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PRESCRIPTION PATTERNS OF ANTIMALARIAL DRUGS AMONG MEDICAL PRACTITIONERS IN OSOGBO METROPOLIS. SOUTH -WEST NIGERIA.

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Abstract.

Objective: In view of the increased prevalence of chloroquine resistance and the recent WHO malaria drug policy recommendation to use a combination of therapies especially artemisinin-based combination therapies (ACTs) in Africa, we tried to assess the prescription pattern and level of knowledge in the use of antimalarial drugs including ACTs among medical practitioners in Osogbo metropolis, southwest Nigeria, an endemic area of *Plasmodium falciparum* infection.

Method: Questionnaires were sent to every medical practitioner working in all the health facilities in the metropolis, namely, a teaching hospital, general hospital, mission hospital, comprehensive health centre and 20 privately owned health facilities. Of the total of 100 questionnaires sent out, 96 were completed and returned while the remaining 4 were not returned. The questionnaires were self-administered.

Result: Sixty-seven percent of the respondents work in the teaching hospital, while the remaining 33% either work in the general hospital or in private medical practice. 82.4% prescribed chloroquine despite the widespread resistance, indicating that this remains the most prescribed antimalarial drug. 45.7% apply the dosage regimen correctly (χ^2 P<0.005); 66.7% prefer the use of chloroquine injection; 85.6% give chlorpheniramine with chloroquine because of pruritus; 14.4% give it because of its synergistic and reversal mechanism. Other commonly prescribed drugs include sulphadoxine-pyrimethamine (71.1%), halofantrine (53.6%), amodiaquine and quinine (51.1%), mefloquine (20.6%), artemisinin or ACTs (18.6%) and co-trimoxazole (17.5%). Of these, the dosage regimen was applied correctly for: sulphadoxine-pyrimethamine (30.9%), halofantrine (12.8%), amodiaquine (3.2%), co-trimoxazole (2.1%), ACTs, quinine and artemisinin monotherapy (1.1%). About 40% of practitioners prefer the use of combination therapy in the future.

Conclusion: There is an obvious paucity of knowledge on the prescription of antimalarial drugs. The proportion of practitioners anticipating the use of combination therapy in the future indicates that with continued medical education the use of combination therapies especially ACTs will be accepted easily.

Key words: Antimalarial drugs, Prescription pattern, Medical practitioners, Osogbo.

INTRODUCTION

Malaria is the second leading health problem in Sub-Saharan Africa. It accounts for more than one million

deaths every year in the region, with about 5% of children under 5 years dying from malaria related illnesses. [1] Therefore, early diagnosis as well as prompt, accurate and effective treatment are principal technical components of

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the global strategy to control this endemic disease. [2]

The rational use of an effective antimalarial drug will not only reduce the risk of severe disease and death but also shorten the duration of the illness, increase man-hour effectiveness help to slow down the development of parasite resistance to antimalarial drugs. It will also prevent misdiagnosis of resistance to antimalarial drugs and over-diagnosis of typhoid infection.

The emergence of and rapid spread of *Plasmodium falciparum* resistance to the first-line antimalarial drug chloroquine in Sub-Saharan Africa has led to the production of several other antimalarial drugs for both monotherapy and combination therapy. Although slightly more expensive, these are available but are not often considered for use in cases of failure to chloroquine, the first-line antimalarial drug in Nigeria. As a response to increasing levels of antimalarial resistance, however, WHO recommends that all countries experiencing resistance to conventional monotherapies such as chloroquine, amodiaquine, and sulphadoxine/pyrimethamine should use combination therapies, preferably those containing artemisinin derivatives (ACTs) for *falciparum* malaria. This has led to increased enthusiasm and pressure on African governments by WHO to move quickly in adopting the use of ACTs in malaria control programs on the continent. [3]

Gradually, several countries are adopting the use of ACTs as first-line malaria chemotherapeutic agents. South Africa adopted artesunate/lumefantrine combination for KwaZulu Natal and Zanzibar adopted artesunate/amodiaquine. [4] Recently in Nigeria, the pressure to change antimalarial drug policy to ACTs is also on the increase.

The low level of education and utilization of these various alternatives prompted our determination to embark on this study to:

1. Assess the level of knowledge of medical practitioners on malarial infection and the available chemotherapeutic approaches.
2. Assess the level of knowledge about dosage regimens and the commonly prescribed antimalarial drugs.
3. Assess the acceptability of combination therapies as a new strategy in combating the development of resistance in *Plasmodium falciparum*.

The objective therefore is to plan an appropriate intervention approach in terms of continuous medical education on new malaria management strategies, especially in areas of high resource constraints such as Sub-Saharan Africa, where the lack of resources has contributed to the continued use of drugs whose effectiveness has been compromised by drug resistance. [5]

MATERIALS AND METHODS

After an ethical approval from a joint university/teaching hospital ethic review committee the study was commenced using semi-structured self-administered questionnaires to interview a total of one hundred medical practitioners working in health facilities situated within Osogbo metropolis between June and August 2004. These health facilities are a teaching hospital, general hospital, mission hospital, comprehensive health centre and 20 private medical practices. The correctness of prescription was assessed using the WHO dosage regimen found in the report on an informal consultation on the use of antimalarial drugs (13-17 November 2000) as a reference for correct dosage regimen prescription.

STATISTICAL ANALYSIS

The statistical package used for data entry and analysis was SPSS version 7.5. Significance was determined using chi-square test for data above five and Fisher's Exact Test for data below five at $P < 0.05$.

RESULTS

Out of 100 questionnaires, 96 were completed and returned while 4 were not returned. The status of the respondents showed that 71 (74%) have basic qualification and are working as residents or general medical practitioners in health institutions, while 25 (26%) have postgraduate fellowship in different specialties in addition to their basic qualification.

The symptoms seen by the respondents include: fever (93%), vomiting and headache (92%), body pains (86%), rigours and chills (85%), abdominal pains (28%), diarrhoea (27%), stuffy or running nose (13%), pruritus (13%), and cough (9%).

Twenty-five (26.0%) always request an investigation before writing a prescription, 45 (46.9%) prescribe drugs without an investigation, while 26 (27.1%) only investigate after a failed initial prescription. ($P < 0.05$).

Eighty-two (85%) prescribed chloroquine as a first-line antimalarial drug, despite the widespread resistance. Of the 45 (46.9%) who prescribed it correctly, 40 (89%) are residents or general medical practitioners while 5 (11%) have postgraduate fellowship. ($P < 0.001$). Of the 51 (53.1%) who prescribed the drug incorrectly, 31 (61%) are residents or general medical practitioners while 20 (39%) had postgraduate fellowship ($P < 0.002$). Table II

Sixty-four (66.7%) give chloroquine by as injection, while 32 (33.3%) prefer oral tablets. The frequency of

Table I: The antimalarial drugs available in the region and the proportion of respondents that prescribe each of these drugs.

