although the patient dying of aortic stenosis may have been in this category. The alteration in the pitch of the mitral systolic murmur observed in three patients is not necessarily indicative of incipient stenosis. The development of right axis deviation can be attributed to the natural progress of rheumatic heart disease without evoking the healing process of the bacterial infection even as a contributory factor. Based on the slender evidence of one case in this series and another in which the infection has not been eradicated long enough, the effect of the healing process, at least on the pulmonary valve, seems to be the opposite of a stenosing tendency.

A boy aged 14 suffering from congenital pulmonary stenosis with superimposed subacute bacterial endocarditis was unable to trot the length of a football pitch before infection. Now, four years after infection, he can partake energetically in a game of football without undue breathlessness. This improvement cannot be the result of the natural evolution of pure pulmonary stenosis, the tendency in such cases being relentless deterioration (Allanby and Campbell, 1949). It would appear that the infection had freed the stenosis after the nature of a Brock (1948) operation. The other patient with infection eradicated from a stenosed pulmonary valve or infundibulum possesses a capacity for effort greater than she has enjoyed for years. Neither patient has a pulmonary diastolic murmur, only a systolic thrill and murmur at the base of the heart with conclusive x-ray and electrocardiographic evidence of the diagnosis. This evidence that healing of the infected process possesses destructive rather than fibrotic powers in the instance of the pulmonary valve has been noted by Pollack *et al.* (1948). As has already been shown, at least in this series, a similar development has fortunately not occurred in healing aortic valves.

Conclusions

In the vast majority of cases of subacute bacterial endocarditis it would appear that, provided the infection is overcome and congestive heart failure avoided at the time of treatment and shortly afterwards, the disease can be regarded as an incident which leaves little or no evidence of additional permanent damage in a heart the seat of congenital or rheumatic disease. In the few cases in which deterioration occurs, it may be anticipated if attention be paid to the following facts: the cardiac grade of the patient when the infection is acquired; the detection of a severe degree of aortic regurgitation after elimination of infection; and the heart size, radiologically, during and immediately after eradication of infection.

Summary

Twenty cases of healed subacute bacterial endocarditis have been followed for periods of between 27 and 63 months. No case relapsed or became reinfected after successful treatment of the bacterial infection. One death occurred.

The effect of the bacterial infection in two cases of congenital pulmonary stenosis is described.

The exercise tolerance, radiological heart-size, and auscultatory features at the time of treatment and after the lapse of years are compared and the significant points identified.

The patients providing the information for this paper were all under the care of Dr. A. Rae Gilchrist, to whom I am grateful for help and criticism.

REFERENCES

- Allanby, K. D., and Campbell, M. (1949). *Guy's Hosp. Rep.*, **98**, 18.
Bloomfield, A. L., Armstrong, C. D., and Kirby, W. M. M. (1945). *J. clin. Invest.*, **24**, 251.
Bramwell, C. (1948). *Lancet*, **2**, 481.
Brock, R. C. (1948). *British Medical Journal*, **1**, 1121.

- Christie, R. V. (1946). *British Medical Journal*, **1**, 381.
— (1948). *Ibid.*, **1**, 1.
— (1949). *Ibid.*, **2**, 950.
DeGraff, A. C., and Lingg, C. (1935). *Amer. Heart J.*, **10**, 459.
Jones, A. M., Herring, R., Langley, F. A., and Oleesky, S. (1947). *Brit. Heart J.*, **9**, 38.
Kaplan, S. R., Rosenman, R. H., Katz, L. N., and Brams, W. A. (1949). *J. Amer. med. Ass.*, **141**, 114.
Kiloh, G. A. (1950). *Brit. Heart J.*, **12**, 33.
Libman, E., and Friedberg, C. K. (1948). *Subacute Bacterial Endocarditis*, 2nd ed. Oxford Univ. Press.
Lichtman, S. S. (1943). *Ann. intern. Med.*, **19**, 787.
MacIlwaine, Y. (1947). *J. Path. Bact.*, **59**, 557.
Matthew, H., and Gilchrist, A. R. (1949). *Edinb. med. J.*, **56**, Trans. Med.-Chir. Soc., **128**, 25.
New York Heart Association (1939). *Nomenclature and Criteria for Diagnosis of Diseases of the Heart*, 4th ed. N.Y. Tuberculosis and Health Association.
Pollack, A. A., Taylor, B. E., Odel, H. M., and Burchell, H. B. (1948). *Proc. Mayo Clin.*, **23**, 516.
Rapoport, B., and Ellis, L. B. (1948). *New Engl. J. Med.*, **239**, 951.
Rosenblatt, P., and Loewe, L. (1945). *Arch. intern. Med.*, **76**, 1.
Seabury, J. H. (1947). *Ibid.*, **79**, 1.
Wagner, B. M. (1948). *Amer. J. med. Sci.*, **215**, 84.

