

60% of Whipple disease patients present with arthritis. DNA for *Tropheryma whippelii* is tested positive in the synovial fluid as well as neutrophil counts are elevated.

**Sampling:** If *Neisseria gonorrhoeae* infection is suspected, Thayer Martin media agar is best inoculated with joint fluid at the bedside.

For microscopy and analysis: 1 mL synovial fluid (or less) in sterile tube and 1 ml (or less) in EDTA tube for cell count.

<b>Reference Interval:</b>	Cell numbers:	up to 200/μl (mean 75/μl)
	Total protein:	11 - 22 g/L
	Uric acid:	3 - 7 mg/dL
	Glucose:	60 - 95 mg/dL
	Lactate:	9 - 16 mg/dL
	LDH:	< 200 U/L

## Tacrolimus (FK 506), Whole Blood

f

**Related Information:** Cyclosporine A (monoclonal)

**Synonyms:** FK-506; Prograf®

**Background:** FK-506 is a macrolide lactone immunosuppressant used in renal, liver, heart, lung and bone marrow transplants and in the treatment of atopic dermatitis. Tacrolimus is more active than cyclosporine, but also nephrotoxic, so co administration is not recommended and kidney function has to be closely monitored.

At least 9 metabolites are known mainly produced by the cytochrome P-450 system.

Bioavailability 5 - 70%; urinary excretion < 1%; plasma binding 70 - 99% mainly to albumin and alpha-1-acid glycoprotein; volume of distribution 0.7 - 1.4 L/kg increased in cirrhosis; half life time 8 - 17 h increased in cirrhosis; peak time 1.1 - 1.9h, peak concentration 21 - 41 ng/ml after a single 7 mg dose. Steady state reached within 2 - 3 days.

**Sampling:** 1 ml whole EDTA blood. Whole blood recommended since tacrolimus binds to erythrocytes and lipoproteins. Plasma levels are up to 20% lower.

<b>Reference Interval:</b>	Therapeutic:	
	for liver transplants	5 - 10 ng/mL
	for renal transplants	5 - 10 ng/mL
	for pancreas transplants	10 - 18 ng/mL
	for bone marrow	10 - 20 ng/mL
	for heart transplantation	5 - 20 ng/mL

for individual dosage please refer to actual guidelines.

S-T

## Teicoplanin, Serum

f

**Synonyms:** Targocid®

**Background:** Close to vancomycin, it is a glycopeptide antibiotic composed of 6 glycopep-

tides. It is effective against Streptococcus species, including Pneumococcus sp., Staphylococcus sp, all aerobic gram positive bacteria including methicillin resistant S. aureus (MRSA), Enterococcus sp., Listeria sp.. Some studies have shown a higher activity against Clostridium difficile as compared to vancomycin.

Resistance: Few strains of S. aureus, moderate numbers of Enterococcus sp. are resistant. Cross resistance with vancomycin is incomplete.

It is not effective against gram negative bacteria.

Teicoplanin is indicated in serious infections with Staphylococcus sp. and Enterococcus sp.

Half life time is 3.6 h, prolonged to 7-30 h after repeated dosages. Protein binding 90%; no crossing of the blood brain barrier; 50% excretion by the kidney within 4 days.

**Sampling:** 2 mL serum

**Reference Interval:** Therapeutic Interval: 5-60 mg/L

(Average serum levels after I.V. dose of 0.4 g are 32 mg/L at 1 h, 5 mg/L at 24 h after first dose)

**Tempra® see** Acetaminophen, Serum

## Testosterone, Serum

f

**Related Information:** Adrenocorticotrophic Hormone, ACTH, Plasma  
Androstenedione, Serum  
Cortisol, Serum or Plasma  
Cortisol, Free, Urine  
Dehydroepiandrosterone Sulphate (DHEA-S), Serum  
Follicle Stimulating Hormone (FSH), Serum  
Luteinizing Hormone (LH)

**Background:** Testosterone (T) is secreted by the testicular Leydig cells, is active and has a more active metabolite, dihydrotestosterone (DHT). DHT is produced by a 5-alpha reductase of the skin, prostate, internal genitals. T is also converted into the estrogenic hormone estradiol (E2) by an aromatase of the fat tissue of the breast. The secretion of T is regulated by a negative loop by the pituitary luteinizing hormone (LH), which is released by the hypothalamic gonadotropin releasing hormone. Peak levels of T occur in the early morning and minimum levels are in the early evening. T is bound in the serum by sex hormone binding globulin (SHBG) to 60% and to 30% by albumin, only 1% - 4% is free. To assess the free T is useful in obese patients who may have low SHBG.

Determination of T is useful in polycystic ovary syndrome which is characterized by androgen excess such as anovulation, hirsutism, acne and is in most cases accompanied by elevated T levels. Useful in male hypogonadism patients with primary testicular insufficiency: Low T values in combination with high LH and FSH levels.

Limitations: Cimetidine may elevate T values. In athletes taking exogenous T, endogenous T may be suppressed.

Morning values are 20% higher than evening levels. Short physical activity may elevate, long term exhausting activities may decrease values, also serve diseases particularly of the liver, kidney and cardiopulmonary system decrease T.

