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A Review on Diagnostic Tests of Malaria

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Abstract: *Malaria is one of the leading causes of death in tropical and subtropical countries, killing more than 1 million people worldwide each year; 90% of deaths occur in African children. Although there are effective ways to control malaria, the number of malaria cases continues to rise for many reasons. Timely and effective diagnosis is essential for the control and management of malaria in this emergency. Routine methods of diagnosing malaria are still problematic; therefore, new technologies are being developed and introduced to overcome these limitations. This review summarizes current malaria diagnostic procedures.*

Keywords: *Malaria*.

I. INTRODUCTION

Sometimes called the "king of diseases," malaria is caused by single celled parasites of the Plasmodium genus. The most severe and sometimes fatal form of malaria is caused by Plasmodium falciparum. Other human malaria species, P. vivax, P. ovale, P. Malaria and sometimes Plasmodium knowlesi can cause severe, severe illness with a low mortality rate. Malaria is the most important infectious disease in the tropics and subtropics and continues to be a global health problem with more than 40% of the world's population at risk, unlike in nearly 100 countries. It is estimated that malaria infects more than 500 million people each year and kills approximately 1-2 million people, 90% of whom are children, in sub Saharan Africa [1]. The number of malaria cases is likely to increase worldwide due to declining malaria control's risk of regional transmission, increased use of antiretroviral drugs among parasites, and in some cases increased international travel and migration [2].

As effective diagnosis reduces malaria complications and mortality, there is a growing need worldwide for effective and efficient malaria diagnosis [3]. It can be difficult to separate the diagnosis from other tropical diseases based on the patient's signs and symptoms or physician findings. Therefore, it is necessary to be careful about diagnosis using the test method. This review discusses malaria diagnoses currently available in a variety of settings and examines their effectiveness in potentially rich and resource-poor environments.

II. DIAGNOSIS OF MALERIA

Timely and accurate diagnosis is essential for malaria control. The global impact of malaria has fueled interest in the development of effective diagnostic strategies, not only in resource-limited areas where malaria places a heavy burden on humans, but also in developing countries where malaria diagnostic information is often lacking [4,5]. Diagnosis of malaria involves identification of Plasmodium parasites or antigens/substances in the patient's blood. While this may seem simple, many factors influence the diagnosis. 5 different types of malaria; different stages of mitosis, spread of different species, level of infection, population movement, parasitemia, immunity, and interaction of signs and symptoms; Vaccination, recurrent malaria, persistent or non-persistent parasitemia, sequestration of parasites

III. LABORATORY ANALYSIS OF MAERIA

Fast and effective malaria diagnosis not only alleviates suffering, but also decreases community transmission. The nonspecific nature of the clinical signs and symptoms of malaria may result in over-treatment of malaria or non-treatment of other diseases in malaria-endemic areas, and misdiagnosis in non-endemic areas [15]. In the laboratory, malaria is diagnosed using different techniques, e.g. conventional microscopic diagnosis by staining thin and thick peripheral blood smears [16], other concentration techniques, e.g. quantitative buffy coat (QBC) method [15], rapid diagnostic tests e.g., OptiMAL [17,18], ICT [19], Para-HIT-f [10], ParaScreen [20], SD Bioline [21], Paracheck [22], and molecular diagnostic methods, such as polymerase chain reaction (PCR) [23,24]. Some advantages and shortcomings of these methods have also been described, related to sensitivity, specificity, accuracy, precision, time

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consumed, cost-effectiveness, labor intensiveness, the need for skilled microscopists, and the problem of inexperienced technicians.

Microscopic diagnosis using stained thin and thick peripheral blood smears (PBS):

