



RISK FACTORS FOR ALZHEIMER'S DISEASE

Family history AD patients often have close relatives who had dementia.

Mild cognitive impairment About 85% of people with early memory problems go on to develop AD within 10 years.

Stroke and risk factors for stroke such as high blood pressure, high cholesterol, smoking and diabetes

Gender Twice as many women as men get AD, possibly because women's production of protective sex hormones drops significantly after age 50. Women also live to older ages and are more prone to diabetes.

Down's syndrome Nearly all people with this chromosomal abnormality develop AD if they live long enough.

A history of depression

Chronic inflammatory conditions such as some types of arthritis

A head injury (particularly with loss of consciousness)

Chronic heavy stress

Social factors such as low socio-economic status, social isolation and little education

THE SILVER TSUNAMI

For our fast-greying population there's a wave of Alzheimer's disease offshore

ALICE FISHER

Brenda Hounam used to be a whiz at doing complicated additions in her head. When the industrial accountant developed problems adding up ordinary rows of figures, she chalked it up to the stress of being a single mom and spending more than 80 hours a week at her job and volunteer work. Then her family noticed uncharacteristic mood swings. "I used to be a very even-keeled person — I never raised my voice. But now I was crying, wearing my emotions on my sleeve," she says today from her home in Paris, Ont.

Her doctor thought she was depressed or menopausal, but Brenda knew it was something else. She became so rattled, she had to go on sick leave. In 2000, she was diagnosed with Alzheimer's disease (AD). She was 53.

What is Alzheimer's?

A form of dementia, AD is a degenerative disease of the brain characterized by a progressive decline of memory and adverse changes in judgment and reasoning. It leads to death and is a leading cause of death in older people. Brenda is among the estimated 300,000 Canadians who suffer from AD.

Ironically, she found it a relief to put a name to what she was experiencing. "You can't become proactive until you know what you have to act against," says the mother of two grown children. Since her diagnosis, she has been a tireless advocate for the Alzheimer Society of Canada.

A more typical AD sufferer is Owen Conrad, 80, of Bridgewater, N.S., who was diagnosed in 2006 with the more common late-onset form of the disease. His wife of 38 years, Cheryl, 58, has had to quit her job in order to serve as Owen's full-time caregiver. His mental health has gone downhill fast. Formerly a quiet man, lately he's been yelling at visitors and getting so agitated that he starts to shake. Cheryl bathes him, feeds him and watches him like a hawk. It's exhausting, but she doesn't complain. "He'd do the same for me," she says.

A-beta: the main culprit

Experts agree that the primary cause of AD in people like Owen is likely the accumulation in brain tissue of a plaque called beta amyloid, or A-beta, which is split off from a larger molecule called APP (amyloid precursor protein). Both are present in the normal brain, but in AD patients A-beta levels are higher, and the usual mechanism for clearing this protein from the system appears to be defective. Tau, another brain protein, has also been implicated. Tau seems to become chemically altered and piles up as threadlike tangles in brain cells.

These accumulations destroy connections between brain cells in different regions. Gradually, they shut down mental function, much like a series of electrical circuit boards blowing, eventually leaving the house in total darkness. The majority of cases surface after age 65, but Brenda, as we saw, developed the disease at a much



REDUCE YOUR RISK OF ALZHEIMER'S

60% of a person's overall risk for AD stems from risky lifestyle factors, so...

- Maintain a healthy weight.
- Maintain a healthy blood pressure and healthy blood sugar and cholesterol levels.
- Be physically and mentally active.
- Eat a diet rich in fresh fruits and vegetables, which contain antioxidants that protect brain cells from damage caused by rogue oxygen molecules called free radicals.
- Eat anti-inflammatory cold-water fish such as salmon, sardines, mackerel and rainbow trout.
- Do not smoke.

younger age. In her case, having had an early stroke at the age of 41 put her at a much higher risk. And her father had shown symptoms of dementia.

Protecting yourself

Even the specialists don't understand how all the risk factors for AD fit together, says Dr. Howard Chertkow, a professor in the department of neurology and neurosurgery at McGill University in Montreal. But they're learning. They know, for example, that lifestyle changes, including diet, can lower your susceptibility (see "Reduce Your Risk of Alzheimer's," above). According to Chertkow, people who consume fruit juice containing antioxidants called polyphenols at least three times a week have a lower risk of dementia. One recent study from Cornell University in Ithaca, N.Y., found that antioxidant-rich apples, bananas and oranges might protect against AD. In other research, people who consume anti-inflammatory omega-3 fatty acids found in oily cold water fish such as salmon may have a lower incidence of AD, says Chertkow. Nutrients such as folic acid and selenium also seem to be protective.