**Sampling:** 1 mL serum or heparin plasma for free testosterone, 1 mL serum for total testosterone.

**Reference Interval:**

Total Testosterone, Serum: (ng/mL)		
Years of age	Male	Female
1 - 9	< 0.4	< 0.4
10 - 11	< 2.0	< 0.7
12 - 13	< 8.0	< 1.2
14	< 12.0	< 1.2
15 - 16	1.0 - 12.0	< 1.2
17 - 18	3.0 - 12.0	0.2 - 1.2
19 - 40	3.0 - 9.5	0.2 - 0.8
> 40	2.4 - 9.5	0.2 - 0.8

Free Testosterone, Serum:

Male	9.0 - 27.0 pg/mL
Female	0.5 - 5.2 pg/mL

## Tetanus Antitoxin Antibody IgG

f

**Background:** Clostridium tetani is a gram positive, spore forming with high environmental resistance, obligate anaerobe. It proliferates at the site of a deep injury and secretes tetanospasmin, a neurotoxin causes the spastic paralysis. The reservoir is the gastrointestinal tract of animals. Although seldom in the industrialized countries, mortality is still 50%. Immunity after vaccination wanes by age, booster immunizations are strongly encouraged.

**Sampling:** 1 mL serum

**Reference Interval:**

< 0.1 IU/mL	no immunity
0.1 - 0.5 IU/mL	immunity may be not protective
0.5 - 1 IU/mL	booster recommended in 3 years
1 - 5 IU/mL	booster recommended in 5 years
> 5 IU/mL	booster recommended in 8 years

S-T

## Theophylline, Serum

f

**Related Information:**

Amiodarone, Serum
Caffeine, Serum
Carbamazepine, Serum
Carbamazepine-10,11-Epoxyde, Serum
Phenobarbital, Serum

Phenytoin (Diphenylhydantoin, DPH), Serum

Verapamil, Serum or Plasma

**Synonyms:**

Aminophylline; Elixophyllin®; Ethylenediamine; Phyllocontin®; Slo-Phyllin®; Sustaire®; Theo-Dur®; Theolair™; Truphylline®.

**Background:** Used in COPD and asthma. Displays anti-inflammatory and immunomodulatory characteristics. Good tolerance if within the therapeutic range.

Half life in healthy and non smoking adults: 6 - 10 h, in healthy children 2 - 9 h, in patients with cirrhosis up to 30 h, with congestive heart diseases up to 24 h, in premature infants 15 - 58 h.

Half life is shorter in smokers; usually smokers need 1.5 - 2 times as much as non smokers and are variable with co-administration of phenobarbital. Possible decrease in theophylline concentrations is caused by rifampin, carbamazepine, phenytoin, aminoglutethimide.

Volume of distribution 0.4 - 0.6 L/kg; protein binding 52 - 60%

**Sampling:** 1 mL serum

In general: Sampling time 2 h after dosage or 6 h for sustained preparations.

Peak concentrations: Oral 1 h, uncoated tablets 2 h, chewable tablets 1-2 h, enteric coated tablets 4-5 h, extended release tablets up to 7 h

**Reference Interval:**

Therapeutic: 10 - 20 µg/mL,

60% of maximal broncho-dilatator effects at 10 µg/mL.

10 - 15 µg/mL are effective in COPD patients.

Toxic effects such as diarrhea, nausea, abdominal pain, headache, dizziness, agitation, tremor may occur at 15 - 25 µg/mL; tachycardia at 25 - 35 µg/mL and at > 35 µg/mL ventricular tachycardia, premature ventricular contractions, seizures.

**Thiamin see** Vitamin B

## Thrombin Time

f

**Related Information:**

Activated Partial Thromboplastin Time

D-Dimers

Fibrinogen, Functional

Applies to Fibrinopeptide A and B

**Background:** The test is measuring the clotting time in the last step of the coagulation cascade (fibrinogen to fibrin). Useful in the diagnosis of hereditary or acquired dysfibrinogenemia.

- Hereditary dysfibrinogenemia, caused by various mutations, leading to mild bleeding or venous or less frequent arterial thrombosis. Prevalence in patients with venous thrombosis is 0.8%. In addition to changed thrombin time, PT or PTT may be prolonged.

- Acquired forms include liver diseases, hepatoma, acute phase reactions with high levels of fibrinogen. Thrombin time can be prolonged in disseminated intravascular coagulation (DIC)

and thrombolytic therapy. Prolongation, together with ReptilaseR time, has been observed in amyloidosis, due to inhibition of conversion fibrinogen to fibrin.

The thrombin time has been used in monitoring heparin therapy if PTT was not reliable, but has been replaced by antifactor Xa assays, since thrombin time is too sensitive.

The assay is performed by adding to the patient's plasma thrombin and clotting time is measured. Thrombin cleaves fibrinogen, releasing fibrinopeptide A and B from fibrinogen and converting fibrinogen into fibrin-clot.

**Sampling:** 2 mL citrate plasma, tube must be approximately completely filled, invert gently to mix well. Separate plasma soon. Plasma is stable on ice up to 4h. Test is highly sensitive to traces of heparin, hirudin or argatroban anticoagulants.

