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Exercise and Weight Loss

By **Dónal P. O'Mathúna, BS (Pharm), MA, PhD**

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THE WORLDWIDE EPIDEMIC OF OVERWEIGHT AND OBESITY CONTINUES to deteriorate.¹ The personal and societal health and economic consequences of obesity have been well documented.² Mention obesity or the need to lose weight, and the next thing to be brought up in many discussions is exercise. Either intuitively, or because of the attention this topic receives, many believe they are not getting enough exercise. If only we could get to the gym more, or at least out for a walk, all those extra pounds would melt away.

The solution seems to be fairly straight-forward: People lose weight when energy output exceeds energy intake. The trend toward obesity is matched by an increasingly sedentary lifestyle, particularly in developed countries. Since physical activity increases energy output, exercise would seem to be an important part of any solution. Hence, a whole exercise industry has arisen claiming that physical activity can burn calories, reduce body fat, control your weight, and reduce your appetite.³ The number of gym club memberships has doubled since 1993, now totaling \$19 billion per year in the United States alone.⁴

Apparently flying in the face of common sense, Yahoo! News published on-line in August 2009 an article entitled “Why Exercise Won’t Make You Thin.”⁵ Later that month, the article was the cover story for *Time* magazine and is currently the most frequently read article on the *Time* magazine web site.⁴ Patients are likely to be wondering whether the advice they may have received to exercise more is justified. Should they join gyms and don shorts or sweat pants when they get home from work? *Time* has raised serious questions, and patients need evidence-based answers.

Clinical Studies

A systematic review was published in 2009 that examined randomized controlled trials (RCTs) of exercise, dietary, and/or behavioral interventions for weight loss in healthy adults.¹ To be included, studies had to compare people engaged in physical training

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or exercise with those who exercised and received a dietary and/or behavioral intervention. Studies were also required to include a one-year follow-up evaluation or to last at least one year. Twelve RCTs met the inclusion criteria. Aerobic training was the exercise method in all studies, with walking being a part of all, but also with some participants using a step-up machine, jogging, or cycling. Combinations of individual and group training were included. Much variability occurred in the duration, frequency, and intensity of training. Similar variability occurred with the dietary recommendations. The purpose of behavioral therapy was consistently stated as changing behavior, thinking, and feelings about body weight, but the interventions themselves were poorly described.

At the end of the intervention period, most studies found that participants had lost significant amounts of weight. The largest weight loss (ranging from 8 to 12 kg, i.e., 17-27 lbs) occurred in those groups that combined aerobic training with dietary and behavioral interventions. The next largest loss of weight occurred in those groups that used exercise and dietary interventions. The least amount of weight was lost in those groups that used aerobic training alone.

Eight of the studies included follow-up periods of up to two years. The same general patterns existed in the degree of successful weight maintenance. The largest effect size was seen in those groups that combined exercise, dietary, and behavioral interventions. Although the groups that included exercise were more successful than

control groups without exercise, groups using exercise as the sole intervention were the least successful. The reviewers concluded that exercise is important in combination with other weight-loss strategies, but that “training alone cannot be expected to lead to any significant weight loss, regardless of the type of training or exercise plan.”¹ Subsequent studies have been published supporting this conclusion.^{6,7}

Looking for Solutions

Part of the problem with exercise and weight loss is that a complex relationship exists between exercise and food intake. In studies where calorie intake was held constant and exercise was added, weight loss occurred. In calorie-restriction programs, weight loss was maintained better when exercise was part of the maintenance program. In one study with a very low-calorie diet and behavior therapy, participants lost an average of 27.2 kg. Two to three years later, those who reported high levels of physical activity had maintained their weight loss better (17.5 kg down from baseline) than those who exercised moderately (9.3 kg) or not at all (5.6 kg).⁸

Another issue is that the number of calories consumed in physical activity is often overestimated by people. The accompanying Table (*see page 111*) lists the number of calories consumed per hour by various activities.⁹ After running for an hour, or hiking in a park for an hour, you decide to reward yourself at a local coffee shop. A muffin and a whole-milk cappuccino will replace 573 calories and negate the run; if you went on the hike, you will need to limit yourself to a skinny muffin and a non-fat latte, which will replace 387 calories.¹⁰

Thirty minutes of physical activity on most days of the week is often recommended. This brings many health benefits, but by itself is insufficient for most people to maintain a desirable body weight (BMI, 18.5-24.9 kg/m²). Sixty minutes of daily physical activity is necessary for most people to prevent undesirable weight gain, and 60-90 minutes per day is necessary for weight loss — in addition to reducing caloric intake.² Thus, many organizations now recommend an hour or more of daily exercise in weight-management programs.¹¹

However, while a small number of studies have shown that short-duration exercise can lead to slightly decreased food intake, as the duration of exercise lengthens, food intake can increase through appetite stimulation.¹² Many studies lasting more than 25 weeks have noted that actual weight loss is often less than that predicted based on the energy expended by the additional exercise.¹³ This phenomenon has been called “compensation” and in some cases people lose only 30% of the weight predicted.¹¹ Anecdotally, this has been explained

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Table	
Calories/hour expended in common physical activities⁹	
Moderate Physical Activity	Calories/hour for a 154 lb person*
Hiking	367
Light gardening/yard work	331
Dancing	331
Golf (walking and carrying clubs)	331
Bicycling (< 10 mph)	294
Walking (3.5 mph)	279
Weight lifting (general light workout)	220
Stretching	184
Vigorous Physical Activity	Calories/hour for a 154 lb person*
Running/jogging (5 mph)	588
Bicycling (> 10 mph)	588
Swimming (slow freestyle laps)	514
Aerobics	478
Walking (4.5 mph)	464
Heavy yard work (chopping wood)	441
Weight lifting (vigorous effort)	441
Basketball (vigorous)	441
* For a 154 lb individual; calories burned per hour will be higher for persons who weigh more than 154 lbs and lower for persons who weigh less.	

