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CLASSIFICATION OF ANTIMALARIAL DRUGS IN RELATION TO DIFFERENT
STAGES OF THE LIFE-CYCLE OF THE PARASITE

(Commentary on a diagram)¹

Introduction

One of the ways of classifying antimalarial drugs is that according to their action on the particular stage of the life-cycle of the parasite. The teaching of principles of chemotherapy of malaria can be greatly facilitated by the use of a diagram indicating clearly the rationale of the use of different antimalarials for different purposes, in the prevention and cure of individual infections as also in the two principal phases (attack and consolidation) of malaria eradication programmes.

It is believed that the accompanying diagram serves a useful purpose. A number of less known or not generally used compounds were not included here. A few remarks concerning the most common drugs mentioned in the diagram provide some additional information.

All the data concerning the rationale of chemotherapy of malaria, the description of individual compounds in common use, the guidance to dosage etc., will be found in the monograph "Chemotherapy of malaria" by Covell, Field & Jaswant Singh (1955).²

A large amount of recent information on the use of chemotherapy in malaria eradication and on the trends of research in this field is contained in the Report of the WHO Technical Meeting on Chemotherapy of Malaria (1961) which has now appeared in print.³

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² Covell J., Coatney G. R., Field J. W. & Singh J. (1955) "Chemotherapy of malaria" World Health Organization: Monograph Series, No. 27.

³ World Health Organization (1961) "Chemotherapy of malaria", Report of a Technical Meeting, Wld Hlth Org. techn. Rep. Ser. 226

Terms pertaining to the action of antimalarial drugs were redefined by the WHO Technical Meeting on Chemotherapy of Malaria (WHO, 1961, Technical Report Series No. 226) and the relevant definitions are as follows:

Causal prophylaxis (True causal prophylaxis): Complete prevention of erythrocytic infections by the administration of drugs destroying either sporozoites or primary tissue forms.

Gametocytocide (Gametocytocidal drug): A drug which destroys the sexual forms of human malaria parasites. (According to this definition, all antimalarial drugs are gametocytocides because they all eliminate P. vivax gametocytes. Gametocytocidal and schizontocidal action should be defined in relation to particular species. The practice of describing the action of antimalarial drugs with general reference to all three species might be confusing.)

Radical treatment (Anti-relapse therapy): Treatment adequate to achieve radical cure viz., complete elimination of erythrocytic stages and persisting tissue stages of the parasite from the body so that relapses cannot occur. (This term should apply to infection with any species of malaria parasite, even though it is now used mainly with regard to P. vivax and P. malariae infections, in which secondary tissue phase of the parasite exists.)

Sporontocidal drug: A drug which when given to the malaria-infected, vertebrate host prevents or interrupts the development of the parasite in the mosquito.

1. Classification of antimalarial drugs

Taking into account their main action on the stage of the life-cycle of the malaria parasite drugs could be classified into five groups:

1.1. Causal prophylactic drugs (primary tissue schizontocides) act on the pre-erythrocytic forms (primary tissue phase) of the malaria parasite. Although primaquine and pamaquine (probably also quinocide) are active in the primary tissue schizonts of P. falciparum and P. vivax they are not used in practice as prophylactic drugs because of their possible side-effects. On the other hand proguanil and pyrimethamine are highly active against the primary tissue forms of P. falciparum and have some action on these forms of P. vivax.

1.2. Schizontocidal drugs sensu stricto (blood schizontocides) act on the asexual erythrocytic forms of all species of malaria parasites. Quinine, mepacrine and 4-aminoquinolines such as chloroquine and amodiaquine have a potent and rapid action and are used for treatment, and also for temporary prevention (suppression) of clinical symptoms. Although proguanil and pyrimethamine have an action on the erythrocytic phase of P. falciparum infection this effect is slow and probably varies in relation to the strain of the parasite. Both drugs (as also chlorproguanil) are particularly useful as suppressants of all species of malaria parasites especially P. falciparum;¹ in the latter case suppressive cure may be achieved.²

1.3. Gametocytocidal drugs (gametocytocides) par excellence are the 8-aminoquinolines of which pamaquine, plasmocide, primaquine and quinocide are most active on sexual forms of all species of malaria parasites. The two last compounds are much less toxic than the others. Quinine, mepacrine, chloroquine and amodiaquine have an action on gametocytes of P. vivax and P. malariae but no direct action on gametocytes of P. falciparum.

1.4. Sporontocidal drugs inhibit the sporogonic phase of development of the parasite in the mosquito. (This effect is also called "anti-sporogonic action" or "gamostatic action" by some workers.) Proguanil, chlorproguanil and particularly pyrimethamine act on the gametocytes of P. falciparum and P. vivax rendering them non-infective to mosquitos; with pyrimethamine this effect may last for two to three weeks after a single dose.

Pamaquine, primaquine (and probably quinocide) have the same effect though the action is somewhat slower and its duration less because of the faster excretion of 8-aminoquinolines.