	CQ	S-P	HF	QN	AQ	ASU	MXP	FMF	CTM	CXZ	MQ
% of prescribers.	82 (85.4%)	68 (70.1%)	52 (53.6%)	49 (51.1%)	49 (51.1%)	36 (37.1%)	27 (28.8%)	19 (20.6%)	17 (18.6%)	16 (17.5%)	14 (15.5%)

CQ=chloroquine: S-P=sulphadoxine-pyrimethamine: HF=halofantrine: QN=quinine: AQ=amodiaquine: ASU=artesunate: MXP=sulphamethoxazole-pyrimethamine: FMF=sulphadoxine-pyrimethamine/mefloquine: CTM=artemether/lumefantrine: CXZ=co-trimoxazole: MQ=mefloquine.

chloroquine injection varies: daily for 3 days (15.6%), 8 hourly for 24 hours (10.4%), 6 hourly for 48 hours (6.3%), 12 hourly for 60 hours (6.2%), 6 hourly for 36 hours (4.2%) and 8 hourly for 60 hours (2.1%).

Eighty-three (85.4%) routinely prescribe antihistamines along with chloroquine to prevent pruritus associated with chloroquine therapy, while 13 (14.6%) do not give antihistamines because of the reversal of chloroquine resistance in *Plasmodium falciparum* parasite.

Sixty-eight (71.1%) prescribed sulphadoxine-pyrimethamine as a second-line antimalarial drug. Of the 30 (31.3%) who prescribed correctly, 23 (76.6%) are residents or general medical practitioners and 7 (23.4%) have postgraduate fellowship. Of the 66 (69.7%) who prescribed incorrectly, 48 (72.7%) are residents or general medical practitioners and 18 (27.3%) have postgraduate fellowship.

Of the 52 (53.6%) prescribed halofantrine, 13 (13.5%) prescribed correctly, 10 (76.9%) are residents or general medical practitioners, while 3 (23.1%) have postgraduate fellowship. Of the 83 (86.5%) who prescribed incorrectly, 61 (73.5%) are residents or general medical practitioners while 22 (26.5%) have postgraduate fellowship.

Forty-nine (51.1%) prescribed amodiaquine and quinine. Three (3.1%) prescribed correctly for amodiaquine, 2 being residents or general medical practitioner and 1 having postgraduate fellowship. Of the 93 (96.9%) prescribed incorrectly, 69 (74.2%) are residents or general medical practitioners, and 24 (25.8%) had postgraduate fellowship.

Other prescriptions are: artesunate 36 (37.1%), sulphamethoxazole-pyrimethamine 27 (28.8%),

sulphadoxine-pyrimethamine/mefloquine 19 (20.6%) artemether/lumefantrine (ACTs) 17 (18.6%), co-trimoxazole 16 (17.2%) and mefloquine 14 (15.5%). The proportion of correct prescription is: sulphadoxine-pyrimethamine/mefloquine (3.1%), co-trimoxazole (2%), artemisinin (1%), artemether/lumefantrine (1%), and mefloquine (0%). Table II

Forty-nine (51%) readily give antibiotics after a failed first prescription, namely, amoxicillin (29%), co-trimoxazole (10%), ciprofloxacin (8%), chloramphenicol (5%), erythromycin (8%), tetracycline (5.2%), and benzylpenicillin (4%).

Antimalarial drugs prescribed after chloroquine failures are: sulphadoxine-pyrimethamine/mefloquine (62.1%), co-trimoxazole (55.5%), artemether/lumefantrine (27.3%), artesunate (24.0%), quinine (20.0%), halofantrine (12.5%), amodiaquine (11.3%) and sulphadoxine-pyrimethamine (10.3%).

Thirty-three (34.9%) give combination therapy, while 63 (65.1%) do not. The following combinations are preferred: amodiaquine/sulphadoxine-pyrimethamine (14.4%), chloroquine/sulphadoxine-pyrimethamine (11.4%), quinine/sulphadoxine-pyrimethamine (7.3%), chloroquine/co-trimoxazole (4.1%), mefloquine / sulphadoxine-pyrimethamine (2.1%), and mefloquine/artesunate (1%).

Forty (41.7%) advised on the use of combination therapy in the future, while 36 (37.5%) advised against it, with 20 (21.8%) not responding. The main reason cited for the use of combination therapy was for treatment of chloroquine resistant strains of *Plasmodium falciparum*.

Table II: The proportion of respondents with correct prescription pattern of all the antimalarial drugs available for common use in Osogbo metropolis, Southwest, Nigeria using WHO dosage regimen of November 2000 as reference.

	CQ	S-P	HF	QN	AQ	ASU	MXP	FMF	CTM	CXZ	MQ
M.B., B.S. Degree + postgraduate N=25	5 (20.0%)	7 (28.0%)	3 (12.0%)	1 (4.0%)	1 (4.0%)	0	0	0	0	0	0
M.B., B.S. Degree only. N=71	40 (56.3%)	23 (32.4%)	10 (14.1%)	0	2 (2.8%)	1 (1.4%)	9 (12.7%)	3 (4.2%)	1 (1.4%)	2 (2.8%)	0
Total no of respondents. N=96	45 (46.9%)	30 (31.3%)	13 (13.5%)	1 (1.0%)	3 (3.1%)	1 (1.0%)	9 (9.4%)	3 (3.1%)	1 (1.0%)	2 (2.8%)	0
P-Value	<0.001	>0.05	>0.05	>0.05	>0.05	>0.05	>0.05	>0.05	>0.05	>0.05	
Chi-square- Value	9.804	0.166	0.069	0.451	0.850	0.356	3.497	1.090	0.356	0.719	
Df	1	1	1	1	1	1	1	1	1	1	
Fisher's Exact test	0.002	0.444	0.547	0.691	0.600	0.740	0.126	0.400	0.740	0.524	

CQ=chloroquine: S-P=sulphadoxine-pyrimethamine: HF=halofantrine: QN=quinine: AQ=amodiaquine: ASU=artesunate: MXP=sulphamethoxazole-pyrimethamine: FMF=sulphadoxine-pyrimethamine/mefloquine: CTM=artemether/lumefantrine: CXZ=co-trimoxazole: MQ=mefloquine.

DISCUSSION AND CONCLUSION

The use of questionnaires to determine the prescription patterns and level of knowledge among medical practitioners in Osogbo metropolis provides the opportunity to critically appraise factors directly or remotely connected with the development of resistance to chemotherapeutic agents in *Plasmodium falciparum*.

Less than fifty percent had sufficient knowledge of the dosage regimen of common antimalarial drugs chloroquine and sulphadoxine-pyrimethamine. Among these, the residents and general medical practitioners showed better prescribing practices than those with postgraduate fellowship. Malaria is an endemic disease; therefore every medical practitioner regardless of area of specialty should be able to correctly prescribe commonly used antimalarial drugs. This finding was inconsistent with from the findings of A.Djimde where all the sanctioned providers prescribed correct dosage regimens for the recommended drugs, i.e. chloroquine and sulphadoxine-pyrimethamine, according to the National Malaria Control Program and World Health Organisation. [6]

The majority of respondents in our survey do not make use of the laboratory in malaria diagnosis. This often led to misdiagnosis of *falciparum* infection or over diagnosis of typhoid infection. The habit of requesting laboratory investigation to confirm *falciparum* infection after an initial failed prescription often contributed to resistance development because of exposure of the *Plasmodium* parasite to drug pressure. The failure to request laboratory investigation often led to misdiagnosis because the majority of cases are usually viral or bacteria upper respiratory tract infections. (*Ogunbamigbe TO, Ojuroungbe O. unpublished data*)

The use of chloroquine injection to treat cases of acute *falciparum* infection is still on the increase despite a serious campaign against it, as shown by the fact that more than two-thirds of the respondents readily prescribe chloroquine by intramuscular injection. The erratic pharmacokinetic profile of chloroquine resulting from this frequent administration at sub-therapeutic dosages has increased the level of resistance. [7]

Most of the respondents give chlorpheniramine, an H₁-receptor antagonist for the prevention of pruritus, in patients with or without history of allergy to the drug. The regular use of this drug has helped inadvertently to promote to a significant degree the susceptibility of *Plasmodium falciparum* to chloroquine because of its advantage in causing a reversal of resistance to chloroquine. [8, 9] (*Ogunbamigbe et al in the press*).

