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THE DISTRIBUTION OF BLOOD GENETIC MARKERS IN IMMIGRANT CHINESE POPULATIONS

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SUMMARY

The current data on the distribution of blood genetic markers in Chinese populations outside China have been reviewed and summarised. The Chinese were found to exhibit varying degrees of heterogeneity in some of the marker systems, and attempts have been made, where appropriate, to relate this heterogeneity to the diverse backgrounds in China of the populations studied.

INTRODUCTION

Since Landsteiner's early reports, at the beginning of the century, that human blood can be divided into groups determined by red-cell agglutinating factors in serum, a formidable collection of data has become available on the distribution of blood genetic markers throughout the world. The Chinese, however, who form a considerable part of the world's population, are proportionately, perhaps, one of the least studied of all ethnic groups in terms of blood genetic markers. In view of the well-established contributions that genetic-marker studies can make to the identification of population migration patterns, attempts are already being made to increase the volume of genetic data on the Chinese, with their long history of extensive migration, both inside, and more recently outside, the Chinese mainland. The time therefore appears appropriate to collate the data currently available on the distribution of blood genetic markers in Chinese as a basis for subsequent comparative studies.

The Chinese Abroad

Most of the blood-group genetic data currently available are from studies undertaken on Chinese outside Mainland China, the majority of the data having originated from the Malay Peninsula, Hong Kong, Taiwan, and from the United States.

The Malay Peninsula, consisting politically of West Malaysia (formerly Malaya) and Singapore, has a total Chinese population of approximately 5 million, of whom just over 1.5

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million are in Singapore (Department of Statistics, Malaysia, 1972; Chief Statistician, Singapore, 1972). The origins of the Chinese in the Malay Peninsula are diverse, and different parts of the region have different distributions of the various specific communities which contribute to the general heading " Chinese ". These communities are most usually described in terms of their dialect subgroups. The most frequently occurring dialect group in the 1957 Population Census for the Federation of Malaya was Hokkien (31.7%), followed by Hakka (Khek) (21.8%), Cantonese (21.7%), Teochew (12.1%) and Hainanese (5.3%) (Department of Statistics, Federation of Malaya, 1957). The minority groups Kwongsai, Hockchiu, Hengkwa, Hokchia, and other unspecified groups, accounted for the remaining 7.4% of the Chinese population. There are no figures available, at present, for the dialect distribution in Singapore, but the distribution is unlikely to differ greatly from that in West Malaysia, apart, perhaps, from a smaller proportion of Hakkas in Singapore.

The 1971 Population Census for Hong Kong enumerated a total of 4 064 400 persons, of whom over 98% were described as Chinese on the basis of language and place of origin (Government of Hong Kong 1972). Most of the Hong Kong Chinese are Cantonese who have originated from Kwangtung Province, but a small number of immigrants from Fukien and Kiangsu are present. The colony also has a unique boat-dwelling Chinese population, consisting of the Tanka and Hoklo groups, whose origins outside the area are not known with any certainty.

The island of Taiwan, by virtue of its geographical location, has also attracted considerable numbers of Chinese from the mainland over the centuries. By the early 17th century a sufficiently large number of migrants from neighbouring Fukien Province had crossed the Strait and settled to have almost completely occupied the western plains and have forced the aboriginal population into the mountains in the east. Migration to Taiwan rapidly increased during the 17th century, when political conditions under the Dutch on the island were considered more favourable than under the failing Ming administration on the mainland.

About 85% of the present Chinese population of Taiwan are known as Fulaus, who are indigenous Chinese from Fukien Province. The remaining 15% are Hakkas, also from Fukien but with complex origins on the mainland. The Hakkas are thought to have originated in Shenshi, Shansi, and Honan Provinces, from which they were forced southwards by frequent invasions from the north. A number of Hakkas settled in Fukien but a further invasion during the early Ming period drove them into Kwangtung. Thereafter, their close proximity to the coast allowed them to join the other residents of Kwangtung in subsequent migration from the province. In addition, they set out alone for Borneo in the mid-18th century, lured by the timber industry which had not attracted the other Chinese communities. By the end of the century a large Hakka community had become established in Borneo.

A population of several hundred thousand Chinese has developed in the United States of America since the mid-19th century, when gold prospectors first began to migrate to California. Most of the Chinese in the United States can be broadly described as Cantonese since most have originated from a small area around Canton and Sze Yap in Kwangtung Province. A detailed account of the migrations of the Southern Chinese is given by Fitzgerald (1972).

BLOOD GROUP STUDIES

The ABO Groups

The early data on the distribution of the ABO blood groups in Chinese, both inside and outside Mainland China, was summarised by Mourant et al. (1958). A number of surveys undertaken since that time have considerably increased the volume of data available. The results of a number of the more recent surveys of ABO blood-group distribution in Chinese are summarised in Table I, which has been prepared in sections corresponding to the areas in which the surveys were undertaken. To maintain uniformity, maximum likelihood estimates of the respective gene frequencies have been obtained from the phenotype data presented in the original reports. These estimates are included in Table I, and each is followed by its standard error. The maximum likelihood estimates for all the genetic marker systems quoted in this paper were obtained using a program written by Dr. W.J. Schull for the IBM 360 at the Australian National University.

A considerable range in the gene frequency estimates is apparent from Table I. However, when 95% confidence limits, as defined by values two standard deviations above and below the individual estimates, are applied, the *A* and *B* frequency estimates from surveys undertaken in Singapore are found to be in mutual agreement. Similarly, the two surveys in Malaysia are concordant in the gene frequency estimates obtained, as are the three surveys in Hong Kong when these confidence limits are employed.

The substantial numbers of subjects studied in Singapore by Chan (1962), in West Malaysia by Duraisamy and Amarasingham (1971), and in Hong Kong by Tong et al. (1962), may be expected to optimally represent the ABO blood-group distribution in these three populations. It is of interest, therefore, that the *A* and *B* gene frequencies obtained by Duraisamy and Amarasingham in Malaysia differ from those obtained by Chan in Singapore by more than four standard deviations, and from the frequencies obtained by Tong et al. in Hong Kong by more than seven standard deviations. Such marked dispersion cannot be expected to have occurred exclusively as the result of biased sampling from a homogeneous population, even when it is considererd that the surveys in Singapore and Malaysia were of blood donors and may have been subject to some form of selection. One possible explanation for such marked heterogeneity may lie in the fact that the population of Hong Kong is predominantly Cantonese, whilst only about 21.7% of the Chinese population of Malaysia are of this dialect group (Department of Statistics, Federation of Malaya, 1957). This inbalance, coupled with the observed heterogeneity, tends to suggest that the ABO blood-group distribution in Cantonese subjects may differ from that in other dialect groups. This view is strengthened in some respects by the high frequencies of *A* and *B* recorded in three of the surveys consisting of essentially Cantonese subjects in New York, compared with frequencies obtained for Chinese in the Malay Peninsula. The surveys in New York, however, have dealt with comparatively small groups of subjects and the standard errors of the gene frequency estimates are high. Further evidence in favour of the suggestion that the ABO blood-group distribution varies in Chinese from different areas is provided by the results of the survey of Nakajima et al. (1967), which show higher frequencies of *A* and *B* in Chinese from North China than

