Discussion and Conclusions

Since the initial case of congenital malaria, three cord bloods in the course of the next 54 deliveries showed subtertian rings, and all three infants subsequently developed symptoms compatible with a diagnosis of malaria. Of the 51 infants whose cord blood smears were negative, only one developed suggestive symptoms. It is concluded that among non-indigenous European women of relatively low immunity, infected with the Lagos strain of *P. falciparum*, congenital transmission of malaria is by no means rare.

As regards predisposing causes, only one of the three mothers admitted to any recent malarial attack, so that placental transmission may occur in the absence of any overt maternal malarial bout during pregnancy. In all three cases the placenta was macroscopically healthy and intact, an observation which does not support Manson-Bahr's (1940) hypothesis that transmission to the foetus can occur only through a placental breach or defect.

There seem to be few effective precautionary or preventive measures. Thus regular suppressive procedures throughout pregnancy, here almost universal, did not seem to give reliable protection; nor, indeed, did a therapeutic course of proguanil, and in one case mepacrine, before delivery. It is, however, strongly urged that in the case of West Coast wives, whether delivered there or in the United Kingdom, the cord blood should be examined at birth as a routine.

Among the salient clinical features in these three cases was the fact that all three mothers were multiparous and past their first youth, being aged 29–37 years. Two had been long resident in the Tropics and previously subject to malaria, though admitting of no recent attack; while the third, a more recent arrival, had suffered an attack of clinical malaria three weeks before delivery. All labours were easy and rapid.

The intervals between birth, when the infants appeared healthy, and the onset of symptoms were 54, 77, and 60 hours, suggesting the possibility of a short-lived passive protection due to maternal antibodies. The earliest manifestations were pyrexia, vomiting of feeds, and a poor colour—a slaty pallor. Convulsions supervened later, and finally pulmonary oedema. One case exhibited hepatomegaly and jaundice, and one splenomegaly.

Quinine, intramuscularly and orally, in one instance combined with oral proguanil, proved quite ineffective. Subsequent experience of two cases of cerebral malaria in European infants under 6 weeks old suggests that intramuscular mepacrine is the treatment of choice and may be dramatically effective. In each case an intramuscular injection of 0.1 g. of mepacrine precipitated an alarming convulsive seizure within 15 to 20 minutes, followed by complete recovery. To avoid this very real danger the dosage should be sufficiently small and divided—0.03 g. daily being suggested as adequate—and preferably begun immediately on discovery of a positive cord blood.

The notable contrast between hyperimmune indigenous populations, among whom placental infection is exceedingly common but congenital malaria very exceptional, and non-indigenous individuals of low immunity, among whom placental infection is very rare but congenital malaria relatively less so, cannot be passed without comment. In Sierra Leone, Blacklock and Gordon (1925) found placental infection in 38% of indigenous deliveries, but consistently failed to demonstrate parasites in foetal cord or peripheral blood, though Walton (1947), in Freetown, found 0.32% of 2,154 newborn infants to be congenitally infected. Bruce-Chwatt (1949—personal com-

munication), in Lagos, reports a 26% placental infection rate in 450 African women but no single case of congenital malaria. Peel and Van Hoof (1948), from the Congo, record that of 400 African mothers 60% showed malarial infection; infection of the placenta was found in 53.9%, and yet no case of congenital malaria was encountered among the 393 newborn infants. In marked contrast, Clark (1915), in Panama, while finding a significant proportion of infected placentas in the West Indian negroes, found none among the European women.

It is suggested that with the increasing degree of immunity to malaria the frequency of infection of the placenta rises, while coincidentally the efficiency of the placenta as a barrier to foetal transmission increases and the incidence of congenital malaria falls.

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FATAL CASE OF POISONING DUE TO INHALATION OF METHYL BROMIDE

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Methyl bromide has been widely used of recent years in fire extinguishers for ships and aircraft, and in refrigeration plants. The dangers of exposure to this compound should therefore be better known than they are. For that reason we are reporting a fatal case with which we were concerned, and which arose from the scrapping of fire-extinguishers from aircraft engines.

Case Report

A man aged 21 was admitted to the Joint County (Fever) Hospital, Elgin, on December 2, 1947, at approximately 5 p.m. with a provisional diagnosis of meningitis. The history then available was that he had felt unwell at his work in the afternoon, had come home, had complained of headache, and quite suddenly at about 3.45 p.m. had had a convulsion, rapidly followed by others and by loss of consciousness. Subsequently it was learnt that the patient had been engaged on emptying and "cleaning" aircraft fire-extinguishers. The method employed was to perforate the lower end of the copper "bottle"—shaped like a vacuum flask—with a fireman's hatchet, and to let the vapour and fluid escape. Thereafter

the brass top was sawn off the bottle. Normally all this was done in the open air, but on the day in question there was severe frost, and the empty bottles were stacked in a shed and later cleaned there under cover. In the course of the morning's work, probably about noon, he had splashed a quantity of liquid methyl bromide over his clothes, a little of it reaching his face.

