and pathological findings in 11–20% of 500 hospital cases; and James, Patton, and Heslin (1955) found 71% of original certificates agreeing with necropsy reports in a survey of 1,889 necropsies, but with wide variation within the groups of different diseases, ranging from 21% agreement in the group of arteriosclerotic heart disease to 93% agreement in the group covering tuberculosis. Pohlen and Emerson (1942, 1943) found consistency in diagnosis in 96% of tumours of the heart, compared with 26% in liver tumours, 99% in measles, and 52% in heart disease.

In the above articles, all of which come from public health departments, there is a tendency to state that errors in registration occur between the few larger groups of causes of death, and that the errors in one direction tend to cancel the others out, making the overall statistics relatively accurate. This seems to be an unfortunate argument, as it would appear to give the published figures false accuracy—the type of accuracy obtained by drawing random diagnoses out of a hat—and minimize the danger of arguing from any of the registrar's statistics.

In assessing the accuracy of certification, any comparison made must be between the cause of death as originally certified and the cause of death after survey of all information obtained by clinical and necropsy examination. Inaccuracies in certification arise in two ways: first, a failure to record accurately the knowledge available at the time of death—that is, negligent certification; and, secondly, the inadequacy of the knowledge available at the time of certification.

In a teaching hospital, where every child, particularly an ill child, is under constant discussion, it is unlikely that faulty certification is due to the absence of available knowledge of diseases; on the other hand, certificates are often filled in by junior housemen who have not acquired the art of avoiding terminology that may lead to inquiries by the coroner. The tendency in both of these instances would be towards a more accurate registration if not conventional. We would thus expect the registration in the present survey to be at least as accurate as is likely to occur in the general field of child deaths.

Summary

A survey of the accuracy of the causes of death given to the registrar at a children's hospital showed that almost one-half of the certifications were not correct as judged by the final pathological diagnosis.

We are grateful to Dr. G. H. Jowett, head of the Department of Statistics of the University of Sheffield, for his advice and comments, and to our clinical colleagues for permitting these diagnostic ablations.

REFERENCES

- Evans, A. G. (1949). Referred to by James *et al.* (1955).
James, G., Patton, R. E., and Heslin, A. S. (1955). *Publ. Hlth Rep. (Wash.)*, 70, 39.
Korns, R. F., and Lintz, W. B. (1949). Referred to by James *et al.* (1955).
Lane, E. A., and Holla, W. A. (1954). *N.Y. St. J. Med.*, 54, 1523.
Pohlen, K., and Emerson, H. (1942). *Amer. J. publ. Hlth*, 32, 251.
— (1943). *Ibid.*, 33, 505.
Registrar General (1956). *Statistical Review of England and Wales for the Year 1955*, p. 220. H.M.S.O., London.
Swartout, H. O., and Webster, R. G. (1940). *Amer. J. publ. Hlth*, 30, 811.
West, H. (1955). *Ibid.*, 45, 211.

In an address on "The Art and Science of Research," before a sectional meeting of the Manchester Medical Society last month, Dr. J. H. SCOTT, lecturer in anatomy at Queen's University, Belfast, defined research as the intellectual fashion of our time. He compared "useless" and "useful" research as illustrated by the discovery of Nasyth's membrane in 1839 and of penicillin in 1929, and the part played by chance in certain cases. Discussing Humphry's work on jaw growth in pigs, he pointed out how the results of research were not always applied successfully to the solution of the problems they were supposed to solve. Research, he said, did not primarily depend on money, or on complicated apparatus, but on a peculiar attitude of mind in which curiosity, persistence, and clarity were essential features.

