The Roll Back Malaria (RBM) Partnership Malaria in Pregnancy Working Group supports the following for all pregnant women living in sub-Saharan Africa:

- In malaria-endemic areas, intermittent preventive treatment using sulfadoxine-pyrimethamine (IPTp-SP) should be provided to pregnant women at each scheduled antenatal care (ANC) visit for protection against malaria. This should start early in the second trimester and continue until the time of delivery, with the doses given at least one month apart [1].
  - IPTp-SP has been shown to reduce maternal anemia, antenatal maternal parasitemia, low birthweight infants and neonatal deaths.
  - Co-trimoxazole provides some protection through its antimalarial activity; however, IPTp-SP should NOT be given to women who are taking daily co-trimoxazole prophylaxis (i.e. mainly those living with HIV) as this increases the risk of adverse events.

- Daily oral supplementation of 30–60 mg elemental iron and 400 \( \mu g \) (0.4 mg) folic acid should be provided as early as possible in pregnancy to meet iron and folic acid requirements [2]. In cases where a combined folic acid–iron tablet is not available, a daily dose of 400 \( \mu g \) (0.4 mg) folic acid can be used separately.

- There is evidence that high doses of folic acid (i.e. 5,000 \( \mu g \) or more) may interfere with the efficacy of sulfadoxine-pyrimethamine as an antimalarial [3]. The higher 5,000 \( \mu g \) (5 mg) dose for pregnant women should be restricted for use in very specific clinical cases. High doses of folic acid are not needed during low-risk pregnancies and may counteract the efficacy of both sulfadoxine-pyrimethamine and co-trimoxazole as antimalarials [4]. The RBM Malaria in Pregnancy Working Group strongly advises that countries currently prioritize the procurement and distribution of the available combined dose of 400 \( \mu g \) (0.4 mg) folic acid plus 30–60 mg elemental iron as part of routine ANC. It also recommends that countries substantially reduce current stores and supplies of folic acid at a dose of 5,000 \( \mu g \) (5 mg) or higher at all facilities, as this dose should only be used for specific medical conditions as outlined by the World Health Organization (WHO) [2], and as indicated below in the answer to Question 2.

**Frequently asked questions about iron and folic acid during pregnancy**

1. **What daily dose of iron and folic acid supplementation does WHO recommend during pregnancy?**

Folate requirements are increased in pregnancy because of the rapidly dividing cells in the fetus and elevated urinary losses. Increased iron is needed to meet the demands for iron of the developing fetus and cell mass expansion. WHO recommends iron and folic acid supplementation for pregnant women, starting early in pregnancy and at a daily dose of 30–60 mg of elemental iron plus 400 \( \mu g \) (0.4 mg) of folic acid, as this has been shown to reduce the risk of low birthweight, maternal anemia and iron deficiency [2]. In settings where anemia in pregnant women is a severe public health problem (i.e. 40 percent or higher) a daily dose of 60 mg of elemental iron is preferred over a lower dose. If a woman is diagnosed with anemia, WHO recommends daily treatment with 120 mg of elemental iron and 400 \( \mu g \) (0.4 mg) of folic acid until her hemoglobin concentration rises to a normal level [5,6].

A combined dose of 60 mg of elemental iron and 400 \( \mu g \) (0.4 mg) of folic acid is included on the WHO Model List of Essential Medicines [7] and is provided by the United Nations Children’s Fund (UNICEF). Using this preparation to treat anemia would provide 800 \( \mu g \) (0.8 mg) of folic acid daily, which would not interfere with sulfadoxine-pyrimethamine as an antimalarial [8]. A trial conducted on pregnant women in Gambia using a 1,500 \( \mu g \) (1.5 mg) daily dose of folic acid showed no reduction.
in sulfadoxine-pyrimethamine efficacy [9]. However, to date, no data are available on sulfadoxine-
pyrimethamine efficacy when administered with daily folic acid doses between 1,500 µg (1.5 mg) and
less than 5,000 µg (5 mg) in pregnant women.

Women should be counseled when they receive iron and folic acid supplements to inform them why
these supplements are needed, how to take them and for what duration. They should also receive
information about how to manage the possible side effects of iron supplementation (mainly mild
gastrointestinal symptoms), which may occur in some women.

2. What are the clinical indications for higher dose folic acid during pregnancy?

Folic acid insufficiency is associated with an increased risk of neural tube defects, a debilitating
congenital anomaly in which the neural tube does not close properly. This occurs in 0.5–6.5 out of
every 1,000 pregnancies. The neural tube forms in the first month after conception, with closure by
about 28 days; thus, in order to prevent neural tube defects maternal intake of folic acid should begin
before conception and continue through early pregnancy.

There are limited cases (e.g. for prevention of recurrent cases of neural tube defects [10] and for
women on anticonvulsant treatment, diabetics and women with sickle cell anemia) where it is
recommended that pregnant women take folic acid at a daily dose of 5,000 µg (5 mg).

In particular, women who have had a previous pregnancy resulting in a baby with neural tube defects
are at higher risk of having another baby with neural tube defects. These women should receive folic
acid at a dose of 5,000 µg (5 mg) a day starting at least one month – though preferably two to three
months – before they conceive, and continuing until 12 weeks of gestation, while increasing their
dietary folate intake. Given the need for supplementation prior to conception, fortification of staple
foods with folic acid should also be considered as a cost-effective public health measure to reduce

3. How does folic acid interfere with the efficacy of sulfadoxine-
pyrimethamine against malaria?

Folic acid is an essential nutrient for all organisms. Humans get folate from food or dietary supplements.
Other organisms, such as the malaria parasite, synthesize folic acid de novo, or endogenously. Both
sulfadoxine-pyrimethamine and co-trimoxazole are anti-folates and prevent malaria by blocking the
synthesis of folic acid. Without folic acid, the parasite cannot complete its lifecycle. However, if blood
folate concentrations are high enough, the malaria parasite can use this folate instead of making its
own, allowing the infection to continue unchecked.

References

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