There is a general lack of adequate knowledge as to

the dosage regimen of the other antimalarial drugs, and this has affected the percentage of prescribers of these drugs, especially the newly introduced ACTs. Less than a quarter of practitioners prefer to use two different antimalarial drugs as combinations, with amodiaquine / sulphadoxine-pyrimethamine ranking highest. Others are: combination of chloroquine, or quinine, or mefloquine with sulphadoxine-pyrimethamine, and mefloquine / artesunate.

These combinations underscore the fact that the basic principle of combination therapy is not well understood, since the majority favour combinations of drugs to which resistance has already developed and those to which resistance is reportedly on the increase. [10]

It is worthy of note, however, that a fairly large number expressed the intention to use combination therapy in the future. This clearly shows that with continued medical education and training it will be possible to improve the prescription pattern, especially with regard to the use of ACTs and other antimalarials in our health institutions.

In conclusion, we observed a general paucity of knowledge about the dosages of various antimalarial drugs, especially chloroquine, as recommended by the National Malaria Control Program and World Health Organization. This may have contributed to the recent increase in chloroquine resistant *Plasmodium falciparum* infection in the region.

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**A SURVEY OF PRESCRIPTION PATTERN OF ANTI-MALARIAL DRUGS AMONG
MEDICAL PRACTITIONERS IN OSOGBO, SOUTHWEST NIGERIA.
QUESTIONNAIRES.**

IDNUM.....

- | | |
|--|----|
| 1. Location i.e Town | |
| 2. Area of Practice | |
| Private Medical Practice | 1 |
| Teaching Hospital | 2 |
| General Hospital | 3 |
| Comprehensive Health Centre. | 4 |
| Others specify | |
| 3. Qualifications | |
| 4. Area of Specialty | |
| General | 1 |
| Surgery | 2 |
| Internal Medicine | 3 |
| Other Specialties Specify | 4 |
| 5. Symptoms of Malaria that are commonly presented in your practice include | |
| (a) Headache | 1 |
| (b) Fever | 2 |
| (c) Chills and rigors | 3 |
| (d) Abdominal pains or cramps | 4 |
| (e) General body pains | 5 |
| (f) Stuffy / running nose | 6 |
| (g) Cough | 7 |
| (h) Pruritus | 8 |
| (i) Vomiting | 9 |
| (j) Diarrhea | 10 |
| 6. What are the common drugs that you will readily prescribe for the treatment of malaria in order of preference using figures 1, 2, 3, e.t.c? | |
| (a) Chloroquine | 1 |
| (b) Amodiaquine (Camoquin) | 2 |
| (c) Halofantrine (Halfan) | 3 |
| (d) Pyrimethamine/ sulphadoxine (Fansidar) | 4 |
| (e) Pyrimethamine/ sulphamethoxazole (Malozone) | 5 |
| (f) Artesunate | 6 |
| (g) Quinine | 7 |
| (h) Trimethoprim/ sulphadoxine (Septrin) | 8 |
| (i) Artemether / Lumefantrine (Coartem)..... | 9 |
| (j) Mefloquine (Lariam) | 10 |
| (k) Mefloquine / Pyrimethamine / sulphadoxine (Fansimef) | 11 |
| (l) Others Specify | 12 |
| 7. If you choose to use (a) and Or (b) above, do you give anti-histamines like | |
| (a) Chlorpheniramine (piriton) | 1 |
| (b) Promethazine (phenergan) | 2 |
| (c) Mepyramine (Antisan) | 3 |
| (d) Any other antihistamine Specify | 4 |
| 8. What in your opinion is the rationale for the above prescription? | |
| (a) To prevent Pruritus | 1 |
| (b) It is routinely used by other practitioners | 2 |
| (c) Do you also give routinely | 3 |
| (d) Because of its reversal properties | 4 |
| (e) Because of its synergistic effect | 5 |
| (f) Any other reason Specify | 6 |

9. The usual dosage you normally prescribe for suspected cases of malaria in mg/kg/day
- (a) Chloroquine
 - (a) Amodiaquine (Camoquin)
 - (b) Halofantrine (Halfan)
 - (c) Pyrimethamine/ sulphadoxine (fansidar)
 - (d) Pyrimethamine/ sulphamethoxazole (Malozone)
 - (e) Artesunate
 - (f) Quinine
 - (g) Trimethoprim/ sulphadoxine (Septrin)
 - (h) Artemether / Lumefantrine (Coartem)
 - (i) Mefloquine (Lariam)
 - (j) Mefloquine / Pyrimethamine / sulphadoxine (Fansimef)
10. Would you prefer to give injections if you are prescribing Chloroquine? Yes 1
No 2
11. How often do you prescribe the injection?
- (a) Daily for 3 days 1
 - (b) 8 hourly for 24 hours 2
 - (c) 6 hourly for 48 hours 3
 - (d) 6 hourly for 36 hours 4
 - (e) Others specify5
12. If prescribing other antimalarial drugs, do you prefer injections to tablets- Yes 1
No 2
13. If yes, how often for each of the drug mentioned below. Using the following answer for each of the drug you commonly prescribe?
- (a) Always 1
 - (b) Not at all 2
 - (c) Occasionally 3
 - (d) After a failed first prescription 4
 - (e) Any other response state5
 - Amodiaquine (Camoquin)(1,2,3,4,5)
 - Halofantrine (Halfan)(1,2,3,4,5)
 - Pyrimethamine / sulphadoxine (fansidar)(1,2,3,4,5)
 - Pyrimethamine / sulphamethoxazole (Malozone)(1,2,3,4,5)
 - Artesunate(1,2,3,4,5)
 - Quinine(1,2,3,4,5)
 - Trimethoprim / sulphadoxine (Septrin)(1,2,3,4,5)
 - Artemether / Lumefantrine (Coartem)(1,2,3,4,5)
 - Mefloquine (Lariam)(1,2,3,4,5)
 - Mefloquine / Pyrimethamine / sulphadoxine (Fansimef)(1,2,3,4,5)
14. How often do you request for laboratory investigation before prescribing Antimalarial drugs?
- (e) Always 1
 - (f) Not at all 2
 - (g) Occasionally 3
 - (h) After a failed first prescription 4
 - (i) Any other response state5
14. Do you have to prescribe antibiotics alongside with your antimalarial drugs?
- (a) Always 1
 - (b) Not at all 2
 - (c) Occasionally 3
 - (d) After a failed first prescription 4
 - (e) Any other response- state5
15. Which of the following groups of antibiotics would you have readily prescribed If your answer is any other than (b) above.
- (a) Amoxicillin / any Penicillin 1

