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ABSTRACTS OF RECENT CHINESE PUBLICATIONS ON MALARIA¹ (XIV)

162. Li, C. J. & Gong, G. Z. Observations on some factors influencing the sporogony of Plasmodium yoelii. Journal of Parasitology and Parasitic Diseases, 1984, 2(1): 9 (In Chinese, with English abstract)

In splenectomized mice, parasitaemia reached a peak level six days after the inoculation of 3×10^7 - 4.5×10^7 cells parasitized with Plasmodium yoelii and remained high for up to 20 days after inoculation. During this 20-day period seven out of 10 test animals died, while all the non-splenectomized control animals survived the peak parasitaemia level that occurred by day 22.

Anopheline mosquitos fed on the non-splenectomized mice two to four days after blood inoculation developed a gland infection rate of 40%, while mosquitos fed on infected splenectomized mice during the same period developed a higher gland infection rate. In the course of pursuing the experiment more statistically significant differences in rates between the two groups of mosquitos became evident ($P < 0.001$).

There was a greater development of parasite oocysts in mosquito vectors receiving para-aminobenzoic acid (PABA) of various concentrations (0.5%, 0.05%, 0.005%) in glucose solution, than in the control mosquitos given glucose only. The PABA concentration found to be most favourable to the development of the oocysts was 0.05%.

Peak infection rates in vectors fed on mice with blood-induced infections varied with the time of the bloodmeal. Peak levels were reached between 20.00 and midnight when bloodmeals had been given at 12.00 noon; on the other hand, peak levels were reached between 8 and 12 in the morning when bloodmeals had been given at 24.00.

163. Huang, W. Z. et al. Study of an agar gel diffusion method for the identification of mosquito bloodmeals. Journal of Parasitology and Parasitic Diseases, 1984, 2(1): 39 (In Chinese, with English abstract)

Agar gel diffusion was carried out to identify the host source of mosquito bloodmeals. For comparison, the precipitin ring test was done simultaneously.

For the agar gel diffusion test, optimal concentrations of antigen and antiserum, as well as optimal temperature and reaction time were determined. Specimens of bloodmeals of Anopheles sinensis artificially fed on fresh cattle blood through a membrane and those naturally fed were collected and tested. It was demonstrated that when the dilution of antigens was 1:500-1:1000 and the dilution of antiserum 1:4 and when the test was performed at 24-37°C for 24 hours, the results were consistent with those of the precipitin ring test. However, in the latter test, 7.8% of the specimens cross-reacted with horse and sheep blood. It appears that the agar gel diffusion test has the advantage over the precipitin ring test of having a higher specificity for identification of mosquito bloodmeals. This method is also simple to perform.

¹ The WHO/MAL series has been chosen as a vehicle for issuing abstracts or translations in English of papers on malaria published in the Chinese medical and scientific press as most of this material is not readily available to interested readers outside China. The numbering of the abstracts in this document is consecutive to that of the abstracts given in the previous WHO/MAL/84.1006.

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164. Malaria Commission, Committee of Medical Sciences. Malaria control and morbidity in China in 1982. Journal of Parasitology and Parasitic Diseases, 1984, 2(1): 1 (In Chinese, with English abstract)

In 1982, 1.97 million clinical cases of malaria were treated; 34.25 million chemoprophylactic doses were given; indoor residual insecticide spraying was carried out in areas covering a total population of 17.54 million; 7.52 million blood examinations were made from pyretic cases and during mass surveys; 14.5% of the total number of malaria cases were confirmed by microscopic examination.

Based upon the statistics from different parts of China, there were 2 041 359 malaria cases in 1982 or 1 018 276 less than that in 1981, giving a morbidity reduction rate of 33.77%. A total of 1483 counties with a population of 583 million were malaria-free or with a morbidity below 1‰.

The total number of malaria cases in the five provinces of Jiangsu, Shandong, Henan, Anhui and Hubei in 1982 was 1.71 million. This figure was 0.93 million less than that in 1981, but still represented 83.7% of the total number of cases for all of China. In the provinces in south China, a similar decline in morbidity was recorded.

The distribution of falciparum malaria in 1982 was similar to that in 1981. The presence of chloroquine-resistant strains of Plasmodium falciparum was confirmed in 28 counties in five provinces.

