EFFECT OF MALARIA ON PREGNANCY

David D. Kulcsar, M.D.

U.N.R.R.A., Shanghai, China

THIS report is a study of the effect of malaria on the course of pregnancy based on the admissions from May 1, 1946 to end of April, 1947, to the Obstetrical Department of the Kweilin Provincial Hospital. Our admissions totalled only 360 cases but in spite of the relatively small number involved, we felt we were justified to undertake this study.

The Province of Kwangsi and also its capital Kweilin is one of the worst malaria-infested regions in China. No accurate statistical data are available but sources of long experience and good judgment estimate that at least 50% of the population suffers from malaria. Our figures are in favour of this opinion. Its effect on pregnant women exhibits itself in several ways. It causes a large proportion of abortions, it precipitates premature labour with corresponding danger to the child, and last but not least it may present difficult diagnostic problems.

In spite of the immense number of malaria cases throughout the world there have been comparatively few studies on its effect on pregnancy, labour and puerperium. To illustrate lack of interest in this field it may be mentioned that DeLee in his wellknown obstetrical textbook does not mention malaria at all. We feel this problem deserves more interest. High fever in labour or puerperium is a shocking experience to all of us; and those who have had to decide on the management of a febrile puerperium will recall what a relief is a positive laboratory report on a blood smear. Possession of penicillin and the knowledge that puerperal sepsis and malaria can coexist will not change much of this statement's value.

Incidence.—The health organization of the League of Nations in 1932 gave a conservative estimation of 300 million cases of malaria throughout the world. (1) This would include about 10 million pregnancies affected with malaria unless chronic malaria would con-

siderably reduce the rate of conception, of which we found no evidence in the literature. (2) Cecil estimates one million cases in the United States, which will no doubt increase on the return of veterans from malaria-infested regions of military operations; 100 million are estimated in India and a great part of the remaining 200 million or more is found undoubtedly in China.

In our series (see Table I) we had 59 cases proved to be positive on laboratory examinations which represents a percentage of 17% of the total admissions. On the other hand there were 173 cases of definite malaria past history, which amounts to 48% of our total admission. We had 8 cases treated on clinical signs only. For definite and lasting experiment only proved cases should be counted. We included those cases with malaria history for the purpose of evaluating the effect of chronicity or as past history as such.

TABLE I.

SHOWING NUMBER AND PERCENTAGE OF ADMISSIONS TABULATED ACCORDING TO LABORATORY FINDINGS, PREVIOUS MALARIA HISTORY AND CLINICAL SIGNS

Classification of cases	*Admission Number*	*Percentage*
Plasmodium positive	59	17
Malarial past history, plasmodium negative	173	48
Negative past history, negative laboratory finding	120	33
Clinically suspect without past history or laboratory findings. Received antimalarial treatment	8	2

EFFECTS OF PREGNANCY

Standers[3] begins his short description of the effect of malaria as follows:

"Despite the somewhat widespread opinion to the contrary it would appear that the ordinary forms of malaria have but little influence upon the course of pregnancy, although Goth[4] has reported 19 out of 46 cases ended in premature labour."

In our series (see Table II) we had 19 premature and 9 threatened or incomplete abortion cases out of 59 proved malaria cases. This figure rather corresponds to Goth's[4] report; 48% of abnormal cases certainly constitute an alarming figure if compared with 18% of abnormal admissions in the so-called malaria free group.

The cause of interruption of the pregnancy is variously given as the reaction to the high fever (Titus[5]), or to uterine contractions caused by the plasmodia and partly to premature separations as mentioned by Jaschke[6] and Pankow in their textbook. Another reason is given by DaLeas, who believes the fetus will become infected very frequently, which is then almost always followed by abortion. Manson-Bahr[8] mentions that "malaria *per se* is a far more potent oxytocic than any drug". He then continues:

"Intra-uterine death of the fetus is fairly frequent, whilst clinical and pathological evidence points to malaria as a powerful predisposing factor in the toxæmias of pregnancy, such as pre-eclampsia, eclampsia and nephritic toxæmia."

We noted the number of cases with albuminuria and œdema; and as is shown in Table VI, there is only a moderate increase in percentage as compared with the free cases. Wickramasuriya's report of 40% of general anasarca out of 357 cases especially investigated in pregnant women is probably due to malnutrition rather than to the specific effect of malaria.

