Annals of Parasitology 2016, 62(1), 17–24
doi: 10.17420/ap6201.27

Review articles

Lessons learnt from 20 years surveillance of malaria drug resistance prior to the policy change in Burkina Faso

Halidou Tinto[1,2], Innocent Valea[1,2], Jean-Bosco Ouédraogo[1], Tinga Robert Guiguemdé[2]

[1]Institut de Recherche en Sciences de la Santé - Unité de Recherche Clinique de Nanoro (IRSS-URCN), Nanoro, Burkina Faso
[2]Centre Muraz, Bobo-Dioulasso, Burkina Faso

Corresponding Author: Halidou Tinto; e-mail: tintohalidou@yahoo.fr

ABSTRACT. The history of drug resistance to the previous antimalarial drugs, and the potential for resistance to evolve to Artemisinin-based combination therapies, demonstrates the necessity to set-up a good surveillance system in order to provide early warning of the development of resistance. Here we report a review summarizing the history of the surveillance of drug resistance that led to the policy change in Burkina Faso. The first *Plasmodium falciparum* Chloroquine-Resistance strain identified in Burkina Faso was detected by an *in vitro* test carried out in Koudougou in 1983. Nevertheless, no further cases were reported until 1987, suggesting that resistant strains had been circulating at a low prevalence before the beginning of the systematic surveillance system from 1984. We observed a marked increase of Chloroquine-Resistance in 2002–2003 probably due to the length of follow-up as the follow-up duration was 7 or 14 days before 2002 and 28 days from 2002 onwards. Therefore, pre-2002 studies have probably under-estimated the real prevalence of Chloroquine-Resistance by not detecting the late recrudescence. With a rate of 8.2% treatment failure reported in 2003, Sulfadoxine-Pyrimethamine was still efficacious for the treatment of uncomplicated malaria in Burkina Faso but this rate might rapidly increase as the result of its spreading from neighboring countries and due to its current use for both the Intermittent Preventive Treatment in pregnant women and Seasonal Malaria Chemoprophylaxis. The current strategy for the surveillance of the Artemisinin-based combination treatments resistance should build on lessons learnt under the previous period of 20 years surveillance of Chloroquine and Sulfadoxine-Pyrimethamine resistance (1994–2004). The most important aspect being to extend the number of sentinel sites so that data would be less patchy and could help understanding the dynamic of the resistance.

Key words: malaria, *Plasmodium falciparum*, drug resistance, Chloroquine, Sulfadoxine-Pyrimetamine, Artemisinin-based combination therapies, Burkina Faso

Introduction

Worldwide use of Artemisinin-based combination therapies (ACT) combined with vector control measures has led to significant decreases in malaria transmission and thus subsequent malaria-related morbidity and mortality in many endemic countries [1]. However, this enthusiasm could be hampered by several reports indicating a decrease of *Plasmodium falciparum* susceptibility to the artemisinin derivatives along the Thailand and Myanmar border [2–6]. More worrying, it has been recently reported a decline of parasitological response rate to treatment with ACTs in Africa patients, possibly due to the emergence of parasites with reduced drug sensitivity [7,8]. From these recent findings, we can predict that artemisinin-resistant malaria found on the border of Thailand and Myanmar could now spread to India and then Africa, repeating the same pattern of resistance similar to what other antimalarial drugs such as chloroquine has done before [9]. Indeed, almost all resistance emerged from either Southeast Asia or South America [10].

