Assessment of Malarial Infection Using Cell Population Data and Peripheral Blood Analysis. Background and Case Study

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Abstract

The malaria parasite causes almost a quarter billion infections and more than a half million deaths yearly. And malaria's impact is most prevalent in children. Diagnosing malaria relies on clinical signs and symptoms, microscopic examination, and advanced diagnostics.

The case report describes a case of *Plasmodium* malaria in a 42-year-old male who returned home to Spain following a 10-day trip to Southern Africa.

While many infectious agents are food or water borne, more than 17% of all infectious diseases are transmitted by vectors,[1] living organisms that transmit infectious agents among animals. While mechanical vectors simply carry the pathogen, biological vectors play a role in the life cycle of the pathogen. Fleas, flies, ticks, and even snails can serve as vectors. Among them, the mosquito is responsible for transmitting disease to nearly 700 million people, which results in more than 725,000 deaths each year.[1] In addition to its role as a mechanical vector for viruses such as West Nile, Dengue, and Zika, the mosquito also serves as a biological vector in the transmission of parasites.

Globally, billions of people are infected with parasites each year.[2] At the most basic level, parasitic diseases include any illness caused by an independently-reproducing infectious agent living on or in another organism and using the resources of the host organism without providing any benefit. Three main groups of parasites cause infections in humans: Ectoparasites, insects that can burrow under the skin and take up residence; helminths, parasitic worms that usually infect the intestinal tract but can also invade skin, brain, eyes, and other tissues; and protozoans, single-celled parasites that can infect the blood and often other parts of the body as well.

Protozoan parasites include diseases like lymphatic filariasis, sleeping sickness (African trypanosomiasis), Chagas disease (American trypanosomiasis), and malaria, a disease causing more than a half million deaths yearly.[3]

Malaria is a potentially life-threatening parasitic infection posing a significant global health threat. According to the World Health Organization, almost half of the global population is at risk of getting malaria,[4] and 247 million cases with over 600,000 deaths in 84 malaria-endemic countries were reported.[5] Once endemic as far north as the Scandinavias,[6,7] malaria is now geographically limited to warmer, more tropical climates (Figure 1). Malaria, literally translated from Italian as bad (mal) air (aria), is currently endemic to 97 countries.[8] African regions carry a disproportionately high burden of malaria infection, with almost 95% of the cases and 96% of the deaths.[3,9] Tragically, 80% of the deaths from malaria in this region are children under the age of 5.[9]

Stopping the spread

Controlling malaria outbreaks relies on controlling the vector, using physical barricades, medications, and potentially, vaccines. The WHO is committed to environmental control of mosquitos with targeted use of insecticides and larvicides coupled with innovation, research and development, and quality care for malaria patients.[3] Destroying available breeding sites may reduce breeding, which in turn will reduce the vector population. Adding insecticides such as, *Bacillus thuringiensis* var. *israelensis* toxin, growth regulators such as methoprene, or biological control agents such as certain fungi can be used to control larval growth.[10] Other control processes rely on changing human behaviors to eliminate the mosquito's habitat. *Anopheles* species can replicate in transient, shallow pools of water, such as those left when rainwater fills tire tracks or the burrowing pits left following

brickmaking.[10] Eliminating these water sources may help to control mosquito levels.

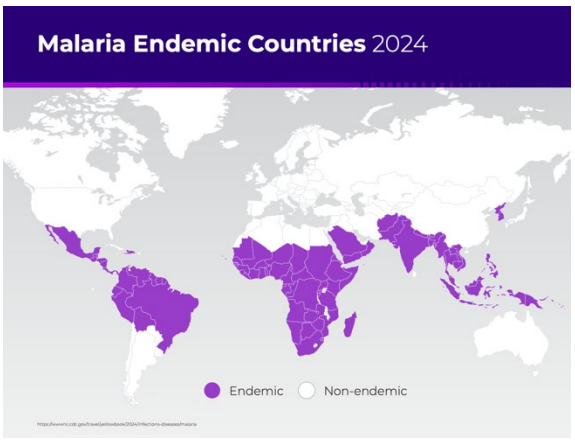

Figure 1. Malaria endemic countries, 2024

While controlling the vector is vital for decreasing malaria transmission, it is impossible to remove all mosquitoes, especially as resistance rises to the drugs designed to kill them.[3,11] Resistance to insecticides has been reported in *Anopheles* spp. since the 1950s,[11–13] and resistance to pyrethroids is now widespread.[11] In the early 2000s, mosquito-control efforts led to a significant reduction in malaria cases, but numbers are rising again due to the spread of insecticide resistance in endemic areas.[3,11] Physical barriers, such as long-lasting insecticide treated mosquito netting around beds, screening on doors and windows, and blocking of holes in eaves and elsewhere in housing,[3,14] are vital to keeping the mosquitoes away from their meal.

