Letters to the Editor

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This series is coordinated by Kenny Lin, MD, MPH, Associate Deputy Editor for *AFP* Online.

Increase in Reported Malaria Cases Prompts Clarification Regarding Diagnosis and Treatment

Original article: Fever in Returning Travelers: A Case-Based Approach

Issue date: October 15, 2013

See additional reader comments at: http://www.aafp.org/afp/2013/1015/p524.html

TO THE EDITOR: We read this article with great interest, and we appreciate the authors highlighting three major sources of fever in the returning traveler. Given the continued steady increase in reported cases of malaria, especially from travelers to sub-Saharan Africa,[1] we would like to make a few points regarding recognition and treatment of this disease.

First, diagnostic studies should be promptly performed, with a low threshold for starting parenteral treatment when there is concern for severe infection. Intensive treatment should not be delayed while awaiting test results.[2] Although rapid testing can be performed, it should not replace direct microscopy, because testing for confirmation of infection and parasite density are needed to follow response to treatment.[2] For help with diagnosis or management, clinicians may call the Centers for Disease Control and Prevention's (CDC's) Malaria Hotline at 770-488-7788 (Monday through Friday, 9 a.m. to 5 p.m. Eastern time) or 770-488-7100 (emergency consultation after hours).

Second, patients with severe infection who may have been exposed to *Plasmodium falciparum* should be given artesunate or quinidine, not chloroquine (Aralen), because patients with *P. falciparum* malaria infection may deteriorate rapidly if improperly treated.[2,3] Worldwide, *P. falciparum* resistance to chloroquine is quite high outside of Latin America and the Middle East, which makes it a poor first choice, especially if there was recent travel to Africa.[4] The CDC's online malaria map provides resistance characteristics for the area of travel (http://www.cdc.gov/malaria/map/).

For less severe infections in recent travelers to Africa or areas where the level of chloroquine resistance is unknown, clinicians should treat with atovaquone/proguanil (Malarone) or artemether/lumefantrine (Coartem) instead of the more cumbersome combination of quinine with doxycycline, tetracycline, or clindamycin.[4] Mefloquine should be used only as a last resort because of neuropsychiatric reactions. A table of treatment recommendations from the CDC is available at http://www.cdc.gov/malaria/resources/pdf/treatmenttable.pdf.

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IN REPLY: I thank Drs. Gibbs and Creech for their interest in our article. First, I agree that malaria smears may need to be performed right away. At our hospital, results are usually available in less than one hour. If results are delayed and the possibility of severe *P. falciparum* infection is high, then empiric

therapy should be started. Second, as stated in the article, many areas in the world have chloroquine-resistant malaria; thus, knowing the area of exposure is needed to choose effective malaria therapy. Lastly, the fixed-dose combination artemether/lumefantrine is an additional first-line option to treat chloroquine-resistant malaria.

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Glycemic Control Is an Important Consideration in Diabetes Care

Original article: "Lending a Hand" to Patients with Type 2 Diabetes: A Simple Way to Communicate Treatment Goals

Issue date: February 15, 2014

Available at: http://www.aafp.org/afp/2014/0215/p256.html

TO THE EDITOR: We appreciate the recommendations in this editorial, and agree that smoking cessation, blood pressure control, the use of metformin (Glucophage) as first-line therapy for diabetes mellitus, and the addition of statins to prevent cardiovascular events are important. However, we disagree with some of the statements regarding the importance of glycemic control. We think that the statement in Figure 1 that glycemic control has no effect on mortality or clinically relevant complications is not supported by the existing evidence.

The literature supports glycemic control (A1C less than 7%) to prevent the onset and progression of microvascular complications, which we think are clinically relevant. Glycemic control is directly associated with the onset and progression of retinopathy and nephropathy.[1-5] In addition, results from the 10-year follow-up of the U.K. Prospective Diabetes Study (UKPDS) found that patients with newly diagnosed diabetes who were randomized to the intensive treatment group (sulfonylurea, insulin, or metformin) had a decreased incidence of microvascular complications, myocardial infarction, and death from any cause.[3] Results of the ACCORD and ADVANCE studies indicated that patients with existing cardiovascular disease may not be candidates for intensive glycemic control.[4,5] However, newly diagnosed patients without significant microvascular or macrovascular complications can benefit from glycemic control in the short term (to prevent microvascular complications) and long term (to potentially prevent myocardial infarction and death from any cause).[3]

As recommended in the current American Diabetes Association standards of medical care in diabetes, the goals of glycemic control must be individualized.[6] Not all patients are candidates for an A1C goal of less than 7%, nor are all patients candidates for an A1C goal of less than 8% or 6.5%. Clinicians should present the potential benefits and risks of various glycemic goals to patients and practice shared decision making to determine individual goals.

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IN REPLY: We thank Dr. Keeble and colleagues for their attention to our editorial and for ▶

the opportunity to clarify our approach. We wholeheartedly agree that management decisions should be tailored to each individual patient. Our model is a helpful way to rank the interventions that maximize length and quality of life for most overweight patients with type 2 diabetes.

There are four key issues pertaining to the concern about glycemic control: (1) the difference between disease-oriented and patient-oriented outcomes; (2) the types of cited studies; (3) our focus on overweight patients with diabetes; and (4) the harm associated with excessive glycemic reduction.

First, the UKPDS showed that only one of its 21 composite outcomes was significantly affected by intensive glycemic control: laser photocoagulation rates. Vision loss—the outcome that matters most—was not affected.[1] Photocoagulation rates are an excellent example of disease-oriented evidence, which supports interventions that affect intermediate outcomes, but not patient-oriented outcomes such as morbidity and mortality.

Second, many studies that support glycemic reduction are invalid. Although the 10-year follow-up of UKPDS showed a reduction in macrovascular events and mortality, it was an open-label follow-up and, thus, prone to bias.[1] In addition, subsequent high-quality studies have not shown a reduction in all-cause mortality,[2,3] but have shown an increased risk of severe complications of hypoglycemia.[3,4]

Third, our article specifically addressed the care of U.S. patients with type 2 diabetes who have a body mass index greater than 25 kg per m^2. In the Japanese study cited by Dr. Keeble and colleagues, the average body mass index was 19 kg per m^2.[5] The 10-year follow-up of UKPDS showed a benefit from glycemic control partially because the study included nonobese patients who do benefit from insulin therapy.[1] When only overweight patients were included, there was no benefit.

Finally, our primary concern is the significant increase in mortality associated with insulin therapy once the A1C falls below 7.5%.[4] We are disappointed that national organizations still recommend pharmaceutically lowering blood glucose levels despite evidence that fails to show benefit and instead demonstrates potential harm.

The reason we based our model on a hand is that regardless of whether aggressive glycemic reduction is beneficial in overweight patients with type 2 diabetes—and the best evidence strongly suggests that it is not—clinicians must spend their time with patients focusing on the other life-prolonging "fingers" of diabetes care. Poor control of hypertension is associated with high blood glucose levels, meaning that clinicians spend too much time on the "pinky" of glycemic control and not enough time on blood pressure control.[6]

Let's stop reversing the hand and start saving lives.

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