So far, malaria control efforts have been hampered mainly by drug resistance. The resistance

of *Plasmodium falciparum* to the two most popular and conventionally used antimalarial drugs namely Chloroquine (CQ) and Sulfadoxine-Pyrimethamine (SP) has led to the change of treatment policy in many endemic countries [10]. As a result, artemisinin-based combination therapies (ACT) have been widely adopted as first-line antimalarial treatments in Africa in the mid-2000s [10]. In Burkina Faso, a new malaria treatment policy was adopted in 2005: for uncomplicated falciparum malaria, artesunate-amodiaquine (ASAQ) or alternatively artemether-lumefantrine (AL) are recommended as first line treatments, whereas quinine is recommended for severe malaria [11]. This change followed a report demonstrating a high chloroquine resistance rate reaching the critical level of >25% over four consecutive years [12]. This history of drug resistance to the previous antimalarial drugs, and the potential for resistance to evolve to ACTs, demonstrate that up-to-date information on efficacy of antimalarial drugs is crucial to provide early warning of the development of resistance [13]. Here we report a review summarizing the history of the surveillance of drug resistance that led to the policy change in Burkina Faso. The lessons learnt could be useful to guide the current strategy for the surveillance of ACTs efficacy in Burkina Faso.

Study area

Burkina Faso is a landlocked country located in the heart of West Africa (Fig. 1). It covers 274,000 kilometers square (km^2) and stretches from north to south on 650 km and from East to West on 850 km. There are two main seasons (rainy and dry): the rainy season occurs from June to November (average rainfall: 700 mm/year; mean temperature >30°C) and it is followed by a cold dry season from December to February (minimum temperature 15°C) and a hot dry season from March to May (maximum temperature 45°C) [14]. According to the last national census carried out in 2010 the population was estimated at 15,730,977 inhabitants with a population growth rate estimated at 3.06% [15]. Like many developing countries, the economy is manly based on agriculture and farming [16]. The epidemiological profile of diseases remains dominated by communicable infectious diseases. Maternal mortality rate is 300 deaths/100,000 live births (2010) and infant mortality rate is 78.3 deaths/1,000 live births. Malaria represents the main public health problem and remains stable over the whole country, with the main transmission season occurring between June and December. The disease represents a significant burden on the population of Burkina Faso, but especially in pregnant women and

