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CLASSIFICATION OF MALARIA CASES

1. Introduction - General

The number and distribution of confirmed malaria cases and their classification according to origin of infection constitute the principal evidence on the basis of which the malaria situation in an area and its progress towards eradication can be judged. It is therefore essential that every case is investigated and thoroughly scrutinized.

This classification is important not only for a clear definition of the epidemiological picture, but also for the decision of appropriate remedial action and eventually for the fulfilment of the criteria of achieved eradication.

The Expert Committee on Malaria has laid down the following categories for classification of cases: indigenous, relapsing, imported, introduced and induced. These terms are fully satisfactory for a purely scientific approach to epidemiology, but in practice several difficulties have been experienced in carrying out classification of cases, and in the proper interpretation of the terms. These difficulties are discussed in the paragraphs below, in which also the interpretation of the various terms is clarified in detail, and in a few instances sub-classifications are given for some of the basic categories and recommendations are made for procedures to be used in the classification of cases. The discussion is chiefly based on the assumption that the classification of cases takes place in an area which is in the consolidation phase but with some modifications it will be possible to apply the interpretations and procedures proposed also for areas in the late stages of the attack phase.

2. Significance of Classification for Criteria of Eradication

One of the criteria laid down for the confirmation of achieved eradication is: "Evidence **that** in this period of three years (three years of careful search for malaria cases) no indigenous cases originating within that time have been discovered" (Eighth Report - Expert Committee on Malaria¹).

The classification of a case as indigenous implies that local transmission has occurred before the discovery of the case and may still be going on, and that the termination of the consolidation phase in the area concerned would be delayed in accordance with the criterion quoted above.

The terms relapsing, imported and induced imply that no recent local transmission is involved in the appearance of these cases. This means that these cases would not spoil the record of a consolidation phase area with regard to the above criterion of three years free from indigenous cases.

The term introduced indicates an intermediate situation in which local transmission has taken place but has not proceeded beyond the first step, the point of origin of this transmission being an imported case. In this special instance, although local transmission has occurred, the case does not spoil the record of the area with regard to the three years freedom from indigenous cases. From all this it will be apparent that the classification of cases as relapsing, imported, introduced or induced has to be made not only honestly but also scrupulously, and that in the absence of definite proof to the contrary the case must be classified as indigenous.

3. Relapsing case

The definition of a relapsing case as laid down by the Expert Committee in their Eighth Report is: "A relapse of a pre-existing infection as shown by the history of the case and the absence of any associated cases in the neighbourhood of its origin". Theoretically this term and its definition is simple and easily interpreted. In practice, however, the classification of a case as relapsing is one of the most difficult to arrive at with assurance.

¹ Wld Hlth Org techn. Rep. Ser. 1961, 205

It is mandatory that a very careful history of the case should be taken to ascertain the "pre-existing infection". By far the best and most desirable proof is a definite record of the case when found during the initial infection, including microscopic diagnosis of the same parasite species as that in the present attack. Here is one of the many reasons for insisting that in a malaria eradication campaign an individual case card should be kept for every malaria case detected, indexed under the locality concerned. This will greatly facilitate the confirmation of the previous history of a relapsing case. If such documentary proof is not available it must be left to the epidemiological, parasitological and clinical judgement of the investigating malariologist to accept or reject the possibility of classifying the case as relapsing on the basis of its history. Regarding the period that may have elapsed since the initial attack, this should as a rule have occurred not more than two years back in the case of Plasmodium vivax infections; however, in some special circumstances infection periods in excess of two years may be exceptionally admitted. In P. falciparum infections the initial attack should not lie back more than one year with the exception of many areas of Africa where a longer period may have to be considered. For P. malariae infections it is impossible to lay down a definite period - the time limit may be longer than two years.

Another limitation with regard to the permissible time for the original infection is that expressed in the definition of a relapsing case given in the forthcoming WHO monograph - Malaria Terminology¹ - which adds to the definition of the Expert Committee a postulate "... that the infection had been contracted before the interruption of transmission was claimed in the relevant locality".