TABLE I

DISTRIBUTION OF ABO BLOOD GROUPS IN SOME CHINESE POPULATIONS

Investigators	Population	N	Percentage of phenotypes				Gene frequencies		
			O	A	B	AB	*A*	*B*	*O*
Levine and Wong 1943	New York	150	30.00	34.00	25.33	10.67	0.2556 ± .0272	0.1996 ± .0244	0.5447 ± .0317
Wiener et al. 1944	» »	138	31.16	32.61	27.54	8.70	.2346 ± .0273	.2021 ± .0256	.5633 ± .0326
Miller et al. 1950	» »	190	36.32	27.89	22.63	13.16	.2283 ± .0230	.1953 ± .0215	.5763 ± .0276
Miller et al. 1951	» »	103	45.63	27.18	22.33	4.85	.1758 ± .0279	.1468 ± .0257	.6774 ± .0345
Sussman 1956	» »	817	40.4	28.6	25.9	5.5	.1882 ± .0102	.1718 ± .0098	.6400 ± .0127
	Malay Peninsula								
Allen and Scott-McGregor 1947	Singapore	624	43.11	24.04	27.72	5.13	.1587 ± .0108	.1810 ± .0115	.6603 ± .0142
Simmons et al. 1950	Malaya Hakkas	100	48.00	25.00	20.00	7.00	.1742 ± .0282	.1446 ± .0259	.6812 ± .0348
	Cantonese	97	46.39	22.68	21.65	9.28	.1729 ± .0285	.1668 ± .0280	.6603 ± .0361
Yeoh 1960	Singapore	1 000	44.30	25.50	26.50	3.70	.1595 ± .0086	.1655 ± .0087	.6751 ± .0111
Chan 1962	»	15 262	43.53	25.99	24.99	5.48	.1724 ± .0023	.1663 ± .0022	.6613 ± .0029
Poon and Amarasingham 1968	W. Malaysia	940	45.85	23.30	25.53	5.32	.1551 ± .0087	.1684 ± .0090	.6766 ± .0114
Lai and Kwa 1968	Singapore	620	48.55	24.52	21.77	5.16	.1611 ± .0109	.1450 ± .0104	.6939 ± .0138
Duraisamy and Amarasingham 1971	Kuala Lumpur	7 586	47.55	24.77	23.36	4.32	.1582 ± .0031	.1498 ± .0030	.6920 ± .0040

Yap et al. 1972	Singapore	1 627	40.87	28.76	25.38	4.98	.1869 ± .0072	.1663 ± .0068	.6469 ± .0089
Hawkins et al. 1974	»	166	40.36	26.51	28.31	4.82	.1722 ± .0218	.1833 ± .0224	.6445 ± .0280
Saha et al. 1974*a*	»	1 181	42.76	26.33	23.37	7.54	.1859 ± .0084	.1680 ± .0081	.6461 ± .0105
Grimmo and Lee 1961	Hong Kong	670	38.51	27.01	26.87	7.61	.1912 ± .0113	.1903 ± .0113	.6185 ± .0143
Tong et al. 1962	» »	13 768	41.74	26.51	25.53	6.22	.1798 ± .0024	.1739 ± .0024	.6463 ± .0031
Ho and Kwan 1973	» »	3 327	39.46	26.39	27.83	6.31	.1800 ± .0050	.1888 ± .0051	.6312 ± . 0063
	Taiwan								
Fraser et al. 1965	Taipeh	98	46.94	28.57	19.39	5.10	.1854 ± .0293	.1309 ± .0250	.6837 ± .0351
	Chung-Li	102	43.14	30.39	15.69	10.78	.2293 ± .0315	.1402 ± .0253	.6305 ± .0363
	Chi-Chi	100	61.00	20.00	15.00	4.00	.1276 ± .0244	.0995 ± .0217	.7728 ± .0307
Nakaiima et al. 1967	Northern Chinese	1 521	30.51	33.00	26.96	9.53	.2423 ± .0083	.2033 ± .0077	.5544 ± .0099
	Southern Chinese	2 223	38.73	30.09	24.52	6.66	.2050 ± .0064	.1706 ± .0059	.6244 ± .0078
	Taiwanese	10 512	43.85	27.03	23.30	5.82	.1805 ± .0028	.1580 ± .0026	.6615 ± .0035
Huang 1970	Fulaus	1 091	41.43	26.86	26.40	5.32	.1770 ± .0086	.1742 ± .0085	.6488 ± .0109
	Hakkas	619	26.49	23.59	43.46	6.46	.1660 ± .0111	.2966 ± .0142	.5374 ± .0157
Layrisse and Arends 1956	Venezuela	100	41.00	32.00	25.00	2.00	.1901 ± .0293	.1475 ± .0261	.6624 ± .0355
Chaudhuri et al. 1967	Calcutta	566	44.52	30.04	19.96	5.48	.1969 ± 0.0125	.1365 ± 0.0106	.6666 ± 0.0149

in those from South China. It is also evident that considerable heterogeneity exists in surveys undertaken within the same geographical area. In Hong Kong, for example, the surveys of Tong et al. (1962) and of Ho and Kwan (1973) both involve large numbers of subjects (13 768 and 3 327 respectively). Despite these large numbers, there is a statistically significant difference between the B gene frequencies from the two surveys ($\chi^2_1 = 8.15$; $p = 0.005$). It should, however, be noted that the blood-group studies conducted by Ho and Kwan were part of a sero-epidemiological study of Epstein-Barr virus infection, and, in consequence, the results may not be representative of the Hong Kong population as a whole.

In view of the heterogeneity which appears to exist in the ABO blood-group distribution in Chinese, no attempt has been made to obtain gene frequencies which would be applicable to Chinese populations in general. It is considered that meaningful ABO gene-frequency estimates for the Chinese can best be obtained through an objective survey in which the participants are listed according to their province of origin in Mainland China.

A number of surveys have investigated the possible association between genes of the ABO system and specific disease conditions in Chinese. However, since marked heterogeneity has been found to exist in the ABO blood-group distribution of healthy Chinese subjects, the results of such surveys may be particularly susceptible to false interpretation. Carcinoma of the stomach in Singapore Chinese was investigated by Yeoh (1960), and carcinoma of the nasopharynx has been studied by Seow et al. (1964), Ho (1967), Shanmugaratnam (1971), and by Hawkins et al. (1974). Saha and Banerjee have investigated pulmonary tuberculosis, glucose-6-phosphate dehydrogenase deficiency, and syphilis (1968, 1971*a*, 1971*b*), and Saha et al. (1971, 1974*a*, 1974*b*), have studied leprosy and myocardial infarction. Only in the survey of Yeoh (1960) has any strong evidence for significant association between blood-group genes and disease been presented, although Saha and Banerjee (1968) found a slight reduction in the frequency of blood group O in subjects with pulmonary tuberculosis compared with that in a group of healthy subjects. Yeoh (1960), without providing a statistical analysis, commented upon the high frequency of group A in a series of patients with carcinoma of the stomach compared with the frequency in a group of normal subjects. Examination of Yeoh's results using the method of Woolf (1955) shows that for the phenotype comparison (A + AB) : (O + B) between the patients and controls the χ^2_1 value is 11.57. This corresponds to a level of statistical significance of less than 0.1% and strongly supports the findings of Aird et al. (1953) and of subsequent workers that there is a significant association between blood group A and carcinoma of the stomach.

The ABO Subgroups

Levine and Wong (1943) tested blood from 58 New York Chinese of groups A and AB, and only two, both of group AB, were of subgroup A_2. A considerable number of samples from Chinese have subsequently been tested for the subgroups of A, but, with the exception of a survey of Chinese in Calcutta (Chaudhuri et al. 1967) and in Venezuela (Layrisse and Arends 1956), A_2 has not been found. Evidence is accumulating through family studies to suggest that, whilst the A_2 gene is rare in Chinese, the A_1 gene is not infrequently suppressed in subjects of phenotype AB resulting in the serological appearance of an intermediate subgroup of A (Hawkins and Simons 1972). This will probably be explained by the existence of weak alleles at the *H* locus with consequential reductions in the amount of precursor substance available for conversion into the A_1 antigen.

