Three case definitions of malaria and their effect on diagnosis, treatment and surveillance in Cox's Bazar district, Bangladesh

R.M. Montanari,[1] A.M. Bangali,[2] K.R. Talukder,[3] A. Baqui,[4] N.P. Maheswary,[5] A. Gosh,[6] M. Rahman,[7] & A.H. Mahmood[7]

Abstract In countries where malaria is endemic, routine blood slide examinations remain the major source of data for the public health surveillance system. This approach has become inadequate, however, as the public health emphasis has changed from surveillance of laboratory-confirmed malaria infections to the early detection and treatment of the disease. As a result, it has been advocated that the information collected about malaria be changed radically and should include the monitoring of morbidity and mortality, clinical practice and quality of care. To improve the early diagnosis and prompt treatment (EDPT) of malaria patients, three malaria case definitions (MCDs) were developed, with treatment and reporting guidelines, and used in all static health facilities of Cox's Bazar district, Bangladesh (population 1.5 million). The three MCDs were: uncomplicated malaria (UM); treatment failure malaria (TFM); and severe malaria (SM). The number of malaria deaths was also reported. This paper reviews the rationale and need for MCDs in malaria control programmes and presents an analysis of the integrated surveillance information collected during the three-year period, 1995–97. The combined analysis of slide-based and clinical data and their related indicators shows that blood slide analysis is no longer used to document fever episodes but to support EDPT, with priority given to SM and TFM patients. Data indicate a decrease in the overall positive predictive value of the three MCDs as malaria prevalence decreases. Hence the data quantify the extent to which the mainly clinical diagnosis of UM leads to over-diagnosis and over-treatment in changing epidemiological conditions. Also the new surveillance data show: a halving in the case fatality rate among SM cases (from 6% to 3.1%) attributable to improved quality of care, and a stable proportion of TFM cases (around 7%) against a defined population denominator. Changes implemented in the EDPT of malaria patients and in the surveillance system were based on existing staff capacity and routine reporting structures.

Keywords Malaria/diagnosis/therapy; Epidemiologic surveillance/methods; Practice guidelines; Outcome assessment (Health care); Bangladesh (*source: MeSH*).

Mots clés Paludisme/diagnostic/thérapeutique; Surveillance épidémiologique/méthodes; Ligne directrice pratique médicale; Evaluation résultats (Santé); Bangladesh (*source: INSERM*).

Palabras clave Paludismo/diagnóstico/terapia; Vigilancia epidemiológica/métodos; Pautas prácticas; Evaluación de resultado (Atención de salud); Bangladesh (*fuente: BIREME*).

Bulletin of the World Health Organization, 2001, **79**: 648–656.

Voir page 655 le résumé en français. En la página 655 figura un resumen en español.

Introduction

Since the inception of the global Malaria Eradication Programme in 1961, malaria blood slide results and related indicators have been at the centre of the malaria eradication strategy worldwide, and have

[1] Medical Officer (Epidemiologist) WHO Dhaka, Bangladesh, at time of study. Currently Public Health Specialist, ICRC Delegation, Bulevar Crvene Armije 144, 11000 Belgrade, Yugoslavia. Correspondence should be addressed to this author.

[2] ICOVED Project Director, Directorate General of Health Services, Ministry of Health and Family Welfare, Dhaka, Bangladesh.

[3] Deputy Director, Malaria & Parasitic Disease Control (M&PDC), Unit, Directorate General of Health Services, Ministry of Health and Family Welfare, Dhaka, Bangladesh.

[4] Civil Surgeon Cox's Bazar District Directorate General of Health Services, Ministry of Health and Family Welfare, Dhaka, Bangladesh.

[5] Senior Entomologist, M&PDC, Directorate General of Health Services, Ministry of Health and Family Welfare, Dhaka, Bangladesh.

[6] Medical Officer, Civil Surgeon's Office, Cox's Bazar District, Directorate General of Health Services, Ministry of Health and Family Welfare, Dhaka, Bangladesh.

[7] Medical Officer (Evaluator), M&PDC, Directorate General of Health Services, Ministry of Health and Family Welfare, Dhaka, Bangladesh.

Ref. No. **99-0206**

Table 1. **Laboratory-confirmed cases of malaria in Bangladesh, 1963–97**[a]

