or accommodative multifocal. Cataracts in FC I/IA are not waiverable, but are potentially waiverable for FC II and FC III.[3]

Enlarged optic nerve cupping and ocular hypertension (OHT) may indicate early glaucoma. Elevated IOP can affect night vision secondary to halos and flare around lights, decreased contrast sensitivity, changes in color vision, loss of central or peripheral visual fields, and loss of VA, all of which can affect performance, mission effectiveness, and safety. OHT is defined as IOPs between 22–29 mmHg in two or more applanation tonometry measurements or 4 mmHg or more difference between the eyes.[‡] OHT is disqualifying for FC I/IA, FC II/IIU, FC III, and air traffic controller/ground-based controller. It is not waiverable for FC I/IA, initial FC II/IIU, and initial FC III. Trained aircrew must show acceptable VA, stabilized IOP, and no evidence of optic nerve damage. Glaucoma is waiverable for FC II and FC III if controlled on aeromedically approved IOP lowering agents such as beta-blockers (timolol), prostaglandin analogues (latanoprost), or laser treatment modalities such as selective laser trabeculoplasty. There should be a full binocular VF, no aeromedically significant central VF defects, and no visual or systemic medication side effects. Lantanoprost has fewer cardiovascular side effects compared to timolol, so it is preferred for high-performance aviators.[9]

The patient was evaluated by local base Optometry and the Ophthalmology Branch of the Aeromedical Consultation Service for waiver for IOL placement. Waiver was approved and he was returned to flying status.

**VanValkenburg K.** ***You're the flight surgeon: a complication of surgical vision correction*****. Aerosp Med Hum Perform 2016; 87(4):426–429.**

## ACKNOWLEDGMENTS

The author wishes to thank Maj. Tighe Richardson, D.O., U.S. Air Force School of Aerospace Medicine, Ophthalmology Branch, and Richard Allnutt, M.D., Deputy Director, Residency in Aerospace Medicine Program, for their professional review of this article. The views expressed in this article are those of the author and do not necessarily reflect the official policy or position of the Air Force, the Department of Defense, or the U.S. Government.

[‡] U.S. Air Force. Section C: eyes and vision USAF medical standards, C8: ocular hypertension (preglaucoma). In: Medical standards directory. 2013:11. [Accessed 15 Dec. 2014]. Available to those with access from https://kx2.afms.mil/kj/kx4/FlightMedicine/Documents/Medical%20Standards%20Directory%20(MSD)/MSD%202013-Dec-2.pdf.

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This article was prepared by Paul A. DeJulio, M.D.

You're the flight surgeon for an F-16 squadron deployed to the Middle East. Your squadron was just tasked with sending a number of personnel forward to a malaria-endemic region. Their projected length of stay is 4 wk. Your pilots are visibly excited when you tell them that they will have to take medication to prevent malaria.

**1. Which of the following antimalarials is not approved for U.S. Air Force pilots?**

A. Atovaquone-proguanil.
B. Mefloquine.
C. Doxycycline.
D. Chloroquine phosphate.
E. Primaquine phosphate.

### ANSWER/DISCUSSION

**1. B.** In accordance with the Official Air Force Aerospace Medicine Approved Medications list, atovaquone-proguanil (Malarone), chloroquine phosphate (Aralen), doxycycline (Vibramycin), and primaquine

DOI: 10.3357/AMHP.4422.2016

phosphate are approved for use as malaria chemoprophylactic agents in flyers. Mefloquine (Larium) is not approved for flyers secondary to the following neurotoxic side effects: optic neuritis, cataracts, decreased night vision, blurred vision, photosensitivity, pseudotumor cerebri, depression, psychosis, and suicide.*

Malaria is caused by parasitic protozoa of the genus *Plasmodium*. The five species that cause disease in humans are *P. falciparum*, *P. vivax*, *P. ovale, P. knowlesi*, and *P. malariae*. Knowledge of the species endemic to the forward location is important when choosing your antimalarial regimen. Using the Centers for Disease Control and Prevention Malaria Map Application,[1] you determine that *P. falciparum* (90%) and *P. vivax* (5–10%) are present and the *P. falciparum* are chloroquine resistant. You confirm your findings with Public Health and review their recommendations for chemoprophylaxis: atovaquone-proguanil, mefloquine, or doxycycline for primary prophylaxis and primaquine for presumptive antirelapse therapy (these recommendations do not take into account the member's flying status). Of note, all five of the antimalarials listed above may be used as primary prophylaxis. Primaquine may be used as primary prophylaxis in areas where *P. vivax* is the primary species; it would not provide adequate coverage in this case.

