findings were kindly confirmed by Dr. H. Lehmann, of St. Bartholomew's Hospital, who also demonstrated 1.9% of foetal haemoglobin (F) in Mrs. P.'s blood. Haemoglobin C moves characteristically slowly at pH 8.6 (the slowest of all the haemoglobins so far described). It is readily denatured by alkali.

Discussion

Since Mrs. P. is homozygous (CC), both of her parents, who were pure-blooded negroes, must have had Hb C. The brothers K. have the same father but a different mother, and, since D.K. has Hb A only, the father must have heterozygous C (AC). Fig. 4 summarizes the genetic data available.

FIG. 4.—Incidence of haemoglobin C in the P. and K. families.

The characteristic haematological findings in haemoglobin C disease are: (1) marked reduction in the osmotic fragility of the erythrocytes; (2) numerous target cells, with boat cells (folded erythrocytes), in the blood film, owing to the abnormal thinness of the cells; (3) demonstration of haemoglobin C only, on electrophoresis. If the disease is in an active phase the features of a haemolytic anaemia are generally present in addition (anaemia, reticulocytosis, increase in serum bilirubin and faecal urobilin, etc.). All cases so far described have had enlarged spleens, and most have complained of joint pains.

The haematological findings in the case of Mrs. P. were complicated by her pregnancy. Although she was grossly anaemic her reticulocyte count was only 2.2%, and her serum bilirubin was normal. Marrow examination revealed a megaloblastic element. As she gives no history of previous ill-health attributable to anaemia the disease may not itself give rise to clinically detectable anaemia in her case. There must be many such persons, with virtually symptomless haemoglobin C disease, if estimates of the frequency of homozygous haemoglobin C are at all accurate. Terry, Motulsky, and Rath (1954) have suggested a frequency of 1 in 6,000 for CC, while Smith and Conley (1953) estimated the incidence of the C trait as 1 to 3%, in North American negroes. It would appear likely, therefore, that with the rapid increase of our negro population other cases of haemoglobin C disease must already be present in this country, and that we must be on the look-out for haemoglobinopathies in non-European patients with anaemia.

Summary and Conclusion

A Jamaican negress immigrant, found to be severely anaemic at routine antenatal investigation, proved to be a case of haemoglobin C disease (CC). Her husband has normal adult haemoglobin (A) only, and her two children have a mixture of A and C. Two of her half-brothers (co-paternal) have been investigated. One has heterozygous C (AC) and one A only.

The abnormal haemoglobins were demonstrated by electrophoresis on filter-paper at pH 8.6.

The characteristic diminished osmotic fragility of the erythrocytes and numerous target cells were well shown in this case.

An incidence of 1 in 6,000 has been suggested for haemoglobin C disease in North American negroes. This and other hereditary haemoglobinopathies should be considered when investigating non-European patients with anaemia.

I wish to thank Dr. H. Lehmann for his help and for confirming the results of electrophoresis; Dr. J. N. Marshall Chalmers for the blood specimens of the brothers K.; Dr. J. D. Procter, the clinician in charge of the patient; and Mr. C. E. Vernon for the electrophoretic determinations. The first report of these cases, apart from the K. brothers, was made at a meeting of the Association of Clinical Pathologists in April, 1956.

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CARDIAC INFARCTION IN MALAYA

BY

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In the changing pattern of medicine in the tropics to-day the degenerative diseases, as elsewhere in the world, are found to be of growing importance. Before the second world war very little was written about cardiac infarction in South-East Asia, mainly because of the urgent need to study the important epidemic diseases, but also because cardiac infarction was still a young subject and because there were few electrocardiographs, without which investigations are unlikely to be carried out. Even to-day there is some difficulty in maintaining an electrocardiograph in good working order in a tropical climate, and servicing is not always possible.

In China an analysis of the incidence of disease in hospitals was given by Gear (1936), but heart disease was not common and degenerative heart disease not separately mentioned. In Canton Karcher (1936), whose patients were mainly female, analysed those who had heart disease. Only 2.1% were classified as having arteriosclerotic heart disease, but 17.7% had hypertensive disease. Snapper (1941) when working in China rarely encountered myocardial infarction. Tung (1948) saw nine patients with it at the Peiping Union Medical College Hospital in 1938-41 and nine patients in private practice in 1945-8. His opinion was that among Chinese, although hypertensive cardiovascular disease was prevalent, coronary thrombosis and angina pectoris were uncommon. Of his 18 patients, 15 were of the upper social and economic class.