Year	Country population	Number of blood slides examined	ABER[b] (%)	No. of malaria positive slides	API[c]	SPR[d] (%)	Pf[e] (n)	SFR[f] (%)	Pf[g] (%)	Malaria deaths[h]	
										Susp.	Conf.
1963	1 895 000	86 345	4.56	402	0.21	0.47	89	1.10	22.14		
1964	8 962 000	474 569	5.30	756	0.08	0.16	279	0.06	36.90		
1965	12 035 000	975 918	8.11	649	0.05	0.07	85	0.01	13.10		
1966	21 203 000	1 715 771	8.09	3 137	0.16	0.20	357	0.02	10.39		
1967	26 874 000	2 485 901	9.25	4 080	0.15	0.16	1 702	0.07	41.72		
1968	47 002 000	2 988 322	6.36	6 244	0.13	0.21	3 069	0.10	49.15		
1969	59 444 000	4 880 511	8.21	7 871	0.13	0.16	2 575	0.05	32.72		
1970	62 810 000	6 107 144	9.72	6 660	0.11	0.11	3 307	0.05	49.65		
1971	63 570 000	2 212 660	3.48	2 944	0.05	0.13	1 556	0.07	52.85		
1972	65 220 000	5 311 988	8.14	18 384	0.28	0.35	6 397	0.12	34.80		
1973	69 288 000	3 259 190	4.70	14 007	0.20	0.43	8 023	0.25	57.28		
1974	71 565 000	1 884 109	2.63	15 855	0.22	0.84	10 726	0.57	67.65		
1975	72 730 000	2 929 935	4.03	31 247	0.43	1.07	19 510	0.67	62.44		
1976	73 930 000	3 537 269	4.78	48 844	0.66	1.38	28 408	0.80	58.16		
1977	76 395 000	1 414 731	1.85	29 673	0.39	2.10	12 923	0.91	43.55		
1978	78 916 000	1 391 055	1.76	33 326	0.42	2.40	6 717	0.48	20.16		
1979	81 520 000	1 374 104	1.69	49 776	0.61	3.62	10 408	0.76	20.91		
1980	84 210 000	2 634 773	3.13	67 717	0.80	2.57	22 184	0.84	32.76		
1981	88 100 000	2 338 853	2.65	45 902	0.52	1.96	15 375	0.66	33.50		
1982	90 300 000	2 808 765	3.11	46 781	0.52	1.67	19 059	0.68	40.74		
1983	92 200 000	2 516 110	2.73	42 529	0.46	1.69	17 546	0.70	41.26		
1984	94 300 000	2 552 513	2.71	32 977	0.35	1.29	14 876	0.58	45.11		
1985	96 400 000	2 823 028	2.93	31 050	0.32	1.10	16 211	0.57	52.21		
1986	98 000 000	2 685 529	2.74	93 128	0.40	1.46	21 064	0.78	53.83		
1987	99 800 000	2 771 577	2.78	35 848	0.36	1.29	20 472	0.74	57.11		
1988	101 500 000	2 704 563	2.66	33 824	0.33	1.25	21 565	0.80	63.76	15	14
1989	103 800 000	3 152 310	3.04	50 738	0.49	1.61	35 780	1.14	70.52	110	103
1990	106 100 000	2 444 415	2.30	53 875	0.51	2.20	34 061	1.39	63.22	67	60
1991	109 900 000	2 081 137	1.89	63 578	0.58	3.05	30 282	1.46	47.63	62	156
1992	112 100 000	1 919 349	1.71	115 660	1.03	6.03	51 775	2.70	44.76	69	378
1993	114 500 000	1 635 589	1.43	125 402	1.10	7.67	54 973	3.76	43.84	136	383
1994	117 000 000	1 661 701	1.42	166 564	1.63	10.0	81 015	4.88	48.63	582	696
1995	119 000 000	1 461 556	1.22	152 729	1.28	10.4	75 860	5.19	49.66	647	742
1996	120 000 000	1 146 736	1.00	100 864	1.00	8.80	54 307	4.73	53.84	50	447
1997	124 300 000	955 542	0.77	68 594	0.55	7.18	42 342	4.43	61.73	12	457

[a] Source: *22*. The country population figures for Bangladesh (column two) refer to mid-year estimates.

[b] ABER = Annual Blood Slide Examination Rate. The total number of blood slides examined annually, as a percentage of the country population.

[c] API = Annual Parasite Incidence. The number of malaria-positive slides per 1000 population.

[d] SPR = Slide Positivity Rate. Number of malaria-positive slides per 100 slides examined, expressed as a percentage.

[e] Pf = *Plasmodium falciparum* infections (including mixed *falciparum* and *vivax* infections)

[f] SFR = Slide Falciparum Rate. The number of *P. falciparum* positive slides per 100 slides examined, expressed as a percentage.

[g] Pf % = Pf Proportion (*P. falciparum* infections per hundred malaria-positive slides).

[h] Malaria deaths were categorized as ''Conf.'' when malaria was confirmed by laboratory results, and ''Susp.'' when laboratory results were not available.

been used to analyse the malaria situation in Bangladesh (Table 1). The justification for this approach came from the definition of epidemiological surveillance used in malaria eradication programmes as a series of epidemiological (and remedial) measures to achieve eradication. Epidemiological surveillance consisted of "the detection of cases through a screening mechanism of the whole population; the screening criterion is the presence of fever, which leads to the microscopic examination of the blood of *every* subject having fever or having recently had fever" (*1*). Cases with parasites in the blood were submitted to radical treatment. This was considered one remedial measure; the other was the administration of a single dose of chloroquine to all fever cases when taking blood samples. In 1969, the global malaria strategy changed from eradication to control, yet the surveillance practices of the malaria eradication era continue to be used in Bangladesh. Bangladesh is not unique in this respect. Following the Amsterdam Ministerial Conference in 1992 a change from specialized information systems to integrated ones was seen as essential, together with "a radical

redefinition of the information that should be collected" (*2*). In many instances, however, general health services continue to follow traditional eradication screening criteria, long after the eradication strategy has been abandoned (*3*).

Epidemiological surveillance has been subject to changes since 1950 when it was first proposed (*3*). Indeed, designing a new epidemiological surveillance system has been part of the effort to improve the Early Diagnosis and Prompt Treatment (EDPT) of malaria patients in areas where *Plasmodiun falciparum* is endemic. EDPT is the first priority technical element of the revised strategy for malaria control endorsed at the 1992 Amsterdam Ministerial Conference on Malaria. Epidemiological surveillance of a malaria control programme provides information on morbidity, mortality, drug consumption and efficacy of treatment, and the data can be used to plan, implement and monitor control measures. The success of control measures can be measured in terms of clinical outcomes with severe malaria (SM) and treatment failure malaria (TFM) cases, as well as in terms of the quality and coverage of the health services (*4, 5*).

