SUPPORT SYSTEM: Left to Right: Kori Morrison, Helen Rucker, Kelli Rucker, Kris Silva.

The Brain Needs Blood

The second most common form of cognitive impairment and dementia may also be preventable.

BY AMY PATUREL, M.S., M.P.H.

Helen Rucker was 70 years old when she lost feeling on her left side. Her face and arm became numb and her speech slurred. After being admitted to the hospital, doctors told her she had experienced a stroke. A series of imaging tests revealed two aneurysms in the base of her brain. An aneurysm is an abnormal widening of an artery due to weakness in its wall. Both of Rucker's aneurysms were pressing on major memory centers of the brain.

"We discussed surgery, but because of where the aneurysms were located, she may not have survived the procedure," says her 43-year-old daughter, Kori Morrison of Irvine, CA. Instead, doctors prescribed Rucker a number of drugs: antihypertensives to lower her blood pressure, antidepressants, and cholesterol-lowering medications. They also urged her to stop smoking. (See box, "Tips to Quit.")

Over the next several years, Rucker—still a smoker—experienced a series of mini-strokes, each time landing in the hospital with further cognitive decline. A mini-stroke, also referred to as a transient ischemic attack (TIA), is caused by a short-lived blockage that affects a small patch of brain cells.

"She would tell stories that sounded logical to strangers, but when my sisters and I heard what she said, we realized she had taken pieces from several different time periods and linked them all together," says Morrison.

For a former schoolteacher who was quick-witted, highly organized, and outgoing—a woman who had performed bookkeeping and scheduling services for five McDonald's restaurants in the San Diego area in her retirement—Rucker's behavior was completely out of character.

STROKE AND VCI

Doctors diagnosed Rucker with vascular cognitive impairment (VCI), a condition that causes symptoms similar to Alzheimer's disease (AD), such as difficulty with reasoning, problem solving, planning, judgment, and memory. (Sometimes, VCI is referred to as vascular dementia. See box, "Vascular Cognitive Impairment: The Basics.") However, instead of resulting from the plaques and tangles that characterize AD, the symptoms of VCI result from reduced blood flow to the brain and ensuing cell death. The longer the blood supply is blocked, and the more brain cells destroyed,

PHOTOGRAPHS BY ANN JOHANSSON

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>
> —RACHEL WHITMER, PH.D.

the greater the cognitive damage. (See the full collection of *Neurology Now* articles on dementia at **http://bitly.com/zG4P7z**.)

"There has been so much focus on AD—as there should be, because it's a devastating, costly, and terrible illness. But we also need to step back and remember the brain is a vascular organ," says Rachel Whitmer, Ph.D., director of the Dementia Epidemiology Research Program at Kaiser Permanente in Oakland, CA, and member of the American Academy of Neurology (AAN). "There's blood flow to it, and there are blood vessels in it. The health of those blood vessels can impact cognitive function."

To understand how VCI progresses, it helps to picture the brain as a field of cells fed by a branching irrigation system. The main arteries enter the brain at the base of the skull (where Rucker's aneurysms were) and split into smaller and smaller blood vessels.

Over a lifetime, that irrigation system can start to break down. A weak patch on an artery wall can balloon outward and form an aneurysm, as in Rucker's case, or the cerebral arteries may develop blockages or blood clots. A severe blockage may affect a large region of the brain, causing a stroke. (See box, "Warning Signs of Stroke," in the story on young adult stroke, page 25.)

Tips to Quit

It's not easy to stop smoking. If you're determined to quit, you can be successful, especially if you enlist help. The following organizations offer resources and programs to help smokers stop lighting up:

- **Freedom from Smoking®, the American Lung Association's smoking cessation program: ffsonline.org; lung.org/stop-smoking/how-to-quit/freedom-from-smoking**
- **North American Quitline Consortium: 1-800-QUITNOW (1-800-784-8669); naquitline.org**
- **QuitNet, the Web's original quit smoking site, launched in 1995 in association with Boston University School of Public Health: quitnet.com**
- **WhyQuit, one of the Internet's leading cold-turkey quit sites: whyquit.com**

"Strokes and mini-strokes are risk factors for VCI," says Dr. Whitmer. In a study published in the medical journal *Brain* of 355 patients over the age of 75 who experienced a stroke, researchers found nearly 24 percent developed dementia. Of the 50 patients who died during the four-year follow up period, 36 percent had evidence of VCI at autopsy.

Experts say Rucker's experience is fairly common. Silent strokes can occur in up to 20 to 30 percent of healthy elderly people, according to Anand Viswanathan, M.D., Ph.D., associate director of Telestroke Services and Hemorrhagic Stroke Research Program at Massachusetts General Hospital, assistant professor of neurology at Harvard Medical School in Boston, MA, and member of the AAN.