165. Gu, G. R. et al. Parasitaemia rate in a malaria endemic region. Chinese Journal of Epidemiology, 1984, 5(1): 35 (In Chinese)

In August 1981, 459 persons randomly selected from four brigades of three communes in Tanghe County, Henan Province, were examined for Plasmodium in blood smears. The results revealed parasitaemia rates of 2.3% (11/459) in the sample population, 4.9% (8/164) in acute malaria patients, 6.5% (2/31) in people with a history of malaria and 0.4% (1/246) in people without a malaria attack for the past two years. The incidence of malaria and the parasitaemia rate were higher in shrubby and hilly regions than in plain areas.

166. Zhang, K. et al. Variation of Plasmodium vivax. Chinese Journal of Medical Laboratory Technology, 1983, 6(4): 231 (In Chinese)

A morphological variation of Plasmodium vivax in Bao-ying, Jiangsu Province, is described. Malaria in this area was found to be usually acute, characterized by continued high fever without chill, and severe anaemia. On Giemsa-stained thin blood films, the red blood cell (RBC) infection rate was 0.83%, and 18% of the infected RBCs were found to harbour more than two parasites, the highest number of parasites being eight in one RBC. In 11.9% of the trophozoites, there were more than two nuclei, the maximum number being five; mature schizonts had 9-24 merozoites with an average of 16. Infected RBCs were enlarged and 4% of them showed Schuffner's dots.

Furthermore, there were some trophozoites in the free state outside the RBCs. The possibility of simian malaria having been ruled out, a polynucleated sub-species of P. vivax was the most likely diagnosis. Biogenetic studies are required to elucidate this phenomenon.

167. Xiang, R. C. Comparison of thin and thick blood film examination for malaria parasites in 40 cases of Plasmodium vivax infection. Chinese Journal of Medical Laboratory Technology, 1983, 6(4): 239 (In Chinese)

Blood was taken from 40 cases of tertian malaria, and both thin and thick blood films stained with Giemsa were prepared and examined for malaria parasites. For each blood film, 100 microscopic fields were examined and the numbers of parasites and positive fields were recorded. Plasmodium vivax was found in all the thin as well as all the thick blood films, with the parasite counts ranging from 1-55 in the thin films and 11-911 in the thick films. The number of fields showing parasites was 2915 (i.e. 72.87%) for the thick films while that for the thin films was 566 (i.e. 14.15%) or five times less, thereby showing the superiority of thick blood film examination. Although the parasites in thick films may be difficult to identify, this problem would be solved by improving the diagnostic ability of the microscopists through training and practice.

168. Luo, Z. Q. Modified dehaemoglobinization of thick films for malaria parasite examination. Chinese Journal of Medical Laboratory Technology, 1983, 6(4): 217 (In Chinese)

Distortion of malaria parasites in the thick films resulting from dehaemoglobinization with distilled water makes species differentiation difficult. The author had more than 10 years experience in using 0.6% formalinized phosphate buffered saline (PBS) (i.e. to 0.6 ml of 40% formaldehyde is added pH 6.8 PBS to make 100 ml) in place of distilled water for dehaemoglobinization. This step takes about 4-5 minutes. The film is then stained with a mixture of Wright-Giemsa (4:1) stain for 5-6 minutes for good results. The incompletely dehaemoglobinized infected erythrocytes are pink and shadowy in outline. The forms of the parasites are retained intact with nuclei in purple, cytoplasm in light blue and distinct pigment dots which facilitate morphological differentiation. The films thus stained can keep for quite a long time.

169. Li, W. L. et al. Characterization of Plasmodium yoelii antigens by monoclonal antibodies. I. Common antigens between erythrocytic stages of Plasmodium yoelii and human malaria parasites. Journal of Parasitology and Parasitic Diseases, 1984, 2(2): 83 (In Chinese, with English abstract)