Population, methods and materials

In Bangladesh, 64 districts are grouped into 5 administrative divisions. Cox's Bazar is one of 15 districts in the Chittagong division and is located in the south-eastern corner of the country. The district has a mostly rural, stable population of 1.5 million people (in 1997) and is divided into 7 major administrative units, or thanas, each with an average population of 227 000 people (*6*). Each of the seven thanas in Cox's Bazar has a Thana Health Complex (THC), which are named Chakaria, Moheshkhali, Ramu, Ukhiya, Teknaf, Sadar and Kutubdia THCs. The THCs include a hospital with laboratory facilities for examining malaria blood slides. A typical THC is a 31-bed institution with an expected complement of 9 doctors, 2 laboratory technicians, and field health assistants (on average one for every 2000–3000 people). The THCs provide daily multipurpose clinics to the catchment area population and act as first-line referral hospitals. Sadar THC is located in the urban district headquarters and acts as a malaria outpatient clinic, while a separate district hospital with a 100-bed capacity, provides both inpatient and outpatient services.

Chittagong division has the highest malaria disease burden in the country. In 1997 there were 42 342 laboratory-confirmed cases of *P. falciparum* in Bangladesh, and 96.9% of them occurred in Chittagong division (Table 1). Malaria in the district is defined as "malaria of forest fringe areas" (*7*), which is characterized by focal, unstable endemic malaria with transmission sustained by forest-related vectors (i.e. *Aedes dirus* and *A. minimus*). These vectors can expand their range under favourable conditions (such as during the monsoon season) and cause outbreaks of varying severity. *P. falciparum* is the predominant species that exhibits moderate chloroquine resistance.

Malaria case definitions

In 1993, WHO recognized the difficulty of diagnosing malaria when skilled microscopists were not available, and this led to the proposal of practical guidelines for the case management of patients with fever (*5*). The WHO study group on the implementation of the global plan of action for malaria control (1993–2000) stressed that the determination of patients' clinical histories, signs and symptoms is an acceptable basis for case management, and that this can produce effective and standardized medical care (*2*). In turn, this standardization can generate surveillance data.

During the last decade, different case definitions for malaria have been developed and tested, mainly in the context of sub-Saharan Africa. Despite the differences, however, the need to improve diagnosis under field conditions has been consistently emphasized by all these studies. Three approaches to defining a clinical case of malaria can be identified from available publications. In the first, algorithms group malaria with other common disease-specific clinical case definitions. This approach improves the recognition and treatment of common conditions in children through standard case management and is central to the development of the WHO Integrated Management of Childhood Illness strategy for preventing childhood mortality (*8–10*).

In a second approach, malaria in children (*11, 12*) or in all age groups (*13*) is defined by specific algorithms that group signs and symptoms of malaria. Attempts have also been made to include "self-diagnosis" by patients as a definition of malaria (*14*). The main objective of this approach is to use a standard clinical case definition of malaria to improve the rational use of antimalarial drugs and reduce wastage and over-treatment.

The third approach is to estimate the proportion of fever or symptomatic cases that are attributable to malaria, given defined cut-off values for parasite density in children (*15, 16*) and in different age groups that self-report malaria illnesses (*17*). The main objective is to elucidate the usefulness of simple diagnostic procedures, such as fever and self-reporting, as epidemiological tools for field trials and for malaria surveys in hyperendemic areas. Limited information is available about efforts to develop "clusters" of malaria case definitions that could differentiate between various clinical presentations and be used to improve the case management, laboratory confirmation and surveillance of malaria control programmes (*18, 19*).

Malaria case definitions in Bangladesh

During 1993–94, three preparatory workshops on *Malaria Case Definitions* (*MCD*), *their use for EDPT and Epidemiological Surveillance* were held in Chittagong and Cox's Bazar. As a result, three MCDs were proposed as outcome measures: uncomplicated malaria (UM), SM, and TFM. The definitions were based on clinical

criteria and were developed through a consensus process that included the faculty from the Chittagong Medical College Hospital, which acts as the main tertiary level referral institution for *P. falciparum* cases in eastern Bangladesh.

Initially, the MCDs were targeted at doctors and other medical personnel working in static health facilities. Reasons for this include the following.

- Government doctors play important roles as health care providers and opinion makers, in both the public and the private sectors.
- There is a need to develop the EDPT component in close collaboration with doctors from areas in which *P. falciparum* is endemic. This would promote appropriate care and a more rational use of drugs, and recognize the role of doctors as teachers and supervisors of field staff.
- The supervisory and surveillance systems at community level are inadequate, while it is widely recognized that the established Disease Profile Monthly Reporting form used in all static health facilities is the most reliable way of reporting MCDs.
- Clinical and laboratory practices need to be reconciled at static health facilities, where it is possible to match and validate clinical data with the results of malaria blood slide examinations.

Cox's Bazar district was chosen as a pilot district to field-test the new MCDs, starting in mid-1994. By the end of 1994, the doctors and health staff (including statistical clerks) in each of the THCs were being trained by staff from the Malaria and Parasitic Disease Control Unit, the Directorate General of Health Services, and the District Health Office (Civil Surgeon's Office). Materials developed during the three preparatory workshops were used. Also, between 1994 and 1997 more than 15 groups, each of 25 medical personnel, underwent a 5-day in-service training programme entitled "Diagnosis and management of severe and complicated falciparum malaria". The programme was held at the Chittagong Medical College Hospital and personnel were drawn from various districts, including Cox's Bazar. A module (*20*) and a practical handbook (*21*) were used in the programme, and training was supported by the medical personnel involved in developing the MCDs. Finally, all THC laboratory technicians were given in-service training using the WHO module on malaria microscopy.

In 1995, the three MCDs were approved as part of national guidelines for Revised Malaria Control Strategy in Bangladesh (*7*). This was followed, in 1997, by the publication of the training module, *Malaria diagnostic treatment and recording charts* (*22*), which was based on the experiences of Cox's Bazar Pilot Project. The module comes with two wall chart algorithms to carry the basic message into the workplace. A maximum of three days is required to complete the training programme, which is expected to be offered to all newly appointed doctors in areas where *P. falciparum* is endemic. An additional five days are required for training in the management of severe and complicated malaria (*20, 21*). The training module used (*22*) shows physicians how to exclude diseases other than malaria and reach a malaria diagnosis by default, according to the three malaria case definitions. Since 1997, efforts have been made to expand the use of the three MCDs to all areas in Bangladesh where *P. falciparum* is endemic by the end of 1999 (*23, 24*).