CONGENITAL MALARIA

REPORT OF THREE CASES

BY

B. S. JONES, M.D., F.R.C.S.Ed.

Surgical Specialist, Colonial Medical Service

A considerable divergence of opinion persists regarding the frequency with which congenital malaria may occur. That it is occasionally encountered there can remain no doubt. Jones and Brown (1924) reported two authentic cases in London, while cases have also been recorded by Beekel (1910), who describes 12 instances of undoubted placental transmission, by Tanner and Hewlett (1935), and by Van Nitsen (1932), who demonstrated malarial schizonts in the spleens of six infants, either born dead or dying soon after birth. Chen *et al.* (1944) have summarized 39 cases of congenital malaria from the world literature, while Wickramasuriya (1935) believes that transplacental foetal infection occurs more often than is normally conceded and records six proved cases of *Plasmodium falciparum* infection.

Most British and American authors, however, while recognizing the possibility of congenitally transmitted malaria, regard its occurrence as a rarity. Thus English (1946), who was in charge of a large maternity hospital in Singapore for 20 years, encountered only one case of congenital malaria amongst the 5,551 deliveries during 1938—a European infant aged 6 days.

During and since the recent war many European women have elected to produce their babies in Nigerian hospitals, and the possibility of congenital malaria has become a significant consideration. Since congenital transmission is still generally regarded as a remote contingency, a pyrexial illness in the first few days of life is more likely to raise suspicions of neonatal infection, while a convulsive seizure will more probably suggest an intracranial birth injury. Even less likely is the possibility of congenital malaria to be entertained in the cases of such women who return to the United Kingdom to have their babies. Therefore three cases personally encountered are recorded.

Most non-African labours in Lagos are conducted at the Creek Hospital, the patients being mainly Europeans, Syrians, or Lebanese of varying duration of residence in the country, though almost all may be assumed to have been subject to subtertian malaria at one time or another.

The occurrence of three confirmed cases of congenital malaria during February, 1949, suggested the possibility that certain of the neonatal deaths in earlier years might have been similarly caused. An investigation of the records, however, showed that of the four deaths occurring within the first 12 days of life in the course of the 143 deliveries conducted during 1947 and 1948 only one could possibly be attributed to congenital malaria. From January 1 to June 30, 1949, the period under consideration, there were 37 accouchements.

Case 1

An Englishwoman aged 29 had been resident in East Africa for some years, and was subject to periodic malarial attacks. She had arrived in Nigeria about one year previously, had taken suppressive quinine somewhat irregularly, but since arrival had had no overt attack of malaria. Her husband was English. She had two children, aged 6 and 4 years, her first labour having been prolonged and followed by subinvolution, the second being easy and normal. Throughout the present pregnancy she had been well, with the exception of one attack of cystitis. Her expected date was February 1, and she was admitted at 4.30 a.m. on February 11 with good pains, os dilated two fingerbreadths, a persistent occipito-posterior presentation, and premature rupture of the membranes. At 7.30 a.m. she was easily delivered of a healthy female infant. The maternal blood on admission showed no malaria parasites.