- (b) Chloramphenicol 2
(c) Ciprofloxacin 3
(d) Erythromycin 4
(e) Septrin 5
(f) Others Specify6
16. Is it in your practice to give two different antimalarial drugs together while treating Malaria?Yes 1
No 2
17. If yes, how often?
(a) Always 1
(b) Occasionally 2
(c) After a failed first prescription 3
(d) Any other response specify4
18. Do you prefer specific combination, state them
19. Based on your experience would you advice combinations in future? Yes 1
No 2
20. If yes, why? State reasons

DISCOVERY OF TWO MORE NEW SPECIES OF *SIMULIUM* (*MONTISIMULIUM*) (DIPTERA: SIMULIIDAE) IN DOI INTHANON NATIONAL PARK, CHIANG MAI, THAILAND

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Accepted 17, November, 2005

Abstract: Two more new black-fly species of the rare subgenus *Simulium* (*Montisimulium*) were discovered in Doi Inthanon National Park, Chiang Mai, Thailand, where *S. (M.) merga* Takaoka and Choochote was known as the only named species. These two new species, *S. (M.) angkaense* sp. nov. and *S. (M.) laoleense* sp. nov., are described on the basis of the pupal and/or mature larvae. Both new species are easily distinguished from *S. (M.) merga* by the pupal gill with 12 slender filaments, and from all the 16 known species with 12 pupal gill filaments in other countries by the long and very long common basal stalk of the gill, respectively.

Key words: black fly, Simuliidae, *Simulium*, Thailand, new species, *Montisimulium*

Simulium (*Montisimulium*) Rubtsov is a small subgenus comprising 46 species [1], of which most species are morphologically very similar in the adult stage and their identification depends upon the differences in the shape and arrangement of the pupal gills [2]. This subgenus is very rarely collected because it often breeds in small temporary watercourses in high mountains and emerges only in certain months of the year. Most *Montisimulium* species are distributed in the Palaearctic Region and only five species have been reported from the Oriental Region [1]. In Thailand, this subgenus was thus far represented by only one unnamed species, *S. (M.)* sp. G, known only by larvae collected at Ang Ka (2,460 m in altitude) in Doi Inthanon National Park, Chiang Mai [3]. In 2004, we were able to collect a few pupae, probably of *S. (M.)* sp. G, at Ang Ka, and we described it as *S. (M.) merga* Takaoka and Choochote from reared adults, pupae and mature larvae, together with *S. (M.) surachaii* Takaoka and Choochote from a single female caught by a hand-net at the same locality [4].

Recently, we discovered several pupae and mature larvae of two more species of this subgenus in Doi Inthanon National Park, bringing the total number to three (so far as immature stages are concerned) in the same mountainous area. Coexistence of more than two species rarely occurs among the subgenus *Montisimulium*. Interestingly, it seems likely that these three species of *Montisimulium*, of which two utilize the same small streams, emerge at different times of the year, i.e., *S. (M.) laoleense* sp. nov. in Febru-

ary and *S. (M.) angkaense* sp. nov. in March and April at Siribhume Waterfall (1,400–1,500 m in altitude), and *S. (M.) angkaense* sp. nov. in February and *S. (M.) merga* in September through December at Ang Ka (2,460 m in altitude) according to our yearly surveys (unpublished data).

In this paper, we describe these two species as new to science on the basis of the pupal and/or larval specimens.

The terms for morphological features used here follow those of Takaoka [5]. Holotype and paratype specimens of the new species are deposited at the Department of Infectious Disease Control, Oita University.

Simulium (*Montisimulium*) *angkaense* sp. nov.

DESCRIPTION. Female and Male. Unknown.

Pupa. Body length 3.2–3.5 mm. **Head** (Fig. 1A). Integument yellowish-brown, moderately covered with large tubercles of various shapes each having several very minute nodule-like secondary projections on surface (Fig. 1B); antennal sheath moderately covered with smaller tubercles; frons with 2 short stout simple dark trichomes on each side, face with 1 long stout simple trichome with coiled apex (a little over twice as long as frontal trichomes) on each side. **Thorax.** Integument yellowish-brown, moderately covered with tubercles similar to those on head except lateral and posterior surfaces with smaller simple tubercles, with 3 long stout simple trichomes with coiled apex mediodorsally, 2 long simple trichomes (1 stout with coiled apex, 1 slender

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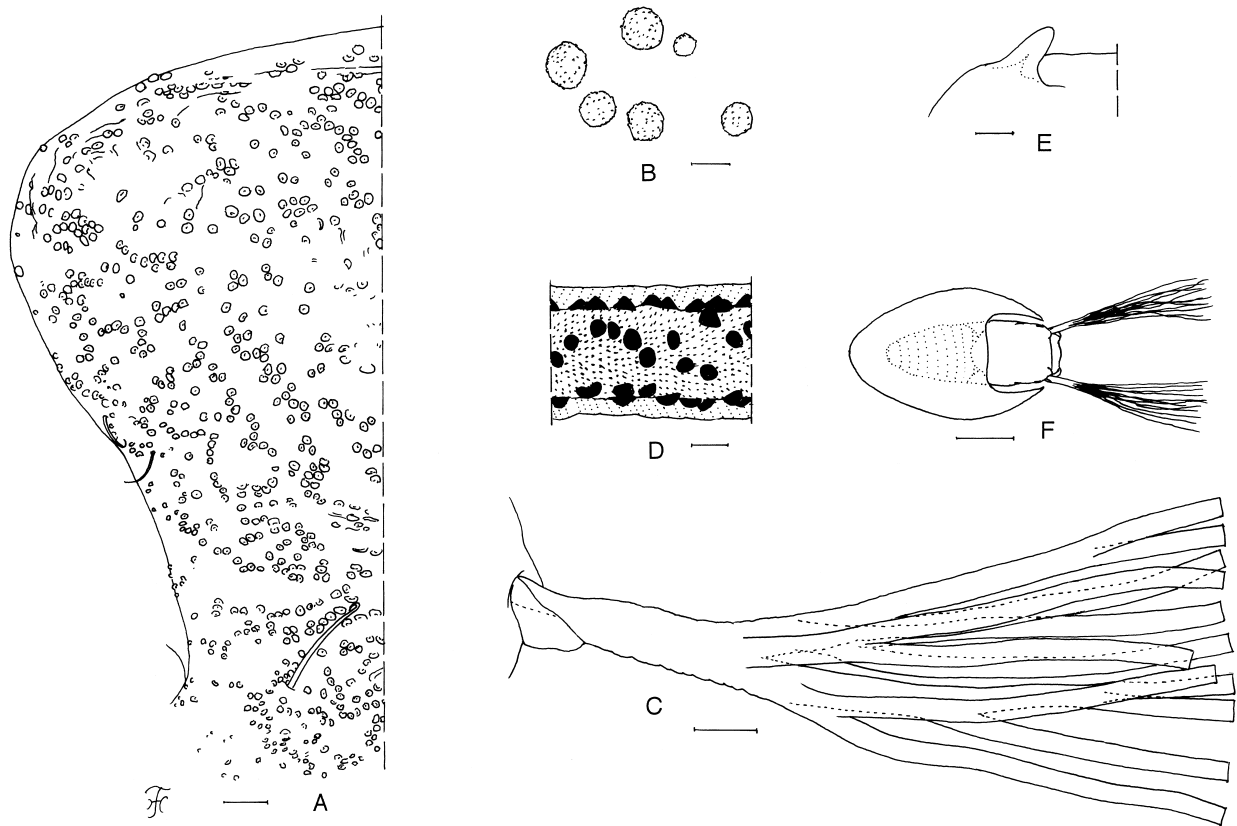


