C1 Esterase Inhibitor, Quantitative, Serum

Synonyms: C1 Inactivator; C1 Inhibitor

Background: The C1 esterase inhibitor is an alpha 2 globulin acute phase protein. It belongs to the serpin family of protease inhibitors, produced by hepatocytes, monocytes, fibroblasts and vascular endothelial cells. It inhibits the catalytic subunits of the first component of the classic complement pathway (C1r and C1s). Deficiency leads to activation of C1 with generation of C2 kinin which mediates angioedema, which may involve the airway and lung to a life threatening extent. Massive swelling of subcutaneus tissue and gastrointestinal tract symptoms may occur.

The C1 esterase inhibitor also inhibits factor XII and kallikrein in the intrinsic pathway of coagulation, and activates plasminogen to plasmin in the fibrinolytic system.

Useful parameter in the assessment of C1 inhibitor deficiency or dysfunction in acquired or hereditary forms in angioneurotic edema.

The inherited forms are autosomal dominant with one normal gene. The common form (85%) of hereditary angioneurotic edema (HAE) is caused by a decrease in the synthesis of the C1 esterase inhibitor, the less common form (15%) is due to altered function. In both forms, C1q is normal, C1s activity is uncontrolled and therefore decreases in C2 and C4 levels occur.

The acquired angioneurotic edema (AAE) affect elder adults with autoimmune or lymphoproliferative disorders. It is characterized by immune complexes consuming large amounts of C1q and C1 esterase inhibitors thus leading to quantitative and functional deficiency of the C1 esterase inhibitor In addition C1q. C2, C3, C4 levels may be reduced as well. The type II form is characterized by autoantibodies which inhibit the functional activity of the C1 esterase inhibitor.

	Antigen	Function	C1q level	C2, C4 level
Type I HAE	decreased	decreased	normal	decreased
Type II HAE	decreased or normal	decreased	normal	decreased
Type I AAE	decreased or normal	decreased	decreased	decreased

Type II AAE in addition to type I autoantibodies are present

Sampling: 1 mL serum

Reference Interval: 15 – 35 mg/dl

C1q Complement, Serum

Related Information: C4-Complement (β1-E), Serum

Background: C1q is a 400kD protein of the classical complement system pathway, able to bind to activated surfaces and to C1s, which split C4 and C2.

Decreased levels of C1q, C1r, C1s (as well as C2,C3,C4) does not significant affect the ability to defend against infections, however patients have a higher incidence of autoimmune diseases (most common are SLE or SLE- like diseases, rheumatic diseases, vasculitis, dermatomyositis).

In liver failure C1q is normal; C3 and C4 are decreased due to decreased production.

In malnutrition state C1q and C3 are decreased, C4 is normal
In nephrotic syndrome C1q, C2, C8 C9 may be decreased, C3 C3c, C4 are normal,
Patients with extended burns have decreased complement levels.

Sampling: 1 mL serum

Reference Interval: 10 – 25 mg/dL

C3-Complement (β1C / β1A-Globulin), Serum

Related Information: C4-Complement (β1-E), Serum
Cryoglobulin, Qualitative, Serum and Plasma

Background: C3 is synthesized mainly in the liver and comprises approx 70% of total complement protein. It is an essential compound for the classical and alternative pathway.
C3 determination is useful in the detection of congenital deficiency and in the evaluation of immunologic disorders with increased consumption of complement such as chronic hepatitis particularly in hepatitis C associated cryoglobulinemia vasculitis, immune complex diseases such as membranoproliferative glomerulonephritis.
Used in the evaluation of the activity of systemic lupus erythematosus. C3 is decreased in lupus nephritis and glomerulonephritis as well as in infective endocarditis and disseminated intravacular cougulation (DIC).
Hereditary C3 deficiency, a rare disorder, presents with recurrent infections particularly caused by encapsulated bacteria such as Neisseria meningitidis; Streptococcus pneumoniae, Hemophilus influenzae, clinically presenting as sinopulmonary infections, meningitis, paronychia, impetigo and immunocomplex diseases.
Deficiency in the complement function may lead to autoimmune diseases possibly due to the lack of clearance of apoptotic cells by macrophages.

Sampling: 1 mL serum

Reference Interval:

Children:	2 - 5 years:	90 – 140 mg/dL
	6 - 10 years:	100 – 150 mg/dL
	11 – 18 years:	100 – 170 mg/dL
Adults:		80 – 200 mg/dL

C4-Complement (β1-E), Serum

Related Information: HLA-B27

Background: C4 protein is encoded in the class III region of the major histocompatibility complex. The 2 known isotypes differ by 4 amino acids (C4A and C4B).
C4 is only involved in the classical pathway. Immune complex production will decrease hemolytic activity (CH50), C3 and C4. Decreased levels are observed in hereditary angioedema since lack of C1 esterase inhibitor leads to the lyses of C2 and C4 by the C1 esterase.

Clinically C4 deficiency presents with an increased incidence of bacterial infection particularly with S. pneumoniae.

In Alzheimer's disease complement activation may play a role.

C4 levels are used in the assessment of autoimmune diseases such as lupus erythematosus, rheumatoid arthritis, glomerulonephritis, chronic hepatitis, cryoglobulinemia, and hereditary angioedema.

Sampling: 1 mL serum

Reference Interval:	Children:	2 - 5 years	14 – 30 mg/dL
		6 - 10 years	16 – 32 mg/dL
		11 – 18 years	17 – 36 mg/dL
	Adults:		20 – 50 mg/dL

C-ANCA see Antineutrophil Cytoplasmatic Antibody (ANCA)

C-Peptide, Serum

Related Information: Glucose, Blood, Urine, Liquor
Insulin Auto-Antibody (human) (IAAB), Serum
Insulin, Serum

Synonyms: Connecting Peptide ; Insulin Connecting Peptide

Background: C-peptide is a 31 amino acid peptide segment connecting the 21 amino acid A chain and the 30 amino acid B chain of proinsulin. Proinsulin is processed to insulin and C-peptide in the secretory granules of the beta cells by the convertases PC2 and PC1/PC3 and by the carboxypeptidase H. Proinsulin has 10%-15% of the biological activity of insulin and has three times the half life time of insulin. C-peptide and insulin are secreted in equimolecular amounts into the portal vein, but in serum the ratio is 5:1 to 15:1 due to hepatic clearance of insulin. 50% of insulin is removed during the first passage through the liver, but there is no removal of C-peptide. In cirrhosis, serum insulin is increased due to reduced hepatic clearance. Half life of proinsulin and C-peptide is 30 min but 4-9 min for insulin.

Useful in differential diagnosis of hypoglycemia: Patients with insulinomas or hypoglycemia from surreptitious insulin administration or insulin secretagogues (sulfonylurea drug) display high levels of C-peptide, insulin and proinsulin.

Useful in the classification of diabetes mellitus: Patients with type 2 diabetes have normal to elevated C-peptide and insulin levels in the absence of beta-cell autoantibodies. In type 1 diabetes mellitus, serum C-peptide and insulin values are low to undetectable, up to 90% have beta-cell autoantibodies.

Further used in beta cell function assessment and evaluation of pancreas transplanted patients.

Limitations: Increased in renal failure, since reduced excretion by the kidney. Some insulinomas may lack the increase of C peptide.

Sampling: 1 mL serum or heparin plasma, fasting sample preferred. Separate serum soon and freeze.

Reference Interval: Fasting C-peptide levels 0.51 - 2.70 ng/mL. Higher in preterm neonates and in infants. After stimulation with glucose or glucagon, levels increase up to 5.6 ng/mL.

C-Reactive Protein, Serum

Related Information: Albumin, Serum
Alpha 1 Antitrypsin, Serum
Haptoglobin (Hp), Serum
Sedimentation Rate

Synonyms: CRP

Background: The increase of CRP starts a few hours after initiation of an inflammatory process. It is sensitive but not specific for acute injuries, bacterial infections, or inflammation.

Use: Assessing cardiac risk: Elevation of CRP may indicate high risk for cardiovascular and peripheral vascular disease. IL-6 and TNF alpha may be produced within plaques, which increase CRP production in the liver. Adding lipid levels, the assessment of cardiovascular risk is more precise.

Cardiac troponins and CRP determines day to month risk of adverse cardiac events, useful in patients with unstable angina pectoris, non-Q wave myocardial infarction, normal CK-MB levels. It is recommended to average the values of 2 samples, 2 weeks apart in a metabolic stable non-fasting or fasting patient. CRP levels <1 mg/L indicate low risk, 1-3 mg/L average risk, > 3 mg/l elevated risk.

CRP was found to be more sensitive in severity assessment in pelvic inflammatory disease or in sepsis, as compared to leukocyte count or temperature and may be useful as an additional marker for appendicitis.

Sampling: 1 mL serum, do not freeze, avoid hemolysis and lipemia.

Reference Interval:

	(mg/L)
Newborn (cord blood)	< 0.6
4 days - 1 month	< 1.6
Children	0.068-8.2

Adults (95% population distribution):

	male	female
25-34 years	0.08- 7.2	0.07-17.8
45-54 years	0.19-13.9	0.15-12.1
65-74 years	0.33-18.5	0.3-16.6
		Pregnancy at delivery <47

CA 15 - 3 (Breast), Serum

Related Information: Carcinoembryonic Antigen (CEA), Serum
HIV Type 1 and 2, Serology

Background: CA 15-3 is a high molecular carbohydrate antigen of 300kd of the mucin family. The marker is useful in monitoring metastasis of carcinomas of the mammary, but it fails, since lacking sensitivity, in screening for carcinomas.

The correlation for the sensitivity of CA 15-3 to detect the carcinoma and the stage of the carcinoma of the mammae are: During stage I sensitivity for detection is 4%-16%, stage II 13%-54%, stage III 65%, and stage IV 54%-91%. There is also a correlation with the location of metastasis.

Combination of CEA and CA 15-3 enhances the sensitivity for monitoring mammae carcinoma and detection of metastasis.

Carcinoma of the ovary increases CA15-3 in 39%-71% of the patients, and in 14%-26% of patients with carcinoma of the uterus, also in 10%-71% in patients with pulmonary carcinomas, and in 10-61% in gastric, pancreatic and liver cell carcinomas.

Limitations: Increased values are observed in dialyzed patients (20% >30U/mL), in HIV positive patients (up to 50% >18U/mL) and to a lesser extent during liver diseases or pulmonary diseases. In 4%-11% of patients with mastopathia or adenomas of the mammae values may exceed 25 U/mL.

Sampling: 1 mL serum

Reference Interval: < 30 U/mL

CA 19 - 9 (Gastrointestinal), Serum

Related Information: Bilirubin, Fractionated, Serum
Carcinoembryonic Antigen (CEA), Serum

Background: The tumor marker CA 19-9 is a monosialoganglioside with similarity to the Lewis-a-blood group antigen. CA 19-9 is mainly prevalent in carcinoma cells of the colon, stomach, and pancreas and in a lesser extend in carcinoma cells of the liver, the bile tract, the bronchial tract and the ovary. Useful in the diagnosis of pancreatic carcinomas, since CA19-9 is the marker with the highest sensitivity (70%-95%) and specificity (70%-90%). Furthermore, values correlate with stage of the tumor.

Lower sensitivity for liver cell carcinomas and bile tract carcinomas (20%-80%); for carcinoma of the stomach (26%-60%) but in combination with CEA a sensitivity of more than 50% is achieved. Sensitivity for carcinomas of the colon is 20%–60% and for ovarian carcinomas 15%-85%, depending on the histopathology.

The marker is useful in monitoring of carcinomas of the colon (second to CEA) and of carcinoma of the ovary (second to CA 125).

Limitations: CA 19-9 is elevated in up to 30% of the patients with cholecystitis, cholangitis, cirrhosis, cystic fibrosis. Complete biliary duct occlusion causes values up to 1000 U/mL. In up to 6% of chronic pancreatitis and up to 20% in acute pancreatitis levels up to 100 U /mL occur.

CA 19-9 is absent from the serum of individuals who have the Le (a-b-) phenotype, which is found in approx. 6% of the white US population and in 22% of the black US population. For Le/le, Se/Se individuals cut off values are < 10.3 U/mL. For Le/Le, se/se individuals cut off values are < 61.3 U/mL. There is also a wide intra and interindividual variability, therefore for monitoring purposes values are considered not to be significant if less than 40 to 50%.

Sampling: 1 mL serum or plasma

Reference Interval: < 37 U/mL (see also limitations)

CA 50, Serum (Gastrointestinal)

Related Information: Bilirubin, Fractionated, Serum
CA 19-9, Serum
CA 72-4, Serum (Stomach, Ovary)
Carcinoembryonic Antigen (CEA), Serum

Background: CA 50 is a non-organ-specific tumor marker and it is elevated in serum in a variety of malignancies, especially in gastrointestinal cancers (stomach, pancreas, liver, and colon). In contrast to CA 19-9, high CA 50 levels can also be seen in malignant tumors outside the digestive tract. CA 50 might be positive in Lewis negative patients not capable to synthesize CA 19-9, an observation which is supported by histoimmunological studies, although the clinical value is doubtful since in serum close correlation between CA 50 and CA 19-9 has been observed even in patients who have Lewis negative phenotype. The marker CA 50 is useful for the follow-up of patients with pancreatic cancers, but less useful in diagnosis. Results are comparable to CA 19-9. Overall sensitivity is reported to be 60%-95%, specificity 30%-40%.

