TEST

Protein electrophoresis - serum

A blood test that separates serum proteins to look for unusual amounts or patterns

WHAT IT MEASURES
Distribution of serum proteins by size and electrical charge

SAMPLE
Blood from a vein

FASTING NEEDED?
No, unless combined tests require it

HOW LONG IT TAKES
About 5 to 10 minutes

RESULTS IN
Usually a few days, varying by laboratory

USED FOR
Diagnosis and monitoring of abnormal blood proteins

MAIN LIMITATION
Small or light-chain proteins may be missed

Overview

Serum protein electrophoresis, often shortened to SPEP, is a blood test that separates proteins in the liquid part of your blood. "Serum" is the fluid left after blood has clotted.

The laboratory places the serum in an electrical field. Different proteins move at different speeds according to their size and electrical charge. This creates a pattern of bands or peaks.

The main protein groups are albumin, alpha-1, alpha-2, beta and gamma globulins. Albumin helps keep fluid inside blood vessels and carries substances through the body. The globulin groups include transport proteins, inflammation-related proteins and antibodies.

SPEP is particularly useful for finding a concentrated group of identical antibodies or antibody fragments. This may be reported as a monoclonal protein, paraprotein, M-protein or M-spike. Finding one does not, by itself, establish its cause or mean that you have cancer.

Why the test is ordered

SPEP may be ordered when another test shows high total protein or an unusual balance

between albumin and globulins. It can also help investigate symptoms or test results that do not yet have a clear explanation.

Reasons for ordering it may include:

The test may contribute to an evaluation for plasma-cell conditions, including monoclonal gammopathy of undetermined significance, known as MGUS, and multiple myeloma. Plasma cells are immune cells that make antibodies. SPEP is only one part of that evaluation.

- Unexplained anemia, kidney problems or high blood calcium
- Persistent bone pain, fragile bones or certain fractures
- Numbness, tingling or other unexplained nerve problems
- Frequent infections or low antibody levels
- Suspected abnormal antibody production
- Monitoring a previously identified monoclonal protein

Who should have the test

SPEP is generally used when your symptoms, medical history or other laboratory results suggest that checking the pattern of blood proteins could be helpful. It is not usually used as a general screening test for people without a specific reason.

You may also have regular SPEP testing if a monoclonal protein is already being monitored. Changes are interpreted alongside your symptoms, blood counts, kidney function, calcium and other tests.

A normal SPEP result cannot rule out every plasma-cell condition. If there is a strong clinical reason for testing, additional blood or urine tests may be needed even when SPEP is normal.

How to prepare

SPEP by itself does not usually require fasting. You can generally eat, drink water and take your usual medicines before the blood draw. If other blood tests are being collected at the same appointment, their preparation instructions may be different.

Tell the healthcare team about your medicines and recent treatments. This is especially important if you have received intravenous immunoglobulin, called IVIG, a plasma-containing transfusion or a monoclonal antibody medicine such as daratumumab. These can affect the pattern.

Being well hydrated can make the blood draw easier. Do not stop a prescribed medicine unless the clinician who prescribed it tells you to do so.

What happens during the test

A healthcare professional places a band around your upper arm and cleans an area of skin. A small needle is inserted into a vein, usually inside the elbow, and blood is collected into a tube.

The needle is then removed and pressure is applied to the area. The collection usually takes only a few minutes.

At the laboratory, the blood is allowed to clot and the serum is separated. Its proteins are then divided into groups by electrophoresis. A graph is produced, and any unusual band or peak may be measured.

Understanding your results

Your report may list the amount of protein in each fraction and show a graph of the electrophoresis pattern. Interpretation focuses on the shape and distribution of the proteins, not just whether one number falls outside a reference range.

Common patterns include:

A monoclonal protein may occur in several different conditions. Some require monitoring only, while others need further assessment or treatment. Its amount can help with follow-up, but the result cannot identify the cause on its own.

Reference ranges and interpretation vary by laboratory, age, sex, pregnancy status, medicines and clinical context. Trends are most useful when testing is repeated with the same method and, where possible, at the same laboratory.

- A sharp, narrow peak, which may suggest a monoclonal protein
- A broad rise in gamma proteins, often linked with general immune activation
- Reduced gamma proteins, which may reflect low antibody levels
- Changes in albumin or alpha proteins associated with inflammation, liver function, kidney function or nutrition

What affects the results

Several factors can change the pattern without indicating a new plasma-cell disorder.