Weak subgroups of B have been reported by Simmons and Kwa (1967) in two apparently unrelated Chinese families in Singapore and by Nakajima et al. (1967) in a Taiwanese, but there appear to be no other reports of this phenomenon occurring in Chinese subjects.

The Rhesus Groups

The low frequency with which Rhesus negative genes occur in Chinese has been recognised since 1943, when Levine and Wong found only one Rhesus-negative subject amongst 150 Cantonese in New York. Large numbers of Chinese have subsequently been studied. Nakajima et al. (1967) found that 99.74% of 17 994 Chinese in Taiwan were Rhesus positive and, also in Taiwan, Huang (1970) found only 15 Rhesus-negative subjects in 6 241 Fu-Laus and Hakkas. Similarly in Malaysia, Duraisamy (1973) found only 6 Rhesus-negative subjects amongst 3 455 Chinese blood donors and hospital patients in Kuala Lumpur.

A number of investigations have included tests for the Rhesus antigens C, E, c, and e. Maximum likelihood estimates of the gene frequencies obtained from some typical surveys are summarised in Table II. These estimates were obtained using a model which assumes the presence of eight gene complexes in the Rhesus system. However, as the complexes *Cde* (r') and *cdE* (r'') cannot normally be identified, except in the rare cases in which they are present in conjunction with another Rhesus-negative complex, and there is no evidence to date that the complex *CdE* (r_y) occurs in Chinese, only five complexes are listed in Table II. For this reason, the estimated frequencies of R_1 in the Table may include a small percentage corresponding to r', and the estimates for R_2 may include a small contribution due to r''.

The gene-frequency estimates in Table II are in substantial agreement considering the relatively small numbers of subjects studied. The major disagreement appears to be centred around the presence or absence of the complexes *r* and R_0 in the populations studied. This point seems to be determined to a large extent arbitrarily by the fortuitous occurrence of subjects of phenotype R_0 (ccDee) or of genotype *rr* (*cdecde*) in the samples. If an *rr* subject is present in the sample, the phenotype CcDee, for example, is most frequently attributed to R_1r, whilst if an R_0 subject is present, phenotype CcDEe appears to be attributed to R_1R_0. Nakajima et al. (1967) found a statistically significant difference in the frequency of complexes containing gene *E* in Northern Chinese than in Southern Chinese, but apart from this finding and the controversy surrounding the presence or absence of R_0 and *r*, the results have added very little information to that summarised by Mourant (1954).

The only investigation for the presence of the C^w variant of the Rhesus system appears to be that of Hawkins and Simons (1972) who did not detect the variant in samples from 250 Chinese in Singapore.

TABLE II

ESTIMATES OF RHESUS GENE FREQUENCIES IN VARIOUS CHINESE POPULATIONS

<table>
<tr><th rowspan="2">Investigators</th><th rowspan="2">Population</th><th rowspan="2">N</th><th colspan="5">Gene frequencies</th></tr>
<tr><th>R_1</th><th>R_2</th><th>R_z</th><th>R_o</th><th>r</th></tr>
<tr><td>Simmons et al. 1950</td><td>Malaya
Hakkas</td><td>100</td><td>0.7349
± .0312</td><td>0.2399
± .0302</td><td>0.0051
± 0.0051</td><td>0.0201
± 0.0100</td><td>0</td></tr>
<tr><td></td><td>Cantonese</td><td>97</td><td>.7835
± .0296</td><td>.1598
± .0263</td><td>0</td><td>0.0567
± 0.0166</td><td>0</td></tr>
<tr><td>Miller et al. 1950</td><td>New York</td><td>190</td><td>.7658
± .0217</td><td>.2237
± .0214</td><td>0</td><td colspan="2">0.0105
± 0.0052</td></tr>
<tr><td>Miller et al. 1951</td><td>»</td><td>103</td><td>.7136
± .0315</td><td>.2087
± .0283</td><td>0</td><td>0.0625
± 0.0506</td><td>0.0152
± 0.0485</td></tr>
<tr><td>Sussman 1956</td><td>»</td><td>511</td><td>.7834
± .0129</td><td>.1552
± .0113</td><td>0.0072
± 0.0027</td><td>0.0153
± 0.0149</td><td>0.0386
± 0.0155</td></tr>
<tr><td>Layrisse and Arends 1956</td><td>Venezuela</td><td>100</td><td>.6949
± .0436</td><td>.1019
± .0232</td><td>0.0555
± 0.0189</td><td>0</td><td>0.1481
± 0.0266</td></tr>
<tr><td>Grimmo and Lee 1961</td><td>Hong Kong</td><td>670</td><td>.7515
± .0154</td><td>.1926
± .0111</td><td>0</td><td>0</td><td>0.0559
± 0.0067</td></tr>
<tr><td>Steinberg et al. 1961</td><td>Kuala Lumpur</td><td>90</td><td>.6720
± .0350</td><td>.2775
± .0334</td><td>0.0058
± 0.0058</td><td colspan="2">0.0447
± 0.0155</td></tr>
<tr><td>Fraser et al. 1965</td><td>Taiwan
Taipeh</td><td>96</td><td>.6679
± .0347</td><td>.1956
± .0351</td><td>0.0613
± 0.0299</td><td>0.0752
± 0.0247</td><td>0</td></tr>
<tr><td></td><td>Chung-Li</td><td>98</td><td>.7428
± .0314</td><td>.2040
± .0295</td><td>0.0072
± 0.0070</td><td>0</td><td>0.0460
± 0.0163</td></tr>
<tr><td></td><td>Chi-Chi</td><td>102[a]</td><td>.7288</td><td>.1684</td><td>0.0457</td><td colspan="2">0.0571</td></tr>
<tr><td>Chaudhuri et al. 1967</td><td>Calcutta</td><td>161</td><td>.6985
± .0256</td><td>.2234
± .0232</td><td>0.0033
± 0.0033</td><td colspan="2">0.0748
± 0.0147</td></tr>
<tr><td>Nakajima et al. 1967</td><td>Taiwan
North. Chin.</td><td>89</td><td>.6292
± .0362</td><td>.3034
± .0344</td><td>0</td><td></td><td>0.0674
± 0.0188</td></tr>
<tr><td></td><td>South. Chin.</td><td>240</td><td>.7458
± .0199</td><td>.1937
± .0180</td><td>0</td><td></td><td>0.0604
± 0.0109</td></tr>
<tr><td></td><td>Taiwanese</td><td>373</td><td>.6898
± .0170</td><td>.2341
± .0155</td><td>0.0072
± 0.0032</td><td>0.0189
± 0.0177</td><td>0.0500
± 0.0188</td></tr>
<tr><td>Shanmugaratnam 1972</td><td>Singapore</td><td>200</td><td>.7542
± .0216</td><td>.1842
± .0194</td><td>0.0158
± 0.0064</td><td></td><td>0.0458
± 0.0105</td></tr>
<tr><td>Hawkins et al. 1974</td><td>»</td><td>166</td><td>.7771
± 0.0228</td><td>.1958
± 0.0218</td><td>0</td><td></td><td>0.0271
± 0.0089</td></tr>
</table>

[a] Values taken from original publication. The particular arrangement of phenotypes did not give a satisfactory maximum likelihood solution after 50 iterations.

The MNSs System

The distribution of the MN blood groups in Chinese has been studied in several surveys since Ride (1935) first examined samples from 1029 subjects in Hong Kong. The results of a number of these surveys are reproduced in Table III. There is considerable variation in the frequency of the *M* gene ranging from 0.505 in Cantonese subjects in Venezuela (Layrisse and Arends 1956) to 0.670 in Cantonese in Malaya (Simmons et al. 1950). The fact that these extreme values both relate to subjects identified as Cantonese seems to preclude any localisation of specific gene frequencies according to geographical origin as was detected for the ABO system. Most of the surveys have involved relatively small numbers of subjects, and the high standard errors associated with the estimates from these surveys may tend to mask any genuine regional localisation of the gene frequencies. In Taiwan, however, Nakajima et al. (1967) studied the distribution of MN types in 2564 Chinese who were able to identify their province of origin in China. A definite cline was observed with higher *M* frequencies in Chinese from the South than in Northern Chinese.

