Gonococcus see Neisseria gonorrhoeae

GPT see Alanine Aminotransferase (ALT), Serum

Growth Hormone (HGH, STH) see Somatotropin

Haloperidol, Serum or Plasma

Related Information: Lithium (Li), Serum

Synonyms: Dozic®; Fortunan®; Haldol®; Haloneural®; Serenace®

Background: Antipsychotic drug, used in the therapy of Tourette syndrome, sedation of agitated or delirious patients.

Sign of overdose: cardiovascular alterations such as EKG changes (depressed T or ST waves), arrhythmias; hyperglycemia; exacerbation of myasthenia gravis.

Bioavaliability 40%-80%; urinary excretion 1%; plasma binding 90%-94% increased in cirrhosis; volume of distribution 11-25 L/kg; half life time 13-23h decreased in children; peak time im: 0.6h, oral: 1.5-5h; peak concentration im: 5-40 ng/mL after a 10 mg single dose, oral: 5-14 ng/mL after a single 20 mg dose.

Haloperidol undergoes reversible metabolism to the reduced, less active form with a half life time of 16-120h. Slow reconversion to the parent drug may be responsible for prolonged half life time in 7 days samples of 70h.

Sampling: 2 mL serum

Reference Interval:			
	Therapeutic values:		4-20 (-40) ng/mL
	Toxic values:	adult	> 50 ng/mL
		children:	> 10 ng/mL

Hantavirus, Serology see Bunyaviruses, Serology

Haptoglobin (Hp), Serum

Related Information: C-Reactive Protein, Serum
Blood Count, Complete
Myoglobin, Blood or Serum or Plasma
Myoglobin Qualitative, Urine

Background: Haptoglobin is a plasma glycoprotein with alpha electrophoretic mobility that binds irreversibly to free hemoglobin, which can be removed by the liver saving hemoglobin from

renal loss. Two major genetic variants Hp1 and Hp2 are known.

Haptoglobin is a sensitive marker for hemolysis which is decreasing haptoglobin levels. If the red blood cells half life is decreased from 26 days to less than 17 days haptoglobin plasma levels are undetectable. Disease causing ineffective erythropoiesis, soft tissue hemorrhage and drug induced hemolytic anemia decrease haptoglobin levels.

Increase may occur in acute inflammation (acute phase reactant) counteracting concurrent hemolysis. Corticosteroids and nephrotic syndrome may elevate haptoglobin levels.

Decreased levels occur in liver disease and during estrogen therapy.

Sampling: 2 mL serum

Reference Interval:			
	1-10 days		5- 48 mg/dL
	10 days – 60 years		26-185 mg/dL
	>60 years	male	35-164 mg/dL
		female	40-175 mg/dL

Helicobacter pylori

Background: Helicobacter organisms are gram negative, spirale shaped, terminal flagellated, microaerophilic, urease positive bacilli (Campylobacter in contrast is urease negative), first isolated in 1982. The natural habitat of H. pylori is the human stomach.

Epidemiology: The infection rate decreases with increasing socio-economic level. Infection occurs in childhood and is likely to persist life long. Due to poor sanitation; the rate of infection in developing countries is high. In western countries in young individuals prevalence is up to 20%. The mode of infection is uncertain but likely to be fecal-oral or oral-oral.

Helicobacter pylori cause chronic gastritis and peptic ulcer and is considered a risk factor for gastric carcinoma.

H. pylori is fragile, biopsies must be kept in transport medium and cultured within 24h. Cultures will be kept for up to 10 days.

Therapy: Clarithromycin plus amoxicillin or clarithromycin plus metronidazole.

Sampling: Serology: 2 mL serum
Antigen detection: approx. 2 g stool
Culture and resistance testing: Gastric biopsy in Portagerm pylori transport medium

Reference Interval:

Serology:	Antibody of the IgG class IgG antibody	negative	<15 U/mL
		borderline	15-20 U/mL
		positive	>20 U/mL
	Validation by immunoblot		

Antigen detection: Negative

Culture: Report on diagnostic finding

Helminths, Microscopy, Feces

Test includes:

Ancylostoma duodenale (old world hookworm)
Ascaris lumbricoides
Cestoda (tapeworms)
Clonorchis sinensis
Diphyllobothrium (fish tapeworm)
Enterobius vermicularis (pinworm)
Fasciolopsis buski
Fasciola hepatica (sheep liver fluke)
Heterophyes heterophyes
Hymenolepis nana (dwarf tapeworm)
Necator americanus (new world hookworm)
Nemathelminthes (Nematodes, roundworms)
Paragonimus westermani (lung fluke)
Schistosomia species
Taenia solium (pork tapeworm)
Taenia saginata (beef tapeworm)
Trematodes (flukes)
Trichuris trichiura (whipworm)
Strongyloides stercoralis (small roundworm)

Background: The multicellular metazoan or helminthes are subdivided in two phyla: the Platyhelminthes (flatworms) and the Nemathelminthes. The phylum Platyhelminthes contains two medical important classes: Cestoda (tapeworms) and Trematoda (flukes).

Cestoda (tapeworms)

The tapeworms consist of two parts, a scolex (head) and multiple proglottids, which replicate from the germinal center next to the scolex to grow worm, the distal end contain gravid proglottids, which are excreted with the feces. The intermitted hosts are pigs, cattle, and fish. Infection of the human is by larvae ingestion or in case of cysticercosis and hydatid disease by egg ingestion.

Taenia solium (pork tapeworm)

The adult worm causes taeniasis. The infection occurs after ingesting uncooked pork containing the larvae. The larvae take 3 months to grow into the adult worm measuring up to several meters. Cysticercosis occurs, if the egg is digested by the definitive host, the human, not by the pig as intermediate host. The egg hatches in the small intestine and the oncosphere disseminate by the circulation system especially into the eye and brain, where they encysted to form cysticerci.

Laboratory diagnosis is made by identifying gravid proglottids with 5-10 primary uterine

branches in the stool. T. saginata proglottides have 10-15 uterine branches. Cysticercosis is diagnosed by finding cysts in tissue after surgical removal. Treatment: Praziquantel, for cysticercosis in addition surgical.

Taenia saginata (beef tapeworm)

Infection is acquired by humans eating undercooked beef containing the larvae which attach in the small intestine and grow in 3 month to the adult, several meters long worm. Detached proglottides passed with the feces infect cattle. The oncosphere emerge from the egg and are carried to the muscle to develop in cysticerci.

Laboratory diagnosis: T. saginata has, in contrast to T. solium, no hooklets at the scolex but also 4 suckers. Treatment: Praziquantel

Diphyllobothrium latum (fish tapeworm)

After ingestion raw or undercooked fish containing the larvae (plerocercoid or sparganum), the larvae develop in the human gut to the adult worm, releasing eggs, which develop in fresh water into embryos to be ingested by copepod Crustacea's as the first intermediate host. When the copepod is eaten by the second intermediate host, (pike, trout, and perch) the larvae differentiate into plerocercoids in the fish muscle.