INFLUENCE OF MATERNAL MALARIA ON NEWBORN INFANTS

BY

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It is well known that schizonts of *Plasmodium falciparum* tend to concentrate in the maternal tissue of placentae in the latter half of pregnancy in women infected with that parasite (Blacklock and Gordon, 1925; Garnham, 1938; Bruce-Chwatt, 1952). There has, however, been considerable controversy about what effect this concentration has on the infant born of such placentae to women who are natives of territories where malaria is so prevalent that adult immunity to it is substantial. On the one hand is the Sierra Leone series of Blacklock and Gordon containing "proof of a very complete association between maternal infection of the placenta and death of the child *in utero* or within a seven-day observation period after birth." On the other hand is Garnham's (1949) diametrically opposite assertion from observations in Kenya that "malarial infection in the mother seldom resulted in stillbirths or in death of the infant in the first week," and that "Luo children are unlikely to suffer ill effects from infection in the mother."

Observations in Lagos (Bruce-Chwatt, 1952) have shown that, although there is no apparent correlation there between neonatal mortality and malarial infection of the placenta, yet there are grounds for believing that such infection is a cause of prematurity and, more generally, of the birth of underweight babies. A further report from Southern Nigeria (Archibald, 1956) confirmed these ill effects.

The present paper presents evidence from Northern Nigeria that this infection commonly prevents African infants born there to malarious mothers from reaching their proper weight at birth.

Present Investigation

The evidence was collected from a number of centres in Northern Nigeria where the birth weight of infants was noted, a number of particulars were obtained from the mother, and blood smears were collected from the maternal surface of the placenta and from the mother's finger at the delivery. The blood smears were examined by the regional malaria unit. The group investigated was mainly drawn from deliveries which took place in medical institutions, and was obviously a selected sample of the population. This was underlined by the finding of malaria parasites in only 15% of the smears examined, a rate much lower than the adult parasite rate generally found in the Northern Region of Nigeria.

The present series consisted of 484 women, 73 of whom were infected at delivery with *P. falciparum* (a few were also infected with *P. malariae*). In most of the mothers, parasites could be detected in the smear both from the finger and from the placenta, but in eight cases they were found only in the placenta and in seven only in the finger. Of the 484 pregnancies, 18 were multiple, two of triplets; and of the 504 infants born, 30 (5.9%) were stillborn, 4 (0.8%) were born alive before term, and 470 born alive after pregnancies which had gone to full term. Of these full-term babies, 440 were single deliveries, and it is with these that the further analysis deals.

Table I shows the distribution of birth weights of these babies. Of the 62 infants born from malarious placentae, 13 (20.6%) were premature—that is, weighing 5½ lb. (2.495 g.) or under (W.H.O., 1950)—as contrasted with 31 (8.2%)

TABLE I.—Record of Birth Weight of 440 Infants Born Alive in Single Deliveries After Full-term Pregnancies

Weight		Infants Born from Malarious Placentae	Infants Born from Non-malarious Placentae
lb.	g.		
Over 2½	1,130	—	1
3	1,360	2	—
3½	1,585	—	2
4	1,815	1	4
4½	2,040	5	8
5	2,270	5	16
5½	2,495	12	50
6	2,720	16	65
6½	2,950	10	74
7	3,175	7	78
7½	3,400	3	38
8	3,630	1	25
8½	3,855	—	11
9	4,080	—	4
9½	4,310	—	1
10	4,535	—	1
Total		62	378
Mean weight in group		6 lb. 2 oz. (2,778 g.)	6 lb. 12½ oz. (3,076 g.)
Standard deviation		14.4 oz. (408 g.)	16.4 oz. (465 g.)

TABLE II.—Record of Birth Weights of 440 Infants Born Alive in Single Deliveries After Full-term Pregnancies, Recorded by Race

Race	No.	Average Weight of Those From Malarious Placentae		No.	Average Weight of Those From Non-malarious Placentae	
		lb. oz.	g.		lb. oz.	g.
Ibo	17	6 5	2,865	124	6 13	3,090
Yoruba	26	6 1	2,750	117	6 11	3,035
Hausa	11	5 12	2,610	70	6 12	3,060
Fulani	—	—	—	12	6 11	3,035
Kanuri	—	—	—	6	6 13	3,090
Others	8	6 4	2,835	49	6 13	3,090
	62			378		

of 378 infants born from uninfected placentae. This contrast is significant ($\chi^2=9.7$; $P<0.01$). The mean weight of the 62 infants born from malarious placentae was 10½ oz. (298 g.) less than that of the 378 infants born from uninfected placentae.

