Exercise Regimens for Men With HIV

To the Editor: Dr Bhasin and colleagues1 reported that testosterone replacement therapy or resistance training resulted in gains in body weight, muscle mass, strength, and lean body mass in men infected with the human immunodeficiency virus (HIV) who have weight loss and low testosterone levels. However, the training protocol does not reflect the scientific basis for effective resistance training.

Bhasin et al described a resistance training protocol that featured whole-body training with 5 exercises 3 times per week. After testing for 1-repetition maximum (1-RM), the first 4 weeks of the protocol involved 3 sets of 12 to 15 repetitions at 60% of the 1-RM. This was followed by 6 weeks of a periodized program using 4 sets of 4 to 6 repetitions with 1 day at 90% of 1-RM, 1 day at 80%, and 1 day at 70%. A similar protocol, but with 5 sets and greater resistance, was used during the last 5 weeks.

There is very little evidence supporting the efficacy of using more than 1 set of repetitions for each exercise.2,3 One set is as effective as multiple sets. Using multiple sets, particularly for people already compromised with health, may cause overtraining and immunosuppression (eg, natural killer cell cytotoxic activity) that can undermine strength gains and body composition changes.4 Also, there is little evidence to suggest that training 3 times per week results in greater strength or lean body mass than training twice per week. Twice-weekly training is recommended over more frequent sessions because it is less time consuming, improves compliance, allows adequate recovery time, and produces the most health and fitness benefits.5 In addition, there is a lack of evidence to recommend periodized programs, which vary the training volume at specific intervals, over training regimens that simply allow sufficient rest between training sessions.6 Most evidence indicates that the key stimulus promoting adaptation in the muscularskeletal system is the intensity of training,7 not volume, as was used in the protocol of this study.

By the last 5 weeks of the intervention, men were receiving an exercise dose that was 7.5 times greater (5 sets of each exercise, 3 times per week) than what appears required for significant improvement (1 set of each exercise, 2 times per week). Resistance training research indicates that the same outcomes could have been produced with a fraction of the training and that weight gain, muscle mass, and strength may have shown better outcomes with a prescribed dose of 1 set per exercise twice per week.

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In Reply: The use of single vs multiple sets of repetitions for resistance exercise training is a controversial issue in the design of resistance training programs. The exercise regimen used in our study was developed in 1995 using multiset and periodization models based on established sources,1 as well as our successful experience with a similar training program in healthy men.2 In that study, the periodized, thrice-weekly, resistance training was safe and effective in substantially increasing fat-free mass and maximal strength in healthy men. Similarly, in HIV-infected men, use of a multiset, periodized, thrice-weekly resistance training protocol was associated with significant gains in fat-free mass and maximal strength.

Our training protocol was safe; no adverse effects were attributable to resistance training. Changes in CD4 and CD8 cell counts and HIV copy number were not significantly different between the exercise and no-exercise groups. Others have reported similar observations in immunologic status using thrice-weekly, multiple-set regimens.3,5

Although the reviews cited by Drs Winett and Carpinelli have suggested that 1 set of repetitions might be as effective as multiple sets, this view is not universally shared.3,6 Recent clinical trials using resistance training in patients with HIV have used multiple sets3,3 with thrice-weekly training. Currently, we do not know whether twice-weekly regimens of resistance training using single sets are as effective as the regimen we used in our study.

Periodization is also an important concept in the design of resistance training programs,4 and there is support for nonlinear periodization models such as those used in our study.5 However, more studies are needed to compare the effectiveness of periodized and nonperiodized regimens in patients with HIV and other populations.

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Letters Section Editors: Stephen J. Lurie, MD, PhD, Contributing Editor; Phil B. Fontanarosa, MD, Deputy Editor.

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Our study demonstrated that the thrice-weekly, multiple-set, periodized regimen was safe and effective in inducing gains in fat-free mass and strength. We do not know if decreasing the volume to 1 set of 8 to 12 repetitions performed twice weekly would yield similar results. Our objective was not to find the lowest training stimulus that would produce clinically detectable changes, but rather to apply established methods for maximizing gains in muscle mass and strength. A more modest approach might provide clinically relevant improvements; however, this has not been demonstrated in clinical trials in this patient population.