Laboratory diagnosis is made by demonstrating in feces the typical eggs or typical parts of the worm: 2 elongated sucking grooves with no hooks at the scolex, eggs are oval with an operculum at one end, proglottides are wider then long, which differentiates the organism from the other cestodes.

Hymenolepis nana (dwarf tapeworm)

The 3-5 cm long worm does not need an intermediate host and eggs can infect humans directly. In the duodenum, hatched eggs develop into cysticercoid larvae and into adult worms, reaching by autoinfection several hundreds of parasites in the gut.

Laboratory diagnosis is made by demonstrating eggs which 6 hooked larvae and 8-10 filaments lying between the membrane of the larvae and the outer shell.

Trematodes (flukes)

including Schistosomia species, Clonorchis sinensis and Paragonimus westermani, Fasciola hepatica, Fasciolopsis buski and Heterophyes heterophyes.

Schistosoma

Three species are known: S. mansoni and S. japonicum live in the mesenteric veins, S. haematobium in the veins of the urinary bladder. Infection occurs by free swimming cercariae, penetrating the skin. The larvae enter the circulation system, enter the liver for maturation into the fluke and migrate into the typical veins system thereafter. The female flukes produce eggs to enter the gut or bladder lumen and eggs can be diagnosed in stool or urine.

The egg hatches in fresh water to penetrate snails and develop into cercariae. S. mansoni is endemic in Africa and Latin America, S. haematobium in Africa and Middle East, S. japonicum in Asia.

Clinically, transient eosinophilia, gastrointestinal hemorrhage, liver granulomas may occur with fibrosis and hepatomegaly, portal hypertension with splenomegaly and esophageal varices. Liver function remains unaltered. In chronic S. haematobium infection, carcinoma of the bladder may occur.

Laboratory diagnosis is made according to the egg form: S. mansoni eggs have prominent lateral spine, S. japonicum small lateral spine and S. haematobium eggs have terminal spine.

Therapy: Praziquantel

Clonorchis sinensis (and closely related Opisthorchis viverrini, Opisthorchis felineus)

also named human liver flukes.

Aquatic snails are infected by human feces containing ova to differentiate to the rediae and further to free swimming cercaria are released from the snails encyst to the stage of metacercariae under the scales of freshwater fish and are capable to infect humans if eaten undercooked. Passing through the duodenum, the metacercariae encyst and enter the biliary ducts and differentiate to the adult hermaphroditic fluke producing eggs which are excreted by the feces. The geographical region is restricted to eastern Asia ans some areas in Siberia. Prevalence in endemic regions up to 35%.There is an association between O. viverrini and cholangiocarcinoma in high endemic areas.

Laboratory diagnosis is made by finding in the stool typical small, brown, operculated eggs.

Paragonimus westermani (lung fluke)

Infection occurs by eating undercooked metacercariae containing crab or crayfish. The larvae encysted in the small intestine and migrate through the mucosa and diaphragma into the lung to differentiate into hermaphroditic adult flukes. Eggs produced are either swallowed or coughed, reaching fresh water and hatch into miracidia, entering snails as the first intermediate host. There, first redia develops and then cercariae which encyst in freshwater crabs as the second intermediate host.

Paragonimiasis is endemic in eastern Asia and central and Western Africa and occasionally in other tropical areas.

Laboratory Diagnosis is made by finding typical operculated eggs in sputum or feces.

Treatment: Praziquantel

Fasciola Hepatica (sheep liver fluke)

causes diseases primary in sheep and other domestic animals. Humans are infected by watercress contaminated with the larvae, they excyst in the duodenum and reach the liver to mature into the adult. Eggs shed into the bile tract are shed by the feces, hatch in fresh

water and enter snails as an intermediate host, develop into cercariae which are shed and encyst on aquatic vegetation.

Laboratory diagnosis is made by identification of eggs in the feces.

Therapy: Praziquantel and bithionol

Fasciolopsis buski

is endemic in Asia and India. Aquatic vegetation is the source of infection when carrying eggs. Attached to the gut mucosa, the fluke differentiate into the adult. Eggs are shed with feces and a snail is necessary as an intermediate host.

Laboratory diagnosis is made by demonstrating characteristic eggs in the feces.

Heterophyes heterophyes

is endemic in Africa, Middle East, Asia. Infection occurs by eating raw fish containing cysts. Mucosa attached larvae produce eggs in the small intestine, passed in the feces and are ingested by snails in brackish water. Cercariae are produced that encyst in certain fish species.

Laboratory diagnosis is made by finding characteristic eggs in the feces.

Nemathelminthes (Nematodes, roundworms)

Nematodes have cylindrical bodies covered with a highly resistant cuticle. The male has a coiled tail, the female is usually larger. The intestinal nematodes include Enterobius (pinworm), Trichuris (whipworm), Ascaris (roundworm), Necator, Ancylostoma (hookworms), and Strongyloides (small roundworm). Diagnosis of Trichinella and Anisakiasis (infection with the third-stage larvae of the round worm Anisakis marinae) is not made by stool examination. Two larvae forms are known: the noninfectious rhabditiform larvae and the infectious filariform larvae.

Symptoms: Itching in the perianal skin area is caused by Enterobius infections, rectal prolapse may occur in Trichuris infection and migrating larvae of Ascaris may cause pneumonia. Anemia occurs in Ancylostoma and Necator infection, Strongyloides may disseminate in various tissues in immunocompromised patients.

Enterobius vermicularis (pinworm)

After ingestion, eggs hatch in the small intestine, differentiate into adult worms and migrate to the colon, where mating occurs releasing eggs which become infectious larvae within 6 h at the anus which may reinfect the host when carried to the mouth.

Enterobius is found worldwide and affects children most commonly.

Laboratory diagnosis is made by recovered eggs from the perianal skin by tape technique. They are not recovered from the feces.

Treatment: Mebendazole or pyrantel pamoate.

Trichuris trichiura

Humans are infected by ingesting eggs in contaminated water or food. Hatching in the small intestine the larvae differentiate in adults who migrate to the colon to mature and produce thousands of eggs daily. Eggs are passed with the feces and form embryos in moist warm soil. Ingestion of eggs completes the cycle.

Laboratory diagnosis is made by demonstrating barrel-shaped (lemon shaped) eggs with a plug at each end in the feces.

Treatment: Mebendazole.

Ascaris lumbricoides

Infection occurs via egg contaminated food or water. Eggs hatches in the small intestine and the larvae migrate through the intestinal mucosa and bloodstream into the lungs, passing through the trachea and are swallowed. In the intestine they develop into adult worms which are up to 25 cm long. Eggs are passed through the feces and form embryos in warm moist soil. Ascariasis is common in the tropics ans in the southeastern US states.

Lab. Diagnosis is made microscopically by detecting oval, irregular surfaced eggs.

Treatment: Mebendazole and pyrantel pamoate.

Ancylostoma duodenale (old world hookworm) and Necator americanus (new world hookworm)

Infection occurs when filariform larvae living in a moist soil penetrate the skin, and are carried to the lungs, migrate to the trachea and are swallowed. In the small intestine they develop into adult worms attached to the mucosa. Eggs are passed in the feces and develop first into feeding, rhabditiform larvae and then into infectious, non feeding filariform larvae.