The distribution of the 440 single full-term deliveries according to the race to which the mother belonged is shown in Table II. The mean weight of infants born from malarious placentae is consistently lower than that of infants born from uninfected placentae, irrespective of the mother's race. It is of interest to note that the mean birth weight of the infants born from uninfected placentae is very much the same for all racial groups represented in this series, whereas the Hausa infants born of infected placentae were on the average of lower weight at birth than either the Yoruba or Ibo babies. This is consistent with the hypothesis that the immunity developed by the indigenous people of Northern Nigeria, where there is a strictly circumscribed wet season and an explosive seasonal intensification of malaria transmission, is less well established than is that developed by Southern Nigerians who have been bred in conditions where malaria is stable.

An attempt was made to classify the families into which those 440 infants were born in accordance with the standard classes used by the Registrar-General of the U.K. (class I, professional; class III, skilled workers; class V,

TABLE III.—Record of Birth Weights of 440 Infants Born Alive in Deliveries After Full-term Pregnancies Recorded by Social Grouping

Social Group	Delivered from Malarious Placentae			Delivered from Non-malarious Placentae		
	No. in Group	Average Weight at Birth		No. in Group	Average Weight at Birth	
		lb. oz.	g.		lb. oz.	g.
I	2	5 10	2,550	1	5 12	2,610
II	1	6 7½	2,935	24	6 12	3,060
III	30	6 1	2,750	206	6 12½	3,075
IV	14	6 5	2,865	76	6 13	3,090
V	4	6 6	2,890	33	6 12	3,060
Not known	11	6 0	2,720	38	6 11½	3,050
	62	6 2	2,780	378	6 12½	3,075

unskilled). This was not very successful because of the large number of families claiming to be "traders," a group which might embrace the merchant prince or the match-box seller. In fact, the average weight of infants at birth was surprisingly similar for all social classes, although for each class the babies born from malarious placentae were under weight as compared with those born from uninfected placentae. The finding that the birth weight did not improve with social class is not in accord with experience in developed countries, but the explanation may be that in the conservative polygamous society of Northern Nigeria a wife may not enjoy her husband's social advantages. Table III shows the social classification of the 440 infants. The small numbers in this series from social classes I and II indicate that advantage of Western obstetric facilities is not taken by the conservative orthodox leaders of Northern Nigerian society.

The influence of maternal parity on the weight of an infant at birth is well known. In the present small series it was found that, in each class, the infants from malarious placentae were less heavy than the others, but the overriding importance of parity was shown by the poor weights of babies born to primiparae.

Discussion

The present series of cases differs from those previously published from Southern Nigeria (Bruce-Chwatt, 1952; Archibald, 1956) in that the effect of malaria on birth weight is more pronounced in this northern than in previous southern groups. This is shown in Table IV.

The proportion of mothers in the series who at the same time showed infection in both blood and placenta was also much higher than has usually been found. In these women in Northern Nigeria, 79% of infections were manifest in both blood and placental smears. Schwetz and Peel (1934) reported a similar coincidence (74%) from the Congo, but in Blacklock and Gordon's (1925) Freetown series only 20% of infections were found in blood and placenta at the same time; in Garnham's (1938) Kenya series it was 59%, and in Bruce-Chwatt's (1952) Lagos group 43%. It is probable that these differences can be explained as being due to

TABLE IV.—Influence of Malarial Infection of Placenta on Birth Weight of Nigerian Babies

Series	Premature		Average Weight	
	In Malarious	In Non-malarious	In Malarious	In Non-malarious
Northern Nigeria	13/62 (20.6%)	31/378 (8.2%)	6 lb. 2 oz. ± 14.4 oz. (2,778 ± 408 g.)	6 lb. 12½ oz. ± 16.4 oz. (3,706 ± 465 g.)
Southern Nigeria	20/68 (29.4%)	65/395 (16.5%)	6 lb. ± 10 oz. (2,722 ± 283 g.)	6 lb. 6 oz. ± 14.6 oz. (2,892 ± 414 g.)
Lagos	15/73 (20.5%)	26/237 (11.0%)	5 lb. 13½ oz. ± 17.4 oz. (2,651 ± 493 g.)	6 lb. 2 oz. ± 15.1 oz. (2,778 ± 428 g.)