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Resistance Exercise and Oxandrolone for Men With HIV-Related Weight Loss

To the Editor: The study by Dr Strawford and colleagues1 contributes important data regarding anabolic steroid treatment of human immunodeficiency virus (HIV)–associated wasting. In an Editorial,2 Dr Dobs noted that this study was “limited by absence of an exercise arm alone.”

We recently completed a pilot study3 on oxandrolone and progressive resistance exercise in a similar group of HIV-positive subjects with a greater than 3% weight loss. All study participants (12 men, 1 woman) received 10 mg of oxandrolone twice a day and were randomized to progressive resistance exercise (n=7) or no progressive resistance exercise (n=6) groups. Study participants had an average of 9.4% and 11.0% muscle wasting and had average logarithmic viral loads of 3.4 and 3.5, in the progressive resistance exercise and control groups, respectively. Group parameters did not differ significantly. Stable physiologic testosterone supplementation in study participants was permitted. Applicants with abnormal liver function test results, pregnancy, active infection or cancer, and those using illicit drugs, appetite enhancers, or anabolic agents within 30 days were excluded. Subjects had at least 3 one-hour, monitored progressive resistance exercise sessions per week. Control subjects did not perform progressive resistance exercise. Weight, body cell mass, and phase angle (a measure of cell membrane integrity) were measured using bioelectric impedance analysis.

At 1 month, the 6 control subjects gained a mean of 1.1 kg (2.4 lb), or 1.9% of entry weight; the 7 exercise subjects gained a mean of 2.0 kg (4.5 lb), or 3.2% of entry weight. One control subject lost weight, 2 lost body cell mass, and 2 lost phase angle at month 1; there were no such losses at month 3. Weight, body cell mass, and phase angle did not decrease for any subjects randomized to exercise. Ten subjects completed 3 months; 5 control subjects gained a mean of 2.7 kg (6.1 lb), or 4.6% of entry weight, and the 5 exercise subjects gained a mean of 3.9 kg (8.7 lb), or 5.6% of entry weight.

While this study was not powered to show the statistically significant improvement with combination anabolic therapy and exercise reported by Strawford et al and while our subjects lacked that study’s advantage of a personal trainer, we also saw gains from anabolic treatment that were enhanced by the addition of progressive resistance exercise. In addition, results from our control group show that oxandrolone can increase weight, body cell mass, and phase angle even in the absence of progressive resistance exercise. Thus, for those patients who cannot or will not exercise, we believe oxandrolone remains a viable option for increasing weight, body cell mass, and phase angle in HIV-related wasting.

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In Reply: Dr Dobs indicated in her Editorial1 that both of our study groups received physiologic testosterone replacement therapy (thus, there was no true “exercise alone” arm). In this regard, the study referred to by Dr Romeyn and Mr Gunn apparently also allowed physiologic carotid stenose replacement. Nevertheless, we await the full report of the study by Romeyn and Gunn with interest.

We certainly were aware of the work reported by Dr Berger. However, this study differed from ours in several important ways that limited its relevance: it did not study the effects of exercise; did not monitor lean body mass changes; and had an oxandrolone-only group, while our study did not.

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Plaque Morphology as a Risk Factor for Stroke

To the Editor: Dr Barnett and colleagues1 have pointed out that not all strokes can be explained by the presence of flow-limiting stenosis. Several other causes of stroke, including cardioembolism, large artery postthrombotic hematologic conditions, and lacunae were considered. However, they did not mention that different forms of plaque, which can be characterized using ultrasound, can also lead to embolic stroke. Heterogeneous plaque is an independent risk factor for stroke regardless of the degree of stenosis. Barnett et al have wisely pointed out that the identification of risk for stroke is complicated, and further study is needed to understand this significant risk factor. In thinking about and analyzing the issues surrounding risk for stroke, the role of characterization of plaque must not be forgotten. Unfortunately, the data on which their study was based originated in the North American Symptomatic Carotid Endarterectomy Trial (NASCET). In the NASCET, plaque type was not characterized and therefore, this could not be included in the analysis by Barnett et al. In future work regarding the etiology of stroke all risk factors, including plaque characterization, should be included in the analysis so that a more comprehensive understanding of the subject can occur. Perhaps if the plaque type had been analyzed, the authors might have rendered a different conclusion.

