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Malaria Prevention Measures in Coalition Troops in Afghanistan

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Statins and Regression of Coronary Atherosclerosis

To the Editor: Dr Nicholls and colleagues¹ found that treatment with statins was associated with regression of coronary atherosclerosis (assessed by intravascular ultrasonography) when low-density lipoprotein cholesterol (LDL-C) was substantially reduced and high-density lipoprotein cholesterol (HDL-C) was increased by more than 7.5%. The authors state that it remains to be determined whether these changes translate to improved clinical outcomes because the small increases in HDL-C observed during statin therapy have never been shown to correlate with clinical outcome.

However, in a post hoc analysis of the secondary coronary heart disease prevention Greek Atorvastatin Coronary Heart Disease Evaluation (GREACE) Study, the composite end point of all vascular events was found to be partly determined by the extent of atorvastatin-induced HDL-C increase in the structured care group compared with usual care.² This was in the setting of achieving an LDL-C level of 100 mg/dL (2.59 mmol/L) in 95% of patients in the structured care group (a 46% decrease in LDL-C from baseline values). After multiple regression analysis, the beneficial effect associated with HDL-C increase was independent of the LDL-C reduction (hazard ratio for each 4 mg/dL [0.10 mmol/L] increase in HDL-C, 0.85; 95% confidence interval, 0.76-0.94; $P = .002$).²

A relatively small increase in HDL-C (mean, 7%) observed during 3 years of statin treatment was associated with clinical event reduction, supporting the findings of Nicholls et al.¹

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1. Nicholls SJ, Tuzcu EM, Sipahi I, et al. Statins, high-density lipoprotein cholesterol, and regression of coronary atherosclerosis. *JAMA*. 2007;297:499-508.

2. Athyros VG, Mikhailidis DP, Papageorgiou AA, et al; GREACE Collaborative Group. Effect of atorvastatin on high density lipoprotein cholesterol and its relationship with coronary events: a subgroup analysis of the GREACE Atorvastatin and Coronary-heart-disease Evaluation (GREACE) Study. *Curr Med Res Opin*. 2004;20:627-637.

In Reply: Dr Athyros and colleagues describe the results of the GREACE study, which demonstrated that a small increase in levels of HDL-C independently predicted the clinical benefit observed during administration of atorvastatin in patients with established coronary heart disease.¹ This observation highlights a number of important points. Their findings provide further evidence to support the concept that small increases in levels of HDL-C are clinically important.

We believe that the beneficial effect of statin therapy is likely derived from several properties beyond the ability of these drugs to lower levels of LDL-C. The findings described by the GREACE investigators also represent an example of the complementary observations between clinical outcomes trials and imaging studies that measure the rate of atheroma progression as assessed by intravascular ultrasound.

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1. Athyros VG, Mikhailidis DP, Papageorgiou AA, et al; GREACE Collaborative Group. Effect of atorvastatin on high density lipoprotein cholesterol and its relationship with coronary events: a subgroup analysis of the GREACE Atorvastatin and Coronary-heart-disease Evaluation (GREACE) study. *Curr Med Res Opin*. 2004;20:627-637.

RESEARCH LETTER

Malaria Prevention Measures in Coalition Troops in Afghanistan

To the Editor: Following the September 11, 2001, attacks on New York and Washington, the International Security Assistance Force (ISAF) was created in Afghanistan in December 2001 with support from 16 nations. By 2006, ISAF support increased to 36 nations, with approximately 115 000 coalition troops serving during this period. Malaria, especially *Plasmodium vivax*, is prevalent between May and November in all areas of Afghanistan less than 6667 feet above sea level.¹ Since 2002, 85 cases of *P vivax* malaria have been reported in British, German, and US troops that have been linked to military service with ISAF,²⁻⁴ and it is likely that additional cases have occurred.

We conducted a survey to compare malaria prevention measures in use by coalition forces in Afghanistan in 2006 and to evaluate the level of international agreement for this area of clinical practice.

