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## Can a troubled mind spell trouble for the heart?

(This article was first printed in the April 2003 issue of the Harvard Mental Health Letter. For more information or to order, please go to www.health.harvard.edu/mental.)

Research confirms that depression may lead to heart disease.
The English language has many words that suggest a connection between depression and the heart. We talk of heartache and describe ourselves and others as heartsick, downhearted, or heartbroken. These words convey an intuition that scientific studies have repeatedly confirmed. What we don't yet know is the exact nature of the connection - or whether treating depression can help prevent heart disease and prolong the lives of people with heart conditions. Because both disorders are so common and so devastating, the answers to these questions have enormous implications for the quality of life and the cost of health care.

A mass of research, much of it conducted since the 1990s, has consistently shown that depressed people are more vulnerable to coronary artery disease, ischemia (lowered blood supply to the heart muscle), congestive heart failure (weakening of the heart muscle), and coronary events - heart attacks, a need for angioplasty or bypass surgery, and death from heart attacks or cardiac arrest. These associations hold even after many other risk factors for heart disease are accounted for, including age, sex, smoking, cholesterol levels, blood pressure, weight-height ratio, and other chronic illnesses. In one of the reviews, covering 11 studies with more than 36,000 participants, analysts found that the risk was up to four times greater in some groups. For example:

- In a six-year study of 5,000 people age 65 and over, those who had frequent depressive symptoms were $40 \%$ more likely to develop coronary artery disease and $60 \%$ more likely to die. For every $5 \%$ increase in the score on a standard rating scale for depression, the risk of developing coronary artery disease within six years rose by $13 \%$ and the risk of dying by 11\%.
- 1,200 Johns Hopkins Medical School students were tracked every five years for nearly 40 years. Clinical depression at any time - even a depressive episode more than 10 years in the past - doubled the risk of developing coronary artery disease and raised the risk for a heart attack by $20 \%$.
- In a four-year study of 2,400 subjects with and without heart disease, those who had depressive symptoms were at a 60\% greater than average risk for cardiac death, and those with clinical depression had a nearly fourfold risk.
- Men in their 50s with high levels of depression and anxiety were over three times more likely than average to have a fatal stroke during the next 14 years.
- 4,500 volunteers with high blood pressure (but no symptoms of heart disease), age 60 and over, answered a questionnaire on depressive symptoms. Clinical depression nearly tripled the risk of congestive heart failure during the next $41 / 2$ years. Eight percent of the depressed subjects developed heart failure, compared to $3 \%$ of those who were not depressed.


## Optimistic hearts do better than angry ones

Even among people who are not clinically depressed, the more optimistic and cheerful have a lower rate of heart disease:

- Among 600 healthy people ages $30-60$ with siblings who had developed heart problems at
an early age, those who showed a "positive outlook" on personality tests were half as likely to experience a cardiac event in the following eight years.
- In a 10-year study of 1,300 men, each increase in level of optimism as indicated by answers to a personality test reduced the chance of developing chest pain and coronary artery disease by $25 \%$. The most optimistic group of men also had a lower risk for heart attack or death from heart disease than the most pessimistic.

The anger that often accompanies pessimism and depression is also a risk factor for heart disease:

- People with normal blood pressure who scored high on a rating scale for anger were nearly three times more likely to have a heart attack or require bypass surgery within the next five years.
- People in their 20s who showed above-average levels of hostility on questionnaires were 2.5 times more likely to develop signs of atherosclerosis within 10 years.
- In a three-year study, hostility as measured by a personality test predicted heart attacks, angina, and ischemic heart disease better than high cholesterol, smoking, or height-weight ratio.


## Depression can wither a damaged heart

Not surprisingly, the prognosis is also worse for existing heart conditions when they are accompanied by depression. Patients who show symptoms of depression while hospitalized for a heart attack or bypass surgery are 3-4 times more likely to suffer another cardiac event or die in the following months or years - independent of the severity of their physical symptoms. That extra risk is especially significant because at least $30 \%$ of hospitalized patients with coronary artery disease have some depressive symptoms, and depression may be even more common in stroke survivors. Consider the following evidence:

- $17 \%$ of patients described as clinically depressed in the aftermath of a heart attack died within six months, compared to $3 \%$ of those who were not depressed. Major depression predicted death within 18 months better than any other risk factor. Patients with major depression were eight times more likely to die than those with mild to moderate depressive symptoms, but even very mild depression raised the risk.
- In a group of heart attack survivors age 65 and over, depression quadrupled the risk of death within four months ( $27 \%$ versus $7 \%$ ).
- Among 400 patients over 50 who were hospitalized with congestive heart failure, more than $75 \%$ had some symptoms of depression. Six months later, only $30 \%$ of patients with no or few depressive symptoms but $60 \%$ of the most depressed had shown a functional decline or had died.


## The biological connection

It makes biological sense that depression should be hard on the heart because depressed people are under chronic stress. In the normal reaction to an acute emergency, called the fight-or-flight response, the adrenal glands release the stress hormones adrenaline and cortisol. The heart speeds up, blood vessels are constricted, and clotting factors in the blood are activated as preparation for a possible injury. This response burdens the heart muscle and reduces the supply of blood to the coronary arteries.

Normally, a feedback system prevents the stress response from persisting when the emergency is over. The brain detects high levels of cortisol in the blood and signals the pituitary gland to stop releasing hormones that activate the adrenal glands. If this feedback loop fails, the emergency response can become a relentlessly malignant condition. Paradoxically, depressed patients seem to be hyper-aroused. Their sleep is disturbed and their appetite poor, and they are often anxious and irritable as well as sad.

Persistent high levels of stress hormones can make the heart less sensitive to the signals it uses to adapt its pumping action to changes in the body's demands. This reduction in heart rate variability raises the risk for serious rhythm disturbances, including ventricular fibrillation, the sometimes deadly rapid and uncoordinated contractions of the lower chambers of the heart.

Stress hormones also stimulate the production of inflammatory substances and oxygen free radicals, the destructive byproducts of metabolism that can damage the lining of arteries. Scientists
using ultrasound measurements have found that the arteries of depressed patients expand and contract less flexibly in response to changes in blood flow.

Emotional stress may raise the risk for heart disease and cardiac events even more than physical stress does. The strain increases the demand for oxygen while reducing the supply carried by the blood. Experiments suggest that the flexibility of coronary arteries increases during strenuous physical activity (a bicycle exercise test), while psychological stress (from public speaking) makes arteries more rigid and resistant to blood flow.

In a study of patients with coronary artery disease, those whose blood pressures increased during a public speaking test were more likely to die within three years. Those who developed chest pain during public speaking were three times more likely to suffer a cardiac event in the next five years. Chest pain during bicycle exercise also predicted cardiac events, but not as strongly.

## Disheartening behavior

Depression affects the heart in indirect as well as direct ways. Because they are often discouraged and believe nothing will help, depressed people don't eat well, don't exercise, and don't consistently follow medical instructions. Studies have shown that they are much more likely to drop out of cardiac rehabilitation programs and fail to take prescribed heart drugs - some of which cannot be omitted for even a day without raising the risk for a stroke or cardiac event.

Depression also leads to social isolation, and isolation is bad for the heart. Support from friends, family, and a community reduces the risk for heart disease even in people with many physical risk factors. In one study, coronary artery disease patients who lacked both a spouse and a confidant had a five-year death rate of $50 \%$, compared with $20 \%$ for those less isolated.
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