

concentration.

Toxicity: Psychosis, CNS depression, ataxia, stupor, coma, hypotension. Chronic: Lethargy, confusion, skin rash, ataxia, proteinuria, hematuria, hepatic alteration.

Urinary excretion 10%-40%; plasma binding <1%; volume of distribution 0.7 L/kg; half life 35-55h decreased in children; peak time 2-5h; peak concentration 24-44 µg/mL after 250 mg orally steady state.

Sampling: 2 mL serum. Steady state is reached after 5 -15 days.

Reference Interval:

Therapeutic:	60 -100 µg/mL (up to 125 µg/mL)
Toxic:	> 150 µg/mL

Extractable Nuclear Antigen (ENA) see

Ribonucleoprotein U1-snRNP Antibody Smith (SM) Antibody; SS-A/Ro and SS-B/La Antibodies

Factor II Mutation (Prothrombin Mutation)

Background: A common hereditary predisposition to venous thrombosis is linked to a mutation at position 20210 in the prothrombin encoding proteingene on chromosome 1q23. The heterozygous form is present in 2% of the population and in 6% of patients with venous thrombosis. In familial thrombosis it is present in 18%. Heterozygous individuals have an up to 3 fold increased risk for venous thrombosis. The risk for arterial thrombosis is still under discussion.

Sampling: 2 mL EDTA or citrate blood. Do not freeze, store at room temperature or at 4°C. Ship to laboratory within 5 days.

Reference Interval: Normal: G20210A Mutation not present

Factor V Leiden Screening Test see Activated Protein C Resistance Protein

Factor V Mutation (Leiden Mutation)

Related Information:

- Activated Partial Thromboplastin Time
- Activated Protein C Resistance Protein
- Antithrombin III
- Protein C
- Protein S, Total

Background: The factor V Leiden mutation is a point mutation on chromosome 1q23 replacing guanine at position 1691 by an adenine, which substitutes arginine with glutamine at amino acid residue 506 leading to activated protein C resistance. There is at least one more, very rare factor V mutation. The DNA based method allows determination of heterozygosity and homozygosity for the mutation.

Clinically, as in other congenital biochemical defects in hypercoagulation states, a family history is usually present. The thromboses are in most cases venous, and may occur in large veins of the abdomen. First episodes usually occur in early adulthood rather than in childhood.

Functional test with high sensitivity and specificity to detect factor V mutation is PTT (activated partial thromboplastin time) done on plasma samples

Sampling: 2 mL EDTA or citrate blood for genetic testing

Reference Interval: Report on diagnostic findings
Factor V gene/chromosome 1q23
mutations not detectable/detectable

E-F

Fecal Pancreatic Elastase 1

Synonyms: Cholesterol-Binding Pancreatic Proteinase ;
Pancreatic Elastase

Background: Human pancreatic elastase is a steroid binding protein and an endoprotease. It binds to bile acids and sterols for transportation of cholesterol and metabolites through the intestinal tract.

There is a linear correlation between elastase 1 secretion and pancreatic secretion of lipase, amylase and trypsin

Elastase 1 is not degraded during intestinal passage, in opposite to chymotrypsin which undergoes a 99.5% degradation, the fecal elastase is a parameter for pancreatic function.

Useful test in the assessment of severity of pancreatitis, in the differentiation malabsorption from maldigestion in cases of steatorrhea. Useful in the diagnosis of Cystic Fibrosis, with a sensitivity and specificity of 90%-100%.

Sampling: Approx 2 g of stool, stable for 3 days at 20°C

Reference Interval:

Children:	Rising during the first month of life and stay	> 500 µg / g during childhood
Adults:	Normal exocrine pancreatic function	200-2500 µg / g stool
	Mild exocrine pancreatic insufficiency	100-200 µg / g stool
	Severe exocrine pancreatic insufficiency	<100 µg / g stool

Ferritin, Serum or Plasma

Related information: Blood Count, Complete
Cooper (Cu), Serum or Urine
Erythropoietin (EPO), Serum
Hemochromatosis, DNA Test
Iron (Fe), Serum
Iron (Fe), Urine

Occult Blood in Stool (Hemoccult)

Porphyrins, Quantitative, Urine, Stool

Transferrin and Total Iron Binding Capacity, Serum

Background: Ferritin is an ubiquitous protein with iron sequestration and storage function. Apoferritin (MW 440 kDa) is composed of heavy and light chains and can bind up to 4000 iron molecules of the Fe^{3+} form, moved into the interior of the molecule and growth of the core of ferric hydroxyphosphate. Ferritin is present in all cells, especially in erythroid precursor cells, in macrophages, and in hepatocytes. Ferritin production is induced by iron and cytokines regulate transcription and translation as well. Small amounts are released into the plasma, which is proportional to the intracellular ferritin stores.

Useful parameter in the diagnosis of hypochromic, microcytic anemias to differentiate into

- 1) iron deficiency anemia with low ferritin, low serum iron, low saturation, high total iron binding capacity (TIBC) and transferrin
- 2) anemia due to chronic diseases with low serum iron, high to normal ferritin, normal to low transferrin and TIBC
- 3) and thalassemia with normal to high ferritin

Increased in iron overload and decreased in iron deficiency anemia.

