MAYO CLINIC

Understanding Immune System Health

A special report from Mayo Clinic Press

Boosting your immune system

4 ways to strengthen your body's natural defenses

By Stephen Kopecky, M.D.

In early 2020, life as most of the world knew it came to a screeching halt. That's when a previously unknown virus began spreading like wildfire, forcing businesses, office buildings, schools, stores, gyms, places of worship, restaurants, movie theaters and other public gathering places to shut their doors.

For our part, those of us who could hunker down in our homes did so as best as we were able. The hope was that by avoiding mingling with others, we would help minimize transmission of the coronavirus and the disease it causes (COVID-19) and avoid all of the possible complications.

Although our knowledge of the virus and how it spread seemed to change by the hour, one fact remained the same: Illness can and did strike all sorts of people, but the vast majority who developed a severe case of COVID-19 had preexisting health problems. Those at higher risk had conditions such as obesity, high blood pressure, diabetes, heart disease, or a history of stroke or smoking.

Small changes in everyday habits, such as eating less red meat or taking the stairs whenever you can, are ways to help prevent long-term chronic illnesses from developing. And these same healthy habits — as well as other habits, such as washing hands and wearing a mask in public — can help prevent communicable diseases such as COVID-19 by protecting overall health and boosting the immune system. And if an infection does occur, it's likely to be much less severe than if you were in poor health.

There will always be risk factors we can't change — genetics, sex, age or a global pandemic. But we can control other risk factors, such as what we put in our bodies and how much exercise and sleep we get. Prevention should be the cornerstone of medicine because it helps to prepare for the unexpected. But more often than not, health care providers end up seeing people only after a problem has developed. COVID-19 highlighted why we need to be more proactive.

A glimpse inside the immune system

We tend to take our immune systems for granted. But they work hard to keep us healthy. This complex system of cells is the body's primary defense system, constantly on the lookout for internal and external threats. To better understand how we can improve or boost the immune system, it helps to have a little background on how it works.

The immune system has two parts. There's the immune function that you're born with, called the innate immune system. The innate immune system is a general defense mechanism that protects you from the time your body is exposed to harmful germs until the time the second part of the immune response — the adaptive immune system — kicks in.

The adaptive immune system identifies and attacks specific germ invaders. It also remembers them, in case of a repeat exposure. This allows your immune system to mount a more effective response the second time around. The process of inoculation develops when you get sick with a virus, or it can be developed intentionally with a vaccine.

Recognizing and destroying potentially dangerous invaders is only half of the job. The other part is being able to turn off that response quickly once the threat has been destroyed.

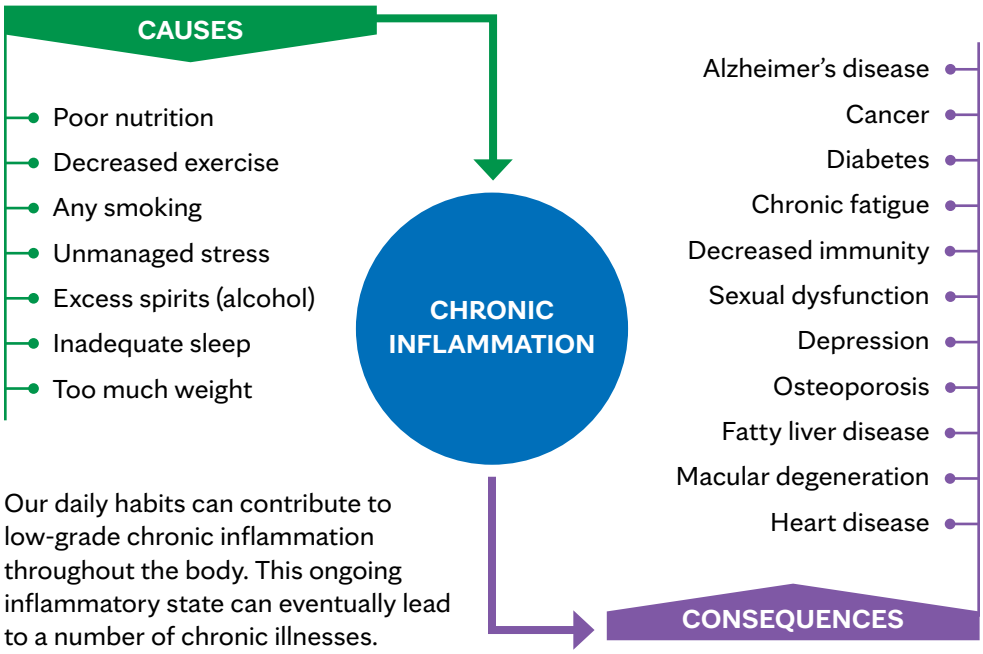
Immune responses take a lot of energy and result in inflammation — just think of the redness, swelling or pain you feel when you have a wound. It's a sign that your immune system is hard at work, and it's usually a good thing.