- Pancreatic carcinoma:

  Up to 80% of the pancreatic cancer patients may display raised CA 19-9 and CA 50 serum levels. Both markers show a significant serum elevation during advanced stages of the disease. However, CA 50 is not considered to have a major advantage as a tumor marker as compared to CA 19-9. Combination of CA 19-9, CA 242, CA 50, and CA 72-4 may increase the diagnostic sensitivity up to 89%, and serial combined examination could increase the diagnostic specificity to 92%. If combining signs and symptoms with CA 50, the sensitivity may be enhanced to 91%, the specificity to 92%.

  The serum tumor markers levels decrease significantly after radical tumor resection.

- Colorectal carcinoma:

  The serum levels of CEA, CA 50 and CA 242 are elevated in 36%, 16% and 20% of colorectal cancer patients, respectively. The intra-individual fluctuations for CA 50 and CA 242 are up to 15%, but in up to 25% of the patients the serum levels of CA 50 are highly oscillating.

  Dukes stage C-D is associated with significantly higher levels of CEA and CA 50 (16%-21% elevated values in Dukes A and B tumors and 44%-47% in Dukes C and D tumors).

Limitations: Moderately elevated serum levels of CA 50 can be seen in benign hepatobiliary diseases, especially in jaundice cases. False positive results may occur in up to 12% of patients

with chronic pancreatitis, a rate which is comparable to CA 19-9. Overall false positive results in up to 33% of the patients.

Sampling: 1 mL serum

Reference Interval: < 19 U/mL

CA 72 - 4 (Stomach, Ovary), Serum

Related Information: CA 19-9, Serum
CA 125, Serum (Ovary)
Carcinoembryonic Antigen (CEA), Serum

Background: The antibody B72.3 reacts with the locus CA72.4 of the tumor associated high molecular weight glucoprotein. Tissue specific reactions are (84%-100%): breast carcinoma, lung-epithelia cell carcinoma, ovaria carcinoma and to a lesser extend with carcinomatous tissue of the endometrium, pancreas, prostata and stomach.

Clinically CA 72-4 is indicated as therapy and follow up marker in carcinomas of the stomach in combination, as a second marker, with CA 19-9 and CEA. CA 72-4 is useful as a second marker in carcinoma of the ovary and carcinoma of the colon.

Limitations: Elevated levels in up to 25% of the patients with cirrhosis, pancreatitis, non-malignant pulmonary diseases, rheumatic diseases, ovarian diseases, diseases of the breast, and GI tract disorders.

- Carcinoma of the stomach:

Diagnostic specificity >95%. Sensitivity overall is 40%-45% but up to 80%, also depending on the stage of the carcinoma. The tumor marker CA 19-9 has a lower sensitivity (30%), also CEA sensitivity is lower (20%-25%). A combined testing for CA 72-4 and CA 19-9 increases sensitivity by 15%. Values return to normal post-operative within 1-2 weeks. A relapse is indicated in 60%-70% of the cases by increasing levels of CA 72-4 (lower sensitivity for relapses for CA19-9 with 50% and CEA with 20%).

- Carcinoma of the colon:

Specificity 95-98%. Sensitivity 20%-43%; combination of CEA and CA 72-4 enhances sensitivity by up to 17%. Post-operative the marker decrease within 3 weeks. Increasing values are reported in up to 80% of the relapse cases and combination of CEA with CA 72-4 enhances sensitivity by 10%.

- Carcinoma of the ovary:

Specificity 85%-95%. Sensitivity 10%-80%, stage dependant. Combining CA 125 with CA 72-4 increase sensitivity by about 10%.

- Other carcinomas:

Increased values of CA 72-4 are reported in carcinomas of the gall ducts (35%-50% of the patients); of the pancreas (up to 35%) and carcinoma of the esophagus (up to 25%).

Sampling: 1 mL serum or plasma, stable for 1 week at 4ºC, otherwise freeze.

Reference Interval: < 5.3 U/mL

CA 125 (Ovary), Serum

Related Information: CA 15-3, Serum
CA 19-9, Serum
Carcinoembryonic Antigen, Serum
Heterophilic Antibodies

Synonyms: Cancer Antigen 125; Carbohydrate Antigen 125

Background: CA 125 is present in healthy individuals at levels < 35 U/mL with a half life time of 5 days. In patients with ovarian carcinomas half life is extended to 12 days and extending further in late stages or large tumor masses.

Clinically the tumor marker is relevant in monitoring ovarian carcinomas and as a second marker in carcinomas of the pancreas (first marker CA19-9).

Diagnostic sensitivity is reported 82%-96% for carcinoma of the ovary at a threshold of 35 U/mL, down to 88 % at 65 U/mL.

Diagnostic specificity is 99% for ovarian carcinomas as compared to healthy individuals, 83% as compared to patients with inflammatory diseases of the ovary or fallopian tubes and 92% as compared to patients with benign tumors of the ovary.

Limitations: Increased to more than 65 U/mL in acute inflammation of the ovary (up to 25%), acute peritonitis (60%), gastrointestinal diseases (8%), cholecystitis (23%), hepatitis (5%), and cirrhosis 35%).

Sampling: 1 mL serum. Since abdominal surgery increases CA 125 levels, specimen should not be drawn within 3 weeks after surgery.

Reference Interval: 0-35 U/mL (for 99% confidence interval)

CA 549 (Breast), Serum

Related information: CA 15 - 3, Serum (Breast)
Carcinoembryonic Antigen (CEA), Serum

Background: CA 549 is a mucinous circulating tumor marker recognized by two monoclonal antibodies (BC4E549 and BC4N154) directed against tumor and milk fat globule membranes.

Overall sensitivity of CA 549 for breast cancer is 77% and specificity 92% (as compared to 61% and 92% for CEA).

No false positive results have been reported in pregnant women.

Early breast cancer:

Sensitivity for detecting early breast cancer is reported 21%-22% for CA 549 (cut off = 12.6 U/mL), as compared to 20% for CA 15-3 (cut off = 25 U/mL) and 11% for CEA (cut off = 6 ng/mL).

CA 549 has a low negative predictive value (0.5) due to a low sensitivity in the detection of early breast cancer. The test has a high positive predictive value (0.9) reflecting a high specificity for the disease. False positive results have been reported in 1.5%-22% of women with benign breast disease, and in up to 26% of patients with nonmalignant liver disease. In metastatic

cancer of prostate, ovary, endometrium, colon, and lung CA 549 was elevated in 12% to 50% of the cases with levels less than 120 U/mL.

Metastatic breast cancer:

Sensitivity in detecting metastatic breast cancer is reported for CA 549 to be between 70% and 83% as compared to CEA 45%, MCA 59%, and CA 15-3 71%. Sensitivity increases only slightly (6%-8%) when two or more markers are simultaneously considered. Overall sensitivity of correlation with objective response is in the range of 50%-70% in patients with abnormal baseline marker values, and in the range of 40%-90% in patients with normal baseline values. The combination of two or more markers did not improve sensitivity, but decreased specificity of correlation with objective response.

Follow up:

In patients without clinical signs of disease after surgery abnormal CA 549 was reported in 11%-16% of the patients, in 82% of the patients with disease progression, in 70% with stationary disease, in 63%-76% with partial remission and in 23%-33% with complete remission.

Sampling: 1 mL serum or plasma

Reference Interval: < 12.1 U/mL

Calcitonin, Serum or Plasma

Related Information: Calcium, Serum
Carcinoembryonic Antigen (CEA), Serum
Catecholamines, Fractionation, Plasma
Catecholamines, Fractionation, Urine
Parathyroid Hormone, Intact, Serum
Phosphate, Inorganic, Urine

Synonyms: Thyrocalcitonin

Background: Calcitonin is synthesized by the parafollicular cells (C-cells)of the thyroid gland and to a minor extend by neuroendocrine cells of the bronchopulmonary system, the thymus and the adrenal medulla, Calcitonin is a monomer of 32 amino acid peptide of 3.5 kDa. The secretion of calcitonin is regulated by iodized calcium and the gastrointestinal peptide hormones in particular gastrin. Calcitonin is metabolized by the kidney within several minutes.

Calcitonin is the main calcium regulating factor, lowering calcium and phosphorus. Furthermore it directly inhibits osteoclastic bone resorption.

Used in assessment of medullary carcinoma of the thyroid, in postoperative monitoring and in the search for metastasis, CEA is the second useful marker in medullary carcinomas.

Increased concentrations occur in familiarly forms of C-cell hyperplasia, some forms of the disease display abnormal values after stimulation only.

Sampling: 1 mL serum, avoid hemolysis and keep refrigerated.

Reference Interval: < 13 pg/mL

Stimulation with pentagastrin or calcium: < 350 pg/mL in men and < 100 pg/mL in women.

Calcium (Ca) Total, Serum

Related Information:
Aluminium, Serum or Urine
Calcium (Ca), Urine
Hydroxyproline, Total, Urine
Magnesium (Mg), Serum
Magnesium (Mg), Urine
Osteocalcin, Serum or Plasma
Parathyroid Hormone, Intact, Serum
Phosphate, Inorganic, Serum
Phosphorus, Inorganic, Urine
Potassium, Serum or Plasma
Potassium, Urine
Pyridinolines
Vitamin D, Serum

Background: With approx 1 kg of calcium it is the fifth most prevalent elements in the body and the most common cation. 99% is bound in the bone as hydroxyapatite. 50% of serum calcium exists in the free ionized form, 10% is complexed with anions (lactate, bicarbonate, phosphate and citrate), 40% is bound to plasma proteins (80% to albumin). Plasma protein binding is ph dependent; alkalosis promotes decreased binding, acidosis an increase.
Ionized calcium in the extracellular fluid is kept around 1.25umol/L by PTH and 1,25-dihydroxyvitamin D_3, targeting bone, kidney and the intestine. PTH in combination with 1,25-dihydroxyvitamin D_3 acts on the bone by releasing calcium and on the kidney by increasing phosphorus secretion and calcium resorption.

Hypercalcemia:
-Primary hyperparathyroidism is characterized by elevated ionized calcium (80% have elevated total serum calcium levels), hypophosphatemia and normal kidney function. In some cases coexistence with endocrine tumors.
-Parathyroid hormone-related protein cause in carcinomas without bone metastasis (primary squamous cell carcinoma of the lung, head, neck, breast, kidney liver bladder, ovary) increase of serum calcium.
-Minor hypercalcemia is seen in dehydration, sarcoidosis, and other granulomatous diseases.
-Abuses of calcium containing ulcer medications and vitamin D-hypervitaminoses.
-Hypercalcemia may occur in hyperthyroidism, Addison disease, acromegaly, pheo-chromocytoma, idiopathic hypercalcemia of infancy, Williams's syndrome, liver diseases, bacteremias, cat-scratch disease.
-Drugs: lithium, thiazides, antiestrogens, estrogens.

Decreased Calcium:
Since about 40% of calcium is bound to albumin, and the important fraction of calcium is the unbound ionized form, total calcium has to be adjusted in a decreased albumin state of the patient. Calculate calcium in a decreased albumin state:

Calcium (mmol/L) = measured calcium (mmol/L) + 0.02 X (mean normal albumin – measured albumin (g/L))

Alternative approximation: Add 0.1 mmol/L to the calcium concentration for every 4 g/L of albumin that albumin is below 40 g/L and a similar subtraction for raised albumin.
Decreased total calcium levels are associated with renal failure, hypoparathyroidism with high phosphorus, vitamin D deficiency, osteomalacia, malabsorption, pancreatitis, bacteremia, hypomagnesemia. .
drugs: Barbiturates, calcitonin, corticosteroids, gastrin, glucagon, glucose, insulin , magnesium, methicillin.
Sampling: 1 mL serum. Hemolysis increase calcium levels therefore avoid any forced blood drawing; take blood samples if necessary uncuffed. Citrate containing blood transfusions increase total calcium but decrease ionized serum calcium.

Reference Interval:

	(mmol/L)
Cord	2.05 - 2.80
Premature	1.55 - 2.75
0-10 days	1.90 - 2.60
10 days -2 year	2.25 - 2.75
2-12 years	2.20 - 2.70
Adults	2.10 - 2.58

Critical value: < 1.75 mmol/L may evoke tetany and seizures.
> 3 mmol/L clinically presents with polyuria, anorexia, nausea, constipation, rare cause of coma.

