

**GLUTATHION REDUCTASE ACTIVITY AND ITS RELATION WITH RIBOFLAVIN LEVELS  
MEASURED BY METHEMOGLOBIN REDUCTION BY CYSTAMINE IN PATIENTS WITH MALARIA  
(PRELIMINARY REPORT)**

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**KEY WORDS:** Malaria; Riboflavin; Glutathion reductase; *Plasmodium falciparum*.

Malaria caused by *Plasmodium falciparum* is characterized by resistance to multiple drugs. Thus, the search for new treatments has included the study of riboflavin-inhibiting drugs as a possible alternative for the control of this endemic disease<sup>5, 6, 7</sup>.

The effect of riboflavin deficiency has been studied since 1944, when SEELER & OTT<sup>10</sup> demonstrated that chickens previously fed riboflavin-free diets and injected with *Plasmodium lophurae* developed attenuated infection and low parasitemia. KAIKAI & THURNHAM<sup>8</sup> reported that the development of *Plasmodium berghei* in the blood of infected rats was impaired when the animals had been previously fed riboflavin-deficient diets.

BATES et al<sup>4</sup>, in a study of children up to 2 years of age in Gambia, detected riboflavin deficiency, and the same phenomenon was observed by THURNHAM et al<sup>11</sup> among children aged up to 18 months in Papua, New Guinea. On the basis of the above information THURNHAM et al<sup>11</sup> and THURNHAM<sup>12</sup> proposed that, even though these findings may be interpreted as geographical coincidence of tropical countries, they may also reflect a physiological

adaptation that would result in decreased severity of malaria.

In view of the above data, in August 1983 in the township of Humaitá, Brazilian Amazon region, we studied 31 patients with malaria caused by *Plasmodium falciparum* and 11 normal individuals native to the Amazon region who had never suffered from malaria. Of the 31 patients, 12 were native to the Amazon region and 19 were migrants from non-endemic regions of Brazil. The control group consisted of 91 normal individuals residing in Anhembi, State of São Paulo, a region where malaria is not endemic. All individuals were adult males and each was tested for glutathion reductase (E.C.1.6.4.2) activity according to the method described by BARRAVIERA<sup>2, 3</sup>. This method utilizes the methemoglobin as a substrate and the cystamine stimulating the glutathion reductase.

The results presented below demonstrate that most of the native Amazonians (81.81%) who had never had malaria and native patients of Amazon region (75.00%) have decreased glutathion reductase activity, whereas most migrants patients with malaria (89.47%) have normal glutathion reductase activity.

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Subjects		Glutathion Reductase Activity				
		Normal		Decreased		Total
		Nº	%	Nº	%	
Normal Individuals (A)	Anhembi (1)	89	97.81	2	2.19	91
	Humaitá (2)	2	18.19	9	81.81	11
Patients (B)	Migrants (3)	17	89.47	2	10.53	19
	Natives (4)	3	25.00	9	75.00	12

Statistical analysis: A x B;  $\chi^2 = 10.51$ ;  $p < 0.01$   
 $A_1 \times A_2 \times B_3 \times B_4$ ;  $\chi^2 = 77.72$ ;  $p < 0.001$   
 $(A_1 + B_3) \times (A_2 + B_4)$ ;  $\chi^2 = 76.73$ ;  $p < 0.001$

The native Amazonian population studied here has peculiar feeding habits, i.e. the basic diet consists of manioc flour and fish, with low consumption of vegetables, legumes, fruit, eggs or dry legumes, foods that are rich in riboflavin. Furthermore, in this population there is high parasitic infestation by *Ascáris lumbricoides*<sup>1</sup>, a helminth which, in addition to consuming albumin and vitamin C, also consumes riboflavin.

Taken together, these data and observations permit us to suggest that the deficiency in glutathion reductase detected here probably occurred owing to a deficiency of flavin-adenine dinucleotide (FAD), a phosphorylated riboflavin derivative. This because the population basically consumes the peculiar diet, has an elevated prevalence of worm infestation and furthermore is submitted to selective malarial pressure<sup>9</sup>.

According to THURNHAM<sup>12</sup>, in areas where malaria is endemic, nutritional deficiencies may be advantageous for the host by suppressing the infection. In this respect, it is possible that the riboflavin deficiency detected in the native population is an additional protecting factor against malaria. Although we know that there are others factors acting in this protection.

Finally, these considerations should be taken into account when indicating riboflavin-inhibiting drugs for the treatment of malaria.

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