

# Mayo Clinic Proceedings

## Khat Chewing: A Smokeless Gun?

Chewing the leaves of the plant *Catha edulis* (referred to as *khat*, *African salad*, *bushman's tea*) likely dates to times of antiquity and may predate the use of coffee.<sup>1</sup> An early written description of khat appeared in Paris in 1697 when Barthelemy d'Herbelot de Molainville traveled to Yemen (*translated*): "[It] is made with a seed which is unknown to us, which has been forbidden by the doctors of the law in the province of Yemen...., where it originated. ...because it is too strong, and affects the brain."<sup>2</sup> It was not until 1975 that United Nations laboratories first discovered the active ingredient of khat to be cathinone, an amphetamine-like substance that has sympathomimetic, euphoric, and mood-altering effects among other health consequences.<sup>3</sup>

An unknown number of people chew khat worldwide. Estimates range from 5 to 10 million, predominantly living in the horn of Africa and the Arabian peninsula, most notably including Ethiopia, Somalia, and Yemen.<sup>1,4</sup> Although khat chewing has been a social custom for centuries in that part of the world, it has largely escaped medical attention. Before the inclusion of khat as a risk factor for acute coronary syndrome (ACS) and early post-ACS death, reported in this issue of *Mayo Clinic Proceedings*,<sup>5</sup> khat chewing had been the subject of few robust clinical studies. In Canada and parts of the European Union, khat possession is illegal.<sup>6</sup> In Australia, to import khat, a license and permit are needed by the Australian Quarantine and Inspection Service,<sup>7</sup> whereas in the United Kingdom, khat possession and use are legal. In the United States, fresh khat is a schedule I drug under the Controlled Substances Act, defined as having a high

potential for abuse and no currently accepted medical treatment.<sup>4</sup> To date, human research involving khat has been limited by low participant numbers; thus, whether khat chewing is dangerous and addictive or rather a way of life that lacks serious long-term health effects for the user remains controversial.

Khat is unique as a substance of abuse. Unlike other abused substances, khat is highly perishable. The leaves are freshly stripped from the *C edulis* trees at dawn and rapidly distributed by airplanes and organized delivery systems in regions where khat chewing is widespread. Cathinone can be found only in fresh *C edulis* leaves. Older leaves contain the substance cathine, which is less sought after by chewers. Notably, cathine lacks the euphoric effects of cathinone.<sup>8</sup> The distribution of khat in some regions of the world is likely as sophisticated as the cold chain delivery of vaccines. Indeed, there may be as many regular khat chewers in Yemen (90% of adult men, up to 50% of adult women)<sup>9</sup> as there are people who have been vaccinated (range, 60%-79%).<sup>10</sup>

Although initially thought to be of limited concern to Western populations because of its complicated cultivation and distribution systems, khat is now confiscated throughout the United States. For example, for a period of 6 months in 2002, US federal officers seized more than 30 metric tons of khat.<sup>4</sup> Arrests of traffickers continue to be publicized, including the jailing of 2 presumed English tourists in March 2010 in Maryland.<sup>11</sup> In England, 7 metric tons of khat is estimated to travel through Heathrow Airport each week, originating from Yemen, Ethiopia, and Kenya.<sup>12</sup> Whether the khat confiscated in the United States is in the form of fresh crimson-brown leaves with higher cathinone content or the aged, leathery, yellow-green variety with minimal cathinone<sup>4</sup> is not reported. Even among khat-producing countries, the cathinone content in fresh *C edulis* leaves naturally varies.<sup>8</sup> Overnight delivery systems, passenger air travel, immigration

See also  
page 974

Dr Mateen is supported by the Sommer Scholars Program at The Johns Hopkins University School of Public Health and the 2010 American Academy of Neurology Practice Research Fellowship Grant.

Address correspondence to Farrah J. Mateen, MD, Department of International Health, Bloomberg School of Public Health, 615 N Wolfe St, Room E8518, Baltimore, MD 21287 (fmateen@jhsph.edu).

© 2010 Mayo Foundation for Medical Education and Research

of khat chewers, and increasing restrictions on cigarette smoking may all contribute to the globalized distribution of fresh and aged khat.