The infant remained quite well till February 13, when it was observed to be fretful and to be vomiting after feeds. At 2 p.m. that day the rectal temperature was 102.6° F. (39.2° C.); the mouth was healthy, the cord was clean, and the chest, cardiovascular system, and abdomen showed no abnormality, but the vulva appeared slightly inflamed, with a scanty thin purulent discharge. A blood smear was taken, and 5,000 units of penicillin intramuscularly three-hourly and 0.125 g. of sulphathiazole six-hourly were prescribed.

At 10 a.m. next day the blood smear was reported to contain scanty subtertian rings, and 2 gr. (0.13 g.) of quinine was given intramuscularly, and 1 gr. (65 mg.) of quinine orally three times a day was prescribed. At 4.30 p.m. the infant was very ill, with a poor slaty colour. At 6.30 p.m. there was a slight improvement; the spleen was found to be palpable and a further 2 gr. of quinine was given intramuscularly. At 9 p.m. there were continuous convulsions and the condition was very poor. The infant, whose temperature was now 105° F. (40.6° C.), was sponged with tepid water, and 3 min. (0.18 ml.) of syrup of chloral was given, this being repeated at 9.30 p.m. At 11 p.m. convulsions had ceased, but diffuse moist rales were heard in the lungs: atropine, 1/600 gr. (0.11 mg.), was given and oxygen administered by oral catheter.

At 12.30 a.m. on February 15 the infant was asleep; the respirations were, however, irregular, and there appeared to be a one-in-three heart-block. At 8.30 a.m. she was quiet, the pulse and respirations were regular, but the temperature, which had been sustained, was 104.4° F. (40.2° C.), and 2 gr. of quinine was given intramuscularly. At 9 a.m. there was renewed respiratory and circulatory depression with cyanosis and occasional twitching of the upper limbs, and death occurred half an hour later. Necropsy was not performed.

Case 2

The mother, aged 37, and her husband were Europeans of French nationality. She had been resident in Nigeria for many years, and had had numerous bouts of malaria, though none recently, but took suppressive proguanil, 100 mg. daily. She had three children, the youngest aged 2½ years, and had had no miscarriages. All previous labours had occurred two or three weeks before the expected date, and all had been easy and rapid. She had been well throughout the present pregnancy and the expected date was March 4. Pains started at 5 a.m. on February 20. She was admitted at 6.30 a.m., and an easy rapid vertex delivery was completed by 7 a.m. The maternal blood showed no malaria parasites.

The infant, a healthy female, was bottle-fed from birth. The cord-blood smear, taken at birth, contained scanty subtertian rings, and ½ gr. (32 mg.) of quinine orally three times a day was prescribed from birth.

At 2 p.m. on February 23 the baby appeared unwell and was vomiting. The rectal temperature was 101° F. (38.3° C.). At 11.15 p.m. 2 gr. of quinine was given intramuscularly. At midnight the vomiting was more severe; it was accompanied by hiccup, a slaty cyanosis, and some twitching of the arms and eyes.

At 1.15 a.m. the next day 3 min. of syrup of chloral was given. At 8.30 a.m. the condition had somewhat improved. The cord was separated cleanly, the chest and cardiovascular system showed no abnormality, but the liver edge was palpable and there was slight icterus. Quinine, 1½ gr. (0.1 g.), was given intramuscularly. At 3.45 p.m. the temperature was 102.8° F. (39.3° C.), the jaundice was deeper, the liver was enlarged to one fingerbreadth below the costal margin, and there were diffuse bilateral moist rales. Penicillin, 5,000 units intramuscularly three-hourly, was prescribed, but death occurred at 5 p.m. Permission for a full necropsy was not obtained, but a post-mortem hepatic puncture smear showed scanty malaria parasites.

Case 3

A Scotswoman aged 29, the wife of an African, had been resident in Nigeria for one year only and took daily suppressive quinine. She had two children, aged 3 years and 1 year 8 months, both labours having been easy, and had had no miscarriage. She had been well throughout the present pregnancy apart from an attack of malaria three weeks before delivery, when she was treated with 0.1 g. of mepacrine orally thrice daily for one week. Her expected date was March 4. She was admitted at 11.15 p.m. on February 25, and an easy vertex labour was completed one hour later. Her blood on admission showed no parasites, but from February 27 to March 1 she had slight pyrexia (99 to 99.8° F.—37.2 to 37.7° C.) accompanied by headache, which responded to a further course of oral mepacrine.