**Reference Interval:** 14 - 20 seconds

**Thromboplastin Time, Partial (PTT) see** Activated Partial Thromboplastin Time

**Thromboplastin Time (Quick's Value) see** Prothrombin Time

## Thyroglobulin, Serum

f

**Background:** Secreted by the thyroid follicular epithelial cells, thyroglobulin stores the thyroid hormones  $T_4$  and  $T_3$ . Used for monitoring patients with differentiated thyroid carcinomas after resection.

**Sampling:** 1 mL serum, do not draw sample soon after needle biopsy, thyroid surgery or radioiodine therapy.

**Reference Interval:** Euthyroid patients and normal TSH: 1.4 - 59 ng/mL  
Total thyrotomy or suppressed TSH: < 0.5 ng/mL

## Thyroglobulin Antibody

a

**Related Information:** Thyroperoxidase Autoantibody  
Thyrotropin Receptor Antibody

**Synonym:** Anti Thyroid Globulin Antibody

**Sampling:** 1 mL serum

**Reference Interval:** Negative < 60 U/mL

## Thyroid Stimulating Hormone, Serum

a

**Related Information:** Thyroglobulin Antibody  
 Thyroid Stimulating Hormone, Serum  
 Thyroxine, Free, Serum  
 Thyroxine, Total, Serum  
 Triiodothyronine, Free and Total, Serum

**Synonyms:** TSH; sTSH; Thyrotropin

**Background:** TSH, synthesized by the anterior pituitary gland, stimulates secretion of  $T_3$  and  $T_4$  and is regulated by a feedback loop, involving TRH from the hypothalamus. The prevalence of hypothyroidism is up to 14% in older individuals, and since subclinical hypothyroidism (increased TSH and normal  $FT_4$ ) has been shown to be a risk factor for atherosclerosis and myocardial infarction, TSH in combination with  $T_4$  or  $FT_4$  has to be considered as a screening test in this population.

- Primary Hypothyroidism: an increased TSH level is an early indicator for later decrease in  $T_4$ .
- Secondary Hypothyroidism: due to the insufficiency of the pituitary gland to react to  $T_4$  level TSH remain low but in part within the normal range. Therefore it is necessary to obtain TSH and  $T_4$  values simultaneously.
- Resistance to thyroid hormone: a familial disease characterized by insensitivity to thyroid hormones, elevated  $T_4$  and  $T_3$  levels and normal to elevated TSH, demanding a clinical evaluation of patients on familiar risk to avoid the diagnose of hyperthyroidism.

To monitor thyroxine therapy, a 8 - 10 week interval has to be considered to achieve a stable steady state of normal TSH levels.

**Sampling:** 1 mL serum, separate serum within 5h and refrigerate for max. 5 days.

TSH release is pulsatile and a diurnal rhythm exists with peak levels around 11 PM. Drugs and diseases often alter TSH, to obtain proper diagnosis, patients should be in a clinically stable state.

**Reference Interval:** Validated for Southern Germany:

Adults	21 - 54 years	0.2 - 2.8 mIU/L
	55 - 87 years	0.2 - 3.0 mIU/L
Newborns/Children	Premature neonates	0.3 - 13 mIU/L
	Birth	0.5 - 20 mIU/L
	2 - 20 weeks	0.8 - 5.0 mIU/L
	21 weeks to 20 years	0.3 - 4.5 mIU/L

For the US reference ranges have been reported as:

Adults	21 - 54 years	0.4 - 4.2 mIU/L
	55 - 87 years	0.5 - 8.9 mIU/L
Newborns/Children	Premature neonates	0.7 - 27.0 mIU/L
	Birth	1.0 - 39.0 mIU/L
	2 - 20 weeks	1.7 - 9.1 mIU/L
	21 weeks to 20 years	0.7 - 6.4 mIU/L

For the Middle East one report systematically investigated TSH:  
Adults 18 - 54 years (average 27 years)

Male	0.52 - 4.89 mIU/L
Female	0.48 - 6.30 mIU/L

Critical value: Less than 0.1 mIU/L indicates wither primary hypothyroidism or exogenous thyrotoxicosis. Patient may be on risk for atrial fibrillation.

## Thyroperoxidase Autoantibody

a

**Related Information:** Thyroglobulin Antibody  
Thyroid Stimulating Hormone, Serum  
Thyroxine, Free, Serum  
Thyroxine, Total, Serum

**Synonyms:** Antithyroid Peroxidase Antibody; Microsomal Antibody; Thyroid;  
Thyroid Antimicrosomal Antibody;

**Background:** Thyroperoxidase is a major antigen in cell mediated cytotoxic thyroid disease. Elevated antibodies titers against thyroperoxidase support the diagnosis of autoimmune thyroiditis in patients with hypothyroidism. However, 10% of the adult population has moderate elevated titers without signs of disease.