variations in the immunity of the mothers. Probably coincident infection of blood and placenta indicates that the woman has not succeeded in mastering the infection. On that postulate, the high coincidence of infection of both blood and placenta in the present series would signify that these women did not have a strong immunity. This is consistent with earlier impressions that immunity to malaria in Northern Nigeria is not firmly established.

Summary

A series of 440 full-term deliveries of single infants is analysed to elicit the effect produced by *P. falciparum* infection of the placentae on the weight at birth of African babies.

The series is analysed by race, social class, and maternal parity, and in each group the effect of malaria infection has been that infants born from infected placentae have a mean weight at birth below that of those born from uninfected placentae.

The effect of *P. falciparum* infection is more pronounced in the present series than in previous groups collected in Southern Nigeria.

The series showed an unusually high proportion of mothers with both blood and placental infections detectable at the same time.

It is postulated from the last two observations that the mothers in the present series were not succeeding in mastering their parasitaemia, and this is thought to strengthen earlier impressions that malarial immunity is not firmly established in the population of Northern Nigeria.

I am indebted to those members of the Medical Department of the Northern Region who assisted in the investigation, and to Dr. R. A. B. Dikko, Acting Principal Medical Officer of the Endemic Diseases Division of the Ministry of Health of the Region, for permission to publish this paper.

REFERENCES

- Archibald, H. M. (1956). *Bull. Wld Hlth Org.*, 15, 842.
Blacklock, D. B., and Gordon, R. M. (1925). *Ann. trop. Med. Parasit.*, 19, 327.
Bruce-Chwatt, L. J. (1952). *Ibid.*, 46, 173.
Garham, P. C. C. (1938). *Trans. roy. Soc. trop. Med. Hyg.*, 32, 13.
— (1949). *Ann. trop. Med. Parasit.*, 43, 47.
Schwetz, J., and Peel, M. (1934). *Trans. roy. Soc. trop. Med. Hyg.*, 28, 167.
World Health Organization (1950). *Wld. Hlth. Org. techn. Rep. Ser.*, No. 27.

ISOLATION OF E.C.H.O. VIRUS TYPE 9 DURING AN OUTBREAK OF MENINGO-ENCEPHALITIS

BY

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During July, 1956, an epidemic of lymphocytic meningo-encephalitis with marked myalgia occurred in Newton-le-Willows, Lancashire (Lyle, 1956). At the same time type I poliomyelitis was occurring in Manchester and Coxsackie B meningitis in Stockport. Neither the epidemiology nor the symptomatology of the Newton-le-Willows outbreak suggested non-paralytic poliomyelitis or the clinically indistinguishable Coxsackie meningitis, but attempts were made in tissue cultures to isolate an agent from the faeces of seven patients.

Virus Studies

Faecal suspensions were prepared in saline and purified by high-speed centrifugation to remove contaminating bacteria. The resulting supernates were inoculated into stationary monolayer tube cultures of monkey-kidney cells prepared by a modification of Youngner's (1954) method.

Two specimens were tested shortly after receipt and both were found to be highly toxic to the culture cells, non-specific degeneration occurring within 24 hours of inoculation.

The residue of these, together with five other prepared specimens, were stored in a low-temperature refrigerator (-25°C), as prolonged storage has been found to diminish the toxicity of faecal extracts.

At the end of four months all the specimens were tested in monkey-kidney cultures as before, and also in stationary HeLa-cell cultures. Negative results were obtained in both types of culture with specimens from two adults and one child taken on the third, seventh, and sixteenth days of illness respectively. Of the other four specimens from children, two showed slight degenerative change in kidney cells with no effect in the HeLa strain, while the other two showed no change in either type of culture. In all four cases subinoculation of culture fluid was made to fresh kidney- and

HeLa-cell cultures. It was not until the fourth blind passage that definite cytopathogenic degeneration was noted in HeLa cells, although it was evident in all the monkey-kidney cultures at the second passage. A further series of blind passages in tissue culture was made with the three negative specimens previously referred to, without results at the fifth passage, when the material was abandoned. Lesions were not produced in 1-day-old mice either by original faecal suspensions or by tissue-culture fluids from cultures showing cytopathogenic effect inoculated by the intracerebral or subcutaneous routes.