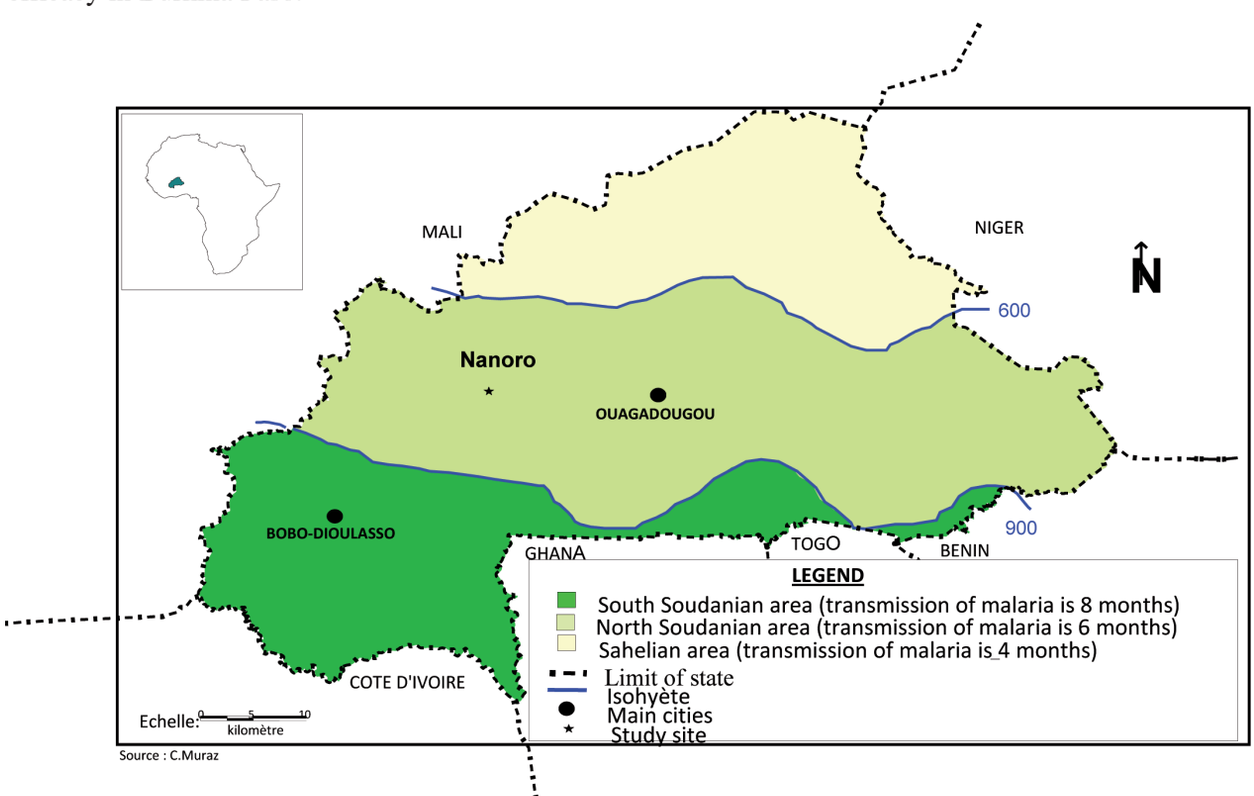

Fig. 1. Map of Burkina Faso highlighting the three main epidemiological settings

children. It is the first cause of consultation (35.12%), hospitalization (40.83%) and death (37.5%) (Ministry of Health [MoH]). Over the last few years, efforts were made to reduce the burden of malaria by providing artemisinin-based combinations treatments (ACTs) and the distribution of long-lasting insecticidal nets (LLINs). Nevertheless in 2010, Burkina Faso health facilities recorded 5,316,411 malaria cases, including 362,919 cases of severe malaria and 7436 deaths [15].

Literature search strategy

A literature search was conducted to identify documents reporting data and information on malaria drug resistance surveillance in Burkina Faso. Our search focused on the period from 1982–2004 and the drugs concerned were CQ and SP. All documents and reports (published and unpublished) available at the National Malaria Control Program (NMCP) level and research institutes were reviewed. A complementary electronic search was done on MEDLINE/PubMed. The key words used for the search were as follow: malaria, *Plasmodium falciparum*, epidemiology, Chloroquine, Sulfadoxine-Pyrimethamine, drug resistance, *in vivo* test, *in vitro* test, Burkina Faso.

Results

From the results of the search, the history of the drug resistance surveillance in Burkina Faso can be divided into three different periods: from 1982 to 1987 the surveillance was carried out by the former West Africa Malaria Resistance Reference Centre (WAMRRC) based at Centre Muraz in Bobo Dioulasso, Burkina Faso [17,18] and was exclusively based on active surveys. The WHO

Table 1. Results of the 7-day *in vivo* test with varying CQ dosage by village and year (period 1982–1987)

Year	Site (village)	Dose (mg/kg)	No. of parasites-positive patients n (%)		
			Day 0	Day 3	Day 7
1982	Bobo-Dioulasso (Nasso, Leguema)	5	82	0	0
		10	92	2 (2.2)	1(1)
Subtotal			**174**	**2 (1.1)**	**1 (0.5)**
1983	Koudougou	5	30	0	0
		10	56	1(1,7)	1(1,7)
		15	20	0	0
		20	24	0	0
		25	19	0	0
Subtotal			**149**	**1 (0.7)**	**1 (0.7)**
1984	Bobo-Dioulasso (Nasso)	5	30	0	0
		10	36	0	0
		25	63	0	0
Subtotal			**129**	**0**	**0**
1985	Bobo-Dioulasso (Leguema)	5	26	1 (3.8)	1 (3.8)
		10	22	2	0
Subtotal			**48**	**3 (6.2)**	**1 (2.1)**
1986	Bobo-Dioulasso (Vallée du Kou)	5	42	5 (11.9)	2 (4.8)
		38	6 (15.8)	2 (5.2)	2(5.2)
Subtotal			**80**	**11 (13.7)**	**4 (5)**
1987	Bobo-Dioulasso (Leguema)	5	35	0	0
	Ouagadougou (Koubri)	25	59	5 (8.5)	0
Subtotal			**94**	**5 (5.3)**	**0**
Total			**674**	**22 (3.3)**	**7 (1)**

