst 40 Malays from Malaya, but subsequent surveys have not revealed the antigen in South African Malays or in blood donors in Kuala Lumpur (Gordon, 1965; Case and Lopez, 1973). None of the 40 Malays tested by Vos and Kirk (1961) possessed either the Js^a (Sutter) or V antigens.

Saha and Banerjee (1973) tested 49 Malay males and 23 Malay females in Singapore for the sex-linked Xg^a antigen. The Xg^a gene frequencies were found to be 0·57 for males and 0·49 for females.

Although not a blood group system, it is convenient to record here that the ability to secrete substances of ABO blood group specificity in the body fluids has not been the subject of genetic surveys amongst the Malays since Polunin and Sneath's study of aboriginal populations in 1953. This survey showed the frequency of the secretor (*Se*) gene to be 0·51 in the Negritos, 0·49 in the Senoi, and 0·48 in the Aboriginal Malays.

THE POLYMORPHIC SERUM PROTEINS

Haptoglobin

Four surveys of the distribution of Haptoglobin types in Malay populations have been documented. Kirk *et al* (1960) reported the Hp^1 gene frequency to be 0·24 in 236 Malays in Malaya whilst Gordon (1964) reported a frequency of 0·33 for this gene in 100 Malay hospital patients in South Africa. In relation to the aboriginal populations, Kirk and Lai (1961) tested samples from 66 Proto-Malays and reported a frequency of Hp^1 of 0·47, and Lie-Injo, Bolton, and Fudenberg (1967) reported an Hp^1 frequency of 0·24 in 202 aborigines from Malayan jungle areas. Haptoglobin was not detectable in 7·5% of the subjects in the latter survey, and the authors were unable to relate this apparent absence to deficiency of red cell Glucose-6-phosphate dehydrogenase, possession of abnormal haemoglobin or to malarial parasites. This situation, however, is not unique to aborigines in Malaysia as it has also been observed in tribal African populations in the Congo and in Nigeria (Giblett, Motulsky, and Fraser, 1966; Barnicot, Garlick, and Roberts, 1960).

Transferrin

A single peptide variation in the structure of the most commonly occurring transferrin type known as Transferrin C provides the D^{CHI} variant which appears to be characteristic of Mongoloid ethnic types (Kirk, Parker and Bearn, 1964; Wang, Sutton and Howard, 1967).

Kirk and Lai (1961) found 11 out of 236 Malays from Perlis and 2 out of 66 Proto-Malays to possess transferrin variants which were subsequently identified as D^{CHI} by Kirk *et al* (1964). The gene frequencies for Transferrin C were reported to be 0·977 in the Malays, and 0·985 in the Proto-Malays. Similarly, Lie-Injo *et al* (1967) found the D^{CHI} variant in six out of 202 aborigines from different jungle areas of Malaya.

Gc

The only survey of the distribution of the Gc factor in Malays appears to be that of Kendrick and Douglas (1967) who examined sera from 51 blood donors in Singapore. The frequencies of Gc^1 and Gc^2 were reported to be 0·8431 and 0·1569 respectively.

THE IMMUNOGLOBULIN ALLOTYPES

The distribution of the Gm and Inv serum groups has not been studied widely amongst the Malay populations of Malaya. Vos, Kirk and Steinberg (1963) examined sera from 156 Malays from Perlis for the Gm antigens Gm^a, Gm^b, and Gm^x. The frequencies of the genes Gm^a, Gm^{ax}, and Gm^{ab} were 0·166, 0·063, and 0·772 respectively. These figures were not significantly different from those obtained for a Chinese population in Malaya examined by the same workers. Similarly, Simons and Ropartz (1973) did not find significant differences in the Gm frequencies in Malay and Chinese blood donors in Singapore.