I say usually because, unfortunately, a lifestyle with little physical activity, unhealthy eating and excess fat create chronic low-level injuries that leave the immune system constantly switched on, similar to having a chronic low-grade infection. Just think about a car idling. Leaving it running all the time would be bad for the car. The immune system is no different. Having it continuously on alert is bad for the body.

Inflammation is part of the body's natural defense process designed to protect against things such as infections, toxins and trauma — and to repair any damage that might occur. The inflammatory response activates a cascade of immune reactions that eliminates germs and repairs injured cells.

For example, if you nick your finger, you'll notice fairly quickly that the area around the wound becomes red and inflamed. This is a sign that the immune system has been activated and is sending immune cells to clean up the area and knit the skin back together.

But scientists have also noticed that a low-grade form of inflammation can occur on a whole-body (systemic) level. This type of inflammation can occur in response to things such as a steady diet of saturated fats and little fiber, or continuously high stress levels.



Our daily habits can contribute to low-grade chronic inflammation throughout the body. This ongoing inflammatory state can eventually lead to a number of chronic illnesses.

This constant state of low-grade inflammation loses its initial purpose of inducing healing and leads instead to increased cellular and tissue damage. It becomes a source of chronic irritation to tissues in the body, and eventually it becomes a problem.

So what can we do to keep our immune systems healthy and strong?

Nutrition

The fuel you put into your body plays a critical role in how well your immune system works. But eating healthy foods and taking vitamins and other supplements after you're already sick doesn't provide the best response. Putting fluid in your car after it's already overheated and broken down will prevent further damage to the engine, but it won't repair the harm that's already been done.

The key is prevention, so you have to make sure your body has what it needs to maintain a strong immune system. A nutrition pattern that's rich in fruits and vegetables, such as the Mediterranean diet, serves up antioxidants and anti-inflammatory nutrients, such as beta carotene, vitamin C, vitamin E and polyphenols, to promote healthy immune responses. (See "Eating the Mediterranean way" page 3.) Polyphenols are plant-based micronutrients that control how the immune system responds.

What we eat also helps the beneficial bacteria in our guts communicate with the immune system and the lungs. This allows for a more effective response to foreign invaders and infection, such as with respiratory viruses.

Any disruption to this delicate balance of bacteria, whether it's from an unhealthy diet or from a medication such as an antibiotic, can make you more susceptible to infections and complications.

Also, and equally if not more important, the Mediterranean diet has proved to be one of the most anti-inflammatory diets ever studied.

EATING THE MEDITERRANEAN WAY

There aren't really single magic foods, supplements or food groups that will deliver health to us on a platter. What research has found, more often than not, is that certain patterns of eating tend to be associated with greater health.