Neutralization tests on tissue-culture fluids were carried out with antisera against poliovirus types 1, 2, and 3, and Coxsackie virus types B1-B5, with negative results. Tests with E.C.H.O. virus type 9 antiserum gave positive results identifying the agent.

Significant rises in neutralizing antibody in E.C.H.O. 9 virus were demonstrated by Dr. D. A. J. Tyrrell, of the Virus Research Laboratory, Sheffield, and by Dr. A. D. Macrae, of the Virus Reference Laboratory, Colindale, in 8 out of 10 cases from which paired sera were available, including one with negative faeces, and three of the four cases from which isolations were achieved. The fourth case had a high neutralizing antibody titre in the first serum specimen, and this was unchanged 15 days later.

Clinical Notes.—The ages of the children from whom isolations of virus were made were 5, 6, 7, and 12 years. All had fever, headache, and enlargement of posterior cervical lymph nodes. In three of the cases axillary glands were also involved, and two of these had inguinal gland enlargement as well. Central nervous symptoms were not prominent, but one child had a positive Kernig sign with slight neck rigidity, one had a transient loss of knee-jerks, and a third had some neck stiffness.

Discussion

The association of E.C.H.O. virus type 9 with cases of aseptic meningitis has been reported from West Virginia (Committee on E.C.H.O. viruses, 1955), and Belgium (Nihoul *et al.*, 1957). In the United Kingdom, Tyrrell and Snell (1956) and Tyrrell (1957, personal communication) recovered this agent from cases similar to Lyle's occurring in the Sheffield area in September, 1956, and a closely related agent with the additional property of pathogenicity for suckling mice has been isolated during outbreaks in East Suffolk (Boissard *et al.*, 1957), Leicester (Rotem, 1957), and Sweden (Wesslén *et al.*, 1958).

The initial negative findings in HeLa-cell cultures suggest that these are less sensitive than monkey-kidney cells for the primary isolation of this virus, and this is confirmed by the findings of Jamieson *et al.* (1958), who isolated five strains in monkey-kidney cells, but could not detect any virus using HeLa-cell cultures.

Although repeated passage in HeLa cells may lead to adaptation to this cell strain (Archetti *et al.*, 1957), this is not normally a practicable diagnostic procedure.

Summary

An agent serologically identical with E.C.H.O. virus type 9 has been isolated from four cases of lymphocytic meningo-encephalitis with myalgia and a rash occurring in an epidemic outbreak.

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REFERENCES

- Archetti, I., Weston, J., and Wenner, H. A. (1957). *Proc. Soc. exp. Biol. (N.Y.)*, 95, 265.
Boissard, G. P. B., Stokes, L. J., Macrae, A. D., and MacCullum, F. O. (1957). *Lancet*, 1, 500.
Committee on E.C.H.O. viruses (1955). *Science*, 122, 1187.
Jamieson, W. M., Kerr, M., and Sommerville, R. (1958). *Lancet*, 1, 581.
Lyle, W. H. (1956). *Ibid.*, 2, 1042.
Nihoul, E., Quersin-Thiry, L., and Weynants, A. (1957). *Amer. J. Hyg.*, 66, 102.
Rotem, C. E. (1957). *Lancet*, 1, 502.
Tyrrell, D. A. J., and Snell, B. (1956). *Ibid.*, 2, 1028.
Wesslén, T., Eriksson, S., Ehinger, A., and Zetterberg, B. (1958). *Arch. ges. Virusforsch.*, 8, 183.
Youngner, J. S. (1954). *Proc. Soc. exp. Biol. (N.Y.)*, 85, 202.