In relation to the aboriginal populations, Lie-Injo, Bolton, and Fudenberg (1967) tested sera from 147 Malayan aborigines and the results show that the majority of the subjects were of the Gm type Gm^{abf}. The antigens Gm^c and Gm^x were not detected. Steinberg and Lie-Injo (1972) tested samples from 266 Malaysian aborigines and from 48 Negritos for eight Gm antigens and for the Inv^1 antigen. The Inv^1 gene frequencies

of the aboriginal Malays did not differ significantly from that of the Negritos, whereas the Semai had a significantly higher Inv^1 frequency (0·315) than the other aboriginal groups. The results of the survey show also that the Negritos have a quite different distribution of Gm phenogroups to the Semai and Aboriginal Malays. For the non-aboriginal population, Simons and Ropartz (1973) found 40% of Singapore Malays tested to possess the Inv^1 antigen.

RED CELL ENZYMES

Only limited studies of the distribution in Malay populations of the polymorphic enzymes involved in erythrocyte metabolism have been reported to date. These are summarised below.

Phosphoglucomutase (PGM)

The distribution of PGM types in non-aboriginal Malay populations has been studied by Gordon Vooijs and Keraan (1966) in Malays in South Africa, and by Blake, McDermid, Kirk, Ong and Simons (1973) in Singapore blood donors. 97 of the Malays in South Africa were of the more common PGM phenotypes, but two possessed the relatively uncommon 3-1 phenotype, and one was thought to be of type 4-1. The PGM 3-1 phenotype was also detected by Blake *et al* (1973) in 2 out of 259 Singapore Malays. The frequency of the PGM_1^2 gene was found by Blake and colleagues to be 0·234 in close agreement with the frequency of 0·245 recorded by Gordon's group in South Africa. None of the samples in the Singapore survey showed any departure from the normal electrophoretic pattern representing PGM locus 2, but Gordon *et al* (1966) reported that one of the Malays tested in South Africa had the Atkinsons' phenotype at this locus, a phenotype that had hitherto been found only in Black populations. The same survey, however, recorded that 3% of 'coloured' South Africans have the Atkinsons' phenotype, and an earlier report by Gordon (1965) commented that contact between the 'coloured' community and the Malays in South Africa has been close for several generations. The possibility that the appearance of this rare phenotype in a Malay has arisen through admixture with another ethnic group remains, therefore, a matter of speculation.

Welch, Lie-Injo and Bolton (1972a) examined samples from 920 aborigines from various parts of West Malaysia and found the PGM_1^1 frequency to vary from 0·51 in Pahang to 0·78 in Perak, with an intermediate value of 0·63 in Kelantan. The sample, however, was found to be somewhat heterogeneous and the combined value of 0·68 for the entire sample was considered to be the most reliable.

6-Phosphogluconate Dehydrogenase (6-PGD)

The distribution of 6-PGD types in Malays has been studied in three surveys. Gordon, Keraan, and Vooijs (1967) reported the frequency of the PGD^A allele in 100 Malays in South Africa to be 0·975, and Blake *et al* (1973) found the PGD^A frequency in 259 Singapore Malays to be 0·940. Lie-Injo and Welch (1972) found the slightly higher PGD^A frequency of 0·958 in 463 Malay newborns in Malaysia compared with that in 581 Malay adults in whom the frequency was 0·969. One of the subjects was reported to have the rare PGD (Thai) variant. In a total of 533 aborigines examined in the same survey, the AC phenotype was reported in 12·8% of 86 Temiar, 7·5% of 214 Semai, and in 10·3% of the remaining group of unclassified aborigines. These figures correspond to PGD^A frequencies of 0·936, 0·963, and 0·945 respectively.

