rial infection particularly in the presence of leukocyturia.
Protease inhibitor medication: Is associated in up to 50% of the patients with crystalluria with radial clusters in starburst form.
White cell casts: Are renal originating leucocytes, particularly in pyelonephritis.
Red cell casts: Are of renal origin, suggest glomerulonephritis as do dysmorphic red cells.
Hyaline casts: Are observed after intensive exercise and in various kidney diseases.
Epithelial casts: Occur in acute tubular injuries, tubular necrosis, in eclampsia, heavy metal poisoning, and ethylene glycol intoxication.
Granular casts: Suggests intensive exercise, glomerular and tubulointerstitial disorders.
Waxy casts: Are characteristic in severe chronic renal diseases.
Fatty casts: Are seen in nephrotic syndrome, glomerular diseases, such as minimal change disease, membranous glomerulopathy, and membranoproliferative glomerulonephritis.
Broad casts: Are shed by damaged tubules or collecting ducts.
Hematuria: Dark brown urine indicates a renal cause, red urine suggest an extrarenal source.
Spermatozoa: Seen after retrograde ejaculation.

Sampling: 10 mL urine. Avoid contamination, use sterile tube and midstream urine. Casts are more likely to be observed in morning urine sample, as well as due to higher concentration erythrocytes and leucocytes. To obtain best results urine should be fresh and warm. If the specimen can not be transported to the laboratory immediately, refrigerate to 4 - 8°C.

Reference Interval: (per high power field)

Casts	rare
Erythrocytes	0 - 5/HPF
Leucocytes	0 - 5/HPF
Bacteria	negative

Uroporphyrins see Porphyrins, Urine, Stool, Quantitative

Valproic Acid, Serum or Plasma f

Related Information: Carbamazepine, Serum
Phenobarbital, Serum
Phenytoin (Diphenylhydantoin, DPH), Serum
Primidone, Serum

Synonyms: Depacon®; Depakene®; Depakote®XR; Depamide®; Dipropylacetic® Acid; Divalproex Sodium; Epilim®; Ergenyl®; Leptilan®; 2-Propylpentanoic Acid; 2-Propylvaleric Acid; Valkote®; Valproate Semisodium; Valproate Sodium

Background: Used in various seizure types and in some bipolar disorders and in migraine headaches. The mechanism the therapeutic effect is by enhancing the inhibiting effect of gam-

ma aminobutyric acid in the brain. The drug is metabolized in the liver. By blocking the P450 enzyme system, valproic acid inhibits the metabolization of other drugs. A substantial to fatal hepatotoxicity, particularly in young children, has been described.
In pregnancy, valproic acid is contraindicated since a higher incidence of neural tube,-cardiac and skeletal defects have been reported.
Bioavailability 100%; urinary excretion 1 - 5%; plasma binding 90 - 95% decreased in renal disease, cirrhosis, pregnancy, elderly, neonates, burn patient; volume of distribution 0.2 L/kg; half life time 11 - 17 h increased in cirrhosis and neonates and decreased in children; peak time 1 - 4 h; peak concentration 26 - 42 ug/mL after a 250 mg oral dose steady state.

Sampling: 2 mL serum. Steady state reached after 3 days

Reference Interval: 50 - 100 µg/mL
Toxic: > 150 µg/mL
In patients with hypoalbuminemia clinical toxicity has been observed within normal serum levels, measurement of the free drug in theses patients may be necessary.

Vancomycin, Serum f

Synonyms: Lyphocin®; Vancocin®; Vancoled®

Background: Vancomycin is a glycopeptide active against gram-positive bacteria, interfering with cell wall synthesis and facilitating, therefore, the uptake of aminoglycosides. As a third line antibiotic, vancomycin should be used only if no other options have remained. It has renal and ototoxic side effects Elimination by glomerular filtration. Bile concentration up to 50% of plasma values; CSF 1 - 30% of plasma concentration.
Urinary excretion 70 - 90%; plasma binding 20 - 40%; volume of distribution 0.4L/kg is decreased in obesity. A half life time of 4 - 7.5 h is increased in renal disease and in elderly and is decreased in obesity.

Sampling: 2 mL serum. Peak after 30 - 60 min after I.V. application.

