LABORATORY DIAGNOSIS OF MALARIA

A panoramic view and update of the diagnostic armamentarium

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The global malaria mortality is larger than expected, in the range of 1.24 million deaths worldwide, as estimated by a systematic analysis published in The Lancet recently. The clinical differential diagnosis of malaria is broad and requires a high index of suspicion. . Laboratory diagnostic tests can be broadly classified as tests used to establish diagnosis/etiology, tests used to assess clinical status and tests used in assistance with therapy. This article provides a panoramic view of our diagnostic armamentarium and current status in terms of the clinical utility of traditional and newer tests against these dangerous microscopic travelers.

GOLD STANDARD FOR DIAGNOSIS

The gold standard for malaria diagnosis is the microscopy of blood smears which is a direct detection method using thick and thin Giemsa stained blood smears. Blood film identification and techniques have been well described in various practical guides such as the WHO (1991) Basic Malaria Microscopy-Learners Guide, WHO.Geneva. Four species account for most human infections: Plasmodium vivax, P.falciparum, P.malariae and P.ovale. Added to that is Plasmodium knowlesi. Ideally, smears should be made every 6-12 hours for 3 consecutive days, Requests for malaria diagnosis should be considered as representing a potential medical emergency so specimens should be transported and tested in a “Stat” manner.

NON BLOOD FILM DIAGNOSTIC TECHNIQUES

Non blood film malaria diagnostic techniques which are currently available include Dipstick antigen capture tests (e.g. Paracheck, ParaSight F, Malaria PFTest,, Optimal test, Quantitative Buffy Coat/QBC method), PCR and sero diagnosis. Rapid dipstick methods such as ParaSight F and Malarial PF test use a monoclonal antibody to detect the histidine -rich protein antibody of P.falciparum. These are useful in those who have not had malaria before and require minimal expertise..However they are not quantitative and detect only P. falciparum. The Optimal test detects parasite lactate dehydrogenase pLDH and this test can be used to detect P falciparum from non falciparum infections. PCR methods have been developed that are very sensitive and specific.

TESTS USED IN CLINICAL STATUS ASSESSMENT

Tests used in assessing the clinical status include Blood Sugar-hypoglycemia in P.falciparum needs immediate treatment, platelet count-thrombocytopenia is suggestive of P falciparum , WBC count, inflammatory markers-ESR,CRP, Blood cultures to exclude secondary infection. Very ill patients are assessed for markers of severity (includes LFTs, blood film for hemolysis, coagulation status, arterial blood gases, glucose and lactate levels etc). The possibility of a co existent second diagnosis, (especially in P. falciparum infestation), such as Salmonella septicemia (so called ‘algid malaria’) should be

considered. Assessment for hemoglobinopathy- sickle cell disease is used when necessary. Tests used in assistance with therapy include G6PD status when clinically indicated.

COMPARISON OF TEST CHARACTERISTICS

The different test methods used in the diagnosis of malaria can be compared using test characteristics such as sensitivity, specificity, parasite density/parasitemia, turnaround time, skill level needed, equipment, and cost/test. The sensitivity for microscopy is estimated as 50 parasites/ul with specificity for all species of plasmodium and an estimation of parasitemia. The skill level needed for malaria microscopy is high but the cost/test is low as the equipment needed is a good microscope. Turnaround time for microscopy is 30-60 minutes. PCR method is estimated to carry the highest test sensitivity estimated as 5 parasites/ul with specificity for all plasmodium species. However, the PCR test does not estimate parasitemia. The skill level and cost/test are high as a PCR apparatus is required. The turnaround time for this test is 24hours. Fluorescence methods of detection are estimated to have a sensitivity of 50 parasites./ ul with a good specificity for P.falciparum and variable for others. The parasite density cannot be accurately estimated by fluorescence .The skill level and cost/test are considered moderate (QBC apparatus/fluorescence microscope required).The turnaround time is 30-60min.The sensitivity of Dipstick tests are estimated as>100parasites/ul. The specificity for Dipstick HRP-2 is for P.falciparum only. Dipstick pLDH ICT Pf/Pv is estimated to have a good specificity for P.falciparum and P.vivax. Dipstick tests provide a crude estimation of parasitemia. The major advantage of dipstick tests are the low skill levels required and rapid turnaround time of approximately 20 minutes with a moderate cost/test. Laboratory professionals may utilize test methods appropriate for their setting based on an evaluation of the above test characteristics and their specific clinical requirements.

RECENT ADVANCES

Scientists at the University of Korea have analyzed typical malaria signals on the nucleated RBC plots of an automated analyzer (DxH800) with a sensitivity of 100% according to a study published in the International Journal of Laboratory Hematology, November 11, 2011. As new research in malaria continues to enhance our understanding of the disease and its diagnostic aspects, our battle goes on.

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