Thirteen cell lines of hybrids secreting monoclonal antibodies against erythrocytic stages of Plasmodium yoelii were established by fusing Sp 2/0 myeloma cells with spleen cells of BALB/c mice immunized with crude preparations of merozoites of the same malaria parasite. The 13 monoclonal antibodies obtained could be classified according to indirect fluorescent antibody (IFA) test results into four groups: (1) those against various developmental forms of P. yoelii in erythrocytes; (2) those against late trophozoites and schizonts; (3) those against schizonts and merozoites; and (4) those against merozoites only. Of the 13 monoclonal antibodies, five showed cross immunofluorescence with human malaria parasites, of which four crossed with P. falciparum only, and one with both P. falciparum and P. vivax. This indicates the existence of common antigens not only between rodent and human malaria parasites, but also between P. falciparum and P. vivax. The distribution and quantity of the common antigens between different malaria parasite species are not always the same. These differences should be carefully considered when heterogenous malaria parasites are used for immunodiagnosis or for vaccination experiments. Immunofluorescence could not be observed on the surface of infected red blood cells when fresh infected cells were used as target cells in the IFA test using monoclonal antibodies.

170. Chen, C. et al. Studies on new antimalarials: synthesis of derivatives of benzo(g)quinoline with double Mannich bases of aminophenol. Acta Pharmaceutica Sinica, 1983, 18(12): 965 (In Chinese, with English abstract)

Since 4- [3,5-bis (pyrrolidinomethyl)-4-hydroxyanilino] benzo(g)quinoline(I) reported in a previous paper exhibited a satisfactory effect against Plasmodium berghei without cross-resistance to chloroquine in mice, it was decided to synthesize a group of derivatives of benzo(g)quinoline with double Mannich bases of aminophenol, 4- [3,5-bis (alkylaminomethyl) 2- or 4-hydroxyanilino] benzo(g)quinolines(II).

2-hydroxy-3-naphthoic acid used as the starting material was first allowed to react with ammonium chloride to yield 2-amino-3-naphthoic acid, and then with acrylonitrile to give 2- [(2-cyanoethyl) amino] 3-naphthoic acid. This intermediate product was hydrolysed to form 3-(3-carboxy-2-naphthylamino) propanoic acid followed by cyclization and hydrolysis to afford benzo(g) 1,2,3,4-tetra-hydroquinoline-4-one, which was subsequently condensed with 2- or 4-hydroxyaniline and reacted with Mannich agents to form the end products II.

Of all the compounds synthesized, compounds I and II_{1-3,6} showed activity against the blood schizonts in mice, and among them, compounds I and II₃ were the most effective, having an activity higher than that of dabequine.

171. Chen, K. Y. et al. Experimental therapy of 7 antimalarials in mice infected with pyronaridine-resistant Plasmodium berghei. Acta Pharmacologica Sinica, 1983, 4(4): 269 (In Chinese, with English abstract)

Seven antimalarials were used in treating mice infected with Plasmodium berghei or a pyronaridine-resistant line of P. berghei. Results showed that the resistant line was

cross-resistant to chloroquine, piperaquine, quinine and quinacrine but susceptible to pyrimethamine and sulfadoxine. The ED₅₀s of pyrimethamine and sulfadoxine were 52.2 and 0.67 mg/kg per day x 3 days respectively. Artemisinin was effective against the pyronaridine-resistant line at a higher dosage, and its ED₅₀ was 1034 mg/kg per day x 3 days. Pyrimethamine in combination with sulfadoxine resulted in a potentiating effect against the pyronaridine-resistant line of P. berghei.

172. Shao, B. R. et al. Effect of pyronaridine and three other antimalarials on gametocytes and sporogony of Plasmodium yoelii. Journal of Parasitology and Parasitic Diseases, 1984, 2(1): 28 (In Chinese, with English abstract)

Mice harbouring Plasmodium yoelii gametocytes were given pyronaridine intragastrically at a dosage of 1200 mg base per kg body weight, this dosage being more or less equal to the LD₅₀. When batches of Anopheles stephensi were fed on these mice 2-12 hours after their inoculation with the drug, no effect was observed on the development of oocysts and infective sporozoites in the mosquitos. Similar results were obtained in mosquitos fed on mice medicated with chloroquine at the dosage of 600 mg base/kg (more or less equal to the LD₅₀). However, the formation of oocysts was inhibited when the mosquitos were fed on mice having received intragastrically a dose of 20 mg base/kg of primaquine or a larger dose of pyrimethamine (10 mg/kg). When 0.005% pyronaridine was fed to mosquitos after their engorgement on a gametocyte-bloodmeal, no influence on gametocyte infectivity or on sporogony was noted. With 0.01% pyronaridine most mosquitos died of intoxication, but normal oocysts could still be found in the survivors. The results in mosquitos exposed to chloroquine were similar, normal oocysts being detected. In contrast, the feeding of 0.001% pyrimethamine to mosquitos led to complete suppression of sporogony. With 0.01% primaquine many mosquitos died, but oocysts could still be found in the survivors. Primaquine at a concentration of 0.1% inhibited infectivity of gametocytes to mosquitos and also oocyst formation, no oocyst being detected in the few survivors.

