CHAPTER 4

DISCUSSION

Normal subjects

The percentage distribution of haptoglobin types in Thai blood donors in the present study was very similar to those of the normal Asian subjects i.e. Chinese , Chinese (Taiwan), Japanese and Malays. However, the distribution of haptoglobin types in Fillipinos and Hong Kong differed distinctly from those of the asian group (Table 19).

Results of Fillipinos based on a small number of subjects taken at random from the general population and representing a mixture of Fillipinos ethnic groups, showed a substantial differences from those of the other south-east Asian subjects. The haptoglobin distribution of the Fillipino group resembled Caucasian haptoglobin distribution more than any other (Blackwell, et al., 1964).

The frequency distribution of the Hp 1-1 in Hongkong also showed higher value but it had been stated that this increase was not statistically significant (Sanford et al., 1966).

Table 19

The distribution of haptoglobin types in some groups of Asian population.

Population	Number tested	Percent Hp group				References
		1-1	2-1	2-2	0	
Chinese	167	10.8	34.1	53.9	1.2	Kirk and Lai(1961)
Chinese (Taiwan)	172	9.3	37.7	52.9	0	Blackwell et al (1962)
Hong Kong (Cantonese)	122	13.9	48.4	37.7	0	Canford (1966)
Japanese	349	6.0	34.9	57.6	1.4	Matsunaga and Murai (1960)
Malays	236	5.1	36.0	58.1	0.8	Kirk and Lai (1961)
Filipinos	293	14.0	48.1	37.2	0.7	Blackwell et al (1964)
Thai	413	4.8	37.5	56.4	1.2	Kirk and Lai(1961)
Thai	632	5.7	37.1	54.8	2.3	Blackwell and Thephusdin(1963)
Thai	662	5.9	38.1	56.0	0	Thephusdin et al (1965)
Thai	213	5.2	40.8	54.0	0	Present study

The results of the percentage distribution of haptoglobin types in Thai blood donors in the present study was in accordance with the results reported previously in Thai normal subjects by Thephusdin et al., (1965); Blackwell and Thephusdin (1963), and Kirk and Lai (1961).

It has been shown that some groups of population had Hp O which represented ahaptoglobinemia or hypohaptoglobinemia in quantity too small to be detected. Blumberg (1961) reported that ahaptoglobinemia and hypohaptoglobinemia had been detected in Africans, in about 4% of American Negroes, and in members of some European and Asiatic population. Blumberg et al. (1963) stated that there were several mechanisms which produced low or absent serum haptoglobin levels in human sera.

Tuttle (1955) and Galatius-Jensen(1957) had shown that newborns have little or no haptoglobin. However, it was present in nearly all children by the age of 4 months.

Many workers had shown that individuals afflicted with a variety of diseases might have decreased or absent haptoglobin levels. This group of diseases includes.

many hemolytic anemias such as paroxysmal nocturnal hemoglobinuria (Allison, 1957), hereditary spherocytosis, thalassemia major, sickle-cell disease and untreated pernicious anemia (Allison, 1958; Mehta and Jensen, 1960; Lathem and Jensen, 1959; Nyman et al., 1959; Nyman, 1957, Whitten, 1962). When the rate of destruction of red blood cells exceeded the rate of production of haptoglobin, the haptoglobin level would be lowered. Haptoglobin levels may also be lowered in a variety of diseases of the liver (Allison, 1958; Mehta and Jensen, 1960; Lathem and Jensen, 1959; Nyman et al., 1959). Although this might be due in part to a hemolytic component, or the effects of estrogen (Borglin and Nyman, 1961) which could decrease haptoglobin levels, it might also be due to impaired haptoglobin synthesis in the liver. All these diseases could account for an ahaptoglobinemia or hypohaptoglobinemia.

In some cases, haptoglobin might fall to very low levels and then returned to detectable level for no apparent reason (Blumberg and Gentile, 1961; Galatius-Jensen, 1958; Sutton et al., 1959).

Finally, in some instances, ahaptoglobinemia appeared to be inherited.

Hypo-and ahaptoglobinemia could be a result of both environmental and genetic factors, i.e., there might be an inherited predisposition to ahaptoglobinemia which was made evident by some environmental force. The highest frequencies of ahaptoglobinemia was found in those parts of West, Central and East Africa which correspond to the distribution of malaria (Allison and Barnicot, 1960).

The ahaptoglobinemia patients were found in the patients, with cardiac sequelae. The most attractive being that persons with low haptoglobin levels might be more susceptible to rheumatic fever leading to complications of this type (Noonan et al 1966).

