ETHNIC DISTRIBUTION OF PATIENTS WITH S.L.E. SEEN IN UNIVERSITY HOSPITAL, KUALA LUMPUR 1967—1976

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INTRODUCTION

SYSTEMIC lupus erythematosus (SLE) is a disease of uncertain aetiology. As awareness of the condition increases and serological techniques for its definition improve, it is being more frequently diagnosed (Fries and Holman, 1975). It has been known for many years that the incidence of the disease is increased in the relatives of patients suffering from the disease (Leonhardt 1967, Arnett and Shulman 1976, and Ermakova 1977), and the genetic component of its pathogenesis has been recently confirmed in twin studies (Block *et al.* 1975). Current thinking, however, is that certain individuals are predisposed by their genetic background to suffer from the illness, and that the trigerring factor is likely to be a virus (Phillips, 1978).

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The effect of race has not been studied very frequently, apart from the major study by Siegal and Lee (1973) which showed that in New York City the disease was more common in black females than white females with Puerto Ricans in between. Siegal and Lee also showed that race can affect the age of onset of SLE. Thus in New York City all the patients diagnosed as SLE before the age of 15 were Puerto Ricans (even though the disease was more prevalent in the Negro population). In one centre in the western United States an increased prevalence of SLE has been noted in people of oriental race (Simon *et al.* 1973).

It is also interesting that 4 out of 110 patients with SLE reported by Lee *et al.* (1977) were 'orientals'. Morton *et al.* (1976) also reported a difference in the annual incidence of SLE in inbred North American Indian tribes. However, Estes and Christian (1971) and Dubois (1974), felt that there was no ethnic or racial predisposition to SLE within the hospital population studied. More recently Hughes (1977) noted a very high prevalence of SLE in the Jamaican population.

At the University of Malaya, SLE appeared to be seen frequently, and in view of the interest of various faculty members in this illness (Lau and White, 1969, and White *et al.* - in press) it seemed reasonable to study the disease in some depth. Consequently in June, 1974, a Systemic Lupus Erythematosus Study Group was set up by members of the Departments of Medicine, Pathology and Psychiatry in order to facilitate the diagnosis and consequent study of the disease and its management. No large study on the effect of race on SLE in West Malaysia has been performed. The study performed in Singapore

(Tay and Khoo, 1971) did not suggest any difference in the prevalence of SLE within minority ethnic groups in comparison with the Chinese majority, but the minority groups were small in size. In West Malaysia, however, the population is derived predominantly from people of Malay, Chinese and Indian origins. It therefore seemed to be of value to determine the ethnic groups of patients with SLE in West Malaysia.

MATERIALS AND METHODS

On admission to University Hospital all patients have their race and date of admission documented on a form by a member of the Medical Records Department. At the time of discharge the Lecturer in charge of the patient enters the diagnosis on the same form, and this information is then computerised by the Medical Records Department, using the code suggested by the International Classification of Diseases (World Health Organisation, 1967). All records of patients coded under number 734.1 were reviewed by the author. The same protocol that was being used in the prospective study of SLE in West Malaysia was completed in this retrospective review, and those patients who fulfilled the A.R.A. criteria (Cohen *et al.* 1971) for the diagnosis of SLE were included in this analysis, whether the information was obtained prospectively or retrospectively. The data from both prospective and retrospective studies were then put on to punch cards for subsequent computer listing and analysis.

Throughout the period of study the Department of Pathology was able to perform on request all the investigations documented in the A.R.A. criteria. However, not all the patients in the retrospective study had the same clinical examination or laboratory investigations performed, and it is clear that there is considerable difference in clinical manifestations found in the retrospective and in the prospective studies (Frank A.O., unpublished data).

Any analysis based on total admissions over a period of time could be biased by a change in the relative proportions of patients of different races being admitted into the hospital. To exclude this possible bias, the date that the patient was first seen at University Hospital was extracted from the computer listings. The numbers of patients of different races admitted in each year were then compared with the numbers of patients of each race admitted during that year with other diagnoses. A chi-square analysis (2 x 2 contingency analysis with Yates correction) between the patients with SLE and the patients without SLE admitted between the years 1967-1971, and 1972-1975 was then performed for each race.