Hookworms are distributed worldwide in tropical areas.

Laboratory diagnosis is made microscopically by observing typical eggs in the stool, frequently occult blood in the stool and eosinophilia.

Treatment: Mebendazole and pyrantel pamoate.

Strongyloides stercoralis

Infection occurs by penetration of the skin by infectious (filariform) larvae which migrate to the lung. After entering the trachea they are swallowed. In the small intestine the larvae differentiate to adult worms, enter the mucosa and produce eggs, which hatch within the mucosa forming rhabditiform larvae which are passed with the feces. Some larvae form filarial larvae which auto-infect the host by penetrating the mucosa and migrate to the lung. In immunocompromised patients, massive autoinfection may occur with dissemination into organs. The rhabditiform larvae passed with the stool, molt through stages in warm moist soil to form adult female and male worms. The entire life cycle can occur in the soil, but after several free living cycles filarial larvae are formed which are capable to enter the parasitic cycle in humans.

Strongyloidiasis is endemic in the tropics, particularly in south eastern Asia. Prevalence in the US: 0.4%-4%

Laboratory diagnosis is made by finding the larvae form in stool and massive eosinophilia.

Sampling: approx. 2 g of fresh stool.

Optimum for obtaining specimens:

Ascaris lumbricoides, hookworms, Trichuris trichiura occur are constantly in feces but Diphyllobothrium latum and Schistosomia species are seen on an irregular base.

Reference Interval: Report on diagnostic finding

Hemochromatosis DNA Testing

Related Information: Ferritin, Serum or Plasma
Transferrin and Total Iron Binding Capacity, Serum

Synonyms: Hereditary Hemochromatosis; HFE Genotyping

Test Includes: Detection of C282, H 63D, S65C mutation

Background: Hereditary hematochromatosis (HH) is an autosomal recessive disease. It is common in Europe and among Caucasians; the prevalence in Caucasians is 1:400 and 1:10 for carriers. Siblings have a 1:4 risk of developing the disease. Caucasian parents and offspring's have a 1:20 risk of being affected.

The HFE gene is located in the HLA region on chromosome 6p21, encoding a cell surface protein which is similar to HLA class I molecules. The normal heterodimer modulates the affinity of the transferrin receptor for transferrin, the mutation prevents expression of the protein at the position at the cell surface.

Clinically, patients in late stage HH present with arthropathy, cardiomyopathy, hypothyrosis, testicular atrophy, abnormalities of the anterior pituitary gland, pancreas, cirrhosis, diabetes mellitus and skin bronzing, which may be preventable by early diagnosis and treatment.

Useful test in the evaluation of patients with persistent elevated AST or ALT or elevated serum transferrin iron saturation in at least two fasting blood samples. Liver biopsy is a complementary procedure particularly in patients to develop cirrhosis. Used also in risk assessment in families with hemochromatosis. For northern Europe 90% of the patients have a mutation at C282Y in the HLA lined HFE gene, in 40%-60% of non C282Y cases a mutation at H63D occurs with lower penetrance. Only 2% of C282Y/H63D or homozygote H63D patients develop clinically significant signs.

Limitations: Expression of heterozygosis of C282Y mutation does not invariably indicate clinical signs of HH. Fibrosis usually does not occur before the age of 40 years.

The test is not diagnostic for neonatal and juvenile hemochromatosis since different genes are affected.

Sampling: 2 mL EDTA blood, do not freeze, ship to laboratory within 5 days. Please provide clinical diagnosis, ethic background, serum iron, ferritin level, family history of HH.

Reference Interval:

Normal:	absence of detectable mutation
Carrier status:	one mutation detected
Hereditary hemochromatosis or predisposition for disease:	two or more mutations

Hemoglobin Electrophoresis

Background: HbA is the predominant hemoglobin (Hb) in the human body, other normal Hb types are HbA_2, which is gene encoded and modified forms such as Hb A_{1a}, HbA_{1b}, HbA_{1c}. During week 5-8 of gestation, HbF replaces precursor Hb forms (HbGower and Portland), newborns still have 80% HbF, which is replaced by adult Hb during the first 12 month of life.

HbA and HbF are composed of four chains out of two classes (alpha, beta, delta, gamma globulin). For HbA the chains are $alpha_2$ and $beta_2$, for HbA_2 $alpha_2$ and $delta_2$, for HbF $alpha_2$ and $gamma_2$.

The electrophoresis method separates Hb into the normal forms HbA_2 or HbF and abnormal forms such as HbC, HbS, and others.

The parameter is used in the diagnosis of hemoglobinopathies (incidence worldwide 0.17%) such as thalassemia, sickling hemoglobulinemias and structural chain abnormalities and in the evaluation of hemolytic anemias. Cord blood is suitable to detect alpha chain variants (HbF, HbG) and HbS or HbC.

Thalassemia is caused by a deficient synthesis of alpha or beta or rarely delta or gamma chain. Patients present increased levels of HbA_2, HbF, HbH (four beta chains) or HbBarts (four gamma chains).

Other forms of hemoglobinopathies are due to abnormal structures of the alpha, beta delta or gamma globulin, there are approx 900 types known so far.

HbA_2 is elevated in beta thalassemia, sickle cell disease, megaloblastic anemias, and hyperthyroidism. HbA_2 is decreased in alpha thalassemia, beta delta thalassemia, delta thalassemia, iron deficiency, and sideroblastic anemias.

Limitations: Avoid test after blood transfusions.

Sampling: 3 mL EDTA whole blood

Reference Interval:

	Adult	Children 1-2 years	newborn
HbA	97-98.5%	95-98%	18%
HbA_2	1.5-3.2%	1.5-3%	0.25%
HbF	0.8-0.5%	0.5-2%	82%

Children HbF	< 2 months	<50%
	2-4 months	<15%
	5 months	<5%
	6 month-1 year	<2%

Hemopexin, Serum

Background: Hemopexin is a beta-migrating single chain polypeptide with a MW 70 kDa and with 20% carbohydrates. Hemopexin binds heme released by degeneration of hemoglobin, contributing by protecting the iron from escaping from the porphyrin molecule and preserving body iron stores.

Deceased to a lesser extend during decreased production in liver failure; a major decrease is caused by intravascular hemolysis, when the amount of free hemoglobin exceeds haptoglobin binding capacity. Heme-hemopexin complexes are cleared by hepatocytes, lowering hemopexin levels in the circulation. Heme subsequently binds to albumin but is redistributed to hemopexin which is newly synthesized by the liver. Therefore depressed levels of free hemopexin are a long term marker for previous hemolysis after haptoglobin levels have returned to normal.