**Sampling:** 1 mL serum, stable 3 days at 4°C.

**Reference Interval:** Negative < 20 IU/mL  
Positive in adults > 20 IU/mL  
In autoimmune thyroiditis > 50 IU/mL

## Thyrotropin Receptor Antibody, Serum

f

**Related Information:** Thyroglobulin Antibody  
Thyroid Stimulating Hormone, Serum  
Thyroperoxidase Autoantibody  
Thyroxine, Free, Serum  
Thyroxine, Total, Serum

**Synonyms:** LATS; Long-Acting Thyroid Stimulator; Thyroid Stimulating Autoantibody; Thyroid Stimulating Immunoglobulins; TRAb; Ts Antibodies;  
TSH- Receptor Antibodies; TSIG

**Background:** Contributes to the pathogenesis in Grave's disease. Sensitivity for Grave's disease 80 - 95%, useful in patients without hyperthyroidism and clinical signs of infiltrative ophthalmopathy or dermopathy and in patients with toxic nodular goiter.

Limitations: Low serum immunoglobulin levels or serum protein may give false negative results.

**Sampling:** 1 mL serum

**Reference Interval:** Negative < 2 U/L

## Thyroxine Binding Globulin

f

**Related Information:** Thyroxine Free, Serum  
Thyroxine Total, Serum  
Triiodothyronine Free and Total, Serum

**Synonyms:**  $T_4$  Binding Globulin; TGB

**Background:** There are at least 3 proteins binding  $T_3$  and  $T_4$ : albumin, transthyretin, thyroxine binding globulin, (see Thyroxine, Total, Serum). Differences in total  $T_3$  and  $T_4$  (abnormal) and free  $T_3$  or  $T_4$  (normal) values suggests altered TBG state, particularly in euthyroid individuals. An increase of TBG may be due to estrogens or a wide variety of drugs. Decrease may be caused by chronic diseases or familial deficiency (1:5000).

Useful in diagnosis of hereditary deficiency of TBG.

**Sampling:** 1 mL serum

**Reference Interval:**

0 - 1 week	3 - 8 mg/dL
1 - 12 months	3 - 6 mg/dL
2 - 10 years	2 - 5 mg/dL
> 15 years	1.2 - 2.5 mg/dL

## Thyroxine Free, Serum

a

**Related Information:** Thyroid Stimulating Hormone, Serum  
Thyrotroponin Receptor Antibody, Serum  
Thyroxine Binding Globulin, Serum  
Thyroxine Total, Serum  
Triiodothyronine Free and Total, Serum

**Synonyms:** Free  $T_4$ ; free Thyroxine; FT<sub>4</sub> free; Unbound  $T_4$

**Background:** Free  $T_4$  is the active form and the precursor of  $T_3$ . Although measurement of  $T_4$  is used in the diagnosis of hyperthyroidism, the levels depend on the amount of thyroxine binding globulin, thus not reflecting the alteration of the clinical state. Mild alterations of the concentration of thyroxine binding proteins does not alter  $T_4$  measurement to a greater extent. A familial form of hyperthyroxinemia is caused by a variant of albumin which binds  $T_4$  abnormally.

Limitations: Rheumatoid factor, anti-thyroxine autoantibodies, low molecular weight heparin therapy, pregnancy, phenytoin may alter free  $T_4$  levels. FT<sub>4</sub> may be increased in amiodarone treatment.

**Sampling:** 1 mL serum

**Reference Interval:** Validated for Southern Germany:  
0.8 - 1.8 ng/dL (10.3 - 23.3 pmol/L)

For the US reference ranges have been reported as:

Adults: 0.8 - 2.7 ng/dL (10.3 - 35 pmol/L)

Newborns: 2.6 - 6.3 ng/dL (33.5 - 81.3 pmol/L)



For the Middle East one report systematically investigated TSH:

Adults: 18 - 54 years (average 27 years)

Male 0.76 - 1.43 ng/dL (9.92 - 18.62 pmol/L)

Female 0.69 - 1.32 ng/dL (9.00 - 17.15 pmol/L)

## Thyroxine Total, Serum

f

**Related Information:** Thyroid Stimulating Hormone, Serum  
Thyroxine Binding Globulin and Thyroxine Free, Serum  
Triiodothyronine Free and Total, Serum

**Synonyms:** T<sub>4</sub>; Tetraiodothyronine; Thyroxine

**Background:** 70% of T<sub>4</sub> is bound to thyroxine binding globulin TBG, 20% to transthyretin and 10% to albumin, most of the T<sub>3</sub> is bound to TBG. 0.03% of T<sub>4</sub> and 0.3% of T<sub>3</sub> remains unbound to protein. About 35% of T<sub>4</sub> is monodeiodinated to T<sub>3</sub> and 15 - 20% is changed to tetraiodothyroacetic acid and excreted in the urine or bile.

Binding to TGB is increased in neonatal state, pregnancy, estrogens, contraceptives, clofibrate, hepatitis, acute intermittent porphyria, and lymphoma. A decrease in TGB binding is observed in nephritic syndrome, androgens administration, prednisone, hepatitis, stress, salicylates, phenylhydantoin.

