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A SHORT REVIEW OF LABORATORY DIAGNOSIS OF MALARIA

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Abstract: Malaria is one of the most important tropical infectious diseases. The gross number of malaria cases is on the increase worldwide mainly due to limitations of traditional methods for malaria diagnosis. The accurate and timely diagnosis of malaria infection is essential if severe complications and mortality are to be reduced by early specific anti malarial treatment. This review details the currently available diagnostic methods for malaria.

Keywords: Malaria, Laboratory diagnosis

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INTRODUCTION

Malaria is a mosquito-borne infectious disease of humans and other animals caused by parasitic protozoan (a type of unicellular microorganism) of the genus *Plasmodium*. Commonly, the disease is transmitted via a bite from an infected female *Anopheles* mosquito, which introduces the organisms from its saliva into the person's circulatory system. In the blood, the protists travel to the liver to mature and reproduce. Malaria causes symptoms that typically include fever and headache, which in severe cases can progress to coma or death. The disease is widespread in tropical and subtropical regions in a broad band around the equator, including much of Sub-Saharan Africa, Asia, and the Americas.

Five species of *Plasmodium* can infect and be transmitted by humans. The vast majority of deaths are caused by *Pl. falciparum* and *Pl. vivax*, while *Pl. ovale*, and *Pl. malariae* cause a generally milder form of malaria that is rarely fatal. The zoonotic species *Pl. knowlesi*, prevalent in Southeast Asia, causes malaria in macaques but can also cause severe infections in humans. Malaria is prevalent in tropical and subtropical regions because rainfall, warm temperatures, and stagnant waters provide habitats ideal for mosquito larvae. Disease transmission can be reduced by preventing mosquito bites by using mosquito nets and insect repellents, or with mosquito-control measures such as spraying insecticides and draining standing water.

Malaria is typically diagnosed by the microscopic examination of blood using blood films, or with antigen-based rapid diagnostic tests. Modern techniques that use the polymerase chain reaction to detect the parasite's DNA have also been developed, but these are not widely used in malaria-endemic areas due to their cost and complexity. The World Health Organization has estimated that in 2010, there were 219 million documented cases of malaria. That year, the disease killed between 660,000 and 1.2 million people,[1] many of whom were children in Africa. The actual number of deaths is not known with certainty, as accurate data is unavailable in many rural areas, and many cases are undocumented. Malaria is commonly associated with poverty and may also be a major hindrance to economic development.

Despite a need, no effective vaccine currently exists, although efforts to develop one are ongoing. Several medications are available to prevent malaria in travellers to malaria-endemic countries (prophylaxis). A variety of anti malarial medications are available. Severe malaria is treated with intravenous or intramuscular quinine or, since the mid-2000s, the artemisinin derivative artesunate, which is superior to quinine in both children and adults and is given in combination with a second anti-malarial such as mefloquine. Resistance has

developed to several anti malarial drugs; for example, chloroquine-resistant *Pl. falciparum* has spread to most malarial areas, and emerging resistance to artemisinin has become a problem in some parts of Southeast Asia.

LABORATORY DIAGNOSIS

Blood films

The most economic, preferred, and reliable diagnosis of malaria is microscopic examination of blood films because each of the four major parasite species has distinguishing characteristics. Two sorts of blood film are traditionally used. Thin films are similar to usual blood films and allow species identification because the parasite's appearance is best preserved in this preparation. Thick films allow the microscopist to screen a larger volume of blood and are about eleven times more sensitive than the thin film, so picking up low levels of infection is easier on the thick film, but the appearance of the parasite is much more distorted and therefore distinguishing between the different species can be much more difficult. With the pros and cons of both thick and thin smears taken into consideration, it is imperative to utilize both smears while attempting to make a definitive diagnosis.[2]

From the thick film, an experienced microscopist can detect parasite levels (or parasitemia) as few as 5 parasites/µL blood.[3] Diagnosis of species can be difficult because the early trophozoites ("ring form") of all four species look identical and it is never possible to diagnose species on the basis of a single ring form; species identification is always based on several trophozoites.

Plasmodium malariae and *Pl. knowlesi* (which is the most common cause of malaria in South-east Asia) look very similar under the microscope. However, *Pl. knowlesi* parasitemia increases very fast and causes more severe disease than *Pl. malariae*, so it is important to identify and treat infections quickly. Therefore modern methods such as PCR (see "Molecular methods" below) or monoclonal antibody panels that can distinguish between the two should be used in this part of the world.[4]

Antigen tests

For areas where microscopy is not available, or where laboratory staff are not experienced at malaria diagnosis, there are commercial antigen detection tests that require only a drop of blood.[5] Immunochromatographic tests (also called: Malaria Rapid Diagnostic Tests, Antigen-Capture Assay or "Dipsticks") have been developed, distributed and field tested. These tests use finger-stick or venous blood, the completed test takes a total of 15–20 minutes, and the results are read visually as the presence or absence of colored stripes on the dipstick, so they are suitable for use in the field. The threshold of detection by these rapid diagnostic tests is in the range of 100 parasites/µl of blood

(commercial kits can range from about 0.002% to 0.1% parasitemia) compared to 5 by thick film microscopy. One disadvantage is that dipstick tests are qualitative but not quantitative – they can determine if parasites are present in the blood, but not how many.

The first rapid diagnostic tests were using *Pl. falciparum* glutamate dehydrogenase as antigen.[6] PGluDH was soon replaced by *Pl. falciparum* lactate dehydrogenase, a 33 kDa oxidoreductase. It is the last enzyme of the glycolytic pathway, essential for ATP generation and one of the most abundant enzymes expressed by *Pl. falciparum*. PLDH does not persist in the blood but clears about the same time as the parasites following successful treatment. The lack of antigen persistence after treatment makes the pLDH test useful in predicting treatment failure. In this respect, pLDH is similar to pGluDH. Depending on which monoclonal antibodies are used, this type of assay can distinguish between all five different species of human malaria parasites, because of antigenic differences between their pLDH isoenzymes.

Molecular methods

Molecular methods are available in some clinical laboratories and rapid real-time assays (for example, QT-NASBA based on the polymerase chain reaction)[7] are being developed with the hope of being able to deploy them in endemic areas.

PCR (and other molecular methods) is more accurate than microscopy. However, it is expensive, and requires a specialized laboratory. Moreover, levels of parasitemia are not necessarily correlative with the progression of disease, particularly when the parasite is able to adhere to blood vessel walls. Therefore more sensitive, low-tech diagnosis tools need to be developed in order to detect low levels of parasitemia in the field.[8]

CONCLUSIONS

The diagnosis of malaria by conventional microscopy remains the gold standard for malaria diagnosis, although it requires highly-skilled personnel and may have a lower sensitivity than the more recent molecular techniques.

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