in terms of people exercising and then compensating in a number of ways that counteract the exercise. Compensation can occur as a high-calorie “reward” for exercising, feeling ravenous and consuming additional food, or being too tired for any further activity later in the day.⁴

The first controlled study to examine different durations of exercise for weight loss was published in 2009.¹¹ More than 400 sedentary, overweight, or obese postmenopausal women were randomized to one of four groups. The four groups averaged either 194, 136, 72, or 0 minutes of supervised exercise per week (beyond normal activities). The women were asked not to change their dietary habits and to complete a monthly health questionnaire. After six months, all four groups lost weight, with the differences between the groups not being statistically significant. However, the group that exercised the most had much less weight loss compared to what was predicted. In the group that averaged 136 minutes per week, the predicted and actual losses matched closely. The group that exercised the least had slightly more weight loss than predicted. The authors concluded that as the amount of exercise increases, people use compensatory mechanisms that counteract weight loss. They encouraged further research to understand the causes and types of compensation, but raised

concerns that current recommendations (to exercise more than 200 minutes per week) may be counterproductive. At the same time, they noted that about one-quarter of the women engaging in the additional exercise did lose weight as predicted, thereby highlighting the importance of individual variability in weight-loss programs.

Conclusion

The health benefits of exercise are many: It protects against the loss of lean body mass, improves cardiorespiratory fitness, reduces obesity-related health risks, and can improve a person’s psychological and emotional sense of well-being.²

However, on its own, exercise is not an effective strategy for reducing weight, and may even contribute to weight

gain. Additional exercise carries the risk of stimulating appetite and leading people to consume more calories. At the same time, exercise has an important role to play within a weight-management program that includes dietary and behavioral interventions. Regular physical activity is particularly important as part of a lifestyle that promotes maintenance of fitness and healthy body weight.

Recommendation

Losing weight is challenging and multifaceted. No one strategy will work for everyone. Exercise, reduced calorie intake, behavioral interventions, and social support are required by most people to be successful in losing weight. Modest, gradual weight loss is most effective, generally in the range of 0.5-1 lb per week.¹⁴ Since people usually become overweight or obese gradually over years, patients should be reminded that it will take time and perseverance to reach their target weight. Physical activity that is regular and incorporated into an active lifestyle will play an important role in maintaining a healthy body weight.

Walking is the most commonly recommended activity because it can be incorporated into most people’s lifestyles relatively easily. The activity can also be carried

out in smaller portions throughout the day. For some obese people, however, even walking can be a strenuous activity and cause discomfort or even pain.¹⁴ Individual considerations must be taken into account in recommending exercise prescriptions. A detailed list of activities at different intensities can be found on the CDC's web site.¹⁵ Even if exercise is not the panacea for weight loss, its health and psychological benefits make it vitally important. ❖

References

- Södlerlund A, et al. Physical activity, diet and behaviour modification in the treatment of overweight and obese adults: A systematic review. *Perspect Public Health* 2009;129:132-142.
- Okay DM, et al. Exercise and obesity. *Prim Care* 2009;36:379-393.
- Hayes C. What is physical activity and why should we do it? *Perspect Public Health* 2009;129:111-112.
- Cloud J. Why exercise won't make you thin. *Time* 17 Aug 2009:26-31. Available at: www.time.com/time/health/article/0,8599,1914857,00.html. Accessed Sept. 7, 2009.
- Cloud J. Why exercise won't make you thin. Yahoo! News 6 Aug 2009. Available at: http://news.yahoo.com/s/time/20090806/hl_time/08599191485700. Accessed Aug. 10, 2009.
- Kerksick C, et al. Effects of a popular exercise and weight loss program on weight loss, body composition, energy expenditure and health in obese women. *Nutr Metab (Lond)* 2009;6:23.
- Caudwell P, et al. Exercise alone is not enough: Weight loss also needs a healthy (Mediterranean) diet? *Public Health Nutr* 2009;12:1663-1666.
- Hartman WM, et al. Long-term maintenance of weight loss following supplemented fasting. *Int J Eat Disord* 1993;14:87-93.
- Office of Disease Prevention and Health Promotion, U.S. Department of Health and Human Services. Nutrition and Your Health: Dietary Guidelines for Americans, 2005. Available at: www.health.gov/DIETARYGUIDELINES/dga2005/report/HTML/table_e6.htm. Accessed Sept. 7, 2009.
- Calculated at: www.calorieking.com on Sept. 8, 2009.
- Church TS, et al. Changes in weight, waist circumference and compensatory responses with different doses of exercise among sedentary, overweight postmenopausal women. *PLoS One* 2009;4:e4515.
- Doucet E, et al. Appetite after weight loss by energy restriction and a low-fat diet-exercise follow-up. *Int J Obes Relat Metab Disord* 2000;24:906-914.
- Ross R, Janssen I. Physical activity, total and regional obesity: Dose-response considerations. *Med Sci Sports Exerc* 2001;33:S521-S527.
- Poirier P, Despres JP. Exercise in weight management of obesity. *Cardiol Clin* 2001;19:459-470.
- Centers for Disease Control and Prevention. General Physical Activities Defined by Level of Intensity. Available at: www.cdc.gov/nccdphp/dnpa/physical/pdf/PA_Intensity_table_2_1.pdf. Accessed Sept. 8, 2009.