Reference Interval: Therapeutic values:
Minimum: 5 - 10 µg/mL
Maximum: 20 - 40 µg/mL
Toxic values: > 80 µg/mL ototoxicity may occur at > 37 µg/mL

Vanillylmandelic Acid, Urine f

Related Information: Catecholamines, Fractionation, Plasma or Urine
Creatinine, Urine
Homovanillic Acid (HVA), Urine
Metanephrines, Urine

Synonyms: 3-Methoxy-4-Hydroxymandelic Acid, VMA

Applies to: Creatinine, measured concomitantly in children

Background: VMA is a metabolite of catecholamines, epinephrine, and norepinephrine. In the diagnosis pheochromocytoma it is less sensitive than metanephrine and equal to norepinephrine, but more sensitive than epinephrine and dopamine.

Sampling: 10 mL of an 24 h urine collected in a container prefilled with 10 mL of a 20% hydrochloric acid (do not use boric acid). Note total quantity.

Reference Interval:		
	1st year	< 27 µg/mg creatinine
	1 - 2 years	< 18 µg/mg creatinine
	2 - 4 years	< 13 µg/mg creatinine
	5 - 9 years	< 8.5 µg/mg creatinine
	10 - 14 years	< 7 µg/mg creatinine
	Adults	< 8 mg / 24 hours

Varicella-Zoster Virus, Serology f

Background: Varicella–zoster virus is an enveloped alpha herpesvirus with a linear, double stranded DNA. The primary disease is Varicella (chickenpox), Zoster (shingles) is the recurrent form. Both forms are infectious.

Varicella: In developed countries peak incidence is at the age of 5 - 9 years in winter and spring epidemics. Maternally derived antibodies protects infants up to 6 - 9 month of life. 90% of the adults are immune by seropositivity. In contrast, in the tropics seropositivity is only 50 - 80% in adults. The risk of infection in day care centers is 50%, incubation period 10 - 25 days. The fatality rate rises with age, at 55 years it reaches 1 per 600 cases.

Herpes zoster as an infection of sensory nerve ganglions it complicates waning immunity affecting elderly or immunocompromised individuals and may be triggered by stress by stress such as diseases, trauma, HIV, malignancy, chemotherapy.

Varicella zoster virus first infects the respiratory mucosa, invading the lymphatics leading to asymptomatic viremia 7 days after infection. The virus replicates further in most tissues and appears in peripheral blood cells. The virus produces the typical Type A intranuclear inclusions, syncytium and gigant cells and in the skin the Tzanck cells. The clinical disease begins about 15 days after infection, including viremia, and skin, lung, gut, reticuloendothelial system infection, and possibly being complicated by pneumonitis, myocarditis, cardiomyopathy, hepatitis, Guillain-Barre syndrome, ventriculitis, granulomatous arteritis, meningoencephalitis. Congenital chickenpox can result in neonatal systemic disease and malformations. Immunity persist after primary infection, and unlike herpes simplex virus, the virus is not detectable during latency. Immune status: IgG positive value indicates immunity, but does not assure, even in high titers, protection from shingles.

Serologic diagnosis: IgM antibodies to VZV are not detectable until 6 days after the exanthema appears and peak around 2 weeks. IgG antibodies start to be detectable at day 9 after onset of the rash in primary varicella and slightly later after reactivation of zoster. Acute and convalescent sera drawn 2 weeks apart are recommended.

Prophylaxis: Live attenuated vaccine is available, 98% of the children and 94% of adults develop protective antibodies. After 5 - 10 years, breakthrough after exposure is 10 - 20%, however as a mild course.

For postexposure prophylaxis, human antiglobulin is available to administer within 96 h.

For treatment of varicella, acyclovir is licensed. For herpes zoster valaciclovir, a prodrug of acyclovir has enhanced bioavailability and famciclovir are in use. Antiviral treatment is without impact in children but reduces severity in adults.

Pregnancy: The congenital varicella syndrome includes microphthalmia, hypoplastic limbs and autonomic nervous system damage with gastroesophageal reflux and CNS abnormalities occurs in maternal varicella infection acquired in most cases before week 20 of gestation, occasional case reports at week 26 - 28. After week 20, manifestations include skin scars and childhood shingles. After gestational zoster, the syndrome has been reported rarely. Subclinical maternal varicella infection may cause neurologic symptoms without other signs of congenital varicella syndrome. Varizella Zoster virus hyperimmune globulin (VZVIG) is effective in prophylaxis for babies born to mothers who have chickenpox 5 days prior and 4 days after delivery. The use of VZVIG is also suggested to nonimmune pregnant women exposed during the first 20 weeks of pregnancy to chickenpox because of a higher risk to develop severe pulmonary complications.

