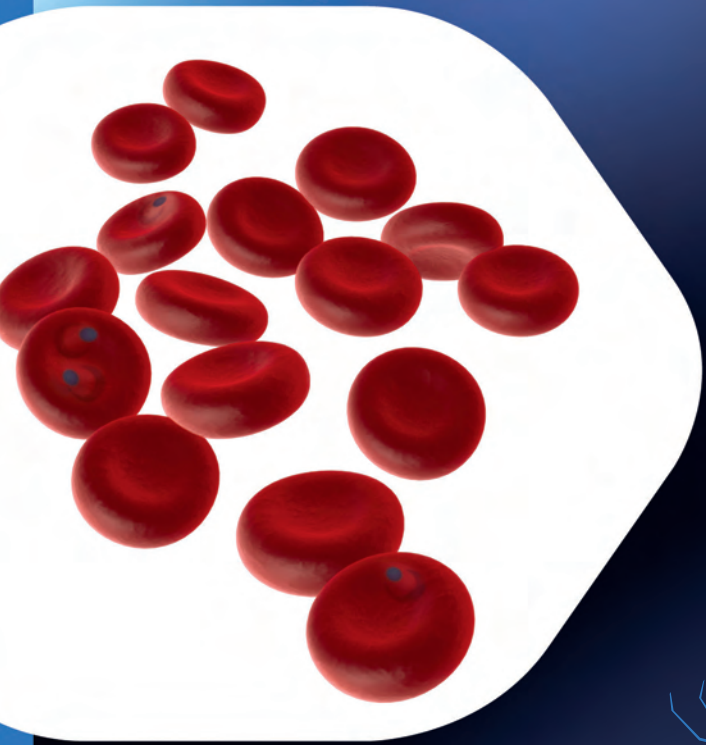
A PRACTICAL HANDBOOK

Third Edition

MANAGEMENT OF SEVERE MALARIA



World Health Organization

ANTIMALARIAL CHEMOTHERAPY OF SEVERE MALARIA

All forms of severe malaria in adults and children

Artesunate[1] 2.4 mg/kg body weight (bw) administered intravenously (iv) or intramuscularly (im) at the time of admission (time = 0), then at 12 h and 24 h, then once a day until the patient is able to take oral medication

If parenteral artesunate is not available, artemether or quinine are acceptable alternatives:

Artemether 3.2 mg/kg bw im given on admission then 1.6 mg/kg bw per day

or

Quinine dihydrochloride 20 mg salt/kg bw (loading dose) on admission, then 10 mg/kg bw every 8 h. Each dose is given as an iv infusion diluted in 10 ml/kg bw of isotonic fluid over 2–4 h at an infusion rate that should not exceed 5 mg salt/kg bw per h. If quinine cannot be administered by iv infusion, it can be given in the same dosage by im injection into the anterior thigh. Each dose for im injection should be diluted in normal saline to a concentration of 60–100 mg salt/ml and injected into two sites to avoid injection of a large volume into one site.

Duration of parenteral treatment

Give parenteral antimalarial agents for the treatment of severe malaria for a **minimum** of 24 h, even if the patient can tolerate oral medication earlier

1 Artesunic acid powder should be dissolved in 1 ml of 5% sodium bicarbonate to make artesunate, then diluted with 5 ml of 5% dextrose and given immediately by iv bolus ('push') injection or by im injection.

Follow-on oral treatment

Complete treatment by giving a full course of effective artemisinin-based combination therapy (ACT) as soon as the patient is able to take oral medication but not before a minimum of 24 h of parenteral treatment. The current ACT options recommended by WHO are:

- artemether plus lumefantrine
- artesunate plus amodiaquine
- artesunate plus mefloquine[2]
- artesunate plus sulfadoxine-pyrimethamine
- dihydroartemisinin plus piperaquine

Pre-referral treatment of severe malaria[3]

If the time between referral and definitive treatment is likely to be > 6 h, give **one** of the following:

- rectal artesunate 10 mg/kg
- im artesunate 2.4 mg/kg
- im artemether 3.2 mg/kg
- im quinine 20 mg salt/kg (split 10 mg/kg into each thigh)

Then refer immediately to an appropriate facility for further treatment.[4]

2 Do not give mefloquine after recovery from cerebral malaria as there is a risk for neuropsychiatric reactions.

3 Pre-referral treatment with broad spectrum antibiotic should also be given.

4 If, however, referral is impossible, the initial treatment should be continued until the patient can tolerate oral medication; at this point, a full course of the recommended ACT for uncomplicated malaria in the locality can be administered.

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TABLE OF CONTENTS

PREFACE

Malaria continues to be a major global health problem, with over 40% of the world's population—more than 3.3 billion people—at risk for malaria to varying degrees in countries with on-going transmission. In addition, with modern, rapid means of travel, large numbers of people from non-malarious areas are being infected, which may seriously affect them after they have returned home. During the past decade, investments in malaria prevention and control have created unparalleled momentum and saved more than 1 million lives. The rates of death from malaria have been cut by over one fourth worldwide and by one third in the World Health Organization (WHO) African Region. Malaria transmission still occurs, however, in 99 countries, and the disease caused an estimated 655 000 deaths in 2010 (with an uncertainty range of 537 000–907 000 deaths), mainly among children under 5 years of age in sub-Saharan Africa.[1]

Plasmodium falciparum is common in the tropics and causes the most serious form of the disease. Infections with this parasite can be fatal in the absence of prompt recognition of the disease and its complications and urgent, appropriate patient management. *P. vivax* and *P. knowlesi* (a species that primarily infects monkeys and may be transmitted to humans in certain forested areas of South-East Asia) may also cause severe infections. Resistance of parasites to antimalaria agents continues to be a threat to malaria control and elimination efforts globally. The emergence of resistance to artemisinins in the Mekong sub-Region is of particular concern. Prompt diagnosis and treatment

1 *World malaria report 2011*. Geneva, World Health Organization, 2011. http://www.who.int/malaria/world_malaria_report_2011/9789241564403_eng.pdf.

are crucial to prevent mortality, especially in high-risk groups such as young children and pregnant women.

This practical handbook on the management of severe and complicated malaria has been revised and updated for the third time, with some key changes, notably, replacement of quinine with artesunate as first-line treatment for severe malaria caused by all *Plasmodium* species. Like previous editions, this handbook is intended primarily for health professionals working in hospitals or health centres with inpatient facilities, who are responsible for the management of patients with severe malaria. As this manual focuses on the practical management of severe malaria, it is based on guidelines and recommendations adopted as standard WHO guidance for the management of severe malaria or severely ill patients, which are listed in Annex 1. When new information or a new recommendation that has not previously been endorsed in a WHO guideline is given, the source of the information or the basis of the recommendation is referenced. The review of the handbook was organised through a consultation of the GMP Technical Expert Group (TEG) on Malaria Chemotherapy co-chaired by Professors Fred Binka and Nick White (Annex 2).