For example, plant-based diets along with lean proteins seem to have the greatest benefit in terms of preventing common chronic diseases such as heart disease, cancer and dementia. And the Mediterranean way of eating in particular seems to lead to a low rate of diet-related disease. In addition, the Mediterranean diet improves the number of healthy bacteria in the digestive tract (gut microbiome) and reduces inflammation in the body. Studies have also shown a reduction in:

- Frailty
- Macular degeneration in people 60 years of age and older
- Childhood asthma
- Erectile dysfunction and female sexual dysfunction
- Metabolic syndrome
- Depression
- Fibromyalgia
- Arthritis pain
- Atrial fibrillation

Following the Mediterranean diet's focus on fruits, vegetables and whole grains increases the consumption of viscous soluble fiber, which scores high marks for anti-inflammatory properties. Consuming healthy sources of fat, such as olive oil, increases our intake of monounsaturated fats, which also have anti-inflammatory properties. Fiber and healthy fats have been found to lower total cholesterol and low-density lipoprotein (LDL cholesterol levels).

Fish, another staple of the Mediterranean diet, are rich in omega-3 fatty acids, a type of polyunsaturated fat thought to curb inflammation in the body and reduce triglycerides, blood clotting, and the risk of strokes and heart failure.

(For more tips on making the switch, see "Eat more this, less that — the Mediterranean way," on page 6.)

Researchers studying the Mediterranean diet and its effects on brain health found an association between eating more fish and a reduced risk of impaired memory and thinking skills (cognitive impairment) and a slower rate of cognitive decline.

Another key component of the diet is to focus on eating as a primary event, rather than an afterthought (think grabbing a burger on the way to the kids' soccer game). Making an event of the meal allows you to eat at a slower pace, which promotes better portion control. There's usually about a 10-minute lag between when your stomach gets full and when your brain realizes it. Therefore, the slower you eat, the less you overeat.

Switching to a Mediterranean-style eating pattern can also benefit our environment. One study showed that moving toward a plant-based diet would decrease agricultural land use by 58%, water consumption by 33%, energy consumption by 52% and greenhouse gas emissions by 72%. ■

When we regularly eat foods that are pro-inflammatory, such as an excess of processed foods, they promote chronic inflammation in our bodies that requires our immune systems' attention. This constant inflammation requires our bodies to address the inflammation and heal it, which in turn diverts and lessens our immune systems' ability to recognize and fight other inflammatory processes such as an invading infection.

As a result, proper nutrition has dual benefits for our immune systems, both for what it does and for what it doesn't do. First, it allows the body to function better to fight infection. Second, it doesn't cause inflammation, which would further divert our immune systems' defenses. There isn't definitive proof that supplementing with vitamins and minerals can ward off any particular virus. But eating nutritious foods as part of an overall healthy diet can help to optimize your immune system, setting you up for the best possible response.

Exercise

Exercise has been shown to give the immune system a boost by maximizing the body's ability to take in and efficiently use oxygen, among other things. Moderate exercise (where you can talk but not sing while exercising) is enough to increase the activity of virus-killing cells both in the short term and the long term. This includes white blood cells and antibodies. Guidelines recommend at least 30 minutes daily, five times a week. But even 20 minutes daily can help quell inflammation and boost immunity, and exercise can be divided up during the day. (See "The benefits of a HIIT workout," on page 5.)

The best part about exercise is that it can be done at home, which we've learned is crucial in the middle of a pandemic shutdown. Leg lunges, situps, squats and stair climbing are all easy exercises you can do at home. If you've been sedentary, start with some stretches and a walk down your street. Then increase your activity as you're able.

Stress relief

During the COVID-19 pandemic, everyone has been feeling more stress than usual. Concern about the health of our loved ones, our jobs and our children's schooling combined with the inability to physically stay in touch with each other has been difficult.

Such added stress increases the production of the hormone cortisol in the body, which in turn can suppress the immune system. Calming activities minimize stress, reduce cortisol production and enhance the immune system's function.

Practicing mindfulness and stepping away from what's causing anxiety can help us stay grounded. (See "Managing stress," on page 7). Exercises that have calming or meditative qualities, such as qi gong and yoga, also are beneficial and can easily be done at home. Video calls can help us stay connected to loved ones and reduce the stress of not being able to get together in person.