Sampling: 1 mL serum

Reference Interval: Differentiation of immunoglobulin class

IgA antibody	negative	< 1.0 COI
IgG antibody	negative	< 250 mIE/mL
IgM antibody	negative	< 1.0 COI
	borderline	1.0 - 1.2 COI
	positive	>1.2 COI

Vasopressin see Antidiuretic Hormone, Plasma

Very Low Density Lipoproteins, Serum f

Related Information: Cholesterol, Total, Serum or Plasma
High Density Lipoprotein Cholesterol, Serum or Plasma
Low Density Lipoprotein Cholesterol
Triglycerides, Serum or Plasma

Synonyms: VLDL

Background: VLDL are smaller than chylomicrons but less rich in triglycerides and have a lower lipid to protein ratio. In the presence of excessive amounts, plasma appears turbid. VLDL are mainly composed in a wide variety in size and composition in the liver: cholesterol 4% - 8%, cholesteryl esters 16 - 22%, phospholipids 15 - 20%, triglycerides 45 - 65% and 6 - 10% are proteins such as apoB-100, apoC and apoE.

Sampling: 2 mL serum. For best results the patient should be on stable diet for 3 weeks. Sample drawing after fasting for 10h is necessary if triglycerides are requested. Total cholesterol is 10 - 15% lower in a recumbent position, as well as 5% lower in a sitting position.

Reference Interval: < 40 mg/dL

Vitamin A, Serum or Plasma f

Related Information: Vitamin E, Serum
Zink (Zn), Serum or Urine or Seminal Fluid

Background: Vitamin A, subdivided in two natural forms: retinol, (vit. A-1) and 3-dehydro-retinol (vit. A-2). It is a fat soluble, essential vitamin utilized by epithelial cells and in the vision cycle. Beta carotene is one of the 50 forms of provitamin A.

The test is used in diagnosis of hypovitaminosis in most of the cases caused by insufficient intake or diet or fat malabsorption.

Hypervitaminosis A may develop in patients with reduced disposal in myxedema, diabetes mellitus, renal diseases.

Teratogenicity has been reported.

Sampling: 2 mL of fasting EDTA or heparin plasma or serum, protect from light, keep refrigerated.

Reference Interval: normal range 200 - 1000 ng/mL
Possible toxic > 14.000 ng/mL

Vitamin B 1 (Thiamin), Serum f

Background: Known for centuries, beriberi polyneuritis disease is a thiamin deficient state.

Thiamine consists of a pyrimidine linked by a methylene bridge to a thiazole nucleus, functioning as a coenzyme in the pyrophosphate form. Thiamine pyrophosphate function in carbohydrate metabolism as a coenzyme in decarboxylation of keto acids (pyruvate, ketoglutarate) and in the hexose monophosphate shunt, thus patients on parenteral nutrition with dextrose thiamine has to be supplied sufficiently.

Toxicity is rare and only sporadically reported after long term parenteral administration.

Deficiency: Beriberi, occurring in Asia due to rice diet, in alcoholics, and clinically presents as a neurological disorder (peripheral neuritis with hyperesthesia, local anesthesia, muscle strength loss, poor memory) or with cardiovascular symptoms (abnormal ECG, cardiac failure).

The inherent subacute necrotizing encephalomyelopathy in children may be linked to thiamin dysfunction, since plasma pyruvate and lactate are elevated.

A form of megaloblastic anemia with deafness and diabetes mellitus has been described and is thiamine responsive. Pregnancy increases slightly thiamine requirement.

Sampling: 3 mL EDTA blood

Reference Interval: 20 - 100 ng/mL

Vitamin B 2 (Riboflavin), Serum f

Background: The water soluble riboflavin acts as a coenzyme after transformation into biological active riboflavin phosphate, also named flavin mononucleotide (FMN) and flavin adenine dinucleotide (FAD).

The conversion by flavokinase to FMN is sensitive to thyroid hormone and is inhibited by chlorpromazine and by tricyclic antidepressants, quinacrine interferes as well. Riboflavin is not stored in the body.

Deficiency: First signs are sore throat and angular stomatitis, later glossitis, cheilosis, seborrheic dermatitis, followed by anemia (normochromic and normocytic with reticulocytopenia) and neuropathy.

