

Is malaria treatment safer than we think? New study investigates

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A new international research collaboration led by Menzies School of Health Research (Menzies) is set to examine whether the risk of severe side effects from vivax malaria medication, primaquine, is lower than assumed to date.

Primaquine is a key component of the standard treatment for *Plasmodium vivax* malaria but is frequently not administered due to fears of life-threatening side effects. The risk of these side effects is highest for patients who have low activity of the enzyme, glucose-6-phosphate dehydrogenase (G6PD).

The [IMPACT study](#), a 3-year project, will assess whether G6PD activity increases during a vivax infection. As adequate activity of the G6PD enzyme is required to safely prescribe malaria medications, the findings will help inform clinical treatment.

This project received almost \$1.3 million as part of the [latest National Health and Medical Research Council \(NHMRC\) Ideas Grant](#) funding round. Ideas Grants are designed to support innovative research projects that address a specific question which looks to improve health for all Australians.

Menzies Senior Research Fellow, Dr Benedikt Ley, will lead a team of researchers to recruit participants in Bangladesh and Pakistan in the latter half of 2024. The researchers will recruit patients with and without malaria and will regularly test participants' G6PD activity levels over 6 months.

Vivax malaria is difficult to eradicate because it's able to remain dormant in the liver. This can result in a relapse in the weeks or months following the initial infection. Treating the liver stage of this disease requires one of 2 medications – primaquine or tafenoquine. However, these drugs can cause life-threatening side effects in people who have insufficient G6PD activity.

Testing for G6PD activity prior to prescribing either drug is considered best practice. Despite this, the limited availability of G6PD testing in some areas means these medications are heavily under prescribed. This undermines elimination efforts, as up to 80% of vivax malaria cases are from relapsing infections.

Preliminary data from studies in Indonesia, Ethiopia and Bangladesh have observed an increase in G6PD enzyme activity in patients with a malaria infection. The IMPACT study looks to further confirm this activity. If proven by the study, it could help lower concern around the safety of liver-stage malaria medications. Greater use of these medications could lead to fewer re-infections with malaria and fewer cases overall, helping to eventually eliminate the disease.

Malaria remains a global health priority. Even though the disease was eradicated from Australia in the 1980s, northern Australian remains at risk of malaria transmission.

Menzies strives to find solutions that support the health of Australians and people in tropical countries at risk of malaria worldwide.

Quotes attributable to Menzies Senior Research Fellow and IMPACT study chief investigator, [Dr Benedikt Ley](#):

“400 to 500 million people worldwide experience low G6PD activity levels. In areas with malaria transmission, this deficiency can be seen in up to 35 per cent of people.

“The lack of knowledge about G6PD activity is hampering the use of liver-stage malaria medications. This study aims to grow the evidence base in this area to support the safe use of these medications.

“If this study proves that a vivax malaria infection increases G6PD activity, it will help expand our understanding on the safe use of primaquine and tafenoquine. It may also simplify prescribing practices and improve malaria elimination efforts worldwide.”

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Menzies School of Health Research

Menzies is one of Australia’s leading medical research institutes dedicated to improving the health and wellbeing of Aboriginal and Torres Strait Islanders, and a leader in global and tropical research into life-threatening illnesses. Menzies continues to translate research into effective partnerships and programs in communities across Australia and the Asia-Pacific region.

Fast Facts: Treating the liver-stage of a *Plasmodium vivax* infection

- *Plasmodium vivax* is one of the most common malaria parasites and has a complex life cycle. It can remain undetectable and dormant in the liver and can reactivate weeks or months after the initial infection.
- This means one bite from a mosquito infected with vivax can result in multiple malaria infections, or “episodes” and more opportunities for the disease to spread.
- Malaria medications target the parasites in the blood or the liver. Treatments that target both areas are known as radical cure.
- Due to the lifecycle of vivax malaria, both blood and liver medication are required to eliminate the parasite.
- Primaquine and tafenoquine are the 2 medications available to treat the liver stage of vivax malaria. While primaquine has been used for more than 60 years (a 7-14 day treatment therapy), tafenoquine is a newer medication (singular dose therapy) and has been approved for use in the last 6 years.
- For patients with insufficient glucose-6-phosphate dehydrogenase (G6PD) activity, both primaquine and tafenoquine can induce acute hemolytic anemia (destruction of red blood cells).
- The World Health Organization recommends G6PD testing of patients before treatment with primaquine as best practice and this testing is mandatory before tafenoquine is prescribed.
- As tafenoquine is provided in a singular dose (therefore cannot be stopped or halved) it should only be prescribed to those with greater than 70% G6PD activity. As primaquine is provided through a 7 or 14 treatment regime, G6PD activity doesn’t need to be as high as those being prescribed tafenoquine, as this treatment can be halted if adverse side effects occur.