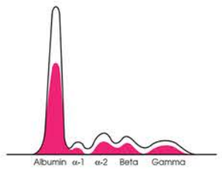
Serum Proteins

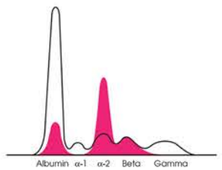
Gastrointestinal Loss



The excessive gastrointestinal loss of albumin, along with other serum proteins, is seen in conjunction with a variety of gastrointestinal disorders. Protein losing enteropathies usually occur secondary to several pathophysiological conditions.

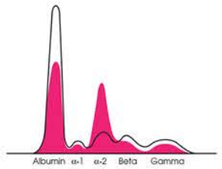
For instance, they may be related to lymphatic abnormalities (e.g. secondary to increased pressure as in patients with constrictive pericarditis, or to congenital abnormalities as in primary intestinal lymphangiectasis). In other cases, the albumin loss may be secondary to mucosal disease, or direct loss of serum into the intestines as in inflammatory bowel disease.

Acute Thermal Injury



Marked hypoalbuminemia may occur in patients with acute thermal burns. As in other conditions where hypoalbuminemia is symptomatic, there is an involved interaction of a number of factors. One of the most important is the loss of albumin through seepage of serum into the burned areas. Another important factor in acute thermal burns is that skin, while only 6% of total body weight, contains 30-40% of total extravascular albumin. The loss of skin will result in significant loss of albumin.

Nephrotic Syndrome



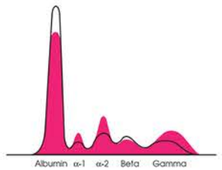
Nephrotic syndrome results from numerous conditions, including diabetes mellitus, collagen vascular disease, glomerular disease and circulatory disease. It is characterized by the loss of albumin and other low molecular weight proteins (e.g. transferrin and alpha$_1$-antitrypsin) and an associated increase of certain large molecular weight proteins (e.g. macroglobulin, IgM, lipoproteins).

Nephrotic syndrome is characterized by:

1. Hypoproteinemia
2. Hypoalbuminemia
3. Edema
4. Lipiduria
5. Hyperlipemia
6. Proteinuria

The electrophoretic pattern may be mimicked by certain inflammatory conditions associated with increased acute/chronic phase alpha$_1$ and alpha$_2$ globulins.

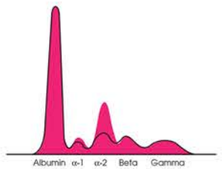
Chronic Inflammation



Chronic inflammatory conditions are also associated with increases of certain proteins. They are usually referred to as chronic phase proteins. Electrophoretically, this chronic response is seen as a moderate to slight increase in the α_2-globulin fraction, and to a smaller degree, in the β-region. The albumin may be slightly suppressed with a gamma globulin increase suggestive of polyclonal increase. Chronic phase proteins are seen in the following disorders:

1. Chronic infectious diseases
2. Connective tissue diseases
3. Allergic diseases
4. Malignancies
5. Autoimmune diseases

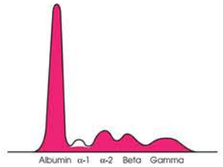
Acute Phase Proteins



Most diseases which are associated with a rapid breakdown of tissue fall under the acute phase phenomenon. Along with rapid tissue breakdown, clinical findings will include fever, elevate sedimentation rate and leukocytosis along with increased levels of acute phase proteins, such as α_1-Antitrypsin, α_1-acid glycoprotein, haptoglobin and C-reactive proteins. Increased acute phase proteins are seen in the following disorders:

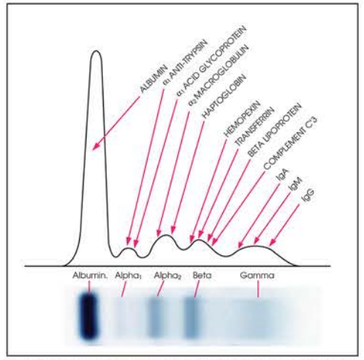
1. Acute infectious diseases
2. Trauma (mechanical, physical, chemical, etc.)
3. Myocardial infarction, thrombolysis, cardiac failure, etc.
4. Auto-toxicosis (uremia, shock, etc.)