Rich in Riboflavin are milk, cheese, organ meets, eggs, green leaf vegetables, whole grain.

Sampling: 3 mL EDTA blood

Reference Interval: 137 - 370 ng/mL

Vitamin B_3 see Niacin, Serum

Vitamin B 6, Plasma or Serum f

Related Information: Homocyst(e)ine, Total, Plasma

Synonyms: Pyridoxal-5-Phosphate; Pyridoxine

Background: Important as a coenzyme in heme synthesis. Deficiency may lead to a hypochromic form of sideroblastic anemia (ring sideroblasts) or to megaloblastic anemia.

Other forms of hypovitaminosis, clinically characterized by dermatitis, cheilitis, glossitis and by laboratory characteristics cystathioninuria, homocystinuria, hyperhomocysteinemia may be due to reduced intake and during therapy with levodopa, disulfiram, contraceptives, theophylline, phenelzine, isoniazid, cycloserine, pyrazinoic acid.

Sampling: 2 mL EDTA plasma or serum, protect from light. Transport to laboratory soon, moderate stable, 50% loss within a week at -20°C.

Reference Interval: 4 - 25 ng/mL

Vitamin B 12, Plasma or Serum na

Related Information: Gastrin, Serum
Homocyst(e)ine, Total, Plasma
Methylmalonic Acid, Serum, Plasma or Urine

Synonyms: Cobalamin; Cyanocobalamin

Background: Cobalamin is an essential vitamin, synthesized by microorganisms, available in dietary animal products and needed for DNA synthesis, methylation reactions and in the citric acid cycle. B-12 applies to all forms of cobalamin, predominant form in the serum is methylco-

balamin and for the cytosol deoxyadenosyl cobalamin.
The daily requirement is estimated to 1 - 4 µg/day. The liver storage can provide B-12 for 4 - 5 years (daily loss approx. 0.1%). Sensitive early indicators for deficiency are an elevation of methylmalonic acid in serum or urine or a significant increase of mean corpuscular volume (MCV). Cobalamins are absorbed through microvilli in the terminal ileum after the release of cobalamins at low ph from proteins by peptic digestion in the stomach, therefore hypochlorhydria cause reduced absorption.
Useful parameter in the evaluation of patients presenting with weakness, anemia (macrocytic, megaloblastic anemia, MCV > 98 fl) or neurologic abnormalities (numbness, loss of vibratory sensitivity). Used in the diagnosis of malabsorption, macrocytosis, hypersegmented neutrophils, leukopenia.
Decreased absorption may be caused by interference with methotrexate, pyrimethamine, diuretics, pentamidine, isethionate, trimethoprim, phenytoin, barbiturates, contraceptives, anti-Tb medication, biguanides.
Decreased serum concentrations are associated with inflammatory bowel diseases, bacterial overgrowth, Diphyllobothrium tapeworm, jejunoileal bypass surgery.
Increased conditions: chronic granulocytic leukemia, chronic renal failure, diabetes mellitus, hepatitis.
Sampling: 2 mL serum
Reference Interval: 250 - 900 pg/mL
Due to the large storage pool by the liver, cut off values are not clearly established.

Vitamin C, Serum or Plasma f

Related Information: Oxalate, Urine
Synonyms: Ascorbate; Ascorbic Acid
Background: Half life approx. 2 weeks, if intake is stopped, for one month vit. C will be compensated, after 2 - 3 month scurvy develops.
Recommended daily intake is 100 mg/day up to a maximum of 1 g/day. High intake may promote oxalate kidney stones. Vitamin C is dialyzed, patients need replacement.
Sampling: 2 mL fasting serum or plasma. Separate serum or plasma very soon (stable 30 minutes at room temperature), freeze to ship at -20°C stable for 4 days. Avoid thawing-freezing cycles.
Reference Interval: Plasma 5 - 20 mg/L
Leukocytes 20 - 50 µg/10^3 cells

Vitamin D, Serum a

Related Information: Calcium, Serum or Urine
Magnesium, Serum or Urine
Osteocalcin, Serum or Plasma
Parathyroid Hormone, Intact, Serum
Phosphate Inorganic, Serum

Synonyms: Cholecalciferol

Applies to: 25–hydroxycholecalciferol (inactive precursor, plasma half life time 2 - 3 weeks), 1,25–dihydroxycholecalciferol, also named calcitriol (biologically active form, plasma half life time is 4 - 6h).