Genetic variants within the MN blood-group system have been reported by Madden et al. (1964) who found 6 out of 420 Chinese in California to possess the St^a (Stones) antigen which appeared to be related to the MN system, and by Cleghorn (1966) who has referred to the finding of the Miltenberger III antigen class in two Chinese families.

The limited investigations for the *Ss* alleles of the MNSs system are summarised in Table IV. The low frequencies for the *S* gene are in substantial agreement in the four surveys, and with Madden et al. (1964), who recorded a frequency for *S* of 7% amongst Chinese in California. The *S* gene has appeared to be more commonly associated with *M* than with *N* in all the surveys undertaken to date.

Other Blood-Group Systems

Whilst the Kell (K) and Duffy (Fy^a) blood groups often prove to be useful markers in population genetics studies, the value of the two systems in studies of the Chinese is clearly limited. Only one subject in over 1750 Chinese tested in Asia and the United States has been reported to possess the Kell antigen. Conversely, the Fy^a gene occurs almost without exception in Chinese. The results of some relevant surveys of the distribution of the Kell and Duffy blood groups are recorded together for convenience in Table V.

The data available on the distribution of the P blood groups in Chinese are somewhat limited. Three surveys were undertaken amongst New York Chinese at a time when the genetic complexity of the P blood-group system was not fully realised. Miller et al. (1950) reported the " incidence of P positives " in 190 subjects to be 32.6%, Miller et al. (1951) found 27.2% of 103 subjects to possess the " P factor ", and Sussman (1956) demonstrated the " P factor " in approximately 40% of 160 subjects. In Taiwan, Huang (1970) found 24.6% of 491 Fu-Lau Formosans to be Q positive, the factor Q having been shown by Henningsen and Jacobsen (1955) to be identical to the P_1 antigen, and Nakaijma et al. (1967) found the phenotype frequency of Q to be 31.85% in 383 Chinese from North China, 28.23% in 464

TABLE III

DISTRIBUTION OF MN TYPES IN CHINESE POPULATIONS

Investigators	Population	N	Percentage of phenotypes			Gene frequencies		
			MM	MN	NN	*M*	*N*	Standard error
Ride 1935	Hong Kong	1 029	33.2	48.6	18.2	0.5753	0.4247	0.0109
Alley and Boyd 1943	Boston	101	38.6	45.6	15.8	.6139	.3861	.0343
Levine and Wong 1943	New York	150	23.3	54.7	22.0	.5067	.4933	.0289
Wiener et al. 1944	» »	138	31.9	46.4	21.7	.5507	.4493	.0299
Simmons et al. 1950	Malaya							
	Cantonese	97	46.4	41.2	12.4	.6701	.3299	.0338
	Hakkas	100	37.0	54.0	9.0	.6400	.3600	.0339
Sussman 1956	New York	817	31.3	49.9	18.8	.5607	.4393	.0123
Layrisse and Arends 1956	Venezuela	100	21.0	59.0	20.0	.5050	.4950	.0354
Grimmo and Lee 1961	Hong Kong	670	30.0	50.9	19.1	.5545	.4455	.0136
Steinberg et al. 1961	Malaya	90	27.8	47.8	24.4	.5167	.4833	.0372
Chaudhuri et al. 1967	Calcutta	209	32.5	42.6	24.9	.5383	.4617	.0244
Fraser et al. 1965	Taiwan							
	Taipeh	98	25.5	52.0	22.5	.5153	.4847	.0357
	Chi-Chi	99	32.3	52.5	15.2	.5859	.4141	.0350
	Chung-Li	102	31.3	51.0	17.7	.5686	.4314	.0347
Nakajima et al. 1967	North of Yellow River	188	21.28	51.60	27.13	.4704	.5296	.0257
	Between Yellow River and Yangtze River	690	24.64	50.87	24.49	.5007	.4993	.0135
	Chekiang, Kiangsi and Hunan	462	25.32	52.60	22.08	.5162	.4838	.0164
	Fukien	422	29.86	50.00	20.14	.5486	.4514	.0171
	Canton	802	30.42	51.37	18.20	.5611	.4389	.0124
	Taiwan	2 984	31.27	50.77	17.96	0.5665	0.4335	0.0064

TABLE IV

ESTIMATES OF *MNSs* GENE FREQUENCIES IN CHINESE POPULATIONS

Investigators	Population	N	Gene frequencies			
			MS	*Ms*	*NS*	*Ns*
Miller et al. 1951	New York	103	0.0374	0.5694	0.0175	0.3757
Grimmo and Lee 1963	Hong Kong[a]	406	0 (0.0166)	0.5854 (0.5647)	0.0096 (0.0019)	0.4050 (0.4168)
Shanmugaratnam 1972	Singapore	200	0.0425	0.5250	0.0062	0.4263
Hawkins et al. 1974	»	166	0.0151	0.5030	0	0.4819

[a] The maximum likelihood estimates for the *MS* and *Ms* frequencies differ significantly from the values (indicated in parentheses) given in the original publication. This appears to be influenced by a significant departure from H-W equilibrium between the observed (6) and expected (0) numbers of subjects of phenotype MS in the sample.

TABLE V

TESTS FOR KELL (K) AND DUFFY (Fy^a) GROUPS IN CHINESE POPULATIONS

Investigators	Population	Kell (K)		Duffy (Fy^a)	
		Number tested	Number positive	Number tested	Number positive
Miller et al. 1951	New York	103	0	103	99%
Sussman 1956	» »	160	0	0	
Layrisse and Arends 1956	Venezuela	0		100	100
Grimmo and Lee 1963	Hong Kong	500	0	500	500
Fraser et al. 1965	Taiwan	300	0	299	291
Chaudhuri et al. 1967	Calcutta	132	1	127	122
Shanmugaratnam 1972	Singapore	303	0	303	303
Hawkins et al. 1974	»	258	0	258	258

Chinese from South China, and 26.14% in 1381 Taiwanese. Hawkins et al. (1974) found 44.1% of 145 Chinese in Singapore to possess the P_1 antigen. Despite the limited availability of data, the surveys appear to indicate significant regional variations in the incidence of the P_1 gene, but no pattern is immediately evident.

Layrisse and Arends (1956) investigated the distribution of the recently discovered Diego blood-group system in Chinese in Venezuela. The Di^a antigen had, until that time, only been found in subjects of Mongoloid extraction. The finding of the antigen in 5 out of 100 Cantonese subjects in Venezuela added weight to the view that the Di^a antigen is a marker of mongoloid ethnic type. Fraser et al. (1965) reported the frequency of the Di^a gene in Taiwan Chinese to be 0.015 which was rather lower than that obtained by Layrisse and Arends (1956). However, preliminary investigations in Singapore Chinese and in the " Boat People " of Hong Kong, (Hawkins, Simons, and Ho: unpublished data) revealed 4 subjects with the Di^a antigen out of a total of 87 tested. These figures correspond to a Di^a gene frequency of similar order to that found in Venezuela.