Vaccines are critical to slowing the spread of the parasite. There are several vaccines currently in development. Of these, 22 are in Phase I, 14 in Phase II, and one each in Phases III and IV clinical trials; 45% target the pre-erythrocytic stage—before reaching the red blood cells, 40% target the blood stage, and 24% target the sexual stage.[15] All are being developed against *P. falciparum* (87%) or *P. vivax* (14%).[15] RTS,S/AS01, the vaccine currently in Phase IV trials, was recently used in over 1 million children in Ghana, Kenya, and Malawi to protect them from *P. falciparum* malaria, supervised by Gavi, the Vaccine Alliance, and the World Health Organization.[3] It is also the only vaccine currently prequalified and recommended by the WHO.[15]

Climate Change and the Rise of Malaria

Weather patterns that lead to global fluctuations in temperature, such as the El Niño-Southern Oscillation (ENSO) phenomenon, have been shown to improve the environment for vectors,[16] subsequently driving increases in vector-borne diseases such as malaria.[17,18] Some models have suggested that increases in global temperatures have the potential to cause increased rates of vector-borne diseases, including malaria.[6,19] And recently, the Intergovernmental Panel on Climate Change warned that by the 2030s, global warming will put an additional 52-62 million people in southern Africa at risk of malaria infection[17]. Higher temperatures drive higher mosquito development and biting rates[20,21] as well as the rate of parasite replication within the mosquito.[21]

Moreover, rising temperatures will expand the transmission season and geographic reach of *Anopheles* mosquitoes, which will allow malaria to spread to populations with limited natural immunity.[16] That said, climate is not the only driver of vector-borne disease spread. For example, prior to the 1950s, much of the southeastern United States was considered malarious,[22] but with concerted malaria-eradication efforts, including the indoor use of DDT sprays,[23] malaria transmission in the United States was eliminated in 1951.[24]

There are five species of malaria that are associated with human disease. *Plasmodium falciparum* and *P. vivax* account for 90-95% of infections.[5,25,26] *P. falciparum* is the most deadly of the malarial parasites and, while declining due to control efforts,[7,27] it is the most prevalent species found in sub-Saharan Africa.[5,27] *P. vivax* is the most prevalent outside of sub-Saharan Africa. *P. ovale curtisi* and *P. ovale wallikeri* (two genetically distinct subspecies[28]) and *P. malariae* less commonly cause significant human disease.

The malaria parasite has a two-host, multistage lifecycle. Human infection begins with the bite of an infected female *Anopheles* mosquito; during the blood meal, malarial sporozoites from the mosquito's saliva are introduced into the host blood stream. The sporozoites travel through the blood to hepatocytes where they infect and mature into schizonts, mature malaria parasites containing many merozoites each. Merozoites, the life stage that infects red blood cells (RBCs), are released when the hepatocytes rupture. (Interestingly, *P. vivax* and *P. ovale* can remain dormant in the liver and cause disease months or years after initial infection.[29]) Released merozoites infect the RBCs and develop into ring forms (trophozoites) or gametocytes. Trophozoites mature in the RBCs, create more schizonts, and rupture releasing more merozoites. Gametocytes differentiate and mature and are transmitted

back to the mosquito vector upon her next blood meal.[8] Malaria does not spread by human-to-human or animal-to-human transmission.