Chertkow stresses, however, that an antioxidant-rich diet is not a treatment but an approach that might mitigate risk factors. "It may be that there are critical times where you have to have your fruit juice or critical times when you have to be eating salmon," he says. As for physical activity, the research is clear: this increases connections between brain cells and may even promote the development of new nerve cells in the brain.

Brenda decided early on that she would try to delay the progression of the disease for as long as possible. "I started drinking antioxidant green tea and having blueberries on my cereal every morning," she says.

Brenda bought a treadmill and now goes walking frequently. She does deep-breathing exercises, believing that this enhances the flow of oxygen to the brain. To challenge her mind, she plays video games and does memory exercises and crossword and jigsaw puzzles.

The gene connection

A small proportion (6% to 7%) of the AD population has the rare inherited form of the disease that manifests itself before age 60. At least three mutated genes are involved in early-onset AD (Brenda has none of these).

As for late-onset AD, no single genetic mutation has yet been identified as the cause, but some genes are known risk factors. Foremost among these is the gene for apolipoprotein E (APOE), a carrier of cholesterol in the brain. Not everyone who has this mutation, however, goes on to develop AD. Another genetic risk factor is the sortilin-related receptor 1 gene (SORL-1), which was discovered at the University of Toronto. SORL-1 is involved in the processing of APP.