Sampling: 1 mL serum

Reference Interval: 50-115 mg/dL

Hepatitis A Antibodies, IgG and IgM (IgG anti-HAV, IgM anti-HAV)

Related Information:
Alanine Aminotransferase (ALT), Serum
Alkaline Phosphatase, Serum
Aspartate Aminotransferase (AST), Serum
Bilirubin, Fractionated, Serum
Hepatitis B (HBV), Serology and Antigen Detection
Hepatitis B Virus DNA Detection (HBV-DNA)
Hepatitis C Genotyping
Hepatitis C Virus RNA Quantification (HCV-RNA)
Hepatitis D Serology
Hepatitis E Antibody (Anti-HEV
Prothrombin Time

Background: Transmission of hepatitis A virus occurs via the fecal oral route. Traveling in endemic areas or consumption of contaminated food are major risk factors. After an incubation period of 2-7 weeks the self limiting disease manifests with fever, jaundice, anorexia, and diarrhea. Fecal excretion peaks before the symptoms develop. Specific IgM antibodies appear in acute hepatitis A infection within a week of the clinical onset and persist for 3-6 month with a peak at 3 month and up to one year in 20% of the patients. IgG specific antibodies persist life long and 50% of the adult population of Western countries have IgG type antibodies. Hepatitis A does not become chronic, subclinical courses, particularly in children are common. Rarely, a fulminant Hepatitis A infection is seen. A vaccine is available.

Sampling: 1 mL serum, EDTA or citrate plasma

Reference Interval:
Hepatitis A IgG antibody (IgG anti-HAV):
IgG positive: Immunity protective for at least 5 years.
Hepatitis A IgM antibody (IgM anti-HAV): negative

Hepatitis B (HBV), Serology and Antigen Detection

Related Information:
Alanine Aminotransferase (ALT), Serum
Alkaline Phosphatase, Serum
Aspartate Aminotransferase (AST), Serum
Bilirubin, Fractionated, Serum
Hepatitis A Antibodies, IgG and IgM (IgG anti-HAV, IgM anti-HAV)
Hepatitis B Virus DNA Detection (HBV-DNA)
Hepatitis C Genotyping
Hepatitis C Virus RNA Quantification (HCV-RNA)
Hepatitis D Serology
Hepatitis E Antibody (Anti-HEV)
Prothrombin Time

Background: HBV is a partially double stranded DNA, enveloped virus of the hepadnavirus family. The major proteins are: The surface antigen (HBsAg), which is part of the envelope, the core antigen (HBeAg) which is located together with the e antigen(HBeAg), a proteolytic product, in the nucleocapsid protein. There are four serologic subtypes of the HBsAg, adw, adr, ayw and ayr for epidemiological use.

The only natural hosts are humans. HBV is distributed worldwide with a high prevalence in Asia. Mode of transmission are via blood, sexual intercourse and perinatally. About 5% of HBV infected patients become chronic carriers defined as HBsAg persisting for more than 6 month. Chronic carriers are more likely to develop in newborns (up to 90%) than in adults, and subsequently with a high risk of developing hepatocellular carcinoma. Immunity lasts lifelong when antibodies directed against HBsAg are produced.

Clinically, many HBV infections are asymptomatic but fulminant courses may occur particularly in patients coinfected with HIV or with preexisting liver damage. The Incubation period varies between 1 and 6 month (usually 4-12 weeks)

Staging of HBV infection:

Test	Acute disease 2-12 weeks	Window phase 10-15 weeks	Recovery years	Chronic carrier
HBs Antigen	positive	negative	negative	positive
HBs Antibodies	negative	negative	positive	negative
HBc Antibodies				
-IGM	positive (early)	positive	negative	negative
-IgG	positive (late)	positive	positive	positive
HBe Antigen	positive	negative	negative	positive or negative
HBe Antibodies	negative	positive	positive	positive or negative

HBs Antigen can be detected 1-7 weeks before liver enzymes levels rise, 50% of the patients are positive 3 weeks after onset of the acute hepatitis, at week 17 only 10 % are still positive. Markers for infectivity are HBs Antigen and HBe Antigen. HBe Antigen usually convert to negative within 3-6 weeks,

persistence for more than 10 weeks suggests risk for development of chronic Hepatitis B. Infectivity is approx. 5 fold as high if HBe Antigen and HBs Antigen are co-present as compared to HBs Antigen alone. In chronic carriers HBeAg may become negative and HBe Antibodies may develop after more than 6 month, but HBs Antigen persists.

A quantification of HBs Antibodies is useful in the assessment of the immune status after vaccination.

Sampling: 1 mL serum citrate plasma or EDTA plasma for each test

Hepatitis B core Antibody (Anti-HBc)

Reference Interval: negative

Hepatitis B core IgM Antibody (IgM anti-HBc)

Reference Interval: negative

Hepatitis Be Antigen (HBeAg)

Reference Interval: negative

Hepatitis Be Antibody (Anti-HBe)

Reference Interval: negative

Hepatitis Bs (surface) Antigen (HbsAg)

Reference Interval: negative

Hepatitis Bs (surface) Antibody quantitative (Anti-HBs)

Reference Interval: negative < 10 IU/L

Quantification for immune status assessment:

Recommendations for vaccination:

< 20 IU/L	immunity not sufficient, immunization necessary	
Immunity present	20–50 IU/L	booster within weeks
	51–100 IU/L	check in 6 month
	101–1000 IU/L	check in 1 year
	1001–7500 IU/L	check in 2–3 years
	>7500 IU/L	check in 5 years

Hepatitis B Virus DNA Detection (HBV-DNA)

Related Information:

Alanine Aminotransferase (ALT), Serum
Alkaline Phosphatase, Serum
Aspartate Aminotransferase (AST), Serum
Bilirubin, Fractionated, Serum
Hepatitis A Antibodies, IgG and IgM (IgG anti-HAV, IgM anti-HAV)
Hepatitis B (HBV), Serology and Antigen Detection
Hepatitis C Serology
Hepatitis C Virus RNA Quantification (HCV-RNA)
Hepatitis D Serology
Hepatitis E Antibody (Anti-HEV
Prothrombin Time

Background: Chronic viral hepatitis is caused by Hepatitis B virus (HBV) or Hepatitis C virus. In most of the HBV infected patients, antibody response to HBs Antigen occurs and persists lifelong. 10% of the HBV infections are characterized by the absence of HBs Antibodies and the presence of HBs Antigen and HBc Antigen. Determination of HBV DNA is a supplement test to determine carrier state and quantification provides information of the infectivity and is of prognostic relevance. It is useful for the measurement of the response to antiviral therapy.

Sampling: 2 mL serum or EDTA blood, (heparinized blood is not accepted)

Reference Interval: Determination of the HB virus load
DNA not detectable: < 1000 Virus particles (VP) / mL

Hepatitis C Antibody (Anti-HCV)

Related Information:
Alanine Aminotransferase (ALT), Serum
Alkaline Phosphatase, Serum
Aspartate Aminotransferase (AST), Serum
Bilirubin, Fractionated, Serum
Hepatitis A Antibodies, IgG and IgM (IgG anti-HAV, IgM anti-HAV)
Hepatitis B Virus DNA Detection (HBV-DNA)
Hepatitis B (HBV), Serology and Antigen Detection
Hepatitis C Genotyping
Hepatitis C Virus RNA Quantification (HCV-RNA)
Hepatitis D Serology
Hepatitis E Antibody (Anti-HEV)
Prothrombin Time

Background: Hepatitis C is a single stranded RNA enveloped virus causing a slowly progressive and often asymptomatic hepatitis. Worldwide 180 million people are chronic carriers. About 30-50% of the patients recover; in 70-50% the infection becomes chronic. Cirrhosis develops in 20% of the patients after more than 20 years. HCV contribute to the prevalence of acute forms of hepatitis 20%, 60% to the cases of chronic hepatitis and 20-30% for cirrhosis of which 1-4% annually may develop hepatocellular carcinoma, whereas alcoholism enhances the rate of carcinoma. Antibody titer rises after 4-10 weeks post exposure. 80% of the infected become positive within 15 weeks post exposure.