Table 2. Results of 7-day *in vivo* test with 25 mg/kg of CQ by year (period 1988–1991)

	1988	1989	1990	1991	Total
No. of patients screened	3,109	4,396	6,763	3,242	17,510
No. enrolled at day 0	315	1,659	950	913	3,837
No. examined at day 7	236	1,363	512	894	3,005
No. of resistant cases	23	71	81	49	224
% resistance	9.7	5.2	15.8	5.5	7.5

standard seven-day test was used for CQ given at variable dosage of 5 mg/kg stat, 15 mg/kg over two days [19] or 25 mg/kg over a three-day period [20]. The second period of the surveillance occurred from 1988 to 1991 and has led to the discovery of the first case of *P. falciparum* chloroquine-resistance (CQ-R) at the standard dose of 25 mg/kg over three days. Finally, the last period of surveillance occurred from 1992 to 2004, just prior to the policy change.

Surveillance from 1982 to 1987. Table 1 summarizes the results of the *in vivo* tests carried out by the WAMRRC through active surveys in five sites and using different doses of CQ. Although some cases remained positive at day 7 with low doses of CQ (5, 10, 15 and 20 mg/kg), when the standard dose of 25 mg/kg over three days was administered, no cases of resistance were observed.

Surveillance from 1988 to 1991. Results of CQ *in vivo* tests (at 25 mg/kg over three days) conducted from 1988 to 1991 are summarized in Table 2. No further tests at lower doses were carried out. The first two cases of *in vivo* CQ-R at the standard dose of 25 mg/kg were detected in September 1988 in a series of 60 tests in a village near Ouagadougou [21]. The resistance appeared in five of the seven study sites. Since 1990, cases of resistance have been observed in all study sites [22]. CQ-R increased until about 16% in 1990 while the following year it was estimated at 5.5%. Higher resistance was observed in the site along the main railway linking the capital cities of Burkina Faso and Ivory Coast (Banfora, Bobo-Dioulasso, Koudougou and Ouagadougou). SP was also tested in 1990 in Bobo Dioulasso, when it was decided to use it as second-line treatment. Among 37 patients tested, two failed to clear their parasites.

Surveillance from 1992 to 2004. The high rate of CQ-R reported in 1990 was later confirmed *in vitro* [23,24]. In 1992, Del Nero et al., reported 24% of *in vivo* CQ-R in the center of the country [24], and it remained stable and varying between 15 and 25% until 2001 [14,25] (Table 3). However, from 2002 high CQ-R, reaching a rate of 40%, was reported over three consecutive years (2002 to 2004) in Nanoro, a sentinel site located in the center of the country [12].

After the two cases of SP resistance reported in 1990 and 1991, a third case was reported in 1997. Since that period, SP resistance was regularly reported every year until 2004, though the rate was relatively low at less than 10% [26].

Discussion

The first *P. falciparum* CQ-R strain identified in Burkina Faso was detected by an *in vitro* test carried out in Koudougou in 1983 [18]. This could be explained by the geographical situation of the latter which is located in the main route of communication between Ivory Coast and Burkina Faso. Indeed, CQ-R was first recorded in West Africa in coastal countries and then it followed the main routes of communication from Abidjan to Bouaké in Ivory Coast, Bobo Dioulasso and Ouagadougou in Burkina Faso and Bamako in Mali [27,28]. This led Charmot to suggest that travelers were responsible of the spread of resistant gametocytes (unpublished data). Nevertheless after this first case of resistance detected in 1983, no further cases were reported until 1987, suggesting that resistant strains had been circulating at a low prevalence before the beginning of the systematic surveillance system established from 1984 by the Ministry of Health [28]. The results presented here, suggest that *P. falciparum* was sensitive to CQ from 1982 to 1987. The few reported failures had been treated with low doses of CQ and responded successfully to the 25 mg/kg.