Life threatening: < 1.5 mmol/L
> 3,5 mmol/L

Calcium (Ca), Urine

Related Information:
Aluminium, Serum or Urine
Calcium (Ca), Total, Serum
Hydroxyproline, Total, Urine
Magnesium (Mg), Serum
Magnesium (Mg), Urine
Osteocalcin, Serum or Plasma
Parathyroid Hormone, Intact, Serum
Phosphate, Inorganic, Serum

Phosphorus, Inorganic, Urine
Potassium, Serum or Plasma
Potassium, Urine
Pyridinolines
Vitamin D, Serum

Background: See also Calcium, Total, Serum. Urinary excretion is useful in the evaluation of the skeletal turnover of calcium. In the fasting state, intestinal and renal calcium resorption and excretion are stable and values > 0.04 mmol/L per 100 mL of glomerular filtration (>0.16mg) indicates osteoclastic bone resorption.

Formula for calculation:

Urine Ca (mg/100mL glomerular filtration) = (Urine Ca (mg/dL) x serum creatinine (mg/dL)) / urine creatinine (mg/dL)

Sampling: 10 mL aliquot of a 24 urine collection, ph < 3 adjusted by 25% hypochloric acid. Note total quantity.

Reference Interval: On a average calcium intake diet of 600-800mg/24h:

Male: < 7.5 mmol/24h
Female: < 6.2 mmol/24h

Calcium to Creatinine ratio:
Adults with constant muscle mass:
Calcium (mmol/L) / creatinine (mmol/L) < 0.4
Children: 2.25 at 1 month and dropping to 1.2 at the age 3 years to adult values at the age of 10 years.

Candida albicans, Serology and Culture

Background: Candida albicans is oval yeast with a single bud. In tissue the organism occur also as pseudohyphae. It is part of the normal flora of the mucous membranes of the upper respiratory, gastrointestinal and female genitale tracts. As an opportunistic pathogen, Candida may overgrow in the mouth as white patches (thrush), in high ph vulvovaginitis, diabetes or during antibiotic therapy and in immunosuppressed patients the organism may disseminate into organs. In warm and moist environments Candida albicans may lead to chronic mucocutaneous candidiasis.

Antibody directed against Candida antigen screening on a regular base (weekly) is a valuable tool to monitor patients for therapy and stage of infection.

In contrast, the value of antigen testing is limited, since the sensitivity of the antigen test is low and a negative result can not preclude an antifungal therapy, particularly in immunocompromised patients. Test specificity is high, but most of the patients also have positive blood cultures.

Risk factors for Candida infection: Prolonged ventilation, urinary catheters, intravascular lines, broad spectrum antibiotic therapy, immunosuppression, iv nutrition, ITU stay.

Sampling: Serology: 1 mL serum
Direct detection by culture: genital swab, tracheal fluid, 2g stool

Reference Interval:

Serology:	Differentiation of immunoglobulin class		
	IgA antibody	negative:	< 60 U/mL
		borderline:	60 – 80 U/mL
		positive:	>80 U/mL
	IgG antibody	negative:	< 40 U/mL
		borderline:	40 – 100 U/mL
		positive:	>100 U/mL
	IgM antibody	negative:	< 60 U/mL
		borderline:	60 – 80 U/mL
		positive:	> 80 U/mL

Culture: Report on diagnostic finding: Direct detection by microscopy and culture.

Cannabinoids (Marijuana Metabolites)

Related information: Ethanol, Blood or Urine

Background: The major active compound of marijuana is tetrahydrocannabinol (THC), leading to euphoria, relaxation, altered reception impaired memory. The major metabolite 11-carboxy –THC is excreted in the urine and detectable in chronic smokers for up to 6 weeks, due to the lipophilic nature it is stored in body fat.

Half Life 1-2 days ; volume of distribution 4-19 L/kg ; protein binding 95-98%

Sampling: 10 mL random urine

Reference Interval:

negative: < 50 ng/mL (Confirmation cut off 15 ng/mL), depending on the legal rules.

Detection: for 3 – 4 days after minor consumption. Detection in heavy smokers for weeks to months after last consumption

Carbamazepine, Serum

Related Information: Carbamazepine-10,11-Epoxide, Serum
Phenytoin (Diphenylhydantoib,DPH), Serum
Valproic Acid, Serum or Plasma
Verapamil, Serum or Plasma

Synonyms: Carpamazepinum; Carbategretal®; Carbatrol®; Carbazep®; CBZ; Epitrol®; Tegretol®-XR

Background: Carbamazepine is a tricyclic antidepressant structurally and mode of action similar to phenytoin.

Carbamazepine blocks sodium channels and inhibits uptake of and release of norepinephrine, but does not influence GABA uptake.

Carbamazepine is the drug of choice in partial seizures and used for generalized tonic clonic seizures, trigeminal neuralgias and mania.

Steady state is reached after 4-8 days. Peak levels after 6-8 h after oral administration; bioavailability 80%; volume of distribution 1L/kg; protein binding 60-80%; half life 36h initially, 20h through.

Carbamazepine is completely metabolized by the liver; one metabolite is the active carbamazepine 10-11-epoxide.

Plasma levels may be decreased by P450 system inducing drugs such as phenytoin, primidone, phenobarbital. Levels may be increased by P450 inhibiting drugs as isoniazid, fluoxetine, propoxyphene, quetiapine, verapamil, stripentol.

Dose related side effects are diplopia, ataxia, gastrointestinal upsets, and drowsiness. The incidence of leukopenia is 10%. There is an up to 8 fold increased risk to develop aplastic anemia and agranulocytosis as compared to the normal population.

Sampling: 1 mL serum, steady state after 4-8 days.

Reference Interval:

Therapeutic	Total level: 4-10 µg/mL ; in combination with other anticonvulsants 4-8 µg/mL
	Free carbamazepine: 0.5-4 µg/mL
Toxic	Total > 15 µg/mL; Free > 4 µg/mL

Carbamazepine-10,11-Epoxide, Serum

Related Information: Carbamazepine, Serum

Background: Carbamazepine-10,11-epoxide is an equipotent active metabolite synthesized in the liver from Carbamazepine. Accumulation of the metabolite, which occurs in patients additionally on valpromide or progabide therapy may lead to toxicity despite normal levels of carbamazepine. Phenytoin and valproic acid may also increase the epoxide to carbamazepine ratio.

Sampling: 1 mL serum

Reference Interval: 0.5-2.5 µg/mL

Carbohydrate Deficient Transferrin (CDT)

Related Information:
Alanine Aminotransferase (ALT), Serum
Alkaline Phosphatase, Serum
Aspartate Aminotransferase (AST), Serum
Bilirubin, Fractionated, Serum
Ethanol, Blood, Serum or Urine
Folic Acid, Serum
Gamma-Glutamyl Transferase (Gamma-GT), Serum

Background: CDT is increased either in alcohol abuses or in patients with autosomal recessive disorders of infancy or childhood, named carbohydrate-deficient glycoprotein syndrome or congenital disorders of glycosylation(CDG), characterized by mental retardation, liver dysfunction, cerebellar hypoplasia, muscular weakness.
Useful as a marker of alcohol consumption, monitoring of alcoholism and for diagnosis of CDG. However, the marker is not highly specific (90%) or sensitive (60%-70%) for alcoholism, since it is affected by smoking, body mass index, hypertension, liver damage.
Half life of CDT is 2 weeks.
Sampling: 1 mL serum. Refrigerate or freeze immediately or ship to the laboratory immediately.
Reference Interval: < 2.9%

Carboxyhemoglobin, Blood

Related Information: Cotinine, Serum, Plasma or Urine
Methemoglobin (MetHb), Whole Blood
Synonyms: Carbon Monoxide Hemoglobin; COHb ; CO-Hemoglobin;
Background: Carbon monoxide is a colorless, tasteless and odorless gas. By binding with a 250 times higher affinity to hemoglobin as oxygen, blood oxygen carrying capacity in the presence of carbon monoxide is reduced. CO also binds to myoglobin and cytochromes oxidases. Half life of carboxyhemoglobin is approx. 6h and even with 100% oxygen administration still remains at 1.5h, which can be reduced under hyperbaric oxygen to 35 min at 3 atmospheres.
Sampling: 1 mL EDTA, citrate or heparin blood. Cape tube tightly, keep tube capped. Keep refrigerated.

Reference Interval			
	Nonsmoker		< 3%
	Smoker	1-2 pack/day	5%
		> 2 packs /day	10%
	Newborn		10%-12%
	Fatal		30%-80%
	Immediate death		> 80%

Carcinoembryonic Antigen (CEA), Serum

Related Information: Alpha1 Fetoprotein, Serum
CA 15-3, Serum
CA 19-9, Serum
CA 125, Serum
Homovanillic Acid (HVA), Urine
Occult Blood in Stool (Hemoccult)
Background: CEA is a 180 kDa glycoprotein (50% carbohydrates). CEA is not organ specific, but highest concentrations up to 500 fold as compared to the normal colon tissue are assayed

in adenocarcinomas of the colon and liver metastasis, to a lower degree in carcinomas of breast (CA15-3 is superior), lung , pancreas and the stomach.
CEA is used in staging and monitoring patients with colorectal carcinoma and as a follow up marker after tumor resection. It is not effective as a screening assay.
Limitations: CEA is moderately elevated in smokers, during infections and inflammations, sometimes during liver diseases, inflammatory bowl diseases, and acute pancreatitis. It is not effective as a screening assay since, in the early stage (Dukes A) 95% are negative, late stage (Dukes D) up to 35% are false negative.
Also recurrent colorectal cancer may be false negative in up to 30%, however CEA is a useful marker for tumor relapse if values progressively increase.

Sampling: 1 mL serum
Reference Interval: < 5.0 ng/mL

Cardiolipin Antibody

Related Information: Prothrombin Time
Very Low Density Lipoproteins, Serum
Synonyms: ACA; Anti-Cardiolipin Antibodies
Background: Cardiolipin is the diphosphadidyl glycerol part of phospholipid membranes. The binding of the antibodies is mediated by beta2 glycoprotein-1 (apolipoprotein H) which is thought to inhibit thrombin generation. The binding changes the phospholipid exposing new epitopes and stimulates antibody production against the new structures.
ACA belong to the group of antiphospholipid antibodies, causing the antiphospholipid antibody syndrome which presents as thrombosis of the arteries and veins and a positive test for lupus anticoagulant or ACA. The autoantibodies are present in patients with systemic lupus erythematosus, in lupus like disease, during infectious diseases, and in drug reactions. Laboratory abnormalities associated with ACA may be thrombocytopenia, reactive VDRL, SS-A/Ro antibodies, prolonged activated partial thromboplastin time. Patients with lupus like disease are often ANA negative. Lupus anticoagulant with anticardiolipin antibodies are present in 70% of the antiphospholipid antibody syndrome patients. Lupus anticoagulant is present in 20-40% and ACA in 50% of patients with SLE.
In chronic hepatitis C patients ACA is higher than in patients with other inflammatory hepatic disease.
Elevated IgG ACA titers are present in cerebrospinal fluid of patients with symptomatic cerebral lupus, probably due to intrathecal IgG production.
Limitations: Cross reactions to a minor extend with reagin antibody of syphilis and lupus anticoagulant.
Sampling: 1 mL serum

Reference interval: Differentiation of immunoglobulin class:

IgA antibody negative:	< 12 RE/mL
IgG antibody negative:	< 12 RE/mL
IgM antibody negative:	< 12 RE/mL

Carnitine, Serum or Plasma

Synonyms: Beta-hydroxy-gamma-trimethylammonium butyrate; Carnitor; Levocarnitine

Background: L-Carnitine, as the active form, is synthesized in tissues from lysine residues starting with the formation of 6-N-trimethyllyine involving S-adenosylmethionine and for further steps, ascorbic acid, niacin, pyridoxine and iron is required.

Dietary carnitine is delivered by meat and dairy products. Cereals do not contain carnitine.

Carnitine is involved in the oxidation of fatty acids, aerobic metabolism of carbohydrates, oxidative phosphorylation, and increases the excretion of organic acids.

Primary deficiency, in part caused by an insufficient transport of carnitine into the muscle cell and faulty renal reabsorption, is observed in inherent disorders leading to storage of fat in muscle cells with dysfunction in cardiac and skeletal muscles. The systemic form is characterized by low plasma, muscle and liver carnitine concentrations with muscle weakness, cardiomyopathy, impaired ketogenesis, and fasting hypoglycemia. The myopathic form presents with muscle weakness, carnitine plasma concentrations are normal.

Secondary deficiencies are characterized by increased urinary excretion due to renal tubular disorders or long term hemodialysis.

Also disorders with increased circulating organic acids may lead to carnitine deficiency due to the excretion promoting function of carnitine.

Toxicity: L-carnitine up to 15 g/day is well tolerated, but DL-carnitine produces myasthenia gravis like symptoms by the inhibitory activity of the D isomer on the L isomer function and uptake.