The distribution of the X-chromosome-linked Xg^a antigen was studied in 64 Singapore Chinese by Wong et al. (1964), who reported the frequency of the Xg^a gene to be 0.46. Saha and Banerjee (1973) found a very similar frequency of 0.446 in 111 Chinese, also from Singapore, but Dewey and Mann (1967) found the frequency to be slightly higher in Chinese in Taiwan. Amongst 171 Mainland Chinese, the Xg^a frequency was found to be 0.5990 and in 178 Taiwan Chinese the frequency was reported to be 0.5253. However, when 95% confidence limits are applied to all of the Xg^a frequencies reported for Chinese, the results are found to be in mutual agreement.

The Kidd blood-group system has been studied in New York Chinese by Rosenfield et al. (1953) who tested 103 samples with anti-Jk^a serum. The frequency of the Jk^a gene was reported to be 0.3103.

THE POLYMORPHIC SERUM PROTEINS

Haptoglobin

Chinese populations in a number of areas have been studied for the distribution of the haptoglobin types. Table VI summarises the results of these investigations. The table has been arranged in order of increasing frequency of the Hp^1 allele. This approach emphasises that, with the exception of the data of Fraser et al. (1965) from a study in Taiwan, surveys undertaken in the same geographical areas have been in very close agreement in their findings. There is, however, a considerable range in the gene frequencies obtained from these surveys, and when 95% confidence limits are applied to the extreme estimates it appears unlikely that the observed range is the exclusive result of sampling errors. The somewhat higher Hp^1 frequencies recorded in New York, Hawaii, and Hong Kong, compared with those in Indonesia, Malaysia, and Taiwan, may suggest that variations exist in the haptoglobin distribution in different groups of Chinese. Support for this view is given when it is considered that the Chinese populations of New York, Hawaii, and Hong Kong, are mainly Cantonese,

TABLE VI

DISTRIBUTION OF HAPTOGLOBIN TYPES IN CHINESE POPULATIONS

Investigators	Population	N	Observed numbers of phenotypes				Gene frequencies		
			0	1-1	2-1	2-2	Hp^1	Hp^2	Standard error
Lie-Injo et al. 1968*b*	Indonesia	85	0	6	28	51	0.2353	0.7647	0.0325
Kirk and Lai 1961	Malaya	167	2	18	57	90	.2818	.7182	.0248
Blackwell et al. 1962	Taiwan	172	0	9.3%	37.7%	52.9%	.2820	.7180	.0243
Steinberg et al. 1961	Malaya	90	3	9	32	46	.2874	.7126	.0343
Shih and Hsia 1969	Taiwan	98	0	11	38	49	.3061	.6939	.0329
Parker and Bearn 1961	New York	118	0.03%	14.8%	38.3%	47%	.3376	.6624	.0309
Shim and Bearn 1964	» »	113	0	16	45	52	.3407	.6593	.0315
Beckman et al. 1964	Hawaii	70	0	7	34	29	.3429	.6571	.0401
Baitsch et al. 1962	»	124		not given			.37	.63	
Sanford et al. 1966	Hong Kong	122	0	17	59	46	.3811	. 6189	.0311
Fraser et al. 1965	Taiwan								
	Taipeh	98	0	10	51	37	.3622	.6378	.0343
	Chi-Chi	100	5	15	55	25	.4474	.5526	.0361
	Chung-Li	101	3	11	54	33	0.3878	0.6122	0.0348

whilst the populations of the other three areas studied include Chinese of other dialect groups. The high Hp^1 frequencies found by Fraser et al. (1965) in Taiwan conflict with this view, but the atypical ABO blood-group distribution found in the Chi-Chi community during this survey tends to suggest that, for Chi-Chi at least, the subjects tested were not entirely representative of the Chinese community of Taiwan as a whole.

Transferrin

Table VII summarises the results of a number of surveys of the distribution of the polymorphic serum-protein transferrin. In view of the comparatively small number of subjects studied, the surveys are in close agreement. The mean frequency of the transferrin *C* gene from the nine surveys is 0.966. Parker and Bearn (1961) discovered that the most commonly occurring variant of transferrin in Chinese, which had previously been regarded as the negroid D^1 variant, was, in fact, distinct in electrophoretic properties from D^1. The Chinese variant was assigned the name D^{CHI} and is now generally regarded as a marker of mongoloid ethnic type.

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TABLE VII

ESTIMATES OF TRANSFERRIN *C* FREQUENCIES IN CHINESE POPULATIONS

Investigators	N	Population	*Tf C* frequency
Kirk and Lai 1961	103	Malaya	0.956
Parker and Bearn 1961	116	New York	0.97
Steinberg et al. 1961	90	Malaya	0.978
Giblett 1962	40	Taiwan	0.95
Beckman 1964	70	Hawaii	1.000
Fraser et al. 1965	300	Taiwan	0.979
Sanford et al. 1966	122	Hong Kong	0.946
Lie-Injo et al. 1968*b*	85	Indonesia	0.971
Shih and Hsia 1969	100	Taiwan	0.945

Gc

Four surveys have investigated the distribution of the Gc polymorphism in Chinese in Hong Kong, Taiwan, the Malay Peninsula, and New York. The frequencies of the Gc^1 and Gc^2 alleles obtained from these surveys are in close agreement as can be seen from Table VIII which summarises the results. Nakajima and Ohkura (1971) suggested that the difference in Gc^1 frequencies in Northern Chinese and Southern Chinese may indicate that a cline exists, but it was emphasised that the difference was statistically insignificant.

THE IMMUNOGLOBULIN ALLOTYPES

Investigations of the Gm allotypic marker system in Chinese were first reported by Steinberg et al. (1961), who tested 90 unrelated Chinese from Malaya for Gm(a), Gm(b), Gm(x), and-Gm-like. All were Gm-like negative and Gm(a) positive, 93% were Gm(b) +, and 5.5% possessed Gm(x). These studies and associated family studies suggested that the Chinese have the alleles Gm^{ab}, Gm^{a}, and Gm^{ax} with frequencies 0.741, 0.231, and 0.028 respectively. Vos et al. (1963) suggested that clinal variation of these alleles occurs in some oriental populations, and Nakajima and Ohkura (1971) verified that such clines exist in China, based upon the results of tests on sera from Chinese in Taiwan with diverse backgrounds on the mainland. Schanfield and Gershowitz (1971) and Schanfield et al. (1972) tested samples from a number of Chinese in Hong Kong, Taiwan, and Michigan (USA), who could provide information on their province of origin on the Chinese mainland. These studies included tests for the markers Gm (a, x, b, c, g, and t). It was found that 4 Gm phenogroups predominate in Chinese:

TABLE VIII

DISTRIBUTION OF *Gc* TYPES IN CHINESE POPULATIONS

Investigators	Population	N	Observed numbers of phenotypes			Reported gene frequencies	
			1-1	2-1	2-2	Gc^1	Gc^2
Cleve and Bearn 1961	New York	117	72	36	9	0.7693	0.2307
Kirk et al. 1963	Taiwanese	86	44	36	6	.721	.279
	Taiwan Chinese	93	52	33	8	.737	.263
	Malayan Chinese	63	41	16	6	.778	.222
Kendrick and Douglas 1967	Hong Kong	72	48	19	5	.7986	.2014
	Singapore	201	119	66	16	.7562	.2438
Nakajima and Ohkura 1971	Taiwan Chinese	100	62	33	5	.785	.215
	Northern Chinese	88	44	33	11	.688	.313
	Southern Chinese	100	56	33	11	0.725	0.275

Gm^{ag}, Gm^{axg}, Gm^{abst}, and Gm^{afb}. The frequencies of Gm^{ag}, Gm^{axg}, and Gm^{abst}, were highest in Chinese with origins in North China and lowest in Chinese from the southern provinces. Conversely, the frequency of Gm^{afb} was lowest in Chinese from the North and highest in those from the South.