That albuminuria and œdema of renal origin occur in tropical malaria is well established. Hypertension is also often noted. Snapper[10] reports a case where tertian malaria was the cause of acute nephritis. Nephritis predisposes to toxæmia, so malaria can be regarded as a predisposing factor as Manson-Bahr[8] mentions. As in our 59 cases no definite toxæmia occurred

TABLE II.

SHOWING COURSE OF PREGNANCY AND COMPLICATIONS GROUPED AS IN TABLE I

	Total No.	*Full term No.*	*%*	*Premature No.*	*%*	*Abortion Threaten. No.*	*%*	*Incompl. No.*	*%*	*Total abnormal cases No.*	*%*
Plasmodium positive	59	31	52	19	32	7	12	2	4	28	48
Malarial past history, plasmodium negative	173	140	81	19	11	7	4	7	4	33	19
Negative past history, negative laboratory finding	120	99	82	15	13	1	1	5	4	21	18
Clinically suspect, no past history, negative lab. finding. Antimalarial treatment ..	8	5	62	0	0	3	38	0	0	3	38

it is unlikely that malaria is such a powerful factor in the etiology of toxæmias.

Type of infection.—We investigated the comparative effect of falciparum to vivax infection. As is shown in Table III, there were 33 cases of falciparum as against 26 cases of vivax infections. Falciparum infections are apt to cause pernicious symptoms and according to Manson-Bahr[8] and others it is especially true in cases of pregnancy. He calls attention to cerebral manifestations which may come unexpectedly, without any previous malarial history and may cause serious diagnostic difficulties. We had no pernicious cases. Although in general in our cases falciparum infection caused the same percentage of abnormality as vivax infections, they caused a considerably higher number of stillbirths as is shown in Table VII. We had one case of double infection; it was a case of incomplete abortion. There were no quartan malaria cases.

TABLE III.
SHOWING DISTRIBUTION AS OF SPECIES OF PLASMODIUM

Species	*Number of cases*	*Percentage*
Plasmodium vivax	26	44.3
Plasmodium falciparum	33	55.7
Total	59	100.0

Effect on the product of gestation. — High percentage of abortion and premature labour will naturally carry high fetal mortality. We had (see Table VII) 18.5% of stillborn and aborted cases as against 9% in the malaria free cases. We also had 10.2% premature babies against 5.8% in the free cases; a great proportion of them will very probably not survive.

The factor of intra-uterine fetal infection should also be considered. This question of congenital malaria gave rise to several conflicting statements and reports. Titus[5] cites Blacklock and Gordon[11] who "advanced evidence against the suggestion that malarial infection of the fetus takes place". The fact that Blacklock and Gordon could not find plasmodium in the fetal blood cannot be accepted in face of positive findings by Schwartz[12] in 6% of the cord-blood and 3.6% of the blood of the infants out of 56 negro women examined in Central Africa. Placental infection on the other hand was shown in 74% in his cases, which made him believe that congenital malaria is of very little importance. Wickramasuriya[9] and DaLeas[7] state fetal infection is more often the cause of death than formerly believed. Chen, Tang and Wang[13] report 39 cases from the literature and one of their own. We had no opportunity to investigate this phase of the problem but after studying related publications and following some of our cases we believe in the occurrence of congenital malaria.

TABLE IV.
EFFECT OF MALARIA AS OF THE SPECIES INVOLVED

	Total	*Full term*		*Premature*		*Abortion Threaten.*		*Abortion Incompl.*	
	No.	*No.*	*%*	*No.*	*%*	*No.*	*%*	*No.*	*%*
Plasmodium vivax	26	14	54	6	23	5	19	1	4
Plasmodium falciparum	33	17	52	13	39	2	6	1	3

TABLE V.
COMPARATIVE RESULTS OF KAHN TEST (BLOOD)

	Number of cases	*Positive*	
		No.	*%*
Plasmodium positive	52	6	11
Malarial past history, negative laboratory findings	142	10	7
Negative past history, negative laboratory findings	83	11	13
Clinically suspect without past history or lab. findings ..	6	0	0

Effect of malarial past history.—Cases with malarial past history but negative plasmodium report on admission were tabulated separately in order to see whether the presence of a