Hepatitis C is transmitted by contact with human blood. There is no insect vector in opposite to the other flavivirus the yellow fever virus. 60% of HCV infections are due to shared needles in IV drug abusers and rarely by sexual contact. The risk of acquiring HCV by sexual contact however increase with coinfectoion with other sexual transmitted diseases. The risk of mother to child transmission is less than 5%, for needlestick infections less than 0.1%.

Limitations: False positive results may occur in pregnant women (0.2%), in recent immunized individuals against influenza virus, hypergammaglobulinemia, positive rheumatoid factor, connective tissue diseases. False negative results occur in patients with essential mixed cryoglobulinemias, hemodialysis, and immunodeficient patients.

Sampling: 1 mL serum EDTA or citrate plasma

Reference Interval: Antibody negative
Validation by Immunoblot

Hepatitis C Genotyping

Related Information:
Alanine Aminotransferase (ALT), Serum
Alkaline Phosphatase, Serum
Aspartate Aminotransferase (AST), Serum
Bilirubin, Fractionated, Serum
Hepatitis A Antibodies, IgG and IgM (IgG anti-HAV, IgM anti-HAV)
Hepatitis B Virus DNA Detection (HBV-DNA)
Hepatitis B (HBV), Serology and Antigen Detection
Hepatitis C Serology
Hepatitis C Virus RNA Quantification (HCV-RNA)
Hepatitis D Serology
Hepatitis E Antibody (Anti-HEV)
Prothrombin Time

Background: There are 6 HCV genotypes and 50 subtypes known. The genotypes are based on differences of the genes that encode one of the two envelope proteins. Genotype 1,2,3 are found worldwide, genotype 4 mainly in Egypt and Zaire, genotype 5 in South Africa, genotype 6 in Asia. Subtypes are described with letters. There is an association between disease progression and genotype: Genotype 1 b and genotype 4 causes a more aggressive form of hepatitis,

Sampling: 5 mL EDTA blood kept at 4°C and ship as soon as possible or freeze to -20°C.

Reference Interval: Report on diagnostic findings:
Genotypes 1, 2, 3
Determination of subtype a, b

Hepatitis C Virus RNA Quantification (HCV-RNA)

Related Information:
Alanine Aminotransferase (ALT), Serum
Alkaline Phosphatase, Serum
Aspartate Aminotransferase (AST), Serum
Bilirubin, Fractionated, Serum
Hepatitis A Antibodies, IgG and IgM (IgG anti-HAV, IgM anti-HAV)
Hepatitis B Virus DNA Detection (HBV-DNA)

Hepatitis B (HBV), Serology and Antigen Detection
Hepatitis C Serology
Hepatitis C Genotyping
Hepatitis D Serology
Hepatitis E Antibody (Anti-HEV)
Prothrombin Time

Background: Hepatitis C is a member of the flavivirus family. It is an enveloped virus with a single stranded positive polarity RNA. The onset of Hepatitis C is usually slow; the mean incubation time is 8 weeks. Patients without receiving treatment remain in 80% chronic carriers for at least one year. Chronic active hepatitis occurs in 10% of theses patients. About 20% of the chronic carriers develop cirrhosis.

HCV–RNA assay becomes positive within days of exposure before ALT or AST becomes usually moderate elevated.

The assay is useful in early diagnosis and therapy monitoring.

Sampling: 3 mL EDTA blood kept at 4°C and ship as soon as possible or freeze to -20°C.

Reference Interval: PCR Report
RNA not detectable: < 100 VP/mL

Hepatitis D Antibody (Anti-Delta), Serology

Related Information: Aspartate Aminotransferase (AST), Serum
Bilirubin, Fractionated, Serum
Hepatitis A Antibodies, IgG and IgM (IgG anti-HAV, IgM anti-HAV)
Hepatitis B Virus DNA Detection (HBV-DNA)
Hepatitis B (HBV), Serology and Antigen Detection
Hepatitis C Antibody (Anti-HCV)
Hepatitis C Genotyping
Hepatitis C Virus RNA Quantification (HCV-RNA)
Hepatitis E Antibody (Anti-HEV)

Background: Hepatitis delta agent (HDV), a RNA virus, occurs only in patients already infected with Hepatitis B virus. Coinfection increases the risk of fulminant and to develop chronic hepatitis with cirrhosis and carcinoma. Mode of transmission is more likely by i.v. drug use than sexual transmitted. Up to 20% of HBV positive individuals may carry in endemic areas HDV, in chronic liver disease patients up to 60%. Antibodies develop 5-7 weeks after infection.

Limitations: Patients with rheumatoid factors or lipemia may have false positive results.

Sampling: 1 mL serum or EDTA plasma

Reference Interval: Negative for IgG and IgM

Hepatitis E Antibody (Anti-HEV)

Related Information: Aspartate Aminotransferase (AST), Serum
Bilirubin, Fractionated, Serum
Hepatitis B Virus DNA Detection (HBV-DNA)
Hepatitis B (HBV), Serology and Antigen Detection
Hepatitis C Antibody (Anti-HCV)
Hepatitis C Genotyping
Hepatitis C Virus RNA Quantification (HCV-RNA)

Background: Hepatitis E is a self limiting hepatitis comparable to Hepatitis A. Route of transmission: Fecal-oral, particularly by contaminated water. The disease is endemic in India, Middle East, Southeast and Central Asia with seroprevalence between 2% and 30%. Acquisition of antibodies occurs predominantly during the first 2 decades of life. Incubation period is 15-60 days; no chronic infection has been described.
Serology: IgM antibodies are detectable 1-4 weeks after exposure, IgG can persist for 2 years. PCR is of limited use since no chronic state is known.

Sampling: 1 mL serum or EDTA plasma

Reference Interval: Negative for IgG

Herpes Simplex Virus Type 1, 2 (HSV), DNA Detection

Related Information: Herpes Simplex Virus Type 1, 2 (HSV), Serology

Background: The test detects nucleic acid of HSV-1 and HSV-2 in blood, CSF or swaps. In culture methods sensitivities are 40%-70% for genital ulcers and 40%-70% for neonatal encephalitis, the PCR improves the sensitivity substantially. PCR is considered as the test of choice for CNS HSV infection due the rapid and sensitive performance, however, a negative result cannot rule out HSV infection. HSV encephalitis is caused in most of the cases by HSV-1, HSV meningitis, which is more frequent, by HSV-2.