Reporting procedures, indicators and training

Based on the three MCDs, indicators were developed to monitor the monthly and yearly incidence and distribution of malaria cases at THC and district levels. The indicators are referred to as "rates" rather than "proportions," and the denominators of the indicators are either the catchment area population or the number of clinical malaria cases.

MCD data were collected routinely by local health staff as part of the Disease Profile Monthly Reporting Form, and forwarded from each THC to the district level. The form, which was normally used to record more than 30 common disease conditions, was amended to include the new MCDs and malaria deaths. Previously, only the total number of slide-positive malaria cases was reported. The new MCDs were integrated into the existing surveillance system and no increase in the number of reporting forms or procedures was instituted (*2, 7*). However, the present reporting does not allow for age or sex differentiation and additional efforts are required to achieve more discrimination in data collection.

Malaria blood slide examination results were reported on the existing Malaria Laboratory Reporting Form. However the rationale for slide collection has been changed. Active case detection, defined as "the process of case-finding by visiting at monthly intervals all houses in a designated area and taking blood specimens of any inhabitants who have, or have recently had, fever" (*25*), was discontinued in Cox's Bazar district in 1994; eventually, it will be phased out in all districts. Guidelines for the collection of blood smears from all cases identified through passive case detection, defined as "the finding of malaria cases through the notification by medical personnel to whom fever cases and other suspected cases are reported" (*25*), were also amended in the revised malaria control strategy (*7*). Emphasis is now placed on the need to collect blood slides from clinically diagnosed malaria patients only when the slide result can be of direct benefit to the EDPT of each case. Blood slides were collected according to the following priorities (*7, 24*):

1. all SM cases (to confirm the diagnosis and follow up);
2. all TFM cases (to confirm the diagnosis);
3. all admitted and very sick patients (for differential diagnosis);

4. UM cases only if the result is of direct benefit to the EDPT of the patient.

These guidelines have established a formal link between MCDs, which are used upon first contact with each patient, and the examination and reporting of malaria blood slides, which follows later. It is critical that the blood slide results are available as soon as possible, to confirm the clinical diagnosis and allow the patient to be treated appropriately. Ideally, blood slides should also be promptly examined for all UM cases; however, each THC is expected to prioritize blood slide collection and examination according to local needs and capacity.

Results

Annual countrywide results of malaria blood slide examinations for the 35-year period, 1963–97, are listed in Table 1, together with standard indicators from the malaria eradication era. The percentage of blood slides positive for malarial parasites (slide positivity rate, or SPR) was calculated using slides from all sources. During 1997, a total of 955 542 blood slides were examined, of which 68 594 were positive for malaria parasites (SPR = 7.2%). *P. falciparum* accounted for 42 342 (61.7%) of the malaria-positive cases. Annual SPRs increased markedly during the 1990s, mainly because active case detection practices have been gradually discontinued, which also makes yearly comparisons difficult.

Since 1992 the active case detection mechanism has been gradually discontinued in favour of passive case detection. This more discriminating activity has led to a relative increase in the proportion of positive slides found. For example, the national SPRs for slides collected by active case detection were 1.7% for 1992 and 0.8% for 1997. By comparison, the corresponding national values for slides collected by passive case detection were 19.0% and 15.3%, and the SPR for Cox's Bazar district was 20.2% in 1997 (Table 2). In this district, active case detection was fully discontinued in 1994 and blood slide collection and examination follow the new criteria outlined previously (*7*). The main reason for discontinuing the active case detection system was that the results of the blood slides only became available long after the patient had been clinically diagnosed and treated (*7*).

Also since 1992, renewed efforts have been made to improve the reporting of malaria deaths from static health facilities (Table 1). As a result, the number of "suspected malaria deaths" has dramatically decreased. The number of confirmed deaths has also decreased from the 1995 peak of 742 confirmed deaths to 457 deaths in 1997. No mortality figures are available prior to 1988.

Countrywide, between 1995 and 1997 a general decline in the number of reported cases, malaria deaths and overall malaria prevalence can be noticed with a 3% decline in the SPR. This decline can be explained in part by the non-reoccurrence of malaria outbreaks along the border area in the north-eastern part of the country (data not shown). The decrease in confirmed malaria deaths is also related to the fact that doctors working in those areas have been trained in the management of severe and complicated malaria (*21*). In addition, there was a decrease in the absolute number of slides examined and very few vector control measures for lack of insecticides (*23*). These last two factors are related to budget cuts and the gradual demise of traditional malaria control programme activities.

The epidemiological data for malaria in the Cox's Bazar district between 1995–97 are shown in Table 2. The data show that between 1995 and 1997 there was a 32% increase in the total number of patients being cared for annually. In 1997, each static health facility provided daily care to an average of more than 200 patients, with malaria patients accounting for 7% of the total. In 1997 the SPR was 34% lower than in 1995, but *P. falciparum* remained the predominant species and accounted for almost 60% of all laboratory-confirmed cases.

Five new rates were derived from the new set of data, based on the MCDs and the reporting of malaria deaths: the malaria rate (MR); UM; TFM; SM; and the case fatality (CF) rate. The new rates are shown in Table 2. The denominator of the CF rate is the total yearly number of SM cases, chosen to relate closely to clinical practice. In 1997, the MR and SM rate were 17.5% lower than in 1995, while the CF rate was 49% lower. During this period, the TFM rate remained stable above 7%. In 1997, the UM rate (83.3%) accounted for the majority of clinical cases.

