TEST

Serum phenylalanine screening

This blood test measures phenylalanine to screen for, confirm, or monitor problems processing this amino acid.

WHAT IT MEASURES
Phenylalanine, an amino acid, in blood

SAMPLE
Blood, usually serum or plasma

FASTING NEEDED?
Sometimes, for confirmatory or monitoring samples

HOW LONG IT TAKES
Usually five to ten minutes

RESULTS IN
Often one to three days; varies by laboratory

USED FOR
Screening, diagnosis support, and treatment monitoring

MAIN LIMITATION
Need for confirmation of elevations and their cause

Overview

Serum phenylalanine screening measures phenylalanine in your blood. Phenylalanine is an amino acid, one of the building blocks used to make proteins.

Your body normally changes phenylalanine into another amino acid called tyrosine. This process requires an enzyme called phenylalanine hydroxylase and a helper substance called tetrahydrobiopterin, or BH4. Problems with this pathway can allow phenylalanine to build up.

One possible cause is phenylalanine hydroxylase deficiency, which includes phenylketonuria, or PKU. Other metabolic conditions, illness, nutrition, and treatment can also affect the result. The test alone does not establish the cause.

Most routine newborn screening uses blood collected from a heel prick and dried on special paper. That is a whole-blood screening test, not a serum test. A quantitative serum or plasma phenylalanine test is often used to check an abnormal newborn screen or monitor someone with a known condition.

Serum is the clear liquid left after blood has clotted. Plasma is the liquid part of blood before

clotting. Laboratories may use either sample, but their methods and reporting can differ.

Why the test is ordered

This test may be ordered to:

A phenylalanine result is usually considered alongside tyrosine. The laboratory may also calculate a phenylalanine-to-tyrosine ratio, which can provide additional information.

- Check an abnormal or uncertain newborn blood spot result
- Investigate a possible problem processing phenylalanine
- Measure phenylalanine after a previous elevated result
- Monitor dietary or medical treatment for PKU
- Monitor phenylalanine before and during pregnancy in someone with PKU

Who should have the test

Newborn screening programmes routinely test babies for PKU in many countries and regions. The timing and collection method are set by the local programme.

A serum or plasma test may be appropriate after an abnormal newborn screen. It may also be used when a clinician suspects a metabolic condition because of medical history, family history, or other test results.

People already diagnosed with PKU or another form of high phenylalanine usually need regular testing. The schedule is individual and may change with age, treatment, illness, or pregnancy.

This is not generally used as a routine wellness test for people without a relevant screening result, history, or clinical concern.

How to prepare

Follow the instructions on your laboratory request. Some samples are collected after fasting, while others are taken without fasting so that they reflect usual eating and treatment.

Do not stop a prescribed low-phenylalanine diet, medical food, supplement, or medicine to prepare for the test unless your metabolic team specifically tells you to. A sudden change can make the result less useful and may be unsafe for someone receiving treatment.

Tell the person arranging the test about:

For repeat monitoring, collecting samples at a similar time and under similar eating conditions can make trends easier to interpret.

- Recent meals, fasting, illness, or unusual exercise
- Medical foods, protein supplements, and tube or intravenous feeding
- Medicines used to lower phenylalanine
- Pregnancy
- A recent blood transfusion

What happens during the test

For a serum test, a healthcare professional places a small needle into a vein, usually in your arm. Blood is collected into a tube and sent to a laboratory.

The blood draw usually takes only a few minutes. Young babies may instead have blood collected from a heel prick, depending on the purpose of testing and local practice.

In the laboratory, the amount of phenylalanine is measured. Many laboratories measure several amino acids in the same sample.

Understanding your results

Results may be reported in micromoles per litre or milligrams per decilitre. Use the reference information provided with your own report rather than converting or comparing results without guidance.

Ranges and interpretation vary by laboratory, testing method, age, sex, pregnancy status, medicines, treatment, and clinical context. Newborn screening cut-offs are also programme-specific and are not the same as treatment targets for someone with diagnosed PKU.

An elevated result means that more phenylalanine than expected was present when the sample was collected. It does not, by itself, confirm PKU. The result may need to be repeated and assessed with tyrosine, other amino acids, and additional metabolic or genetic tests.

A result within the laboratory's expected range makes an important phenylalanine elevation less likely at that time. It may not rule out every mild or intermittent disorder, especially if the sample was collected unusually early, after transfusion, or while treatment was already lowering the level.

A low result usually does not suggest PKU. In someone receiving treatment, however, a persistently low level may mean that nutrition or treatment needs review. Do not change a prescribed diet based on one result.