Difficulties have arisen in the interpretation of the second clause in the Expert Committee's definition, "... as shown by the absence of any associated cases in the neighbourhood of its origin." If this is taken verbatim it could be understood to signify that a case, defined as a relapse on the basis of its history, must be classified as indigenous if any additional case or cases were found simultaneously or within a short period in the neighbourhood, even if these cases were not indigenous.

¹ Revised edition 1961 to be published shortly

In fact, however, the words "associated cases" should be interpreted as epidemiologically related cases, and the simultaneous discovery of several cases in one locality may be pure coincidence and not due to an epidemiological (transmission) link. The simultaneous discovery of other cases in the neighbourhood should always arouse suspicion of local transmission and lead to an intensive epidemiological investigation of the locality with a full study of social, entomological and other relevant conditions. But if such an investigation has furnished a reasonable explanation of the other cases and proved the absence of transmission, the case can be classified as relapsing.

It should be noted that the term relapsing case applies in the first instance to late relapses of infections acquired naturally in the same area prior to interruption of transmission (i.e. relapses of indigenous cases). However, it also applies to relapses of imported, introduced and - at least theoretically - induced cases, (but see paragraph (8) "Priority of Classification"). In the latter instances it is recommended that on the individual case card the case should be marked as: Relapsing (from imported, etc., case).

4. Imported case

The definition of an imported case as laid down by the Expert Committee in their Sixth and Eighth Reports is:

"Imported, as shown by tracing the case to its origin in an acknowledged malarious area."

When the whole malarious area (or formerly malarious area) of a given country is in the same phase of an eradication programme and can be considered as one unit from an epidemiological and operational point of view, this term can be simply interpreted as signifying a case the origin of which could be traced to a malarious area outside the country. In reality, however, in many programmes different parts of a country are in different phases of a malaria eradication programme and/or form large geographically separated epidemiological/operational units. In these instances each of these units has to be separately assessed with regard to its progress towards malaria eradication and the term imported can no longer be confined to cases imported from abroad but must also be applied to cases imported from areas within the national boundaries of the

country. From both an epidemiological and an operational point of view it is, however, important to define in regard to imported cases whether the origin of infection was abroad or within the country. Furthermore, assuming that the case was found in a consolidation phase area it would be important to define whether the case originated in an attack phase area of the same country (by far the most common occurrence) or from another consolidation phase area in the same country. In the latter instance the classification as imported would only be permissible if that other consolidation phase area is geographically separated from the consolidation phase area in which the case was found, and if that area of origin formed a distinct, separated, large administrative unit. In accordance with these concepts, imported cases should be sub-classified as follows:

- (a) imported from abroad
- (b) imported from within the country from an attack phase area; or an area in an earlier stage than attack phase;
- (c) imported from within the country from another geographically separated consolidation phase area.

Theoretically speaking a case may also be imported from a maintenance phase area in the same country but in practice this will occur very rarely, if ever.

In connexion with cases imported from within the country the question may arise whether in consolidated reports these cases should be recorded and registered for the area of detection or the area of origin. It goes without saying that for a proper epidemiological assessment of a national malaria eradication campaign, information both on the place where the infection was acquired and where it was detected is of importance and provision should always be made to ensure knowledge of the case in both locations. A decision has to be made, however, as to the place for which the case should be recorded. Taking the most common occurrence of a case contracted from local transmission in an attack phase area and imported to and detected in a consolidation phase area, the case should be recorded as imported in the consolidation phase area and not as indigenous in the attack phase area. This is taking into consideration the importance of the fact that imported cases in a consolidation phase area constitute an additional work load in treatment and follow-up for the surveillance mechanism. In the situation considered here this information in regard to the place