Sampling: Swap or vesicle fluid: Cytobrush in transport buffer
CSF/liquor: 2 mL
EDTA blood: 2 mL
Bronchial lavage fluid

Rapid transport to laboratory required, if more than 2h transit time expected, keep at 4°C, if 8h expected, freeze. Do not use heparinized tubes.

Reference Interval: HSV-1 or HSV-2 DNA not detected

Herpes Simplex Virus Type 1, 2 (HSV), Serology

Related Information: Herpes Simplex Virus Type 1, 2 (HSV), DNA Detection

Background: Herpes simplex virus (HSV)-1 and Herpes simplex virus (HSV)-2 also ICTV named as Human herpesvirus-1 and -2 are members of the subfamily Alphaherpesviridae in the genus Simplexvirus.

Herpesviridae have an icosahedral core surrounded by a lipoprotein obtained when budding from the nuclear membrane, a large seize of 120 – 200 nm, and a double stranded DNA.

HSV-1 peak incidence of primary infection occurs in childhood, for HSV-2 during adolescence. Adult seroprevalence in HSV-1 is 75% to 100%, for HSV-2 5%-95%. Main route of transmission for HSV are oral secretions, for HSV-2 genital secretions.

Herpes simplex virus types 1 and 2 and varicella viruses causes vesicular rash, HSV-1 causes lesion appears above the waist, HSV-2 below. HSV-1 causes acute gingivostomatitis, recurrent herpes labialis, keratoconjunctivitis, and temporal lobe encephalitis. HSV-2 causes neonatal disseminated disease, aseptic meningitis, recurrent genital herpes; HSV-1 is transmitted by respiratory secretions and saliva, HSV-2 via sexual contact and perinatal infection. Nearly all of the HSV-2 seropositive individuals shed virus intermittently from the mucosa.

Herpes simplex -1 or HSV-2 encephalitis, although rare with an incidence of 1 case per 250 000 population per year is the most common form of sporadic fatal encephalitis. 95% of HSV encephalitis is caused by HSV-1. One third of the adults developing herpes encephalitis have a primary infection, and those who have antibodies to HSV at the onset of encephalitis, 90% did not have had recurrent HSV-2 infection.

Neonatal herpes infection occurs if the mother has a primary infection during delivery. Infants born to seronegative mothers have an increased risk to acquire HSV-2 during delivery than infants born by seropositive mothers. More than 50% of the newborns become infected, mortality in disseminated infection in newborns exceed 70%. Prompt initiation of antiviral therapy may prevent development of neurologic impairment.

Therapy: For HSV -1 and-2 the DNA polymerase inhibitors acyclovir, valaciclovir, famciclovir, and in case of resistance foscarnet or cidofovir are available. Theses drugs have been shown to reduce duration of viral shedding, time of healing of lesions, duration of pain, complication rate. Intravenous administration of acyclovir is indicated even before laboratory confirmation in patients suspected systemic disease or herpes encephalitis.

Sampling: 1 mL serum

Reference Interval:	Differentiation of immunoglobulin classes	
IgA antibody	negative	< 0.9 COI
	borderline	0.9 – 1.0 COI
	positive	> 1.0 COI
IgG antibody	negative	< 20 RE/mL
IgM antibody	negative	< 0.9 COI
	borderline	0.9 – 1.0 COI
	positive	> 1.0 COI

IgG differentiation to IgG-HSV-1 and IgG-HSV-2 type

IgM antibodies are produced in primary infection and to a lesser extend during recurrent disease. Unspecific reactivity occurs. Increased IgA antibodies support the diagnosis of recent or recurrent infection.

Herpes-Zoster see Varicella-Zoster Virus, Serology

High Density Lipoprotein Cholesterol, Serum or Plasma

Related Information: Apolipoprotein A-1 and B-100, Serum
Cholesterol, Total, Serum or Plasma
Lipoprotein (a), Serum
Low Density Lipoprotein Cholesterol
Triglycerides, Serum or Plasma

Synonyms: Alpha1 Lipoprotein Cholesterol ; HDL ; HDLC ; HDL Cholesterol

Background: The HDL fraction summarizes a heterogenous class of lipoprotein particles. The level of HDL is considered as a major risk factor for coronary heart diseases (CHD) in an inverse related manner.

CHD risk increases 2%-3% for every 1 mg/dL decrease in HDL.

Increase in HDL is seen in physical exercise, weight loss, and moderate alcohol consumption as well in medications as niacin, fibrates, statins, resins, estrogens. A decrease is associated with smoking, obesity, pregnancy, stress, hospitalization, and medications as probucol, corticosteroids, androgens, progestins, diuretics, propanolol. Decrease also occurs during chronic renal failure, type II diabetes, myocardial infarction, thyroid dysfunction.

Hereditary defects of metabolism are: Familial hyperalphalipoproteinemia which is a deficiency of the cholesterol ester transfer protein, causing an increase in HDL and decrease in LDLC and triglycerides.

Tangier disease, apolipoprotein A-I deficiency, lecithin–cholesterol acyltransferase deficiency and fish eye disease are further types of genetic disorders affecting HDL.

Sampling: 1 mL serum or plasma. For optimal results, the patient should be on a stable diet for 2-3 weeks, stable body weight and fasting for 10h.

Reference Interval:	Male standard risk	30–50 mg/dL
	favorable or protective	> 50 mg/dL
	Female standard risk	40–60 mg/dL
	favorable or protective	> 60 mg/dL

Histamine, Urine or Plasma

Related Information: Immunoglobulin E

Background: Histamine is a mediator of anaphylaxis or other allergic states such as urticaria, flushing, asthma, and tachycardia. Histamine is released by basophil cells and mast cells via IgE receptor mediation. May also be elevated in myeloproliferative diseases and in carcinoid tumors (gastric origin).

Limitations: False positive during urinary tract infections.

Sampling: Plasma: 2 mL of EDTA plasma, freeze immediately and ship frozen.
Urine: ship a 10 ml aliquot of a 24h urine collected in a clean container. Keep cool. Note total quantity.

Reference Interval: Plasma: 0.3-1.0 ng/mL
Urine: 10-35 ng/mL or < 45 µg/g creatinine

Histone-Antibodies

Related Information: Antinuclear Antibody, Antibodies, dsDNA, Antibodies, ssDNA, Smith (Sm) Antibody

Background: Histones are tetrameric proteins located at the nucleolus. The tetramers are composed of H2A-H2B and H3-H4.

Useful test in drug induced systemic lupus erythematosus (SLE). Relevant antibodies are of the IgG and IgA type, IgM antibodies are present in healthy individuals and are directed against complexed DNA with H2A-H2B. In drug induced systemic lupus erythematosus antibodies directed against histones are present in 95% in high levels, and in 20%-70% in non-drug induced systemic lupus erythematosus. Absence of SLE antibodies such as Antinuclear Antibody, native ds-DNA Antibody, Smith (Sm) Antibody and high levels of Histone Antibodies favor the diagnosis of drug induced SLE. Clinically the drug induced SLE is characterized by skin and joint symptoms without renal involvement. Antibodies to ssDNA are present in 70%-90%, but no antibodies to dsDNA.