The marked increase of CQ-R reported in 2002-2003 as compared to previous years could be explained by the length of follow-up. Indeed, the follow-up duration was 7 or 14 days before 2002 and 28 days from 2002 onwards. Therefore, pre-2002 studies have probably under-estimated the real

Table 3. Results of *in vitro* and *in vivo* tests in Burkina Faso from 1992 to 2004

	Site	Epidemiological facies	Duration of follow-up	Parasitological failure %		Clinical failure %		Source
				CQ	SP	CQ	SP	
1992	Ouagadougou	Central area	14	24.4	0	–	–-	Del Nero et al. 1994
	Bobo-Dioulasso	South-west	14	32	0	–	–-	Coulibaly et al., 1996
1993	Bobo-Dioulasso	South-west	14	-	3.2	–	–	Aouba et al., 1992***
1994	***Not found***	***Not found***	***Not found***	***Not found***	***Not found***	***Not found***	***Not found***	–
1995	Bobo-Dioulasso	South-west	*In vitro* test	20	–	–	–	Ouedraogo et al., 1998
1996	Bobo-Dioulasso	South-west	*In vitro* test	19	–	–	–	Ouedraogo et al., 1998
1997	Bobo-Dioulasso	South-west	14	20	1.5	17	0	Ouedraogo et al.,997***
1998	Bobo-Dioulasso	South-west	14	–	–	22.2	2.6	Sanou et al., 2003***
1999	Koudougou	Central area	14	43.3	–	21.7	0	Tinto et al., 1999***
	Banfora	South-west	14	22.4	–	18.4	–	
	Bobo-Dioulasso	South-west	14	–	–	15.2	1.7	Sanou et al., 2003***
2000	Bobo-Dioulasso	South-west	14	–	–	28.5	5.7	Sanou et al., 2003***
2001	Bobo-Dioulasso	South-west	14	–	–	28.8	7.8	Sanou et al., 2003***
	Gaoua	South-west	14	5.3	6.3	5.3	6.3	Ouedraogo et al., 2001***
2002	Bobo-Dioulasso	South-west	14	27.3	–	21.7	–	Ouedraogo et al., 2001***
	Gaoua	South-west	14	18.7	–	8.3	–	
	Dori	Sahelian area	28	20*	–	13.4*	–	
	Nanoro	Central area	28	58.5*	–	35.1*	–	
2003	Bobo-Dioulasso	South–west	14	42.8	–	19	–	Ouedraogo et al., 2001***
	Gaoua	South–west	14	26.8	–	8.3	–	
	Dori	Sahelian area	28	–	–	18.7*	–	
	Nanoro	Central area	28	63.3*	–	33.3*	8.2**	
2004	Bobo-Dioulasso	South-west	28	–	–	–	11.5*	Ouedraogo et al., 2001***
	Gaoua	Sahelian area	28	–	–	–	8.1*	
	Dori	Central area	28	–	–	–	–	
	Nanoro	Sahelian area	28	–	–	–	21.8*	
	Gourcy	Central area	28	–	–	–	2.7*	
	Koupéla	South-west	28	–	–	–	23.5*	

*PCR uncorrected data ; ** PCR corrected data; ***unpublished data come mainly from students thesis or reports

prevalence of CQ-R by not detecting the late recrudescence [29]. The data collected in 2002–2003 are probably more representative of the true prevalence of resistance, both for CQ and SP. Indeed, an analysis achieved in 2003 showed significant differences between failures detected within the 14-day and 28-day follow-up [26]. However, with a rate of 8.2% (PCR corrected) treatment failure reported in 2003, SP was still efficacious for the treatment of uncomplicated malaria in Burkina Faso compared to the results reported from other African countries [30–32], while CQ-R has reached the critical level for change. Nevertheless, SP resistance might rapidly increase in the next few years as the result of its spreading from neighboring countries [33,34] and of high drug pressure, due to its current use for both the Intermittent Preventive Treatment in pregnant women (IPTp) and Seasonal Malaria Chemoprophylaxis (SMC) [35,36].