of detection for the purpose of consolidated reports is more important than the information of one more indigenous case in an attack phase area where presumably other indigenous cases were occurring at the same time. As stated above, however, this should not preclude the rapid information of the Malaria Eradication Service unit in the attack phase area where the case originated. If a case in a consolidation phase area had been imported from another consolidation phase area in the same country, where the infection was due to recent local transmission, the fact of the occurrence of an indigenous case in the originating consolidation phase area is of at least equal importance to that of the importation of a case in the other consolidation phase area. In these, on the whole rare, instances it will be necessary to include the case in consolidated reports for both areas, appearing as indigenous in one and as imported in the other. In consolidated reports for a whole country such doubly recorded and counted cases should be specially marked and explained.

5. Introduced case

The definition of an introduced case as laid down by the Expert Committee in their Sixth and Eighth Reports is:

"... directly secondary to a known imported case".

The principal epidemiological consideration for giving these cases a special status is that if transmission can be detected at a moment when it has not progressed beyond one step then the situation can still be handled with relative ease through appropriate actions so as to prevent the re-establishment of endemicity. The postulate that the original case must be an imported case is an additional safeguard for the assumption that transmission is limited to one step only an assumption that could not be made with a similar degree of assurance with regard to directly secondary cases originating, for instance, from relapsing cases. In practice it will not be easy to obtain conclusive proof that only one step of local transmission is involved and to find the direct link of the case in question with a known imported case. The classification "introduced" should therefore be made with extreme caution and in case of doubt cases should be classified as indigenous. In order to provide the fullest possible justification for classifying a case as introduced - signifying that not more than one step of local transmission was involved - strict epidemiological observation of the locality subsequent to the detection of the case should be made a rule. Such subsequent observation will, in the event of no further cases being detected, provide additional proof for the absence of transmission beyond the first step.

6. Induced case

The definition of an induced case as laid down by the Expert Committee in their Sixth and Eighth Reports is:

"Induced, as shown by its relation to a blood transfusion with an appropriate interval, or to another form of parenteral inoculation to which infection could be properly attributed."

This definition of the Expert Committee refers mainly to those induced cases which are due to blood transfusion or other accidental causes. These are admittedly the most frequent types of induced cases. However, it should not be forgotten that another type of case comes under the same classification, viz, those brought about deliberately for the purpose of malaria therapy or experimentation.

Induced cases can usually be defined as such without great difficulty on the basis of a carefully taken case history. In the instance of transfusion malaria the epidemiological evidence is usually straightforward and convincing even if, as so often happens, parasites cannot be demonstrated microscopically in the peripheral blood of the suspected donor. It may be pointed out here that during the late phases of a malaria eradication campaign, induced cases may give an indication of an otherwise undetected parasite reservoir and should therefore be the starting point of a full epidemiological investigation.

7. Indigenous case

In their criteria for malaria eradication (Sixth and Eighth Reports) the Expert Committee have not given a positive definition of the term indigenous. This term is thus defined by the Expert Committee only per exclusionem implying that any case that cannot be classified as relapsing, imported, introduced or induced (which terms are defined) must be considered as indigenous. An official definition of the term indigenous would, therefore, have to read as follows:

"Indigenous - any case which cannot be proved to be relapsing, imported, introduced or induced."

For operational purposes we would amplify this strict official definition by the following:

"A malaria infection which has been proved or cannot be disproved to be due to recent local transmission."

The concept "recent" cannot easily be defined in terms of a specific number of weeks or months but must be interpreted on an epidemiological basis. It may be safe to state that "recent local transmission" should refer to a period not exceeding one year.

While it would be always desirable to arrive, through patient investigation, at a positive proof of local transmission, the rule has to be followed that also cases in which such positive proof has not been reached but which cannot be proved to belong to any of the other categories, must be classified as indigenous. (See also "Undeterminable case" below.)