173. Dai, Z. R. et al. Some biological characteristics of the simian malaria model with the Plasmodium cynomolgi-Anopheles stephensi system and its response to current antimalarials. Acta Pharmaceutica Sinica, 1983, 18(12): 881 (In Chinese, with English abstract)

Under certain conditions the Plasmodium cynomolgi infection rate of Anopheles stephensi was $77 \pm 0.15\%$. The rhesus monkeys were fairly susceptible to the parasite infection. All monkeys were infected after having been inoculated intravenously with more than 10^5 sporozoites each. The testing of current antimalarial drugs in this model showed that primaquine and pyrimethamine exhibited causal prophylactic activity. Primaquine (2.5 mg base/kg x 5 days) used in combination with chloroquine (20 mg base/kg x 3 days) showed radical curative effect, while chloroquine exhibited only suppressive activity when used alone (20 mg base/kg x 3 days).

174. Ding, L. Y. 40 cases of pyrimethamine induced megaloblastic anaemia. Chinese Journal of Internal Medicine, 1983, 22(9): 578 (In Chinese)

Forty males aged 19-23 years were hospitalized from October 1980 to September 1981 due to megaloblastic anaemia caused by pyrimethamine medicated salt at a dose of 11.4-41.7 mg per day taken for more than two months as prophylaxis against malaria. The main manifestations were: anorexia, constipation, dizziness, lethargy, sallow withered face, gingival and nasal haemorrhages, dark phalange joints, petechiae on the trunk and extremities, and mouth ulcers. It was found that 75% of the patients had 6-11 g haemoglobin, the lowest being 4.1 g; red blood cells varied in size with megalocytosis; 90% of the patients had less than 4000 white blood cells with an average lymphocyte rate of 50%; all had less than 90 000 platelets; 30 patients had reduced reticulocytes (< 0.5%). The bone marrow was hyperplastic in 35 patients, depressed in four and attenuated in one. Four severe cases were cured with blood transfusion, steroids, haemostatics and a supply of iron; the rest responded well to folic acid, vitamin B₁₂ and other appropriate medication.

175. Xiao, R. M. et al. Evaluation of toxic effect of para-fluoro-5-phenoxy-primaquine citrate (MP-0090). Chinese Journal of Infectious Diseases, 1983, 1(4): 209 (In Chinese, with English abstract)

The toxic effects of a newly synthesized antimalarial, para-fluoro-5-phenoxy-primaquine citrate (MP-0090) were studied by double-blind test in 38 healthy volunteers and 78 patients

infected with Plasmodium vivax. At the dose of 22.5 mg base given daily for five days (total 112.5 mg), it caused mild gastro-intestinal disturbances, such as nausea, vomiting and dyspepsia, without any impairment of hepatic or renal functions. Electrocardiograms were essentially normal. It did not lead to acute haemolysis and methaemoglobulinaemia. The drug may be less toxic than primaquine.

176. Chen, L. J. A malaria case in a 4-day-old infant. Journal of Public Health and Disease Control, 1984, 3(1): 61 (In Chinese)

A male infant was hospitalized four days after birth due to abrupt high fever. His mother had had an attack of malaria at eight months of gestation and had been treated inappropriately with only four tablets of chloroquine. Routine physical and laboratory examination revealed a temperature of 39.7°C but no abnormality in development or in the blood picture. This baby did not respond to penicillin or streptomycin. Malaria parasites were finally found in a thick blood smear. This infant was then treated with 1/8 ampule of quinine compositus and 0.02 g of chloroquine. His temperature returned to normal and he was discharged two days after treatment.

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