Felty syndrome is associated in up to 85% with high level histone antibodies, 5%-15% of patients with rheumatoid arthritis or primary biliary cirrhosis have elevated histone antibody levels as well as in autoimmune hepatitis, scleroderma, and neoplastic diseases.

Sampling: 1 mL serum

Reference Interval: Negative: < 20 U/mL

HIV-1/HIV-2 Serology

Test includes: HIV antibody detection by ELISA, confirmation of ELISA positives by Western Blotting, p-24 Antigen detection on request

Background: Human immunodeficiency virus (HIV) is the etiologic agent of AIDS. Acute infection is either symptome free or presents with flu-like disease. During the stage of acute infection at week 2-3 post infection virus can be detected in the plasma by p24 antigen assay or by PCR based viral DNA test. After 3 weeks, antibodies can be detected in serum or plasma.

Screening for HIV is performed by highly sensitive and specific ELISA (EIA) method; positive results have to be repeated by a second sample due to serious consequences of the diagnoses to rule out switched samples or contaminations and subsequently has to be confirmed by the Western blot method. HIV-2 is closely related to HIV-1, endemic in West Africa causing the same clinical disease, but time to develop AIDS may be longer.

Limitations: A positive HIV EIA must be confirmed by a second method that has to be based on an alternative principle of antibody detection. Cross reactivities in the screening EIA based test have been rarely described. Cross-reactions may be due to histocompatibility antigen mismatches or very rare in other viral diseases such as influenza.

Serology cannot be used in infants born to an HIV positive mother due to maternal antibody transfer by the placenta. Virus cultivation or DNA detection are more appropriate.

Sampling: 1 mL serum

Reference Interval: p-24 antigen detection: negative
HIV1/HIV-2 antibody detection: negative

HLA-B27

Related Information: C4Complement
Rheumatoid Factor, Serum or Body Fluid
Yersinia enterocolitica and Yersinia pseudotuberculosis, Culture and Serology

Background: HLA-B27 is an allele of the HLA-B locus. It is predictive marker for ankylosing spondylitis (AS). A patient tested positive has a 100 times greater like hood to develop AS than a negative patient.

Epidemiology: HLA B-27 allele is present in 3%-4% of African-Americans, in 6%-8% of Caucasians, and in 1% of Asians.

Sensitivity and specificity: 90% of patients with ankylosing spondylitis (AS) are positive. 10% of normal subjects are HLAB27 positive. Most of the HLAB27 subtypes are associated with AS.

The antigens is also associated, but to a lesser extend with Reiter syndrome, psoriatic arthritis, juvenile rheumatoid arthritis, or post infectious arthritis as well as congenital deficiency of C4 and C2, adrenal hyperplasia.

Sampling: 3 mL EDTA or ACD blood

Reference Interval: Negative

Homocyst(e)ine Total, Plasma

Related Information: Cholesterol, Total, Serum or Plasma
Factor V Mutation (Leiden Mutation),
Folic Acid, Serum
Methylmalonic Acid, Serum, Plasma or Urine
Vitamin B 12 , Plasma or Serum

Background: 80%-90% of the homocysteine is protein bound in the plasma, 5%-10% circulates as homocysteine, 5%-10% is bound to mixed disulfides, 2% is unbound (free).

Metabolized from the essential amino acid methionine, it undergoes either remethylation to methionine, transsulfuration to cysteine and glutathione (vitamin B 6 and riboflavin needed) or oxidation to homocysteine and mixed disulfides.

Useful as an independent risk factor for atherosclerosis. An increased value is a marker for thrombophilic state on risk for thrombosis (arteria and venous).

When increased a marker for vitamin deficiency (B6, B12 riboflavin) and folic acid.

Raised levels in newborns may indicate inborn errors of cobalamin and folate metabolism and the rare autosomal recessive disorder of homocystinuria.

Elevated levels are found in patients with renal insufficiency and hypothyroidism.

Highly prevalent, in 10%-15% of the population, a thermolabile variant of 5,10-methylenetetra hydrofolate reductase present with raised blood homocysteine levels and require higher folic acid intake.

Sampling: Optimal is fasting 2 mL serum and immediately centrifuged.

10% increase per hour if not separated, slowed by placing on ice.

Reference Interval:

0-30 years		4.6-8.12 µmol/L
30-59 years	male	6.3-11.2 µmol/L
	female	4.5-7.9 µmol/L
> 59 years		5.8-11.9 µmol/L

Alternative: overall 95 th percentile 5-15 µmol/L

Homovanillic Acid (HVA), Urine

Related Information: Catecholamines, Fractionation, Plasma
Catecholamines, Fractionation, Urine
Vanillylmandelic Acid, Urine

Background: HVA is a major terminal metabolite of dopamine.

Patients with neuroblastoma excrete dopamine and vanillylmandelic acid. Neuroblastomas are third (7%-11%) among malignancies during childhood, behind leukemia and gliomas. Diagnostic sensitivity depends on the tumor stage, in early stages 60%-70% stage I/II and 80% for stage II increasing to 98% in stage IV.

In pheochromocytoma sensitivity of urinary excretion for tumor detection is 96% for catechol-

amines, 96% for metanephrine, and 89% for vanillylmandelic acid.

Sampling: Ship an aliquot of 10 mL of a 24h urine, collected in a container prefilled with of 10 ml of a 20% hydrochloric acid solution. Ph should be between 2 and 4. Note total quantity! Avoid aspirin, disulfiram, reserpine, pyridoxine 2 days prior to collection; avoid levodopa 2 weeks prior to the testing.

Reference Interval:

age in years	mg/g creatinine, 95% percentile
0-1	32.6
2-4	22
5-9	15.1
10-19	12.8
>19	7.6

Alternative value for adults: < 6.9 mg/24 h

Human Herpesvirus Typ 6, Serology

Synonyms: HHV-6; Herpesvirus-Typ 6

Background: HHV-6 is a member of the subfamily beta-Herpesviridae and in the genus Roseolovirus. HHV-6 was originally isolated from T cell cultures derived from the blood of patients with AIDS. In contrast to CD4 T cell infection with HIV, HHV-6 infection is rapidly controlled by the immune system. HHV-6 is closely related to cytomegalovirus and HHV-7 viruses. There are two HHV-6 variants; HHV-6 B is the primary etiologic agent of exanthema subitum, for HHV-6 A (and HHV-7) no single disease has been associated with. HHV-6 (and HHV-7) infection occurs early in life, virus is present in saliva of most adults. Virus replicate in CD4 and in CD8 T cells, in natural killer cells, monocytes, epithelial cells and in brain cells.

Exanthema subitum (roseola infantum) in young children is characterized by fever, sometimes associated with a mild respiratory illness and lymphadenopathy, followed by the appearance of a fine maculopapular rash spreading from the trunk to the extremities. High fever for 3-4 days and inflammation of the tympanic membranes may occur, but rash may be present in only 10% of the patients. It was estimated that up to 25% of all hospital admissions of children under the age of 3 years with acute febrile illness is due to HHV-6 infection. Primary HHV-6 infection may also cause seizures in infants which accounts for up to 30% of all febrile seizures under the age of 3 years. Rarely, serve courses have been described such as meningoencephalitis, fulminant hepatitis or pancytopenia. In adolescents, HHV-6 may cause mononucleosis like illness.