A personal survey of patients admitted on to a female medical ward during the six month period from the 1st April, 1976, to the 1st October, 1976, was then conducted. This survey specifically excluded patients who were a) being admitted for the second or subsequent time over the six month period, b) were known to be suffering from SLE or c) were suspected to be suffering from SLE.

RESULTS

Table I shows the ethnic groups of patients who were known to have, or not to have, SLE during the period 1967-1975. This table assumes patients with SLE to have been admitted on one occasion only, and does not make any allowances for patients without SLE who may have been re-admitted on one or more occasions, nor for patients who might have been suffering from SLE but for whom the diagnostic criteria suggested by Cohen et al. 1971, were not fulfilled.

TABLE I

PATIENTS WITH SLE AND ALL OTHER COMPLAINTS IN U.H. K.L. 1967 — 1975			
RACE	**SLE**	**NON SLE**	**TOTAL**
CHINESE	142	66357	66499
INDIAN	16	36754	36770
MALAY	17	22793	22810
TOTAL	175	125904	126079

$x^2 = 57.68$ $p > 0.001$

An analysis was performed on the numbers of Chinese, Malay and Indian patients who were or who were not suffering from SLE between the

years 1967-1972 and 1973-1975. A chi-square test showed no significant difference in any racial group in the frequency of admissions of new patients with SLE during the two time periods. This finding supports the contention that, although the proportions of Chinese, Indian and Malay patients who were admitted to University Hospital over the years studied varied (see Table II), the proportion of patients of any individual race suffering from SLE remained constant.

TABLE II

ADMISSIONS TO UNIVERSITY HOSPITAL
KUALA LUMPUR 1967 — 1975
[excluding obstetric patients]

YEAR	CHINESE %	INDIAN %	MALAY %	OTHER %	TOTAL No. of patients
1967	50.1	32.4	13.5	4.0	1431
1968	55.7	27.2	13.4	3.7	8359
1969	55.6	25.8	14.2	4.4	13554
1970	58.1	25.4	12.7	3.8	11905
1971	54.6	27.4	14.7	3.3	13364
1972	49.3	29.4	18.6	2.7	18380
1973	48.6	29.8	19.0	2.6	18933
1974	48.4	29.0	20.2	2.4	20672
1975	47.6	29.4	21.2	1.8	23229
TOTAL	51.22	28.32	17.57	2.89	129827

Table III shows that there was a highly significant difference in the incidence of SLE in hospital admissions between Chinese patients and other patients ($p < 0.001$) and Table IV shows that there was no significant difference between the incidence in hospital admissions of SLE in

TABLE III

COMPARISON OF CHINESE AND INDIAN AND MALAY ADMISSIONS
1967 — 1975 WITH AND WITHOUT SLE

RACE	WITH SLE	WITHOUT SLE	TOTAL
CHINESE	142	66,357	66,499
INDIAN & MALAY	33	59,547	59,580
TOTAL	175	125,904	126,079

x^2 (Yates Correction) = 55.5690 $p < 0.001$

TABLE IV

COMPARISON OF INDIAN AND MALAY ADMISSIONS
1967 — 1975 WITH AND WITHOUT SLE

RACE	WITH SLE	WITHOUT SLE	TOTAL
INDIAN	16	36,754	36,770
MALAY	17	22,793	22,810
TOTAL	33	59,547	59,580

x^2 (Yates Correction) = 1.9180 $p > 0.1$

Indian and Malay patients over these years. It is concluded that SLE is a more frequent occurrence in Chinese admissions to University Hospital, Kuala Lumpur, than in Indian or Malay admissions, and this is independent of the proportion of admissions of each race over this period. Table V compares the ethnic composition of admissions to a female medical ward in a six month period in 1976 to the ethnic composition of all hospital admissions from 1967 to 1975 (excluding obstetric admissions). There was no significant difference, and this confirms the validity of the total figures of admissions between 1967-1975 regardless of sex or readmissions, and also confirms that there is no changing trend in 1976.