Adenylate Kinase

Three surveys have studied the distribution of the enzyme Adenylate kinase in Malays, and a recent survey by Welch, Lie-Injo and Bolton (1972b) has investigated the distribution in West Malaysian aborigines. The results of these surveys are summarised in Table V. Ethnic variations in this system make it of particular interest in the Malay Peninsula where several ethnic groups are present. Although the system is polymorphic in most populations, only one Chinese has to date been found to have a phenotype other than AK 1 (Shih *et al*, 1968). In contrast to the virtual absence of the AK^2 gene in Chinese, and the frequency of about 0·015 in the Malays, a survey of Indians and Pakistanis in England reported by Rapley *et al* (1967) showed very high frequencies of the AK^2 gene of 0·098 and 0·130 respectively.

Lactate Dehydrogenase (LDH)

Although variations in the electrophoretic pattern of LDH are rare, Blake *et al* (1973) found two separate variants of the enzyme in samples from 259 Malays in Singapore. One of the variants was electrophoretically indistinguishable from the LDH (Calcutta-1) variant which is widespread in India, and the other was similar, but not identical, to the LDH (Calcutta-2) variant which is also found in Indians. The two variants were given the trivial names LDH (Malay-1) and LDH (Malay-2).

Red Cell Acid Phosphatase

Two surveys have investigated the distribution of red cell Acid phosphatase variants in Malays in Singapore. Lai and Kwa (1968) reported the frequency of the p^a gene to be 0·344 in 260 subjects, and Blake *et al* (1973) reported the frequency of this gene to be 0·3263 in 259 subjects. Both surveys revealed a subject with the p^c gene.

TABLE V

ADENYLATE KINASE TYPES IN MALAY POPULATIONS

Investigators	Malay Population	Number Studied	Observed Numbers of Phenotypes			Gene Frequencies		Standard Error
			1-1	2-1	2-2	AK^1	AK^2	
Gordon *et al* (1966)	South Africa	100	93	7	0	·9650	·0350	·0130
Chan (1971)	Blood Donors West Malaysia	400	385	15	0	·9813	·0187	·0048
Welch *et al* (1972b)	Malays West Malaysia	324	314	10	0	·9846	·0154	·0048
Welch *et al* (1972b)	Aborigines West Malaysia	483	470	13	0	·9865	·0135	·0037
Blake *et al* (1973)	Blood Donors Singapore	259	252	6	1	·9846	·0154	·0054

Phosphohexose Isomerase (PHI)

Omoto and Blake (1972) reported the results of their tests for PHI in over 4000 subjects from South East Asia and Oceania. Only 9 subjects possessed variant PHI phenotypes of whom 2 were Malays from Singapore with phenotype 3-1. Lie-Injo and Welch (1972) also found a subject of phenotype 3-1, and, in addition, three subjects of phenotype 4-1 in a total of 579 Malays tested in Malaysia.

Invariant Systems

No departures from the normal electrophoretic patterns were detected in tests for Malate dehydrogenase (MDH), Phosphoglucokinase (PGK), Peptidase B, "Oxidase" and Diaphorase in the Malay blood donors tested by Blake *et al* (1973). Similarly, Welch, Lie-Injo, and Bolton (1972a) detected no variations from the normal Carbonic Anhydrase electrophoretic pattern shown by haemolysates from 534 aborigines from various parts of West Malaysia.

RED CELL GENETIC DEFECTS

Two of the most widespread red cell genetic defects in South East Asia are the presence of the E variant of haemoglobin and deficiency of the enzyme Glucose-6-phosphate dehydrogenase (G-6-PD). These conditions affect both Malays and Malayan aborigines with varying degrees of severity.

The first attempts to demonstrate abnormal haemoglobins in Malayan populations were those of Polunin and Sneath (1953) who used the sodium metabisulphite test for sickle cells on the blood of 178 Negritos and 46 Orang Darat but were unable to observe the sickling phenomenon. A number of subsequent studies have shown that whilst Haemoglobin S apparently does not exist amongst the Malay populations, Haemoglobin E occurs quite commonly. The results of some of these surveys are summarised in Table VI.

