Implementation of G6PD testing and radical cure in *P. vivax* endemic countries: considerations

Malaria Policy Advisory Committee
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WHO Guidelines on Radical Cure

WHO guidelines for the treatment of malaria 2015 (3rd ed)
Control and elimination of *Plasmodium vivax* malaria: A technical brief

Launched in WHO SEARO on 29 July 2015 at a Global Meeting in New Delhi attended by countries in all WHO Regions with endemic *P. vivax*

Discussions on translating guidelines into policy and strategy in programmes
WHO Guidelines on Radical Cure

- In both, recommendations are based on:
  - the need to radically cure patients using primaquine
  - minimizing the risk of primaquine-induced acute haemolysis in those who are deficient in the enzyme glucose-6-phosphate dehydrogenase (G6PD)
2.4.4 RECOMMENDATIONS

- Where feasible, all patients should be tested for G6PD deficiency before administering primaquine. Testing for G6PD deficiency in vivax malaria cases should be considered an integral part of ensuring universal access to diagnosis and treatment.

- G6PD testing should be incorporated into treatment guidelines, and services made available as tools are developed (possibly with referral of patients from lower to higher level health facilities).

- Where no G6PD test is available, it is difficult to generalize on the correct approach to patient management, because each individual assessment depends on the risk of adverse consequences (related to the likely dose of primaquine required, the prevalence and severity of G6PD deficiency in the area, the degree of anaemia and the availability of blood transfusion) and the potential benefits (related to the probability of relapse). In some circumstances, the assessment will favour withholding primaquine, and in others it will favour starting radical treatment after educating the patient about the possible risks, and informing the patient that they should stop the drug if they become ill or their urine becomes red or black.
Difficulties in Implementation Expressed by Countries

- The lack of a robust, easy-to-use point-of-care test for G6PD
  - makes it difficult to test at the lower levels of the health system.
  - Referral to higher levels is problematic, and may result in *P. vivax* patients not being treated.

- Some countries (eg, in the Americas) are already implementing radical cure at HF level without testing for G6PD
  - G6PD deficiency allele frequency is very low (and variants are mild) or absent. Benefits exceed the risks
  - Full compliance with recommendations could prevent expansion and reverse implementation
Countries Request Practical Guidance from WHO

- To move towards testing and radical cure when improved tools are available, & until then, not compromise the early treatment of *P. vivax* in settings where G6PD testing is currently not feasible.

- How to perform risk-benefit assessment when G6PD status is unknown on making a decision on administering or withholding radical cure
Current WHO recommendations remain unchanged in both documents.

In translating these recommendations to action plans in countries, the following (or similar) guidelines be provided by WHO in (or as an addendum to) the *P. vivax* technical brief.
MPAC Advice to WHO

- Where feasible, all patients with confirmed *P. vivax* and *P. ovale* should be tested for G6PD deficiency before administration of 14-day radical treatment with primaquine.
- Because current G6PD tests may not be appropriate for use at the lower levels of the health system, countries may use the following guiding principles:
MPAC Advice to WHO

- All countries in the phases of malaria elimination and/or in prevention of re-introduction:
  - ensure that all *P. vivax* patients who do not know their G6PD status are tested before the administration of primaquine anti-relapse therapy.

- Countries where the prevalence of G6PD deficiency is known to be very low, and where G6PD testing is not currently considered mandatory:
  - should continue, while taking all precautions to educate the patient about the possible risk and strengthen their pharmacovigilance systems and the response arm.
MPAC Advice to WHO

- Where both the burden of *P. vivax* malaria and the prevalence of G6PD deficiency is considerable:
  - *P. vivax* patients should continue to be tested for malaria and treated for the blood-stage infection at all levels of the health system, particularly at the community level.
  - A decision to administer primaquine anti-relapse therapy should be on one or both of the following:
    - individual patient assessment of the risk/benefits
    - referring the patient to a higher level health facility for G6PD testing and primaquine treatment after providing treatment for the blood-stage infection.
MPAC Advice to WHO

- WHO should provide more specific guidance to countries on:
  - determining the population prevalence of G6PD and variants;
  - making risk–benefit assessments for radical cure;
  - assessing the feasibility of managing an acute haemolytic event when the G6PD status is unknown;
  - G6PD testing of patients, where it is feasible, and interpretation of test results.
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"To achieve a radical cure (cure and prevention of relapse), a 14-day course of primaquine is recommended, after exclusion of G6PD deficiency….”