Sampling: Plasma: 2 mL serum or plasma .
Urine: 10 mL aliquot of a 24h urine, collected without preservatives in a clean container.
Seminal fluid: 1 mL

Reference Interval:

Plasma	0.8 – 1.5 mg/dL
Urine	15 – 40 mg/24h
Seminal fluid	> 4.0 mg/dL

Cat Scratch Disease see Bartonella Henselae, Antibody, Serum

Catecholamines Fractionation, Plasma

Related Information: Catecholamines, Fractionation, Urine
Homovallinic Acid (HVA), Urine
Vanillylmandelic Acid, Urine

Synonyms: Adrenalin®, Noradrenalin®

Test includes: Epinephrine (E) (Adrenalin®) and Norepinephrine (NE) (Noradrenalin®) and Dopamine (D)

Background: The catecholamines are synthesized in the adrenal medulla, brain, sympathetic nervous system. Pheochromocytoma secrete large amounts of E, NE or both. Half live is 2 min.

Sampling: 2 mL EDTA or heparin plasma. Patient must be in calm, relaxed state and in a supine position for 30 min prior to collection. Catecholamine levels vary with posture, cold anxiety, pain. Epinephrine like drugs such as Aldomet®, Inderal®, should be withdrawn 8 days prior to sampling. Place EDTA or heparin blood specimen immediately after drawing on ice. Transport the specimen on ice to laboratory for separation of plasma within 1h or separate plasma by centrifugation at 4°C and freeze at –70°C.

Clonidine suppression test: Test to be conducted after an overnight fasting period. Patient remains in recumbent position during the test. After baseline specimen is drawn, 4.3 ug/kg body weight is given per os. Clonidine suppresses catecholamines in patients with essential hypertension but not in pheochromocytoma.

Reference interval:

Norepinephrine	supine 70 – 750 pg/mL	upright: 200-1700 pg/mL
Epinephrine	supine < 110 pg/mL	upright <140 pg/mL
Dopamine	< 30 pg/mL (independent of posture)	

Catecholamines Fractionation, Urine

Related Information: Calcitonin, Serum or Plasma
Catecholamines Fractionation, Plasma
Homovanillic Acid, Urine
Metanephrines, Urine or Plasma
Vanillylmandelic Acid, Urine

Background: Please see Catecholamines Fractionation, Plasma.

Useful in the diagnosis of catecholamine secreting tumors. Most of them (>95%) are adrenal pheochromocytomas, less common are paragangliomas and neuroblastomas.

Limitations: Increased values occur post surgery, injuries cold, anxiety, and some acute or chronic illnesses.

Sampling: 20 mL aliquot of a 24h urine, collect in 10 mL of 20% hydrochloric acid (do not use boric acid). Store during collection refrigerated. Please note total quantity.

Reference Interval:

Epinephrine (µg/24 h)	
< 1 year	0-2.5
1-2 year(s)	0-3.5
2-3 years	0-6.0
4-9 years	0.2-10
10-15 years	0.5-20
>16 years	0-20

Norepinephrine (µg/24 h)	
<1 year	0-10
1 year	1-17
2-3 years	4-29
4-6 years	8-45
7-9 years	13-65
>10 years	15-80

Dopamine (µg/24 h)	
<1 year	0-85
1 year	10-140
2-3 years	40-260
>4 years	65-400

CD4$^+$ and CD8$^+$ Cells see Lymphocyte Immunophenotyping

Cell Count, Liquor see Cerebrospinal Fluid (CSF, Liquor)

Cerebrospinal Fluid (CSF, Liquor)

Background (general): Useful in the evaluation of meningitis, encephalitis, meningoencephalitis, bacterial, viral or fungal infections, parasitic diseases, malignancies, lymphomas of the CNS, trauma, vasculitis, degenerative processes.

Sampling (general): CSF. Concurrently, a sample of peripheral blood should be obtained in case CSF glucose levels (infectious diseases) or oligoclonal bands (demyelinating diseases) are due to investigation. Blood cultures are valuable in infectious causes, particularly prior of initiation of antibiotic therapy.

Samples should be delivered to the lab promptly.

For the diagnosis of meningitis, culture and gram stain and cell count have priority over antigen or other testing, followed by glucose and protein.

1. Cell count

Reference Interval:

Premature neonates	<29 cells / mm^3
<1 month	<32 cells / mm^3
1 month to12 month	< 10 cells/ mm^3
1-4 years	< 8 cells/ mm^3
5-14 years	< 5 cells/ mm^3
adults	0-5 cells/ mm^3 , lymphocytes and monocytes, no red cells.

2. Protein

Background: The protein concentration in the CSF is less than 1% of plasma concentration. Proteins in the CSF are of lower molecular weight as compared to plasma proteins, normally comparable small amounts of beta lipoproteins, alpha $_2$ macroglobulin, IgM or haptoglobulins are part of CSF.

Elevated protein should trigger further tests such as IgG / albumin index, IgG synthetic rate, electrophoresis for oligoclonal bands.

Increased:

- Bacterial meningitis (100-500 mg/dL, occasionally higher) including mycobacteria
- Brain abscesses
- Syphilis in 10-20% with primary syphilis, up to 70% with secondary stage disease
- Carcinomas
- Diabetes mellitus
- Arachnoiditis
- Demyelinating diseases (MS patients display normal or slightly elevated levels)
- Dehydration
- Disc herniation
- Drug related such as gentamicin, vancomycin, ampicillin, phenothiazine
- Subarachnoid hemorrhage
- Trauma
- Obstruction of the spinal canal (e.g. tumor) due to lacking reabsorption of protein by arachnoidal cells
- Froin syndrome (protein >200 mg/dL, clotting of CSF due to fibrinogen)
- AIDS patients with CNS involvement (up to 50% of the patients display elevated CNS protein, 10-30 % oligoclonal bands, the percentage is stage dependent.)

Normal to slightly (50-80 mg/dL) elevate:

- In some psychiatric disorders
- Multiple sclerosis

Viral meningitis (usually less than 100mg/dl)

Decreased (10-20mg/dL):

Water intoxication,

CSF leaks (beta 2 transferrin typically elevated)

Leukemia

Hyperthyroidism

Limitations:

Fresh blood increases CSF protein test values. The protein levels can be adjusted by the CSF erythrocyte count

Ery / ul	corrected protein concentration by subtraction of
500	7.7 mg/L (2%)
1000	15.4 mg/L (4%)
2000	30.8 mg/L (8%)
4000	61.6 mg/L (15%)
8000	123.0 mg/L (30%)

Reference Interval: Protein

Infants (lumbar) (approximate)

1-8 days	26-135 mg/dL
3-30 days	26-115 mg/dL
1-2 month	18-86 mg/dL
2-3 month	10-74 mg/dL
older 6 month	15-45 mg/dL

Adults

lumbar	18-43 mg/dL
ventricular	5-15 mg/dL
cisternal	15-25 mg/dL

The higher protein levels in infants can be explained by increased blood brain barrier permeability.

3. Glucose

Background: CSF glucose is useful in the distinction of bacterial versus viral meningitis. CSF glucose is low <40mg/dL (<2.2 mmol/L) in bacterial or tuberculous meningitis and normal in viral meningitis.

Low CSF glucose occurs in sarcoidosis and neurosyphilis, in meningeal cysticercosis, trichinosis, and during intrathecal drug therapy. Subarachnoid hemorrhage, carcinomas and leukemias may also lower CSF glucose.

Limitations: High contamination with blood may increase CSF glucose due to higher blood glucose levels. Delayed delivery to the laboratory in cases of bacterial presence or contami-

nation may decrease glucose due to utilization of glucose.
CSF. Blood glucose is valuable, ideally taken 2h prior to lumbar puncture (equilibration time)

Reference Interval:

Adults:	50-80 mg/dL or 60-70% of plasma glucose
Infants and young children:	Slightly higher than adults: 60-80 mg/dL (SI 3.4-4.5 mmol/L). Plasma/CSF ratio: In premature and newborn infants, CSF glucose may be 80% or more of blood glucose levels (adults: 60%-70%). Critical value: less than 40%.

4. Humoral Immunoglobulin Production

Background: Antibodies are not synthesized during healthy state of the CNS. Antibodies entering via the blood brain barrier from the blood are as low as 0.2% for IgG and 0.03% for IgG of the blood concentrations. The humoral reaction in the CNS may characterize a CNS disease and is a valuable tool in diagnosis. Humoral reactions of the CNS may last in diseases such as neurosyphilis and herpes encephalitis after successful treatment for several years to decades.

Early stage CSF pattern:

No IgG, IgA or IgM	Early stage of bacterial, virus encephalitis, Guillain Barré
Predominant IgG	Multiple sclerosis (but up to 20% IgM or rarely IgA), neurosyphilis (sometimes IgM), HIV encephalitis
Predominant IgA	Neurotuberculosis (sometimes IgG or IgM), abscesses
Predominant IgM	Neuroborreliosis (sometimes IgA and IgG), mumps encephalitis, non-Hodgkin lymphoma of the CNS, neuro trypanosomiasis
Mixed IgG, IgA, IgM	Infections during immunodeficiency

Reference Interval:

IgG 10-40 mg/L (serum 7-18 g/L)
IgA 0.5- 6.0 mg/L (serum 0.9-4.5 g/L)
IgM 0.05-0.8 mg/L (serum 0.6-2.8 g/L)

5. Albumin

Background: Albumin is synthesized outside of the CNS. It is the ideal protein to represent changes in the blood brain barrier. For other parameters such as IgG, IgA IgM and known serum and CSF concentrations the intrathecal production can be determined if the serum Albumin to CSF ratio has been determined.
The ratio for proteins in CSF/serum depends on molecular seizes:

Protein	MW (kDa)	ratio [mean]
Albumin	69	1:205
IgG	150	1:440
IgA	160	1:800
IgM	971	1:3400

The ratio of the concentrations of CSF albumin / albumin serum (Q alb) is considered as a parameter for the function of the blood brain barrier and serves as the reference for other proteins such as immunoglobulins NSE, S100B, cystatin c resulting in an blood-brain barrier function independent measurement of intrathecal production of the protein of interest.

Ratio CSF IgG / CSF albumin <0.27

Index (CSF IgG / CSF albumin) / (serum IgG / serum albumin) < 0.7

The CNS IgG production rate in mg/day is calculated by Tourtellotte as used for the diagnosis of MS:

5 x [{CSF IgG - serum IgG/369} - {(CSF albumin - serum albumin /230) x 0.43 x (serum IgG/serum albumin) }]

Reference Interval: CSF albumin: 110-350 mg/L (serum albumin: 35-55 g/L)

6. Electrolytes

Reference Interval:

	CSF	Serum
Osmolality	281 mosm/kg	289 mosm/kg
Urea	16.3 - 34.7 µmol/L	16.7 - 32.5 µmol/L
Calcium ionized	1.05 -1.35 mmol/L	1.15 - 1.35 mmol/L
Chloride	116 - 127 mmol/L	92-105 mmol/L
Glucose	1.1 - 4.4 mmol/L (20-79 mg/dL)	3.9 - 6.1 mmol/L (70 - 110mg/dl)
Lactate	1.2 - 2.1 mmol/L	0.5 - 2.2 mmol/L
Magnesium	0.9 - 3.2 mg/dl (0.38-1.4 mmol/L) total Mg	total Mg: 1.8 - 2.7 mg/dl (0.75 - 1.1 mmol/L) Ionized Mg : 1.1 - 1.5 mg/dl (0.46 - 0.6 mmol/L)
Phosphate anorganic	1.1 mmol/L	0.8 - 1.45 mmol/L
Potassium	2.7 - 3.9 mmol/L	3.6- 4.8 mmol/L
Sodium	138 - 150 mmol/L	135 - 145 mmol/L

7. Lactate, CSF

Background: Used, but not reliable parameter to differentiate between bacterial from other forms of meningitis. Elevated also in cerebral infarct, Creutzfeldt Jacob disease, cerebral hemorrhage, subarachnoid hemorrhage, hypertension, hepatic encephalopathy, diabetes mellitus, head injury.

Reference Interval: Increased in the first 2 weeks of life
Adults 10-22 mg/dL (1.1-2.4 mmol/L)

8. Interpretation, CSF

Infectious condition for lumbale CSF of adults

	pressure mmH2O	cell count	protein mg/dl	glucose
normal	50-150	<5 lymphocytes	15-60	60-70% of serum glucose (74-106 mg/dl = 4.1-5.9 mmol/L)
bacterial meningitis	elevated	200-10 000, 95% PMN	usually>100	lower(<50mg/dl)
viral meningitis	elevated	normal -1000, predom.lymphocytes	usually 50-100	normal
tuberculosis or fungal	elevated	normal -500, predom.lymphocytes	100-several thousands	low (<50 mg/dl)
brain abscess	elevated	usually <500 predom.lymphocytes	50-100	normal to low

Non infectious condition for lumbale CSF of adults

subarachnoidal hemorrhage	normal to elevated	slightly elevated	elevated	normal to low
Guillain Barré syndrome	normal	normal	elevated	normal

Infectious condition for lumbale CSF of adults

Parasitic Disease	Protein g/L	Glucose mg/dL	Cell count/ul	
Neurocysticercosis	up to 16	mean 42 mg/dl decreased down to 6 mg/dl	mean 60 up to 2000	In up to 60 % of the patients display CSF abnormalities, most common: elevated protein, predominant mononuclear cells, seldom decreased glucose. In 50% eosinophils increased
Bilharziosis of the CNS	elevated	Occasionally decreased	Up to 100	200 mio humans affected by schistomiasis, but CNS infection rare. Oligoclonal IgG, antibodies in the CSF occur in 70% of the patients.
Nematode infection of the CNS	Elevated		Elevated	Usually presents as meningitis, myelitis, radiculitis. Predominant eosinophiles in the CSF
Strongyloidiasis infection of the CNS			Elevated	High eosinophile count, IgG and IgA elevated in 80% of the patients
African Trypanosomiasis				IgM predominant (95% of the cases present with intrathecal IgM production, with IgG 70% only). Note that the European population has higher serum albumin levels (35-55 g/l) as compared to the African population, but the albumin ratio CSF/serum is comparable in trypanosomiasis patients.