The Weight of the Evidence: Hypertension in Women

ABSTRACT & COMMENTARY

By Susan T. Marcolina, MD, FACP

Dr. Marcolina is a physician at the HealthPoint Community Health Clinic in Kent, WA; she reports no financial relationship to this field of study.

Synopsis: Lifestyle and dietary modifications are important tools for both prevention and adjunctive treatment of hypertension, an important risk factor for cardiovascular disease, the leading cause of death for women. The strongest risk factor for developing new-onset hypertension in this prospective 14-year cohort study was a BMI > 25 kg/m², a designation encompassing both overweight and obese individuals. After controlling for multiple variables in a population of healthy, young female professionals, overweight women (BMI, 25-29.9 kg/m²) had an almost three-fold risk of developing hypertension, whereas obese women (BMI ≥ 30 kg/m²) had almost a five-fold increased risk. This adds to the compelling evidence that weight loss is a prudent strategy for young overweight women to decrease their risk of incident hypertension.

Source: Forman JP, et al. Diet and lifestyle risk factors associated with incident hypertension in women. *JAMA* 2009;302:401-411.

THE JOINT NATIONAL COMMITTEE ON HYPERTENSION, 7th report (JNC-7), established a threshold of systolic blood pressure of 120-139 mm Hg or diastolic blood pressure of 80-89 mm Hg as prehypertension and advised health-promoting lifestyle modifications for all patients to prevent cardiovascular disease.¹ Forman et al, in this longitudinal cohort study of more than 83,000 healthy, young professional women from the second Nurses' Health Study, convincingly quantified the rela-

Table	
Low-risk factors for hypertension ²	
Factors	Explanation
BMI < 25 kg/m ²	30 minutes duration
Daily vigorous exercise	Diet rich in fruit, vegetables, low-/non-fat dairy and no more than 2.3 g of sodium (100 mmol) daily
DASH diet adherence	Up to 10 g/d or 1 alcoholic beverage daily
Modest alcohol intake	Tylenol, nonsteroidal anti-inflammatory drugs
Use of non-narcotic analgesia more than once weekly	At least 400 µg/d
Supplemental folic acid	

tive importance of six low-risk lifestyle and dietary factors (see Table, above) to incident hypertension using the population attributable risk (PAR) statistic,² which estimates the percentage of all cases of disease attributable to specific risk factors for a given population. These researchers dichotomized each lifestyle factor into risk vs. no risk for this analysis and adjusted for age, race, family hypertension history, use of oral contraceptives, and smoking status. Over the 14 years of this study, the strongest risk factor for hypertension was an increased BMI. In fact, the authors calculated the PAR for new-onset hypertension to be 40% for subjects with a BMI ≥ 25 kg/m². They found that the other five modifiable risk factors were also associated with long-term development of hypertension, but to a lesser degree than increased BMI. Specifically, non-narcotic analgesic use greater than once weekly, not following a DASH-style diet, not exercising vigorously daily, consumption of more than 10 g/d of alcohol, and folate supplementation less than 400 µg daily were associated with PARs of 17%, 14%, 14%, 10%, and 4%, respectively. Upon further analysis, they found that women with specific combinations of 3, 4, 5, and 6 low-risk factors progressively lowered their risk for developing hypertension. For women with a normal BMI, daily vigorous physical activity, and a DASH-style diet, 53% of new-onset hypertension might be prevented; if they had all six low-risk factors, 78% of new cases of hypertension might be prevented. Notably, only 0.3% of this young, professional study population had all six low-risk factors.

■ COMMENTARY

The prevalence of hypertension in women is 30%; in certain subgroups, such as African-American women, the prevalence is up to 44%.³ Although the 2nd Nurses' Health Study population was primarily white, other studies involving more ethnically diverse cohorts, such as the Coronary Artery Risk Development in Young Adults (CARDIA) study, also showed that the lifestyle

and dietary practices mentioned above were important risk contributors to the development of hypertension and coronary artery disease.⁴

The National High Blood Pressure Education Program, established in 1972, has been instrumental in increasing public and professional awareness of the importance of blood pressure control through resources available on the web and in printed form in multiple languages.⁵ The following National Heart Lung and Blood Institute web site also has specific resources targeted for women: www.nhlbi.nih.gov/hbp/issues/issues.htm.

Hypertension is a known risk factor for cardiovascular disease as well as stroke, congestive heart failure, and renal disease, and the prevalence increases with age.⁶ Given that 66% of non-institutionalized U.S. adults older than age 20 and 17% of children ages 6-19 years are overweight or obese and at risk for the development of hypertension,^{7,8} interventions to assist patients with weight loss have enormous potential to improve quality of life on an individual level and to reduce disease burden and medical costs in the aggregate.

Primary care physicians play a central role in the early identification of patients at risk for hypertension due to an elevated BMI. It is important, therefore, to evaluate patients for cardiometabolic risk by calculation of BMI with height and weight measurements, as well as a measurement of the waist circumference, the clinical determinant of abdominal adiposity.

Waist circumference should be measured on the skin with a tape in the horizontal plane at the level of the iliac crest. The measurement should be made at the end of a normal expiration and the tape should be tight without compressing the skin. Women with a waist circumference greater than 35 inches (31.5 inches for women of Chinese, Japanese, South Asian, or South or Central American descent) should be considered as one risk category above that defined by their BMI and are at higher risk of diabetes, dyslipidemia, hypertension, and cardiovascular disease.⁹

As physicians evaluate overweight and obese women, there are elements from the history that can help in the management such as:

1. Family history
2. Age of onset of weight gain
3. Minimum/maximum adult weight
4. Events associated with weight gain
5. Most recent weight-loss attempts
6. Previous weight-loss modalities used and complications thereof.

