

## CLINICAL INQUIRIES

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### ■ CLINICAL COMMENTARY

#### Infants may have complications; evaluate if there is apnea or significant cough

Immunity to pertussis wanes following vaccination, leaving many adolescents and adults susceptible to infection. In older children and adults, there is often little in the clinical presentation that distinguishes chronic cough due to pertussis from that associated with other causes. Clinicians should consider evaluating for pertussis in older children and adults with chronic cough (>2 weeks) if there is reason to suspect they have been exposed, if the cough is associated with inspiratory whoop, or if the individual has household or frequent contact with infants.

Infants may suffer severe complications from pertussis, and should receive evaluation when presenting with apnea or significant cough of any duration. In current practice, evaluation usually includes obtaining a nasopharyngeal swab for culture and PCR, though these tests may be insensitive, especially in later phases of illness. The usefulness of single, quantitative immunoglobulin G titers with comparison to pop-

impact the epidemiology of pertussis in the US.

*Michael Ohl, MD, University of Missouri–Columbia*

## Does quinine reduce leg cramps for young athletes?

### ■ EVIDENCE-BASED ANSWER

Very little evidence exists regarding the use of quinine for cramps in young adult athletes. Quinine may be an effective treatment for heat cramps in athletes (strength of recommendation [SOR]: **C**, 1 case series involving 2 patients). Quinine is better established as an effective treatment for nocturnal leg cramps in the general adult population (SOR: **A**, 1 meta-analysis and 2 randomized controlled trials).

### ■ EVIDENCE SUMMARY

Leg cramps (heat cramps) in athletes are defined as painful involuntary muscle contractions, usually in the large muscle groups of the legs, which occur during or in the hours following exercise. Oral quinine is sometimes used to treat nocturnal leg cramps in the general adult and elderly populations. However, its use is controversial secondary to concerns regarding efficacy and safety.

Efficacy of quinine in young athletes has not been well studied. A case series reported on 2 athletes: 1 college basketball player and 1 professional football player.<sup>1</sup> The basketball player experienced heat cramps during games that were resistant to hydration and dietary treatment. A regimen of 60 mg oral quinine sulfate taken 1 hour before game time and again at half-time eliminated cramps during the first game and the subsequent 15 games. The football player's heat cramps were only partially improved with oral electrolyte repletion and oral hydration. However, he suffered no further cramps after initiating a regimen of 120 mg oral quinine sulfate

before games and 60 mg oral quinine during games for an undisclosed period of time. Both players had normal blood chemistries before starting quinine. No side effects were mentioned.

Several trials involving the general adult population exist. A meta-analysis of 4 published and 3 unpublished reports of randomized, double-blind controlled crossover trials (n=409) showed that adult patients had significantly fewer nocturnal cramps when taking quinine compared with placebo.<sup>2</sup> The absolute reduction in number of leg cramps was 3.6 (95% confidence interval [CI], 2.15–5.05) over a 4-week period, and the relative risk reduction was 0.21 (95% CI, 0.12–0.30).

Two randomized controlled trials were not included in the meta-analysis discussed above. One double-blind, randomized, controlled parallel group trial of 98 adult patients with a mean age of 50 years demonstrated that a regimen of daily quinine sulfate therapy of 200 mg with the evening meal and 200 mg at bedtime significantly reduced the number of nocturnal muscle cramps compared with placebo.<sup>3</sup> Over a 2-week treatment period the quinine group experienced a median of 8 fewer cramps (95% CI, 7–10), while the placebo group experienced a median of 6 fewer cramps (95% CI, 3–7). However, patient evaluation of global efficacy of treatment was not statistically significant between the quinine and placebo groups.

A second double-blind, randomized, controlled parallel group trial of 102 adult patients, mean age approximately 50 years, showed that a 2-week treatment period of hydroquinine (not available in the US) also produced a significant reduction in day- and nighttime muscle cramps compared with placebo.<sup>4</sup> This study used a regimen of two 100-mg hydroquinine or placebo tablets with the evening meal and one 100-mg tablet or placebo at bedtime. The median difference in the number of cramps between the treatment and control groups was 5 (95% CI, 2–8).