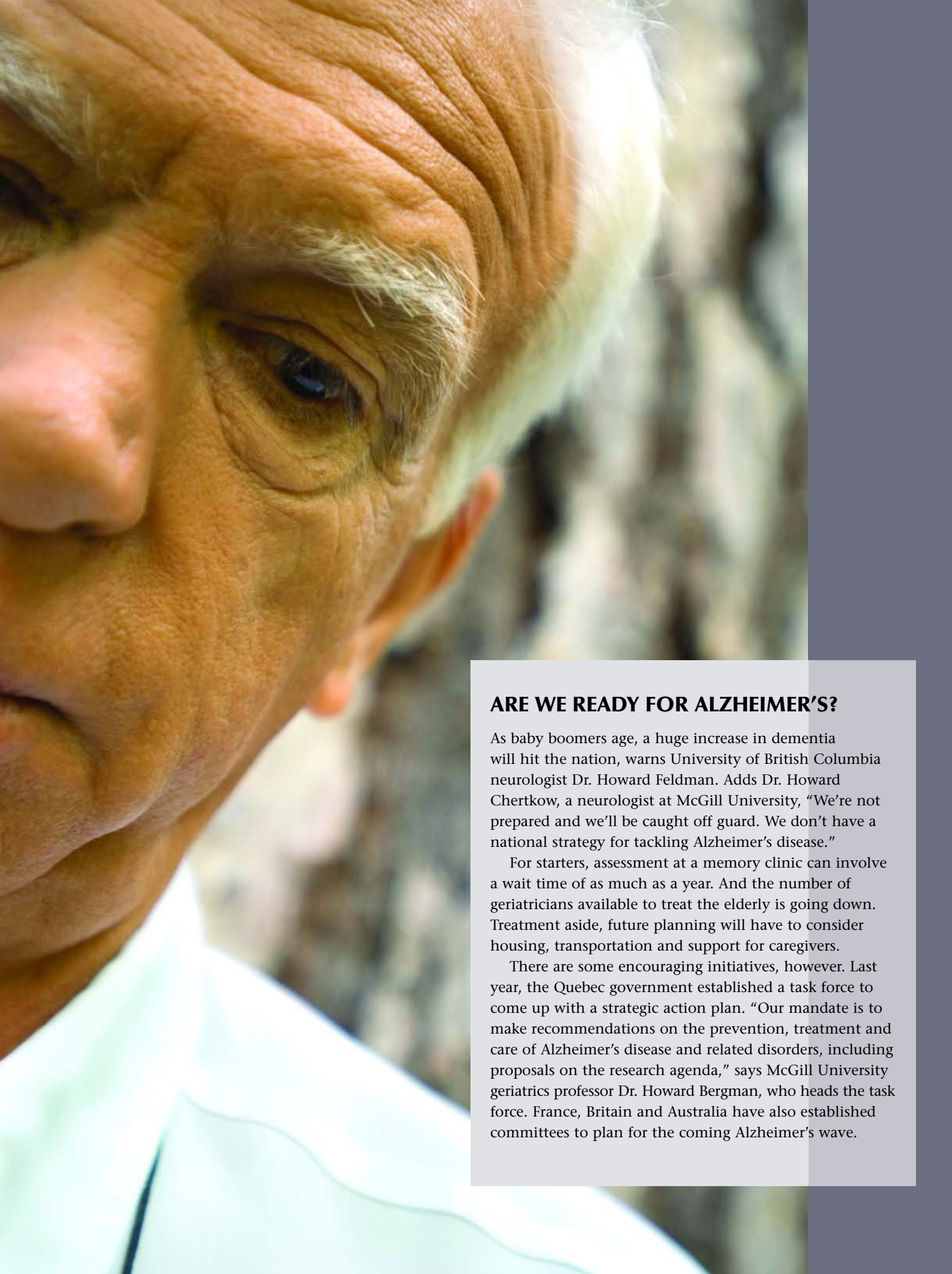
Tests

AD is still diagnosed mainly through clinical assessment of cognitive function. "There's no magic blood test that states, 'You have Alzheimer's disease' or 'You're going to develop Alzheimer's disease,'" says Dr. Howard Bergman, a professor of geriatric medicine at McGill. Nor is there a diagnostic X-ray image, nuclear medicine test, CT scan or MRI, although those tests may rule out similar conditions such as vascular dementia, which can be brought on by multiple strokes and brain tumours.

But that is changing. Identifying the early signs of mild cognitive impairment is an exciting research area. Although AD often doesn't turn up until a person's 70s or 80s, it may have started 30 or 40 years earlier. "The cutting edge of diagnosis is the development of PET [positron emission tomography] scans that display hot spots in the brain that are caused by the presence of amyloid, says Chertkow.

Early intervention

To prevent AD, we may need to intervene in the early stages — just as with diabetes, whose early phase can be picked by a blood test for impaired glucose tolerance when a patient complains of fatigue years before full-blown diabetes sets in. "It's not clear," says Chertkow,



ARE WE READY FOR ALZHEIMER'S?

As baby boomers age, a huge increase in dementia will hit the nation, warns University of British Columbia neurologist Dr. Howard Feldman. Adds Dr. Howard Chertkow, a neurologist at McGill University, "We're not prepared and we'll be caught off guard. We don't have a national strategy for tackling Alzheimer's disease."

For starters, assessment at a memory clinic can involve a wait time of as much as a year. And the number of geriatricians available to treat the elderly is going down. Treatment aside, future planning will have to consider housing, transportation and support for caregivers.

There are some encouraging initiatives, however. Last year, the Quebec government established a task force to come up with a strategic action plan. "Our mandate is to make recommendations on the prevention, treatment and care of Alzheimer's disease and related disorders, including proposals on the research agenda," says McGill University geriatrics professor Dr. Howard Bergman, who heads the task force. France, Britain and Australia have also established committees to plan for the coming Alzheimer's wave.



WHAT'S NEW IN RESEARCH?

More than 50 new compounds are undergoing testing and a few are entering early human trials. Some could actually change the course of the disease, says McGill University neurologist Dr. Howard Chertkow.

PLAQUE FIGHTERS Flurizan and other chemicals called secretase inhibitors block the process that splits off A-beta from the larger APP protein, thereby stemming the accumulation of A-beta in the brain. Alzhemed prevents A-beta molecules from sticking together and might even prevent the telltale plaques of AD. Ubiquitin, a naturally occurring chemical found at decreased levels in AD patients, helps mop up A-beta.

VACCINATION There's also renewed interest in an Alzheimer's vaccine to prompt the immune system to block or remove A-beta from the brain. Following a disappointing early vaccine that was withdrawn after some patients suffered brain inflammation, new hope has emerged. "At least half a dozen forms of the vaccine have been reworked to make them safe, and these are now being tested in humans," says Chertkow. If upcoming trials are successful, at least one vaccine should be on the market within five to seven years.

STATINS These are drugs that reduce blood cholesterol and may also decrease the production of A-beta.