It is important to note that cigarette smoking complicates treatment because smoking cessation is often accompanied by weight gain.

A complete review of systems can uncover comorbidities such as obstructive sleep apnea, endocrine disorders such as polycystic ovarian syndrome, Cushing's disease, diabetes, depression, eating disorders, chronic pain syndromes, or substance abuse, which may require additional evaluation with diagnostic testing and referral to different specialists for treatment.⁹ Many types of medications can cause weight gain or prevent weight loss such as antipsychotics, anticonvulsives, antidepressants, oral contraceptives, antihypertensives (particularly alpha and beta blockers),¹⁰ corticosteroids, antihistamines, or diabetes treatments such as insulin, thiazolidinediones, or sulfonylureas.^{10,11} Often there is an alternative medication that can be used that is weight-neutral. The overweight/obese patient can be more successful with weight loss if comanaged by the primary physician with a team of professionals that includes a dietitian, psychologist/support group, and a fitness trainer, depending upon the patient's needs.

The National Weight Control Registry has identified four specific behaviors key to successful long-term weight management¹²:

1. **Self-monitoring:** Record/monitor daily food diaries and limit certain foods or food portions, monitor weight > once weekly.
2. **Low-calorie, low-fat diet:** Total energy intake: 1,300-1,400 kcal/d with 20%-25% fat.
3. **Daily breakfast intake.**
4. **Regular physical activity:** 2,500-3,000 kcal/week.

A useful National Institutes of Health (NIH) Publication (No. 08-4992) from the Weight-control Information Network (WIN) entitled "Healthy Eating & Physical Activity Across Your Lifespan" provides information to patients about menu planning, portion control, exercise ideas, and implementation tools, as well as additional resources. It can be downloaded from the NIH web site at www.win.niddk.nih.gov.

Clinical guidelines from the American Heart Association and the National High Blood Pressure Education

Program recommend limiting alcohol intake to two drinks (10-20 g alcohol) or less daily in men and only one drink or less (10 g) in women for the primary prevention of hypertension.¹³ Among the studies that form a basis for these recommendations is a meta-analysis by Xin et al of randomized clinical trials that included patients who initially consumed 3-6 daily alcoholic beverages. They found that with an average of 67% reduction in alcohol consumption, the net change in systolic blood pressure was -3.3 mm Hg and -2.0 mm Hg in diastolic blood pressure.¹⁴

Sesso et al, in a cohort of patients from the Women's Health Study and the Physicians' Health Study, found that the risk for developing hypertension for both sexes substantially increased if patients consumed more than two alcoholic beverages daily.¹⁵ Interestingly, among hypertensive patients with greater daily consumption of alcoholic beverages (more than two daily), blood pressure reductions occurred relatively rapidly (i.e., within weeks) after reductions in alcohol intake.¹⁴ The blood pressure-lowering effects of alcohol reduction are similar to the blood pressure-lowering effects of dietary sodium reduction.^{16,17}

Cook et al, in an overview of data from observational studies and randomized trials, suggested that the 2 mm Hg diastolic blood pressure reduction seen in studies of dietary sodium restriction and alcohol intake could be expected to result in a 17% decrease in the incidence of hypertension, a 6% decrease in coronary artery disease and a 15% reduction in the risk of strokes and transient ischemic attacks.¹⁸

This longitudinal cohort study demonstrated the importance of encouraging patients to adopt as many of the six low-risk lifestyle and dietary habits as possible, the most important of which is maintenance of a normal weight. Within the realm of realistic possibility in daily practice, it is important not to let perfect be the enemy of good. If patients are adopting some of the low-risk lifestyle measures, even if not optimally, they should be applauded and encouraged in their efforts to improve their overall health and decrease their risk for developing hypertension. Continuous reinforcement and monitoring of individual patient progress in adoption of low-risk lifestyle and dietary factors can help to reduce the risk of hypertension for women during their lifetime. ❖

References

1. Chobanian AV, et al; Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure. National Heart, Lung, and Blood Institute; National High Blood Pressure Education Program Coordinating Committee. Seventh report of