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In Reply: Dr Bluth correctly notes that the degree of stenosis is not the only variable that increases the risk of stroke. He cites studies showing that modern ultrasound done in well-equipped and closely supervised laboratories can distinguish between echodense and echolucent carotid lesions. Echolucency (corresponding to soft and friable plaques) along with the degree of stenosis led to an increased risk of stroke. However, such sophisticated ultrasound technology did not exist when NASCET was launched in 1987. At that time it was an inadequate method to evaluate either the severity of stenosis or the nature of the carotid lesion causing the symptoms. A major study contemporaneous with NASCET could not conduct risk and benefit analyses based on the degree of stenosis as evaluated by ultrasound.1 Thus, the NASCET protocol appropriately required conventional angiography.

Despite the presence of carotid lesions, whether echolucent or echodense, the same proportion of patients in NASCET probably would have had their subsequent strokes attributed to cardiac sources and to lacunar (usually small-vessel) disease. The patients with cardioembolic strokes had overt evidence of cardioembolic disorders (eg, atrial fibrillation, acute anterior myocardial infarction) and the lacunar strokes had the appropriate clinical and radiological features.2 Lacunae have been proven infrequently to be of embolic origin, reflecting disease of the penetrating arteries. While some lacunae might be caused by emboli arising from an echolucent plaque, most appear to be of small-artery origin. Imaging technology is on the verge of being able to visualize the small arteries that cause lacunar stroke.3 Improvement in computed tomography and magnetic resonance imaging intracranial arterial imaging and in cardiac, aortic, and extracranial artery studies may render both conventional angiography and the current varieties of ultrasound obsolete for stroke prevention studies.

Some large-artery strokes may originate from soft friable plaques. Early observations indicate that such echolucent plaques are an independent risk factor for stroke. A large multicenter study examining plaque characteristics is under way in Europe and the results are eagerly awaited.4

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Quality of Life in Maintenance vs Prolonged Induction Therapy for HIV

To the Editor: The feasibility of induction-maintenance therapy for human immunodeficiency virus type 1 (HIV) infection has been studied as a strategy to simplify antiretroviral regimens. In the Amsterdam Duration of Antiretroviral Medication study, maintenance dual therapy after 26 weeks of quadruple induction therapy resulted in less viral suppression than prolonged induction therapy. However, a prolonged quadruple regimen may have a negative impact on patients’ quality of life (QOL) because of pill burden and adverse effects. We compared QOL in maintenance vs prolonged induction therapy.

Methods. Antiretroviral-naïve HIV-infected patients with a CD4 cell count of at least \(200 \times 10^6/L\) (200/µL) and 1000 HIV RNA copies/mL received 26 weeks of induction therapy comprising stavudine, lamivudine, saquinavir, and nelfinavir. If the plasma HIV RNA concentration at weeks 24 and 25 was less than 50 copies/mL, patients were randomly assigned to receive prolonged 4-drug induction or maintenance therapy (either stavudine and nelfinavir or saquinavir and nelfinavir). From week 26, plasma HIV RNA concentrations were assessed by an ultrasensitive assay procedure (Amplicor HIV-1 Monitor Ultrasensitive; Roche Diagnostics, Branchburg, NJ) with a variable quantification limit. Clinical results have been reported elsewhere.

In a subsample, QOL was assessed at weeks 24 and 48 by the Medical Outcomes Study (MOS) HIV Health Survey, comprising 10 subscales. We calculated changes in QOL scores from week 24 to week 48. Effect sizes for between-group differences were calculated by dividing mean differences by pooled SDs. Effect sizes equaling 0.2, 0.5, and 0.8 are considered to indicate small, moderate, and large effects, respectively. We calculated correlation coefficients between the plasma HIV RNA concentration at week 48 and changes in QOL scores. Analysis was by intention to treat.