Fig. 1. Pupa of *Simulium (Montisimulium) angkaense* sp. nov. A, head integument with 2 frontal and 1 facial trichomes and with tubercles (right half, front view); B, large tubercles with secondary projections; C, basal portion of gill showing long common basal stalk and arrangement of 12 filaments (right side, outer view); D, enlargement of basal portion of gill filament showing many dark dots in outer cuticular layer; E, terminal hook (left side, end view); F, cocoon and pupa (dorsal view). Scale bars. 1.0 mm for F; 0.1 mm for C; 0.04 mm for A; 0.01 mm for B, D and E.

with uncoiled apex) mediolaterally, 1 long stout simple trichome with uncoiled apex posterolaterally, and 3 stout simple trichomes with uncoiled apex (1 long, 1 medium-long, 1 short) ventrolaterally, on each side. Gill (Fig. 1C) composed of 12 slender thread-like filaments closely arranged in 2-4 groups of filaments: e.g., $2+[2+(1+2)+2+(1+2)]$ or $[2+(1+2)]+2+[2+(1+2)]$ or $[1+1+(1+2)]+2+2+(1+2)$ or $2+2+[(1+2)+2]+(1+2)$, each group arising nearly at same level from long common basal stalk; all filaments light to medium brown, subequal in thickness to one another but somewhat different in length (2.5-3.5 mm long including common basal stalk) and, with numerous brownish-black to black small dots in surface cuticular layer at least on basal 3/4 (Fig. 1D), without annular ridges though annular furrows present irregularly. **Abdomen.** Dorsally, segments 1 and 2 weakly sclerotized and yellowish or yellowish-brown; segments 1 and 2 sparsely tuberculate; segment 1 with 1 long slender or stout simple dark hair with coiled or uncoiled apex on each side; segment 2 with 1 medium-long

slender dark hair and 5 short dark spines on each side; segments 3 and 4 light yellow, each with 4 dark hooks and 1 short dark spine on each side; segments 5-9 covered with comb-like groups of many minute spines on each side; segments 5 and 6 bare; segments 7 and 8 each with distinct spine-combs directed backward in transverse row on each side; segment 9 light yellow, with distinct horn-shaped terminal hooks (Fig. 1E). Laterally, segments 2-4 each with 3 short dark spines on each side; segment 9 without grapnel-like hooklets on each side. Ventrally, segments 3-8 nearly transparent and segment 9 weakly sclerotized and yellow; segments 3-8 with comb-like groups of minute spines; segment 4 with 1 simple or bifid dark hooklet submedially and a few slender dark setae on each side; segment 5 with pair of bifid dark hooks submedially and a few slender setae on each side; segments 6 and 7 each with pair of bifid inner and outer dark hooks and a few slender setae on each side. **Cocoon** (Fig. 1F). Wall-pocket-shaped, thin, moderately woven with no open spaces in webs, without anterodorsal

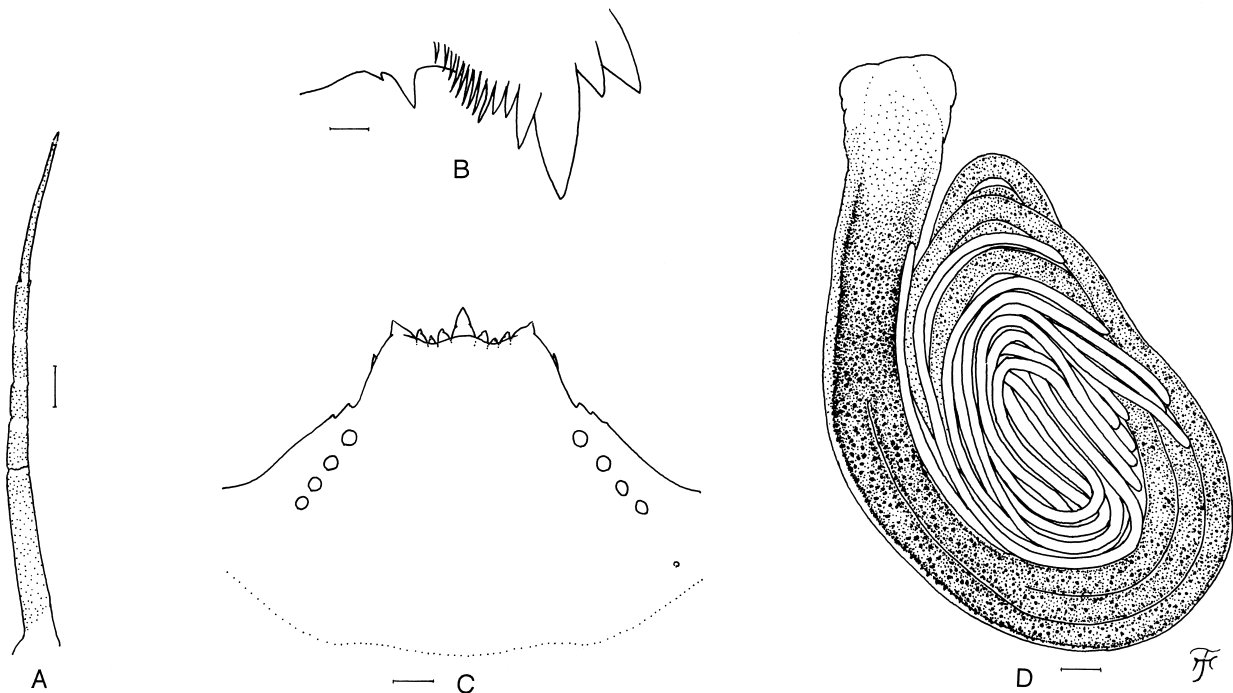


Fig. 2. Mature larva of *Simulium (Montisimulium) angkaense* sp. nov. A, antenna showing 3 thin unpigmented annular bands on segment 2; B, mandible; C, hypostomium; D, Pharate pupal gill (left side, outer view). Scale bars. 0.04 mm for A and D; 0.02 mm for C; 0.01 mm for B.

projection, and slightly extending ventrolaterally; individual threads invisible; 3.0–3.5 mm long by 1.8–2.4 mm wide.