Malaria is conventionally diagnosed by microscopic examination of stained blood films using Giemsa, Wright's, or Field's stains [25]. This method has changed very little since Laverran's original discovery of the malaria parasite, and improvements in staining techniques by Romanowsky in the late 1,800s. More than a century later, microscopic detection and identification of Plasmodium species in Giemsa-stained thick blood films (for screening the presenting malaria parasite), and thin blood films (for species' confirmation) remains the gold standard for laboratory diagnosis [26]. Malaria is diagnosed microscopically by staining thick and thin blood films on a glass slide, to visualize malaria parasites. Briefly, the patient's finger is cleaned with 70% ethyl alcohol, allowed to dry and then the side of fingertip is picked with a sharp sterile lancet and two drops of blood are placed on a glass slide. To prepare a thick blood film, a blood spot is stirred in a circular motion with the corner of the slide, taking care not make the preparation too thick, and allowed to dry without fixative. After drying, the spot is stained with diluted Giemsa (1 : 20, vol/vol) for 20 min, and washed by placing the film in buffered water for 3 min. The slide is allowed to air-dry in a vertical position and examination using a light microscope. As they are unfixed, the red cells lyse when a water-based stain is applied. A thin blood film is prepared by immediately placing the smooth edge of a spreader slide in a drop of blood, adjusting the angle between slide and spreader to 45° and then smearing the blood with a swift and steady sweep along the surface. The film is then allowed to air-dry and is fixed with absolute methanol. After drying, the sample is stained with diluted Giemsa (1 : 20, vol/vol) for 20 min and washed by briefly dipping the slide in and out of a jar of buffered water (excessive washing will decolorize the film). The slide is then allowed to air-dry in a vertical position and examined under a light microscope [27]. The wide acceptance of this technique by laboratories all around the world can be attributed to its simplicity, low cost, its ability to identify the presence of parasites, the infecting species, and assess parasite density-all parameters useful for the management of malaria. Recently, a study showed that conventional malaria microscopic diagnosis at primary healthcare facilities in Tanzania could reduce the prescription of antimalarial drugs, and also appeared to improve the appropriate management of non-malarial fevers [16]. However, the staining and interpretation processes are labor intensive, time consuming, and require considerable expertise and trained healthcare workers, particularly for identifying species accurately at low parasitemia or in mixed malarial infections. The most important shortcoming of microscopic examination is its relatively low sensitivity, particularly at low parasite levels. Although the expert microscopist can detect up to 5 parasites/µl, the average microscopist detects only 50-100 parasites/µl [28]. This has probably resulted in underestimating malaria infection rates, especially cases with low parasitemia and asymptomatic malaria. The ability to maintain required levels of in malaria diagnostics expertise is problematic, especially in remote medical centers in countries where the disease is rarely seen [29]. Microscopy is laborious and ill-suited for high-throughput use, and species determination at low parasite density is still challenging. Therefore, in remote rural settings, e.g. peripheral medical clinics with no electricity and no health-facility resources, microscopy is often unavailable [30].

IV. MOLECULAR DIAGNOSIS METHODS

oted above, traditional malaria diagnostic methods are problematic. Many laboratories need new diagnostic methods with high requirements and high features, no difference. Recent advances in molecular biology techniques such as PCR, loop-mediated isothermal amplification (LAMP), microarray, mass spectrometry (MS), and flow cytometry (FCM) analysis have enabled the spread of malaria parasites, and new techniques have been developed for malaria diagnosis. .

PCR technology

PCR-based technology is a new development in the molecular diagnosis of malaria and has been shown to be one of the most specific and effective methods for diagnosis, particularly in malaria patients with hypoparacythemia or a combination [55]. PCR technology continues to be widely used to confirm malaria, monitor response to treatment, and identify vaccine [27]. It has been shown to be more sensitive than QBC and some RDTs [56,57]. As the gold standard for malaria diagnosis, PCR has been shown to be more sensitive and specific than stained microscopy of peripheral

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blood smears and now appears to be the best way to diagnose malaria [55]. PCR can detect as few as 1-5 bacteria/µl of blood (≤ 0.0001% infected erythrocytes compared to approximately 50-100 parasites/µl blood detected by microscopy or RDT). In addition, PCR will be useful in the detection of parasites, infectious diseases and can use large samples of these samples in their work [58,59]. Some modified PCR methods such as nested PCR, real-time PCR, reverse PCR have been proven to be reliable and have emerged as the second method of 96 Korean J Parasitol. roll 47, no. 2: 93-102, June 2009 The usual diagnostic criteria for patients with signs and symptoms of malaria are not included; it also allows the identification of correct species [58,60-62]. Recently, PCR methods for the identification of P. knowlesi [63-65] have gained widespread acceptance. Although PCR seems to have overcome the two main problems (sensitivity and specificity) in diagnosing malaria, the use of PCR is limited by its complex process, high cost and need for skilled specialists. Therefore, PCR is not routinely used in developing countries due to the complexity of the tests and the lack of resources to perform these tests adequately and routinely [66]. Quality control and maintenance of equipment is also important for PCR technology, so it may not be suitable for diagnosing malaria in remote areas or even in modern laboratories [67].