Background: IIncreased in patients with hypercalcemia due to extrarenal production of 1,25–dihydroxycholecalciferol (sarcoidosis, lymphoma, cat-scratch disease). Also in patients with primary hyperparathyroidism, vitamin D intoxication, lack in response by issue to 1,25 OH vitamin D. Decreased 1,25 OH cholecalciferol in hypoparathyroidism, hypercalemia in malignancy, renal failure, hyperphosphatemia, hypomagnesemia, vit D dependant rickets.

Sampling: 1 mL serum or plasma for 25-hydroxycholecalciferol; 3 mL serum or plasma for 1,25-dihydroxycholecalciferol;

Reference Interval:

Varies with sunlight exposure and diet

25-hydroxycholecalciferol	30 - 96 ng/mL (depending on sun exposure time)
1,25-dihydroxycholecalciferol	35 - 80 pg/mL

Vitamin E, Serum f

Related Information: Cholesterol, Total, Serum or Plasma
Vitamin A, Serum or Plasma

Synonyms: Alpha Tocopherol, Tocopherol

Background: As a fat soluble, widely distributed vitamin in diet, deficiency is less likely to occur. Deficiency may occur in premature infants, biliary atresia, cystic fibrosis, hemolytic anemia, neurologic disorders, long term dialysis and in acanthocytosis.

Sampling: 1 mL serum, protect from light

Reference Interval: 3 - 20 µg/mL

Vitamin H (Biotin), Serum f

Background: Tissue biotin is a cofactor for carboxylation of pyruvate, acetyl-coenzyme A (CoA), propionyl CoA, and beta-methylcrotonyl CoA .

Deficiency presents as severe exfoliative dermatitis and alopecia, similar to zinc deficiency.

Secreted in the urine as intact biotin, and to a lesser amounts as bis-norbiotin and biotin sulfoxide.

Sources for biotin are, egg yolk, milk, fish, and nuts. Biotin is cooking stable vitamin.

Daily recommended intake approx. 30 µg, the bacterial intestinal flora contributes in part to the

supply. Therapeutic large doses (5 - 10 mg) are applied to infants with seborrhea or genetic alteration of biotin dependent enzymes, no toxicity has been reported so far.

Sampling: 2 mL serum

Reference Interval: > 200 ng/L
< 100 ng/L interpreted as a biotin deficiency

Vitamin K-1, Serum f

Related Information: Factor II Mutation (Prothrombin Mutation)
Factor V Mutation (Leiden Mutation)
Protein C
Protein S, Total

Background: Vitamin K is a fat soluble vitamin, essential for the synthesis of clotting factors by the liver as a co factor in carboxylation of glutamic acid residues to form gamma-carboxyglutamic acid. Since bile salts are necessary for absorption, an obstruction of the bile ducts may cause vitamin K deficiency. Besides dietary intake, the vitamin is also synthesized by intestinal bacteria; antibiotic treatment may cause a deficiency. Vitamin K deficiency is characterized by decrease of factor II, VII, IX, X, Protein C and Protein S. Prolongation of PT occurs.
Coumarin blocks vitamin K dependent carboxylation, therefore, according to the half life time of the clotting factors, factor VII, and Protein C in the serum decreases first, thereafter factor X, II and IX .
Cephalosporins interfere directly with vitamin K regeneration.

Sampling: 2 mL serum

Reference Interval: 50 - 900 ng/L

Willebrand factor, Plasma f

Related Information: Coagulation factors
Bleeding disorders
Willebrand Disease

Synonyms: von Willebrand factor (vWF)

Background: Willebrand factor (WF) regulates important steps in primary and secondary hemostasis. Deficiency or functional defects of WF lead to bleeding disorders affecting both plasmatic coagulation as well as platelet function. In rare cases also increased risk of thrombosis may occur. Furthermore, WF deficiency is involved in thrombotic thrombocytopenic purpura or hemolytic-uremic syndrome. Deficiency of WF also leads to increased turnover rate of coagulation factor VIII resulting in low levels of this factor.
Both hereditary and acquired defects of WF are known, leading to bleeding disorders involving skin, mucosa and gingival bleedings, nosebleeds, menorrhagia or gastrointestinal and urinary tract bleedings. Please note that persons with blood group 0 reveal lower levels of WF without