Results of serum haptoglobin levels in 238 blood donors in the present studies (as shown in table 3) were similar to the values reported previously in Thai subjects (Areekul & Chantachum, 1972) and in other European and American people. Many methods were developed for the determination of haptoglobin levels. Jayle and Boussier (1955), used titrimetric or iodometric method based on measurement of the peroxidase activity of the haemoglobin-haptoglobin complex. Nyman (1959) determined the haemoglobin-binding capacity of

the haptoglobin by titration with haemoglobin, followed by electrophoresis on filter paper. Owen et al. (1964), Shinton et al. (1965), Areekul & Chantachum (1972) and our studies determined the peroxidatic activity of the complex with a spectrophotometer. Ratcliff and Hardwicke (1964), Rajendran et al. (1975) had estimated the serum haptoglobin by gel filtration on Sephadex G.100, followed by elution with 2% sodium chloride solution, Miale (1964) analysed by densitometry of electrophoresis strips and Colfs and Verheyden (1965) determined the serum haptoglobin levels by using the gelatinised cellulose acetate as supporting medium for the electrophoresis. Although various different methods were used , the haptoglobin levels appeared to be nearly the same.

Pregnant women

The results in the present study showed that the percentage distribution of haptoglobin types 1-1, 2-1, and 2-2 in 213 pregnant women was not much different from those of the 101 non-pregnant women. No relationship between the haptoglobin levels and the duration of pregnancy or the number of gravida were demonstrated in these subjects.

The mean value of serum haptoglobin levels in the pregnant women was found to be lower than that of non-pregnant women. Finding that 86 of 220 pregnant women (39.1%) had haptoglobin levels less than 40 mg% were in accordance with the result reported by Schumacher and Schlumberger (1963). These authors found that during pregnancy there was a rise of the alpha-2 lipoprotein while haptoglobin levels decreased. The mechanism that caused low haptoglobin level in pregnant women was not exactly known. One possible factor was due to the haemodilution in these subjects. In pregnancy, particularly during the last trimester, the blood volume is usually increased because of an increase in plasma fluid. The serum haptoglobin concentrations could therefore be lower than normal. However, the increased plasma volume during pregnancy alone could not decrease the haptoglobin concentrations to such low levels as in the present studies. Since it has been well established that the mother's phenotypes appear to be completely independent of the haptoglobin type of the foetus, the possibility of the leakage of haptoglobins from mother to foetus was therefore very unlikely.

The most likely explanation was probably due to the high blood estrogen concentration during pregnancy which may cause low haptoglobin levels. During pregnancy, the blood estrogen

concentration rose and was excreted in the urine in increasing amount especially during the last six months of pregnancy (Wright, 1956). This estrogen of pregnancy was formed by the placenta and the amount excreted was related to the size of the placenta. The blood estrogen concentration fell rapidly to the normal level after the expulsion of the placenta. Findings that haptoglobin levels are decreased in woman after the administration of estrogen and increased after the administration of androgen (Borglin and Nyman, 1961; Studnitz and Nyman, 1957) also supported the explanation described above.

Patients with hookworm infection

The distribution of haptoglobin types in patients with hookworm infection was similar to that of the normal subjects.

The mean serum haptoglobin level in these patients was significantly lower than that of the normal subjects. Fourteen out of 67 patients had the haptoglobin level less than 40 mg%. The lower haptoglobin level in these patients could be due to the blood and plasma protein loss which has been shown to be occurred in this disease (Areekul et al, 1971).

Patients with malaria infection

The result in the present study showed that the Hp O in patients with malaria infection was 31.9%. Hp O designated ahaptoglobinaemia or hypohaptoglobinaemia. The absence or almost absence of haptoglobin in the serum was a common feature in patients with increased red cell destruction, so that the genetically determined phenotype was often masked in such cases. In human experimentally infected with malaria, the haptoglobin levels were generally decreased during the height of fever and red blood cell haemolysis (Blumberg et al, 1963). Areekul et al (1971) also reported that the serum haptoglobin levels in subjects with malaria was lower than those of the normal subjects. It has been reported that malaria could account for some of the ahaptoglobinaemia found in malaria regions (Allison and Barnicot, 1960). Allison et al (1958) found no demonstrable haptoglobin in about a third of the Nigerians, and similar high frequencies of ahaptoglobinaemia had been observed in certain other African tribal groups (Allison and Barnicot, 1960; Blumberg and Gentile, 1961; Giblett et al 1966). The highest frequencies of ahaptoglobinaemia were also found in those parts of West, Central and East Africa which correspond to the distribution of malaria (Blumberg et al, 1963).

Patients with liver diseases

The results in the present studies showed that the frequency distributions of the phenotypes of serum haptoglobin in patients with opisthorchiasis, amoebic liver abscess, hepatomegaly, obstructive jaundice, cirrhosis, infectious hepatitis, carcinoma of the liver, hepatoma were very similar to those of the normal subjects. However, their serum haptoglobin levels were usually lower than those of the normal subjects. Since the parenchymal cells of the liver were responsible for synthesis of serum proteins including alpha and beta globulins, the liver diseases described above could caused hepatocellular damage, therefore this damage may impair haptoglobin synthesis. These findings were in accordance with the results reported previously in patients with hapatitis and cirrhosis of the liver (Owen and McKay, 1959).