**Sampling:** 1 mL serum

<b>Reference Interval:</b>	1 - 3 days	11.8 - 22.6 ug/dL
	1 - 2 weeks	9.8 - 16.6 ug/dL
	1 - 4 months	7.2 - 14.4 ug/dL
	4 - 12 months	7.8 - 16.2 ug/dL
	1 - 5 years	7.3 - 15.0 ug/dL
	5 - 10 years	6.4 - 13.3 ug/dL
	10 - 15 years	5.6 - 11.7 ug/dL
	> 15 years	5.0 - 11.0 ug/dL
	Pregnancy	5.5 - 16.0 ug/dL

S-T

## Tissue Polypeptide Antigen (TPA), Serum

f

**Related Information:** Carcinoembryonic Antigen (CEA), Serum  
CA 19-9 (Gastrointestinal), Serum

**Synonyms:** Tissue Polypeptide Specific Antigen; TPS; TPA

**Background:** TPA is composed of low molecular weight epithelium associated cytokeratines predominant in cells undergoing mitosis but in minor concentrations during the interphase. TPA concentration is a marker of disease progression and remission, occurring in inflammatory diseases and many tumors.

Useful in combination with CEA to monitor breast, colorectal, ovarian, bladder, lung tumors. It may be helpful in the distinction between cholangiocarcinomas, which are positive, and hepato-

cellular carcinomas, which are negative.

Limitations: Increased values during pregnancy

**Sampling:** 2 mL serum

**Reference Interval:** Negative < 80 U/L

**Total Iron Binding Capacity see** Transferrin and Total Iron Binding Capacity, Serum

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## Toxocara canis, Serology

f

**Background:** *Toxocara canis* is the major cause of visceral larva migrans. The hosts are canids, including the domestic dog and feral fox. The dogs are usually less than 6 month old when the larvae undergo all four larval stages and are caught up and adult parasites develop in the small intestine. In older dogs larval maturation is halted at the second larval stage (L2). Nearly all dogs are infected due to a reactivation of the L2 stage in pregnant bitches, crossing the placenta and are excreted with the milk.

The eggs produced in the dog's intestine by the adult female nematode are passed by the feces into the soil. If humans ingest contaminated soil, the egg hatches into larvae in the small intestine. The larvae migrates into liver, brain, eyes and are halted at the second larval stage , thus humans and other animals are paratenic hosts. Infection however can follow ingestion of fertilized embryonate eggs or uncooked tissue of another paratenic host.

Serology studies show that 2 - 8% of the population has evidence of previous infection, in children prevalence is up to 35% in tropical areas, peaking between 3 - 10 years of age. Main route of transmission is fecal oral.

Treatment: albendazole or mebendazole

**Sampling:** 2 mL serum

**Reference Interval:** Antibody negative

## Toxoplasmosis, Serology

f

**Background:** *Toxoplasma gondii* is an obligate intracellular protozoan parasite. The hosts are domestic cats and other felines. Humans, other mammals and birds are intermediate hosts, where the *T. gondii* occurs in two forms: rapidly multiplying (intracellular) tachyzoites and dormant bradyzoites which persist for years in the form of tissue cysts (most common in brain and muscle). The host can be infected by the oral route with oocysts, tachyzoites and bradyzoites.

Cats become infected by eating birds or other sources of raw infected meat. Other animals and humans become infected either from oocysts in soil or contaminated food or tissue cysts in undercooked meat. During pregnancy, tachyzoites invade the placenta and the fetus.

Epidemiology: Beef, pork and lamb meat are infected in 5 - 92%. Oocyte shedding in cats is estimated to be 1%. Prevalence increase with age, in child bearing age it is estimated in

Europe, North America and Australia to be 37 - 58%, in South America and Sub-Saharan Africa 51 - 77%, Southeast Asia India and China it is 4 - 39%.

In 90% of cases no clinical symptoms are apparent during acute phase. Symptoms are enlarged lymph nodes mainly at head and neck.

Maternal immunity due to toxoplasmosis passed before conception protects the fetus from infection. The risk of congenital infection depends on the time of acquisition of an acute maternal infection. 15% - 25% in the first trimester, 30% - 54% in the second and 60 - 65% in the third. The severity of congenital disease is conversely related to the gestational age. Signs of infection at delivery are present in 21% - 28% if infection occurred in the second trimester and up to 11% in the third trimester. 10% are born with severe disease such as strabismus, chorioretinitis, encephalitis, microencephaly, hydrocephalus, convulsions. Nonspecific signs are anemia, jaundice, thrombocytopenia, diarrhea, and pneumonitis. For confirmation of fetal infection, amniotic fluid should be assayed by PCR for *T. gondii* as well as culture assays.

Therapy: In gestational toxoplasmosis drug therapy may be considered with spiramycin if the fetus is not infected since spiramycin concentrates in the placenta but does not cross the placenta. In case of a confirmed (for example by toxoplasmosis-DNA test in amniotic fluid, test not reliable before week 18) infection of the fetus sulfadiazine plus pyrimethamine plus folic acid may be an option after week 16 of pregnancy until delivery. Pyrimethamine should not be used in the first 12 - 16 weeks of pregnancy because the concern of teratogenicity. All infected newborns should stay on therapy. Symptomatic *T. gondii* infection in immunocompetent, non-pregnant individuals without visceral involvement does not need treatment. In immunocompromised hosts, sulfadiazine plus pyrimethamine and folic acid is recommended.