LAMP technology

LAMP technology has been described as a simple and inexpensive molecular malaria diagnostic test for the conserved 18S ribosomal RNA gene of Plasmodium falciparum [68]. Other studies have shown good sensitivity and specificity not only for P. falciparum but also for P. vivax, P. ovale and P. malariae [69,70]. The principle of microarray technology is similar to Southern hybridization. Targets separated from the nucleic acid in the test sample are hybridized to the probes in the array, allowing multiple genetic targets to be analyzed in a single test. Best of all, this technique can be miniaturized and used for point-of-care diagnosis [23]. A panmicrobial oligonucleotide microarray was developed for the diagnosis of infectious diseases and confirmed the presence of Plasmodium falciparum in clinical specimens [74]. However, these diagnostic methods are still in the early stages of development [30].

FCM detection

Flow cytometry has been reported for the diagnosis of malaria [75–77]. Briefly, the principle of the process is based on the discovery of plasmodium, which occurs when the malaria parasite in red blood cells digests hemoglobin and crystallizes the toxic hemi released by plasmodium in the acidic vacuole, and forms plasmodium. Plasmodium in phagocytic cells can be detected by depolarization of laser light as the cells pass through the flow cytometer channel. This method can provide 49-98% sensitivity and 82-97% specificity in the diagnosis of malaria [78,79] and can be used in the diagnosis of unscreened malaria. The disadvantages are labor intensive, highly trained professionals required, expensive diagnostic equipment, and the possibility of being negative for other diseases or conditions. Therefore, this method should be considered as a malaria screening tool.

Automatic blood cell counter (ACC)

The ACC is a useful diagnostic tool for malaria [80] and 3 methods have been reported. The initial detection of malaria pigment (plasmozoin) in monocytes using the Cell-Dyn® 3500 test showed 95% sensitivity and 88% specificity compared to standard heat spread [81]. The second method also used Cell-Dyn® 3500 and examined the depolarized light laser (DLL) to detect malaria with an overall sensitivity of 72% and a specificity of 96% [82]. A third method used the Beckman Coulter ACC to measure monocytes by volume, conductivity, and scattering (VCS) with 98% sensitivity and 94% specificity [83]. Although promising, none of these 3 techniques are routinely available in clinical settings; More research is needed to develop and validate the device and its software. The promising accuracy of this technique in diagnosing malaria means that the ACC can be an important diagnostic tool for routine malaria diagnosis.

Mass spectrometry

A new method for the detection of malaria in vitro with a sensitivity of 10 parasites/µl blood has been recently reported. It includes a procedure for cleaning whole blood samples followed by direct UV laser desorption mass spectrometry (LDMS). SSSFor the diagnosis of malaria, the principle of LDMS is to identify specific biomarkers in clinical samples. In malaria, heme from plasmodium is a biomarker specific to the parasite of interest. LDMS is fast, highly efficient and

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automated. Compared to the microscopic technique, which requires skilled technicians and up to 30-60 minutes to analyze each peripheral blood smear, LDMS can identify the sample in <1 minute [84]. However, rural areas without electricity are not suitable for the existing large-scale electricity supply. Future developments in equipment and technology should make this approach even more effective.

V. CONCLUSION

Routine microscopic examination of peripheral thick and thin blood smears remains the gold standard for diagnosing malaria. Although this method requires microscope training and differs in sensitivity and specificity compared to the latest technologies, it is inexpensive and reliable. Quick and easy RDT is currently used in many remote areas, but is expensive and requires advanced quality control. Serological tests are useful for detecting infectious diseases, but not for diagnosing acute malaria. Molecular biology methods are related to laboratory science; They can be used to detect antibody development, can be used for species identification, and can be used to assess disease severity in hypoparacytemia.

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