8. Priority of Classification

A question of priority sometimes arises when a case presents elements for two different classifications. One such example has already been given when discussing the classification of cases imported within a country, which cases may be indigenous at the point of origin (e.g. in an attack phase area of the country) and imported in the locality of detection (e.g. in the consolidation phase area of the same country). For this example we have indicated the classification to be chosen.

Another example frequently met in practice is that of cases which may be defined as either relapsing or imported depending on the importance given to one or other aspect of the case. The following rules may help in the decision in such an instance:

- (a) a case having contracted the infection outside the area under consideration should at the time of its first discovery in the locality invariably be classified as imported, irrespective of whether this is his first manifestation of the disease or not;
- (b) a case previously detected and then defined as imported into an area and presenting later on a relapse in the same area should in this second instance be classified always as relapsing (the operational implication being that his treatment and follow-up in this area were insufficient).

9. Unclassifiable/Undeterminable Cases

In every malaria eradication programme, even one with the very best epidemiological service, unavoidably some cases will be met which are impossible to classify for a variety of reasons.

A distinction should be made between:

- (a) cases which could not be classified because a proper investigation was not, or could not have been, carried out, and
- (b) cases which have been properly investigated but in which it was impossible to reach a valid conclusion as to the nature and origin of the cases.

(a) Cases may become lost for investigation for operational reasons such as shortage of staff at the time of detection and the impossibility to conduct a useful investigation a long time afterwards. In other instances it may be impossible to trace a case after the positive microscopic diagnosis of a blood slide because the person has moved out of the locality and cannot be found or because the identification of the blood slide was insufficient. In consolidated quarterly reports on surveillance operations or similar reports such cases should be listed as "unclassified", it being understood that this refers always to cases which have been "lost for investigation" for reasons like the ones mentioned above or for similar reasons. If such "unclassified" cases form a large proportion of all cases in a series of subsequent reports this should alert the higher echelons of a malaria eradication service to the unsatisfactory situation in epidemiological operations. It will be necessary eventually to classify these cases as indigenous in the absence of proof to the contrary.

(b) There will be other cases where a proper investigation has been carried out but where there was neither sufficient evidence to show that the case was relapsing, imported, introduced or induced, nor any evidence of local transmission. These will usually be isolated cases occurring in a locality where none had been detected for a considerable time, and where no additional cases were found during the epidemiological investigation and during subsequent close observation of the locality. According to what has been said on the classification of indigenous cases these cases will have to be classified immediately as indigenous and will have to be registered as such in quarterly and other reports. A note should, however, be made in the summing up

paragraph of the individual case card indicating that it had to be classified as indigenous because in spite of a thorough investigation no conclusive proof as to its true nature was obtainable. For internal purposes such a case may be marked on the case card as "Indigenous, single, source undeterminable, not followed by further transmission". It will be important to have such a record for the time when the question of certification of achieved eradication arises, as it may be possible to permit a limited number of such cases during the consolidation phase, in spite of their classification as indigenous, if sufficient evidence on the circumstances of the case and on the absence of transmission during the subsequent period in the locality is available.

It can be seen from the discussion above on classification of the various categories of malaria cases that such classification can rarely be made only on the basis of investigation of the individual case and that a final conclusion can only be reached when the situation in the whole locality (focus) has been duly investigated and critically assessed. This concept may be formulated as a rule as follows:

Classification of malaria cases should never be made on the basis of the investigation of the relevant case alone. This first investigation will merely indicate a tentative classification which should be confirmed - or rejected - on the basis of a full epidemiological investigation of the locality and all the factors involved.

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TABLE I

QUARTERLY DATA ON SURVEILLANCE OPERATIONS

Country District
Year Quarter Phase

Phase of the programme	Area with combined active and passive case detection methods	Area with either active or passive case detection methods
<p>1. <u>Passive case detection</u></p> <p>1.1 Approximate population under passive case detection</p> <p>1.2 Number of malaria detection posts:</p> <p>(a) Health units</p> <p>(b) Voluntary collaborators</p> <p>2. <u>Active case detection</u></p> <p>2.1 Population under active case detection</p> <p>2.2 Actual number of households under active case detection</p> <p>2.3 Average interval between visits</p> <p>2.4 Number of people seen during the quarter*</p> <p>2.5 Number of surveillance agents on last day of quarter</p>		

* Record each separate visit; i.e. if a person is seen 3 times during the quarter, each visit should be counted and the figure recorded would be "3".