The current study reported in *Mayo Clinic Proceedings*, performed by the Gulf Registry of Acute Coronary Events (Gulf-RACE) collaboration in 64 hospitals and involving more than 8000 patients, represents the largest group of khat chewers formally studied to date (nearly 1000 chewers) and does so by using a multinational prospective design of hospitalized ACS patients. Khat use was analyzed by self-report, which is necessary because there is no laboratory test for khat intake in the clinical setting. While controlling for other major risk factors, the Gulf-RACE group found that khat chewers were more likely to die after ACS and more likely to develop post-ACS stroke and cardiogenic shock. Non-khat chewers were more likely to experience a recurrent myocardial infarction. Khat chewers were less likely to be treated with coronary reperfusion therapy, probably because they presented late to the hospital (defined as >12 hours after symptom onset).<sup>5</sup>

The strengths of the study include the high number of khat chewers, the clarity with which the outcomes are reported, and the duration of follow-up of the patients (including both chewers and nonchewers). The results are supported by those from other studies, including case-control and case reports, that suggest that khat may be a risk factor for myocardial infarction, ischemic stroke, and increased blood pressure and heart rate in both humans and laboratory animals.<sup>13-16</sup>

Some questions, however, remain unanswered by the current study. Gulf-RACE did not enroll African blacks.<sup>17</sup> The number of Arab women presenting to hospitals, and thus eligible for inclusion in this study, is relatively small (23%). By comparison, approximately 55% of the participants in the Framingham Heart Study are women.<sup>18</sup> It is also difficult, in nearly every study on khat chewers, to separate the potentially collinear effects of cigarette smoking from khat because most khat chewers concomitantly smoke tobacco (including 61% in Gulf-RACE).<sup>5</sup>

Importantly, the income level of the countries in this study varied widely from some of the highest gross national incomes per capita in the world (Qatar [ranked as the sixth highest gross national income in the world in 2009] and Kuwait [10th]) to one of the lowest (Yemen [ranked 165th at 950 US dollars per capita]).<sup>19</sup> Because all khat chewers in the study were of Yemeni origin and survival was related to delayed presentation to the emergency department, khat chewing and risk of ACS death may be confounded with low income. Yemen is the poorest and most populous country in the Arabian peninsula, with 70% of the population inhabiting rural areas.<sup>20</sup> Access to primary care varies widely between urban and rural dwellers (80%

vs 25% of the population).<sup>21</sup> Long distances to hospitals,<sup>22</sup> reduced health care literacy (overall literacy in Yemen is 69%),<sup>21</sup> and general lack of health care infrastructure and access<sup>21-23</sup> could partially explain the relationship between khat, delays in care seeking, and higher post-ACS death found in Yemen in this study. By comparison, separate studies in Yemen have found that severe malarial disease and reduced vaccination uptake were both more likely among patients who had longer distances to travel.<sup>22,24</sup> Therefore, it is possible that higher ACS mortality in khat chewers in Yemen represents higher overall mortality in poorer, rural people in a country experiencing protracted armed conflict.

Khat therefore remains a controversy. If khat is indeed on the causal pathway toward death after ACS, does it begin the pathway by creating poor insight into one's own cardiac symptoms, thereby delaying prompt presentation for treatment? Or perhaps the postulated physiologic effects, namely a heightened sympathomimetic response with transiently raised heart rate and blood pressure, are to blame. Or do regions where khat chewing is common also suffer from a general lack of health care infrastructure and income diversion so that ACS cannot be ideally treated? As one Arab proverb goes, "Many are the roads that do not lead to the heart." Of course, some do. Finding these paths and their exact mechanisms will become increasingly important, not just in the Middle East but worldwide.

Farrah J. Mateen, MD  
Department of Neurology and  
Department of International Health  
The Johns Hopkins University  
Baltimore, MD

Gregory D. Cascino, MD  
Department of Neurology  
Mayo Clinic  
Rochester, MN

1. Balint EE, Falkay G, Balint GA. Khat—a controversial plant. *Wien Klin Wochenschr*. 2009;121:604-614.

2. Krikorian AD. Kat and its use: an historical perspective. *J Ethnopharmacol*. 1984;12:115-178.

3. United Nations. Etude sur la composition chimique du khat: recherches sur la fraction phenylalkylamine. UN document MNAR/11/1975.

4. US Department of Justice; National Drug Intelligence Center. Intelligence Bulletin: Khat (*Catha edulis*). Intelligence Bulletin 2003. Product No. 2003-L0424-002. Published May 2003. <http://www.justice.gov/ndic/pubs3/3920/index.htm>. Accessed October 4, 2010.

5. Ali WM, Zubaid M, Al-Motarrab A, et al. Association of khat chewing with increased risk of stroke and death in patients presenting with acute coronary syndrome. *Mayo Clin Proc*. 2010;85(11):974-980.