What affects the results

Phenylalanine reflects both inherited metabolism and what was happening in your body near the time of collection. Important influences include:

Strenuous exercise is not usually the largest influence, but unusual or prolonged exercise can change amino acid metabolism. Kidney function is also not usually the main reason for a misleading phenylalanine result, although serious kidney or liver illness can affect overall amino acid balance.

- Food and fasting: A recent protein-containing meal can affect amino acid measurements. Prolonged fasting may increase protein breakdown.
- Age at newborn collection: A sample taken very soon after birth, before enough feeding, may not show the same elevation as a later sample.
- Prematurity or illness: Premature birth, severe illness, and increased breakdown of body tissue can alter amino acid levels.
- Intravenous nutrition: Amino acid solutions used in parenteral nutrition can raise phenylalanine and produce an abnormal screening result.
- Treatment: A low-phenylalanine diet, medical foods, sapropterin, or pegvaliase can lower the measured level.
- Pregnancy: Phenylalanine targets and interpretation are different during pregnancy. Levels may also change as pregnancy progresses.
- Recent transfusion: Donor blood can dilute or alter newborn screening results. The screening programme may require another sample at a specific time.
- Sample type and method: Dried blood spot, serum, and plasma values are not automatically interchangeable.
- Collection and handling: Poor sample quality or incorrect storage can occasionally prevent reliable measurement.

Accuracy and limitations

Modern laboratory methods can measure phenylalanine accurately in a good-quality sample.

However, measuring the number accurately is not the same as identifying why it is high.

Screening can say "possible problem" when no lasting disorder is present. This can happen with prematurity, illness, intravenous nutrition, early feeding changes, or temporary newborn elevations. For that reason, an abnormal screen requires confirmation.

Screening can also miss a problem. Possible reasons include collection too early, a recent transfusion, treatment already lowering phenylalanine, poor sample quality, or a mild condition that does not cross the programme's cut-off. How often this happens differs among screening programmes, methods, and cut-offs, so there is no single rate that applies everywhere.

A quantitative plasma or serum amino acid test is usually better than a screening blood spot for confirming the amount present. Further tests may include a phenylalanine-to-tyrosine ratio, urine or blood tests for BH4-related disorders, enzyme studies, or genetic testing. Even genetic testing may not find every relevant change.

Risks and complications

A blood draw may cause brief discomfort, a small bruise, or light-headedness. Serious complications are uncommon, and pressure over the site usually stops minor bleeding.

What happens next

If the result is within the expected range, no further testing may be needed. Monitoring continues as scheduled if you already have PKU or another metabolic condition.

An uncertain or mildly elevated result is often repeated under clearer collection conditions. The next sample may be serum or plasma rather than another screening blood spot.

A clearly elevated newborn screening result usually leads to prompt contact from the screening programme and assessment by a metabolic specialist. Follow the timing they provide, but an abnormal screening result does not automatically mean that your baby has PKU.

For someone with known PKU, results are used to guide routine follow-up. Do not change medical food, diet, or medicine without the clinician or dietitian managing that treatment.

Seek urgent medical care for serious symptoms such as a seizure, severe breathing difficulty, unusual unresponsiveness, or a baby who cannot be woken normally. These symptoms have many possible causes and should not be attributed to a phenylalanine result alone.

Common questions

Can I drink coffee before the test?

If you have been told to fast, have only water unless the laboratory says otherwise. Milk, cream, or protein-containing drinks can affect amino acid measurements. If fasting was not requested, follow your usual routine.

Does the time of day matter?

There is no universal collection time. For ongoing monitoring, using a similar time of day and similar timing around meals can make results easier to compare.

Can I exercise beforehand?

Normal daily activity is usually acceptable. Avoid unusually strenuous or prolonged exercise immediately beforehand if possible, especially when the result will be compared with earlier monitoring samples.

Do I need to avoid protein before the test?

Not unless you have been specifically instructed to do so. Continue your usual prescribed diet and medical food because changing protein intake can make the result unrepresentative.

Is this the same as the newborn heel-prick test?

Not exactly. Newborn screening usually measures phenylalanine in a dried whole-blood spot. Serum or plasma testing uses liquid blood and is commonly used for confirmation or monitoring.

Can one high result diagnose PKU?

No. A high result needs confirmation and interpretation with other tests. These help distinguish PKU from temporary elevations, treatment effects, BH4-related disorders, and other causes.

Sources

- American College of Medical Genetics and Genomics: ACT Sheets and Algorithms, Elevated Phenylalanine
- GeneReviews: Phenylalanine Hydroxylase Deficiency, NCBI Bookshelf
- Health Resources and Services Administration: Phenylketonuria, Newborn Screening Information Center

- van Wegberg AMJ and colleagues. The complete European guidelines on phenylketonuria: diagnosis and treatment. Orphanet Journal of Rare Diseases . 2017;12:162
- UK Government: Newborn blood spot screening programme handbook