Mature larva. Body length 6.5–6.8 mm. Body greyish, mottled with reddish-brown markings dorsally and laterally on segments 5–9 (Fig. 4A); abdomen, when viewed dorsally, equally narrow from segment 1 to segment 4, abruptly widened posteriorly from anterior margin of segment 5 to anterior margin of segment 6, then gradually narrowed toward segment 9; maximum width near border of segments 5 and 6 (though maximum width on segment 6 when viewed laterally). Cephalic apotome (Fig. 4D) yellow, with well-defined positive head-spots, or dark yellow to light brown (except narrow portions along both lateral margins light yellow), with positive head spots, of which posterolateral spots connected posteriorly to dark areas just anterior to posterior margin; lateral surface of head capsule dark yellow to light brown except eye-spot region clear yellowish-white, with dark broad eyebrow and dark area widely posterior to eye-spot region; 2 large and 3 small spots near posterior margin and 1 small spot just below eye-spot region positive, usually 2 large spots (and also all or 1 or 2 of 3 small spots) merged into dark background color; ventral surface of head capsule (Fig. 4E) dark yellow to medium brown (though narrow area along anterior margin and/or large area medially somewhat lighter in some larvae),

with dark brown basal area on each side of postgenal cleft; horizontal and round spots on each side of postgenal cleft distinctively positive (these spots seemed to merge into dark background color in a few larvae). Cervical sclerites composed of 2 small elliptical pieces, not fused to occiput, very widely separated medially from each other. Antenna (Fig. 2A) consisting of 3 segments and apical sensillum, much longer than stem of labral fan; proportional lengths of 1st, 2nd, and 3rd segments 1.0 : 1.0 : 0.8; all segments light yellow, with 3 thin unpigmented annular bands on segment 2. Labral fan with ca. 34 main rays. Mandible (Fig. 2B) with mandibular serrations consisting of 2 teeth (1 large, 1 small); large tooth nearly at right angle to mandible on apical side; comb-teeth composed of 3 teeth, of which 1st tooth longest, 2nd tooth subequal to, or slightly longer than, 3rd one; supernumerary serrations absent. Hypostomium (Fig. 2C) with 9 apical teeth in row; median and corner teeth well developed; median tooth of 3 intermediate teeth on each side smallest; lateral serrations weakly developed anteriorly; 4–6 hypostomal bristles per side, lying slightly divergent posteriorly from lateral margin. Postgenal cleft (Fig. 4E) very small, vestigial. Pharate pupal gill (Fig. 2D) with 12 thread-like filaments arising from long common basal stalk; each filament without transverse ridges but with numerous brownish-black to black small dots in surface cu-

ticular layer. Abdominal cuticle bare except both sides of anal sclerite moderately covered with simple colorless setae. Rectal scales present but scarcely visible. Rectal organ compound, each of 3 lobes with 11–16 finger-like (except apical 2 or 3 thumb- or nodule-like) secondary lobules. Anal sclerite X-shaped, with anterior arms 0.8 times as long as posterior ones; sensilla absent on and just posterior to basal juncture area; accessory sclerite absent. Last abdominal segment much expanded ventrally forming double bulges on each side, visible as a large ventral papilla when viewed from side. Posterior circling with ca. 76 rows of up to 14 hooklets per row.

TYPE SPECIMENS. Holotype pupal exuviae, collected from a small seasonal stream (water temperature 18.0 °C, shaded, altitude ca. 1,400 m), Siribhume Waterfall, Doi Inthanon National Park, Chiang Mai, Thailand, 16. III. 2005, by W. Choochote. Paratypes: 2 pupae, 2 pupal exuviae and 8 mature larvae, same data and date as those of holotype; 1 pupa, 1 pupal exuviae and 1 mature larva, same data as those of holotype except date, 28. IV. 2005, and water temperature 24.0 °C; 1 pupal exuviae (only right gill), 1 mature larva and 6 immature larvae, same data as those of holotype except date, 13. III. 2004; 1 immature larva, same locality as that of holotype but 100 m upstream (same data and date as those of holotype of *S. (M.) laoleense* sp. nov.); 10 mature larvae and 60 immature larvae, Ang Ka (altitude 2,460 m), Doi Inthanon National Park, Chiang Mai, Thailand, 28. II. 2004, by W. Choochote.

ECOLOGICAL NOTES. The pupae of this new species were found in small depressions formed on the surface of rocks in a small forest stream of Siribhume Waterfall, while larvae of this new species were collected from fallen leaves as well as the surface of rocks at both Siribhume Waterfall and Ang Ka. The pupae and/or mature larvae of this new species were collected only in March and April at Siribhume Waterfall, and in February at Ang Ka. Associated species were *S. (M.) laoleense* sp. nov., *S. (Simulium) doipuiense* at Siribhume Waterfall, and *S. (Gomphostilbia) inthanonense*, *S. (Nevermannia) caudisclerum*, *S. (S.) setukoae* and *S. (S.) suchariti* at Ang Ka.

DISTRIBUTION. Thailand.

ETYMOLOGY. The species *angkaense* refers to Ang Ka, where this new species was collected for the first time.

REMARKS. This new species is assigned to the subgenus *Simulium (Montisimulium)* by the pupal gill with 12 thread-like filaments (Fig. 1C) and the larval postgenal cleft absent

or very small (Fig. 4E). This species is characterized by the pupal gill with 12 thread-like filaments arising from the long common basal stalk. The arrangement of gill filaments separates this new species from all the 16 known species of this subgenus which have 12 filaments on the pupal gill [2, 6–8]. The mature larva of this new species is readily distinguished from *S. merga* by the greyish body with reddish-brown markings dorsally on the abdominal segments 5–9 (Fig. 4A), the head capsule almost entirely dark between the eye-spot region and the posterior margin (this dark area connected to the marked dark eyebrow) (Fig. 4D), and the antenna with unpigmented annular bands on the second segment (Fig. 2A).

It should be noted that there is a possibility that this new species is conspecific to *S. (M.) surachaii* described from a single female captured by a hand-net at Ang Ka, although this female was caught in July [4], different from the possible emergence time (February) of *S. (M.) angkaense* sp. nov. at Ang Ka.

***Simulium (Montisimulium) laoleense* sp. nov.**

DESCRIPTION. Female, Male and Pupa. Unknown.

Mature larva. Body length 5.5–6.1 mm. Body light yellow to greyish yellow (Fig. 4B); abdomen (Fig. 4B) shaped as in *S. (M.) angkaense* sp. nov. Cephalic apotome (Fig. 4F) clear yellow except narrow portion along posterior margin always darkened, with well-defined positive head-spots, of which posterolateral spots usually connected posteriorly to dark narrow area in front of posterior margin; lateral surface of head capsule clear yellow, with no dark well-defined eyebrow (somewhat darkened at most near both ends if present); 2 large and 2 (or 3) small spots near posterior margin distinctively positive, and 1 small spot just below eye-spot region faintly or moderately positive; ventral surface of head capsule (Fig. 4G) yellow, with dark basal area on each side of postgenal cleft; horizontal and round spots on each side of postgenal cleft distinctively positive. Cervical sclerites composed of 2 small elliptical pieces, not fused to occiput, very widely separated medially from each other. Antenna consisting of 3 segments and apical sensillum, much longer than stem of labral fan; proportional lengths of 1st, 2nd, and 3rd segments 1.0 : 0.8 : 0.8; all segments not or only slightly pigmented, then pale annular bands not visible, if any. Labral fan with ca. 32 main rays. Mandible (Fig. 3A) with mandibular serrations consisting of 2 teeth (1 large, 1 small); large tooth nearly at right angle to mandible on apical side; comb-teeth composed of 3 teeth, shortened from 1st to 3rd; supernumerary serrations absent. Hypostomium (Fig. 3B) with 9 apical teeth in row; median and corner teeth well developed; median tooth of 3 interme-