Sixteen potential sentinel sites representing the whole country have been identified by the NMCP for the surveillance of antimalarial drugs resistance. However, due to lack of resources only 3 are really active. The activation of the other 13 sites would have improved the applicability of the data collected.

Conclusions

We reviewed in this paper, the history of malaria drug resistance surveillance from the period of the establishment of the systematic surveillance system until the policy change in 2005. We observed a heterogeneous distribution of the resistance with the highest prevalence found in the center of the country. The current strategy for the surveillance of the ACT resistance should build on lessons learnt and positive accomplishments achieved under the previous period of 20 years surveillance of CQ and SP resistance (1994–2004). The most important aspect being to extend the number of sentinel sites so that data would be less patchy and could help understanding the dynamic of the resistance.

Acknowledgements

We are grateful to the Institute of Tropical Medicine, Belgium (FA3–DGCD program) for the financial support through a post-doc grant provided to Halidou Tinto for his research activities in Burkina Faso.

References

[1] WHO. World malaria report 2011. Geneva: WHO, 2011. 2011.

[2] Maude R.J., Pontavornpinyo W., Saralamba S., Aguas R., Yeung S., Dondorp A.M. et al. 2009. The last man standing is the most resistant: eliminating artemisinin-resistant malaria in Cambodia. *Malaria Journal* 8: 31. doi:10.1186/1475-2875-8-31.

[3] Rogers W.O., Sem R., Tero T., Chim P., Lim P., Muth S. et al. 2009. Failure of artesunate-mefloquine combination therapy for uncomplicated *Plasmodium falciparum* malaria in southern Cambodia. *Malaria Journal* 8: 10.

[4] Noedl H., Se Y., Sriwichai S., Schaecher K., Teja-Isavadharm P., Smith B. et al. 2010. Artemisinin resistance in Cambodia: a clinical trial designed to address an emerging problem in Southeast Asia. *Clinical Infectious Diseases* 51: e82-89. doi:10.1086/657120.

[5] Lim P., Alker A.P., Khim N., Shah N.K., Incardona S., Doung S. et al. 2009. Pfmdr1 copy number and arteminisin derivatives combination therapy failure in falciparum malaria in Cambodia. *Malaria Journal* 8: 11.

[6] Dondorp A.M., Nosten F., Yi P., Das D., Phyo A.P., Tarning J. et al. 2009. Artemisinin resistance in *Plasmodium falciparum* malaria. *New England Journal of Medicine* 361: 455-467. doi:10.1056/NEJMoa0808859.

[7] Beshir K.B., Sutherland C.J., Sawa P., Drakeley C.J., Okell L., Mweresa C.K. et al. 2013. Residual *Plasmodium falciparum p*arasitemia in Kenyan children after artemisinin-combination therapy is associated with increased transmission to mosquitoes and parasite recurrence. *Journal of Infectious Diseases* 208: 2017-2024. doi:10.1093/infdis/jit431.

[8] Borrmann S., Sasi P., Mwai L., Bashraheil M., Abdallah A., Muriithi S. et al. 2011. Declining responsiveness of *Plasmodium falciparum* infections to artemisinin-based combination treatments on the Kenyan coast. *PLoS One* 6: e26005. doi:10.1371/journal.pone.0026005.

[9] Gharbi M., Flegg J.A., Hubert V., Kendjo E., Metcalf J.E., Bertaux L. et al. 2013. Longitudinal study assessing the return of chloroquine susceptibility of *Plasmodium falciparum* in isolates from travellers returning from West and Central Africa, 2000-2011. *Malaria Journal* 2: 35. doi:10.1186/1475-2875-12-35.

[10] Mita T., Tanabe K. 2012. Evolution of *Plasmodium falciparum* drug resistance: Implications for the development and containment of artemisinin resistance. *Japanese Journal of Infectious Diseases* 65: 465-475. doi:10.7883/yoken.65.465.