Ceruloplasmin (Cp), Serum or Plasma

Related Information: Copper (Cu), Serum or Urine

Background: Cp is a glycoprotein, MW 132 kDa, with 9% carbohydrates. Cp binds 6-9 Cu atoms. Cp is synthesized in hepatocytes and Cu is intracellular ATP dependent incorporated. In patients with Morbus Wilson, the ATPase is impaired. The physiologic function of Cp is to make Fe available for erythropoiesis by ferroxidase activity, inhibiting the oxidizing properties of lipids, thus preventing atherosclerosis and neurotoxicity.

70% of the body copper is bound to Cp, 7% to transcuprein, 20% to albumin, and 2% to amino acids.

Cp is decreased in 75% of the patients with Morbus Wilson (WD). WD is characterized by toxic accumulation of copper in liver, basal ganglia e.g. globus pallidus hypodensity in some cases fronto-temporal, cerebellar, and brain stem atrophy. WD is autosomal recessive hereditary disease with a homozygote prevalence of 1:50.000 to 1:100.000. Symptoms occur in late puberty, and since the disease is treatable with the chelating penicillamine or trientine dihydrochloride, it is advisable to screen young patients with cirrhosis or CNS signs such as tremor, dysarthria, dysphagia, dyskinesias, dementia, micrographia, personal changes, and psychiatric symptoms. In liver failure caused by WD characteristically the ratio aspartate aminotransferase (AST) to ALT (alanine aminotransferase) is >2, alkaline phosphatase more likely to be decreased and AST is moderate increased. Cp in WD is usually < 20 mg/dL, however 20% of the patients with hereditary Cp defects, renal Cp losses, after severe burning, or decreased synthesis in serve liver diseases present decreased Cp.

Menkes disease, a defect liked to the chromosomal locus Xq13.3 lacking an intracellular Cu binding protein and presenting in early childhood with seizures, mental retardation, impaired joint function and facial dysmorphism. The prognosis is poor. Cp and serum copper is decreased.

Limitations:

Cp is an acute phase protein, interpretative caution is necessary. Oral contraceptives or estrogens cause dose dependent an increase of Cp up to 30%.

Sampling: 1 mL serum, transport to laboratory soon, otherwise centrifuge and freeze.

Reference Interval:

Children	(mg/dL)
1 day to 4 month	15-56
5-6 month	26-83
7-18 month	31-91
18-36 month	32-90
4-9 years	26-46
10-12 years	25-45

Female	(mg/dL)
13-19years	22-50
>19 years	25-60
>19 and on oral contraceptives	27-66
>50 and on estrogen therapy	30-50
Pregnancy	<130

Male	(mg/dL)
13-19 years	15-37
>19 years	22-40

Chagas see Trypanosoma cruzi, Serology

Chlamydia

Test includes: Chlamydia trachomatis serology, C. trachomatis direct DNA detection, C. pneumoniae serology

Background: The genus Chlamyddia includes C. trachomatis. The genus Chlamydophila includes C. pneumoniae, C. psittaci. Chlamydiaceae are obligate intracellular organisms. The cell wall resembles gram negative bacteria but lack muramic acid.Two forms are known, a non-replicating, infectious dense particle (elementary body) and a larger intracellular form (the metabolically active reticulate body). C. trachomatis is transmitted by direct contact and by vectors such as flies and contaminated towels. In industrialized countries, C. trachomatis is the most common bacterial STD, reaching 20% in young sexually active people. C. pneumoniae is a respiratory pathogen worldwide distributed. In tropical countries infections are common in the first year of life. Seroconversion reaches 25%-50% at the age of 15, rising further in the elder population which indicates either chronic or repeated infection.

Diseases caused by C. trachomatis are in female's cervicitis (incidence 30%), endometritis, pelvic inflammatory disease (10%-70%), and rarely perihepatitis, bartholinitis; in male's urethritis (10%-30%) and epididymitis. Conjunctivitis and reactive arthritis are seen in both sexes, in neonate's conjunctivitis and infant pneumonitis.

Diseases caused by C. pneumoniae are pneumonia: endemic (10%) or epidemic (up to 50%). Also acute bronchitis (5%) and rarely otitis media, sinusitis, carditis, vasculitis, reactive arthritis. Chronic infections may lead to chronic obstructive lung disease, asthma, sarcoidosis, in up to 50% to arteriosclerosis.

Classification

In the rRNA-based tree of life, four bacterial phyla comprising the Planctomycetes, Verrucomicrobia, Chlamydiae and Lentisphaerae, form together with the candidate phyla Poribacteria and

OP3 a monophyletic group referred to as the PVC superphylum. The Chlamydiaceae is a phylogenetically distinct Gram-negative bacterial family, encompassing two genera (Chlamydia and Chlamydophila), which are subdivided into three (Chlamydia muridarum, Chlamydia suis, and Chlamydia trachomatis) and six (Chlamydophila pneumoniae, Chlamydophila abortus, Chlamydophila caviae, Chlamydophila felis, Chlamydophila pecorum, and Chlamydophila psittaci) defined species, respectively.

Sampling: 1 mL serum

A PCR assay for direct detection is available for Chlamydia trachomatis. For swabs use a special swab, STD-PEN for males, STD-EZE for females. Punctate, tracheal fluid and 10ml first void urine is suitable for direct detection. Collect in a sterile container.

Reference Interval:

Chlamydia trachomatis; Serology
Differentiation of immunoglobulin class

IgA antibody	negative:	< 8 RE/mL
	borderline:	8 – 10 RE/mL
	positive:	> 10 RE/mL
IgG antibody	negative:	< 8 RE/mL
	borderline:	8 – 10 RE/mL
	positive:	> 10RE/mL

Chlamydia trachomatis, Direct detection by PCR
Report: DNA not detectable, detectable

Chlamydophlia pneumoniae, Serology
Differentiation of immunoglobulin class

IgA-Antibody	negative:	< 11 RE/mL
	borderline:	11 – 15 RE/mL
	positive:	>15 RE/mL
IgG-Antibody	negative:	< 11 RE/mL
	borderline:	11 – 15 RE/mL
	positive:	> 15 RE/mL

Chloride (Cl), Liquor see Cerebrospinal Fluid (CSF, Liquor)

Chloride (Cl), Serum

Background: Used in the diagnosis of alkalosis or acidosis and in the calculation of the anion gap. Increased in mineralocorticoid deficiencies, hyperchloremic metabolic acidosis, hyperinfusion of saline, diarrhea, renal tubular acidosis.

Decreased in overhydration, inappropriate ADH syndrome, vomiting, respiratory acidosis, Addison's disease, burn wounds, metabolic alkalosis, diabetic ketoacidosis, pyloric stenosis in early infancy, diuretic drug therapy.

Sampling: 1mL serum or plasma

Reference Interval:

	(mmol/L)
Adults	95-105
Children	
1day – 1 week	96-111
1 week – 1 month	96-110
1month – 6 months	96-110
6 months – 1 year	96-108
older than 1 year	96-109

Critical: < 80 mmol/L or > 115 mmol/L

Chloride (Cl), Urine

Related Information: Potassium, Urine
Sodium, Urine

Background: Used in the differentiation between Cl sensitive form and Cl resistant form of hypochloremic metabolic alkalosis:

The Cl sensitive (responding to chloride intake by restoring body stores) form is associated with vomiting, diuretic drugs medication and is caused by loss of H and Cl ions or it is caused by Cl loss in the feces by villous adenomas. Urinary Cl may be as low as <10mmol/L.

The Cl resistant forms are caused by primary and secondary hyperaldosteronism and Bartter Syndrome. Urine Cl varies according to Cl intake, urinary Cl is usually > 20mmol/L.

Sampling: Random urine 5 mL or to obtain more reliable results send in an aliquot of 5mL of a 24h collected urine, note total quantity.

Reference Interval:

Infants	2-10 mmol/24h
Children	10-40 mmol/24h
Adults	85-200 mmol/24h

Cholesterol, Total, Serum or Plasma

Related Information: Apolipoprotein A-I and B-100, Serum
C-Reactive Protein, Serum
Endomysial Antibodies
High Density Lipoprotein Cholesterol, Serum or Plasma
Homocysteine, Total, Plasma
Low Density Lipoprotein Cholesterol, Serum or Plasma
Triglycerides, Serum or Plasma

Background: Elevated serum cholesterol levels are considered a major risk factor for coronary heart disease (CHD). Screening is advisable in persons with diabetes mellitus, elevated blood pressure, family history of hyperlipidemia or early CHD, xanthomata or xanthelasmata.
In the diagnosis of anemic patients, levels below 150 mg/dL may indicate celiac disease.

Sampling: 1 mL serum

Patient preparation:
Stable diet for 3 weeks, stable body weight and fasting for 10h.
Cholesterol levels may be 10%-20% lower in recumbent position after 20 min.
Plasma cholesterol may be 10% lower than serum values.

Reference Interval:

Newborn	60 – 120 mg/dL
Children	90 – 190 mg/dL
Adults Desiderable	< 200 mg/dL
Borderline	200-239 mg/dL
High	>240 mg/dL

Chorionic Gonadotropin (hCG, β-hCG), Serum

Related Information: Alpha$_1$-Fetoprotein (AFP), Serum
Progesterone, Serum

Background: HCG is used to assess pregnancy, to support ultrasound diagnosis of ectopic pregnancy and to detect trisomy 21. It is also used as a marker for gestational trophoblastic neoplasias (molar gestations, placental trophoblastic carcinomas, choriocarcinomas), nonseminomatous germ cell tumors and for seminomas.
During pregnancy beta-hCG doubles every 1-3 days, in ectopic pregnancies more slowly. It is recommended to determine hCG and progesterone every other day to detect slower than normal rising levels in ectopic pregnancy.
Mothers carrying fetuses with in trisomy 21 have lower serum AFP levels, lower unconjugated estriol levels but an increased concentration in hCG at week 16.
Decreased levels of hCG are found in trisomy 18.
Limitations: Rarely false positive results are due to heterophilic antibodies.

Sampling: 1 mL serum. Serum is stable at room temperature for 1 day and 4 days at 4°C, otherwise freeze.

Screening:

First (day 74-97) and second (week 16-18) trimester screening (including AFP and unconjugated estriol) of maternal serum for Down syndrome (trisomy 21) and Edwards syndrome (trisomy 18).

Reference Interval:

Male	< 2,0 mIU/mL
Female	< 3,0 mIU/mL
Pregnancy	
Week of gestation	
1	5 – 50 mIU/mL
1 – 2	50 – 500 mIU/mL
2 – 3	100 – 5 000 mIU/mL
3 – 4	500 – 10 000 mIU/mL
4 – 5	1 000 – 50 000 mIU/mL
5 – 6	10 000 – 100 000 mIU/mL
6 – 10	15 000 – 200 000 mIU/mL
10 – 12	10 000 – 100 000 mIU/mL

HCG increases rapidly during the first 6 weeks of pregnancy, peaking between day 60-70. Concentrations less than 2000 mIU/mL and increase of hCG less than 65% within 48h may suggest abortion or ruptured ectopic pregnancy.

Chromogranin A, Serum

Related Information: Catecholamines, Fractionation, Plasma
Calcitonin, Serum or Plasma
5-Hydroxyindoleacetic Acid (5-HIAA), Quantitative, Urine

Background: Chromogranin A is a soluble 50 KD protein of neuroendocrine cells mainly stored in chromaffin granules. It is released from the adrenal medulla together with catecholamines. It is also present in other neuroendocrine tissues.

It may be elevated in pheochromocytoma and small cell lung carcinomas.

Sampling: 1 mL serum or EDTA plasma, separate immediately, freeze and ship frozen.

Reference Interval: < 100 ng/mL

CK-Isoenzyme (CK-MM, CK-BB, CK-MB) see Creatinine Kinase Isoenzymes, Serum

Clobazam, Serum

Background: Clobazam, a 1,5 benzodiazepine, is metabolized to N-desmethylclobazam. Clobazam is used as adjunctive therapy in the treatment of epilepsy, however with waning effectiveness after weeks of continuous therapy. It may be used in short term treatment of anxiety disorders.

Bioavailability 85%-90%, peak time 0.5-2.5h, half-life time 11-77h (average 18h, longer in elderly than young males (48h versus 17h), peak time 1-4h after dosing, peak plasma concentrations were 290-410 ng/mL decreased in cirrhosis and hepatitis after a dose of 20 mg.