On examination the patient was having recurring convulsive seizures at the rate of about 10 a minute. These affected the jaw, back, both arms, and both legs, and were in the nature of clonic spasms. He was unconscious. An alcoholic odour in the breath was most pronounced. Attempts were made to control the spasms. Thiopentone was given, and, by adjusting the dose, control was effected for a few minutes at a time. During the first interval of freedom from spasm a further rapid examination was made, but there were no additional positive findings except that moist sounds were heard on auscultation of the chest. Samples of blood, urine, C.S.F., and stomach content were secured. The urine was blood-stained. A further dose of thiopentone at a later hour had the same effect. Between 10.30 and 11 p.m., after the intramuscular administration of paraldehyde had proved fruitless, 2 ml. of this drug was given intravenously, with 1/50 gr. (1.3 mg.) of atropine. This combination immediately controlled the seizures. In the course of the next few hours the general condition steadily deteriorated. Nikethamide was injected intravenously to combat respiratory depression, but large amounts counteracted the sedative action of the paraldehyde, leading to recurrence of the clonic spasms. The patient died at 5.15 a.m. on December 3.

At the necropsy on December 5 the stomach showed submucous haemorrhages at the distal end. The duodenum also showed submucous haemorrhages. The remainder of the bowel was normal. The liver, pancreas, and spleen showed no obvious changes. The chest cavity was normal in size; the pericardium was healthy; there was no evidence of valvular disease of the heart, and the heart muscle appeared healthy. The kidneys were very congested. The capsule stripped off easily; there was no evidence of inflammation of any duration, and the appearance of the cortex was in keeping with the condition of haematuria which developed on the night of the onset of illness. The brain showed no evidence of meningitis; the ventricles were normal; the surface of the brain was considerably congested and there were numerous small haemorrhages.

The appearances of the organs accorded with the absorption of an acute irritant poison which had caused submucous haemorrhages of the stomach and duodenum and had acted as a convulsant, causing congestion and haemorrhage of the cerebral cortex and acute congestion of the kidneys in the process of elimination.

Biochemical Findings.—Urine: a slight degree of albuminuria was found on direct examination; there were no other abnormal constituents. Blood: 30 mg. of NaBr per 100 ml. C.S.F.: No NaBr. Stomach contents: 30 mg. of NaBr per 100 ml. These findings suggest that a derivative of bromine was not the cause of death.

Discussion

Methyl bromide (CH_3Br) is a gas at normal temperatures, the boiling-point of the liquid being 4.5°C . (40.1°F). It is a heavy gas, its weight being approximately six and a half times that of air. Like chloroform, ethyl chloride, and carbon tetrachloride it is not inflammable. Its use as an agent for extinguishing fires depends on its weight, which leads to a blanketing effect and the exclusion of oxygen, or on its non-inflammability, which is utilized in aircraft engines, where it is played on the carburettor, thus lowering the flash-point of the petrol.

Poisoning by its agency was first noted in 1901, and up to 1940 a total of 42 cases had been reported in the literature. Of these, 12 were fatal, 23 recovered, and in

the remaining 7 information was incomplete. From 1939 to 1944 an additional 22 cases were reported in the Royal Navy, with fatalities (Clarke *et al.*, 1945). Cases may have occurred among Air Force personnel, but under conditions of national emergency they would not be disclosed. Inquiry of R.A.F. medical personnel in the neighbourhood suggested that little was known of methyl bromide as a toxic agent.

Its mode of action depends largely on the concentration. If this is of the order of 10,000 parts per million the gas acts as a lung irritant. The victim seeks to escape, and if he does so the duration of exposure is unlikely to be sufficient to produce the chain of events described below. If he fails to escape, the signs, including post-mortem signs, are those of lung irritation, with haemorrhage and oedema of the lung and pleural effusion. Oxygen may be effective in treating this class of case.

If the concentration is in the neighbourhood of 1,000 parts per million the sequence described by Leschke (1934) is typical. After inhalation of the poison there are slight non-characteristic symptoms, such as headache, giddiness, fatigue, vomiting, and double vision. There is then a free interval of hours or even days, followed by the sudden onset of twitching, lockjaw, cramps, double vision, delirium, and raving madness. Leschke thinks that these symptoms are due to some intermediate metatoxic process, and not to the methyl bromide as such. In support of this view is the fact that methyl bromide has never been recovered from man or experimental animals. When death occurs in this class of case there has usually been some degree of pulmonary oedema and pleural effusion. Necrosis of the renal cortex is also a fairly constant sign. In only one other instance have we ascertained that haemorrhages into the cerebral cortex have occurred. This was one of a group of boys from an approved school who were living in a disused naval launch.

No curative treatment is known when convulsions have begun; indeed, in only one instance have we found a report of recovery after the onset of convulsions. Exposure to minimal concentrations of the order of 200–400 p.p.m. results in loss of appetite, nausea, headache, and muscular pains, the symptoms rapidly disappearing on cessation of exposure. Prolonged application of methyl bromide to the skin may lead to burning. It is clear, however, that this does not always happen, as workmen have used it to remove grease from their hands without ill effect. There is, in fact, a strong suggestion of idiosyncrasy.

One feature common to all the reported cases we have studied is its occurrence in an enclosed space, such as a ship, covered railway wagon, or workshop. In our case the actual opening was carried out in the open air, but the "cleaning" was done in a shed, and on a cold day. In our opinion this combination of circumstances led to imperfect emptying of the fire-extinguishers in the open air, with a consequent rise in the methyl bromide content of the shed to dangerous levels.

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