- the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure. *Hypertension* 2003;42:1206-1252.
2. Forman JP, et al. Diet and lifestyle risk factors associated with incident hypertension in women. *JAMA* 2009;302:401-411.
 3. National Center for Health Statistics. Health, United States, 2008, with Special Feature on the Health of Young Adults. Hyattsville, MD: 2009. Available at: [www.cdc.gov/nchs/data/08.pdf](http://www.cdc.gov/nchs/data/hus/08.pdf).
 4. Liu K, et al. Blood pressure in young blacks and whites: Relevance of obesity and lifestyle factors in determining differences. The CARDIA study. Coronary Artery Risk Development in Young Adults. *Circulation* 1996;93:60-66.
 5. U.S. Department of Health and Human Services. National Heart Lung and Blood Institute: National Institutes of Health. National High Blood Pressure Education Program. Available at: www.nhlbi.nih.gov/about/nhbpep/index.htm. Accessed Aug. 3, 2009.
 6. Fields LE, et al. The burden of adult hypertension in the United States, 1999 to 2000: A rising tide. *Hypertension* 2004;44:398-404.
 7. Centers for Disease Control and Prevention. Overweight and Obesity. Data and Statistics. Available at: www.cdc.gov/obesity/data/index.html. Accessed Aug. 2, 2009.
 8. Centers for Disease Control and Prevention Fast Stats on the Prevalence of Obesity: Table 76: Overweight among children and adolescents 6-19 years of age, by selected characteristics: United States 1963-1965 through 2003-2006. Available at: www.cdc.gov/nchs/data/08.pdf. Accessed Aug. 2, 2009.
 9. The Practical Guide: Identification, Evaluation and Treatment of Overweight and Obesity in Adults. October 2000. NIH Publication Number 00-4084.
 10. Cheskin LJ, et al. Prescription medications: A modifiable contributor to obesity. *South Med J* 1999;92: 898-904.
 11. Lebovitz HE. Differentiating members of the thiazolidinedione class: A focus on safety. *Diabetes Metab Res Rev* 2002;18(Suppl 2):S23-S29.
 12. Klem ML, Wing RR. A descriptive study of individuals successful at long-term maintenance of substantial weight loss. *Am J Clin Nutr* 1997;66:239-246.
 13. Whelton PK, et al. Primary prevention of hypertension: Clinical and public health advisory from the National High Blood Pressure Education Program. *JAMA* 2002;288:1882-1888.
 14. Xin X, et al. Effects of alcohol reduction on blood pressure: A meta-analysis of randomized controlled trials. *Hypertension* 2001;38:1112-1117.
 15. Sesso HD, et al. Alcohol consumption and the risk of hypertension in women and men. *Hypertension* 2008; 51:1080-1087.
 16. He J, et al. Role of sodium reduction in the treatment and prevention of hypertension. *Curr Opin Cardiol* 1997;12:202-207.
 17. Puddey IB, et al. Alcohol is bad for blood pressure. *Clin Exp Pharmacol Physiol* 2006;33:847-52
 18. Cook NR, et al. Implications of small reductions in diastolic blood pressure for primary prevention. *Arch Intern Med* 1995;155:701-709.

Patients With the Common Cold: Empathy Helps Heal Faster

ABSTRACT & COMMENTARY

By Joseph E. Scherger, MD, MPH

Dr. Scherger is Clinical Professor, University of California, San Diego; he reports no financial relationship to this field of study.

This article originally appeared in the Aug. 29, 2009, issue of Internal Medicine Alert. It was reviewed at that time by Gerald Roberts, MD, Assistant Clinical Professor of Medicine, Albert Einstein College of Medicine, New York, NY; he reports no financial relationship to this field of study.

Synopsis: *A randomized controlled trial demonstrated that “perfect” empathy with patients results in a better immune response, reduction of symptoms, and faster recovery from a common cold.*

Source: Rakel DP, et al. Practitioner empathy and the duration of the common cold. *Fam Med* 2009;41:494-501.

EMPATHY IS A CORNERSTONE OF MEDICAL PRACTICE, but something that is considered more a part of the art of medicine than its science. A group of investigators at the University of Wisconsin performed a randomized controlled trial in two primary care clinics of added empathy to encounters for patients with the common cold. Three hundred and fifty patients age 12 and older were randomized to a standard and an empathy-enhanced physician visit. The treatment group physicians were trained in delivering empathy as defined by Mercer and Reynolds, “the ability to understand a patient’s situation, perspective, and feelings (and their

attached meanings); to communicate that understanding and check its accuracy; and to act on that understanding with the patient in a helpful and therapeutic way.”¹

The patients rated the degree of empathy using the Consultation and Relational Empathy (CARE) measure. CARE assesses 10 areas of empathy on a scale of 1 to 5: 1) made patients feel at ease, 2) allowed them to “tell their story,” 3) really listened, 4) were interested in them as a whole person, 5) fully understood their concerns, 6) showed care and compassion, 7) were positive, 8) explained things clearly, 9) helped them take control, and 10) helped create a plan of action. Eighty-four patients rated their encounter as a perfect 50 and this group was compared with the rest.

The duration and severity of the cold was measured in two ways. The patients self-reported their symptoms at baseline and twice daily for 14 days using the Wisconsin Upper Respiratory Symptom Survey.² The patients’ colds were considered ended if they gave two consecutive “No” responses to the question, “Do you think you still have a cold?” The patients’ immune responses were measured using interleukin 8 (IL-8) from a nasal wash done at enrollment and at a follow-up visit approximately 48 hours later. IL-8 is an inflammatory cytokine found in nasal secretions that rises rapidly with upper respiratory infections and then falls over days to weeks. This correlated with the determination that the patients had a cold by having one of the following four symptoms: nasal discharge (runny nose), nasal congestion, sneezing, and sore throat.

The 84 patients reporting “perfect” empathy had similar demographics to the rest of the group (n = 266). The severity of their cold symptoms fell faster than the others starting on day 2 and remained lower until resolution of the cold. The perfect empathy group had a mean duration of 7.10 days compared with 8.01 for the others ($P = 0.017$). The perfect empathy group showed a rise in the IL-8 immune marker more than double the control group, suggesting a much greater immune response to the cold related to empathy ($P = 0.015$).

■ COMMENTARY

The lead author and investigator of this study is David Rakel, MD, son of Robert Rakel, MD, legendary author and editor of numerous textbooks in medicine. I know David well and he is a true scholar and serious investigator. After completing his family medicine residency, he attended the integrative medicine fellowship program at the University of Arizona. David Rakel single authored a textbook, *Integrative Medicine*, published by Saunders.³ David’s research team at the University of Wisconsin is conducting high-quality, evidence-based investigations

of integrative medicine.