Remarks:

TABLE II

QUARTERLY INFORMATION ON SOURCE OF SLIDES

Country District
 Year Quarter Phase

	Slides examined	Slides found positive
1. <u>Passive case detection</u>		
1.1 Health units (M.D.P.)		
1.2 Voluntary collaborators (M.D.P.)		
1.3 Medical persons or institutions (not M.D.P.) and Compulsory notifications *		
2. <u>Active case detection</u> (House-to-house fever case surveys)		
3. <u>Mass blood examinations</u>		
4. <u>Epidemiological survey</u> (in the neighbourhood of confirmed cases)		
5. <u>Follow-up</u> (of confirmed malaria cases)		
6. <u>Special surveys</u> **		
Total number:		

M.D.P. = Malaria Detection Post

* Those not included anywhere else under nos. 1 to 6.

** Indicate type of survey. Infant surveys should always be recorded under item 6 and not under item 3.

N.B. Data should be recorded once only - no duplication under separate items.

Remarks:

TABLE III

QUARTERLY INFORMATION ON SPECIES OF PARASITES AND ORIGIN OF INFECTION
 OF CONFIRMED MALARIA CASES BY AGE GROUPS

Country District

Year Quarter Phase

A.

Species of Malaria Parasites	Number of Infections
<u>Plasmodium vivax</u>	
<u>Plasmodium falciparum</u>	
<u>Plasmodium malariae</u>	
<u>Plasmodium ovale</u>	
Mixed	
Unclassifiable	

B.*

Origin of infection	age group (in years)				Total
	Under 1	1 - 4	5 - 14	15 and over	
Indigenous					
Relapsing					
Imported (a)					
Imported (b)					
Imported (c)					
Induced					
Introduced					
Unclassified**					
Total:					
				From quarter under review	
				From previous quarters	

Imported (a) = from abroad

Imported (b) = from within the country - attack phase area

Imported (c) = from within the country - consolidation phase area

* Record under III B, the actual number of cases which have been investigated during the quarter whether they were detected in previous quarters or during the quarter under review and omit those cases where the investigation has not been completed. They should be reported in the next quarterly report.

** This category should be used only for cases lost for investigation. Cases investigated but whose origin cannot be clearly defined ("unclassifiable") must be recorded as "indigenous".

Remarks:

TABLE IV

QUARTERLY INFORMATION ON RADICAL TREATMENT

Country District
 Year Quarter Phase

Drug(s)		Total number of:			
Name	Mg. base per tablet	Confirmed malaria cases			Tablets administered
		encoun-tered	Treatment started	Treatment completed	

Remarks:

TABLE V

QUARTERLY INFORMATION ON LABORATORY SERVICES

Country

Year Quarter Phase

1. Number of microscopists employed full-time in ME laboratories on last day of the quarter	
2. Number of microscopists employed part-time in ME laboratories on last day of the quarter	
3. Number of positive slides re-examined	
4. Number of negative slides re-examined	
5. Proportion of total slides examined in laboratories outside the ME Service	

Remarks:

The purpose of the WHO/Mal Series of documents is three-fold:

- (a) to acquaint WHO staff, national institutes and individual research or public health workers with the changing trends of malaria research and the progress of malaria eradication by means of summaries of some relevant problems;
- (b) to distribute to the groups mentioned above those field reports and other communications which are of particular interest but which would not normally be printed in any WHO publications;
- (c) to make available to interested readers some papers which will eventually appear in print but which, on account of their immediate interest or importance, deserve to be known without undue delay.

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