[11] Gansané A., Nébié I., Soulama I., Tiono A., Diarra A., Konaté A.T. et al. 2009. Change of antimalarial first-line treatment in Burkina Faso in 2005. *Bulletin*

de la Société de Pathologie Exotique 1990 102: 31-35.

[12] Zongo I., Tinto H., Drabo K.M., Rouamba N., Guiguemdé T.R. 2005. Historique de la chloroquino résistance de 2001 à 2004 au Burkina Faso: les raisons d'un changement de la politique nationale de traitement du paludisme simple 30: 47-53.

[13] Sibley C.H., Guerin P.J., Ringwald P. 2010. Monitoring antimalarial resistance: launching a cooperative effort. *Trends in Parasitology* 26: 221-224.

[14] Tinto H., Zoungrana E.B., Coulibaly S.O., Ouedraogo J.B., Traoré M., Guiguemde T.R. et al. 2002. Chloroquine and sulphadoxine-pyrimethamine efficacy for uncomplicated malaria treatment and haematological recovery in children in Bobo-Dioulasso, Burkina Faso during a 3-year period 1998-2000. *Tropical Medicine and International Health* 7: 925-930. doi:10.1046/j.1365-3156.2002.00952.x.

[15] EDSBF-MICSIV 2012. Institut National de la Statistique et de la Démographie, Ouagadougou, Burkina Faso.

[16] Derra K., Rouamba E., Kazienga A., Ouedraogo S., Tahita M.C., Sorgho H. et al. 2012. Profile: Nanoro Health and Demographic Surveillance System. *International Journal of Epidemiology* 41:1293-1301. doi:10.1093/ije/dys159.

[17] Ouedraogo J.B., Guiguemde T.R., Somda A., Gbary A.R., Baudon D. 1987. Une méthode simplifiée de surveillance active de la chloroquinosensibilité de *Plasmodium falciparum* par les centres de santé périphériques. *Medecine d'Afrique Noire* 34: 711-717.

[18] Baudon D., Decouvoux Roux J., Sondo B. 1984. Etude de la sensibilité de *P. falciparum* ala chloroquine dans une savane de Haute-Volta apaludisme hyper-endémique: utilisation des tests in vivo et in vitro. *Bulletin de la Société de Pathologie Exotique* 77: 658-665.

[19] Payne D. 1982. Aspects pratiques des épreuves in vivo de la sensibilité des plasmodies humaines aux antipaludiques. WHO/MAL/82,1986, Genève.

[20] Baudon D., Guiguemde T.R., Ouedraogo J.B. 1987. Surveillance de la sensibilite de *Plasmodium falciparum* a la chloroquine en Afrique de l'Ouest: interet de l'utilisation de tests in vivo a 5 et 10 mg/kg. *Bulletin de la Société de Pathologie Exotique* 80: 469-476.

[21] Ouédraogo J.B., Lamizana L., Toe A.C.R., Kumilien S., Gbary A.R., Guigemdé T.R. et al. 1991. Emergence du Paludisme chimiorésistant au Burkina Faso. *Medecine d'Afrique Noire* 38.

[22] Ouédraogo J.B., Guiguemdé T.R., Gbary A.R. 1990. Surveillance passive de la chimiosensibilité palustre à Bobo-Dioulasso (Burkina Faso). *Medecine d'Afrique Noire* 37: 261-264.

[23] Ouédraogo J.B., Dutheil Y., Tinto H., Traoré B., Zampa H., Tall F. et al. 1998. In vitro sensitivity of *Plasmodium falciparum* to halofantrine compared with chloroquine, quinine and mefloquine in the region of Bobo-Dioulasso, Burkina Faso (West Africa). *Tropical Medicine and International Health* 3: 381-384.

[24] Del Nero L., Lamizana L., Pietra V., Nebié I. 1994. Sensitivity to antimalarial drugs by *Plasmodium falciparum* in Goundry, Oubritenga province, Burkina Faso. *Parassitologia* 36: 287-293.