6. World Health Organization (WHO) Expert Committee on Drug Dependence. Assessment of khat (*Catha edulis* Forsk). [http://www.who.int/medicines/areas/quality\\_safety/4.4KhatCritReview.pdf](http://www.who.int/medicines/areas/quality_safety/4.4KhatCritReview.pdf). Accessed October 4, 2010. Published 2006.

7. Australian Government: Department of Health and Ageing. Application forms and guidelines: guidance for completing licence and import permit applications (khat). <http://www.health.gov.au/internet/main/publishing.nsf/Content/ocs-tc-guidance-imp-khat.htm>. Accessed October 4, 2010. Published December 2009.
8. Patel NB. Mechanism of action of cathinone: the active ingredient of khat (*Catha edulis*). *East Afr Med J*. 2000;77:329-332.
9. Al-Mugahed L. Khat chewing in Yemen: turning over a new leaf. *Bull World Health Organ*. 2008;86(10):741-742.
10. World Health Organization (WHO). Global Health Observatory. Yemen: data and statistics. <http://www.who.int/gho/countries/yem/data/en/index.html>. Accessed October 4, 2010.
11. US Department of Homeland Security; Customs and Border Protection. 2 U.K. khat smugglers sent packing after release from Maryland jail. US Customs and Border Protection Web site. Published March 2, 2010. [http://www.cbp.gov/xp/cgov/newsroom/news\\_releases/archives/march\\_2010/03022010\\_3.xml](http://www.cbp.gov/xp/cgov/newsroom/news_releases/archives/march_2010/03022010_3.xml). Accessed October 4, 2010.
12. Holligan A. Khat use spreads to British youth. BBC News. March 16, 2009. [http://news.bbc.co.uk/2/hi/uk\\_news/7942432.stm](http://news.bbc.co.uk/2/hi/uk_news/7942432.stm). Accessed October 4, 2010.
13. Vanwalleghem IE, Vanwalleghem PW, De Bleecker JL. Khat chewing can cause stroke. *Cerebrovasc Dis*. 2006;22(2):198-200.
14. Al-Motarreb A, Briancon S, Al-Jaber N, et al. Khat chewing is a risk factor for acute myocardial infarction: a case-control study. *Br J Clin Pharmacol*. 2005;59:574-581.
15. Hassan NA, Gunaid AA, Abdo-Rabbo AA, et al. The effect of Qat chewing on blood pressure and heart rate in healthy volunteers. *Trop Doct*. 2000;30:107-108.
16. Nencini P, Ahmed AM, Amiconi G, Elmi AS. Tolerance develops to sympathetic effects of khat in humans. *Pharmacology*. 1984;28:150-154.
17. Al-Menyar A, Zubaid M, Sulaiman K, et al. In-hospital major clinical outcomes in patients with chronic renal insufficiency presenting with acute coronary syndrome: data from a registry of 8176 patients. *Mayo Clin Proc*. 2010;85(4):332-340.
18. Parikh NI, Gona P, Larson MG, et al. Long-term trends in myocardial infarction incidence and case fatality in the National Heart, Lung, and Blood Institute's Framingham Heart Study. *Circulation*. 2009;119:1203-1210.
19. World Bank. Gross national income per capita 2009, Atlas method and PPP. <http://siteresources.worldbank.org/DATASTATISTICS/Resources/GNIPC.pdf>. Accessed October 4, 2010.
20. Central Intelligence Agency (CIA). The World Factbook: Yemen. <https://www.cia.gov/library/publications/the-world-factbook/geos/ym.html>. Accessed October 4, 2010.
21. World Health Organization (WHO). Country profiles: Yemen. [http://www.emro.who.int/emrinfo/index.asp?Ctry=yem#PHC\\_Concluded](http://www.emro.who.int/emrinfo/index.asp?Ctry=yem#PHC_Concluded). Accessed October 4, 2010.
22. Al-Taiar A, Clark A, Longenecker JC, Whitty CJM. Physical accessibility and utilization of health services in Yemen. *Int J Health Geogr*. 2010;9:38.
23. Fares S, Zubaid M, Al-Mahmeed W, et al. Utilization of emergency medical services by patients with acute coronary syndromes in the Arab Gulf states [published online ahead of print June 25, 2010]. *J Emerg Med*. doi:10.1016/j.jemermed.2010.05.002.
24. Al-Taiar A, Jaffar S, Assabri A, et al. Who develops severe malaria? Impact of access to healthcare, socio-economic and environmental factors on children in Yemen: a case-control study. *Trop Med Int Health*. 2008;13(6):762-770.