Psychoneuroimmunology is the study of psychological processes (like empathy) and their impact on both the nervous and immunologic systems.⁴ Evidence of these connections is vast and this is an emerging area of science. It is the biology of the mind-body connection. The bottom line from this study is that empathy heals, at least for the common cold. We all know that the physician is a therapeutic agent, at least as powerful as any medication. In the busy practice of primary care, taking the time to show empathy, the time to heal, is a real challenge.⁵ Maybe with the new patient-centered medical home models there will be more time for better communication with our patients. Much of the care coordination work in patient care may be done outside of visits, giving us more time to communicate with patients and show empathy.

Empathy is not just the soft side of medical practice. As this randomized controlled trial shows, empathy with patients makes them respond to sickness better and heal faster. The only cost is our time, attention, skill, and caring. That would be real health care reform for America! ❖

References

1. Mercer SW, Reynolds WJ. Empathy and quality of care. *Br J Gen Pract* 2002;52(Suppl):S9-S12.
2. Barrett B, et al. The Wisconsin Upper Respiratory Symptom Survey is responsive, reliable, and valid. *J Clin Epidemiol* 2005;58:609-617.
3. Rakel DP. *Integrative Medicine*. Philadelphia, PA: Saunders; 2003.
4. Ader R, ed. *Psychoneuroimmunology*. 4th ed. New York, NY: Academic Press; 2007.
5. Ludmerer KM. *Time to Heal*. New York, NY: Oxford University Press; 1999.

Throw in the Zinc? Minerals and Acute Childhood Diarrhea

ABSTRACT & COMMENTARY

By Bridget S. Bongaard, MD, FACP

Dr. Bongaard is the Director of the Integrative Medicine Service Line at CMC-NorthEast Medical Center; she reports no financial relationship to this field of study.

Synopsis: *This novel, large randomized controlled trial of 808 Indian children with acute dysentery, ranging in*

age from 6 to 59 months, assigned each subject to one of three arms of treatment for 14 days using a base of standard oral hydration formula for each group: placebo having no additives, zinc 20 mg/5 mL supplementation, or zinc 20 mg/5 mL plus copper 2 mg/5 mL supplementation. The authors concluded that despite prior data showing favorable response to zinc additive therapy, there was no difference in the severity, duration, or relapse of the illness between their study cohorts.

Source: Patel A, et al. Zinc and copper supplementation in acute diarrhea in children: A double-blind randomized controlled trial. *BMC Med* 2009;7:12.

MORBIDITY AND MORTALITY FROM ACUTE INFANTILE dysentery in underdeveloped countries is staggering, and represents a significant public health issue. There are 4.6 million pediatric deaths due to dysentery (25%-30% of all deaths of children younger than age 5) in underdeveloped countries, and though there are a number of potential infectious etiologies, rotavirus leads the pack (possibilities typically include rotavirus, adenovirus, astrovirus, and Norwalk-like virus).¹

Diarrhea has a significant impact on intestinal absorption, nutrition, and childhood development, as well as global mortality.² There has been a remarkable reduction in death from this malady, from 4.6 million annual deaths 20 years ago to approximately 1.6-2.1 million current deaths, largely due to the development and institution of protocols utilizing glucose-electrolyte oral rehydration solutions.² Severe, unrelenting diarrhea precipitates significant zinc and copper losses in the body. Zinc is a critically important mineral that regulates the transport of water and electrolytes across the intestinal mucosal, preventing villous atrophy and improving overall immunity.³ Copper is speculated to be helpful; however, it has yet to be proven clinically to be synergistic with the administration of zinc. The zinc:copper ratio is also important to maintain, as excessive amounts of copper can interfere with zinc absorption and lead to zinc deficiency, and large oral doses of zinc can interfere with copper bioavailability. It is not known, however, whether severe diarrhea can lead to total body deficiency of both mineral stores. Children with malnutrition or recurrent diarrhea may already be at high risk due to total body deficiencies of both minerals, further complicating the issue.

The authors of this community-based, controlled study note that a recently published Cochrane review reported a reduction in acute diarrhea within 12 hours with the addition of supplemental zinc to standard World Health Organization (WHO) oral dehydration therapy in

affected children.⁴ The studies, however, were heterogeneous for method and amount of zinc, and did not control for additional supplements in the form of multivitamins or vitamin A, making it difficult to determine the effectiveness of zinc therapy alone. The study by Patel et al uniquely utilized strict protocols for supplementation with copper and zinc in the same ratio as is customarily seen in the diet to limit adverse effects.

Children were excluded if there was known HIV infection, kwashiorkor, or another chronic or severe complicating illness. Also excluded were those who required IV hydration (though if successfully rehydrated and able to take oral replacement afterward, they were included in the study). Participants were required to have acute dysentery > 72 hours and be able to take oral fluids or feedings. Patients were discontinued from the study if they developed complications such as electrolyte imbalance, azotemia, convulsions, acidosis, congestive heart failure, hemolytic uremic syndrome, septicemia, loss of consciousness or death, or if the patient left against medical advice.

An independent laboratory checked the replacement syrup solution contents for accuracy and ensured the zinc sulfate solution contained 20 mg/5 mL of elemental zinc, while the zinc with copper sulfate solution contained an additional 2 mg/5 mL of elemental copper. Any child who vomited the chosen experimental preparation was given a second dose to achieve a total of 0.5 mL/kg/d of the syrup. The doses were administered on a daily basis, and continued until the 14th day of follow-up even if the patient had been discharged from the hospital. Bottles were weighed periodically to measure treatment compliance. All patients were monitored for dehydration, and fluid balance was achieved by administering a solution of WHO standard guideline of 100 mg/kg oral rehydration solution to match oral or fecal losses on a volume-to-volume basis until diarrhea ceased. Mothers were encouraged to nurse or feed their children when tolerated. Stools were measured by volume but were not cultured for infectious agents. Venous blood samples for baseline serum zinc and copper were performed on admission and a second sample was obtained at day 14 of follow-up for comparison.