Sleep

The interaction between the immune system and sleep is a two-way street. When your immune system response kicks in, it changes your sleep. You may find yourself sleeping longer, for example, as your immune system stages an attack against a virus.

On the flip side, when you don't get enough sleep, your immune system can be altered. When you're not sleeping well, you may notice that you get sick more easily. Getting adequate sleep can help support the way your immune system functions by increasing the number of immune cells circulating in your body.

Sleep has been associated with reduced infection risks, improved infection outcomes and better vaccination responses. Getting adequate sleep before receiving a vaccination can double the immune response in humans. Animal studies have shown that increasing the length of sleep positively affects infection outcomes.

Lack of sleep appears to be a trigger of low-grade inflammation and related diseases. Studies in humans on the relationship between sleep and infection link shorter sleep duration with increased risk of pneumonia and respiratory infections. The amount of sleep the immune system needs to function properly is very individual.

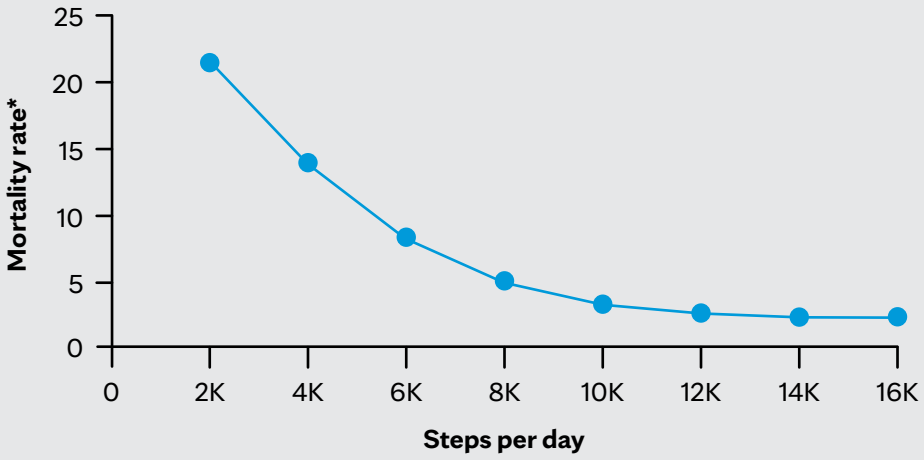
DOES COUNTING STEPS HELP?

Something I frequently ask patients to do is walk 10,000 steps every day. This has been a popular trend for a while now and it's a good one. You can even download apps on your phone or wear activity monitors that help you measure your steps. But why 10,000 steps?

Because that's right around the number that achieves the greatest reduction in premature deaths before the effects start to level off. A *JAMA* study published in 2020 showed that increasing daily steps reduced the mortality rate from any cause, but more specifically from heart disease and cancer.

The average American walks just under 5,000 steps a day. In the study, making the change from 4,000 daily steps to 8,000 steps led to the steepest decline in mortality. After about 8,000 steps for women and 12,000 steps for men, the benefits started to plateau. Older adults benefited the most since they're at the highest risk. The study also showed that walking fewer steps, but speeding up every so often, can provide about the same benefit as walking more steps at a steady rate. ■

Steps per day and mortality rate in U.S. adults over 40



*Per 1,000 adults a year
Based on *JAMA*. 2020;323:1151.

But if suboptimal sleep is leaving you tired and run-down, it's likely that your immune system is feeling the same effects. (See "Breaking the disrupted sleep cycle," page 8.)

Slow and steady

It would be really great if we all could make major lifestyle changes with a little willpower and a flip of the switch. But we might as well be honest — that expectation isn't logical or reasonable. It sets us up for disappointment and reinforces the negative mindset many of us have about our ability to change.

When we set big goals for ourselves that require sudden, drastic changes to our daily lives, those changes might last for a day or two but not much longer. We might be able to maintain an austere diet, an intense fitness plan or a dramatic sleep program for a while. But these extreme behaviors usually don't become enduring habits. In moments of stress or exhaustion, we quickly regress to our old habits because they're easier and they're what we're used to. The next morning, we wake up with a feeling of failure that discourages us from reaching our earlier goals.