The InV allotypic marker system was studied in the same series of investigations by Schanfield et al. (1972). There was found to be very little variation in the frequency of the InV^1 gene in Chinese from various regions. In Southern Chinese and Taiwan Chinese the frequency of InV^1 was found to be 0.303, whilst in Chinese from the northern provinces a slightly higher frequency of 0.361 was reported. Nakajima and Ohkura (1971) also noted a slightly higher InV^1 frequency in Northern Chinese than in Southern Chinese, but the differences were not statistically significant. Simons and Ropartz (1973) found a very similar InV^1 frequency in Singapore Chinese to those reported by Schanfield et al. (1972).

THE DISTRIBUTION OF RED-CELL ENZYMES

Amongst the red-cell enzymes found to be polymorphic in populations tested to date, only three, phosphoglucomutase, 6-phosphogluconate dehydrogenase, and acid phosphatase, can reasonably be described as polymorphic in Chinese populations.

Phosphoglucomutase (*PGM*)

Four surveys have investigated the distribution of PGM phenotypes in Chinese in various parts of South-East Asia and in San Francisco (Lie-Injo et al. 1968*a*, Shih and Hsia 1969, Lie-Injo and Poey-Oey 1970, Blake et al. 1973). Table IX shows that the frequencies of the PGM_1^1 and PGM_1^2 alleles obtained from these surveys are in close agreement. The surveys have also demonstrated that the low frequency alleles PGM_1^6 and PGM_1^7 occur in Chinese.

Variants in the electrophoretic pattern representing the PGM-2 locus are rare. No variants at this locus were detected in the 378 Singapore Chinese tested by Blake et al. (1973).

TABLE IX

DISTRIBUTION OF *PGM* TYPES IN CHINESE POPULATIONS

Investigators	Population	N	Observed numbers of phenotypes				Gene frequencies	
			1	2-1	2	Others	PGM_1^1	PGM
Lie-Injo et al. 1968*a*	San Francisco	110	64	36	6	4[a]	0.7636	0.2182
	Kuala Lumpur	276	155	103	17	1[b]	.7482	.2500
	Djakarta	41	23	11	4	3[c]	.7317	.2317
Shih and Hsia 1969	Taiwan	100	53	41	6	0	.7350	.2650
Lie-Injo and Poey-Oey 1970	Indonesia	88	51	28	5	4[d]	.7614	.2159
Blake et al. 1973	Singapore	378	204	143	27	4[e]	0.7315	0.2632

[a] 6-1 × 3 7-1 × 1 $PGM_1^6 = 0.0136$ $PGM_1^7 = 0.0046$
[b] 6-2 × 1 $PGM_1^6 = .0018$
[c] 6-1 × 1 7-1 × 2 $PGM_1^6 = .0122$ $PGM_1^7 = .0244$
[d] 6-1 × 2 7-1 × 2 $PGM_1^6 = .0114$ $PGM_1^7 = 0.0114$
[e] 6-1 × 2 6-2 × 2 $PGM_1^6 = 0.0053$

6-*Phosphogluconate Dehydrogenase* (6-*PGD*)

Chinese subjects in Taiwan, Singapore, and Malaysia, have been investigated for the distribution of 6-PGD types (Shih et al. 1968, Shih and Hsia 1969, Lie-Injo and Welch 1972, Blake et al. 1973). The results of these surveys are summarised in Table X. Apart from a slightly lower PGD^A frequency in the Taiwan Chinese studied by Shih and Hsia (1969) compared with the other groups, there appears to be little variation between the results of these

TABLE X

DISTRIBUTION OF 6-*PGD* TYPES IN CHINESE POPULATIONS

Investigators	Population	N	Observed numbers of phenotypes				Reported gene frequencies		
			A	AC	C	Other	PGD^A	PGD^B	Other
Shih et al. 1968	Taiwan								
	Mainland Chinese	111	98	13	0	0	0.941	0.059	—
	Taiwanese	117	101	15	1	0	.927	.073	—
Shih and Hsia 1969	Taiwan	100	79	21	0	0	.895	.105	—
Lie-Injo and Welch 1972	Malaysia								
	Adults	435	409	25	1	0	.969	.031	—
	Newborn	494	453	40	0	1[a]	.959	.040	0.001
Blake et al. 1973	Singapore	378	327	50	0	1[b]	0.9325	0.0661	0.0013

a PGD^{Thai}

b $PGD^{\text{Singapore}}$

surveys. One of the Singapore Chinese studied by Blake and colleagues had a hitherto undescribed 6-PGD phenotype to which the trivial name PGD (Singapore) was assigned, and Lie-Injo and Welch (1972) found the rare PGD (Thai) variant in a newborn Chinese in Malaysia.

Red-Cell Acid Phosphatase

The first investigation of genetic polymorphism for red-cell acid phosphatase in a Chinese population was undertaken by Lai and Kwa (1968), who studied the distribution of the enzyme in 620 Chinese blood donors in Singapore. Shih and Hsia (1969) subsequently conducted a survey in Taiwan, and Blake et al. (1973) made a further study amongst blood donors in Singapore. The results of the three surveys are shown in Table XI. It is of interest to note that, in 998 subjects in the two surveys in Singapore, only the genes p^a and p^b were present, whilst amongst only 100 Taiwan Chinese, 10% possessed the p^c gene. This finding may reflect the divergent origins in China of the present populations of Singapore and Taiwan.

ENZYMES SHOWING LITTLE OR NO GENETIC VARIATION IN CHINESE

Variations in the electrophoretic pattern of lactate dehydrogenase (LDH) are rare in most populations tested to date. No variants were detected amongst samples from 100 Chinese

TABLE XI

FREQUENCIES OF RED-CELL ACID-PHOSPHATASE ALLELES IN CHINESE POPULATIONS

Investigators	Population	N	Gene frequencies		
			p^a	p^b	p^c
Lai and Kwa 1968	Singapore	620	0.220	0.780	0
Shih and Hsia 1969	Taiwan	100	0.193	0.743	0.050
Blake et al. 1973	Singapore	378	0.2143	0.7858	0

in Taiwan tested by Shih and Hsia (1969), but Blake et al. (1973) detected two hitherto unreported variants in three of 378 Chinese blood donors tested in Singapore. The variants were assigned the trivial names LDH (Chinese-1) and LDH (Chinese-2).

The investigation of over 1 000 subjects from Taiwan, Malaysia, and Singapore, has shown that the Chinese are essentially monomorphic for the enzyme adenylate kinase (Shih et al. 1968, Shih and Hsia 1969, Chan 1971, Blake et al. 1973). Only one of the subjects in these surveys had a phenotype other than AK 1, the exception being a Chinese in Taiwan with origins in the Chinese mainland, whose phenotype was 2-1 (Shih et al. 1968).

Severe haemolytic anaemia due to hereditary deficiency of the enzyme phosphoglycerate-kinase (PGK) in two male members of a large Chinese family was reported by Valentine et al. (1969) and provided the first evidence that the structural locus for PGK is linked to the X-chromosome. There have been no reports to date of electrophoretic variants of PGK having been detected in Chinese.

Chen and Giblett (1971) tested samples from 120 Chinese in Taiwan for variants of glutamic oxalacetic transaminase. One subject had the GOT phenotype 2-1 and the remainder were of the GOT-1 phenotype.

Amongst samples from 378 Chinese blood donors in Singapore, Blake et al. (1973) found only one variant of phosphohexose isomerase (PHI 2-1) and one variant of diaphorase (Dia 4-1) but detected no variations from the normal electrophoretic patterns for the enzymes, malate dehydrogenase, peptidase B, and " oxidase ". In Malaysia, Lie-Injo and Welch (1972) reported two subjects with PHI phenotype 4-1 in 545 Chinese.