Classification: *Toxoplasma gondii* belongs to the phylum Apicomplexa (together with *Plasmodium* spp., *Cryptosporidium* spp., and *Theileria* spp.) which is an early-branching eukaryotic lineage containing a number of important human and animal pathogens. Their complex life cycles and unique cytoskeletal features distinguish them from other eukaryotes. Apicomplexans rely on actin-based motility for cell invasion. Closely related genera are *Neospora* and *Hammondia*.

**Sampling:** 2 mL serum

**Reference Interval:** Differentiation of immunoglobulin class:

IgA antibody	negative:	< 20 AU/mL
IgG antibody	negative:	< 6 IU/mL
	borderline:	6 - 8 IU/mL
	positive:	> 8 IU/mL
IgM antibody	negative:	< 6 AU/mL
	borderline:	6 - 8 AU/mL
	positive:	> 8 AU/mL

Enhanced marker for acute infection:

IgG avidity test low:	< 0.15 (acute infection)
borderline:	0.15 - 0.25
avidity test high:	> 0.25 (past infection)

## Transferrin and Total Iron Binding Capacity, Serum

f

**Related Information:** Copper (Cu), Serum or Urine  
 Erythropoietin (EPO), Serum  
 Ferritin, Serum or Plasma  
 Hemochromatosis DNA  
 Iron (Fe), Serum or Urine  
 Occult Blood in Stool (Hemoccult)  
 Soluble Transferrin Receptor, Serum or Plasma  
 Applies to Transferrin Saturation (%)

**Background:** Please see also Iron (Fe), Serum

After absorption, iron is bound to transferrin, a single chain protein of 80 kDa, synthesized in the liver. Binding to transferrin is pH dependent, at pH 7.4, very strong, no binding at pH 4.5. Cells acquire iron from transferrin by the transferrin receptor (TfR) a transmembrane glycoprotein which is predominant in all cells and particularly in placenta, liver and erythroid precursor cells. Serum Iron concentrations reflects the  $\text{Fe}^{3+}$  bound by transferrin. Approx 30% of transferrin is occupied by  $\text{Fe}^{3+}$ , a large capacity to bind iron is left. Transferrin saturation is the ratio of plasma iron to total iron binding capacity (TIBC).

Interpretation of transferrin and iron is difficult since serum iron is decreased by infection, inflammation, malignancy, ascorbate deficiency and it may be increased by liver diseases, iron ingestion and decreased erythropoiesis. There is a great circadian fluctuation (30% higher iron values in the morning) and a more than 30% day to day variation in serum iron.

Therefore, measurement of transferrin and iron is of limited use for

- Iron deficiency caused by inadequate absorption (celiac disease, inflammatory bowel disease, dietary, red cell defects).
- Increased losses: Tumors, gastritis, ulcer, parasitic disease, genitourinary diseases.

Useful parameter in:

- Iron overload state: If the transferrin binding capacity is exceeded, iron is deposited in parenchymal cells or reticuloendothelial system (transfusion overload). To establish the diagnosis of hemochromatosis: Transferrin saturation > 55% and ferritin > 400  $\mu\text{g}/\text{L}$  together with the clinical signs. In the classical HLA related hemochromatosis, saturation increases before ferritin goes up and in 90% of the patients homozygosity for the C282Y mutation is responsible for this type of iron storage disease.

Overview on iron status indicators changes:

Status	Ferritin	Transferrin	Serum Iron	Iron Saturation
Iron deficiency	down	up	down	down or normal
Anemia in chronic diseases	up or normal	down or normal	down	down or normal
Sideroblastic anemia	up	down or normal	up or normal	up
Hemolytic anemia	up	down or normal	up	up
Hemochromatosis	up	normal or down	up	up
Acute liver impairment	up	variable	up	up
Protein deficiency		down or normal	down or normal	down or normal

Limitations: TIBC and transferrin are elevated in patients on oral contraceptives, saturation is normal. Transferrin saturation is low in acute or chronic infection, iron may be low as well but does not indicate iron deficiency. Some patients have anemia but normal transferrin concentrations. In very high iron level and iron poisoning, TIBC may give false high results.

**Sampling:** 2 mL serum, due to circadian rhythm, fasting morning sample is preferred.

**Reference Interval:** Transferrin:

Adults		200 - 400 mg/dL
Children	2 - 5 years	280 - 350 mg/dL
	6 - 10 years	260 - 360 mg/dL
	11 - 18 years	260 - 360 mg/dL

TIBC is an approximation to transferrin and can be calculated as

$$\text{TIBC } (\mu\text{g/dl}) = \text{transferrin } (\text{mg/dL}) \times 1.25$$

Percent saturation (Tfs%): Please see Iron, Serum to calculate:

$$\text{Transfe. Saturation, Tfs } (\%) = \text{Iron, Serum } (\mu\text{g/dL}) \times 70.9 : \text{transferrin } (\text{mg/dL})$$

Newborn		29.4 - 46.0%
Premature		11.4 - 42.2%
1 - 5 years		7.0 - 44.0%
6 - 9 years		17.0 - 42.0%
10 - 14 years	female	11.0 - 36.0%
	male	2.0 - 40.0%
14 - 19 years		6.0 - 33.0%
Adult		16.0 - 45.0%

**Transferrin Saturation see** Transferrin and Total Iron Binding Capacity, Serum

## Treponema pallidum (TPAH) Serology

f

S-T

**Related Information:** Borrelia, Serology

**Synonyms:** Lues Serology; Syphilis Serology; Treponemal Antibodies

**Background:** Members of three genera of spirochetes are known to causes human diseases: Treponema (syphilis and nonvenereal treponematoses) ; Borrelia (B. burgdorferi: Tick born Lyme disease, B. recurrentis: Louse born relapsing fever); Leptospira (leptospirosis).