You don't need to go cold turkey and implement changes at once. Keep in mind that no goal is too small. For example, one study found that replacing just half a tablespoon of margarine, mayonnaise or butter a day in your diet with the same amount of olive oil can help reduce your risk of heart disease. When you set goals that you can easily attain, your confidence will grow and you'll be able to build on your success incrementally.

Taking little steps eventually takes us further. And every little step we take toward a healthier lifestyle will help us live our lives to their fullest and longest. ■

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Stephen Kopecky, M.D., is a two-time cancer survivor and cardiologist at Mayo Clinic in Rochester, Minn. This publication contains excerpts from his book, "Live Younger Longer: 6 Steps to Prevent Heart Disease, Cancer, Alzheimer's, Diabetes and More," a comprehensive guide to understanding and improving your health. Look for it from Mayo Clinic Press.

THE BENEFITS OF A HIIT WORKOUT

High-intensity interval training (HIIT) is a way to get in the same cardiovascular shape as you would with traditional training, but with less time spent exercising. It's also a form of exercise that's very helpful for our bodies since it replicates what we've been doing on Earth for millennia.

If you were a cave dweller hundreds of thousands of years ago, what you did long ago was a primitive form of interval training: You would run like crazy to catch your food or run like crazy to avoid being caught for food. You would usually do this for very short periods. All of the activity you did was in short bursts of high-energy activity to maximize survival and minimize energy expenditure.

Research has shown that just three intervals over 10 minutes three times a week increases your muscles' capacity to extract oxygen and do more work. This improves both cardiorespiratory fitness and cardiometabolic health in overweight adults and reduces belly fat.

How it's done

High-intensity interval training is performed a bit differently from continuous exercise at a moderate intensity. Continuous exercise is when you warm up, move to a moderate intensity level, and then keep it at that level for 10, 20 or 30 minutes.

There's nothing wrong with the continuous approach. If you're doing it already, that's great and it makes it easier to switch to intervals. But if you're looking for a more time-efficient way to get fit, then interval training might be for you.

Interval training is appropriate even for people who are older, inactive or overweight. It's also been shown to be safe and effective for people with heart disease and diabetes. It's all based on your own perception of intensity. You only go as hard as you can go, improving as you're able. The three key components of intervals are: 1. Once you warm up, go hard (hard enough that you think this is difficult; I can't keep this up very long). 2. Before you give out and have to stop, slow down and get your breath fully back so you can go just as hard on the next interval (this may take four or five minutes as you start to get in shape). 3. Do not go too long because if you go too long, you can't go that hard; 30 to 120 seconds is long enough.

You can do interval training with just about any activity. Depending on what you like to do, you can simply increase your speed or other intensity variable such as the incline or the tension. For example, you might:

- Go from walking to walking briskly or jogging
- Alternate between walking and climbing stairs
- Pedal faster, stand up to pedal or increase the resistance when bicycling
- Maintain or increase your speed as you run or walk up a hill
- Alternate between dancing to music that has faster and slower tempos
- Swim several laps at your regular pace followed by a lap that is faster

Six sessions of repeated 30-second sprints over two weeks with interval training is equal to 90 to 120 minutes of moderate continuous activity a session. In other words, 11 minutes a day of interval activity can equal 45 minutes a day of continuous moderate-intensity activity in terms of the fitness that you can achieve. ■

EAT MORE THIS, LESS THAT – THE MEDITERRANEAN WAY

EAT MORE

- Fruits
- Vegetables
- Nuts
- Legumes
- Extra-virgin olive oil
- Minimally processed foods
- Fish and seafood
- Lean poultry

EAT LESS

- Butter
- Full-fat dairy
- Red meat
- Ultraprocessed foods
- Sugary beverages

WINE

- Limit to one glass a day (5 oz. for men; 3 oz. for women)