TABLE V

	Comparison between admissions to a female Medical Ward 1.4.76 — 1.10.76 and all admissions 1967 — 1975 by racial group				
	MALAY	**CHINESE**	**INDIAN**	**OTHER**	**TOTAL**
% of admissions 1967 — 1975	17.57	51.22	28.32	2.89	100
Expected number of 320 admissions	56.2	164.	90.6	9.2	320
Observed number of 320 admissions	56	162	102	0	320
$x^2 = 2.9$			$P > 0.05$		

DISCUSSION

These results support the clinical impression held for some years in West Malaysia that SLE is more frequently seen in the Chinese population, and noted in previous publications from the University Hospital (White *et al.* - in press). It cannot be explained by the numbers of Chinese patients who seek treatment at the University Hospital. Unfortunately these results tell us nothing about the prevalence of systemic lupus erythematosus in West Malaysia and this information is unlikely to be obtained for many years, as it is unlikely that resources will become available for the expensive epidemiological study that would be necessary. However, the numbers noted in this study are probably only a small proportion of the reservoir of patients treated in West Malaysia. Patients with minor complaints are unlikely to seek help, and of those that do seek help many will be treated in the district and state hospitals. It is, of course, true that some of our patients had been treated elsewhere prior to being seen in the University Hospital. However, the numbers are sufficiently large regardless of this to suggest that a significant reservoir of SLE exists in West Malaysia.

SLE is widespread in the East, and has been reported from Singapore (Tay and Khoo, 1971), Hong Kong (Wong, 1969), and Japan (Fukase and Ofuzi, 1973). In this Japanese study, 689 patients were thought to have SLE, and of these, 275 were thought to have fulfilled the A.R.A. criteria (Cohen *et al.* 1971). The finding of an increased frequency of SLE in Chinese in West Malaysia suggests that the Chinese may be at increased risk. This suggestion is supported by the scarcity of reports from India. Menon *et al.* (1976) thought that this was because SLE was a rare disease in India, but this view was challenged by Malaviya *et al.* (1973), at the All India Institute of Medical Sciences in New Delhi, who reviewed the positive anti-nuclear factor tests found in one year and noted 22 cases of SLE. This, however, contrasts with the 81 new patients seen by Hughes (1977) in one year in Jamaica.

Further support for a racial influence on the risk of having SLE comes from the reports of SLE from Africa. Up until 1960, no reports of SLE had been noted in Africans, although one had been noted in a Cape Coloured (Trowell, 1960). Greenwood (1968) noted that a few cases had been reported in Africans, and he reported two more cases from Western Nigeria. No definite cases of SLE were encountered during three years observation in Tanzania (Yudkin J, personal communication). Recently 46 patients were reported from Cairo by Grennan *et al.* (1977) but presumably none of these were Africans.

SLE has also been reported from South Africa (Jessop and Meyers, 1973, and Seedat and Pudifin, 1977). Both series noted SLE to be less common in Africans than in Indians and Coloureds. Whilst the authors acknowledged that the reports were clinical studies, they felt that this supported the general experience that Negroes in Africa tend not to suffer from Autoimmune Disease in any great frequency.

SLE is probably a world-wide disorder, with reports from Australia (Nanra and Kincaid-Smith, 1973), the United States of America (Kellum and Haserick, 1964, Howell *et al.* 1969, Estes and Christian, 1971, Lie and Rothfield, 1972, Foad *et al.* 1972, Gibson and Dibona, 1972, Fessel, 1974, Fries and Holman, 1975, Ropes, 1976, Morton *et al.* 1976, Fish, 1977), Canada (Lee *et al.* 1977) and Western Europe. There have been two recent reports from the United Kingdom (Grennan *et al.* 1977, and Grigor *et al.* 1978). Reports from France (Morel-Maroger *et al.* 1976), Scandinavia (Leonhardt, 1967, and Eyrich and Borulf, 1974), Poland (Checinska *et al.* 1974, and Maldykowa and Chwalinska-Sadowska, 1974) and Russia (Ivanova, 1974 and Ermakova, 1977) demonstrate its distribution throughout Europe.