Natural Selection

The link between the sickle cell trait and protection against malaria was first suggested in the mid-1900s.[30,31] Similarly, the Duffy glycoprotein, a receptor for chemicals secreted by blood cells during inflammation, also serves as a receptor for *P. vivax*\. RBCs that lack the Duffy antigens are relatively resistant to invasion.[32] Blood types in endemic populations lean toward O and Duffy negative.[31–33]

Symptoms

Symptoms of malaria infection may be mild or may be life threatening and depend on the species and the individual. The incubation period leading up to manifestation of symptoms depends on the species of *Plasmodium*. Patient presentation may be mild or life-threatening.[9] Initially, symptoms are generalized, which may make diagnosis difficult. In severe disease, symptoms may progress to include fever and flu-like illness, with headache, shaking chills, muscle aches, and extreme tiredness. Some patients may present with anemia, jaundice, and stupor as well.[9] Pregnant women, children, and those with underlying medical conditions such as HIV/AIDS are more likely to develop severe infection.[3,5] If not promptly treated, malaria infection, especially with *P. falciparum* and *P. vivax*, may result in multi-organ failure[34] and have neurological complications including mental confusion, seizures, and coma.[34,35]

Treatment

Quinine, an alkaloid, is a traditional treatment and cure for malaria originally extracted from the bark of the cinchona tree. When the British Empire took control of India in the mid-1800s, British troops were leveled by malaria.[7,36] Unfortunately, the bitter taste of quinine was off-putting. To make the quinine more palatable, it was mixed with soda, sugar, lime, and gin to mask the bitter taste—and the gin and tonic was born.[7]

"The gin and tonic has saved more Englishmen's lives and minds than all the doctors in the Empire."
~Sir Winston Churchill[37]

In the early 1900s, Chloroquine phosphate became the treatment of choice and remains so today when the parasites are sensitive to the drug. Resistance to both quinine and chloroquine is growing around the world, necessitating new treatments.

Treatment resistance

Plasmodium spp. have evolved extensive mechanisms to evade host immunity that allow them to maintain host infection. First, when a trophozoite invades a host cells, it exports hundreds of proteins to the cell's internal and external surfaces and restructures the infected RBC's (iRBC) cytoskeleton.[8,38] These events are involved in creating new pathways for the parasites to obtain nutrients and expel wastes. Second, each of the Plasmodium spp. genomes has its own array of variant surface antigens (VSAs),[39] making the proteins expressed by the parasite highly variable. Parasites change expression of these antigenically distinct surface proteins, making them unrecognizable to the immune system.

CASE STUDY

A 42-year-old previously healthy male presented to the Emergency Department with a four-day-long fever. Three days prior to symptom onset, the patient had returned from a 10-day trip to Angola. As a result, the patient underwent a rapid malaria test at the pharmacy prior to admission. He was clinically stable, conscious, and collaborative.

Peripheral blood was drawn, and a standard complete blood count with differential (CBC-Diff) was performed (DxH 900 Hematology Analyzer, Beckman Coulter, Miami, FL). The CBC was flagged for thrombocytopenia (PLT=27* 109/L), and lymphopenia (LY#=0.7*109/L) (Figure 2). A peripheral blood smear was performed and analyzed using X100HT with Full-Field PBS application (Scopio Labs, Tel Aviv Israel) and showed 0.36% parasitemia (Figure 3). Upon diagnosis, the patient was transferred to a different hospital for further treatment.

Additional test results are listed below.[1]

- Total bilirubin: 44.0 µmol/L
- Non-conjugated bilirubin: 33.4 µmol/L
- GPT: 71 µmol/L
- GOT: 51 µmol/L
- CRP: 150.6 mg/L