Results. Ten of 16 patients assigned to receive maintenance therapy and 9 of 15 patients assigned to receive prolonged induction therapy participated in the QOL study. Both groups were comparable (P > .20) in terms of age (39 vs 44 years), sex (91% vs 100% men), Centers for Disease Control and Prevention HIV classification A (73% vs 67%), median baseline CD4 cell count (370 \(\times 10^6/L\) vs 420 \(\times 10^6/L\)), and median baseline HIV RNA log10 copies/mL (4.50 vs 4.58).

Participants were similarly comparable to those who did not participate. Patients assigned to receive maintenance therapy showed more decline in QOL scores than patients assigned to receive prolonged induction therapy on the following MOS-HIV subscales: physical function (−11 points; effect size, 0.4), role function (−18 points; effect size, 0.4), social function (−17 points; effect size, 0.5), overall QOL (−19 points; effect size, 0.7), health distress (−17 points; effect size, 0.7), health perceptions (−13 points; effect size, 0.5) and energy/fatigue (−8 points; effect size, 0.3). At week 48, plasma HIV RNA was higher in the maintenance group than in the prolonged induction group (2.3 log10 copies/mL vs 1.6 log10 copies/mL; P = .05), although concentrations in both groups were quite low. A higher plasma HIV RNA concentration was correlated with more decline in QOL scores for energy/fatigue (\(r = −0.51; P = .03\)), social function (\(r = −0.66; P = .003\)), health distress (\(r = −0.64; P = .005\)), health perceptions (\(r = −0.55; P = .02\)), and overall QOL (\(r = −0.58; P = .009\)) (Figure)

Comment. Quality-of-life scores declined more during maintenance therapy than during prolonged induction therapy. The data from this small unblinded study raise the interesting possibility that the negative effects of inferior viral suppression on QOL were greater than the added burden of a 4-drug regimen.

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Funding/Support: This work was supported by grant 1325 from the AIDS Fund, Amsterdam, the Netherlands. The original antiretroviral study was financially supported by Roche and Bristol-Myers Squibb.
Directly Observed Therapy to Treat HIV Infection in Prisoners

To the Editor: The efficacy of highly active antiretroviral therapy (HAART) in the treatment of human immunodeficiency virus (HIV) infection has been demonstrated in a number of clinical reports. However, current regimens are complex and poor adherence to therapy is the main cause of both treatment failure and emergence of drug resistance. Adherence to multidose treatment regimens may be more difficult in certain settings, such as prison. Herein we report data from HIV-positive prisoners treated using a directly observed therapy (DOT) program. To our knowledge, DOT for HIV infection has not been evaluated in this setting.

Methods. We selected 9 Italian prisons in which antiretroviral drugs are always administered by prison nurses who observe the patient taking every dose (DOT schedule), and 9 prisons in which nurses leave all drugs with the patient once a day with no directly observed control (NDOT schedule). Eighty-four HIV-infected intravenous drug users were consecutively enrolled from April 1997 to September 1998. All patients received counseling about their HIV infection and provided informed consent. The study received institutional review board approval.

Of these 84 patients, 37 (n=36 men) aged 23 to 48 years (mean, 34 years) with plasma HIV RNA levels between 4.04 and 5.94 log copies/mL (mean, 5.30 copies/mL; median, 4.92 copies/mL) were treated according to the DOT schedule. Median CD4 cell count was 173 × 10^6/L (range, 12-558 × 10^6/L), and 23 patients (62.1%) had a CD4 cell count of less than 200 × 10^6/L. Nine patients were antiretroviral therapy naive. The remaining 47 patients (n=44 men), aged 22 to 51 years (mean, 34 years) with plasma HIV RNA levels between 2.77 and 5.81 log copies/mL (mean, 5.12 copies/mL; median, 4.78 copies/mL) were treated with the NDOT schedule. Median CD4 cell count was 163 × 10^6/L (range, 5-669 × 10^6/L), and 25 patients (53.2%) had a CD4 cell count of less than 200 × 10^6/L. Ten patients were antiretroviral therapy naive. Plasma HIV RNA levels were determined by the Amplicor polymerase chain reaction assay (Roche Diagnostic Systems, Basel, Switzerland; detection limit, 400 copies/mL). We followed the guidelines of the Italian Health Ministry for decisions about antiretroviral therapy.