TABLE VI.
SHOWING NUMBER AND PERCENTAGE OF CHILLS, ALBUMINURIA AND ŒDEMA

Classification	*Total admission*	*Chills*		*Albuminuria*		*Œdema*	
		No.	*%*	*No.*	*%*	*No.*	*%*
Plasmodium positive							
Vivax	26	5	19	2	8	3	12
Falciparum	33	7	21	8	24	5	15
Total	59	12	20	10	17	8	13
Malaria past history, negative laboratory findings	173	3	2	30	17	19	11
Cases with no malaria past history, laboratory or clinical findings	120	5	4	24	20	7	6

TABLE VII.
COMPARISON SHOWING CONDITION OF PRODUCT OF GESTATION

Classification	Healthy No.	Healthy %	Premature No.	Premature %	Stillborn No.	Stillborn %	Aborted No.	Aborted %	Pregnancy carried No.	Pregnancy carried %
Plasmodium positive										
Vivax	14	53.8	0	0	3	11.5	3	11.5	6	23
Falciparum	19	57.5	6	18.2	5	15.1	0	0	3	9
Total	33	55.9	6	10.2	8	13.5	3	5	9	15.2
Malaria past history, neg. lab. findings	142	82	3	1.7	6	3.5	9	5.2	13	7.5
Cases with no malaria past history, laboratory or clinical findings	101	83.9	7	5.8	7	5.8	4	3.3	1	0.8

malarial past history has any effect on the course of pregnancy. We had 173 cases, 48% of total admission. It appears that a past history as such has no adverse effect except in the possibility of recurrency. Vivax malaria may be expected to relapse in 55%, falciparum in 45% of the treated cases (Mackie, Hunter, Worth[1]). One wonders whether the so-called suppressive malaria medication would not be worthwhile in order to prevent complications. In our 59 cases 50 were recurrences and only 9 primary infection. A major part of the recurrent attacks could have been prevented and no doubt most of the premature labours would have continued to full term and some of the stillborns born alive. The author has not heard of any investigation in this line; it is hoped this possibility will be explored in the near future.

Clinically suspect malaria cases and pregnancy.—Stander[3] says in his textbook: "Too many sins of omission and commission on the part of the obstetrician have undoubtedly been cloaked under the diagnosis of malaria" and continues "the existence of malarial fever should not be entertained until all other possibilities have been practically eliminated and the characteristic parasites have been found in the blood." There is no question of the advisability of a most thorough search for the cause of any fever; but one perhaps should not delay such a relatively harmless medication as atabrine or quinine where there is considerable clinical suspicion of malaria. Imperati and his co-workers[14] have depended as often on the leucopenia and relative mononucleosis of malaria as on the actual finding of the parasite in the blood. We had 8 cases of such a nature and we were convinced of having been right in initiating anti-malarial treatment.

Some other observations.—Chills had occurred in 20% of the plasmodium positive cases; 3% of all the other cases showed chills during their hospitalization.

Red cell count per c.mm. averaged 3,680,000; for the clear cases 3,820,000, and for those with past malarial history it averaged 3,720,000. The difference does not justify special comment except to note that it was quite low in all categories, which in itself makes complications more serious and prevention more important.

White cell count averaged 8,960 per c.mm. as against 9,610 in the malaria-free cases.

Results of Kahn tests. Cecil[2] mentions that "sometimes" in malaria a false positive reaction was obtained. Potter[15] tested 100 men with malarial infection, who all had previously negative Wassermann and Kahn test and were presumably free from syphilis, and found 12 positive and 10 doubtful cases. They all became negative within 30 days. Rosenberg[15] made a study to determine which serological test would give the smallest percentage of false positive reactions in malaria. Hinton test was found to be most reliable and Rosenberg advises to suspect syphilis if a positive reaction persists beyond 6 weeks in the absence of continued malarial infection. We had, as shown in Table V, 11% positive reactions as against 9% of the malarial negative cases. Our figures will put us more on guard for syphilis.

Public and private ward admissions show the same distribution in plasmodium positive as in the free cases which indicates the necessity and value of proper education, as those in higher economic brackets should at least show a lower admission rate for malaria.

Treatment of malaria in pregnancy and puerperium. — Williams[3] advises unhesitating use of quinine because its oxytoxic properties apparently are in abeyance in the presence of malarial infection, so that it can be used with impunity without fear of setting up uterine contractions. Manson-Bahr[8] is more cautious

and recommends care in giving quinine because, "Undoubtedly, if administered in large doses, it may sometimes cause miscarriage". He advises that quinine should be given in the minimum dose likely to be effective, say 3 grains q.8h. for 2 days. Acton[16] concluded from his pharmacological studies that miscarriage can only be brought about by doses of quinine sufficiently large to poison the patient.