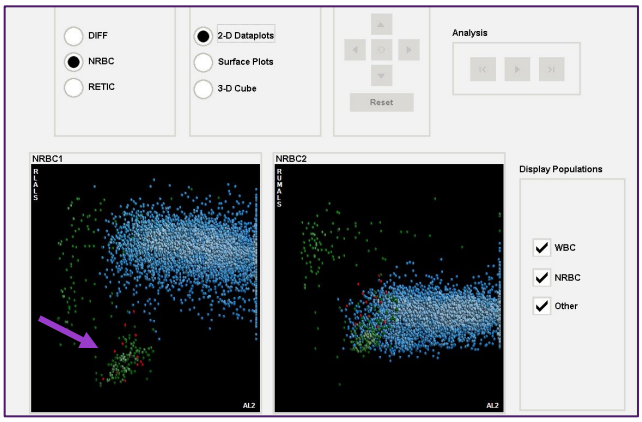

Figure 2. Patient images from DxH 900 Hematology analyzer

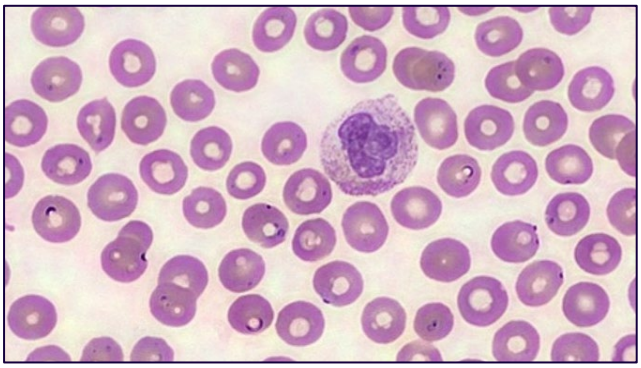

Figure 3. Patient images showing trophozoites from X100HT with Full-Field PBS application (Scopio Labs)

How Technology Aids in the Identification of *Plasmodium*

The CBC-Diff is one of the most commonly performed laboratory tests and is used to identify a wide range of disorders. While the CBC-Diff is not a diagnostic test for malaria, certain hematological test result patterns coupled with patient symptoms may raise the suspicion of malarial infection,[40–42] especially in non-endemic areas, where initial diagnosis is missed in almost 60% of cases.[43] For example, red blood cell distribution width (RDW), hemoglobin, leukocytes, and platelet counts,[42,44–46] as well as nucleated red blood cells (nRBCs) and monocyte anisocytosis[45] have all been shown to have potential as CBC markers of *Plasmodium* infection.[2] The ability to observe the biophysical characterization of WBCs in their near native state using Beckman Coulter hematology analyzers provides information about cytoplasmic granularity and membrane surface (MALS†/LMALS†/UMALS†), cellular transparency and optical size (AL2†), and cellular complexity (LALS†). Conductivity characterizes the nuclear and granular constituents, nucleus to cytoplasm ratio, and the chemical composition of the cell interior, while volume measurements correlate to cell size. Cell Population data (CPD)† are used to identify morphological changes in cells. CPD are available for the laboratory and as research use only (RUO) tools and may help arouse suspicion of abnormal cells in the blood.

Several publications have demonstrated the usefulness of monocyte and lymphocyte anisocytosis (Standard deviation of monocyte volume and Standard deviation of lymphocyte volume) in malaria to detect activated monocytes and lymphocytes, which are involved in immune response against the parasite.[45,47] Coupling the standard deviations of lymphocyte and monocyte volumes was shown to be a highly sensitive (98%) and specific (94%) screening test for the presence of *Plasmodium*, even in patients with HIV coinfection, likely due to cellular activation in response to infection.[45,47]

In another study, Sharma et al. aimed to differentiate malaria from dengue and from other febrile illnesses using multivariate analysis and demonstrated that leukocyte morphological abnormalities quantitated by automated analyzers can successfully identify malaria and dengue and distinguished them from other fevers.[48] These discriminant functions can be used to rapidly calculate and generate flags to trigger specific testing.

The patient in the case described herein presented with an abnormal WBC differential plot pattern and high values for @SD-V-LY† (28.06) and @SD-V-MO† (25.62) as compared with the normal specimen. The patient's blood sample also showed thrombocytopenia and eosinopenia—which are often present in malaria.[45,49] The green population at the low-left part of the NRBC plot (arrow, Figure 2) is example of the "malaria signal," as described by Lee et al.[50]

All these findings—anisocytosis of monocytes and lymphocytes, thrombocytopenia, eosinopenia and presence of abnormal population on NRBC1 plot—may help the lab to suspect cellular abnormalities associated with malaria and request additional testing.

Microscopy

Malaria is a common disease in tropical areas; however, in patients outside of malaria-endemic areas without a pre-existing suspicion, diagnosis can be challenging.

†These parameters are research use only (RUO), and their clinical use would require validation through controlled clinical trials.

Microscopic examination of peripheral blood remains the gold standard for detecting malaria infection, but it is labor intensive and requires a high skill level for accurate assessment,[45,49,51] which may be unattainable in endemic areas.[49] Fortunately, with the advent Scopio's Full-Field Digital morphology technology, the presence and prevalence of malarial trophozoites can be easily evaluated in a time-efficient manner.[52]

In the current case, the patient's blood smear showed the presence of trophozoites in the RBCs, further confirming infection with *Plasmodium* spp. (Figure 3).