Mode of transmission: Intimate contact of skin or mucous membranes containing spirochetes and during pregnancy across the placenta typically after the third month of pregnancy (congenital syphilis) to the fetus.

During the first stage of infection the spirochetes multiply at the site of inoculation to form a local, nontender ulcer (chancre) in 2 - 10 weeks. The ulceration heals spontaneously but the organism is widely spread into various tissues forming lesions of the secondary syphilis characterized by

maculopapular rash, moist papules on skin or mucous membrane which are highly infectious. Approx 30% of primary and secondary stages will clear without treatment, one third will stay latent with positive serology and in some patients with reappearing second stage infectious episodes. One third of patients will develop the tertiary stage with only rarely seen treponema containing lesions. Immunity is incomplete, antibodies can not prevent disease progression and multiple infections can be acquired but patients with late stage syphilis are less likely to acquire a new infection. Treatment: Penicillin or erythromycin.

Laboratory diagnosis:

Direct detection: Spirochetes can be demonstrated in the lesions of primary and secondary syphilis by darkfield microscopy or by direct fluorescent antibody DFA test.

Nonspecific serologic tests: Nontreponemal antigens (cardiolipins) react with antibodies in the serum of patients with syphilis. The VDRL (Venereal Disease Research Laboratory) and RPR (Rapid Plasma Reagin) are positive in most cases of primary and always in secondary syphilis. The titers decreases and become negative during efficient treatment. False positive may occur in leprosy, hepatitis, infectious mononucleosis, autoimmune diseases.

False negative titres occur as a result of the prozone phenomena occurring when the antibody is in excess in the patient's serum.

Specific serologic tests: Specific *T. pallidum* antigens react with patient's antibodies in immunofluorescence based test such as FTA-ABS or hemagglutinin based tests such as TPAH or MHA-TP. These tests become positive in the primary stage of syphilis and remain positive for life. The titer does not correlate with treatment or reinfection.

**Sampling:** 1 mL serum

**Reference Interval:**      TPHA nonreactive      < 1:80  
    TPHA reactive              > 1:80

Validation of the result: antibody differentiation by immunoblotting

## Triglycerides, Serum or Plasma

a

**Related Information:** Apolipoprotein A-1 and B-100, Serum  
 Cholesterol, Total, Serum or Plasma  
 Glycosylated Hemoglobin A1c , Blood  
 High Density Lipoprotein Cholesterol, Serum or Plasma  
 Low Density Lipoprotein Cholesterol

**Background:** Triglycerides (TG) are composed of a glycerol backbone esterified with three fatty acids. Transportation in the blood in form of chylomicrons or as very low density lipoproteins. Tissue storage fat consists of 95% TG.

Useful in coronary risk assessment: TG is needed to calculate the LDLC value using the Friedewald formula:

$LDLC \text{ (mg/dL)} = \text{Cholesterol, Total (mg/dL)} - HDLC \text{ (mg/dL)} - [\text{triglycerides (mg/dL)} / 5]$

But TG must be below 400 mg/dL and chylomicrons must not be present and not to use in

familial dysbetalipoproteinemia.

Elevated TG may be due to hypothyroidism, nephritic syndrome, diabetes mellitus, ethanol intoxication, pancreatitis, glycogen storage diseases, estrogen therapy, oral contraceptives, thiazides, beta adrenergic blocking agents. Pregnancy may be associated with increased TG.

**Sampling:** 1 mL of fasting serum or plasma, fasting should last for 10 - 12h and patient should be on a stable diet for 3 weeks.

**Reference Interval:** According to Executive Summary of the Third Report of the National Cholesterol Education Program (NCEP). Expert Panel on Detection, Evaluation and Treatment of High Blood Cholesterol in Adults. JAMA, 2001, 285(19) pp 2486-97

Normal TG	< 150 mg/dL
Borderline TG	150 - 199 mg/dL
High TG	200 - 499 mg/dL
Very high TG	> 500 mg/dL

## Triiodothyronine Free and Total, Serum

a

**Related Information:** Thyroglobulin, Serum  
Thyroid Stimulating Hormone, Serum  
Thyrotropin Receptor Antibody, Serum  
Thyroxine Free and Total, Serum

**Background:** Mainly (70 - 80%) produced by conversion of  $T_4$  to  $T_3$  is more metabolic potent (3 fold as compared to  $T_4$ ) and with less affinity to TBG than  $T_4$ . Approx 30 - 40% of  $T_4$  is converted to  $T_3$ . 0.3% is free in peripheral blood as compared to 0.02% of  $T_4$ . Only the free fraction of  $T_4$  and  $T_3$  parallel the cellular uptake and determines the status of the thyroid function in an individual. Increasing total  $T_3$  and unchanged protein bound fraction may occur during pregnancy or estrogen therapy, Total  $T_3$  may be reduced in androgen therapy, prednisone, dexamethasone, glucocorticoids well as in iodine deficiency and anorexia nervosa.

