

What is homocysteine?

Homocysteine is a chemical found in the blood that is produced when the amino acid *methionine* (a building block for proteins) is broken down. High levels are linked to an increased risk of [PAD](#), [heart disease](#), and [stroke](#).

The connection between homocysteine and heart and blood vessel disease was first suspected about 25 years ago. Doctors noticed that people with a rare genetic disease called *homocystinuria*, which causes very high levels of homocysteine to build up in the blood, often developed heart disease in their teens and twenties. Since then, studies have found that higher-than-normal levels of homocysteine increase the risk of developing heart and blood vessel disease in otherwise healthy people as well.

It is thought that homocysteine damages the linings of the blood vessels and makes the blood more likely to form clots (especially in the arteries).¹ In patients with PAD, homocysteine reduces the ability of the blood vessels to expand (*dilate*) when muscles need more blood, and causes other problems with the artery lining.

So far, trials have failed to show that lowering homocysteine levels can reduce a person's risk of developing PAD or PAD complications.

See also:

[Homocysteine & Vein Disease Risk](#)
[Homocysteine & Heart Risk](#)

How does homocysteine affect my risk of PAD?

Women with high homocysteine levels are twice as likely to develop PAD than with women with lower levels.^{4,5} However, it is still not clear if homocysteine is the cause of this increased risk, or if women with high homocysteine are simply more likely to have other conditions and characteristics that put them at risk for PAD.

One in five women with PAD have high homocysteine levels (see [What do my homocysteine numbers mean?](#)).⁶ PAD patients tend to have higher homocysteine levels than people without PAD.

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One study of 631 people (half were women) found that people with homocysteine levels about 50% above average had a 44% higher risk of developing PAD.

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However, homocysteine may be only a sign, rather than a cause, of artery problems. A large study in women found that the link between homocysteine and PAD disappears after other factors are taken into account. The Nurse's Health Study examined 27,935 healthy women and monitored them for 12 years. Women who developed PAD had slightly higher homocysteine levels than women who stayed PAD-free. However, homocysteine levels were not linked to the risk of developing PAD after other PAD risk factors were taken into account.⁹ Another analysis that looked at a cross-section of the US population found that the link between homocysteine and PAD was explained by differences in smoking habits, kidney function, and levels of certain metals in the blood.

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In women who have already been diagnosed with PAD, higher homocysteine levels indicate your PAD is more likely to get worse, and to progress more quickly.¹¹ In patients with leg symptoms of PAD, each 1-point rise in homocysteine corresponds to a 6% higher risk of dying from heart and blood vessel disease.

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Again, it is not clear whether homocysteine is a cause of worsening PAD, or simply an indicator of more severe disease.

How is homocysteine measured? Should I be tested?

Homocysteine is measured with a routine blood test. The homocysteine test is not widely available, costs about \$100, and is not currently covered by insurance. In rare cases, your healthcare provider may order a *methionine-load test*, a more precise test that measures homocysteine before and after you swallow 100 mg/kg of methionine (dissolved in orange juice).

Since it has not been proven that lowering homocysteine levels reduces your risk of PAD and other problems, most women do not need to be tested. Your doctor may test your homocysteine level if you have a personal or family history of early heart or blood vessel disease, but you do not have any well-established risk factors (such as [smoking](#) , [high cholesterol](#) , [high blood pressure](#) , lack of exercise, [obesity](#) or [diabetes](#)).

What do my homocysteine numbers mean?

HA Fasting Blood Homocysteine Levels¹³

Normal	5 to 15
Moderately High	16 to 30
Intermediately High	31 to 100
Very High	More than 100

Levels are measured in micromoles of homocysteine per liter of blood ($\mu\text{mol/L}$)

What causes high homocysteine levels?

Homocysteine levels are determined by your diet and genetic makeup. Folic acid and other B vitamins, such as B₆ and B₁₂, break down homocysteine in the body. If you do not get enough of these vitamins, your homocysteine levels will go up.

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Click [here](#) to learn how to make sure you get enough B vitamins in your diet.

Your age, hormonal status, and other conditions and medications can also affect your homocysteine levels. See [What causes high homocysteine levels?](#) to learn more.

Can lowering homocysteine prevent future problems?

Because women with high homocysteine levels are at increased risk for PAD, it was thought that lowering homocysteine might reduce this risk. However, so far trials have failed to show that lowering homocysteine levels with B vitamins can reduce the risk of developing heart and blood vessel disease, including PAD.

Most studies of homocysteine-lowering have looked at heart disease, rather than PAD. One study examined at 5,442 women aged with a history of heart or blood vessel disease or at least three major heart disease risk factors. A B vitamin pill lowered homocysteine by about 20% over 7 years, but did not lower the risk of heart attack, stroke, procedures to treat heart disease, or dying of heart and blood vessel disease.¹⁴ No randomized clinical trials (the gold standard way to determine if a treatment is effective) have examined whether lowering homocysteine can reduce the risk of developing PAD.

Despite this lack of success, it is possible that these studies did not lower homocysteine enough, or that the populations studied did not have high enough homocysteine levels to see a benefit. For now, it is not recommended that women take B vitamin supplements to prevent PAD or heart disease by lowering homocysteine.^{4,15}

If you are at high risk for heart and blood vessel disease ([calculate your risk here](#)

) and have had a homocysteine test that showed **very high** levels, your doctor may advise you to take B vitamin supplements.

How can I lower my homocysteine levels?

Although it has not been proven that lowering homocysteine levels reduces your risk of PAD and its complications, you are strongly advised to get enough folic acid in your diet, especially if you have risk factors for PAD. This means eating at least five servings of fruits and green, leafy vegetables daily.

Recommended intakes of

homocysteine-related vitamins ¹³

Micronutrient	Recommended	Good Sources
Daily Allowance		
Vitamin B ₆	1.3 to 1.7 mg	Beef, chicken, m...
Vitamin B ₁₂	2.4 µg	Fortified cereals,
Folic acid 400 µg (same for pregnant women*)		Citrus fruit, orange juice, beans, liv...

*Folic acid supplements are recommended for women who may become pr...

Hearty-healthy lifestyle choices such as the [DASH Diet](#) (Dietary Approaches to Stop Hypertension) and quitting smoking can also help

lower homocysteine levels.

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Even if homocysteine is not the culprit,

[quitting smoking](#)

and sticking to a

[heart-healthy diet](#)

are proven ways to lower your risk for PAD.

For more on how to lower your PAD risk, see [Preventing PAD: The Basics](#)

References

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