While clinicians are taught to think horses when hearing hoofbeats, understanding the interconnectedness of laboratory results can help them identify the zebras in the herd to detect disease earlier, which can ultimately save lives.

References

1. World Health Organization. Vector-borne diseases. World Health Organization Fact Sheets. March 2, 2020. Accessed October 20, 2023. https://www.who.int/news-room/fact-sheets/detail/vector-borne-diseases
2. Tigabu A, Taye S, Aynalem M, Adane K. Prevalence and associated factors of intestinal parasitic infections among patients attending Shahura Health Center, Northwest Ethiopia. *BMC Res Notes*. 2019;12(1):333. doi:10.1186/s13104-019-4377-y
3. World Health Organization. *World Malaria Report 2022*. World Health Organization; 2022.
4. World Health Organization. Malaria. Q&A. World Health Organization. January 12, 2024. Accessed August 7, 2024. https://www.who.int/news-room/questions-and-answers/item/malaria#:~:text=Nearly%20half%20of%20the%20world's,contracted%20malaria%20in%2085%20countries.
5. World Health Organization. Malaria. March 29, 2023. Accessed October 11, 2023. https://www.who.int/news-room/fact-sheets/detail/malaria
6. Fernanco SD. Climate Change and Malaria - A Complex Relationship. United Nations Chronicle. Accessed October 13, 2023. https://www.un.org/en/chronicle/article/climate-change-and-malaria-complex-relationship
7. Roser M, Ritchie H. Malaria - Our World in Data. *Our World in Data*. November 12, 2019.
8. Cowman AF, Healer J, Marapana D, Marsh K. Malaria: biology and disease. *Cell*. 2016;167(3):610-624. doi:10.1016/j.cell.2016.07.055
9. World Health Organization. Malaria Fact Sheet. WHO | Malaria. March 29, 2023. Accessed October 25, 2023. https://www.who.int/news-room/fact-sheets/detail/malaria
10. Centers for Disease Control and Prevention. How Can Malaria Cases and Deaths Be Reduced? - Larval Control and Other Vector Control Interventions. CDC - Malaria - Malaria Worldwide. July 16, 2020. Accessed October 16, 2023. https://www.cdc.gov/malaria/malaria_worldwide/reduction/vector_control.html
11. Suh PF, Elanga-Ndille E, Tchouakui M, et al. Impact of insecticide resistance on malaria vector competence: a literature review. *Malar J*. 2023;22(1):19. doi:10.1186/s12936-023-04444-2
12. Elliott R, Ramakrishna V. Insecticide resistance in Anopheles gambiae Giles. *Nature*. 1956;177(4507):532-533. doi:10.1038/177532a0
13. Davidson G. Insecticide resistance in Anopheles sundaicus. *Nature*. 1957;180(4598):1333-1335. doi:10.1038/1801333a0
14. Boggild A, Brophy J, Charlebois P, et al. Summary of recommendations for the prevention of malaria by the Committee to Advise on Tropical Medicine and Travel (CATMAT). *Can Commun Dis Rep*. 2014;40(7):118-132. doi:10.14745/ccdr.v40i07a01
15. World Health Organization. WHO Review of Malaria Vaccine Clinical Development. WHO GOHRD. November 2022. Accessed September 19, 2024. https://www.who.int/observatories/global-observatory-on-health-research-and-development/monitoring/who-review-of-malaria-vaccine-clinical-development
16. Rocklöv J, Dubrow R. Climate change: an enduring challenge for vector-borne disease prevention and control. *Nat Immunol*. 2020;21(5):479-483. doi:10.1038/s41590-020-0648-y
17. Samarasekera U. Climate change and malaria: predictions becoming reality. *Lancet*. 2023;402(10399):361-362. doi:10.1016/S0140-6736(23)01569-6
18. Anyamba A, Chretien J-P, Britch SC, et al. Global Disease Outbreaks Associated with the 2015-2016 El Niño Event. *Sci Rep*. 2019;9(1):1930. doi:10.1038/s41598-018-38034-z