Alpha$_1$ Antitrypsin Deficiencies



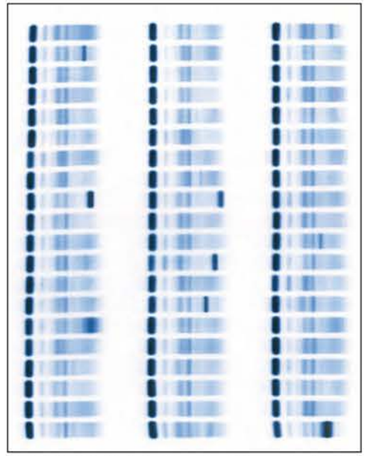
1. Normal concentration of α_1-AT is 200-400 mg/dL. In heterozygous α_1-AT deficiency, there is a severe drop in α_1-AT to approximately 30-50% of normal. Homozygous deficiency varies according to ethnic group, but α_1-AT levels usualy fall to 10-15% normal concentration. This condition is seen in 3-5% of the population. Patients with homozygous deficiency are highly predisposed to pulmonary emphysema, hepatic cirrhosis, pancreatic insufficiency and other abnormalities.
2. Acquired deficiency may result in liver disease or severe nephrotic syndrome. Urinary loss of α_1-AT may be seen. Alpha$_1$ antitrypsin phenotyping is essential for precise diagnosis of deficiency types.

Classic 5-Banded Pattern



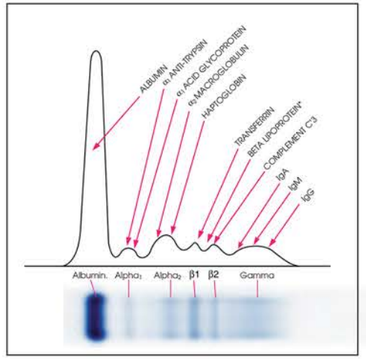
Classic 5-banded separations are a mainstay in the clinical laboratory, providing critical information to clinicians to both diagnose and follow treatment progress.

Knowledge of the proteins in each fraction can aid in interpretation. Each fraction contains 1-3 specific proteins: elevation or depression of the area where each protein migrates can reflect concentration. Follow-up testing can then be performed to characterize or quantity.



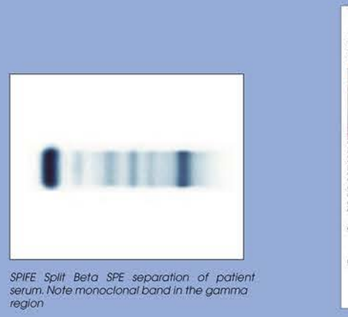
SPIFE Split-Beta Protein Gel – 60 Sample. Gel sizes ranging from 10 to 100 samples are available to meet the workloads of any laboratory. Both the classic and split-beta formulations provide crisp, clear separation of the protein fractions.

Split Beta Pattern

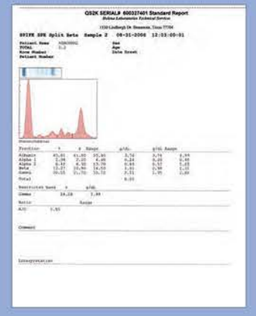


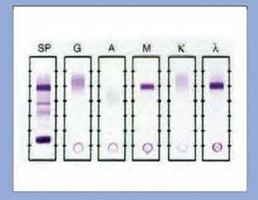
While some laboratories prefer classic five-banded serum protein separations, others prefer a split-beta pattern. With SPIFE Split-Beta gels, the proteins migrating in the beta region are split into two fractions, β1 and β2, between transferrin and C3 complement. *Beta lipoprotein can migrate in either the B1 or B2 region. In some instances, the split-beta separation may allow easier detection of beta-migrating monoclonal gammopathies.

How to Evaluate Monoclonal Gammopathies



SPIFE Split Beta SPE separation of patient serum. Note monoclonal band in the gamma region





Immunofixation of patient serum characterized the monoclonal protein as an IgM - λ.

1. Perform serum and urine protein electrophoresis. A 24-hour urine specimen is preferable, but a first-morning specimen is adequate to characterize the monoclonal protein. Only electrophoresis can demonstrate the monoclonal nature of protein.
2. Quantitate monoclonal peak by densitometry. Modern densitometry allows quantitation of serum monoclonal proteins separate from normal immunoglobulins.
3. Identify the monoclonal protein(s) using immunofixation on serum and urine. Specific serum immunoglobulins may be quantitated by nephelometry to assess general immune competence and provide base values of immunoglobulin concentrations.