Two ratios were used to compare the old and new reporting practices. The first ratio showed that in 1995, 2 slides were collected and examined for each reported MCD; in 1997, this ratio narrowed to 1.5 slides for each reported MCD. This indicates that even in 1997, up to one third of the blood slides examined were still not requested by clinicians treating malaria patients. The second ratio compared the total number of MCDs reported in a year to the total number of positive slides reported in the same year. In 1997, 3.32 MCDs were reported for every malaria-positive blood slide, compared to a value of 1.65 for 1995. The same data were used to calculate the positive predictive value (PPV) of the combined MCDs, using the number of positive slides reported as the true standard. Between 1995 and 1997, the PPV fell from 60.7% to 30.1%; the MR fell from 29.2 to 24.0 cases per 1000 population; and the SPR from 30.6% to 20.2% (Table 2). The decreasing PPV correlates well with a decreasing prevalence of malaria, it indicates that MCDs become less reliable as a diagnostic tool (i.e. over-diagnosis increases) when malaria is less. It can also be said, when considering that Cox's Bazar was a pilot district benefiting from special inputs and supervision, that the 30% decrease in the absolute number of blood slides collected and examined over the same period

reflects increased awareness among the health staff of the changing malaria epidemiological situation.

Discussion

Where *P. falciparum* is endemic in Bangladesh, as in other developing countries, the EDPT of malaria patients continues to rely on a mix of clinical and laboratory diagnostic skills. These skills are poorly coordinated and in short supply, with demand for malaria laboratory services and antimalarial drugs far outweighing available resources. In rural areas of Bangladesh, it is estimated that only 12% of patients with acute illnesses use government facilities (*6*). This is not uncommon in developing countries, because access to health care is often limited and traditional healers provide an alternative source of care throughout these countries. Also, the average consulting time (54 seconds), the proportion of adequate examinations (37%) and the availability of essential drugs (54%) at THCs are all unsatisfactory (*26*). Often, for example, only half the sanctioned posts at the THCs are filled with doctors in areas where falciparum malaria is endemic. There are several reasons for this, including high staff turnover, poor communication and working conditions, and lack of amenities and schools for family dependants. Consequently, to provide essential needs such as antimalarial drugs, the health system needs to be strengthened with more resources and become more efficient.

The surveillance data from Cox's Bazar district (Table 2) are on disease occurrences in populations (*5*). While trends from the malaria data analysed are consistent with each other, it should be noted that the parasitological and clinical data for each patient are recorded and reported separately at the THC level, with formal collation and analysis at the district level. The total number of slides collected annually exceeded the number of clinical cases by a factor ranging from 2 in 1995 to 1.5 in 1997. This indicates that many of the slides that are collected are not related to the EDPT of malaria patients. One explanation for this is that blood slides are taken for all fever episodes, in a practice dating from the malaria eradication era. The local population is used to this and may demand that slides be taken as a part of the "treatment" for malaria. Traditional healers may also refer patients to the government laboratory facility for the same reason. These individuals are likely to escape clinical reporting, while receiving some treatment before the slide result becomes available. Multiple blood slides are also taken to monitor SM and TFM cases, and severely ill patients with a diagnosis other than malaria, which would also contribute to the high ratio of slides taken per clinical malaria case. Nevertheless, the data in Table 2 show an encouraging trend between 1995 and 1997, with a 25% reduction in the ratio. This reduction indicates a shift to a surveillance system in which health care provision drives the demand for blood slide collection. More progress could reduce the ratio to a level approaching unity.

Table 2. **Epidemiological surveillance data for malaria in Cox's Bazar District, 1995–97**

Parameter	1995	1996	1997
Total population	1 383158	1 456 964	1 555 347
Total number of slides collected	80 141	79 225	55 976
Total number of malaria-positive slides slide positivity rate (SPR)	24 540 (30.6%)	22 577 (28.5%)	11 280 (20.15%)
Total number of slides positive for *P. falciparum* *P. falciparum* rate (PfR)	15 385 (62.7%)	12 686 (56.2%)	6 665 (59.1%)
Total number of patients (inpatients + outpatients)	467 337	565 200	618 052
Total number of malaria (TM) cases	40 437	46 326	37 463
Malaria rate (MR) (TM cases/ 1000 population)	29.2	31.8	24.0
Uncomplicated malaria (UM) cases UM rate (UM cases/TM cases, %)	32 835 (81.2%)	37 799 (81.6%)	31 214 (83.3%)
Severe malaria (SM) cases SM rate (SM cases/TM cases, %)	4 574 (11.3%)	5 389 (11.6%)	3 518 (9.4%)
Treatment failure malaria (TFM) cases TFM rate (TFM cases/TM cases, %)	3 028 (7.5%)	3 138 (6.8%)	2 731 (7.3%)
Total malaria deaths Case fatality rate (CFR) (CFR = Total malaria deaths/SM cases x 100)	278 (6%)	234 (4.3%)	110 (3.1%)
Ratio of TM cases to total slides collected	1.98	1.71	1.49
Ratio of TM cases to total number of malaria-positive slides	1.65	2.05	3.32
(Positive predictive value of the TM cases compared to the total number of malaria-positive slides as the true standard, expressed as a percentage[a])	(60.7%)	(48.7%)	(30.1%)

[a] Example: PPV for 1995 = $\frac{24\,540 \text{ positive slides} \times 100}{40\,437 \text{ TM cases}} = 60.7\%$

In reviewing the data, the main concern was to validate the case definitions (assuming adequate clinical skill), so as to ensure the most appropriate use of antimalarial drugs under field conditions. It has been recognized that the clinical diagnosis of malaria at the periphery needs to be improved, even though there is no absolute criterion to establish a definite diagnosis of malaria on clinical grounds alone, and it is likely that many patients continue to be treated inappropriately because of inadequate diagnosis and in order to save the lives of those at risk from untreated falciparum malaria (*2, 12, 27*).