You start your pilots on doxycycline with instructions to take 100 mg daily starting 2 d prior to the forward deployment and ending 4 wk after leaving the malaria endemic region. You warn them of the potential for gastrointestinal upset and photosensitivity. As you are handing them the medication, one of your pilots asks, "Hey Doc, they gave us this yellow spray can at home and said that it was to be used to prevent malaria. It starts with a 'p.' Do I need to bring it?"

**2. How do you respond to this question?**

A. "Yes, that's permethrin; spray it on your civilian clothing AND your flight suits."
B. "Yes, that's permethrin; spray it on your civilian clothing but NOT your flight suits."
C. "Yes, that's permethrin; spray it on your skin to prevent sunburn."
D. "Yes, that's permethrin; spray it on your mustache for added shine."

## ANSWER/DISCUSSION

**2. B.** *Plasmodium* is spread through the bite of an infected female *Anopheles* mosquito. Mosquito bite prevention is the first line of defense against malaria and should be used in conjunction with chemoprophylaxis. Mosquito bite prevention includes avoiding outdoor exposure from dusk to dawn (when *Anopheles* mosquitoes feed), wearing long clothing, sleeping in air-conditioned/screened rooms, and applying insect repellents [e.g., picaridin, DEET (N,N-diethyl-meta-toluamide)] to the skin and insecticides (e.g., permethrin) to bed netting and clothing.[4] Permethrin spray is applied to civilian clothing and some military uniforms. The Armed Forces Pest Management Board recommends against spraying flight suits with permethrin. Contrary to popular belief, this is not because permethrin affects the flame retardant capacity of Nomex®. Instead, preliminary studies of factory and Individual Dynamic Absorption kit (aerosol spray has not been tested) treated Nomex® uniforms have shown that the fabric does not properly absorb the permethrin solution, leaving some areas untreated while others contain a high concentration of the chemical. These areas of high concentration may exceed the Environmental Protection Agency's exposure limits and present a hazard to the pilot (Perry M. Personal communication; 7 July 2015).

Your pilots carry out their mission downrange and return in good health. When you see them next you remind them to continue to take the doxycycline an additional 4 wk and tell them you have another antimalarial medication—primaquine—that they must take for 14 d. They inquire as to why they need a second medication.

**3. What is your response to this inquiry?**

A. "Antimalarials are like JDAMs; the more I use, the more *Plasmodium* I can kill!"
B. "I'm concerned the doxycycline won't work."
C. "We must treat the 'sleeping' form of malaria in your liver."
D. "Primaquine also prevents Rocky Mountain spotted fever."

## ANSWER/DISCUSSION

**3. C.** The life cycle of *Plasmodium* in the human consists of both hepatic (exoerythrocytic) and blood (erythrocytic) stages (**Fig. 1**). When a female *Anopheles* mosquito infected with *Plasmodium* bites her victim, she injects sporozoites into the bloodstream. This spindle-shaped form of the protozoa travels to the liver and divides in a process called schizogony. Schizogony produces hepatic schizonts: structures that contain merozoites. Hepatic schizonts rupture, releasing merozoites into the bloodstream, where they invade erythrocytes. The continual release of merozoites into the bloodstream after leaving a malaria-endemic region is the reason that primary prophylaxis is continued for days to weeks (depending on the agent). Once in the blood, a second round of schizogony produces a blood-stage schizont. Upon maturation of the schizont, hemolysis occurs, releasing merozoites into the bloodstream; this is what causes the characteristic fevers and chills of malaria. The merozoites go on to invade other red blood cells, which perpetuates the disease process.

Hypnozoites represent another hepatic stage that exists only with *P. vivax* or *P. ovale* infections. In this stage, *Plasmodium* may remain quiescent for months before reactivating and entering the bloodstream. Primaquine is unique among antimalarials in that it is the only one with proven activity against the hypnozoite stage. It is prescribed as presumptive antirelapse therapy: 30 mg base (two tablets) daily for 14 d postexposure. Because your pilots were in a region with *P. vivax,* you tell them you must treat the "sleeping" form of malaria in their liver. Primaquine use is contraindicated in patients who are glucose-6-phosphate dehydrogenase (G6PD) deficient as it may induce a hemolytic anemia. Before you prescribe primaquine, you should verify your pilots' G6PD status. If you find that a pilot is G6PD deficient, it does not preclude him or her from deploying. You should emphasize the importance of mosquito bite prevention and taking the chemoprophylaxis. The U.S. Air Force Infectious Disease Service recommends a consultation upon redeployment so that they may further counsel the member.