Erythrocyte Glucose-6-phosphate dehydrogenase deficiency in Malays was first recognised by Weatherall (1960) in three Malay infants in Singapore with kernicterus due to deficiency of the enzyme. In West Malaysia, the distribution of G-6-PD deficiency has been investigated by Lie-Injo and colleagues and the data was reviewed by Lie-Injo (1969). In Malays, the frequency of G-6-PD deficiency ranges from between 1-5% in the Kuala Lumpur area to 11% in the east of the country. In relation to the aboriginal populations, Lie-Injo and Chin (1964) found 17% of 607 aboriginal hospital patients and military personnel to be deficient of the enzyme. A subsequent study of aborigines in Perak and Kelantan showed that 21% of the subjects tested were G-6-PD deficient (Lie-Injo and Bolton, 1969). In Singapore, Vella (1961) found 0·65% of male Malay blood donors to be deficient of the enzyme, and Saha and Banerjee (1971) found the deficiency in 2·02% of 1384 Malays. Wong (1973) studied the cord blood of 29,720 Malays born in Singapore between 1965 and 1972 and found 3·5% of the males and 0·8% of the females to be deficient.

TABLE VI

ABNORMAL HAEMOGLOBINS IN MALAY POPULATIONS

Investigators	Population or Propositus	Number Studied	Number with Abnormal Haemoglobin	Abnormal Haemoglobins Detected
Lehmann and Singh (1956)	Malaysians*	346	26	Hb E × 25, Hb H × 1.
Vella (1961)	Malays Singapore & Malaya Senoi (Semelai)	4984 41	259 13	Hb E × 247, Hb D × 7. Hb K × 4, Hb J × 1. all Hb E.
Vella and Tavaria (1961)	Malays, Kuching	166	5	all Hb E.
Lie-Injo and Chin (1964)	Semai Temiar Temuan Semelai Unclassified aborigines	111 62 37 29 29	30 29 3 6 9	all Hb E.
Wong (1968)	Malay Child, Singapore	Family of 11	8	5 with hereditary persistent Hb F, 3 with hereditary persistent Hb A_2.
Lie-Injo and Bolton (cited by Lie-Injo, 1969)	Aborigines Perak & Kelantan	not stated	38%	all Hb E.
Wong (1969) Clegg *et al* (1969)	Malay Infant Singapore	1	1	Hb Singapore $\alpha_2$141PROβ_2
Welch, Lie-Injo and Bolton (1972a)	West Malaysian aborigines	1028	323	all Hb E.
Wong (1972)	Malay female, Singapore	Family of 6	4	Hb J Singapore α 78 ASN→ASP. α 79 ALA→GLY.
Lie-Injo *et al* (1972)	Malay male, Kuantan	Family of 6	3	Hb Köln ($\alpha_2\beta_2$98 VAL→MET).
Wong (1973)	Cord Blood Malay Infants, Singapore	1326	54	Hb Barts × 8, Hb E × 46.

*The survey was undertaken at a time when the term 'Malaysian' was used specifically to refer to the Malay population of the Malay Peninsula and did not have the present interpretation implying citizenship of Malaysia.

Allison (1960) and Motulsky (1960) have advanced the view that the G-6-PD deficiency trait may be selectively maintained as a protective mechanism against the malarial parasite *P. falciparum* based on the attraction of the parasite to the oxidative shunt in the unaffected red cell. Similarly Allison *et al* (1963) noted a positive correlation between deficiency of the enzyme and abnormal haemoglobin genes but added that this correlation would be expected if the genes are, in fact, favoured by malarial selection. Lie-Injo and Chin (1964) and Lie-Injo and Poey-Oey (1964) have noted that this correlation is well evidenced in South-East Asian populations. Nevertheless, the malarial hypothesis has not been unquestionably accepted. However, in the absence of reliable evidence with which to discredit the theory, it seems attractive that it should be contributed as an explanation for the high frequency of Haemoglobin E and G-6-PD deficiency in the Malay populations of the Malay Peninsula.

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