There was not a statistically significant difference between the groups' intake of the oral syrup while completing 14 days of oral therapy, whether the full treatment was rendered at home, in the hospital, or both. There was an average daily zinc intake of 14.3 mg of zinc in the zinc group, and 13.5 mg of zinc and 1.3 mg of copper in the zinc and copper group. Neither mean duration of diarrhea nor mean stool weight differed between the trial groups. Also, there was no significant

cohort difference between the amounts of oral rehydration solution or IV fluids, the mean duration of diarrhea, or the proportion of patients with diarrhea for > 5 days or > 14 days. As a final note, between the three groups, there was an insignificant difference in time to cessation of diarrhea and reduction in duration of diarrhea, and neither baseline serum zinc nor serum copper levels had an effect on the duration or volume of diarrhea.

■ COMMENTARY

The mean absolute difference in serum zinc from baseline to the 14th day increased significantly in the zinc-supplemented groups, indicating adherence and bioavailability of the supplements due to the study's meticulous methods ensuring that all children received similar doses, frequency, and duration of syrups (of identical appearance) for the entire 14 days. The lack of improvement despite the addition of zinc sulfate or copper sulfate to the standard oral rehydration solution protocols could be due to many reasons. The doses of zinc used in this study were lower than other studies that showed effectiveness, with the dose differing between the average intakes of 13.9 mg in this study compared to 20 mg fixed-dose administration in other studies. This difference may not be valid, however, as the other studies did not report the actual mean consumption.

This study scrupulously determined the variances in each treatment cohort, as well as calculated the baseline serum zinc compared to end of study levels, and showed a corresponding increase in the cohorts treated with zinc. Total body zinc deficiency (serum zinc level ≤ 60 $\mu\text{g/dL}$) could affect the outcomes despite supplementation; however, there are other studies to support that despite initial low levels of zinc, there is no difference in morbidity and mortality between placebo and supplemented groups. It certainly may be important to note that serum zinc levels do not necessarily reflect the measure of body zinc status; however, they do play a role in intestinal inflammation.⁵ Measurement of dietary zinc or copper intake and tissue zinc or copper status perhaps may better explain the impact of zinc supplementation on tissue function. Also, not all studies that reported a positive effect were in children with zinc deficiency. Therefore, it seems there are other critical factors involved. A potential confounding variable considered was that breastfeeding or increased zinc store acquired in utero may create a selective advantage in the younger children, although in this current study, 41% of children were between age 6 and 12 months and 56% had received breastfeeding yet achieved no improvement with supplementation of zinc or copper during their illness.

Could the difference be due to the infectious etiology of the dysentery? This is an interesting point as zinc has a positive effect on enteropathogenic *Escherichia coli*, but a much less significant effect on rotavirus and *E. coli* heat-stable enterotoxin. As stated in the introduction, rotavirus is an extremely common cause of dysentery in this population and may have accounted for the lack of response to the zinc or copper/zinc treatment arms. Unfortunately, the diarrheal pathogens were not indexed in the treated population, or correlated to age or severity of illness. Furthermore, there may have been a positive difference in the meta-analysis studies due to less rigorous measurement of diarrheal volume losses as compared to this meticulous study, which could account for a perceived difference in overall outcome of treatment.

This trial is the first to evaluate the impact of oral zinc and copper administration on the duration of acute diarrhea. The results shed light on the variance in outcomes in treatment of severe childhood dysentery (a leading cause of childhood morbidity and mortality), and a re-examination of available trial results is needed to determine how to stop this debilitating process. Zinc and copper supplementation are relatively innocuous

CME Instructions

Physicians participate in this continuing medical education program by reading the articles, using the provided references for further research, and studying the CME questions. Participants should select what they believe to be the correct answers, then refer to the list of correct answers to test their knowledge. To clarify confusion surrounding any questions answered incorrectly, please consult the source material.

After completing this activity, participants must complete the evaluation form provided at the end of each semester (June and December) and return it in the reply envelope provided to receive a credit letter. When an evaluation form is received, a credit letter will be mailed to the participant.

CME Objectives

- After completing the program, physicians will be able to:
- present evidence-based clinical analyses of commonly used alternative therapies;
 - make informed, evidence-based recommendations to clinicians about whether to consider using such therapies in practice; and
 - describe and critique the objectives, methods, results and conclusions of useful, current, peer-reviewed clinical studies in alternative medicine as published in the scientific literature.

when properly dosed, and may present advantage in some cases of childhood dysentery; however, further trials are necessary before making this a universal recommendation. ❖

Reference

1. Nguyen TV, et al. Diarrhea caused by rotavirus in children less than 5 years of age in Hanoi, Vietnam. *J Clin Microbiol* 2004;42:5745-5750.
2. Petri WA, et al. Enteric infections, diarrhea, and their impact on function, and development. *J Clin Investigation* 2008;118:1277-1288.
3. Patel A, et al. Zinc and copper supplementation in acute diarrhea in children: A double-blind randomized controlled trial. *BMC Med* 2009;7:22.
4. Lazzerini M, Ronfani L. Oral zinc for treating diarrhoea in children. *Cochrane Database Syst Rev* 2008;(3):CD005436; doi: 10.1002/14651858.CD005436.pub2.
5. Al-Gindan Y, et al. Intestinal inflammation in rats induces metallothionein in colonic submucosal. *J Clin Biochem Nutr* 2009;44:131-141.