In the Malaysian regions reports are also rare. Kouwenaar (1937) described a case, including a necropsy report, in a Javanese. Van Wesel (1939), in writing on cardiac infarction, reported five cases of coronary artery disease, but these were all in Europeans or Indo-Europeans. Soetano Tjokronegoro (1940) reported six

cases of aneurysm of the heart, of which four were in natives. Zuidema (1941) stated that cases are seen in Europeans, Indo-Europeans, and Chinese, but rarely in natives of Java, although hypertension and arteriosclerosis are common. He reported the cases of two Javanese, one of whom was a doctor. An extensive review of heart disease in Thailand was made by Bisal (1938). He analysed 530 cases admitted to Siraraj Hospital in Bangkok, of which 4.5% were described as arteriosclerotic in type. Although this group was further broken down the diagnosis of cardiac infarction was not mentioned.

Sengupta (1940) collected the cases seen at the Medical College Hospital, Calcutta, from 1931 to 1936. The total in this period was only 21, which was 2.1% of all cardiac cases. From correspondence I have had with Indian physicians I find the condition is not regarded as rare to-day, and Vakil (1949) has published a series of cases. In Ceylon the disease also seems fairly common now, Jayewardene and Jayasekera (1954) having collected 270 cases from the General Hospital, Colombo, during 1952 and 1953.

Scope of Investigation

This investigation covers the four years 1952-5. During this time all patients attending the Penang General Hospital who were found to have suffered from cardiac infarction were studied. Those with an old infarction diagnosed for the first time as well as those seen during an attack are included. The hospital is the main medical centre in the Settlement of Penang and Province Wellesley, which is situated in the north of the Malay Peninsula. Accommodation is graded into first, second, and third class. For third-class accommodation a small charge may be made, but most of the patients are treated free. The general medical beds of the hospital are divided into two medical units, each of which has 60 third-class beds and further beds in the better-class wards as required. Nearly all the cases were in-patients, but a few out-patients were seen in consultation. The diagnosis of cardiac infarction was based on definite changes in the QRS complex of the electrocardiogram, and a series of tracings was taken from each patient when that was possible. The customary twelve leads, occasionally more, were usually recorded at each examination. Post-mortem examinations are rarely permitted, and in only 4 of the 18 deaths was necropsy performed, and in these the diagnosis was confirmed.

In the four years 89 cases of cardiac infarction were diagnosed, an average of only 22 a year. During the same period a yearly average of 562 E.C.G.s were taken. The population of the Settlement from which these patients were drawn was 527,770 (estimation for 1954) and the average yearly admissions to the hospital were 9,396. The figure of 89 cases in four years is probably a little less than it should be, as fewer cases were diagnosed in the earlier part of the investigation. This may be attributed to shortage of staff and difficulties with the electrocardiograph, resulting in rather fewer recordings being taken.

Distribution by Sex, Age, Social Class, and Race

Of the 89 patients only 13 were women. Although this low figure for women may be partly due to the fact that fewer women than men are admitted to hospital, this explanation is quite inadequate, and the difference can be attributed to the different sex incidence for the disease. The ages of the men, by decades, are given in Table I.

TABLE I.—Age Incidence of 76 Male Patients

Age	No. of Cases	Age	No. of Cases
20-29 years	2	50-59 years	30
30-39 "	7	60-69 "	13
40-49 "	20	70+ "	4

The average age of the men was 52 and of the women 57. The youngest patient was an Indian Moslem aged 25 who worked as a boatman, and the oldest an Indian cowherd who gave his age as 81. The average age of the men by nationality was: Chinese, 55 years; Indians, 51; Malays, 50; and Europeans and Eurasians, 52. Thirty-two of the patients were admitted to first-class wards, nine to second-class wards, and 48 to third-class wards. The total admissions by class are not recorded in the hospital, but it is estimated that there are at least four times as many third-class admissions as first and second in the medical units.