In Table 2, a yearly Positive Predictive Value (PPV) combining the three MCD totals was calculated by taking the total number of laboratory-confirmed cases as the "true" standard. PPVs were calculated on the assumption that the blood slides positive for malaria were taken from the same patients reported under the three MCDs. This is likely

to be true in most cases, since the THC health staff were adequately trained. Nevertheless, the clinical diagnosis and recording precedes laboratory testing and recording, and both sets of data are subsequently reported separately and unmatched. As a result, the PPVs are likely to be an overestimation. Field-level training emphasizes that supervisors should check laboratory results against the SM, TFM and UM cases reported. If the cross-checking is poor and results are inconsistent, especially with TFM and SM cases, remedial action is required. Ideally, the sensitivity and specificity of each of the three MCD definitions needs to be tested to determine their value as a diagnostic test with changing prevalence of the disease. This would also help shed light on the proportion of missed "asymptomatic" malaria patients who would be classified as "false negative".

PPV rates halved between 1995 and 1997 (from 60.7% to 30.1%; Table 2), coinciding with a substantial decrease in malaria prevalence, while no major change in the incidence of other communicable diseases was reported (data not shown). The 1997 PPV is considered low but plausible, even if results are difficult to compare with similar findings (*11–14*). PPV rates also indicate that the number of patients unnecessarily treated increases as the prevalence of malaria decreases. For example, in 1997 more than three times as many patients were likely to have received antimalaria treatment as needed it, most commonly with UM clinically diagnosed cases. For example, compare the total number of malaria (TM) cases to the total number of positive slides (Table 2). It is important to measure overtreatment because of the spread of drug-resistant strains, and the rising cost of drugs, as more expensive alternatives to chloroquine become necessary (*11, 27, 28*).

The most striking finding of this study is that when MCDs were used to monitor disease outcomes the case fatality rate fell by half over the 3-year study period. We attribute this to the capacity-building effort deployed, which included training health staff in all static health facilities; improving supervision and referral; better case management (particularly the widespread introduction of quinine dihydrochloride, 10 mg salt/kg body weight, IV/IM); and adequate reporting of malaria deaths. It is also possible that the improved EDPT for malaria has made the overall delivery of health services more effective and reliable, and increased local appreciation for public health facilities. This would lead to an overall increase in demand for services, and indeed, no particular disease or condition contributed disproportionately to the increased number of patients.

The TFM diagnosis aims to identify patients who exhibit an inadequate response to a full treatment course over a period of one month. Malaria blood slide examination is always required to validate the case history and clinical assessment. Surveillance of TFM rates from all static health facilities allows trends in the efficacy of standard treatment regimens to be identified, as well as "TFM hot spot areas." Data generated from each THC also relate to a smaller, well-defined population denominator, from which a representative sample of malaria patients can be fully tested for therapeutic efficacy. While the overall district TFM rates did not change significantly (Table 2), a "TFM hot spot area" was identified in Ramu THC, where yearly TFM rates of 11.1%, 16.2% and 13.8% were reported during the 1995–97 period (*22*). These rates were the highest in the district. On account of these findings, therapeutic efficacy trials (*28*) have been carried out in Ramu THC.

Given the standard treatment regimens adopted[a] for the three MCDs, TFM cases include both chloroquine and sulfadoxine–pyrimethamine failure cases. While the majority of TFM cases reported refer to outpatients treated with chloroquine (data not shown), disaggregation of TFM data by treatment regimen or severity was considered too cumbersome to be included in the regular reporting. For this reason, local analysis of raw data at the THC level is emphasized during training (*22*). The case fatality, SM and TFM rates act as an early warning, and guide the Malaria and Parasitic Disease Control unit in monitoring therapeutic efficacy (*7, 27, 29*) and reviewing antimalarial drug policy. When TFM monitoring leads to appropriate treatment, it should reduce the risk of transmitting drug-resistant strains of *P. falciparum*.

The long-term sustainability and credibility of the new EDPT and surveillance strategy hinges on regular procurement and supply of essential antimalarial drugs, but no standard procedure for the collection of data on antimalarial drug procurement and supplies data has been established. At present, the procurement of antimalarial drugs is mainly the responsibility of the District Civil Surgeon's Office, which in the past has mainly used the number of positive malaria slides to estimate drugs and supplies requirements. We believe data from the new surveillance system need to be incorporated into the drug requisition plans for falciparum malaria-endemic areas and used to develop a policy for monitoring drug procurement and distribution. The new MCDs have shown their usefulness by improving the EDPT of malaria patients at the THC and district level and strengthening the overall health system. In turn, these changes should gradually modify the way malaria surveillance is defined at the national level (Table 1).

Successfully changing consolidated surveillance practices largely depends on the degree of adoption and utilization of the proposed changes by the primary beneficiaries or users. In our case, the new users have been identified as the health care

[a] The drug regimen for each MCD is as follows:
UM = Chloroquine tab./3 days plus primaquine tab. (single dose)/day 4.
TFM = Quinine tab. 3 times a day/3 days plus fansidar tab. (single dose)/day 3 and primaquine tab. (single dose)/day 4.
SM = Quinine IV/IM every 8–12 hrs until able to take quinine tab. orally 3 times a day/3–7 days plus fansidar tab. (single dose)/from day 3 and primaquine tab. (single dose)/from day 4.