It is not suggested that these reports represent all published reports, nor that the frequency of SLE is greater in the United States. Indeed, population studies in New York and Malmo, Sweden, suggest a similar prevalence of SLE (Siegel and Lee, 1973). It is likely that in the industrial states the frequency of reports is proportional to the interest in the condition, and the resources available to investigate it. However, in the "third world", this is less likely to hold true, and many of the reports from the "third world" emanate from ex-British colonies, where a similar pattern of medical care might have been expected. It is reasonable to suggest that the infrequent reports of SLE in Black Africans from Africa may indeed represent a different frequency in expression of the disease.

Little work has been performed on serological changes in populations. However, Siegel and Lee (1973) found increased gamma globulins in Negro patients compared to White patients, with levels in Puerto-Ricans in between. These values mirrored the incidence of SLE in these ethnic groups. Raised gamma globulins are frequently seen in African patients (Trowell, 1960) although SLE is reported infrequently in Africans. Meyers (personal communication, 1978) has reported only one instance of a positive anti-nuclear factor in 547 sera taken from a tribal population. Clearly no definite conclusions can be drawn, but the parallel with Rheumatoid Arthritis (RA) is noteworthy. In Western Nigeria RA is uncommon and mild, and the incidence of sero-positivity is no different from that of the general population (Greenwood, 1969). In West Malaysia, sero-positivity was noted in approximately 50% of the Chinese cases studied by Toh *et al.* (1973), and the disease appeared to be intermediate in frequency between Western Nigeria and the United Kingdom, where sero-positivity is commonly accepted to be approximately 85% of patients with RA. Sero-positivity was lower, however, in the Indian and Malay patients (Toh *et al.* 1973) than in the Chinese patients.

None of our 202 patients with SLE were 'Orang Asli' (the indigenous population of West Malaysia). If it should subsequently be confirmed that SLE is infrequent in the Orang Asli, it would support the suggestion by Greenwood (1968), that the infrequent occurrence of autoimmune disease in parts of tropical Africa may be related to the immunological disturbance produced by multiple parasitic infections.

The interesting contrast between the suspected decreased susceptibility to SLE in West African patients and the increased susceptibility in their North American Negro and West Indian descendants has been noted (Greenwood, 1968). Environmental factors almost certainly play a role

here, and it has been shown that serum gamma globulin levels in West African people residing in the United Kingdom decrease as their length of stay in England increases (Schofield, 1957).

It is concluded that the finding of an increased susceptibility to SLE in Chinese patients from Peninsular Malaysia suggests that racial factors play a part in the pathogenesis of SLE, and this is not likely to be explained purely by genetic or geographical factors. Other environmental factors probably exert a role. SLE appears to be reported frequently from Chinese communities and infrequently from tropical Africa. A recent review (Lancet, 1978) discussed the genetic and environmental factors thought to be influencing the expression of SLE. This author believes that a careful study of geographical and racial factors would contribute usefully in this discussion.

SUMMARY

Following the opening of the University Hospital of the University of Malaya in 1967, over 126,000 patients (excluding obstetric patients) have been admitted. A retrospective review, run concurrently with a prospective study, of over 200 patients thought to have suffered from systemic lupus erythematosus (SLE) revealed that, up until the 31st December 1975, 175 patients fulfilled the criteria for the diagnosis of SLE. There was a highly significant increase in the diagnosis of SLE over this period among Chinese patients compared to all other races, and no significant difference in the diagnosis of SLE among Indian and Malay patients.

A review of the literature revealed that SLE appears to be a worldwide disease, reported frequently from Chinese communities but infrequently from tropical Africa.

It is concluded that SLE is more common in the Chinese from Peninsular Malaysia than the other races, and that a careful study of geographical and racial factors in SLE may contribute to further understanding of its pathogenesis.

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