Use: Diagnosis of hyperthyroidism as  $T_4$  and  $T_3$  are increased. Diagnosis in the rare form of thyrotoxicosis of isolated  $T_3$  increase. To investigate patients with supraventricular tachycardia, fatigue, weight loss, proximal myopathy. Monitoring  $T_4$  therapy.

Limitations: Patients with chronic diseases and altered nutrition may have decreased  $T_3$  levels. Oral contraceptives, pregnancy. Subclinical hyperthyroidism may display normal  $T_3$ , also  $T_3$  is normal in mild hypothyroidism. Changes in TGB can affect total  $T_3$  but to a lesser extent free  $T_3$ .

Half life:  $T_3$  1 day;  $T_4$  7 days. Production per day  $T_3$ : 33 µg;  $T_4$ : 80 µg

**Sampling:** 1 mL serum

**Reference interval:** Triiodothyronine, Free

Validated for Southern Germany (MEDLAB)

Adults 2.19 - 3.49 pg/mL (3.4 - 5.4 pmol/L)

Children 3.10 - 4.14 pg/mL (4.8 - 6.4 pmol/L)

Validated for Germany

Adults 2.0 - 4.4 pg/mL (3.1 - 6.8 pmol/L)

For the Middle East one report systematically investigated TSH:

Adults 18 - 54 years (average 27 years)

Male 2.82 - 4.43 pg/mL (4.36 - 6.85 pmol/L)

Female 2.19 - 3.76 pg/mL (3.39 - 5.82 pmol/L)

Triiodothyronine, Total

Age	ng/dL
1 - 3 days	100 - 740
1 - 11 months	105 - 245
1 - 5 years	94 - 241
6 - 10 years	94 - 241
11 - 15 years	82 - 213
16 - 20 years	80 - 210
20 - 50 years	70 - 204
50 - 90 years	40 - 181

## Troponin T, Serum

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**Related Information:** Creatine Kinase (CK, NAC-activated)  
Creatinine Kinase Isoenzymes, Serum  
Myoglobin, Blood, Serum or Plasma

**Background:** Cardiac troponin T is a highly specific and sensitive test in myocardial infarction. Other markers are MB fraction of creatinine kinase (CKMB), cardiac troponin I. CKMB and myoglobin are less sensitive than the troponins. The troponins remain elevated for 5 - 7 days. Limitations: May be elevated in renal failure and muscle injuries.

**Sampling:** 2 mL serum. First sample should be drawn at admission, a second sample at 6 - 9h and a third sample at 12 - 24h.

**Reference Interval:** TnT < 0.2 ng/mL  
hs TnT < 0.014 ng/mL

For therapeutic decisions see actual guidelines.



## Trypanosoma cruzi (Chagas Disease), Serology f

**Background:** The cycle in the reduviid bug begins with the ingestion of trypomastigotes present in the blood of the reservoir host including domestic animals and wild species as armadillo, raccoon and rats, further differentiation in the insects gut into epimastigotes and trypomastigotes which are shed into the insects feces and enter the blood of the the reservoir host when the bug bites. Non-flagellated amastigotes form within the host cells, preferentially in reticoendothelial, myocardial and glia cells. Amastigotes differentiate to trypomastigotes to enter the flood and are taken by the reduviid bug.

Chagas disease occurs in Central and South America in rural areas due to the bugs spread in the walls of the rural houses.

Clinically, edema near the bite site occurs with fever, lymphadenopathy and hepatosplenomegaly, resolving within 2 month. Progression to the chronic phase is characterized by the cardiac muscle involvement with myocarditis, arrhythmias and loss of tone due to infected glia cells which leads to megacolon or megaesophagus.

Laboratory diagnosis is made by demonstrating trypomastigotes in the thick or thin film of patient's blood. However trypomastigotes are rare in the acute phase and absent in the chronic phase. Bone marrow aspirates or muscle biopsy specimens may reveal amastigotes.

Serology is helpful in acute and chronic forms.

**Sampling:** 1 mL serum

**Reference Interval:** Antibodies not detectable

## Tumor Necrosis Factor (Cachectin), Serum f

**Background:** A useful marker in sepsis, trauma, heart diseases and in unspecific monitoring of chronic inflammatory diseases. In heart failure, TNF alpha may be considered as an indicator of poor prognosis.

In the CSF, it is used to monitor the activity of multiple sclerosis and to distinguish between bacterial and other forms of meningitis.

Plasma half life time of the active trimer is < 5 min. The levels of the active TNF-trimer will be elevated for 4 - 6 h, the levels of the total TNF for 24 h.

**Limitations:** Therapy regimes in transplant patients using antibodies may cause false positive results.

**Sampling:** 2 mL serum. Separate cells within 2 h. Freeze immediately at -20°C if test will be performed within one week; otherwise freeze at -70°C, ship frozen.

**Reference Interval:**

Total TNF alpha	5 - 15 pg/mL
Active Trimer	< 5 pg/mL