providers in static health facilities at the THC and district levels. The fundamental change is to emphasize the surveillance of case management and disease outcomes, rather than emphasize malaria parasites and blood slide results. This means using data based on actual health care provision rather than laboratory services alone. Since 1961, malariologists have relied on a simple, all-encompassing case definition where "fever = malaria = blood slide". Slide-based reporting has continued to define malaria as a positive/negative outcome, even though blood slide data alone are no longer considered an adequate basis for surveillance. Surveillance data based on the EDPT approach is an attempt to define new ways to look at blood slide data in combination with clinical findings and develop local solutions for improving patient care, epidemiological surveillance and programme management. ■

Acknowledgements

This programme received support from the WHO Country Office (BAN/CTD/001 project). We are grateful to the health professionals in Cox's Bazar district who contributed to the activities reported in this paper. We are also grateful to Abul Fayez, Ridwanur Rahman, Emran Bin Yunus and Amir Hossain, from the Malaria Research Group in Chittagong, for their support in developing the MCDs and in training Cox's Bazar health personnel in diagnosing and managing severe and complicated falciparum malaria. We also thank Nurun Nabi, A.K. Shamsuddin Siddiquey and A.K.M. Nurul Anwar, of the Ministry of Health and Family Welfare, for their support.

Conflicts of interest: none declared

Résumé

Trois définitions de cas de paludisme et leur effet sur le diagnostic, le traitement et la surveillance dans le district de Cox's Bazar (Bangladesh)

Dans les pays où le paludisme est endémique, l'examen en routine des lames de sang demeure la principale source de données pour le système de surveillance de la santé publique. Cette approche est toutefois devenue insuffisante car on met désormais l'accent non plus sur la surveillance des infections palustres confirmées au laboratoire mais sur la détection et le traitement précoces de la maladie. Il a en conséquence été préconisé de modifier radicalement les informations recueillies sur le paludisme et de les faire porter sur la surveillance de la morbidité et de la mortalité, les pratiques cliniques et la qualité des soins. Afin d'améliorer le diagnostic et le traitement précoces des cas de paludisme, trois définitions de cas ont été élaborées, avec des indications pour le traitement et la notification, et appliquées dans tous les établissements de santé fixes du district de Cox's Bazar au Bangladesh (1,5 million d'habitants). Les trois définitions de cas concernaient le paludisme simple, l'échec thérapeutique et le paludisme grave. Le nombre de décès dus au paludisme a également été noté. Cet article examine la justification des définitions de cas et leur nécessité dans les programmes de lutte contre le paludisme et présente une analyse des informations de la surveillance intégrée recueillies sur la période de trois ans considérée, de 1995 à 1997. L'analyse conjointe des lames de sang et des données cliniques ainsi que de leurs indicateurs montre que l'examen des lames de sang n'est plus utilisé pour les investigations d'épisodes fébriles mais pour la détection précoce et le traitement immédiat des cas, en donnant la priorité aux cas de paludisme grave et d'échec thérapeutique. Les données indiquent une baisse de la valeur prédictive positive totale des trois définitions de cas à mesure que la prévalence du paludisme diminue. Elles permettent donc de chiffrer la façon dont le diagnostic essentiellement clinique du paludisme simple conduit à un surdiagnostic et à un surtraitement dans un contexte de conditions épidémiologiques changeantes. Les nouvelles données de la surveillance ont également montré une diminution de moitié du taux de létalité parmi les cas de paludisme grave (de 6 % à 3,1 %), qui peut être attribuée à l'amélioration de la qualité des soins, et une proportion stable des échecs thérapeutiques (environ 7 %) par rapport à une population définie. Les modifications intervenues au niveau de la détection et du traitement précoces des cas de paludisme et au niveau du système de surveillance ont été réalisées avec le personnel existant et en utilisant les structures de notification courantes.

Resumen

Tres definiciones de los casos de paludismo y su efecto en el diagnóstico, tratamiento y vigilancia en el distrito de Cox's Bazar (Bangladesh)

En los países con paludismo endémico, el examen sistemático de los frotis de sangre sigue siendo la principal fuente de información para el sistema de vigilancia de salud pública. Este enfoque se ha vuelto inadecuado, sin embargo, toda vez que el énfasis de la salud pública se ha desplazado de la vigilancia de las infecciones palúdicas confirmadas en el laboratorio a la detección y el tratamiento precoces de la enfermedad. Como consecuencia, se ha propuesto modificar radicalmente la información reunida sobre el paludismo para que incluya la vigilancia de la morbilidad y la mortalidad, la práctica clínica y la calidad de la asistencia. A fin de mejorar el diagnóstico precoz y el tratamiento inmediato (DPTI) de los enfermos de paludismo, se elaboraron tres

definiciones de casos de paludismo (DCP), con directrices para el tratamiento y la notificación, que fueron utilizadas en todos los servicios de salud estáticos del distrito de Cox's Bazar (Bangladesh) (1,5 millones de habitantes). Las tres DCP fueron las siguientes: paludismo no complicado (PNC), paludismo tratado infructuosamente (PTI), y paludismo grave (PG). Además, se notificó el número de defunciones por paludismo. En este artículo se examinan las razones y la necesidad de adoptar DCP en los programas de lucha antipalúdica y se presenta un análisis de la información de vigilancia integrada reunida durante el periodo de tres años considerado, 1995-1997. El examen combinado de los datos basados en los frotis y los datos clínicos y sus indicadores relacionados muestran que los análisis de los frotis sanguíneos ya no se usan para documentar los episodios de fiebre sino como apoyo del DPTI, dándose prioridad a los pacientes aquejados de PG y de PTI. Los datos muestran una disminución del valor predictivo positivo global de las tres DCP conforme disminuye la prevalencia de paludismo. Los datos permiten así cuantificar en qué medida el diagnóstico fundamentalmente clínico del PNC conduce al sobrediagnóstico y el sobretratamiento cuando cambia la situación epidemiológica. Los nuevos datos de vigilancia muestran asimismo una reducción a la mitad de la tasa de letalidad entre los casos de PG (del 6% al 3,1%), atribuible a la mejora de la calidad de la atención, y una proporción estable de los casos de PTI (en torno al 7%) respecto a una población definida. Los cambios introducidos en el DPTI de los enfermos de paludismo y en el sistema de vigilancia se basaron en el personal y los sistemas de notificación sistemática existentes.