Sampling: 2 mL serum

Reference Interval:

Therapeutic	100 – 400 ng/mL
Desmethylclobazam	1000 – 4000 ng/mL

Clonazepam, Serum

Related Information: Diazepam, Serum

Synonyms: Iktorivil®; Klonopin®; Rivatri®

Background: Clonazepam belongs to the class of benzodiazepines. It is a long acting drug used in prevention of absence seizures, in myoclonic seizures, tonic-clonic seizures and in reducing tardive dyskinesia. The drug is under investigation in infantile spasm, neuralgia, Parkinson's disease, and bipolar disorders. Pronounced sedative effects limit the use, by paradoxical hyperactivity in children and by development of tolerance.

Bioavailability 98%; urinary excretion 1%; plasma binding 86% lower in neonates; volume of distribution 3.1-3.3 L/kg ; half life time 18-28h, increased in the elderly; peak time 1.2-3.8h after a 2 mg oral dose; peak concentration 12-22 ng/mL after a single 2 mg dose orally.

Steady state reached after 5-10 days. Active metabolites have longer half-life times.

Sampling: 2 mL serum

Reference Interval:

Therapeutic:	30-60 ng/mL
Steady state for seizure control:	5-70 ng/mL
Toxic:	>80 ng/mL
Highly toxic:	>100 ng/mL

Clostridium difficile

Background: C. difficile antibiotic-associated diarrhea and pseudomembranous colitis is a major cause of hospital acquired diarrhea. Toxic strains usually produce toxin A, an enterotoxin and toxin B. Since not all C. difficile strains produce toxin and the amount of toxin must exceed a level to cause colitis, false positive culture results are common. Toxin testing is a more reliable parameter.

Limitations: In up to 20% of adults and in up to 50% of newborns non-toxin producing C. difficile may be isolated. In 40%-60% of hospitalized patients, toxin may be detected but without any symptoms.

Sampling: Fresh stool, patient must have diarrhea. Keep specimen cool and process soon. Repeated testing does not improve sensitivity.

Reference Interval:

Report on diagnostic finding:

Culture result: Growth of C. difficile

Toxin detection by EIA: Toxin A and B

Clostridium tetani

Related Information: Tetanus Antitoxin Antibody IgG

Background: Spores are widespread in nature and wound sites even very small (such as skin popping by drug abusers) are portals of entry. Hypoxic sites such as necrotic tissue favor infection. Neonatal tetanus (the C. tetani enters through a contaminated umbilicus) is a major problem in developing countries. After infection, the C. tetani produces an polypeptide toxin which is carried intra-axonal and blocks the activity of inhibitory mediators at ganglioside receptors.

Clinically, patients present with lockjaw, risus sardonicus, opisthotonus, and spastic paralysis (botulism: flaccid paralysis).

Laboratory diagnosis: C. tetani is rarely isolated from the wound site, there is no the serologic diagnosis in the early stage.

Treatment: Immunoglobulin for neutralization of the toxin, metronidazole and penicillin.

Sampling: Biopsy material, wound swap

Reference Interval:

Report on diagnostic finding

Culture result

Clostridium Tetani Immunity see Tetanus Antitoxin Antibody IgG

Cocaine, Urine

Synonyms: Coke; Crack; Dama Blanca; Gold Dust; Liquid Lady; Nose Candy; Rock; Snow; Toot; White Lady

Background: Cocaine is a highly potent natural central nervous system stimulant. The hydrochloride salt or the sulfate salt appears as a fine powder for inhalation, mixed with sodium bicarbonate it becomes the solid form for smoking called crack. Administration via smoking, intravenous injection or orally, also sublingual, rectal, vaginal.

Alcohol inhibits cocaine degradation. Cocaine is the cause of microvesicular steatosis and necrosis of the liver. Myocardial effects are cardiomyopathies, myonecrosis, dysrhythmias, angina

pectoris, ischemia, and infarction. Renal failure, rhabdomyolysis, disseminated intravascular coagulation may occur. Fetal growth and development are altered.
Metabolites are benzoylecgonine and ecgonine methyl ester. Benzoylecgonine is detectable in the urine as early as 2-3h for 1-3 days after intake. For long term exposure, hair analysis indicate cocaine use for month, assuming a hair growth rate of 13 mm per month
Half life : Cocaine 1h; benzoylecgonine 5-10h; ecgonine methyl ester 3-4h;
ethylcocaine 2h. Bioavailability for cocaine 30-70%, volume of distribution 3-5 L/kg
Sampling: 5 mL random urine. Keep refrigerated. To rule out dilution for forensic purposes, request urine creatinine.
Reference Interval: Immunological drug screen: negative : < 300 ng/mL

Cold Agglutinin Titer

Related Information: Cold Fibrinogen
Cryoglobulin, Qualitative, Serum or Plasma

Background: Mycoplasma activates several classes of immunoglobulins. Cold isohemaggglutins are usually of the IgM class, clumping erythrocytes at 4°C. M. pneumoniae has an I antigen similar to an I like antigen on human RBC s . During Mycoplasma pneumoniae infection, 50% of the patients develop titers against I antigen. Cold agglutinins rise at week one after onset, peaking after 2-3 weeks and decline after 4 weeks.
Limitations: False positive results are linked to rubella, adenovirus, infectious mononucleosis, connective tissue diseases.
Sampling: 10 mL whole blood, allow to clot warm (37°C), separate cells from serum in a prewarmed centrifuge, send in blood clots and serum
Reference Interval:
Negative: not detectable
Positive: Titers > or = 64 or 4 fold increase in titer

Cold Globulins see Cryoglobulin, Qualitative, Serum or Plasma

Copper (Cu), Serum or Urine

Related information: Ceruloplasmin (Cp), Serum or Plasma
Iron (Fe), Serum
Transferrin and Total Iron Binding Capacity, Serum
Zinc (Zn), Serum or Urine or Seminal Fluid

Background: Copper is an essential trace element, serving as a cofactor in metalloenzyme systems and is part of the hemoglobin synthesis pathway. Cu is necessary for bone formation, pigmentation, CNS development, growth, and connective tissue. In the serum it is bound to

ceruloplasmin as the major transport protein. Cu is absorbed in the stomach and duodenum regulated by metallothionein (MT). MT is induced by Cu and to a higher degree by zinc to a low degree by cadmium and iron), both binding to MT. Zinc inhibit Cu absorption by strongly inducing MT, leading to a high amount of MT in mucosal cells with trapped Cu. The cells are sloughed into the intestinal lumen and lost into the stool.
Absorption is inhibited by molybdenum by forming insoluble complexes with Cu, used in therapy of Wilson disease.
Cu is transported into the liver by albumin and histidine, and synthesized to ceruloplasmin. Peripheral tissue uptake of Cu depends on the ceruloplasmin form; 50%-80% of the Cu in the peripheral blood is bound to ceruloplasmin.
Ceruloplasmin usually parallels serum Cu, except in acute Cu intoxication, were ceruloplasmin may remain normal with elevated fee serum Cu and elevated levels of total serum Cu and in Wilson's disease with chronic low ceruloplasmin leading to more free serum Cu with normal or decreased total Cu.
Secretion occurs largely eliminated by excretion into the bile; a small fraction is secreted into the urine. Abnormal urine excretions occur in burns, Menkes syndrome or during therapy with chelating drugs.

Useful test

- in combination with serum ceruloplasmin for screening for Morbus Wilson with decreased or normal serum Cu but, due to decreased excretion of Cu into the bile, increased excretion into the urine. In addition, for Wilson's disease and ICC, the liver tissue Cu concentrations are diagnostic.
- to monitor adequate parental nutrition.
- in the diagnosis of primary biliary cirrhosis and primary sclerosing cholangitis.
- to monitor Cu deficiency in premature infants during serious illnesses leading to decreased Cu absorption.
- in Cu intoxication (increased serum Cu, increased urine Cu)
- in the diagnosis of Indian Childhood Cirrhosis (ICC) during penicillamine therapy. ICC is caused by inherited factors, such as defective basal production of MT, and toxic exposure of the child to milk boiled in brass vessels.
- in Menkes syndrome (decreased serum Cu, increased urine Cu). Menkes disease is a severe X-linked Cu deficiency syndrome presenting early at the age of 2-4 month and is due to a defective Cu transporting ATPase, leading to Cu accumulation in the intestinal mucosa and kidney and subsequently a lack of Cu in the peripheral tissue and in the liver.
- in the diagnosis of Occipital Horn Syndrome (OHS) (Ehlers-Danlos syndrome type IX), an inherited disorder. OHS which is characterized by low serum Cu and ceruloplasmin and low fibroblast lysyl oxidase activity as well as low intestinal Cu absorption.
- to rule out Cu deficiency in iron resistant anemia, characterized by reduced ceruloplasmin synthesis leading to a microcytic or normocytic anemia.

- to rule out Cu deficiency in scurvy like bone disease
- to rule out Cu deficiency in depigmentation

Limitations:
Cu binding Ceruloplasmin increases during acute inflammations such as rheumatoid arthritis, therefore increasing serum Cu. Estrogen increases ceruloplasmin, elevating Cu during pregnancy and during contraceptive drug intake.
Drugs increasing Cu: carbamazepine, phenobarbital, phenytoin, valproic acid.
Decreased serum Cu levels occur: Low serum protein, malnutrition, ACTH therapy, glucocorticoid therapy.

Sampling:
Serum:
2 mL serum. Container must be metal free (certified trace metal free blood collection tubes), draw sample through a plastic catheter preplaced in the vein. Use during drawing powder free gloves.

Urine:
Collect 24h urine in a pre-washed metal free plastic container. Acidify to ph 2 with hydrochloric acid. Avoid contamination with dust. Ship 10ml to the laboratory, note total quantity.

Reference Interval:

Serum:	70-140 µg/dL

Diurnal variation with a peak in the morning

Urine:	5-60 µg/24h

Coproporphyrin see Porphyrins, Urine, Stool, Quantitative

Cordarone® see Amiodarone, Serum

Cortisol, Serum or Plasma

Related Information: Adrenocorticotropic Hormone (ACTH), Plasma
Androstenedione, Serum
Cortisol, Free, Urine
17-alpha-Hydroxyprogesterone
Testosterone, Serum

Synonyms: Compound F; Hydrocortisone

Background: Cortisol is secreted in a circadian rhythm with a maximum in the morning (5-25ug/dL) and a minimum in the early evening (3-16ug/dL).

Cortisol is bound to cortisol binding globulin (CBG), with serum concentration of 35-40 ng/L and albumin. Estrogens can increase CBG up to 120 ng/L. Half life of serum cortisol is approx 90 min. After inactivation in the liver the metabolites are excreted in the urine, only 1% is excreted in the free, unchanged form.

High cortisol levels are caused by adrenocortical hypersecretion, adrenocortical hyperplasia, adenoma, carcinoma excess pituitary or ectopic (small cell carcinoma of the lung) ACTH production.

To verify a cortisol excess, at least one of the following tests should be done: Midnight serum cortisol, urine free cortisone determination, a dexamethasone suppression test (DST).

DST overnight: 1 mg oral dose of dexamethasone at 11 PM, sampling at 8 AM: cortisol <3ug/dl is evidence against Cushing syndrome.

DST low dose: Protocol includes collection of 24h urine samples at day 1 through 4. At day 2 in the morning, the patient is given a dose of 0.5 mg dexamethasone and subsequently every 6 h 0.5 mg for a total of 8 doses. Baseline cortisol levels are drawn at day 1 at 8 AM and 8 PM and at day 5 at 8AM. Normal suppression: Corticol (Urine and Serum) on day 4: 50% below baseline.

DST high dose: Same as low dose, but dose is 2mg dexamethasone. A 50% suppression in urine and serum levels < 10 µg/dL occurs in patients with pituitary ACTH secreting adenomas, but lacks in patients with adrenal tumors secreting cortisol or ectopic corticotropin releasing tumors.

Low cortisol levels may be due to pituitary failure, failure of the adrenal glands (adrenogenital syndrome, primary adrenocortical insufficiency, Addison disease. Expected values at 8 AM for serum cortisol are < 5 µg/dL, exclusion of diagnosis if values> 20 µg/dL in patients without stress factors.

Sampling: 1 mL serum or heparin plasma. Diagnosis can not be based on one single test!

Reference Interval:

Children:		8 AM	
		5 days:	0.6 - 20 µg/dL
		2 - 12 months:	2.4 - 23 µg/dL
		5 - 15 years:	2.5 - 23 µg/dL
		16 - 18 years:	2.4 - 29 µg/dL
Adults:	> 18 years	8 AM:	5.0 - 25 µg/dL
		4 PM:	3.0 - 16 µg/dL
		8 PM:	50% of 8 AM leveL
		Midnight:	< 1.8 µg/dL

Cortisol free, Urine

Related Information: Cortisol, Serum or Plasma
17-alpha-Hydroxyprogesterone, Whole Blood, Plasma or Serum

Background: Please see also Cortisol Serum or Plasma.