* U.S. Air Force. Official Air Force aerospace medicine approved medications. 2014 Oct. 3:20. [Accessed 1 Feb. 2015]. Available to those with access from https://kx2.afms.mil/kj/kx4/FlightMedicine/Documents/Forms/ShowFolders.aspx.

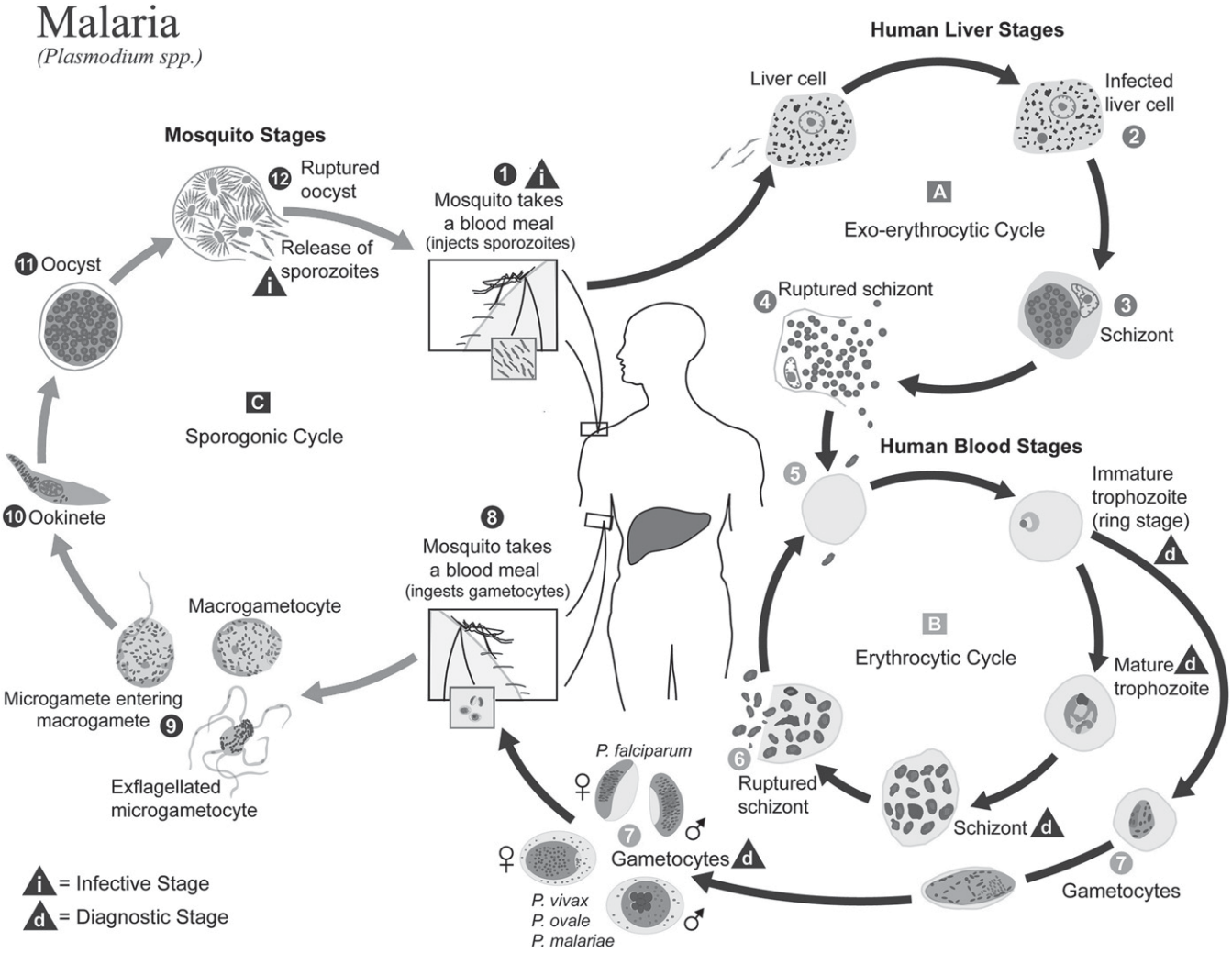


**Fig. 1.** Life cycle of *Plasmodium*. Image credit: CDC/DPDx; Alexander J. da Silva, Ph.D.; and Melanie Moser.

Approximately 72 h after their return, you run into one of your pilots in the dining facility and he reports, "I stopped taking that second medicine (primaquine). It makes me feel like crap!" You ask him for specifics. "I have muscle aches and feel fatigued. It also makes me feel nauseous. I felt fine on doxycycline."