Methods. In June 2006 the malaria prevention policy of each ISAF force was evaluated through a standardized 7-part questionnaire (BOX) sent to each senior national representative, a designated staff officer stationed within the ISAF headquarters in the city of Kabul. The senior national representatives were requested to verify national policy with their respective medical personnel in theater. Drug dosage was not ascertained, assuming that all countries

Table. Malaria Prevention Measures Reported by ISAF Senior National Representatives, June 2006*

Nation	No. of Troops Deployed With ISAF	Antimalarial Drug	Exceptions/Alternatives to Antimalarial Drug Measures	Start Time for Drugs (Before Entering Theater), w	Stop Time for Drugs (After Departing Theater), w	Nondrug Malaria Prevention
Austria	5	Mefloquine	Not required in Kabul city	1	As soon as departed	Repellent, warning card
Belgium	250	Mefloquine	Not required in Kabul city	2	4	Treated bed net, treated uniform, repellent
Canada	2200	Mefloquine	Atovaquone-proguanil if deploying <4 weeks	3	4	Treated bed net, treated uniform, repellent
Croatia	120	Mefloquine	Not required in Kabul city	2	4	Treated bed net, repellent
Czech Republic	100	Mefloquine		1	3	Treated bed net, treated uniform
Denmark	300	Atovaquone-proguanil	Not required in Kabul city	1 Day	1	Treated bed net, treated uniform, repellent
France	700	Chloroquine-proguanil				
Germany	2200	Mefloquine	Not required in Kabul city	2-3	4	Treated bed net, treated uniform, repellent
Greece	180	Mefloquine	Or chloroquine or doxycycline			
Hungary	200	Doxycycline	Not required in Kabul city	1	4	Untreated bed net
Irish Republic	10	Chloroquine-proguanil				
Italy	1200	Doxycycline	Or mefloquine	1	4	Treated bed net, treated uniform, repellent, vaporizing mats
Lithuania	135	Mefloquine		On entering	4	Treated bed net, treated uniform, repellent, warning card
Luxembourg	10	Chloroquine-proguanil	Not required in Kabul city			
Macedonia	120	Mefloquine		2	4	Untreated bed net, repellent, mosquito coils, vaporizing mats, electronic buzzers
Netherlands	1700	Proguanil	Not required in Kabul city Atovaquone-proguanil if deploying <2 weeks			
New Zealand	100	Doxycycline		2	2	Untreated bed net, treated uniform, repellent, warning card
Norway	350	Doxycycline		1	4	Untreated bed net, treated uniform, repellent
Poland	100	Chloroquine		1	4	Repellent
Portugal	180	Mefloquine	Not required in Kabul city			
Romania	750	None				
Slovakia	60	Mefloquine				
Slovenia	50	Chloroquine		1	4	Untreated bed net, repellent, electronic buzzers
Spain	600	Mefloquine	Atovaquone-proguanil if deploying <4 weeks Doxycycline for pilots and drivers	1	4	Treated bed net, treated uniform, repellent, mosquito coils, vaporizing mats
Sweden	350	Mefloquine	Atovaquone-proguanil if based in Kabul city, and also for short deployments	1	1	Treated bed net, treated uniform, repellent
Turkey	475	Mefloquine		15 Days	15 Days	Untreated bed net, repellent, warning card
United Kingdom	4500	Chloroquine-proguanil		1	4	Treated bed net, treated uniform, repellent, warning card
United States	18 500	Mefloquine	Doxycycline is an alternative drug, although not for all personnel	2	4	Treated uniform, repellent

Abbreviation: ISAF, International Security Assistance Force.

*Blank table cells denote no response to questionnaire item (ie, no actual response, respondent replied "don't know", data unavailable, or question not understood by respondent due to language barrier).

Box. Malaria Prevention Questionnaire, ISAF Senior National Representatives, June 2006

1. What is your nation's officially recommended anti-malaria drug regimen for Afghanistan as of June 2006? (Please give drug names)
2. What is your nation's official policy for when anti-malaria drugs should be started before entering Afghanistan?
3. What is your nation's official policy for when anti-malaria drugs should be discontinued after leaving Afghanistan?
4. During which months of the year are troops of your nation, deployed in Afghanistan, officially advised to take antimalaria drugs?
5. Which of the following additional antimalaria measures are officially recommended to troops of your nation deployed in Afghanistan?
 - a. Use of mosquito net?
 - b. Mosquito net treated with insecticide?
 - c. Uniform treated with insecticide?
 - d. Skin-applied insect repellent?
 - e. Mosquito coils?
 - f. Vaporizing mats?
 - g. Electronic buzzers?
 - h. Carrying of personal-issue malaria warning card?
6. Have there been any cases of malaria in your national force in Afghanistan?
7. Please mention any other factors relevant to your nation's malaria prevention policy in its troops deployed in Afghanistan.

