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A NETWORK FOR THE EVALUATION OF CHEMORESISTANCE OF *PLASMODIUM FALCIPARUM* IN WEST AFRICA

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SUMMARY: The resistance of *Plasmodium falciparum* to common drugs has been contributing to a worsening of the malaria situation in West Africa. Since the problem of chemoresistance crosses national borders, West African countries need to coordinate surveillance and control efforts. In 1985 the eight member states of the Organisation de Coordination et de Coopération pour la lutte contre les Grandes Endémies (O.C.C.G.E.) set up a chemoresistance surveillance network. By using standard methods and by holding regular workshops it has been possible to get a global view of the problem of drug resistance and to coordinate disease control programmes. The network could be rendered more efficient and effective with greater resources and a membership covering a greater number of West African countries.

KEY WORDS: *Plasmodium falciparum*, drug resistance, surveillance network, West Africa.

INTRODUCTION

Malaria remains one of the major causes of morbidity and mortality in tropical areas. Between 300 and 500 million cases occur each year, causing more than one million deaths, mainly in African children under 5 years old (see KONDRACHINE & TRIGG, 1998). It is considered that malaria represents 2,3% of the general morbidity burden in the world and 9% of this burden in Africa. This disease is consequently an important source of economic loss (WHO/TDR, 1996). In Burkina Faso, the mean expenditure on mosquito control and malaria treatment is estimated at US $ 75 over the six months of high transmission, representing 5% of total family income (GUIGUEMDE *et al.*, 1994b). Direct and indirect costs related to malaria were estimated at US $ 800 million in 1987.

Chloroquine, the most widely used antimalarial drug, has progressively lost its efficacy in Asia, South-East Asia, and in South America since its introduction in 1959. Resistance has since spread to other parts of the world, reaching the African continent relatively recently. The first documented cases were reported in East Africa in 1978 (ANONYMOUS, 1985; CDC, 1978; CAMPBELL *et al.*, 1983), in Kenya and Tanzania. Further cases were reported in much of Eastern Africa: Mozambique, Burundi, Zimbabwe, Rwanda, Zambia and Democratic Republic of the Congo (BRYSKIER & LABRO, 1988). It continued towards Central Africa: Angola, Congo, Gabon, Central African Republic, Cameroon and Chad and then reached West Africa in the second half of the eighties (GUIGUEMDE *et al.*, 1988a, b, 1991; BOURRÉE *et al.*, 1986; CHARMOT *et al.*, 1991).

CHEMORESISTANCE IN WEST AFRICA

The emergence of resistance of *Plasmodium falciparum* to drugs worsens the malaria situation in endemic countries by reducing the list of effective treatments. The consequences are a re-emergence of the disease both in mild and severe cases in children, pregnant women and other adults. As a result, malaria mortality increases in the overall population, and more in pregnant women and children under five years old.

The first cases of chemoresistance notified in West Africa before 1986 were isolated cases, or *in vitro* cases of reduction in drug efficacy (BOURGEADE, 1993; CHARMOT *et al.*, 1991; COULIBALY *et al.*, 1994). In addition, *in vivo* chemoresistance cases were reported in tourists (CRCP/OCCGE, 1997).

Between 1987 and 1990, the Reference Centre for Malaria Chemoresistance (Centre de Référence de la Chimiorésistance du Paludisme, CRCP) in collaboration with national Ministries of Health, evaluated chemoresistance in the member countries of the Organisation de Coordination et de Coopération pour la lutte contre les Grandes Endémies (OCCGE) (GUIGUEMDE *et al.*, 1991). This study determined the phenomenon more in coastal countries: Bénin, Togo and Côte d'Ivoire (probably the first reached) and to a lesser extent in the Saharan countries: Burkina Faso, Mali, Niger and Sénégal. By 1990, all of the 8 countries of the OCCGE were covered, finishing with Mauritania (COULIBALY *et al.*, 1994). Chemoresistance rates were generally less than 30% until 1990 (GUIGUEMDE *et al.*, 1991), and rarely exceeded 30% after. Resistance was found to: Chloroquine (CQ), Amodiaquine (AQ), Mefloquine (MQ), and to a lesser extent Quinine (Q).

In the countries of the OCCGE, the resistance to CQ reported for 1995 and 1996 was generally less than 30% and was type I resistance, whilst therapeutic failures rarely exceeded 10% (CRCP/OCCGE, 1997). AQ and SP (Sulfadoxin-pyrimethamine), when tested showed a good level of efficacy (Togo).

Globally, a trend towards stagnation and even reces-

sion of chemoresistance (principally to CQ *in vivo*) was noted, and CQ remains the first-line drug for the treatment of mild cases.

There is, however, considerable local variation in resistance both in time and in space (GUIGUEMDE *et al.*, 1991, 1994a; BOURGEADE, 1993; CHARMOT *et al.*, 1991). Related factors include the date of emergence of resistance, whether the setting is urban or rural, and patterns of migration.

Countries outside of the OCCGE have carried out a number of chemoresistance studies but differences in the methods employed makes comparison problematic. The language barrier between Anglophone and Francophone countries contributes to poor communication between OCCGE and non-OCCGE countries.

THE NEED FOR A CHEMORESISTANCE SURVEILLANCE NETWORK

Chemoresistance needs observation on a regional, or better, continental scale. A chemoresistance network is urgently needed to:
- standardise study methods to make their results comparable;
- choose suitable sites for study based on geographical and epidemiological considerations;
- make better use of expensive diagnostic technologies;
- allow for regular scientific exchange.

EXAMPLE OF THE CRCP/OCCGE

In 1985 the «Centre de Référence de la Chimiorésistance du Paludisme» (CRCP) was created in Bobo-Dioulasso (Burkina Faso) at the Centre Muraz under the auspices of the OCCGE (GUIGUEMDE *et al.*, 1988b). A pyramidal structure was set up to include peripheral surveillance centres, national centres, and the reference centre. Surveillance strategies and methods were laid out for each centre.

The objectives of the CRCP were to:
- set up and train specialised teams in all OCCGE member states to carry out *in vivo* and *in vitro* tests with a common methodology within the national surveillance systems;
- provide permanent support and continual training to these teams;
- advise these teams;
- suggest appropriate therapeutic regimes to avoid and/or limit the spread of drug resistance;
- collaborate with foreign countries so as to keep abreast of technical progress and to follow up resistance in travellers.

The results of the network have been encouraging: the studies carried out in each country used standard methods and workshops have been held every two years to compare the results of surveillance. These workshops have allowed:
- exchange of experience;
- evaluation of the general situation of chemoresistance;
- re-orientation of malaria control policy;
- protocols for rational drug use.

CONCLUSION

The setting up of a chemoresistance surveillance network is necessary to cover all of the geographical region confronted by the problem of endemic malaria. The malaria network of CRCP/OCCGE, which was created in 1985, has contributed to a better understanding of the phenomenon of chemoresistance and to the formulation of national malaria control strategies. The network should be widened to cover the other endemic countries of the region, and be strengthened in its operational capacities. It should serve as an example for other regions where malaria is endemic.

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