Results. There were no significant differences between groups with regard to sex, age, CD4 cell count, or viremia and no significant difference in the HAART schedule for the 2 groups. Mean duration of therapy was 8.7 months (range, 3-19 months) for the DOT group and 8.5 months (range, 3-16 months) for the NDOT group. Two patients in the DOT group discontinued therapy after 3 months because of peripheral neuropathy and relapsing renal colic. No drug switching was required for any patient. We identified adverse effects in 15 patients (9 in the DOT group and 6 in the NDOT group) without discontinuation of therapy, including 1 case of anemia, 3 cases of peripheral neuropathy, 5 cases of renal colic, and 6 cases of gastrointestinal tract problems. All subjects reported a favorable attitude toward DOT.

All patients in the DOT group showed a significant decrease in viral load (>2 log) after therapy; of these, 23 (62.1%) had a plasma HIV RNA level below the detection limit compared with 16 patients (34.0%) in the NDOT group (odds ratio, 3.18; 95% confidence interval, 1.18-8.67; $\chi^2=7.44; P<.01$). In the DOT group, only 2 patients (5.4%) had a CD4 cell count that remained less than 200 × 10^6/L; by contrast, 15 patients in the NDOT group (31.9%) had a CD4 cell count less than 200 × 10^6/L (odds ratio, 0.12; 95% confidence interval, 0.02-0.62; $\chi^2=7.44; P<.001$).

Comment. These findings suggest that DOT may be an acceptable and feasible intervention for HIV-positive Italian prisoners. Ensuring adherence to treatment regimens by DOT results in a higher efficacy of HAART. We assume that the DOT group had 100% adherence to the treatment regimen. The cost of implementing DOT in this setting is low; no additional staff was required to administer this therapy.

DOT has been used for many years as an approach for the treatment of tuberculosis. This strategy also could be considered for treatment of HIV disease, especially in difficult-to-reach populations such as prisoners. The optimal duration for this intervention strategy remains to be evaluated. However, current trends toward simplified HAART schedules could facilitate DOT programs.

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Acknowledgment: We would like to thank all the members of the Infettivologi Penitenziari study group: A. Abbinante, MD; F. Alberti, MD; G. Barbarini, MD; F. Cac-
Lead Exposure From Candles

To the Editor: Blood lead levels as low as 0.43 μmol/L (10 μg/dL) in children can result in developmental and behavioral problems, including lower intelligence.1 For this reason, lead has been restricted in paint and banned in gasoline and vinyl mini-blinds in the United States. However, most physicians are probably unaware that household candlewicks may still include lead as a stiffener. In 1974, the candle industry agreed with the Consumer Product Safety Commission (CPSC) to voluntarily stop making candles with lead-containing wicks. In February 2000, we conducted a systematic survey to determine the prevalence of such candles. We also estimated atmospheric lead levels produced by burning lead wick candles.

Methods. We purchased 1 of each type of candle with a metallic wick from 11 chain stores and 1 dollar store in the Baltimore-Washington area and tested these for lead by using inductively coupled plasma spectroscopy (R. J. Lee Group, Inc, Monroe-Washington, Pa). We then used these measured lead contents to estimate the average 24-hour ambient air lead levels that would result from burning these candles for 3 hours by solving the following rate equations:

\[
\begin{align*}
(1) \quad \frac{dl(t)}{dt} &= -0.2 \times l(t) \quad \text{for } 0 \leq t \leq 3 \text{ h} \\
(2) \quad \frac{dl(t)}{dt} &= -0.2 \times l(t) \quad \text{for } t > 3 \text{ h}
\end{align*}
\]

Here, \(l(t)\) is the concentration of lead in a 51-m\(^3\) room as a function of time, \(\gamma\) is the rate at which lead enters the room (micrograms of lead per centimeter of wick [determined empirically] × length of wick consumed per hour [1.33 cm/hr] [written communication, K. Bridbord, MD, December 14, 1973]) × fraction of lead vaporized [20%],2 and 0.2 is the typical fraction of air exchanged per hour in an energy-efficient home.3