The great diversity of races in Malaya gives an opportunity of comparing the incidence of cardiac infarction among them. Table II shows the estimated population of each

TABLE II

Race	Population of Penang and Province Wellesley (1954)	Average Yearly Admission	No. of Cases in 4 Years	Yearly Rate per 10,000 Admissions
Chinese ..	291,252	4,971	24	12
Indians ..	70,845	2,723	44	40
Malays ..	157,873	1,141	8	17.5
Europeans and Eurasians ..	5,226	454	11	60.5
Others ..	2,574	107	2	
Total ..	527,770	9,396	89	

race for 1954. As these races do not make comparable use of the hospital facilities the average yearly admissions by race are also given. The significance of the figures in Table II are discussed below. It should be pointed out that nearly all the Chinese originally came from South China, those from the Fukien Province being the commonest. Some of the Chinese patients were born in Malaya and most of the others have spent many years there. The Indians are mostly from South India, and include both Hindus and Moslems. Although the habits of these two religious groups differ it is not possible with such small numbers to make any subdivision. Like the Chinese, most have spent many years in Malaya.

Symptoms

A comparatively large number of patients in whom sound electrocardiographic evidence of infarction was found were unable to give a history of any definite episode to indicate the attack (Table III). Of those included under "typical

TABLE III

Class	Typical Episode	No Episode
First ..	30	2
Second ..	9	0
Third ..	26	22
Total ..	65	24

episode," two collapsed suddenly and died within three days, and one became unconscious but recovered. A fourth collapsed a week after childbirth, and the E.C.G. demonstrated infarction. Soon after this she suffered from hemiplegia. Practically all these patients had electrocardiographic tracings which indicated a recent infarction. A few gave a history of chest pain some time before coming to hospital. On the other hand, among the 24 without a history of an acute episode most of the tracings suggested old infarctions. This group usually presented with symptoms of cardiac failure, but one presented with a hemiplegia, one with cirrhosis of the liver and heart failure, and one with a vague history of weakness and oedema.

Two factors that are related to atheroma and so to cardiac infarction are diabetes and hypertension. Both these conditions are common in Malaya, but I do not know of any

significant figures regarding their incidence. Of the 89 patients with cardiac infarction, 11 were noted to have glycosuria, and consisted of six Indians, four Chinese, and one Eurasian. It is not so easy to assess the incidence of hypertension in the series, as many cases were on the borderline. If the diagnosis is based on the blood-pressure readings and E.C.G. tracings taken after an attack, there were only 15 with clear evidence of hypertension. This number is probably too small, and little weight can be attached to it.

Cases Outside the Hospital Practice

During the inquiry into cardiac infarction it became evident that the total number of patients with the disease was small and that the incidence seemed particularly low among the Chinese. It was therefore decided to seek further information on the subject from the 54 private practitioners of the Settlement. A simple questionnaire was sent to each asking for the number and nationality of patients with cardiac infarction that they had seen in the previous twelve months, excluding all who had been referred to the hospital. Answers were obtained from 44. Twenty-six had no cases, but the other 18 had seen 48—38 Chinese, 7 Indians, 2 Malays, and 1 other.

A further source of information was in the coroner's cases investigated by the Government pathologist. The only figures available were for a period of two years. In this time there were 16 cases—6 in Chinese, 4 in Indians, 5 in Malays, and 1 in Europeans.

When these figures are added to the hospital figures of Table II a more complete picture can be obtained (Table IV).

TABLE IV

	Population	No. of Cases per Year	No. of Cases per 100,000 of Population per Year
Chinese	291,252	47	16
Indians	70,845	20	28
Malays	157,873	6.5	4
Europeans and Eurasians	5,226	2.75	55

Discussion

The number of patients found suffering from cardiac infarction is not large or complete enough to allow of any dogmatic statements about the incidence of the disease among the peoples of Malaya. Other factors influence the value of some of the figures, and these are mentioned below. It is, however, interesting to note that the same trends for age, sex, and social status appear in Malaya as elsewhere. The distribution of hospital patients according to class shows that those of higher social classes are more often sufferers. There were nearly as many patients in the first- and second-class wards as in the third-class wards, in spite of the great difference in numbers admitted to these respective wards. About a third of those admitted to the third-class wards were engaged in the less strenuous or better-fed occupations such as coffee-shop keepers, clerks, etc. It should be added, however, that in some cases age or early heart failure may have driven them from manual work. More patients were treated by private doctors than were admitted to hospital, and this fact supports the opinion that the rich are more likely than the poor to be affected.