[25] Tinto H., Sanou B., Erhart A., D'Alessandro U., Ouédraogo J.B., Guiguemdé T.R. 2006. [In vivo sensitivity of *Plasmodium falciparum* to chloroquine and sulfadoxine pyrimethamine in the Bobo Dioulasso region (1998-2001): risk factors associated with treatments failures to the two drugs]. *Bulletin de la Societe de Pathologie Exotique* 99:161-165 (in French).

[26] Tinto H., Ouédraogo J.B., Zongo I., van Overmeir C., van Marck E., Guiguemdé T.R. et al. 2007. Sulfadoxine-pyrimethamine efficacy and selection of *Plasmodium falciparum* DHFR mutations in Burkina Faso before its introduction as intermittent preventive treatment for pregnant women. *American Journal of Tropical Medicine and Hygiene* 76: 608-613.

[27] Guiguemdé T.R., Gbary A.R., Ouedraogo J.B., Gaybor A.., Lamizana L, Maïga A.S. et al. 1991. Point actuel sur la chimiorésistance du paludisme des sujets autochtones dans les états de l'OCCGE (Afrique de l'Oest). *Annales de la Societe Belge de Médecine Tropicale* 71: 199-207.

[28] Guiguemde T.R., Aouba A., Ouedraogo J.B., Lamizana L. 1994. Ten-year surveillance of drug-resistant malaria in Burkina Faso (1982-1991). *American Journal of Tropical Medicine and Hygiene* 50: 699-704.

[29] Stepniewska K., Taylor W.R., Mayxay M., Price R., Smithuis F., Guthmann J.P. et al. 2004. In vivo assessment of drug efficacy against *Plasmodium falciparum* malaria: duration of follow-up. *Antimicrobial Agents and Chemotherapy* 48: 4271-4280. doi:10.1128/AAC.48.11.4271-4280.2004.

[30] Curtis J., Duraisingh M.T., Trigg J.K., Mbwana H., Warhurst D.C., Curtis C.F. 1996. Direct evidence that asparagine at position 108 of the *Plasmodium falciparum* dihydrofolate reductase is involved in resistance to antifolate drugs in Tanzania. *Transactions of the Royal Society of Tropical Medicine and Hygiene* 90: 678-680. doi:10.1016/S0035-9203(96)90432-0.

[31] Deloron P., Mayombo J., Cardinal A.Le., Mezui-Me-Ndong J., Bruzi-Baert C., Lekoulou F. et al. 2000. Sulfadoxine-pyrimethamine for the treatment of *Plasmodium falciparum* malaria in Gabonese children. *Transactions of the Royal Society of Tropical Medicine and Hygiene* 94:188-190.

[32] Plowe C.V., Cortese J.F., Djimde A., Nwanyanwu

O.C., Watkins W.M., Winstanley P.A. et al. 1997. Mutations in *Plasmodium falciparum* dihydrofolate reductase and dihydropteroate synthase and epidemiologic patterns of pyrimethamine-sulfadoxine use and resistance. *Journal of Infectious Diseases* 176:1590-1596. doi:10.1086/514159.

[33] Driessen G.J.A., Van Kerkhoven S., Schouwenberg B.J.J.W., Bonsu G., Verhave J.P. 2002. Sulphadoxine /pyrimethamine: An appropriate first-line alternative for the treatment of uncomplicated falciparum malaria in Ghanaian children under 5 years of age. *Tropical Medicine and International Health* 7: 577-583.

[34] Henry M.C., Niangue J., Kone M. 2002. [Which medication should be used to treat uncomplicated malaria when chloroquine becomes ineffective in Western Cote d'Ivoire?]. *Medecine Tropicale* (Mars) 62: 55-57 (In French).

[35] World Health Organization. Seasonal malaria chemoprevention with sulfadoxine-pyrimethamine plus amodiaquine in children: A field guide 2013:1-56.

[36] Headquarters WHO. Technical Expert Group meeting on intermittent preventive treatment in pregnancy (IPTp) 2007:11-13.

Received 8 December 2015
Accepted 21 January 2016