In the puerperal state sufficiently large doses can safely be given as according to Standers[3] the drug exerts no appreciable influence upon the mammary secretion or the well-being of the child. On the other hand Greenhill[17] has a different opinion; he believes:

"Quinine may injure the baby; frequently the liquor amnii is stained with meconium; in a few instances babies have been born dead presumably as a result of the action of quinine, and in some instances deafness caused by injury of the auditory nerve can be traced to the use of quinine in labour."

Apparently this aspect of quinine therapy requires further investigation and experimentation. Quinine is excreted in the milk of nursing women. Manson-Bahr[8] makes the suggestion to give a few 5 grain doses of quinine during labour or soon after in order to prevent a latent infection to become active. Labour seems to have the same effect as any other shock or strain in precipitating a recurrence.

The comparatively recently developed atabrine is well borne by pregnant women in relatively large doses and is replacing quinine, especially in the treatment of pregnant cases. As for the comparative value of the two drugs Titus[5] states atabrine is more prompt and effective. Many of the doctors in South China believe quinine acts faster. Mackie, Hunter and Worth[1] state atabrine and quinine are approximately equally effective in the treatment of acute clinical malaria. The plasma concentration determines the efficiency of action. With the usual plan of dosage an effective plasma level is attained more rapidly with quinine than with atabrine.

We treated 30 cases with quinine and 20 with atabrine; 50% of atabrine treated cases were controlled after one febrile attack, while only 22% of those treated by quinine were controlled after the first febrile attack. But we do not believe the number is sufficiently large to warrant conclusion in this respect.

We experienced no untoward effect from either of the 2 drugs. The new synthetic drug paludrine will probable replace atabrine in the near future.

TABLE VIII.
SHOWING COMPARATIVE EFFECT OF QUININE AND ATABRINE

Plasmodium positive	*No.*	*%*
Total admission	59	
Quinine after one febrile attack	13	22
Checked after more attacks	26	44
Atabrine after one attack	10	16.9
Checked after more attacks	10	16.9

SUMMARY

1. A statistical study on the effect of malaria on pregnancy is presented on the basis of 360 admissions to the Obstetrical Ward of the Kweilin Provincial Hospital.

2. There were 59 plasmodium positive cases which represented 17% of the total admission; and another 48% had a definite malarial past history.

3. Forty-eight per cent of the plasmodium positive cases showed complications as against 18% of the malaria free cases.

4. Complications occurred in the form of abortions (16%), premature labours (32%), and stillbirths (13.5%).

5. Contrary to previous reports malaria does not seem to be a serious predisposing factor to toxæmias.

6. Falciparum infections occurred in 33 cases (55.7%) and vivax in 26 cases (44.3%).

7. Falciparum and vivax infections appeared to have the same percentage of total complications, *but falciparum caused more premature labours and more stillbirths.*

8. A suggestion is put forward to investigate suppressive malarial medication in cases of known malarial past history in order to prevent recurrences during pregnancy, labour and puerperium.

9. Comparative therapeutic effect of quinine and atabrine discussed.

10. The author emphasizes the importance and frequency of complications due to malaria.

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RÉSUMÉ

Etude étiologique des effets de la malaria sur la grossesse, basée sur 360 cas. Il se trouva 59 malades porteuses de plasmodium ou 17% du total des cas admis; dans un autre groupe de 48% on relevait dans le passé une histoire de malaria. 48% des cas porteurs de plasmodium eurent des complications par rapport aux 18% qui n'avaient pas eu la malaria. Ces complications furent l'avortement (16%), le travail prématuré (32%) et la naissance d'enfants morts (13.5%). Il ne semble pas que la malaria prédispose aux toxémies. On releva le falciparum dans 33 cas (55.7%) et le vivax chez 26 (44.3%). L'un et l'autre se partagèrent également le total des complications, mais *le falciparum détermina plus souvent le travail prématuré et la naissance d'enfants morts.* On devrait faire enquête sur le nombre de celles qui ont cessé la médication antimalarique afin de prévenir les rechutes au cours de la grossesse, de l'accouchement et des suites de couches. La quinine et l'atabrine ont des effets à peu près comparables.

JEAN SAUCIER