RED-CELL GENETIC DEFECTS

The distribution of red-cell genetic defects in South-East Asian populations has been reviewed by Lie-Injo (1969). The most serious defects occurring in Chinese are hereditary deficiency of glucose-6-phosphate dehydrogenase and the haemoglobinopathies, particularly the thalassaemias.

Glucose-6-Phosphate Dehydrogenase (G-6-PD)

One of the earliest attempts to demonstrate deficiency of G-6-PD in Chinese was by Beutler et al. (1959) who, using the glutathione stability test, did not detect any G-6-PD deficient subject amongst 77 Chinese students in the United States. In Singapore, however, T. Vella (1959) found 2.22% of 225 males to be G-6-PD deficient, and Smith and Vella (1960) found that of 13 Chinese infants severely affected by neonatal jaundice not attributable to foeto-maternal incompatibility within the ABO or Rhesus blood-group systems, 12 were deficient of the enzyme. The frequency of G-6-PD deficiency has since been studied extensively in Chinese populations. The findings have been in substantial agreement and there appears to be no reason to consider all of the surveys in detail. Typical findings are those of Chan et al. (1964), who found 5.5% of 200 male hospital-patients in Hong Kong to be G-6-PD deficient, and of Yue and Strickland (1965), who found 3.74% of 1177 cord blood samples from male births in Hong Kong to be deficient of the enzyme. In Taiwan, Lee et al. (1963) noted that the frequency of G-6-PD deficiency in 442 Hakka males from Hsin-Pu was considerably higher at 6.79% than in 343 Taiwanese males in whom the frequency was 0.29%. A further point of interest was that in 78 Hakka females from Hu-Kou a comparitively high frequency of 5.13% were G-6-PD deficient. In an extended survey in Singapore, Wong (1973) has tested the cord blood of 202 816 Chinese infants born over a seven-year period. G-6-PD deficiency was found in a total of 1.81% of the subjects consisting of 3.0% of the males and 0.6% of the females. Studies of the families of G-6-PD deficient Chinese subjects have confirmed the finding in other ethnic groups that the inheritance of G-6-PD is an X-chromosome-linked phenomenon (Lee et al. 1963, Chan and Lai 1971).

The observation of Kirkman et al. (1960), that G-6-PD from persons deficient of the enzyme had different biochemical properties to that purified from persons with normal levels, led to extensive biochemical and electrophoretic studies attempting to classify the various types of G-6-PD. Beutler (1969) lists 45 different variants from the normal B (+) type of G-6-PD, but McCurdy et al. (1970) suggest that this number may be in excess of the true figure because of methodological differences which exist within the laboratories undertaking the identification of these variants. However, at least 5 variant types are known to exist in the Chinese. McCurdy and colleagues (1966, 1970) identified three G-6-PD variants to which they assigned the names " Canton ", " Taiwan-Hakka ", and " Taipeh-Hakka ", and Chan and Todd (1972) have reported the " B (—) Chinese " and " Hong Kong " variants. Chan and Todd (1972) showed that these variants were widely distributed throughout Kwangtung Province, and, based on the rarity of mutation at the G-6-PD locus (Azevedo et al. 1968), suggested that the presence of several different variants in this region was related to the diverse origins in China of the present Southern Chinese population.

The Haemoglobinopathies

A considerable number of investigations for abnormal haemoglobins in Chinese have been published since 1955, when Rigas and colleagues first discovered the unique H variant of haemoglobin in two members of a Chinese family. In general, the incidence of abnormal haemoglobins in Chinese is low. Indeed, most of those reported have been detected in population surveys rather than as the result of clinical investigations since they are often benign in the heterozygous state. However, when such haemoglobins coexist with a thalassaemia condition, serious anaemia may result (Wong 1971).

In a review of the distribution of haemoglobinopathies in Singapore, Wong (1967) reported that the thalassaemia occurring most frequently in Chinese is that associated with haemoglobin H. This condition appears to be compatible with a normal lifespan. Classical β-thalassaemia occurs less frequently and is almost entirely restricted to the paediatric age group, since it invariably proves fatal before the patient reaches adulthood. No figures are available for the overall frequency of the heterozygous thalassaemia states, since there is no specific test for the reliable diagnosis of the condition.

A thalassaemia condition, which is almost exclusively restricted to the Chinese, is the Barts Haemoglobin-Hydrops Foetalis Syndrome. This condition was first described by Lie-Injo and Jo (1960) and Lie-Injo et al. (1962) in Chinese from Kuala Lumpur and Indonesia, but has subsequently been reported in Chinese from Hong Kong, Singapore, and Canada (Todd et al. 1967, Wong 1965, Yuet et al. 1967). The condition appears to be due to impaired γ-chain production in the foetus resulting in a surplus of γ-chains leading to the formation of haemoglobin Barts with the structure γ^4. When the genes determining this condition are present in homozygous state, the situation is incompatible with life and infants so affected are either stillborn or die within a very short time of delivery. A detailed account of the haemoglobin constitution in such cases is given by Weatherall et al. (1970).

A number of relevant findings relating to haemoglobinopathies and abnormal haemoglobins in Chinese are summarised in Table XII. The summary is far from exhaustive, but it does demonstrate similar patterns of abnormal-haemoglobin distribution in a number of Chinese populations. Particularly outstanding is the complete absence of references to the findings of Haemoglobins S or C in Chinese subjects. Haemoglobin E appears to be the most frequently occurring variant due to aminoacid substitution, whilst the variants D, G, J, and K, also occur sporadically. A number of distinct variants of the latter three types have been reported in the extensive surveys in Taiwan by Dr. Blackwell and his colleagues. Identical variants of haemoglobin G having the structure $\alpha_2^{30\ \mathrm{Glu}\rightarrow\mathrm{Gly}}\ \beta_2$ have been found in Chinese subjects from Hong Kong, Singapore, Hawaii, and Taiwan (Swenson et al. 1962, Blackwell and Liu 1970), and the structure appears to be unique to Chinese subjects.

DISCUSSION AND CONCLUSION

It seems hardly surprising that subjects originating from different parts of an area as large as China should exhibit some degree of heterogeneity in terms of blood genetic marker distribution. The ABO blood-group system has been the most extensively studied genetic marker in Chinese populations, and the preceding account of some of the work that has been undertaken to date reveals the considerable variations in ABO blood-group distribution which exist in this ethnic group. In view of such heterogeneity, it is difficult to make valid comparisons of the Chinese with other ethnic groups. From the gene frequencies tabulated by Mourant et al. (1958) for several Japanese populations, however, it is apparent that, with minor