19. Wang Z, Liu Y, Li Y, et al. The relationship between rising temperatures and malaria incidence in Hainan, China, from 1984 to 2010: a longitudinal cohort study. *Lancet Planet Health*. 2022;6(4):e350-e358. doi:10.1016/S2542-5196(22)00039-0
20. Blanford JI, Blanford S, Crane RG, et al. Implications of temperature variation for malaria parasite development across Africa. *Sci Rep*. 2013;3:1300. doi:10.1038/srep01300
21. Mordecai EA, Paaijmans KP, Johnson LR, et al. Optimal temperature for malaria transmission is dramatically lower than previously predicted. *Ecol Lett*. 2013;16(1):22-30. doi:10.1111/ele.12015
22. CDC - Malaria. About Malaria - History - Elimination of Malaria in the United States (1947-1951). July 23, 2018. Accessed November 20, 2023. https://www.cdc.gov/malaria/about/history/elimination_us.html
23. Andrews JM, Quinby G, Langmuir A. Malaria Eradication in the United States*. *Am J Public Health*. 1950;40:1405-1411.
24. Williams LL. Malaria Eradication in the United States. *Am J Public Health*. 1963;53(1):17-21.
25. Garcia LS. Malaria. *Clin Lab Med*. 2010;30(1):93-129. doi:10.1016/j.cll.2009.10.001
26. Snow RW. Global malaria eradication and the importance of Plasmodium falciparum epidemiology in Africa. *BMC Med*. 2015;13(1):23. doi:10.1186/s12916-014-0254-7
27. Weiss DJ, Lucas TCD, Nguyen M, et al. Mapping the global prevalence, incidence, and mortality of *Plasmodium falciparum*, 2000-17: a spatial and temporal modelling study. *Lancet*. 2019;394(10195):322-331. doi:10.1016/S0140-6736(19)31097-9
28. Miller RH, Obuya CO, Wanja EW, et al. Characterization of Plasmodium ovale curtisi and P. ovale wallikeri in Western Kenya utilizing a novel species-specific real-time PCR assay. *PLoS Negl Trop Dis*. 2015;9(1):e0003469. doi:10.1371/journal.pntd.0003469
29. Centers for Disease Control and Prevention. Malaria Biology Lifecycle. July 16, 2020. Accessed November 20, 2023. https://www.cdc.gov/malaria/about/biology/index.html#:~:text=P.%20vivax%20(as%20well%20as,after%20the%20infecting%20mosquito%20bite.
30. Asmerom H, Gemechu K, Sileshi B, Arkew M. Hematological Abnormalities Among Malaria Infected Adult Patients in Association with ABO Blood Groups at Jinella Health Center, Harar, Eastern Ethiopia. *J Blood Med*. 2023;14:463-476. doi:10.2147/JBM.S419815
31. Sacomboio ENM, Zua SD, Tchivango AT, et al. Blood count changes in malaria patients according to blood groups (ABO/Rh) and sickle cell trait. *Malar J*. 2024;23(1):126. doi:10.1186/s12936-024-04886-2
32. Picón-Jaimes YA, Lozada-Martinez ID, Orozco-Chinome JE, et al. Relationship between Duffy Genotype/Phenotype and Prevalence of Plasmodium vivax Infection: A Systematic Review. *Trop Med Infect Dis*. 2023;8(10). doi:10.3390/tropicalmed8100463
33. Vigan-Womas I, Guillotte M, Juillerat A, et al. Structural basis for the ABO blood-group dependence of Plasmodium falciparum rosetting. *PLoS Pathog*. 2012;8(7):e1002781. doi:10.1371/journal.ppat.1002781
34. Bhutani A, Kaushik RM, Kaushik R. A study on multi-organ dysfunction syndrome in malaria using sequential organ failure assessment score. *Trop Parasitol*. 2020;10(2):86-94. doi:10.4103/tp.TP_12_19
35. Idro R, Marsh K, John CC, Newton CRJ. Cerebral malaria: mechanisms of brain injury and strategies for improved neurocognitive outcome. *Pediatr Res*. 2010;68(4):267-274. doi:10.1203/PDR.0b013e3181eee738
36. Achan J, Talisuna AO, Erhart A, et al. Quinine, an old anti-malarial drug in a modern world: role in the treatment of malaria. *Malar J*. 2011;10:144. doi:10.1186/1475-2875-10-144
37. Award Winning Gin | Highclere Castle Gin - Award Winning Gin | Highclere Castle Gin. Accessed November 20, 2023. https://highclerecastlegin.com/highclere-meets-winston-churchill/