Black and Blue and Purple: Pomegranate and Coumadin

By Russell H. Greenfield, MD, Editor

Synopsis: Studies on the effects of pomegranate juice on CYP-mediated drug metabolism have yielded inconsistent results, but this recently published case report raises the specter of interaction between the juice and warfarin, a drug whose narrow therapeutic window and potential for significant complications are well known.

Source: Komperda KE. Potential interaction between pomegranate juice and warfarin. *Pharmacotherapy* 2009; 29:1002-1006.

THE AUTHOR DESCRIBES THE CASE OF A 64-YEAR-OLD woman with a history of pulmonary embolism and deep vein thrombosis referred to an anticoagulation clinic for care. She had been on a stable drug regimen, and

CME Questions

34. Most guidelines currently recommend how much exercise per day for weight loss?

- a. 30 minutes or less
- b. 45 minutes or so
- c. 60 minutes or less
- d. 60 minutes or more

35. Compensation as discussed in the exercise article refers to:

- a. The payment received by participants in research studies.
- b. The reduced amount of weight loss actually recorded compared to what was predicted.
- c. The way the body responds to being obese.
- d. The loss of weight that accompanies exercise.

36. The most effective strategies for weight loss involve a combination of:

- a. exercise with restricted calorie diets.
- b. exercise with behavioral therapy.
- c. exercise with restricted calorie diets along with behavioral therapy.
- d. restricted calorie diets along with behavioral therapy.

37. Which of the following medications can result in weight gain when taken regularly?

- a. Insulin
- b. Beta blockers
- c. Corticosteroids

- d. Antihistamines
- e. All of the above

38. Which of the following was the most powerful predictor of incident hypertension?

- a. BMI ≥ 25 kg/m²
- b. Alcohol intake of > 10 g daily
- c. Non-adherence to DASH diet
- d. Lack of daily vigorous physical exercises
- e. Use of non-narcotic analgesics more than once daily

39. A perfect empathy score with patients demonstrated which of the following with patients suffering with the common cold?

- a. A lower rise in the immune maker for response to the infection
- b. Shorter duration of the cold but no reduction in symptoms
- c. A reduction in symptom severity but no reduction in the duration of the cold
- d. Both a reduction in the severity and duration of the cold symptoms

40. Which of the following is the most common infectious etiology for childhood infectious diarrhea?

- a. *Escherichia coli*
- b. Rotavirus
- c. *Giardia lamblia*
- d. Antibiotics

Answers: 34. d, 35. b, 36. c, 37. e, 38. a, 39. d, 40. b.

her use of supplements, including fish oils and a multivitamin, had not changed in a long time. She had been taking warfarin for approximately 4 years as directed by her primary care physician, using a stable dose of 4 mg/d for the prior 9 months except for a brief period of time 4 months before presenting to the clinic, when it was noted that her International Normalized Ratio (INR; typically deemed to be therapeutic between 2.0-3.0 while on warfarin) was fluctuating. A short series of warfarin dosage changes occurred before she was returned to the 4 mg/d dose.

The patient was present at a clinic educational session where she learned of the potential impact of certain foods on warfarin, as well as concerns about the use of cranberry juice while on the medication. At her clinic visit one week earlier, the patient's INR was 2.2 and was deemed therapeutic. After the educational session, she reported to the clinic physician that she had been drinking pomegranate juice 2-3 times a week for a number of months. The staff pharmacologist identified data suggesting a potential inhibition of CYP3A4 and CYP2C9 and recommended she stop drinking the juice. One week later, having had no pomegranate juice for 10 days, her INR was subtherapeutic at 1.7 in the face of no other medication changes and no missed warfarin doses. She required an increase in the dosage of warfarin to maintain a therapeutic INR.

The author forthrightly states there are limitations to her conclusions, including lack of a re-challenge of the patient with pomegranate juice (unethical) and the fact she was on other medications, albeit at stable doses.

■ COMMENTARY

Case reports are rarely covered in the pages of *Alternative Medicine Alert*, chosen only when concern about a widespread or generally accepted intervention is raised. Such are the circumstances with this case report, though the intervention in question is largely a patient-initiated one.

As noted in Dr. Kiefer's review article, "Imported Fruits: Drink Their Juices?" (see August 2009 issue of *Alternative Medicine Alert*), pomegranate juice is perhaps the only one of the heavily marketed fruit juices (think açai and mangosteen, among others) associated with compelling supportive data for a potential health benefit from its ingestion. Widely touted potential anticancer, antioxidant, and cardiovascular health effects have created significant consumer demand for the often

pricey drink, and physicians have had little reason for concern apart from the drink's sugar content. Years ago the same could be said for grapefruit juice, until it was discovered that drinking the juice could interfere with CYP3A4-metabolized drugs. Of late, concerns have been raised about cranberry juice and cytochrome P450 inhibition (CYP), though the data are contradictory. Now comes word of a possible interaction between pomegranate juice and warfarin, a drug whose therapeutic window is notoriously narrow.

In the case report at hand, the patient suffered no untoward consequences. In fact, it appears her INR was therapeutic because of her drinking pomegranate juice. The warfarin dose employed was likely too low to attain the desired therapeutic effect. The concern grows out of the potential for a patient to unknowingly augment warfarin's effects by drinking pomegranate juice, thereby creating a supertherapeutic INR and risking hemorrhagic complications.

As is often quoted, "What is natural is not synonymous with what is safe," at least not in all circumstances. It seems important to keep in mind the potential inhibitory effects of pomegranate juice on CYP activity for patients on CYP-metabolized drugs, especially warfarin, until more is known. ❖

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