Hemochromatosis: ferritin and iron saturation are usually increased, but a better screening test for hemochromatosis is transferrin saturation which may indicate hemochromatosis if levels are in men >60% or in women >50%.

Please also see Iron (Fe), Serum.

Limitations: Loss of ferritin from hepatocytes in liver cirrhosis, autoimmune hepatitis, chronic hepatitis increases ferritin levels. As an acute phase reactant ferritin may be elevated in infectious diseases, acute renal failure. It may be elevated hemolytic anemias, malignancies such as leukemias, or lymphomas.

Extreme high levels up to 400 000 $\mu\text{g/L}$ have been reported in HIV infected patients with histoplasmosis or hemophagocytosis.

Sampling: 1 mL serum or plasma

Reference Interval:		($\mu\text{g/L}$)
Newborns		25-200
First month		200-600
2-5 month		50-200
0.5 – 15 years		22-75
Adults		
Male		35-250
Female	< 40 years	35-122
	> 40 years	35-250

Fetoprotein, Alpha, see Alpha,-Fetoprotein (AFP), Serum

Fibrinogen Functional

Related Information: Activated Partial Thromboplastin Time
D-Dimers
Prothrombin Time
Thrombin time

Synonyms: Factor I

Background: Thrombin converts fibrinogen to a fibrin clot. Fibrinogen is synthesized by the liver; it may be decreased during liver diseases, particularly in late stages. In disseminated intravascular coagulation (DIC) fibrinogen is decreased by excessive thrombin generation; in advanced DIC with poor prognosis, fibrinogen may be elevated. Fibrinogen is decreased during thrombolytic therapy or fibrinolysis, since plasmin split fibrinogen and fibrin.

Fibrinogen is an acute phase reactant. It is elevated during pregnancy, physical activity, and may be a marker for increased risk for myocardial infarction.

Rare forms of hereditary deficiencies of fibrinogen have been described. Clinically they may present with bleeding symptoms such as epistaxis, gastrointestinal bleeding, miscarriage, intracranial hemorrhage. Usually, symptoms are milder than those caused by factor VIII or IX deficiencies.

Genetics allow classifying three forms: The homozygous quantitative form or afibrinogenemia with bleeding, the heterozygous quantitative form or hypofibrinogenemia with a moderate decreased fibrinogen level and little tendency of bleeding and the qualitative form or dysfibrinogenemia, with little or no bleeding history which is characterized by various mutations, producing dysfunctional fibrinogen. Clinically it may present with an increased risk for venous thrombosis and in a minor group of arterial thrombosis. Prevalence in patients with thrombosis is estimated 0.8%.

Useful in the evaluation of disseminated intravascular coagulation, prolonged PT and PTT and in the evaluation of bleeding.

Limitations: Fibrinolytic degradation products >100 µg/mL and heparin >0.6 U/mL falsely lower fibrinogen values. Dysfibrinogenemia also lowers fibrinogen test results.

Moderate hemolyzed, icteric or lipemic plasma will not interfere with the assay.

Sampling: 2 mL citrate plasma, mix well, tube must be filled no less than 80% of the maximum volume. Separate plasma soon, plasma is stable for 5h at 4°C.

Reference Interval: For the functional, Clauss based method:
150-450 mg/dL

Fibrinopeptide A and B see Thrombin Time

FK- 506 see Tacrolimus (FK 506), Whole Blood

Folic Acid, Red Blood Cells

Related Information: Blood Count, Complete
 Folic Acid, Serum
 Homocysteine, Total, Plasma
 Phenobarbital, Serum
 Primidone, Serum
 Vitamin B 12 , Plasma or Serum

Background: Red blood cell (RBC) folate is a more reliable parameter to assess folate deficiency than serum due to minor variations caused by diet. Celiac disease can be ruled out when RBC folate and D-xylose absorption is normal.

Megaloblastic anemia present, if due to folate deficiency, values < 100 ng/mL erythrocytes.

Sampling: 2 mL of EDTA blood, fasting sample preferred, stable for 2 days at room temperature.

Reference Interval: 150 – 600 ng/mL erythrocytes

Folic Acid, Serum

Related information: Blood Count, Complete
 Folic Acid, Red Blood Cells
 Homocysteine, Total, Plasma
 Phenobarbital, Serum
 Primidone, Serum
 Vitamin B 12 , Plasma or Serum

Background: The reduced form of folic acid is essential for the synthesis of amino acids, purines and DNA. Clinically, anemia, congenital malformation in newborns and vascular diseases are seen in deficiency.

Folic acid is composed of p-aminobenzoic acid and glutamic acid. Dihydrofolate dehydrogenase catalyses the reduction reaction to dihydrofolic acid and to tetrahydrofolic acid, which are transformed to folate cofactors serving as donators of one carbon units for oxidation, particularly in purine and pyrimidine synthesis and amino acid conversions such as homocysteine to methionine (cobalamin also required). Elevated homocysteine levels are linked to vascular diseases. Nucleoside synthesis impairment, through decreased synthesis of precursors may cause megaloblastic anemia.