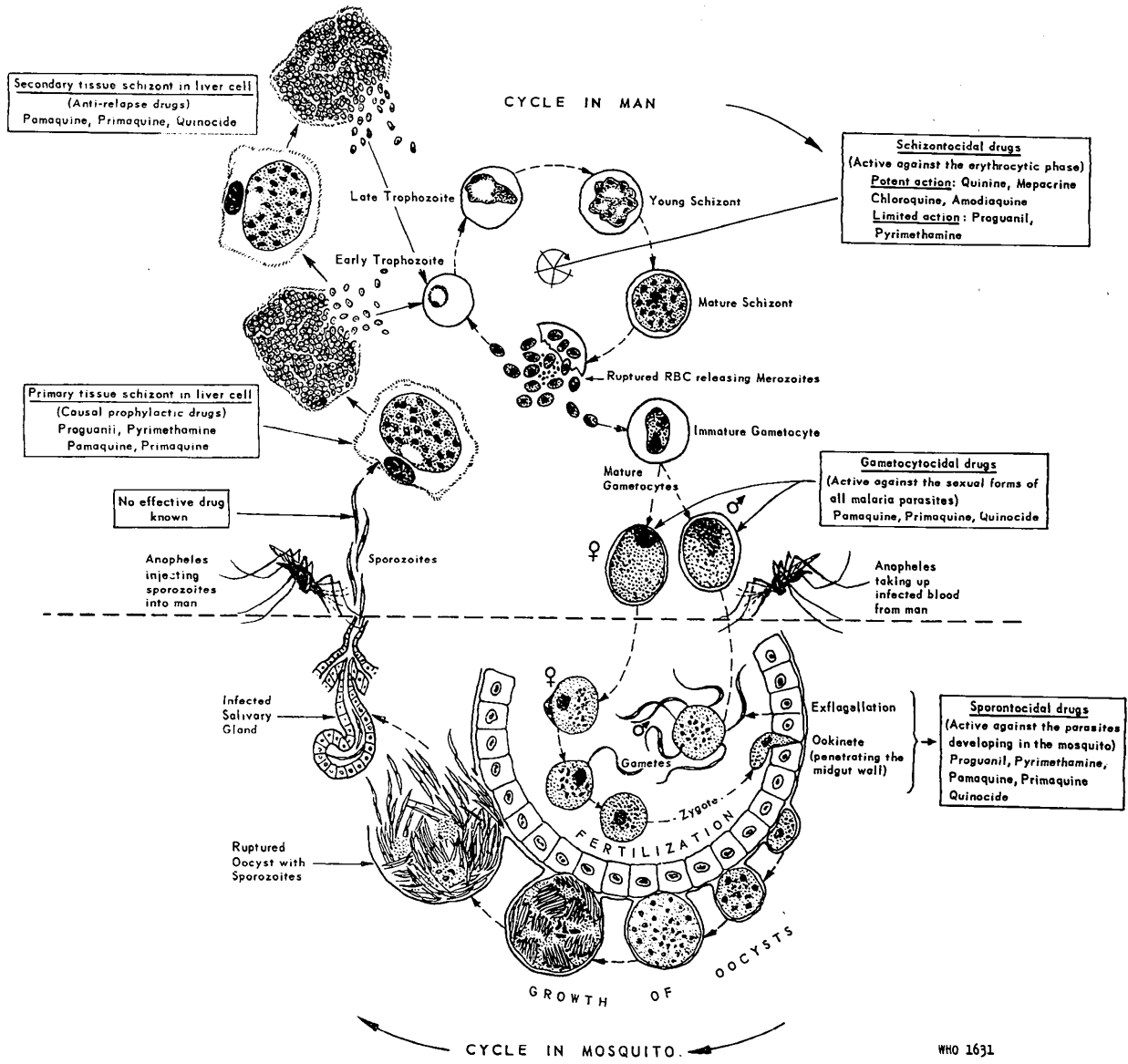
¹ In some cases proguanil and pyrimethamine can produce a suppressive cure of P. vivax infections. Many 8-aminoquinolines show an activity on asexual forms of malaria parasites in the blood but only in doses which are likely to be followed by undesirable side-effects.

² Suppressive treatment (suppression, chemosuppression, clinical prophylaxis, chemoprophylaxis, drug prophylaxis, etc.): treatment the aim of which is the prevention - or elimination - of clinical symptoms and parasitaemia, and which does not necessarily prevent or eradicate the infection. Suppressive cure: complete elimination of the parasite from the body while the patient is receiving continuous suppressive treatment.

1.5. Anti-relapse drugs or secondary tissue schizontocides have a pronounced action on the secondary exo-erythrocytic phase of P. vivax and P. malariae infections in the liver. The only compounds of high activity are pamaquine, primaquine and quinocide. They effect radical cure of all relapsing infections and are usually administered after the treatment of the primary attack though they can also be given during a relapse or at the time of latency. The completeness of the curative effect in vivax infections depends somewhat on the strain of the parasite.

Primaquine and quinocide are better supported with less side-effects than pamaquine or plasmocide.

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