It should be noted that during the 2 weeks immediately following the treatment period, num-

bers of cramps were still low compared with the pretreatment period and no significant difference was seen in number of cramps between groups. This raises suspicion that the improvement in both groups was due to the self-limited nature of cramps and represented the regression-to-the-mean phenomenon rather than a true treatment effect of hydroquinine. In addition, extrapolating results from studies of nocturnal cramps to heat cramps is problematic, as it is unknown whether these differ in physiology or cause.

Use of quinine for common cramps in nonathletes has been controversial. In 1994 the Food and Drug Administration (FDA) issued a statement banning over-the-counter sale of quinine for nocturnal leg cramps, citing lack of adequate data to establish efficacy and concern for potential toxicity.<sup>5</sup> Between 1969 and 1990 the FDA received 26 adverse reaction reports in which quinine was concluded to be the causative agent. The 3 studies discussed above consistently mention only tinnitus as likely related to quinine use. However, the descriptions and inference testing of side effects were inadequate in each study.

Of note, quinine is a category X drug and should not be used during pregnancy.<sup>6</sup>

## ■ RECOMMENDATIONS FROM OTHERS

No specific recommendations exist regarding the use of quinine in athletes. The American Medical Society of Sports Medicine recommends rest, stretching, and oral hydration for simple heat cramps, and intravenous fluids for very severe cases.<sup>7</sup> Several texts also recommend rehydration with an oral electrolyte solution, as well as rest, stretching, and massage.<sup>8–10</sup>

*Noelle Robertson, MD, Wayne Hale, MD, Leslie Mackler, MSLS, Moses Cone Health System, Greensboro, NC*

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## Hydration before, during, and after activity remains the cornerstone to approaching cramping in athletes

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### CLINICAL COMMENTARY

#### Hydration and salt intake best approach for cramping in athletes

The use of quinine for the treatment or prevention of leg cramps in young adult athletes is not well studied. Safety and efficacy issues make it an unappealing option in the treatment of cramps and consequently it is not recommended for use in athletes. Hydration before, during, and after activity remains the cornerstone to approaching cramping in athletes. Appropriate salt intake for those who lose high concentrations of salt in their sweat may also

be useful in prophylaxis. Once cramps occur, rehydration, stretching, massage, and rest work best.

*Sourav Poddar, MD, Team Physician, University of Colorado Buffaloes, University of Colorado Health Sciences Center, Denver*

## Can type 2 diabetes be prevented through diet and exercise?

### EVIDENCE-BASED ANSWER

Diets that result in long-term weight loss of 5% to 7%, along with moderate-intensity exercise for more than 150 minutes per week, reduce the incidence of type 2 diabetes for patients with impaired glucose tolerance (IGT) (strength of recommendation [SOR]: **A**, based on multiple randomized controlled trials [RCTs]). Each of the trials demonstrating this finding included fairly intensive counseling as part of the successful intervention. Diet and exercise reduce the incidence of diabetes in both lean (body mass index [BMI] <25) and overweight patients with IGT (SOR: **B**, based on a single, large RCT).

### EVIDENCE SUMMARY

Three large prospective RCTs evaluated the effect of dietary and exercise interventions in populations at risk for developing diabetes.

The **Diabetes Prevention Program Research Group**<sup>1</sup> randomized 3234 patients age >24 years without diabetes but with IGT and a BMI >24 to 1 of 3 groups: intensive lifestyle modification, metformin, or control; they then compared the incidence of diabetes over 3 years. Patients were men and women from primary care populations and represented diverse ethnic backgrounds. Investigators defined IGT as plasma glucose of 140 to 200 mg/dL 2 hours after a 75-g glucose bolus when the fasting glucose was <140 mg/dL. Intensive lifestyle intervention comprised individual training sessions on a