The advantage of urine cortisol is the independence from cortisol binding globulin and since collection covers 24h, independence of circadian rhythm.

In patients with Cushing, free urine cortisol usually is >120 µg/24h, but additional testing is needed.

Sampling: 10 ml aliquot of a 24h urine, collected in a container prefilled with 1 g acid, note total quantity. Creatinine variation between several 24h urine collection periods should not exceed 10%, otherwise collection may be incomplete and results due to ciardian variation may be false.

Reference Interval: 30-120 µg/24 h

Corynebacterium diphtheriae (Diphtheria)

Background: Corynebacteria species organisms are gram positive rods, arranged in palisades or V and L formation and appear beaded by polymerized polyphosphate. Humans are the only host for C. diphtheriae. C. diphtheriae resides in the upper respiratory tract and transmission occurs by air borne droplets. Skin can be infected if lesions are present, predominant in the tropics. Endotoxin production, mediated by a temperate beta bacteriophage, is necessary for infection.

Diphtheria is now a rare disease in industrialized countries due to vaccination, performed by three doses at the age of 2, 4, 6 month of age and a booster at 1 and 6 years. Immunity does not last life long.

Sampling:

Serology: 1 mL serum

Culture: Throat swab, nasopharyngeal swab, if pseudomembranes are present, swab should be taken from beneath the membrane.

Reference Interval:

Serology:

Diphtheria toxoid specific IgG antibodies, quantitative

Recommendations for vaccination

Immunity absent:		
	< 0.1 IU/mL	immunization immediately
	0.1 – 0.2 IU/mL	borderline, booster immediately
Immunity present:		
	0.2 – 1.0 IU/mL	booster recommended in 3 years
	> 1.0 – 1.5 IU/mL	booster recommended in 5 years
	> 1.5 – 2.0 IU/mL	booster recommended in 7 years
	> 2.0 IU/mL	booster recommended in 10 years

Culture:

Report on diagnostic finding

Corynebacterium sp. or Corynebacterium diphtheria isolated. Toxin producing strains can not be distinguished from non-toxin producers.

Coxiella burnetii (Q-Fever) Serology, Screening

Background: First recognized in Queensland in the 1930s, Coxiella burnetii is now known worldwide as an obligate intracellular organism. It has been included into the Rickettsiaceae, but it is more closely related to Legionella species and Francisella species. It is as Gram-negative, pleomorphic coccobacillus 0.2-1.0 um, displaying morphologic and phase changes. The bacterium is resistant to extreme environmental conditions for years and a low dose (one organism) of infection is needed, resulting in ready transmission of infection by aerosol inhalation. The most important animal reservoirs are cattle, sheep, goat besides a wide range of arthropods and mammals. The infected animals have high numbers of bacteria in blood and tissue, shedding viable organism in milk. Target cells for Coxiella spp. are monocytes and macrophages, particularly alveolar macrophages. Protected by a potent acid phosphatase it replicates intracellular.

Coxiella can be recovered from blood, urine, body fluids during acute infection.

Serology:

IgG phase II antigen peak at week 8 after onset of symptoms, whereas phase I develop very slow and remain on low titers. In chronic Q fever, IgG titers to phase I and phase II are high, and IgA phase I is usually associated with chronic infection. Thus elevated levels of IgG (>1:200) and IgM (1:25) to phase II but not phase I antigens indicate acute infection, while high titers of IgG (1:800) and IgA (1:50) to phase I antigen is more predictive to chronic infection.

Sampling: Highly infectious organism. Handle with extreme care. Serology: 1 mL serum.

Reference Interval:

Antibody titer including IgA, IgG and IgM phase I and II: <1:10

Coxsackie Virus, Serology

Related Information: Echo Viruses Serology

Background: Coxsackieviruses belong to the enteroviruses. Two groups are known. Group A (24 serotypes) causes herpangina, characterized by fever, sore throat, vesicles in the oropharynx and hand-foot-and-mouth disease which presents with a vesicular rash on hands and feet and ulcerations in the mouth. Group B coxsackieviruses (6 serotypes) causes pleurodynia (Bornholm disease, epidemic myalgia) with fever, chest pain, and signs of congestive failure and in severe cases dilated cardiomyopathy. In the mouse model Coxsackie B4 causes diabetes due to pancreatic damage.

Coxsackie A and B both are the cause of respiratory symptoms, rash, and aseptic meningitis.

The viruses are transmitted via the fecal oral route; respiratory aerosols play a minor role. Replication takes place in the oropharynx and in the intestinal tract. There is a summer and fall peak.

Sampling: 1 mL serum. Acute and convalescent sera should be drawn 2 weeks apart.

Reference Interval:

Differentiation of immunoglobulin class

IgA antibody	negative:	< 30 IU/mL
	borderline:	30 – 50 IU/mL
	positive:	>50 IU/mL
IgG antibody	negative:	< 80 IU/mL
	borderline:	80 – 100 IU/mL
	positive:	> 100 IU/mL

Creatine Kinase (CK, NAC-activated)

Related Information: Creatinine Kinase Isoenzymes, Serum
Lactate Dehydrogenase (LDH), Serum
Myoglobin, Blood,Serum or Plasma
Troponin T, Serum

Synonyms: CK; CPK; Creatinine Phosphokinase

Background: Please see: Creatinine Kinase Isoenzymes, Serum

Useful in diagnosis of acute myocardial infarct.

CK is a marker in patients with skeletal muscular disease or damage particularly in Duchenne's muscular dystrophy, levels reaching up to 5000 - 40000 U/L; CK is increased in females carrying the disease.

Increased levels occur in muscular stress, polymyositis, dermatomyositis, myocarditis, myositis after grand mal seizure, rhabdomyolysis and in advanced stages of cancer as well as obstructive lung disease. Multiple cardioversion shocks may give false positive CK and CK-MB results.

Limitations: Reference values in persons of African ancestry are up to 30% higher than those of European ancestry.

There is a day to day variation of CK in healthy adults of 20% to 30%.

Exercise has a major influence on CK values: Persons exercising aerobically have lower levels than those who do not exercise but complete inactivity (hospitalized patients) lowers CK. Short intensive exercise can increase values 10 -100 fold.

Sampling: 1 mL serum, avoid hemolysis.

Reference Interval:

Cord blood		175-402 U/L
Neonates		468-1200 U/L
< 5 days		195-700 U/L
5 days – 6 month		41-330 U/L
6 month -18 years		24-229 U/L
Adults:	male	55-170 U/L
	female	30-135 U/L

Creatine Phosphokinase MB-Isoenzyme see Creatinine Kinase Isoenzymes, Serum

Creatinine Clearance

Related Information: Creatinine, Serum or Plasma
Creatinine, Urine
Cystatin C, Urine
Protein, Quantitative, Urine
Uric Acid, Serum

Background: Useful in the evaluation of renal function. Due to exponential rise in serum creatinine with the decline in GFR, slight changes in serum creatinine represent a far greater decrease in GFR.

Sampling: 1 mL aliquot of a 24h urine collection, note total quantity and 1 mL serum. Exact timed collection period is essential. Also provide patients sex, age, height and weight. Patient must be well hydrated during the collection. Urine flow above 2 mL/minute is required. Keep collected urine refrigerated.

Reference Interval:

Newborn:	40 – 60 mL/min
up to 6 months:	60 – 75 mL/min
6 – 12 months:	75 – 100 mL/min
> 1 year:	100 – 140 mL/min
Male:	98 – 156 mL/min
Female:	95 – 160 mL/min

Critical value for moderate renal impairment: 40 mL/minute; severe renal impairment: less than 30 mL/minute

Alternatively, corrected for body surface area

(Body surface area in cm^2 = weight in kg $^{0.425}$ x height in cm $^{0.725}$ x 71.84)

Corrected creatinine clearance in ml/minute = ((urine volume per minute x urine creatinine) / serum creatinine) / (1.73/surface area body in m^2)

Children	70-140 mL/minute/1.73 m^2
Adults male	85-140 mL/minute/1.73 m^2
Adults female	75-115 mL/minute/1.73 m^2

For each decade after 40 years, decrease is 6-7 mL/minute/1.73m^2

For more precise calculation of GFR in adults:

GFR = 170 serum creatinine in mg/dL $^{-0.999}$ x age $^{-0.178}$ x (0.762 if female or 1.180 if black) x serum urea nitrogen in mg/dL $^{-0.170}$ x serum albumin in g/dL $^{+0.318}$

Creatinine Kinase Isoenzymes, Serum

Related Information: Creatine Kinase (CK, NAC-activated)
Myoglobulin, Blood, Serum or Plasma
Troponin T, Serum

Synonyms: CK-Isoenzymes (CK-MM, CK-BB, CK-MB), CK Isoforms ;
CK-MB and Total CK; CPK Isoenzymes ;
Creatinine-Phosphokinase-MB and Total Creatinine Phosphokinase;
Creatinine-Phosphokinase-MB Isoenzyme.

Background: Energy for muscle contractions are supplied by ATP and restored by CK through converting creatinine phosphate to creatinine and ATP. CK requires Mg. It is a dimer with a M (muscle) subunit and a B subunit (brain) of 40 kDa each. Three resulting forms may be released into the serum: CK_1 (BB); CK_2 (MB) and CK_3 (MM). There is a different mitochondrial form of CK (64kDa). Rarely CK_1 or CK_2 form oligomers with a molecular weigh of up to 250 kDa, (Macro CK). CK is found in small amounts in nearly all tissues, but high concentrations are only reached in the brain, which do not cross the blood brain barrier and in the muscle.

Tissue distribution in relative percentage:

	CK_1 (BB)	CK_2 (MB)	CK_3 (MM)
Skeletal muscle	0	0-7	93-100
Cardiac muscle, normal	0	2-3	97-98
Cardiac muscle, injured	0	10-15	85-90
Lung	20-50	0-5	30-60
Brain	97-98	2-3	0
Smooth muscle of the intestinum	90-95	0	5-10
Prostate	95-100	0-2	0-5
Placenta	100	0	0

Day to day variation of CK: 20%-30%; The half life of CK-MM is 20-24h; of CK-MB is 10-12h and of CK-BB is 1-2h.

Useful in the diagnosis of acute myocardial infarct (AMI). CK-MB usually starts to raise 6 h after onset of chest pain, peeks at 15-20h and returns to baseline by 72 h. Troponins stay elevated up to 2 weeks, CK-MB therefore serves as a good marker for reinfarction.
Limitations: The abrupt rise and fall of CK-MB is characteristic for AMI, for other damaging agents such as chronic myopathies or renal failure values change with a slower rate.
CK-MB elevation may occur in hypothyroidism.
CK-BB may be elevated in intestinal ischemia, malignancies, prostate cancer, small cell carcinoma of the lung and intestinal malignancies
In neonates CK-MB may be increased to 5%-10% of total CK, due to an increased skeletal

muscle proportion during fetal life.

Macro CK may increase total CK levels mainly in older women, in patients with HIV infection, in autoimmune diseases, in association with autoantibodies to CK-BB.

Sampling: 2 mL serum, avoid hemolysis.

Reference Interval:

CK-MM	< 174 U/L (= CK, total)	(95 – 100% of total CK)
CK-MB	< 12 U/L	(0 – 6% of total CK)
CK-BB >18 years	< 2 U/L	(< 1% of total CK, neonates < 12%)
Makro-CK	not detectable	
CK mitochondrial	< 2 U/L	

Creatinine, Serum or Plasma

Related Information: Creatinine, Urine
Creatinine Clearance
Cystatin C, Urine
Digoxin, Serum
Lactic Acid, Whole Blood, Plasma or CSF
Osmolality, Serum
Osmolality, Urine
Parathyroid Hormone, Intact, Serum
Uric Acid, Serum

Background: Creatine is the storage compound for high energy phosphate. Synthesized in the liver from arginine, glycine, methionine and to 98% distributed into the muscle to be converted in phosphocreatine and spontaneously into the cyclic amide creatinine. Creatinine is not metabolized further and is excreted.

Creatine is filtered by the glomeruli but completely reabsorbed, whereas creatinine is filtered and not reabsorbed under normal conditions.

Creatine and creatinine are proportional to the muscle mass with a daily turnover rate of creatine approx. 1.6% to 1.7%.

Serum creatinine is an approximation to the glomerular filtration rate to be used as a renal function test, particularly to monitor nephrotoxicity of drugs.

Causes of Increased creatinine: Renal diseases and insufficiency, urinary tract obstructions. Shock, dehydration, heart failure increases creatinine by reduction of renal filtration. Serum creatinine >2mg/dL in necrotizing pancreatitis indicate poor prognosis. Hypertension, diabetes mellitus may increase creatinine levels.

Low creatinine is associated with small stature, decreased muscle mass, liver disease, corticosterol therapy, muscle diseases, dermatomyositis.

Limitations: Creatinine is a late indicator for renal dysfunction, abnormal serum creatinine occurs

after destruction of more than half of the nephrons.