References

1. **Pampana E.** *A text book of malaria eradication*, 2nd edition. London, Oxford University Press, 1969.
2. *Implementation of the global malaria control strategy: report of a WHO study group on the implementation of the global plan of action for malaria control, 1993–2000.* Geneva, World Health Organization, 1993 (WHO Technical Report Series, No. 839).
3. **Declich S, Carter AO.** Public health surveillance: historical origins, methods and evaluation. *Bulletin of the World Health Organization*, 1994, **72**: 285–304.
4. **Litsios S.** Which way for malaria control and epidemiological services? *World Health Forum*, 1993, **14**: 43–51.
5. *A global strategy for malaria control.* Geneva, World Health Organization, 1993.
6. *The dancing horizon. Human development prospects in Bangladesh.* Dhaka, Bangladesh, United Nations Development Programme, 1997.
7. *Guidelines for the implementation of the revised malaria control strategy in Bangladesh.* Country Working Group Proceedings, 10–13 December 1994. Kotbari, Comilla, Bangladesh, Malaria and Parasitic Disease Control Unit, Directorate General of Health Services, Ministry of Health and Family Welfare, 1995 (unpublished document).
8. **Redd SC et al.** Usefulness of clinical case-definitions in guiding therapy for African children with malaria or pneumonia. *Lancet*, 1992, **340**: 1140–1143.
9. **Weber MW et al.** Evaluation of an algorithm for the integrated management of childhood illness in an area with seasonal malaria in the Gambia. *Bulletin of the World Health Organization*, 1997, **75** (Supplement 1): 25–32.
10. **Perkins BA et al.** Evaluation of an algorithm for integrated management of childhood illness in an area of Kenya with high malaria transmission. *Bulletin of the World Health Organization*, 1997, **75** (Supplement 1): 33–42.
11. **Redd SC et al.** Clinical algorithm for treatment of *Plasmodium falciparum* malaria in children. *Lancet*, 1996, **347**: 223–227.
12. **Olaleye BO et al.** Clinical predictors of malaria in Gambian children with fever or history of fever. *Transactions of the Royal Society of Tropical Medicine and Hygiene*, 1998, **92**: 300–304.
13. **Bassett MT et al.** Clinical diagnosis of malaria: can we improve? *Journal of Tropical Medicine and Hygiene*, 1991, **94**: 65–69.
14. **Philipps J et al.** Clinical diagnosis of malaria: can the patients help us improve? – Short report. *Transactions of the Royal Society of Tropical Medicine and Hygiene*, 1996, **90**: 42.
15. **Armstrong Schellenberg JRM et al.** What is clinical malaria? Finding case definitions for field research in highly endemic areas. *Parasitology Today*, 1994, **10**: 439–443.
16. **Smith T, Armstrong Schellenberg JRM, Hayes R.** Attributable fraction estimates and case definitions for malaria in endemic areas. *Statistics in Medicine,* 1994, **13**: 2345–2358.
17. **Smith T et al.** Is fever a good sign for clinical malaria in surveys of endemic communities? *American Journal of Tropical Medicine and Hygiene*, 1995, **52**: 306–310.
18. **Montanari RM, Pyalalyia TR, Ake IN.** The malaria control programme in Papua New Guinea: epidemiological surveillance and a look into the future. *Papua New Guinea Medical Journal*, 1992, **35**: 233–242.
19. *The epidemiological approach to malaria control.* Geneva, World Health Organization, 1998 (Control of Tropical Diseases Division, unpublished document).
20. *The diagnosis and management of severe and complicated falciparum malaria.* Geneva, World Health Organization, 1995 (Control of Tropical Diseases Division, unpublished document).
21. **Gilles HM.** *Management of severe and complicated malaria: a practical handbook.* Geneva, World Health Organization, 1991.
22. *Malaria diagnostic treatment and recording charts. A training module for medical officers.* Trial Edition. Dhaka, Bangladesh, Malaria and Parasitic Disease Control Unit, Directorate General of Health Services, 1997 (unpublished document).
23. *Country report: Bangladesh.* Intercountry consultative meeting of national malaria control program managers, Chiang Mai, Thailand, 20–24 October 1997. Dhaka, Bangladesh, Malaria and Parasitic Disease Control Unit, Directorate General of Health Services, 1997 (unpublished document).
24. *Country report: Bangladesh.* Intercountry meeting of national malaria control program managers, Pattaya, Thailand, 22–27 February 1999. Dhaka, Bangladesh, Malaria and Parasitic Disease Control Unit, Directorate General of Health Services, 1999 (unpublished document).
25. *Terminology of malaria and of malaria eradication. Report of a drafting committee.* Geneva, World Health Organization, 1963.
26. **Guyon AB et al.** A baseline survey on use of drugs at the primary health care level in Bangladesh. *Bulletin of the World Health Organization*, 1994, **72**: 265–271.
27. *WHO Expert Committee on Malaria. Twentieth report.* Geneva, World Health Organization, 2000 (WHO Technical Report Series, No. 892).
28. **Shapira A, Beales PF, Halloran ME.** Malaria: living with drug resistance. *Parasitology Today*, 1993, **9**: 168–173.
29. *Assessment of therapeutic efficacy of antimalarial drugs for uncomplicated P. falciparum malaria.* Geneva, World Health Organization, 1997 (Control of Tropical Diseases Division, unpublished document).