ANTI-DIABETIC DRUGS Anti-diabetics called glitazones may help maintain brain function (some researchers believe that AD might actually be a sort of diabetes of the brain). When the diabetes drug insulin, for example, is administered through the nasal passages, thereby taking a more direct route to the brain, some AD patients experience improved memory and cognition.

STEM CELLS Derived from bone marrow and other tissues, these immature cells can be trained to grow into nerve cells with the help of growth factors. The growth factors trigger nerve cells to produce new connections to other nerve cells. The hope is that these new neurons will migrate to brain regions that have suffered cell damage or loss.

ALZHEIMER'S DISEASE BY THE NUMBERS

- By 2031, an estimated 750,000 Canadians will have Alzheimer's, and two million will have other dementias and mild cognitive impairment.
- Today, this disease costs the Canadian economy \$5.5 billion a year, making it the third most costly illness after heart disease and cancer.
- That price tag will rise to \$11 billion a year by 2011 and to \$17 billion by 2031.
- Nearly half of those with dementia live at home, where they are looked after by a caregiver.



"if it's going to be with a scan or a blood test, but there's a lot of research under way to find tools to make the AD diagnosis earlier — before people have a lot of memory loss or maybe before they have any memory loss."

Adds Dr. Howard Feldman, head of the division of neurology at the University of British Columbia in Vancouver, "Some researchers want to see new criteria that would establish a diagnosis of AD when the disease is still in its precursor stage." Scientists are already looking to a future in which AD would be diagnosed through changes in biological markers, such as spinal fluid protein levels, as well as MRI and PET scans. MRI research from the University of Western Ontario in London, for example, shows that fluid-filled cavities in the brain increase in size with only mild cognitive impairment — well before a diagnosis of full-blown AD.

Researchers expect that future treatments will prevent the disease from progressing in persons in the early stages of AD. "Our mantra is that if we could delay the disease by a year, then over three decades, we would reduce the prevalence of AD by 10%," says Feldman. "If we could delay it by five years, it's been calculated that we could reduce the prevalence by 50%."

Early diagnosis also allows patients to plan for the future. "People who know their diagnosis early may make different life decisions," says Feldman. "For younger individuals, diagnosis has career implications, as well as implications for their fitness to drive a car."

One advocate for early diagnosis is Dave Fost, a resident of Edmonton. He was diagnosed with AD six years ago at age 58. "If you sense your memory is not as it was, don't decline to be evaluated in favour of assuming that this is a natural progression," he says. "The earlier the diagnosis, the more can be done."

Targeted treatments

Current AD therapies target the amyloid protein — in an attempt either to suspend its production or mop it up. Cholinesterase inhibitors prevent an enzyme called cholinesterase from destroying acetylcholine, the

neurotransmitter used by nerve cells in brain regions that control thinking and memory. These agents include donepezil (Aricept), galanthamine (Reminyl) and rivastigmine (Exelon). Meantine (Elixia) goes after the neurotransmitter glutamate, which also has important roles in brain function.

None of these drugs will stop the progression of the disease. They all merely treat the symptoms and may improve or stabilize cognitive function for a limited period of time — and only in some patients. "It's a very, very individual thing as to who is going to benefit for how long and how much," says McGill's Bergman.

New outlook

Although he freely admits to "grasping for words" and at times feeling "stupid," Dave maintains a sense of humour about his failing memory. "I don't look at Alzheimer's as being a hindrance. It's given me a different outlook on the future," he says. Dave's advice to recently diagnosed patients is never to hide their condition. "Being upfront about it makes other people much more comfortable."

Brenda, too, preaches honesty and openness. One of her regrets is that she didn't reveal all her alarming symptoms to her doctor. "I walked in and complained, 'I'm so tired,'" she recalls. "I didn't tell him I was having trouble with my math. I didn't tell him about my mood swings. I didn't tell him I had difficulty multi-tasking."

Once diagnosed with the disease, AD patients are strongly advised to wear identification bracelets coded with their personal information. This is invaluable in case they wander off and get lost. "We want to ensure minimal stress on our caregivers and families," says Dave. His wife, Janet, persuaded him to get an ID bracelet before he actually needed one (he still doesn't).

It's also crucial to stay motivated about living and to keep interacting with others, says Dave, who helps facilitate support groups for affected people. Alzheimer's has totally refocused my thinking on what's really important in life." 