Results. Eighty-six (30%) of the 285 types of candles contained metallic wicks and 9 of these (10%) contained lead, for an overall 3% lead-wick prevalence. Total lead content per wick ranged from approximately 24 000 μg to 118 000 μg (Table) (33%-85% lead by weight). When the rate equations are solved, these 9 candles are calculated to result in average 24-hour air lead concentrations ranging from 13.2 to 54.0 μg/m\(^3\), which is 10.1 to 36.0 times the US Environmental Protection Agency standard of 1.5 μg/m\(^3\).

Comment. Because each 1-μg/m\(^3\) increase in ambient air lead concentration in this range can increase a child’s blood lead level by 0.22 μmol/L (5 μg/dL),4 chronic exposure to only 1.5 μg/m\(^3\) could raise a child’s blood lead level from 0.13 μmol/L (2.7 μg/dL) (the median for US children younger than 5 years)1 to 0.48 μmol/L (10 μg/dL), which is the upper limit recommended by the Centers for Disease Control and Prevention. Thus, all 9 candles that we tested have at least 10 times enough lead to achieve this increase.

We estimated that the candle containing the least lead would produce an average air lead concentration of 30.6 μg/m\(^3\) during 3 hours of burning; a 6-year-old, inhaling 0.66 m\(^3\) of this air per hour during average daily activity5 would exceed the CPSC’s recommended daily lead limit for children (15 μg) in 45 minutes. According to the National Candle Association, $2.3 billion worth of candles were projected to be sold in 1999, a figure that is increasing by 10% to 15% annually.6 Physicians must warn patients that burning candles with lead-containing wicks may cause lead poisoning and that there is no reliable method to distinguish metallic candlewicks containing lead from those that do not. Families exposed to candles with metallic wicks should have their blood lead levels checked. Most importantly, the CPSC should ban and recall all candles containing wicks with lead; we have recently filed a petition requesting this (http://www.citizen.org/hrq/PUBLICATIONS/1510.htm).

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Table. Lead Content of Lead-Containing Candles Purchased in the Baltimore-Washington Area in February 2000*

<table>
<thead>
<tr>
<th>Candle Number</th>
<th>Lead in Wick, μg</th>
<th>Lead Emitted by Wick, μg</th>
<th>Average 24-Hour Air Lead Level, μg/m(^3)</th>
<th>Multiples of EPA Lead Standard</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>39 400</td>
<td>7 880</td>
<td>21.2</td>
<td>14.1</td>
</tr>
<tr>
<td>2</td>
<td>68 058</td>
<td>13 612</td>
<td>27.4</td>
<td>18.3</td>
</tr>
<tr>
<td>3</td>
<td>117 936</td>
<td>23 587</td>
<td>47.5</td>
<td>31.7</td>
</tr>
<tr>
<td>4</td>
<td>66 957</td>
<td>13 391</td>
<td>54.0</td>
<td>36.0</td>
</tr>
<tr>
<td>5</td>
<td>32 113</td>
<td>6 423</td>
<td>18.8</td>
<td>12.5</td>
</tr>
<tr>
<td>6</td>
<td>37 795</td>
<td>7 559</td>
<td>24.4</td>
<td>16.2</td>
</tr>
<tr>
<td>7</td>
<td>62 152</td>
<td>12 430</td>
<td>25.0</td>
<td>16.7</td>
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<tr>
<td>8</td>
<td>25 786</td>
<td>5 157</td>
<td>16.6</td>
<td>11.1</td>
</tr>
<tr>
<td>9</td>
<td>23 618</td>
<td>4 723</td>
<td>15.2</td>
<td>10.1</td>
</tr>
</tbody>
</table>

*EPA indicates Environmental Protection Agency. Mean multiple of EPA lead standard was 18.5 and median, 16.2. Adapted from Table 1 published on Public Citizen’s Website (http://www.citizen.org/hrq/PUBLICATIONS/1510.htm) with column 3 equal to column 4 and rates computed by rate equations described in “Methods” section.