Is the disease less common in Malaya than in the United Kingdom? In comparing figures for these two countries a correction must be made for age because cardiac infarction is a disease of older people. In the last Malayan Census Report (1947) the number of the population aged 40 years and over is given as 219 per 1,000. This is only a little over one-half of the corresponding figure for England and Wales as given in the report of the Ministry of Health for 1953. My estimate for the Settlement of Penang and Province Wellesley is 78 cases in a population of 527,770. If an increase is allowed for the age distribution one has an inci-

dence of about 30 per 100,000 to compare with any United Kingdom figures. Unfortunately it is not easy to find in the literature suitable statistics for comparison. However, through the courtesy of Dr. G. M. Fyfe, who is studying coronary sclerosis in a Scottish county, I can make use of some of his observations. In a total population of 219,502 there were 429 cases in one year. This incidence is six to seven times greater than that which I have found in Malaya. Dr. Fyfe's figures were, however, obtained by a special scheme of notification by the medical practitioners of the area and should be more accurate and more complete than mine. They also include angina pectoris in the 429 cases. The difference, therefore, is probably less than the figures indicate.

The comparison of hospital figures is most difficult. The Penang General Hospital admits patients suffering from pulmonary tuberculosis, infectious diseases, and tropical diseases as well as those with general medical and surgical complaints. In two small hospitals in Scotland the average yearly admission for coronary sclerosis (mostly cardiac infarction) was 110 out of a total admission of 1,840. The Penang figures were 22 out of a total admission of 9,396. This difference is very great, but probably can be taken as little more than evidence of the different use that is made of the hospitals in these countries.

A further point of interest is the racial incidence. The impression gained in hospital work was that it was commoner among the Indians than among the Chinese. Further considerations modify this opinion and demonstrate how many fallacies there may be in attempting to analyse statistics in such a country as Malaya. For example, tuberculosis was one of the common causes for admission to hospital, the figures by nationality being available. In 1954 there were 491 Chinese admissions to 98 Indian. Whatever the cause of this difference it means that for other diseases the Chinese were even more reluctant to use the hospital than the figures in Table II indicate. Furthermore, the age incidence in hospital for these two races also differs, there being comparatively fewer Chinese in the middle group of 30–49 years. Out of 500 Chinese admissions, 196 were over 39 years of age and 124 over 49. The corresponding figures for Indians were 203 and 93. The number of patients reported by the general practitioners was dependent upon memory and cannot be accepted as more than approximately accurate. As nearly all the doctors work in the municipal area of Penang, and as the percentage of Chinese in this area is higher than in the Settlement as a whole, the figures have limited value in demonstrating incidence. The figures shown in Table IV, based on total population, indicate that the incidence among the Indians is nearly twice as high as among the Chinese, but this apparent higher susceptibility of the Indian must remain only a suspicion, as the evidence collected here is not good enough to offer statistical support.

In proportion to their numbers the Malays use the hospital less than the other races. It is certain, too, that they make little use of the services of the general practitioners. The figures available can be accepted only as evidence that infarction does occur in this race. The majority of Malays living a traditional country life as farmers or fishermen have little representation in the figures give in this paper.

One would like to give particulars of the diets and the people concerned. Some figures are available for the poorer section of the community, and these indicate that the intake of fat is low; but among the middle and upper classes the intake is probably quite high. Financially Malaya is more prosperous than most other Asian countries and the diet therefore correspondingly richer. So far as racial incidence is concerned it is of no value, however, to add inadequate diet figures to my own inconclusive incidence figures.

Lastly, it is of interest to consider the difference in symptoms as shown by the large number of patients who did not give a history of an acute episode. Parkinson and Bedford as long ago as 1928 described the type with dyspnoea and

heart failure without pain. In two recent papers (Papp, 1952; Roseman, 1954) on painless cardiac infarction the incidence is given as 4.6% (7 out of 150) and 4.5% (10 out of 220). In the present series it was 27% (24 out of 89), and this painless infarction was much commoner in the patients in the third-class wards; while Hunter (1946), in the U.S.A., found painless infarction commoner in the poor negro than in the poor white patient. The cause for this high proportion of painless infarctions must be conjectural. Perhaps some patients had forgotten the pain. To the educated man of to-day a pain in the chest is alarming, but to one who has never heard of coronary thrombosis and in whose life there have been many pains and hardships it may, unless very severe, be passed over as of little importance. One of the patients included here as a typical case came to hospital complaining of dyspnoea and swelling of the feet. It was only when the history was fully taken that it was learnt that he had had a pain in the chest two weeks earlier. It may be, too, that the pain in the poorer man is actually less severe; that just as the disease is less common, each attack may also be on the average less acute. Possibly the explanation is a combination of both suggestions. Whatever the reason may be, it is evident that the painless cardiac infarction is one of the causes of the not infrequent cases of heart failure of obscure aetiology found in the poor Asian patient.