Table XII

Abnormal Haemoglobins Affecting Chinese

Investigators	Haemoglobin reported	Locality	Comments
Rigas et al. 1955	H	USA	First report of Hb H
Vella et al. 1958*a*	G	Singapore	First finding of Hb G in Chinese
Vella et al. 1958*b*	Q + H	»	Found in investigation of severe anaemia
Vella F. 1959	Fessas and Papaspyrou	»	63 cases in 1962 cord bloods
	Barts	»	2 cases in 1962 cord bloods
	Alexandra	»	8 cases in 1962 cord bloods
Lie-Injo 1959	Fessas and Papaspyrou	Indonesia	21 cases in 633 cord bloods
Raper et al. 1960	Singapore-Bristol	Singapore	Redesignation of Fessas and Papaspyrou
Lie-Injo and Jo 1960	Unspecified Fast Haemoglobin	Indonesia	First report of association with hydrops foetalis
Vella and Tavaria 1961	E	Kuching	2 cases in 742 subjects
Schneider and Jim 1961	Honolulu	Hawaii	
Dixon et al. 1961	Q	Singapore	Second case reported in Chinese
Vella 1962	E	Singapore and Malaya	24 cases in 10 165 subjects
	D	»	1 case in 10 165 subjects
	G	»	1 case in 10 165 subjects
	J	»	3 cases in 10 165 subjects
	Q	»	1 case in 10 165 subjects
Swenson et al. 1962	G $\alpha^{30\ \mathrm{GLU}\to\mathrm{GLN}}$		Identical structural anomaly in Hb G from Hong Kong, Singapore and in Hb Honolulu
Lie-Injo et al. 1962	Barts + H	Malaya	Second report of association with hydrops foetalis
Lie-Injo and Hart 1963	Q + H	Indonesia	Present in 2 sisters
McFadzean and Todd 1964	E	Hong Kong	4 cases
	E thalassaemia		2 cases
McFadzean and Todd 1964	H	Hong Kong	17 cases
	Barts	»	In 6 cases of hydrops foetalis
Wong 1965	Barts	Singapore	In 16 cases of hydrops foetalis
Lie-Injo et al. 1966	Q + H	W. Malaysia	Present in 4 subjects in two families
Blackwell and Liu 1966	J Meinung	Taiwan	
Todd et al. 1967	Barts	Hong Kong	In 7 cases of hydrops foetalis
Ranney et al. 1967	New York $\beta^{113\ \mathrm{VAL}\to\mathrm{GLU}}$	New York	
Blackwell et al. 1971*b*	K Kaohsiung	Taiwan	In 9 unrelated subjects. Same structural anomaly as Hb New York (Ranney et al. 1967)
Yuet et al. 1967	α and β thalassaemia in one family	Canada	Resulted in hydrops foetalis
Wong 1968	J Bangkok $\beta^{56\ \mathrm{GLY}\to\mathrm{ASP}}$	Singapore	
Blackwell et al. 1968*a*	E	Taiwan	9 cases confirmed to have structure $\alpha_2\beta_2^{26\ \mathrm{GLU}\to\mathrm{LYS}}$
Blackwell et al. 1968*b*	G Hsin-Chu $\beta^{22\ \mathrm{GLU}\to\mathrm{ALA}}$	»	Identical to variant found in North American Indians
Blackwell et al. 1969*a*	J Taichung $\beta^{129\ \mathrm{ALA}\to\mathrm{ASP}}$	»	
Blackwell et al. 1969*b*	G Szu-Hu $\beta^{80\ \mathrm{ASN}\to\mathrm{LYS}}$	»	
Blackwell et al. 1969*c*	G Taipei $\beta^{22\ \mathrm{GLU}\to\mathrm{GLY}}$	»	
Blackwell and Liu 1970	G Taichung $\alpha^{74\ \mathrm{ASP}\to\mathrm{HIS}}$	»	
Wong 1971	Q	Singapore	2 further cases
Blackwell et al. 1971*a*	J Kaohsiung $\beta^{59\ \mathrm{LYS}\to\mathrm{THR}}$	Taiwan	
Blackwell et al. 1972	G Hsi-Tsou $\beta^{79\ \mathrm{ASP}\to\mathrm{GLY}}$	»	
Wong 1973	E	Singapore	46 cases in 1643 cord bloods
	Barts	»	3 cases in 1643 cord bloods

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exceptions, the Chinese populations tested outside China have lower *A* and higher *O* frequencies than the Japanese. Conversely, the Malays of the Malay Peninsula, whose ethnic relation to the Chinese is markedly different to that of the Japanese, have little to distinguish them from the Chinese in terms of ABO blood-group distribution (Hawkins 1974). All of the studies to date have agreed on the almost total absence of the A_2 antigen in Chinese.

Within the Rhesus blood-group system, all of the surveys have agreed on the high frequency of R_1 and on the low frequency of R_0 and/or *r*. Occasional reports of the presence of Rhesus negative complexes other than *r* have been made, but these complexes must be regarded as a rarity (Nakajima et al. 1967, Hawkins and Simons 1973). Nakajima et al. (1967) have commented also upon clinal variation for the *E* gene of the Rhesus system between Northern and Southern Chinese.

For the MNSs system, there is little to distinguish the Chinese from either Japanese, Malays, or, indeed, from Europeans, when their *M* and *N* gene distribution is considered alone. However, when these alleles are considered in conjunction with *S* and *s*, the distinction becomes quite apparent. The low *S* frequency of the Chinese is very similar to that of both Japanese and Malays, but differs considerably from that of Europeans. In common with the situation which exists in most European populations, *S* appears to be associated more frequently with *M* than with *N*, but this is in contrast to the situation which exists in Japanese (Lewis et al. 1957). Clinal variations for the *M* and *N* alleles between Chinese in Taiwan with origins in the north and south of Mainland China have been reported by Nakajima et al. (1967). Also in relation to clinal variation in Chinese, Schanfield et al. (1971, 1972) have discussed the existence of north-south clines within the Gm immunoglobulin system.

All of the studies on Chinese populations to date have agreed on the almost total absence of the Kell antigen and on the presence in practically all Chinese of the Fy^a antigen. In common with other mongoloid groups, the Chinese possess the Di^a antigen of the Diego blood-group system and the D^{Chi} gene of the serum-transferrin system. Genetic variants within other systems, that at the present time appear to be unique to the Chinese, include the " Singapore " variant of 6-PGD and the " Chinese-1 " and " Chinese-2 " variants of LDH (Blake et al. 1973) and the " Canton ", " Taiwan-Hakka ", " Taipeh-Hakka ", " B (—) Chinese ", and " Hong Kong ", variants of G-6-PD (McCurdy et al. 1966 and 1970, Chan and Todd 1972). Identical variants of Haemoglobin G, having a structure which appears to be unique to Chinese, have been found in subjects from Hong Kong, Singapore, Hawaii, and Taiwan (Swenson et al. 1962, Blackwell and Liu 1970), and, together with the numerous other haemoglobins which have been characterised in members of this ethnic group, these may be valuable in tracing the migration patterns of early Chinese populations. A finding relating to the red-cell acid-phosphatase system may already be of value in this respect, when it is considered that the p^c gene occurs in 10% of Chinese in Taiwan (Shih and Hsia 1969) but appears to be absent in Chinese in the Malay Peninsula (Lai and Kwa 1968, Blake et al. 1973).

The relative paucity of available data on a number of genetic-marker systems in Chinese populations leaves the significance of some of the data open to various interpretations. As further genetic polymorphisms are discovered, however, and their distributions are investigated in Chinese populations, it is possible that the new information, together with that available on the polymorphisms known at the present time, may be pieced together to reveal their true significance in terms of the migrations and history of this vast proportion of the world's population.

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RIASSUNTO

Vengono passati in rassegna e riassunti i dati disponibili sulla distribuzione dei marcatori sanguigni nelle popolazioni cinesi emigrate dalla Cina. Un variabile grado d'eterogeneità è stato riscontrato per alcuni dei sistemi di marcatori e, dov'era possibile, si è cercato di riferire tale eterogeneità alla diversa origine della popolazione studiata.

RÉSUMÉ

Les données courantes sur la distribution des marqueurs génétiques sanguins chez les populations chinoises émigrées de la Chine sont analysées et résumées. Un degré variable d'hétérogénéité a été remarqué pour certains des systèmes de marqueurs et ceci a été rapporté, là où il était approprié, aux différentes origines en Chine des populations étudiées.

ZUSAMMENFASSUNG

Übersicht und Zusammenfassung der verfügbaren Daten über die Verteilung der Blut-Markierungsgene chinesischer aus China ausgewanderter Bevölkerungen. Einige Markierungssysteme erwiesen sich als mehr oder minder heterogen; soweit möglich wurde daher versucht, eine Beziehung zwischen dieser Heterogenität und der jeweiligen Vorgeschichte im Ursprungsland der einzelnen Bevölkerungen festzustellen.

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