Dehydration concentrates proteins and may make measured amounts appear higher. Receiving a large amount of fluid can dilute them. Kidney or liver disease can alter several protein fractions because these organs remove, produce or process proteins.

Infection, inflammation, autoimmune illness and recent immune stimulation can cause a broad increase in antibodies. Pregnancy may lower albumin through blood-volume changes and alter other fractions. Normal patterns can also shift with age.

Some treatments create especially important interpretation problems. Therapeutic monoclonal antibodies, including daratumumab, can appear as a small monoclonal band. IVIG contains antibodies from donors and can produce temporary bands or a broad increase. A recent plasma-containing transfusion may also introduce donor proteins.

Sample quality matters. Blood that has not clotted completely may contain fibrinogen, a clotting protein that can resemble an abnormal band. Breakdown of red blood cells or a very fatty sample can make the tracing harder to interpret.

Tell the person reviewing the result about recent medicines, infusions and transfusions. The laboratory may be able to use another method or compare the band with previous results.

Accuracy and limitations

SPEP is good at finding many moderate or large monoclonal proteins, but it can miss small amounts. It may also miss conditions that produce mainly free light chains, which are small antibody components that may not create a clear peak.

There is no single miss rate that applies to every person. Performance changes with the amount and type of protein, the laboratory method and the condition being investigated. A normal result is therefore not always the final answer.

The test can also produce a suspicious-looking pattern when no harmful plasma-cell disorder is present. Inflammation may create restricted bands, while IVIG, fibrinogen and monoclonal antibody medicines can imitate an M-protein. Even a genuine monoclonal protein may come from a condition that does not currently need treatment.

Immunofixation is better at confirming whether an abnormal band is monoclonal and identifying its antibody type. A serum free light-chain test is better for detecting excess free light chains. Urine electrophoresis, imaging or a bone marrow biopsy may be appropriate in selected situations, but SPEP alone cannot determine whether these are needed.

Risks and complications

The risks are those of an ordinary blood draw. You may have brief discomfort, a small bruise or feel light-headed; serious complications are uncommon.

What happens next

A result without an abnormal monoclonal band may need no further action if the original concern has been resolved. Further testing may still be arranged if symptoms or other results continue to suggest a protein disorder.

If a monoclonal band is found, routine follow-up often includes immunofixation, serum free light chains, blood counts, calcium and kidney tests. Your clinician may compare the amount with earlier results or arrange repeat testing before deciding whether specialist assessment is needed.

An abnormal SPEP result is not usually an emergency by itself. Arrange the recommended follow-up rather than trying to interpret the graph alone.

Seek urgent medical help for severe symptoms such as new chest pain, severe difficulty breathing, fainting, sudden confusion or being unable to pass urine. These symptoms require assessment because of how you feel, not simply because an SPEP result is abnormal.

Common questions

Can I drink coffee before the test?

Yes, if SPEP is the only test being performed. Milk, sugar or other ingredients may matter if you are also having tests that require fasting, so follow the instructions for the full set of blood tests.

Does the time of day matter?

Time of day is not usually important for SPEP. Follow-up samples may be collected under similar conditions to make comparisons easier.

Can I exercise beforehand?

Normal activity is generally fine. Very intense exercise can affect hydration and some blood proteins, so avoid arriving dehydrated and mention unusually strenuous recent activity.

Do I need to stop my medicines?

Usually not. Tell the healthcare team about all medicines and infusions, particularly monoclonal antibody treatments and IVIG, because they can change the pattern.

Does an M-spike mean multiple myeloma?

No. An M-spike means that a group of similar antibodies or antibody fragments was detected. Further tests are needed to identify the protein and understand why it is present.

Why might I need more tests after a normal result?

SPEP can miss small monoclonal proteins and free light chains. Immunofixation and serum free light-chain testing may find proteins that do not create a clear SPEP peak.

Sources

- National Institute for Health and Care Excellence. Myeloma: diagnosis and management , guideline NG35
- College of American Pathologists. Laboratory Workup of Monoclonal Gammopathies: A Clinical Practice Guideline , Archives of Pathology & Laboratory Medicine, 2020
- International Myeloma Working Group. Screening panels for monoclonal gammopathies , Leukemia, 2009
- MedlinePlus. Protein Electrophoresis by Immunofixation Blood Test
- ARUP Consult. Monoclonal Gammopathies
- American Family Physician. Understanding and Interpreting Serum Protein Electrophoresis , 2005