"So the absence of a clinical stroke does not exclude VCI," Dr. Viswanathan says. It just means the symptoms may emerge differently. A prolonged period of TIAs may lead to a more gradual cognitive decline, while bigger strokes often produce profound, immediate effects.

DEPRESSION, SLEEP DISORDERS, AND VCI

Less well-known risk factors like depression and sleep disorders may also contribute to the development of VCI.

It's difficult to tease out whether depression is an early symptom of dementia or a risk factor for it. Dr. Whitmer and her colleagues believe that depression can be an independent risk factor for VCI. When they examined the association between depression and dementia, they discovered that people with late-life depression had a two-fold increase in AD risk, while people with midlife and late-life depression had more than a three-fold increase in risk of VCI.

Sleep disorders and VCI also seem to coexist. "Some evidence suggests an association between sleep disturbances and cognitive decline," says Dr. Viswanathan. He explains that patients with cognitive decline often exhibit marked sleep disturbances. However, as in the case of depression, it isn't clear yet whether sleep disorders are a cause of cognitive decline, or a consequence, or both.

WHICH DEMENTIA?

In 2010, about a month after Rucker was released from the hospital following another stroke, she called Morrison in the middle of the night demanding to talk to her grandson Troy. Trouble is, Troy is not Morrison's son; he is the son of Morrison's sister and lives with his father 65 miles away. Even more painful than the confusion, Rucker got mean and angry when Morrison couldn't produce Troy.

This is considered standard behavior for someone with AD, but for someone with VCI?

It's possible, experts say. "We're finding more and more in our practice that patients with VCI can have similar symptoms to those with AD," says Dr. Viswanathan. "There's a large overlap between the two conditions."

Alzheimer's disease nearly always includes some degree of memory loss. But VCI symptoms can vary widely, depending on the severity of the blood vessel damage and the part of the brain affected.

"People tend to worry a lot about losing their memory, but not as much if they can't do the banking anymore," says Vladimir Hachinski, M.D., D.Sc., professor of neurology and epidemiology at the University of Western Ontario in Canada and Fellow of the AAN. "Executive function, having the ability to plan, solve problems, and multitask, is as meaningful as the ability to remember important information."

Another distinction between AD and VCI concerns the way in which the major symptoms take hold. Typically, AD is gradual and insidious, reflecting the slow accumulation of abnormal proteins in the brain. In contrast, the symptoms of VCI may worsen noticeably from one day to the next as large numbers of brain cells die from lack of oxygenated blood. If AD is often a shallow, downward slope, then VCI is often a staircase.

But here's where it gets tricky: The only way to definitively diagnose someone with AD, VCI, or a combination of the two, is to perform an autopsy. (For more on brain autopsy and donation, see "One Precious Gift," **http://bit.ly/VCxDY1**.) The majority of patients who are diagnosed with AD also show some evidence of VCI, and vice versa.

Autopsies suggest that the brain of up to 45 percent of people with dementia have signs of both AD and VCI, according the Alzheimer's Association. Vascular factors have become increasingly recognized as either causing or contributing to cognitive impairment in the elderly.

"Someone could have AD and then subsequently develop vascular problems in the brain that exacerbate their AD," says Dr. Whitmer. "It can work the other way as well: Someone can be diagnosed with VCI and go on to develop the signature plaques and tangles of AD."

TREATMENT STRATEGIES

The U.S. Food and Drug Administration (FDA) has not approved any drugs to specifically treat changes in judgment, planning,

Vascular Cognitive Impairment: The Basics

WHAT CAUSES IT? Vascular cognitive impairment (VCI), sometimes referred to as vascular dementia, results from conditions and behaviors that damage the brain's blood vessels, depriving it of vital oxygen and nutrients. Strokes, which block an artery leading to the brain, are a common cause of VCI. Conditions and behaviors that narrow or damage brain blood vessels—such as aging, smoking, high blood pressure, hardening of the arteries, diabetes, and brain hemorrhage—are also common causes.

WHO IS AT RISK? People over the age of 65, people who smoke, and people who have a history of heart attack, stroke, mini-strokes, clogged arteries, high blood pressure, and high cholesterol are all at increased risk for VCI.

WHAT ARE THE COMMON SYMPTOMS? Symptoms often overlap with those of Alzheimer's disease (AD), but they are most clear-cut when they occur suddenly following a stroke or a series of mini-strokes. Difficulties with personal finance (which often occur early in the dementia process), reasoning, problem solving, planning, judgment, memory, and other thought processes are all common in VCI.