A definite role in Multiple sclerosis and lymphoproliferative disorders has not been established and is still under investigation.

In immunocompromised patients, HHV-6 has been associated with intestinal pneumonia and encephalitis.

Serology: IGM antibody is the first antibody to be produced in response to acute (primary) as well as in recurrent disease, although the amount of produced IgM is generally higher during primary infection. Paired samples 10-20 days apart are recommended for serological diagnosis.

Therapy: Some effect was seen with Foscarnet and Cidofovir

Sampling: 1 mL serum

Reference Interval: Differentiation of immunoglobulin class

IgG antibody negative:	< 0.9 COI
borderline:	0.9 – 1.1 COI
positive:	> 1.1 COI
IgM antibody negative:	< 0.9 COI
borderline:	0.9 – 1.1 COI
positive:	> 1.1 COI

Human Papillomavirus (HPV) DNA

Synonyms: HPV, HPV Test, HPV screen

Background: HPV primarily infects keratinizing mucosal squamous epithelium. HPV is a member of the family of Papovaviruses, which are double stranded, circular, supercoiled DNA viruses with an icosahedral nucleocapsid. Carcinogenesis by HPV involves two proteins encoded by gene E6 and E7, interfering with the tumor suppressor gene p53 and Rb. More than 100 types of papilloma viruses are known, some highly correlated to carcinoma of the cervix.

Although prevalence of HPV infection as a sexual transmitted disease (STD) among women is high, only a faction develops high grade squamous intraepithelial lesions with few progressions to cervical carcinoma. Co-risk factors are smoking, oral contraceptives, nullipara, and other STDs. Immunocompetent women are able to clear the infection within 1-2 years. The test is useful in monitoring patients demonstrating minor cytological abnormalities by Pap test or any abnormal cytologic results or clinical finding such as koilocytosis, condyloma acuminatum, low grade squamous intraepithelial lesions, high grade squamous intraepithelial lesions, invasive cervical squamous cell carcinomas and adenocarcinomas.

Of the 30 known anogenital HPV types, 13 types are implicated in the pathogeneses of cervical cancer: 16,18,31,33,35,39,45,52,58,59,68. The most common high risk types are: 16,18,31,33,35,45. Low risk types are: 6,11,42,43,44.

Sampling: Cytobrush in special transport medium on request to obtain from MEDLAB

Reference Interval: Report on diagnostic finding

Humoral Immunoglobulin Production, Liquor see Cerebrospinal Fluid (CSF, Liquor)

Hydantoins see Phenytoin, Serum

5-Hydroxyindoleacetic Acid (5-HIAA) Quantitative, Urine

Related Information: Serotonin, Blood

Background: 5-HIAA is a serotonin metabolite excreted in larger amounts by carcinoid neoplasms of the gastrointestinal tract or respiratory tract and other sites. Used in the diagnosis and monitoring of carcinoid tumors. Urinary excretion > 24 mg/24h favors the diagnosis, particularly if clinical signs are present as flushing, hepatomegaly, diarrhea, and bronchospasm.

Limitations: However, some tumors release non-hydroxylated indole acid which is not measured in the assay. Renal diseases may lower urinary secretion.

Increase in patients with malabsorption, (celiac disease, tropical sprue), chronic obstruction.

Urinary increase after ingestion of food rich in serotonin such as avocados, bananas, cantaloupe, chocolate, eggplants, dates, kiwi, melon, nuts, pineapples, plantain, plums, tomatoes.

Drugs increasing 5-HIAA are acetaminophen, salicylates, phenacetin, naproxen, methocarbamol, imipramine, isoniazid, MAO-inhibitors, methenamine, methyldopa, reserpine, phenothiazine.

Sampling: 10 mL aliquot of a 24h urine, collect in a prefilled container with 10 mL of 20% hydrochloric acid, note total quantity.

Reference Interval: 0.6 – 8.2 mg/24h

17-alpha-Hydroxyprogesterone (17-OHP)

Related Information: Adrenocorticotropic Hormone, ACTH, Plasma
Androstenedione, Serum
Cortisol, Serum or Plasma
Progesterone, Serum

Background: 17-OHP is a precursor of cortisol and synthesized by the adrenal cortex, ovaries, testes, and placenta.

It is a marker for patients with congenital adrenal hyperplasia (CAH), characterized as an autosomal recessive disorder by deficiency of cortisol due to 21 hydroxylase deficiency (90% of the cases) which leads to ACTH induced adrenal hyperplasia. Patients present with virilization and mineralocorticoid deficiency, increased 17-ketosteroid and pregnanetriol urine values.

The test is used

- In CAH newborn screening and diagnosis and therapy monitoring on cortisol medication.
- In the evaluation of hirsutism, infertility, hermaphroditism which may be caused by 17-hydrolase deficiency.
- In the diagnosis of endocrine active tumors.

Limitations: 17-OHP is elevated to a lesser extend in 11 beta hydroxylase deficiency. To differentiate both 11-deoxycortisol and desoxycorticosterone have to be determined.

Sampling: 2 mL serum or heparin plasma, peak level in the morning. Separate serum or plasma within 6h. Newborn screening at the age of 2-4 days recommended, not earlier than day 2.

Reference Interval:				(ng/mL)
	Infants	cord blood		7.4-18.7
		3 days to 60 days		0.1-9.4
		3 month to 11 years		< 0.9
		12-20 years		< 1.8
	Adult	male		0.4-3.3
		female	follicular	0.1-1.2
			luteal	0.4-4.8
			postmenopausal	0.1-0.6

Newborn screening (ng/dL) (dryed whole blood spot)

weight	borderline	congenital adrenal hyperplasia suggested
<1299 g	>13500	
1300-1699 g	11500-13400	>13500
1700-2199 g	6500-8900	>9000
>2200 g	4000-8900	>9000

Hydroxyproline, Total, Urine

Related Information: Alkaline Phosphatase, Serum
Alkaline Phosphatase, Liver-Intestine-Bone-Isoenzymes, Serum
Calcium (Ca), Total, Serum
Osteocalcin, Serum or Plasma
Pyridinolines

Test includes: Creatinine, Total, Urine

Background: A marker for bone metabolism and bone turnover. Elevated in Paget s disease, healing phase after fractures, primary and secondary hyperparathyroidism. The parameter is sensitive to diet, low dose gelatin were used for establishing reference intervals. For best results avoid foods containing gelatine (cooked collagen) and meat for 1-2 days prior to collection. Ice cream, candies, desserts may contain gelatine as well. Avoid aspirin.

Sampling: Ship to the laboratory a 10 ml aliquot of a 24h urine, collect in container pre filled with 1 mL glacial acetic acid. Note total quantity.

Reference Interval:	Children	up to 1 month	2000 µmol/g creatinine
		1-12 month	1500 µmol/g creatinine
		1-6 years	1000 µmol/g creatinine
		7-14 years	200 µmol/g creatinine
	Adults	> 15 years	30 µmol/g creatinine

Ident Card see Paternity Testing