Daily 50-200 ug of folic acid is usually absorbed from an average intake of 500-700 ug (US). The richest sources are yeast, liver, kidney and green vegetables. In the human liver 2-20 mg are stored. Stores are sufficient for 1-6 month. Before absorption, alpha 1-glutamyl transferase within the intestinal mucosa must hydrolyze all but one glutamyl residues of the polyglutamate form of N-methyltetrahydrofolate. Excretion via urine and stool.

Limitations: Hemolysis increase falsely folic acid levels. Decreased by contraceptives. Significant fluctuations with diet.

Sampling: 1 mL serum, overnight fasting sample preferred. Avoid hemolysis and exposure to light. 20% loss per day at room temperature and light exposure.

Reference Interval:

Adult: 5.89 nmol/L - 33.08 nmol/L (2.6 - 14.6 ng/ml)
(convert: ng/ml x 2.266 = nmol/L)

Children: (nmol/L)

year	Male	Female
0-1	16.3-50.8	14.3-51.5
2-3	5.7-34.0	3.9-35.6
4-6	1.1-29.4	6.1-31.9
7-9	5.2-27.0	5.4-30.4
10-12	3.4-24.5	2.3-23.1
13-18	2.7-19.9	2.7-16.3

E-F

Follicle Stimulating Hormone (FSH), Serum, Urine

Related information: Estradiol, Serum
Estrone, Serum
Luteinizing Hormone (LH)

Background: Please see Luteinizing Hormone (LH), Serum.

Limitation: FSH increases with age and is increased in smokers.

Sampling: Serum: 2 mL of serum. Avoid hemolysis. FSH is stable for 4h at room temperature, 2 weeks at -20°C. Avoid freezing thawing cycles.

Urine: 10 mL of urine. Since FSH is less pulsatile, a less than 24h collection period is suitable. Note total quantity and length of collection period.

Reference Interval:

Serum:	Male		1.0 - 8.0 IU/L
	Female	follicular phase:	2 - 8 IU/L
		ovulatory peak:	5 - 25 IU/L
		luteal phase:	2 - 8 IU/L
		post menopausal:	30 - 100 IU/L
Children		1.5 - 8.0 IU/L	
Urine:	Male > 8 years		< 20 IU/24h
	Female	9-15 years	< 22 IU/24h
		> 15 years	< 30 IU/24h
		post menopausal:	< 60-90 IU/24h
	Children		< 5 IU/24h

Free Light Chains Structure (FLC), Serum

Related Information: Albumin, Urine
Free Light Chains Structure, Urine
Immunoglobulin G (IgG), Serum, Urine, CSF
Protein Electrophoresis, Serum

Background: Monoclonal gammopathies are characterized by the clonal expansion of plasma cells. The disorders can be diagnosed and monitored by monoclonal immunoglobulins secreted by plasma cells. Monoclonal gammopathies include multiple myeloma (MM), light chain myeloma, Waldenstrom macroglobulinemia, nonsecretory myeloma (NSMM), smoldering multiple myeloma, monoclonal gammopathy of undetermined significance (MGUS), primary systemic amyloidosis (AL) and light chain deposition disease (LCDD). AL, LCDD and NSMM display low concentrations of serum monoclonal light chains which cannot be detected by protein electrophoreses or immunofixation techniques but by more sensitive techniques detecting light chains not bound to immunoglobulins (free light chains). Sensitivity (referred to the reference interval) for detecting polyclonal hypergamma globulinemia, AL, LCDD, MM is 90%-100 % for a 95% confidence interval, specificity 92%-98%.

The ratio may be used for discrimination between monoclonal gammopathy of undetermined significance (MGUS) and MM. Kappa/ lambda ratio between 0.6 and 4.2 increase the probability of MGUS in asymptomatic patients. For AL an abnormal ratio in 90% of the patients has been reported.

Sampling: 1 mL Serum

Reference Interval:

	95% reference interval	diagnostic range
Kappa free light chain	3.3-19.4 mg/L	
Lambda free light chain	5.7-26.3 mg/L	
Ratio kappa/lambda free light chain	0.3-1.2	0.26-1.65

Free Light Chains Structure, Urine

Related Information: Immunoglobulin G (IgG), Serum, Urine, CSF
Albumin, Urine
Protein Electrophoresis, Serum

Synonyms: Bence Jones Protein, Urine

Background: Normal renal function renders protein excretion < 150 mg per day. 70% of filtered protein are albumin; transferrin, low molecular weight protein and immunoglobulins. An excretion rate of the fraction of light chains of more than 50 mg/24h favors a diagnosis of malignant monoclonal gammopathy.

Sampling: Aliquot 5 mL of a 24h urine, collected in a sterile container without preservatives, keep refrigerated. Note total quantity.

Reference Interval: Type kappa: < 22 mg/L
Type lambda: < 12 mg/L