WHAT TREATMENTS ARE AVAILABLE? Controlling conditions that affect the underlying health of your heart and blood vessels can sometimes slow the progression of VCI. Doctors may prescribe medications to manage blood pressure, cholesterol, and blood sugar levels. They may also prescribe medications normally prescribed to people with AD to minimize symptoms like memory deficits and difficulty planning.

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>
> —ANAND VISWANATHAN, M.D., PH.D.

memory, and other thought processes caused by VCI. However, medications typically used to treat AD may also improve the symptoms of VCI. Cholinesterase inhibitors, for example, (brand names Aricept, Exelon, Razadyne, and Cognex) boost levels of a chemical messenger called acetylcholine, which is involved in memory and judgment. Memantine (Namenda) regulates another chemical messenger called glutamate, which is important for information processing, storage, and retrieval.

"Unfortunately, no treatment currently exists that can repair vascular damage in the brain. What we have are symptomatic therapies that don't necessarily alter the course of the disease itself," says Dr. Viswanathan. "But controlling risk factors—high blood pressure, high cholesterol, diabetes, and especially smoking—can actually prevent the development of strokes, which can tremendously alter the disease course." (See box, "Use Your Head: Protect Your Heart.")

A study published in the AAN's medical journal *Neurology* found that high blood pressure, high cholesterol, smoking, and diabetes at midlife were each associated with a 20 to 40 percent increased risk of dementia. Individuals with all four of those risk factors at midlife had more than a two-fold greater risk of dementia than those with no risk factors.

Rucker, who died in October 2011, was active and fit. However, she also had high blood pressure and a genetic predisposition to develop thinness in the arterial walls. Perhaps most importantly, she was a lifetime smoker.

But her outcome isn't inevitable for people who are diagnosed with VCI.

"The most important thing is to minimize the likelihood of additional strokes that could lead to worsening dementia," explains Dr. Viswanathan. That includes taking the appropriate medications and addressing cardiovascular risk factors—especially quitting smoking. These steps, according to some studies, may both reduce symptoms and slow the progression of VCI.

Use Your Head: Protect Your Heart

What's good for your heart is good for your head. Taking the following steps to keep your heart healthy may also help reduce your risk of VCI:

- **Don't smoke**
- **Keep your blood pressure and cholesterol levels in check**
- **Eat a low-fat, healthy diet**
- **Get plenty of exercise**
- **Maintain a healthy weight**
- **Limit alcohol consumption**
- **Get blood sugar levels (and diabetes, if you have it) under control**

DOING AWAY WITH LABELS

Identifying dementia may seem simple. After all, those affected often become confused and forgetful. But, it turns out clinically diagnosing dementia is more difficult than one might expect.

Part of the problem with diagnosing dementia is that the widely accepted definition includes memory impairment. That may work well for identifying patients with AD, says Dr. Hachinski, but it often misses the problems with executive function typical of people with VCI. (Executive function allows for abstract thought, the planning and taking of actions toward a goal, and adaptation to the unexpected.) This is where a neuropsychologist can be extremely valuable: By evaluating a patient's thinking and behavior, a neuropsychologist can help determine the type and degree of impairment early on.

Dr. Hachinski's Ischemic Scale is perhaps the most frequently used method to identify a vascular component both AD and VCI. It is based on the presence or absence of risk factors such as history of stroke, abrupt onset of cognitive symptoms, and history of hypertension. But even that falls short, he argues.

"We have to do better by developing a minimum standard description of impairment, so that every doctor or researcher who looks at cognitive impairment—whether in AD, VCI, Parkinson's disease, and so on—uses the same descriptive terms. Then, if we follow those patients to an outcome like dementia or death, we can develop evidence-based criteria for diagnosing these conditions." (As Dr. Hachinski points out, such minimal standards have been proposed: The National Institute of Neurological Disorders and Stroke-Canadian Stroke Network Vascular Cognitive Impairment Harmonization Standards were published in the medical journal *Stroke* in 2006.)

In the meantime, experts agree the focus should be on identifying VCI early in the disease process before symptoms set in.

Morrison is convinced her mom knew something was off long before doctors found the aneurysms. "But my mom wasn't one to see a doctor, hoping instead that if she ignored major symptoms or changes, they would go away," she says.

Unfortunately, ignorance isn't a feasible option with VCI. Instead, say experts, focused attention on risk factors and careful management is key.

"Our doctors told us that if we knew about mom's aneurysms sooner, surgery may have been possible," says Morrison. "Coupled with medication and lifestyle changes, that could have lengthened her life—or at least improved the quality." NN