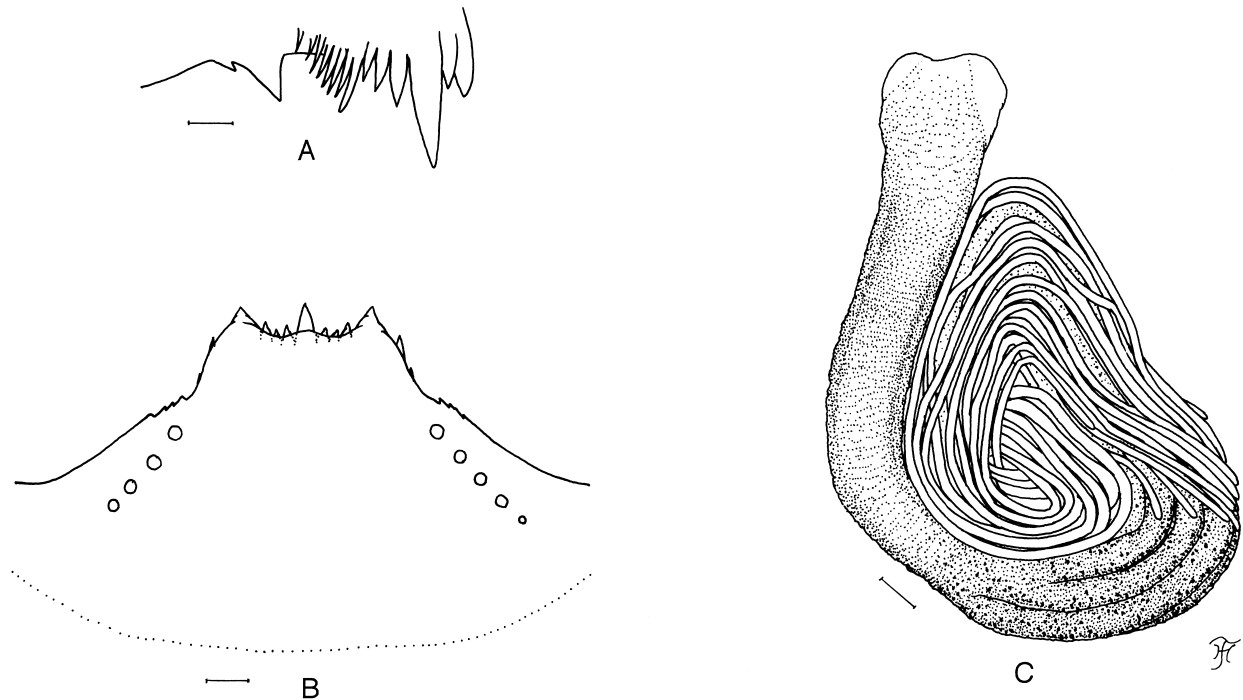


Fig. 3. Mature larva of *Simulium (Montisimulium) laoleense* sp. nov. A, mandible; B, hypostomium; C, Pharate pupal gill (left side, outer view). Scale bars. 0.04 mm for C; 0.02 mm for B; 0.01 mm for A.

diate teeth on each side smallest; lateral serrations weakly developed anteriorly; 4 or 5 hypostomal bristles per side, lying slightly divergent posteriorly from lateral margin. Post-genal cleft (Fig. 4G) very small, vestigial. Pharate pupal gill (Fig. 3C) with 12 thread-like filaments arising from very long common basal stalk about 1.6 times as long as that of *S. (M.) angkaense* sp. nov.; each filament with sharp transverse ridges and with numerous brownish-black to black small dots in surface cuticular layer. Abdominal cuticle bare except both sides of anal sclerite moderately covered with simple colorless setae. Rectal scales present. Rectal organ compound, each of 3 lobes with 13 or 14 finger-like secondary lobules. Anal sclerite X-shaped, with anterior arms 0.9 times as long as posterior ones; sensilla absent on and just posterior to basal juncture area; accessory sclerite absent. Last abdominal segment much expanded ventrally forming double bulges on each side, visible as a large ventral papilla when viewed from side. Posterior cirlet with ca. 78 rows of up to 14 hooklets per row.

TYPE SPECIMENS. Holotype mature larva, collected from a small seasonal stream (width 0.5 m, water temperature 18.5 °C, shaded, altitude ca. 1,500 m) very slowly flowing in a forest, Siribhume Waterfall, Doi Inthanon National Park, Chiang Mai, Thailand, 28. II. 2004, by W. Choochote. Paratypes: 4 mature larvae and 20 immature larvae, same

data as those of holotype; 5 immature larvae, same locality as that of holotype but 100 m downstream (same data and date as those of holotype of *S. (M.) angkaense* sp. nov.).

ECOLOGICAL NOTES. The larvae of this new species were found on fallen leaves in a small stream. Associated species were *S. (G.) inthanonense*, *S. (M.) angkaense* sp. nov., *S. (S.) crocinum* and *S. (S.) doipuiense*.

DISTRIBUTION. Thailand.

ETYMOLOGY. The species *laoleense* refers to Laolee, the Mong's name for Siribhume Waterfall, where this new species was collected.

REMARKS. This new species is also assigned to the subgenus *Simulium (Montisimulium)* as in the preceding species.

This new species is remarkable in having the pupal gill composed of 12 thread-like filaments arising from a very long common basal stalk (Fig. 3C). Within this subgenus, none of the known species has such a long common basal stalk except one unnamed species, i.e., *S. (M.)* sp. C reported from India [9], which has, though, 14 pupal gill filaments per side. The mature larva of this species is somewhat similar in the body and antennal colors to *S. (M.)*