INSTEAD OF	TRY
Butter or margarine	Olive oil for cooking or for dipping whole-wheat bread in
Red meat	A meatless meal, such as one based on legumes (think peas) or beans; vegetable-based recipes Grilled or baked lean, skinless chicken breast; grilled or baked fish or shellfish (tuna, salmon, trout, mackerel and herring are good choices)
Full-fat dairy	Low-fat or fat-free dairy, such as low-fat or fat-free milk, low-fat cheeses, and low-fat or fat-free Greek or regular yogurt; milk alternatives, such as almond or oat milks
Salt	Herbs and spices first, which can eliminate or lessen your need to add salt
Peanuts	Almonds, walnuts, hazelnuts
White bread or pasta, processed cereals	Whole-grain breads, pasta and cereal Alternative grains, such as bulgur wheat and faro
Cream-based sauces	Olive oil-based sauces, tomato-based sauces
Soda, diet soda, juice	Water, carbonated or sparkling mineral water, seltzer, unsweetened tea
Prepackaged, store-bought desserts, cookies, cakes or other baked goods.	Homemade sweet treats (remember, don't deprive yourself; everything in moderation)

Since we're all different, stress is different for each of us. What causes stress in one person might not cause stress in another. And there are different kinds of stress.

Some stress is actually good stress, such as when competing in a sport with friends. Win or lose, you tried your best and had fun, coming away feeling energized. Some stress is manageable, like the stress of driving and getting slowed by a stoplight that lasts longer than we'd like. In the big picture of life, it's not important.

But some stress can be toxic. This is the kind of stress where you have little to no control, such as in the death of a loved one or a large personal financial crisis you can't change. With toxic stress, it's critical to have help and support from family or professionals.

The good news is that you can learn to tackle stress — even sudden, large amounts of stress — by engaging in small, daily habits that keep stress from becoming overwhelming or taking over. Stress may be a fact of life, but it doesn't have to rule your life. Learning healthy ways to react to and relieve stress can have profound effects on your health, longevity and well-being. Adopting even one new healthy habit and practicing it each day can help to fight the harmful effects of stress.

- **Practice positive self-talk.** Self-talk is the endless stream of positive or negative thoughts that run through your head every day. The goal of positive self-talk is to weed out misconceptions and challenge them with self-compassion and rational, positive thoughts. Start by following one simple rule: Don't say anything to yourself that you wouldn't say to a friend or loved one. Be gentle and encouraging with yourself. If a negative thought enters your mind, evaluate it rationally and respond with statements of what is good about you. Instead of saying, "I can't handle this," remind yourself, "Hey, I've handled bigger challenges before, and I can handle this too."
- **Harness the power of optimism.** Some research suggests that optimists may cope better with stressful situations, such as major life transitions, and that optimists have a lower risk of heart attack and premature death. A simple but effective habit is to practice gratitude when you first wake up in the morning or before you go to sleep at night. Instead of dwelling on your worries during these times, try thinking of three things you're grateful for — big or small.
- **Get outside.** Studies show that spending time in nature reduces stress, lowers cortisol levels, decreases blood pressure and improves well-being. For many of us, the sounds, sights and smells of green spaces — such as forests, wetlands, city parks and gardens — have a powerfully calming effect. Studies have linked being outdoors with a greater reduction in inflammation in your body.
- **Appeal to your senses.** A simple way to de-stress is to engage your senses — touch, smell, sight, taste and hearing. Hang a colorful poster or cheerful family photo in your workspace. Listen to some peaceful music or a recording of ocean waves. Pleasant smells can be another stress reliever. Essential oils that may help you relax include lavender, frankincense, jasmine, and lemon or orange.
- **Help others.** Studies on helping others show that shifting the focus from yourself to other people may not only relieve stress but improve your overall health and well-being. Consider serving at a food bank or raking an older neighbor's lawn. Even small acts of kindness, such as giving a stranger a compliment, can affect your attitude, outlook and health.
- **Take care of your body.** Sleep, diet and exercise are vital for your physical health. They can also impact how you cope with stress. Get proper sleep to rejuvenate your body and help you tackle the stressors of your day in a refreshed state. Use exercise to release brain chemicals (neurotransmitters such as dopamine, serotonin, melatonin and endocannabinoids) that can leave you feeling happier, more relaxed and less anxious. Seek out healthy meals and snacks and limit caffeine. Too much caffeinated coffee, tea or soda will increase your stress level.
- **Seek help.** If you're having difficulty coping with the stressors in your life, consider enrolling in a stress reduction class at a community or health care center or online. Your doctor or a mental health professional also can provide treatment options if stress is building or if you're not functioning well.

