Monitoring the response of malaria infections to treatment*

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A simplified schema for assessing the response of malaria patients to treatment is described. It involves collection and examination of blood films prior to the first dose and on days 2 and 7 after the onset of treatment.

Introduction

Huge quantities of antimalarial drugs are being consumed unnecessarily by patients who are presumed to have malaria. This practice is not only costly and potentially harmful to the recipients but also promotes the development of drug-resistant parasites. Fortunately, current efforts to improve laboratory diagnostic facilities at health centres and health subcentres should also be helpful in limiting the use of antimalarials to patients who really need them. Microscopic examination of blood films will be just as useful in establishing a definitive diagnosis of malaria as, say, helping to differentiate between a bacterial and viral infection. Identification of the plasmodial species by suitably-trained technicians also ensures that patients will not receive medication that is inappropriate for their infection.

Greater use of the microscope also provides the opportunity for monitoring the parasitological response to treatment. This should be done, wherever possible, for the well-being of the patient because it indicates the response to treatment more precisely than clinical observations alone. It also alerts health personnel to the need for early treatment with alternative drugs, an especially important consideration in the management of severe infections.

Regular and widespread reporting of the response to treatment will also provide an early warning of changes in the drug susceptibility of parasites and help to define the extent and severity of drug resistance. It will then be possible, for the first time, to formulate rational drug policies and to plan for optimal use of antimalarial drugs based on extensive information collected from rural health facilities.

Method and discussion

Routine assessment of the response to treatment should obviously be kept as simple as possible. The standard WHO 7-day or 28-day *in vivo* test would be impractical because 7 to 10 follow-up blood examinations are required after treatment. However, collection and examination of blood films on two occasions, on days 2 and 7 after the onset of treatment, are much more feasible and would provide a reasonable insight into the drug susceptibility of local infections.

In monitoring the response to treatment, health personnel in most rural areas will frequently not have the time or inclination to carry out conventional parasite counts as part of their routine work, e.g., the enumeration of parasites against 1000 leukocytes and then applying appropriate formulae to obtain parasite densities per μl of blood. On the other hand, the widely applied method of recording parasite densities according to a 1+ to 4+ scale is also not satisfactory for assessing the parasitological response to treatment. It is just as easy and much more meaningful to count the number of parasites per 100 leukocytes. If no parasites are seen, particularly on day 7, the microscopist should try to examine the blood film over an area covering 1000 leukocytes. Although the precision of such a procedure may not be optimal, a quick counting method applied widely is preferable to one that is more precise but rarely used outside of a research or hospital setting.

Using this simple procedure for assessing parasite densities on days 0, 2 and 7, the response of infections to treatment can be classified as follows:

1. *Good response: S or RI (late).* Parasite density declines to less than 25% of the pre-treatment level by day 2 and no parasites are seen by day 7. The patient is either cured or experiences a recrudescence within a few weeks if some parasites have evaded drug action.

2. *Partial response: RI (early) or RII.* Parasite density declines to less than 25% of the pre-treatment level by day 2, but the patient may require alternative treatment because parasites are still present on day 7.

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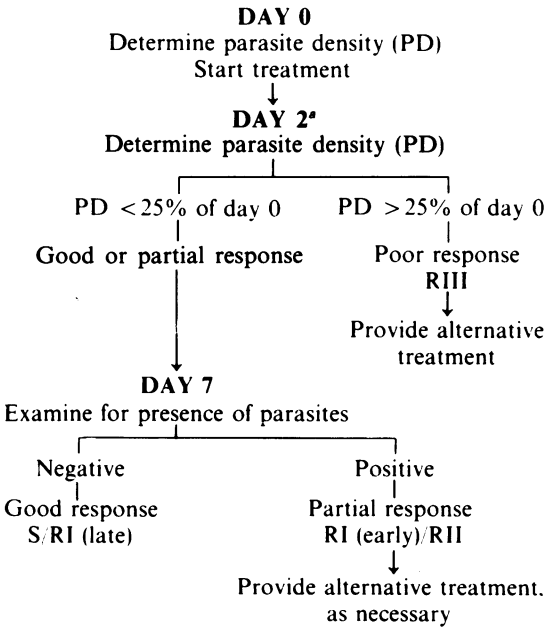
3. *Poor response: RIII.* Parasite density is more than 25% of the pre-treatment level on day 2, usually indicating that alternative treatment is required.

This procedure for assessing and classifying the response to treatment can be used for chloroquine as well as for other drugs and drug combinations (Fig. 1). It cannot be used for assessing the response to drugs that act slowly, e.g., tetracyclines. However, since such drugs should only be used in combination with more rapidly-acting drugs anyway, the procedure would be useful for determining the response of infections to the drug combination. From time to time, there are reports that parasite clearance takes longer than 7 days after starting treatment with a rapidly-acting drug, despite the fact that such patients are cured of their infections. The reasons for this are unclear at present, but they may be due to the presence of parasites with a reduced drug susceptibility that are eventually suppressed by the patient's immune response. At any rate, such a slow clearance of parasites should always alert health personnel to the possibility that drug-resistant parasites may be present in the area.

Fig. 1. **Schema for monitoring the response of malaria infections to treatment (based on the WHO standard field test).**



* This examination on day 2 should be carried out no sooner than 48 hours after the first dose of treatment. If this is not possible, the collection of blood films can be delayed until the morning of day 3.

Widespread monitoring of the *in vivo* response of malaria infections to treatment should be supplemented by *in vitro* assessment of the susceptibility of *Plasmodium falciparum* to various drugs. The *in vitro* test is particularly useful for investigating unusual *in vivo* findings and detecting subtle changes in drug susceptibility without having to take into consideration factors such as host immunity and the possibility of reinfection. *In vitro* assessment should be carried out by a central or regional drug monitoring team. The team would follow up reports of any unexpected response to treatment, and carry out periodic monitoring of drug susceptibility in designated indicator areas. In addition, it would be involved in the training and supervision of *in vitro* testing at stationary facilities, such as laboratory-staffed hospitals.

In vivo and *in vitro* findings should be expressed in a format that is easily understood by rural health workers. This would encourage their active participation in drug monitoring activities even further and lead to the more effective control of drug-resistant malaria.

Résumé

Surveillance de la réponse des parentes du paludisme au traitement

L'emploi accru de microscopes dans les centres de santé pour aider au diagnostic du paludisme et à celui d'autres maladies favorisera l'emploi plus rationnel et plus économique de médicaments dans les régions rurales. Cela bénéficiera également aux malades atteints de paludisme en rendant possible la surveillance de la réponse parasitologique au traitement et, si cette réponse n'est pas satisfaisante, en permettant de commencer un traitement précoce avec des médicaments de remplacement. L'évaluation de la réponse au traitement devrait rester aussi simple que possible, pour qu'elle soit largement adoptée par les centres de santé ruraux. Cet objectif peut être atteint en recueillant des gouttes de sang épaisses deux fois seulement, le deuxième et le septième jour après le début du traitement, et en effectuant une numération rapide des parasites. Le schéma de surveillance de la réponse au traitement est basé sur l'épreuve-type de terrain de l'OMS. La surveillance étendue, par des installations de santé rurales, de la réponse *in vivo* des infections paludéennes au traitement, complétée par l'emploi prudent du test *in vitro*, permettra aux autorités sanitaires de formuler des politiques pharmaceutiques rationnelles et de faire des plans pour l'emploi optimal des antipaludéens.