The infant was a healthy half-caste male, and the cord blood at birth contained scanty subtertian rings. On the day of birth, February 26, 3 gr. (0.2 g.) of quinine was given intramuscularly, and ½ gr. thrice daily by mouth and proguanil, 25 mg. twice daily, were prescribed. Next day a further 3 gr. of quinine was given intramuscularly. On the 28th there was slight pyrexia, but the infant seemed to be well and was taking his feeds. The chest, abdomen, and cardiovascular system were normal, and the blood showed no malaria parasites. There was slight swelling of the left buttock, probably post-injection. Another 3 gr. of quinine was given intramuscularly. At 4.30 p.m. the baby was unwell, with slaty colour and vomiting, and 2 gr. of quinine was given intramuscularly. On March 1 there was rapid deterioration, with coffee-ground vomits, and death occurred at 5.30 a.m. Necropsy was not carried out.

Subsequent to Case 1 every expectant mother was prescribed, in addition to her customary daily suppressive, 400 mg. of proguanil daily, beginning 10 days before the expected date and continuing until admission in labour; a cord-blood smear was also taken at every birth and examined for malaria parasites. Of the 37 deliveries, the first six were not cord-tested: the 31 which occurred after Case 1 were all cord-tested at birth, and only Cases 2 and 3 showed positive smears. Placental smears were not examined as a routine, as it was felt that the universal daily suppressive habit would certainly invalidate the results.

Since my departure from the Creek Hospital there have been a further 23 deliveries during July and August, 1949, all infants being cord-tested at birth. Of these only one showed parasites in the cord blood: a febrile illness developed within a few days of birth, but responded to treatment. A second infant, despite a negative cord blood, developed high pyrexia 26 hours after birth, and was tentatively diagnosed on clinical grounds and therapeutic response as a case of malaria.

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.

It is a pleasure to acknowledge my thanks to Dr. G. B. Walker, Director of Medical Services for Nigeria, for permission to publish this paper; to Dr. L. J. Bruce-Chwatt, Government malariologist, for much helpful information and advice; and to Dr. I. G. MacGregor, senior specialist, for information concerning cord-blood results subsequent to my departure from the Creek Hospital.

REFERENCES

- Beekel, F. (1910). *Cleveland Med. J.*, **9**, 879.
Blacklock, D. B., and Gordon, R. M. (1925). *Ann. trop. Med. Parasit.*, **19**, 327.
Chen, K. T., et al. (1944). *Chin. med. J.*, **62**, 199.
Clark, H. C. (1915). *J. exp. Med.*, **22**, 427.
English, J. S. (1946). *British Medical Journal*, **1**, 701.
Jones, J. L., and Brown, H. C. (1924). *Lancet*, **2**, 1058.
Manson-Bahr, P. H. (1940). *Manson's Tropical Diseases*, 11th ed., p. 61.
Peel, E., and Van Hoof, L. (1948). *Ann. Soc. belge Méd. trop.*, **28**, 413.
Tanner, N. C., and Hewlett, R. F. L. (1935). *Lancet*, **2**, 369.
Van Nitsen, R. (1932). *Ann. Soc. belge Méd. trop.*, **12**, 249.
Walton, G. A. (1947). *Ann. trop. Med. Parasit.*, **41**, 396.
Wickramasuriya, G. A. W. (1935). *J. Obstet. Gynaec. Brit. Emp.*, **42**, 816.

FATAL CASE OF POISONING DUE TO INHALATION OF METHYL BROMIDE

BY

A. C. MacDONALD, M.A., M.B., Ch.B.

I. C. MONRO, M.D., D.P.H.

AND

G. I. SCOTT, F.R.C.S.Ed.

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