Try the strategies that appeal most to you. But remember to be open. A suggestion you're skeptical of could end up being surprisingly helpful. By developing and practicing these techniques now, you can reduce your stress, prevent negative impacts on your health and boost your ability to manage future challenges. ■

BREAKING THE DISRUPTED SLEEP CYCLE

If you have trouble with falling asleep or staying asleep, you can start to develop negative associations with sleep. If these associations persist, they can create a harmful cycle that leaves you chronically sleep deprived. Negative associations can develop around your nightly habits before bed, the sleep environment in your bedroom or the process of falling asleep.

Negative conditioning created by the way you prepare for bed or approach bedtime may in fact increase your brain's alertness and make it very difficult to fall asleep. Say, for example, that you always are late to bed, which increases your worry that you won't get enough sleep before the next day.

In your rush to get to sleep, you ignore bedtime rituals and jump straight in between the sheets. Once there, though, your brain is so wound up that you're nowhere near feeling drowsy. You toss and turn, but sleep remains elusive. Once again, you've failed at getting a good night's rest. The next night, your brain remembers the difficulty falling asleep, and the whole process reignites.

To undo this cycle, you need to expose your brain to the glow of success. And to do that, you need to break the conditioned responses that happen when you repeatedly try to sleep without success. How do you do this?

- **Refresh your bedtime rituals.** They don't have to take up a lot of time, but you do need a few rituals signaling bedtime, such as brushing your teeth or getting into proper pajamas. Relax your mind by reading a book, contemplating a few things you're grateful for or focusing on slowing your breathing. Do your best to go to bed at the same time every night and wake up around the same time every morning.
- **Reclaim your bedroom.** Only use your bedroom for sleep or sex. Remove prompts for activities that don't belong in the bedroom, such as watching TV, working on a computer or browsing apps on your phone. It may also help to remove pets from the bedroom. If you can't sleep, get up and go read a boring book or magazine in an upright chair. Do this until you start to feel very sleepy, and then go back to bed. The important thing is that you don't want to associate your bed with not sleeping.
- **Rinse and repeat.** You'll likely need to do this routine repeatedly until your brain starts to feel good about bedtime and sleeping. The trick is to make it easy to fall asleep but hard to do other things like worry, watch TV or anything else that will hype your brain.

Although getting more sleep may seem like the least urgent change you need to make in your life, the truth is that quality sleep creates a halo that touches all other areas of your life. When you're rested, you make better choices about what to eat and how much to eat, you have more energy for physical activity and exercise, you're more patient and attentive to those around you, you're less prone to getting sick, and you're mentally better equipped to handle stressors large and small.

Some people have more specific sleep problems, such as insomnia, obstructive sleep apnea or a snoring partner. It's important to get these sorts of sleep problems evaluated by a doctor so that they can be treated appropriately and you can get the rest you need for your health (and, in many cases, the health of your partner). ■

SLEEP CHECKLIST

- ☐ Cut back on caffeine if needed.
- ☐ Get enough daytime exercise.
- ☐ Avoid heavy meals before bed.
- ☐ Reduce screen time an hour before bed.
- ☐ Relax with a bedtime routine (for example, gratitude meditation, practicing optimism, journaling or reading).
- ☐ Cool bedroom temperature.
- ☐ Keep room dark, comfortable.
- ☐ Take slow, deep breaths.