Supplemental Oxygen and Mountaineer Death Rates on Everest and K2

To the Editor: The use of supplemental oxygen by Himalayan mountaineers has been debated for more than 8 decades.1,2 Although sometimes viewed as unsporting, supplemental-oxygen use may improve survival rates by increasing performance and lowering hypoxic stress.1,3 Analyses of death rates of mountaineers descending from high summits may reveal an impact of supplemental oxygen on survival because descending mountaineers are often near exhaustion and vulnerable to accident, storm, or illness during their descent.

Methods. We analyzed interview data3 of more recent data (Elizabeth Hawley, oral communication, May 4, 2000) on all mountaineers reaching the summit of the 2 highest peaks (Everest and K2) from 1978 (year both summits first reached without supplemental oxygen) through 1999. For “summit-team” analyses on Everest, we excluded recent data (1993-1999) to reduce the impact of guided expeditions, which may include inexperienced climbers. We used exact logistic regression (conditional maximum likelihood) with survival as the dependent variable and supplemental oxygen (used and not used) as a factor, stratified by mountain (Everest and K2). In a preliminary analysis, the year of summiting (covariate) was unrelated to individual death rates on Everest (either directly or via an interaction with supplemental oxygen, P>.27) and hence excluded from final analyses.

Results. Individual mountaineers not using supplemental oxygen had significantly higher death rates during descent than did those using supplemental oxygen (Table, P<.001). This pattern is especially evident on K2, where approximately 1 in 5 climbers not using supplemental oxygen died during descent (Table).

To control for nonindependence of climbers in a team, we used a “summit team” as a complementary unit of analysis and determined (for each team reaching the summit on a given day and route) whether supplemental oxygen was used and whether any descending mountaineer died. Number of summitters was a covariate because the probability of a death(s) may increase with the number of climbers exposed to risk. Even by this conservative analysis, teams not using supplemental oxygen had relatively high death incidences (P=.03).

Comment. Reaching the summit of Everest, and especially of K2, is dangerous. Overall, 1 in 29 climbers died during descent on Everest, and 1 in 7 died on K2 (Table). Reaching those summits without supplemental oxygen is associated with an even higher risk: 1 climber in 12 died on Everest, and approximately 1 in 5 died on K2 (Table). The survival impact of supplemental oxygen may be greater than suggested because mountaineers not using supplemental oxygen are probably relatively more experienced and therefore might be expected to have lower death rates. The association may be causal because supplemental oxygen decreases exposure time and reduces physical deterioration.1,3 Nevertheless, alternative explanations (eg, mountaineers using supplemental oxygen are more risk averse) cannot be excluded. Moreover, a full risk assessment of supplemental oxygen use awaits incorporation of data on death rates during ascent, risk to porters ferrying oxygen canisters, actual causes of death, and weather conditions. In any case, Himalayan mountaineering is a dangerous activity1 that balances adventure against risk. Mountaineers considering whether to use supplemental oxygen should consider the risk of death during descent.

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Funding/Support: This study was funded by a fellowship to Dr Huey from the J. S. Guggenheim Fellowship.

Acknowledgment: We thank T. Hornbein, MD, University of Washington, Seattle, and C. Houston, MD, University of Vermont, Burlington, for advice, and E. Hawley, Consul for New Zealand, Kathmandu, Nepal, for sharing data.


CORRECTION

Incorrect Wording: In the Original Contribution entitled “The Accuracy of Patient History, Wheezing, and Laryngeal Measurements in Diagnosing Obstructive Airway Disease” published in the April 12, 2000, issue of The Journal (2000;283:1853-1857), there was incorrect wording in the abstract. On page 1853, in the “Results” section, the sentence that read “maximum laryngeal height of at least 4 cm” should have read “maximum laryngeal height of 4 cm or less.”

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as courses longer than 6 days with standard doses (details are available from the authors). Patients with several courses of antibiotics were classified as having received a high-dose based on at least a single high dose course. Analysis was by conditional logistic regression analysis using version 2.0.3 for Windows (Cytel Software Corp, Seattle, Wash).