38. Moxon CA, Grau GE, Craig AG. Malaria: modification of the red blood cell and consequences in the human host. *Br J Haematol*. 2011;154(6):670-679. doi:10.1111/j.1365-2141.2011.08755.x
39. Frech C, Chen N. Variant surface antigens of malaria parasites: functional and evolutionary insights from comparative gene family classification and analysis. *BMC Genomics*. 2013;14:427. doi:10.1186/1471-2164-14-427
40. Abro A, Ustadi AM, Younis N, Abdou A, Hamed DA, Saleh A. MALARIA AND HEMATOLOGICAL CHANGES. *Pakistan Journal of Medical Sciences*. 2008;24(2):287.
41. Price RN, Simpson JA, Nosten F, et al. Factors contributing to anemia after uncomplicated falciparum malaria. *Am J Trop Med Hyg*. 2001;65(5):614-622. doi:10.4269/ajtmh.2001.65.614
42. Omarine Nlinwe N, Nange TB. Assessment of Hematological Parameters in Malaria, among Adult Patients Attending the Bamenda Regional Hospital. *Anemia*. 2020;2020:3814513. doi:10.1155/2020/3814513
43. Kain KC, Harrington MA, Tennyson S, Keystone JS. Imported malaria: prospective analysis of problems in diagnosis and management. *Clin Infect Dis*. 1998;27(1):142-149. doi:10.1086/514616
44. Singh A, Narang V, Sood N, Garg B, Gupta VK. Malaria Diagnosis Using Automated Analysers: A Boon for Hematopathologists in Endemic Areas. *J Clin Diagn Res*. 2015;9(10):ED05-EC08.
45. Briggs C, Da Costa A, Freeman L, Aucamp I, Ngubeni B, Machin SJ. Development of an automated malaria discriminant factor using VCS technology. *Am J Clin Pathol*. 2006;126(5):691-698. doi:10.1309/0PL3-C674-M39D-6GEN
46. Shin S, Park SH, Park J. Incidental Identification of Plasmodium vivax During Routine Complete Blood Count Analysis Using the UniCel DxH 800. *Ann Lab Med*. 2018;38(2):165-168. doi:10.3343/alm.2018.38.2.165
47. Fourcade C, Casbas MJC, Belaouni H, Gonzalez JJD, Garcia PJJ, Pepio MAE. Automated detection of malaria by means of the haematology analyser Coulter GEN.S. *Clin Lab Haematol*. 2004;26(6):367-372. doi:10.1111/j.1365-2257.2004.00648.x
48. Sharma P, Bhargava M, Sukhachev D, Datta S, Wattal C. LH750 hematology analyzers to identify malaria and dengue and distinguish them from other febrile illnesses. *Int J Lab Hematol*. 2014;36(1):45-55. doi:10.1111/ijlh.12116
49. Singh A, Narang V, Sood N, Garg B, Gupta VK. Malaria diagnosis using automated analysers: A boon for hematopathologists in endemic areas. *J Clin Diagn Res*. 2015;9(10):EC05-8. doi:10.7860/JCDR/2015/15108.6696
50. Lee HK, Kim SI, Chae H, et al. Sensitive detection and accurate monitoring of Plasmodium vivax parasites on routine complete blood count using automatic blood cell analyzer (DxH800(TM)). *Int J Lab Hematol*. 2012;34(2):201-207. doi:10.1111/j.1751-553X.2011.01383.x
51. Kim H, Hur M, Yi J-H, et al. Detection of blasts using flags and cell population data rules on Beckman Coulter DxH 900 hematology analyzer in patients with hematologic diseases. *Clin Chem Lab Med*. November 27, 2023. doi:10.1515/cclm-2023-0932
52. Katz B-Z, Feldman MD, Tessema M, et al. Evaluation of Scopio Labs X100 Full Field PBS: The first high-resolution full field viewing of peripheral blood specimens combined with artificial intelligence-based morphological analysis. *Int J Lab Hematol*. 2021;43(6):1408-1416. doi:10.1111/ijlh.13681

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