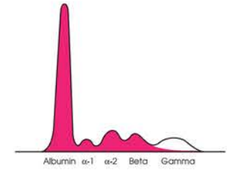
Electrophoretic Characteristics of Serum Proteins in Certain Clinical Conditions

	Albumin	Alpha 1	Alpha 2	Beta	Gamma
Acute Inflammation	↓N	↑	↑		N↓
Subacute Inflammation	N↓	N	↑	N	N
Chronic Inflammation	↓N	↑	↑	N↑	↑
Chronic Cirrhosis	↓↓		↓	↓	↑
Acute Cirrhosis	↓↓		↓	Beta-Gamma Bridge	
Nephrotic Syndrome	↓↓		↑↑		N↓
Hypogammaglobulinemia					↓↓↓
Paraprotein	↓	↓	↓	Homogeneous Peak	
Hypergammaglobulinemia	↓				↑
Hypoproteinemia (Protein Loss)	↓↓	N↑	N↑	↓	↓N or ↑
Alpha$_1$ Antitrypsin Deficiency		↓↓			

	Albumin	Alpha 1	Alpha 2	Beta	Gamma
Carcinomatosis	↓	↑	↑		
Diabetes Mellitus	↓		↑	↑	
Hepatitis, Viral	↓	↓	↓	↑	↑
Hodgkins Disease	↓		↑		↑
Leukemia, Myelogenous	↓				↑
Lupus Erythematosis	↓		↑		↑
Lymphoma	↓				↓
Macroglobulinemia	↓			↑	↑
Myeloma	↓				↑
Rheumatoid Arthritis	↓		↑		↑
Ulcerative Colitis	↓	↑	↑	↓	↓

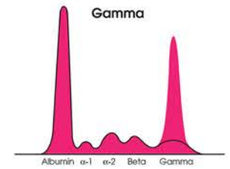
↓: decrease ↑: increase N: normal

Hypogammaglobulinemia

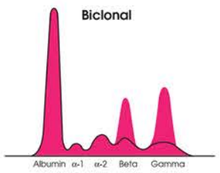


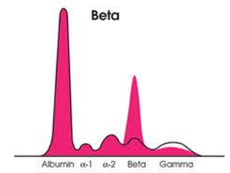
Decreased amounts of most or all immunoglobulins occurs in immunodeficiencies such as Wiskott Aldrich syndrome, infantile X-linked globulinemia and transient hypogammaglobulinemia deficiency. Decreases may involve selective immunoglobulin classes as in selective IgA deficiency, IgG variable common deficiency, sub-class deficiency and selective kappa or lambda light chain deficiency. Most of these are hereditary and manifest in childhood. Immunoglobulin deficiencies acquired in adulthood can be secondary to disease states such as monoclonal gammopathies, or can be induced by immunosuppressive therapy. The occurrence of hypogammaglobulinemia requires immunofixation or immunoelectrophoresis analysis.

Monoclonal Gammopathies

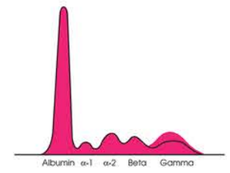


Monoclonal gammopathies are disorders of immunoglobulin synthesis consisting of a proliferation of B cell clones. This increase of plasma cells results in a single homogenous spike (M protein) in the beta-gamma region. When M protein is present, there is usually a decrease in normal immunoglobulins. High M protein levels and decreased levels of other immunoglobulins may be associated with a malignant clinical course.





Polyclonal Gammopathies



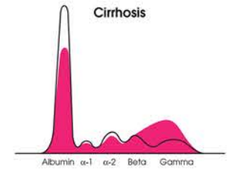
Polyclonal gammopathy is a secondary disease state characterized by a broad, diffuse increase of the gamma fraction. Usually all three major immunoglobulins (IgG, IgA and IgM) are increased in variable concentrations. Polyclonal gammopathy is the second most commonly seen abnormality after hypoalbuminemia.

Continued evaluation of polyclonal gammopathies has some prognostic value. Clinical improvement in a primary disease state is marked by a decrease of the gamma fraction.

Polyclonal gammopathy is seen in a wide variety of disorders:

1. Chronic liver disorders
2. Collagen disorders
3. Chronic infections
4. Metastatic carcinoma
5. Cystic fibrosis
6. Thermal burns

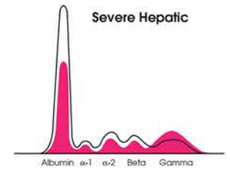
Liver Disease



Since the liver is the site of albumin synthesis, it is to be expected that diseases affecting this organ would also affect the level of albumin within the body. The liver, however, has considerable reserve synthesis capability, and only in advanced hepatocellular diseases are decreased levels of albumin seen.

Listed below are major hepatic problems and the expected serum protein profiles:

1. Acute viral hepatitis – increase of IgG and IgM.
2. Chronic liver disease (including cirrhosis) – marked increase of IgG and IgM with a decrease of albumin and transferrin.
3. Biliary destruction – may show an increased level of C4 and beta lipoproteins.



Normal

Abnormal

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An Educational Service of

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