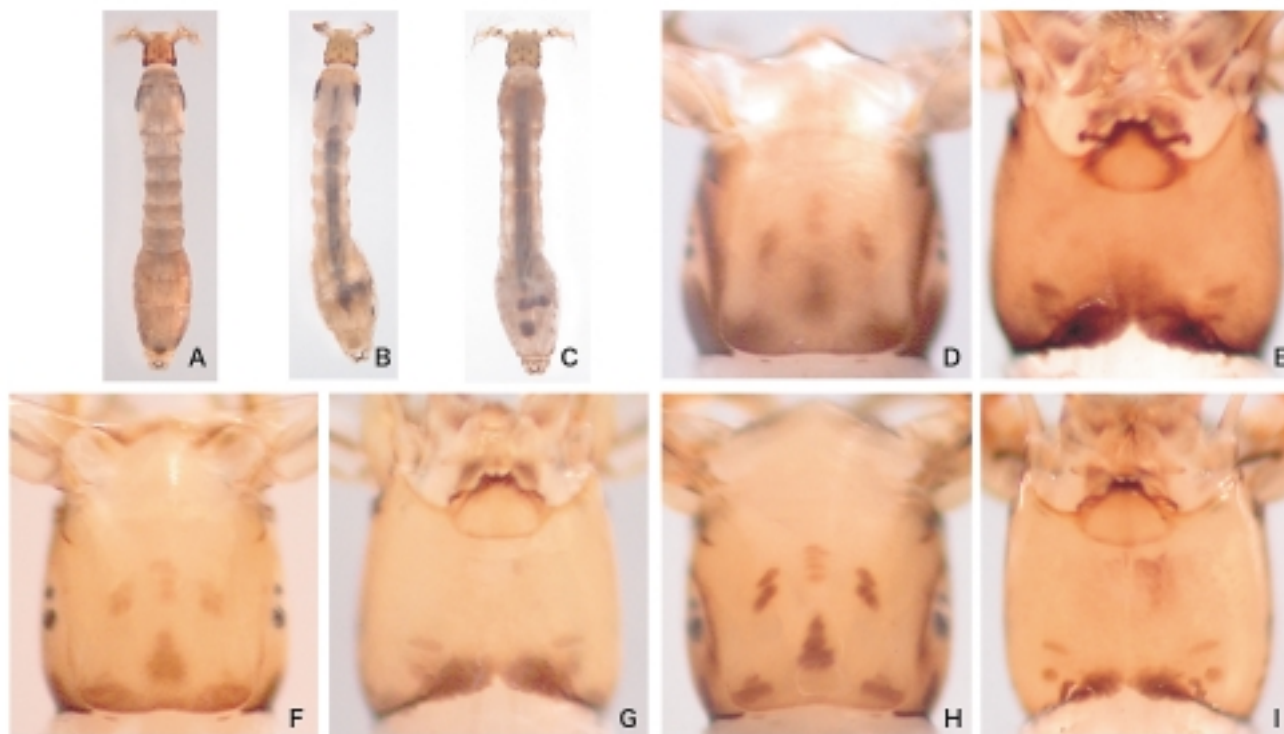


Fig. 4. Whole bodies and head capsules of mature larvae of three species of *Simulium* (*Montisimulium*) in Doi Inthanon National Park. A C, whole bodies (dorsal view); D I, head capsules, D, F and H, dorsal view; E, G and I, ventral view; A, D and E, *S. (M.) angkaense* sp. nov.; B, F and G, *S. (M.) laoleense* sp. nov.; C, H and I, *S. (M.) merga*.

merga (Fig. 4C), but differs from the latter species by the ill-defined eyebrow, the cephalic apotome with dark area just before the posterior margin which is connected to the posterolateral spots (Fig. 4F), and the fifth abdominal segment lacking a pair of dark small markings dorsally (Fig. 4B). *Simulium (M.) laoleense* sp. nov. seems to be related to *S. (M.) angkaense* sp. nov. in having the 12 pupal gill filaments but is easily distinguished from it by the light yellow body color (Fig. 4B), the antenna without distinctive hyaline annular bands on the second segment, the ill-defined faint eyebrow (Fig. 4F), and the pharate pupal gill with a very long common basal stalk (Fig. 3C).

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Information of the first master course for Tropical Medicine in Japan

INAUGURATION OF THE MASTER COURSE IN TROPICAL MEDICINE AT NAGASAKI UNIVERSITY: A MILESTONE IN TROPICAL MEDICAL EDUCATION IN JAPAN.

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Abstract: We now live in a world where the threat of emerging and re-emerging infectious diseases crosses continental and national borders. In recognition of this trend the world realizes the importance of nurturing expertise in the control of infectious diseases based on sound knowledge, experience, and evidence. The introduction of a Master of Tropical Medicine course at the Graduate School of Biomedical Sciences in Nagasaki University, Japan is expected to provide a whole new opportunity for eager doctors to acquire necessary knowledge and skills to combat the world-wide burden of infectious diseases.

Key words: Master course; tropical medicine; infectious diseases

Year 2006 shall witness a new start to tropical medical education in Japan when the Master Course of Tropical Medicine, the first of its kind in this country, begins at the Graduate School of Biomedical Sciences, Nagasaki University. Since we shall take part in the course as course director and course coordinator, it should not be out of place for us to briefly introduce this course in the context of tropical medicine and international health at large.

Perhaps a few words may be necessary to clarify the use of the word "tropical medicine". In the 19th century medicine became global as exemplified by the inauguration of International Medical Congress in Paris in 1867. As a natural consequence of such globalization in medicine, tropical medicine emerged and developed towards the end of the 19th century. The first tropical medical school, Liverpool School of Tropical Medicine in the United Kingdom, opened in April 1899 followed by Tropical School in London six months afterwards. Globalization at that time period strongly mirrored the spirit of imperialism in which great powers competed against each other in order to enlarge their colonies in Africa, Asia, the Americas and Oceania. Such imperial expansion was hampered by infectious diseases prevalent in the tropics. Thus, the primary purpose of tropical medicine then was for better medical protection of their nationals in the tropics where it was infamously dubbed as the grave of white men.

While we recognize the dark side of the image that has always accompanied the term tropical medicine, it is also true that tropical medicine represented the passion and goodwill of the doctors heading for steaming tropical countries where a full range of maladies flourish.

After a short period of optimism in the middle of the 20th century that many of the infectious diseases would be overcome before the turn of the millennium, we are now facing the threat incurred by a number of emerging and re-emerging infectious diseases. The speed at which these infectious diseases spread from one country to another has been accelerating due to ever-expanding economic activities and international travels. Such evolvement has brought tropical medicine back into the limelight and the world now demands experts with knowledge and enthusiasm to combat this current trend. In addition, a further reflection on the issue reveals that the role that tropical medicine is expected to play will not differ much from the one that it played a century ago. In other words, tropical medicine is again playing a vital role to assure the health of the people living in the developed countries, and for this reason developing expertise in tropical medicine has significant merits in developed countries as well as in developing countries.

The Graduate School of Biomedical Sciences at Nagasaki University is the only school in Japan that runs a PhD course specializing in emerging infectious diseases and tropical medicine. Furthermore, the Institute of Tropical

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Medicine at this University has been playing a central role in medical research in the tropics, human development and provision of human resources for disease control programs overseas. We are launching a Master course in Tropical Medicine in this prestigious venue with the intent of contributing to the global efforts to reduce the burden of tropical and infectious diseases. To achieve this goal, we will provide students with opportunities to attain a broad range of skills and knowledge relating to tropical medicine by introducing a structured program maximizing the utility of teaching resources available at the Institute of Tropical Medicine. Specifically, we will place emphasis on acquisition of knowledge required for management and control of infectious diseases backed up by solid foundation of microbiology and advanced molecular biology tools.

The details of the course can be obtained by visiting our website at: <http://www.mdp.nagasaki-u.ac.jp/eng/index.html> (see Section 'Student Center'). We describe below the outline of this 12-month course due to commence in April 2006 with students recruited from countries world-wide (the course will be taught in English). We are targeting medical doctors with at least two years of clinical experience who have strong interests in infectious diseases occurring primarily in the tropics or have future plans of working in tropical countries.

The course consists of three components: a) lectures, tutorials and practicals (laboratory practices); b) overseas clinical training; and c) a research project (Master dissertation).

a) Lectures, Tutorials and Practical (from April to July 2006)

Lectures and practicals aim to cover essential knowledge of clinical infectious diseases with frequent reference to relevant information of microbiology (including virology), parasitology, and entomology. There are epidemiology and public health sessions designed for building up basic skills in study design, data management and medical statistics. The course will hold a series of tutorial sessions for discussion on clinical cases and disease outbreaks with particular emphasis on diagnosis, treatment, prevention and control.

b) Overseas Training (August 2006)

All students will attend overseas training for four weeks where they will have exposure to real clinical cases in the local hospitals by attending ward rounds and outpatient clinics and having clinical case discussions. In addition, students will visit community health facilities, ministry offices, internationally recognized research groups, and international governmental and non-governmental organizations.

c) Research Project (from September 2006 to March 2007)

All students will be assigned to conduct a research project under the supervision of professors and will submit a Master dissertation.

In closing, we are in the process of reaching the first milestone in the tropical medical education in Japan with the imminent establishment of the Master Course in Tropical Medicine at Nagasaki University. In modern tropical medicine now is the time when opportunities are greater than ever.