Summary

The literature on cardiac infarction in South-East Asia is reviewed.

A series of cases in a Malayan hospital is described and further figures of patients seen by private practitioners are also given.

The difficulties in comparing the incidence either between Malaya and the United Kingdom or among the races of Malaya are discussed.

The figures that are given show that the disease is not a rarity in Malaya, but suggest that it may be less common than in the United Kingdom.

Among the different races of Malaya the figures available for Malays are too few for comparison. There is a suspicion that the incidence is higher among the Indians than among the Chinese.

In the symptomatology a high incidence of painless infarction is noted.

I wish to thank Dr. H. A. Reid, who has allowed me to include all his cases and has given other help; all the doctors of the Settlement who so kindly replied to my questionnaire; Dr. J. T. Boyd, of the London School of Hygiene and Tropical Medicine, for advice on statistics; Dr. G. M. Fyfe for figures of incidence in the U.K.; Dr. H. I. Williams for necropsy figures; and the following for answering other inquiries: Drs. F. R. Dieuaide, H. S. Gear, C. Gopalan, E. W. Graham, C. K. Menon, R. Subramaniam, and I. Simpson. I am indebted to Dr. R. E. Anderson, Director of Medical Services, Federation of Malaya, for permission to publish.

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Medical Memoranda

Toxic Psychosis Caused by "Preludin"

"Preludin," a new drug for controlling the appetite, is, I believe, gaining popularity among those who for a number of different reasons try to slim. It was discovered in 1953 and first marketed in Germany in 1954. It has been on sale in this country for about twelve months. Below is reported the case of a young woman who took preludin in large doses for its central stimulant effect, and as a result developed a toxic psychosis. This was at first thought to be a schizophrenic illness. I have not seen this danger reported before.

CASE REPORT

The patient, aged 29, was an assistant matron at an infants' boarding school run by her mother. She suddenly began to complain that the floor was magnetized and her jewellery electrified. In an attempt to insulate herself she had cut up her hot-water bottle. Her family looked after her at home until her admission to hospital three days later. On admission she was dishevelled, tense, depressed, and emotional, but otherwise there were no abnormal findings. Formal psychometric testing showed no confusion, no clouding of consciousness, and no disorder of perception. She was co-operative and expressed remorse for all the trouble she had caused. Chlorpromazine was given, and within a few days she calmed down.

On her third day in hospital her father telephoned to say that he had found amongst her belongings at home a large number of empty preludin tablet containers. He estimated that she must have taken at least 1,400 tablets during the previous 12 weeks. He said that three months previously he had discovered she was taking dexamphetamine sulphate ("dexedrine") tablets, and had asked the near-by chemist shops to stop supplying her with this drug. The patient, when asked about the preludin, admitted that her father was quite right. She had taken preludin tablets in order to forget everything and to be able to go off and enjoy herself with her friends. She had needed about a dozen preludin tablets to get the same effect as a few dexamphetamine tablets gave her.

A review of her behaviour over the three months before she had startled her family with her complaints that the floor was magnetized and her jewellery electrified revealed that she had been very irritable and suspicious. Her fiancé had commented that she seemed to "babble" at times. It had been noticed that she had seemed restless at night and unduly fearful of burglars. In fact, she had gone to the trouble of putting talcum powder on her window-sill so that fingerprints of any intruder would be readily available, and had placed small articles against the inside of her bedroom door in order to have warning if it was being opened.

Her previous personality was that of an unstable erratic girl who from childhood had been unreliable. Her personal history showed that thread of instability, lack of conscience, and disregard for others in her behaviour so characteristic of a psychopathic personality.

COMMENT

Preludin is claimed to produce early satiety of the appetite without disturbing side-effects. Any central effect is said to be only that of a very mild elation. Its chemical formula shows that it is an oxazine derivation of ephedrine, which is more closely related to caffeine than amphetamine. However, it is known that a toxic psychosis may occur when excessive quantities of either of these drugs are taken.

The toxicity of preludin has been studied in mice by Thomä and Wick (1954), who found that, compared with amphetamines, the lethal dose of preludin by the oral route is nearly five times as great. They also found that to produce the same degree of excitement in unanaesthetized dogs the amount of preludin needed was six times that of