**4. Based on his presentation, which of the following should you NOT do?**

A. Confirm that he is still taking the doxycycline.
B. Double-check his G6PD status.
C. Evaluate him for malaria.
D. Give him some Afrin and tell him to follow up tomorrow.

## ANSWER/DISCUSSION

**4. D.** Symptoms of an uncomplicated malaria infection are nonspecific and may include fevers, tachycardia, tachypnea, chills, malaise, fatigue, diaphoresis, headache, cough, anorexia, nausea, vomiting, abdominal pain, diarrhea, arthralgias, and myalgias.[6,9] Your pilot has just returned from a malaria-endemic region and is experiencing symptoms consistent with the disease; a full evaluation is indicated. During your history you confirm that that he is still taking his doxycycline, which makes an active infection less likely. His vital signs are blood pressure 112/85, pulse 77, respiratory rate 12, oxygen saturation 99%, and temperature 98.7°F. Upon further questioning, his review of systems is negative. During the physical exam you evaluate him for jaundice, abdominal tenderness, hepatosplenomegaly (indicating hemolysis and sequestration) or evidence of dehydration,[3] all of which are negative. You draw blood and with your limited resources run a complete blood count, basic metabolic panel, and urinalysis looking for anemia, leukocytosis, thrombocytopenia, bilirubinemia, or evidence of kidney damage. Fortunately, his labs are also unremarkable. While you are comforted by the pilot's normal exam, you maintain a high index of suspicion as you do not have access to giemsa stain, a light microscope, or more advanced tests (e.g., rapid diagnostic antigen testing, polymerase chain reaction) necessary to definitely rule out the disease. Recognizing that hemolysis could explain some of your pilot's symptoms, you double check his G6PD status and confirm that it is normal.

**5. While his complaints of myalgias and fatigue are not common among patients taking primaquine, they may represent an idiosyncratic reaction. Your next steps should include all BUT**

A. Discontinue the primaquine; it is a threat to flight safety.
B. Continue the primaquine, as tolerated; place on duties not including flying (DNIF).
C. Educate the pilot on ways to mitigate the side effects.
D. Closely monitor him for signs and symptoms of malaria.

## ANSWER/DISCUSSION

**5. A.** The benefits of primaquine generally outweigh any minor side effects. Before deciding that your pilot cannot tolerate the primaquine, you should educate him on ways to mitigate the side effects such as taking it with food and splitting the dose: 15 mg base (one tablet) twice daily. In the meantime, you should continue the primaquine, as tolerated, and DNIF him for 14 d. This will undoubtedly be an unpopular decision, as you are requiring your pilot to take a medication that makes him feel sick and takes him out of the fight. In response, you should reaffirm the benefits of the primaquine (i.e., preventing malaria), counsel the pilot that by grounding him now you could be saving him from a much longer DNIF in the future, and remind him that his health is more important than any sortie. In this case, your pilot's symptoms resolve when he takes the primaquine with food. You return him to flying status for the remainder of his treatment course and closely monitor him for signs and symptoms of malaria.

## AEROMEDICAL DISPOSITION

Chloroquine, doxycycline, and primaquine are approved for malaria chemoprophylaxis in Air Force, Army, and Naval aviators. The Air Force and Navy have also approved the use of Malarone. All three services require their aviators undergo a ground trial of these medications to exclude idiosyncratic reactions.[5,7,8] The length of the DNIF varies according to the service and the drug. For specifics regarding ground trials, refer to the Air Force and Navy waiver guides and the Army Flight Surgeon's Aeromedical Checklists. The Federal Aviation Administration Guide for Aviation Medical Examiners does not provide a comparable list of approved antimalarials for civilian aviators. If a pilot experiences adverse effects from any of the approved antimalarials, they should be grounded until their symptoms resolve. The Air Force, Army, Navy, and Federal Aviation Administration all prohibit the use of mefloquine in flyers. If a pilot mistakenly takes mefloquine, he or she should be grounded for 4 wk and observed for neurological and psychiatric symptoms.[2,8]

**DeJulio P.** ***You're the flight surgeon: malaria prevention in U.S. Air Force aviators.*** **Aerosp Med Hum Perform. 2016; 87(4):429–432.**

## ACKNOWLEDGMENTS

The author wishes to thank Dr. Daniel Van Syoc, Deputy Chief, Aeromedical Consultation Service, and Dr. Nicholas G. Conger, Infectious Diseases Consultant, Wright-Patterson Air Force Base, for their expert reviews of the contents of this article, and Lt. Col. Matthew Ayres, 77th Fighter Squadron, for his outstanding leadership. The views expressed in this article are those of the author and do not necessarily reflect the official policy or position of the U.S. Air Force, the Department of Defense, or the U.S. Government.

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