Abbreviation: ISAF, International Security Assistance Force

would follow manufacturers' standard dosing recommendations.

The survey was administered in English, the working language of the North Atlantic Treaty Organization, after piloting on a multinational convenience sample of clinical and nonclinical personnel and minor revision. Representatives were sent 1 written reminder.

Results. Of the 36 troop-contributing nations, representatives of 28 (78%) responded to the survey, with 20 (55%) answering all questions. The nonresponders were Albania, Azerbaijan, Bulgaria, Estonia, Finland, Georgia, Latvia, and Switzerland. Eighteen (64%) of the 28 responders validated their responses in theater and reported more than 98% accuracy.

Except for France and the Irish Republic, no countries had identical malaria prevention policies (TABLE). Divergence in the antimalarial drugs routinely used by ISAF troops was notable, with 15 nations (54%) reporting the use of mefloquine as their preferred agent, 4 (14%) chloroquine-

proguanil, 4 (14%) doxycycline, 2 (7%) chloroquine alone, 1 (4%) atovaquone-proguanil, and 1 (4%) proguanil alone for all deployments in Afghanistan of longer than 2 weeks. One nation (Romania) replied that it did not routinely use malaria prophylaxis for its ISAF force in Afghanistan.

Twenty ISAF nations used at least 1 additional nondrug technology to prevent malaria. Eighteen nations (64%) reported using topically applied insect repellent and 13 (46%) insecticide-treated uniforms. Seventeen nations (61%) reported using bed nets, although only 11 (39%) stated that these were pretreated with insecticide. Five nations (18%) reported issuing malaria warning cards to their ISAF troops. Three (11%) reported using vaporizing mats, 2 (7%) mosquito coils, and 2 (7%) electronic buzzers.

No representatives of any nations reported cases of malaria occurring in Afghanistan except New Zealand (in Bamyán) and Norway (1 in 2004).

Comment. These results indicate discrepancies in malaria prevention policies between ISAF nations with troops serving in Afghanistan, although this lack of concordance may be partly due to differing perceptions of disease risk. There is compelling evidence that insecticide-treated bed nets are effective in preventing malaria in travelers, and insecticide-treated clothing and certain drugs (atovaquone-proguanil, doxycycline) are also likely to be beneficial.⁵ However, the use of chloroquine for chemoprophylaxis in a region known to have chloroquine-resistant *Plasmodium falciparum* and the use of electronic buzzers and mosquito coils conflicts with current evidence.⁵⁻⁷

There are limitations to this study. The survey was conducted in English, which may have introduced a response bias or resulted in inaccurate responses. The survey does not measure adherence to policy by individual military personnel, and as such cannot be directly linked to outcomes. Nevertheless, these national differences have the potential to engender confusion locally and contribute to malaria acquisition.

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Acquisition of data: Darbyshire, Jackson.

Analysis and interpretation of data: Croft, Darbyshire, Jackson, van Thiel.

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CORRECTION

Incorrect Example: In the Original Contribution entitled "An Empirical Examination of the Stage Theory of Grief" published in the February 21, 2007, issue of *JAMA* (2007;297:716-723), an incorrect example was provided for natural causes. On page 717, column 1, second full paragraph, the third sentence should be "Because approximately 94% of US deaths result from natural causes (eg, heart disease, cancer),¹⁵ deaths from unnatural causes (eg, car crashes, suicide) were excluded thereby enabling the results to be generalized to the most common types of death."

Medicine requires not only the intellectual cultivation of a science, but the patience and the practical skill of an art. At the bedside we must be animated by the feeling of faithful artisans, of men whose object and duty is practical work; for when the art of medicine is needed by the suffering and the dying it is no question of mere theoretical knowledge and extraneous acquirement. But skill in the commonest art it is not to be attained without much practice, far less in the complicated and difficult art of healing, where every case presents some peculiarities. To practice it successfully, we must have made our home at the bedside, and, if I may say so, have lived with disease, observing it in all its forms and changes.

—Sir William Withey Gull (1816-1890)