Sampling: 1 mL serum or plasma (heparin or EDTA or citrate)

Reference Interval:

Children	1-5 years	0.3-0.5 mg/dL
	5-10 years	0.5-0.8 mg/dL
Adults	Men	0.6-1.2 mg/dL
	Women	0.5-1.0 mg/dL (during pregnancy slightly lower)

In children with normal muscle mass GFR can be calculated:

GFR in ml/minute/1.73 m^2 = (a x body length in cm) / serum creatinine in mg/dL

Mean values for a

Low birth weight infants under 1 year	0.33 mg/dL
At term born under 1 year of age	0.45 mg/dL
Children 2-12 years	0.55 mg/dL
Male13-21 years	0.7 mg/dL
Female 13-21 years	0.55 mg/dL

Critical value

Chronic renal insufficiency:	1.5 – 3.0 mg/dL
Chronic renal failure:	> 3.0 mg/dL

Creatinine, Urine

Related Information:
Creatinine Clearance
Creatinine, Serum or Plasma
Osmolality, Serum
Osmolality, Urine
Sodium, Serum or Plasma
Sodium, Urine
Uric Acid, Urine
Vanillylmandelic Acid, Urine

Background: Creatinine, Serum or Plasma

In combination with serum creatinine a useful marker for renal function.

To differentiate between prerenal and renal causes in acute renal failure the following urinary parameters are useful:

Parameter	pre-renal	renal-tubular
Sodium concentration (mEq/L)	< 20	>40
Fraction Na%	<1	>1
Urine to plasma creatinine	>40	<20
Urine osmolality (mOsm/kgH2O)	>500	<350

Fraction Na% = [(Urine Na/serum Na) + (urine creatinine/serum creatinine)] x 100

Sampling: 5 mL aliquot of a 24h collected urine, keep cool, no preservatives added, note total quantity.

Reference Interval:

Children	2-3 years	6 - 22 mg/24h
	>3 years	12 - 30 mg/24h
Adults	Male	1.0 - 2.0 g/24h
	Female	0.8 - 1.8 g/24h

Alternatively, given per kg body weight:

Infants	8-20 mg/kg/day
Children	8-22 mg/kg/day
Adolescents	8-30 mg/kg/day
Adults male under the age of 40	14-26 mg/kg/day
Adults female under the age of 40	11-20 mg/kg/day

For each decade after 40 years, urine creatinine decreases up to 10 mg/kg/day

Cryoglobulin Qualitative, Serum or Plasma

Background: Cryoglobulins are immunoglobulins aggregating below 37°C in vivo and in vitro. They are associated with lymphoproliferative, infectious and autoimmune diseases, particularly such as Sjoegren syndrome, hepatitis C, macroglobulinemia Waldenstroem.

Clinically patients present with purpura, vasculitis, polyarthralgia, peripheral neuropathy, renal impairment, Raynaud syndrome.

Classification

Type 1: Cryoglobulins are composed of IgA or light chains complexed with monoclonal IgM or IgG immunoglobulins and are associated with lymphoproliferative or plasma proliferative diseases. Patients are asymptomatic or present with Raynaud syndrome, purpura or acrocyanosis. Typically precipitation occurs within 24h, concentrations are high (>500 mg/dL)

Type 2: Monoclonal IgM complexes with polyclonal IgG as an antigen (mixed cryoglobulinemia). As the most common form, it is often associated with hepatitis C, also with lymphoproliferative diseases and connective tissue diseases.
Clinically it presents also as arthralgias, glomerulonephritis, vasculitis, neuropathy and purpura.
Typically precipitation occurs within 1-7 days at 4°C

Type 3: Polyclonal IgM complexes with polyclonal IgG (mixed cryoglobulinemia). Associated with hepatitis C, chronic infections (such as CMV, bacterial endocarditis, leprosy, fungal and parasitic infections), autoimmune diseases (SLE, rheumatoid arthritis) and inflammatory bowl diseases.
Clinically often asymptomatic.

Precipitation may take 7 days at 4°C, concentrations are low (<1 mg/dL)

Sampling: Patient preferably in a fasting state. 10 mL whole blood drawn into a pre-warmed container, allow to clot at 37°C, centrifuge at 37°C, ship serum and clots to laboratory. Do not refrigerate or freeze. Results cannot be interpreted if the specimen is improperly handled. Please give brief clinical history.

Reference Interval: Not detectable

Cyanocobalamin see Vitamin B 12, Plasma or Serum

Cyclic Citrullinic Peptide (CCP) see Anticyclic Citrullinated Peptide Antibody

Cyclosporine A Monoclonal

Synonyms: Ciclosporin, Neoral®, Sandimmun®

Background: Cyclosporine is an immunosuppressive agent used in organ transplant in the treatment of graft versus host disease in hematopoietic stem cell transplantation. Also used in autoimmune disorders as a low dosage regime (less than 7 mg/kg/day).

The drug is a fat soluble cyclic polypeptide of 11 amino acids produced by the fungus species Beauveria nivea and acting in the antigen induced differentiation of T cells. Cyclosporine binds to cyclophilin, an intracellular protein of the class immunophilins, forming a complex that inhibits a phosphatase (calcineurin) which is part of the activation pathway for a T cell specific transcription factor NF-AT involved in the production of IL-2, IL-3, and IFN-gamma.

Oral bioavailability 10%-46%; urinary excretion <1%, plasma binding 90%-95%, volume of distribution 0.1 -15 L/kg decreased in aged and increased in children, half life time 4h-53h decreased in children, peak time after oral administration 1.5h-6h depending on the formulation, peak concentration 900–1800 ng/mL for soft gelatin capsules or 500-1600 ng/mL for Sandimmune®.

Cyclosporine is metabolized by the P-450 system and excreted by the bile.

Toxicities including nephrotoxicity, hypertension, hyperglycemia, liver function impairment, hirsutism, cholelithiasis. Possibly increases the risk for lymphomas.

Sampling: 3 mL EDTA plasma

Therapeutic Values 150 – 400 ng/mL

CYFRA 21 – 1, Serum

Related Information: Carcinoembryonic Antigen (CEA), Serum

Synonyms: Cytokeratin -19-fragment

Background: Cytokeratins is a class of approx 20 polypeptides which account with actin and microtubuli for the cytoskeletal structure of the cell.

CYFRA 21-1 is a fragment of cytokeratin 19 which is soluble in the serum and expressed in normal epithelia cells and malignant epithelial derived cells, predominant in lung tissue.
Useful in diagnosis of squamous cell carcinoma of the lung and as a prognostic marker, indicating poor prognosis
Used also in the diagnosis of carcinoma of the bladder.
Limitations: Since CYFRA 21-1 is present in various tissues in the body, it may be elevated in benign diseases. This feature influences the usefulness of the CYFRA 21-1 for lung carcinoma monitoring. Elevated levels are associated with pneumonias, sarcoidosis, bronchitis, asthma, tbc, emphysema.

Sampling: 1 mL serum.

Reference Interval:

Normal individuals: 80% display CYFRA 21-1 < 1.5 µg/L

Upper limit for a 95% specify for malignant diseases by organ:

Healthy individuals	1.7 µg/L
Disease of the lung	3.3 µg/L
Disease of the gastrointestinal tract	6.9 µg/L
Diseases of the ovary and uterus	3.1 µg/L
Disease of the bladder	2.4 µg/L
Renal insufficiency	5.2 µg/L

Cystatin C, Urine

Related Information: Creatinine Clearance
Creatinine, Serum or Plasma
Creatinine, Urine

Background: Cystatin C is a 13 kDa proteinase inhibitor prevalent in all nucleated cells. It is filtered in the glomerulus and reabsorbed by the proximal tube. No extrarenal route of excretion. Children over 1 year of age display the same serum level as adults. There is no diurnal variation, but day to day levels variation averages 13%, which is higher than creatinine variation. In renal transplant patients, cystatin c correlates better with GFR than serum creatinine.

Sampling: 10 mL aliquot of a 24h urine, no preservatives required. Note total volume. Stable at 20°C for 1 week.

Reference Interval: 0.5 – 1.0 mg/L

Cystic Fibrosis (CF) Gene Mutation

Synonyms: CFTR Gene Mutation

Background: CF is an autosomal recessive disease linked to mutations in the cystic fibroid transmembrane conductance regulator gene on chromosome 7q31.2, encoding a 1480 amino acid protein (CFTR), regulating chloride channels in epithelia cells in the lung, the pancreas, and

sweat glands. The deltaF508 mutation accounts for 70% of all CF mutant alleles in Caucasians, 10 mutations contribute to 85% of the more than 1000 known alleles. Using a panel of 31 mutations approx. 90% of mutations are detected and in 1%-2% no so far known mutation is detectable in clinical diagnosed CF patients. Carrier rate in Caucasians is 4%, prevalence 1 in 3000 live birth.

Useful in the diagnosis of CF, to evaluate chronic respiratory diseases, to assess carrier state, to evaluate infertility in men with congenital bilateral absence of the vas deferens (in 70% of the patients CFTR gene mutations, causing 5% of male infertility, but some of the patients without CF), to evaluate chronic idiopathic pancreatitis (up to 35% have a CFTR mutation without CF), to investigate infants with foul smelling stools or hepatosplenomegaly, to evaluate newborns with meconium ileus.

Limitations: Although the 31 one mutations included in the test panel, not detecting a mutation does not rule out CF.

The detection of 2 mutations confirms CF. 20%-30% of CF patients have one mutation, 70%-80% have two. 1%-2% have no mutation detectable. In carrier status, 90% have one detectable mutation.

Sampling: 2 mL EDTA blood. Amniotic fluid to be taken between the 12th and 14th week of gestation, chorionic villus specimens between week 8 and 12. Do not freeze, transport to laboratory soon.

Reference Interval: Report on diagnostic finding
Mutations on CFTR-gene out of 31 mutations tested for

Cystine, Urine

Related Information: Amino Acid Screening, Plasma or Urine

Background: Cystinuria is an autosomal recessive disease. Patients present frequently cystine urinary stones and urinary tract infections.

Not a diagnostic test for cystinosis.

Limitations: Chelating agents such as penicillamine cause false negative results

Sampling: An aliquot of 10 mL of a 24 h urine, collected in a clean container prefilled with 1 mL of glacial acetic acid. Note total quantity.

Reference Interval:

Normal	40 - 60 mg cystine / g creatinine
Heterozygotes	< 300 mg cystine / g creatinine
Homozygotes	> 250 mg cystine / g creatinine

Cytomegalovirus (HCMV, CMV), Antigen

Related Information: Cytomegalovirus (HCMV, CMV), DNA Detection
Cytomegalovirus (HCMV, CMV), Serology

Synonyms: CMP pp65 Detection

Background: The presence of the CMV specific protein (pp65) in infected peripheral blood leucocytes can be used to quantify the amount of CMV particularly in immunocompromised patients. As compared to viral CMV culture as the gold standard for active replicating virus, the assay has a sensitivity of 70-90% and a specificity of 95%-99%. Patients with antigenemia may be asymptomatic.

Sampling: 1 mL EDTA blood. Specimen must be processed within 6 hours.

Reference Interval: Report on diagnostic finding
Negative: pp65-AG not detectable

Cytomegalovirus (HCMV, CMV), DNA Detection

Related Information: Cytomegalovirus (HCMV, CMV), Serology
Cytomegalovirus (HCMV, CMV), Antigen

Background: 80% of the adult population has been infected with CMV in the past, usually asymptomatic, as indicated by antibodies.

In immunosuppressed in individuals early CMV detection has become a marker for intervention. CMV DNA detection is also useful in the diagnosis of congenital CMV infection, which may lead, if infection occurs during early pregnancy, to multiorgan failure CNS disorders. A high CMV load in amniotic fluid correlates with symptomatic infection. Infected newborns shed CMV with the urine.

Although DNA detection is highly sensitive false negative results occur. False positive results may be due to contamination.

Sampling: 1 mL CSF, EDTA blood, bronchoalveolar lavage, 10 mL urine, cervical swab

Reference Interval: Negative: CMV DNA not detectable

Cytomegalovirus (HCMV, CMV), Serology

Related Information: Cytomegalovirus (HCMV, CMV), Antigen
Cytomegalovirus (HCMV, CMV), DNA Detection

Background: Primary CMV infection can establish as an infectious mononucleosis like disease, interstitial pneumonia, hepatitis, meningoencephalitis intrauterine infection with congenital infection. After the primary phase CMV in the latent phase may be reactivated particularly in immunocompromised patients presenting as retinitis, colitis, and pneumonitis.

However the majority of CMV infections remain asymptomatic. The IgG type antibody will persist for lifetime. IgM antibodies are synthesized in low levels during reactivation and in higher levels during primary infection.

Intrauterine infection can occur even if a maternal immunity exists due to reinfection with a different CMV strain. However, maternal antibodies protect to a higher degree the fetus from infection.

Sampling: 1 mL serum

Differentiation of immunoglobulin class

IgG antibody negative:	<0.4 IU/mL
borderline:	0.4 – 0.6 IU/mL
positive:	> 0.6 IU/mL
IgM antibody negative:	< 15 AU/mL
borderline:	15 – 30 AU/mL
positive:	> 30 AU/mL