Results. Case and control groups were not different with respect to age, sex, person-years of registration (median, 4.5 years), number of hospitalizations, treatment for respiratory complaints, or presence of chronic diseases. The median age was 57 years (25th-75th percentile, 49-65 years). Nearly 80% of the complaints, or presence of chronic diseases. The median age was 57 years (25th-75th percentile, 49-65 years). Nearly 80% of the

## Table. Hospitalization for Acute Myocardial Infarction for Use of Selected Antibiotics by Dose

<table>
<thead>
<tr>
<th>Group of Antibiotics</th>
<th>Cases (n = 628)</th>
<th>Controls (n = 1615)</th>
<th>Matched Odds Ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Fluoroquinolones</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low dose</td>
<td>5 (0.8)</td>
<td>14 (0.9)</td>
<td>1.05 (0.35-3.15)</td>
</tr>
<tr>
<td>High dose</td>
<td>5 (0.8)</td>
<td>32 (2.0)</td>
<td>0.34 (0.12-0.93)</td>
</tr>
<tr>
<td><strong>Quinolones</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low dose</td>
<td>1 (0.2)</td>
<td>3 (0.2)</td>
<td>1.01 (0.09-10.8)</td>
</tr>
<tr>
<td>High dose</td>
<td>4 (0.6)</td>
<td>11 (0.7)</td>
<td>0.81 (0.24-2.73)</td>
</tr>
<tr>
<td><strong>Tetracyclines</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low dose</td>
<td>170 (27.1)</td>
<td>379 (23.5)</td>
<td>1.13 (0.90-1.42)</td>
</tr>
<tr>
<td>High dose</td>
<td>6 (1.0)</td>
<td>13 (0.8)</td>
<td>0.95 (0.35-2.62)</td>
</tr>
<tr>
<td><strong>Macrolides</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low dose</td>
<td>11 (1.8)</td>
<td>25 (1.5)</td>
<td>1.02 (0.48-2.14)</td>
</tr>
<tr>
<td>High dose</td>
<td>13 (2.1)</td>
<td>22 (1.4)</td>
<td>1.58 (0.74-3.36)</td>
</tr>
<tr>
<td><strong>Other</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low dose</td>
<td>131 (20.9)</td>
<td>290 (18.0)</td>
<td>1.22 (0.95-1.57)</td>
</tr>
<tr>
<td>High dose</td>
<td>100 (15.9)</td>
<td>247 (15.3)</td>
<td>1.04 (0.78-1.38)</td>
</tr>
</tbody>
</table>

**Use** is defined as receiving a course of antibiotics for more than 5 days; **high dose** as a course longer than 6 days with standard doses. Data are presented as number (percent) of subjects hospitalized for acute myocardial infarction. CI indicates confidence interval.

Fluoroquinolones and quinolones have been reported to have a stabilizing effect on the cytoskeleton of endothelial cells and have an effect on chondrocytes in humans. Because calcification also plays a major role in the later stages of plaque formation in atherosclerosis, it is possible that the negative association of fluoroquinolones with MI may be mediated via their nonbacterial inhibitory actions.

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CORRECTIONS

Incorrect Wording: In the Research Letter entitled “Supplemental Oxygen and Mountaineer Death Rates on Everest and K2” published in the July 12, 2000, issue of THE JOURNAL (2000;284:181), the final sentence was worded incorrectly. The sentence that read “Mountaineers considering whether to use supplemental oxygen can now consider the risk of death during descent” should have read “Mountaineers considering whether to use supplemental oxygen can now consider the associated fatality risks during descent.”

Incorrect Wording: In the Commentary entitled “Current and Future Public Health Challenges” published in the October 4, 2000, issue of THE JOURNAL (2000;284:1696-1698), there was incorrect wording. On page 1697, under “Achieve a Longer Healthspan,” the sentence that read “In 1900, about 1 in 25 Americans was elderly; in 1990, the proportion was 1 in 8, or 10 times greater than in 1900” should end after “1 in 8.” A new sentence should then read, “In absolute terms, the number of elderly Americans had increased 10-fold.”