Hematology

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Plasma is the liquid part of fluid blood. Outside the vascular system, blood can be kept fluid by either removing fibrinogen or by adding anticoagulants, most of which prevent coagulation by chelating or removing calcium ions. Citrate, oxalate and EDTA are chelating category anticoagulants. Heparin prevents coagulation via direct thrombin inhibition, and fibrinogen to fibrin conversion by augmenting a natural anticoagulant antithrombin III molecule to neutralize thrombin. Heparin fails to influence the calcium concentration in its anticoagulant effect. Freshly drawn plasma contains all the proteins of circulating blood; in stored plasma, however, factor V and VIII activity gradually declines.
Serum is the fluid which remains after blood coagulates. Coagulation converts all fibrinogen into solid fibrin, consuming factors V, VII and prothrombin in the process. Other coagulation proteins and proteins not related to hemostasis remain in serum as in plasma levels. Normal serum lacks fibrinogen, prothrombin, factors V, VIII, XIII, but contains factors VII, IX, X, XI, XII. If the coagulation process proceeds abnormally, serum may contain residual fibrinogen and fibrinogen cleavage products in unconverted prothrombin.

Acetylcholinesterase in Erythrocytes

(syn: RBC cholinesterase, erythrocytic cholinesterase, red cell cholinesterase, "true" cholinesterase) The enzyme is limited to the outer membrane surface. The red cell enzyme is synthesized during erythropoiesis. Activity is higher in young erythrocytes, decreasing rapidly with age. Red cell cholinesterase is a better chronic organic phosphate poisoning indicator than serum pseudocholinesterase (better measure of acute toxicity). The cholinesterase activity in human red cells is highly but not exclusively specific for acetylcholine. Cholinesterase activity present in the serum/plasma hydrolyses both choline and aliphatic esters, has a broader range of esterolytic activity and is referred to as "pseudo-" or "nonspecific" cholinesterase. It hydrolyses acetylcholine only slowly. Test is used also to detect atypical forms of the enzyme. Cholinesterase is irreversibly inhibited by organophosphate insecticides and reversibly inhibited by carbamate insecticides.

Increased Values

sickle cell anemia, hemolytic conditions, thalassemias, spherocytosis, acquired hemolytic anemias

Decreased Values

paroxysmal nocturnal hemoglobinuria, organophosphate toxicity, pyridostigmine therapy for myasthenia gravis, megaloblastic anemia relapse

V. Marks et al., *Differential Diagnosis by Laboratory Medicine*

Activated Protein C Resistance

(syn: APC resistance) It is an anticoagulatory protein C system action disorder with high thrombotic risk, caused by molecular F V defect (i. e. factor V Leiden is less sensitive to anticoagulative activated protein C influence than normal F Va) with modified activated protein C splitting properties.
Test Purpose. 1) differential diagnosis of thrombophilic conditions (APC resistance is the most frequent genetic thrombosis cause).

Positive Resistance
inborn APC resistance, acquired APC resistance in – (protein C/S deficiency, increased F VIII values, antiphospholipid syndrome)

Adenylate Kinase in Erythrocytes

Decreased Values
autosomal recessive hemolytic anemia

Aminolevulinate Dehydratase in Erythrocytes

Decreased Values
ALAD deficiency, lead poisoning, hereditary tyrosinemia
Interfering Factors: medicaments – (EDTA)

Alpha-2-Antiplasmin

(alpha-2 AP, syn: alpha-2-plasmin inhibitor) Antiplasmin is a glycoprotein, the primary plasmin inhibitor synthesized in the liver.
Function. Antiplasmin serves as a regulator of fibrinolysis – a) it blocks the enzymatic activity of plasmin, b) inhibits binding of plasminogen to fibrin, c) it binds to fibrin with factor XIII, making the clot more difficult to lyse by plasmin.
Test Purpose. 1) to evaluate serum alpha-2-antiplasmin functional activity, 2) differential diagnosis of bleeding conditions (e.g. accelerated fibrinolysis).

Increased Values
diabetes mellitus

Decreased Values
congenital antiplasmin deficiency, primary fibrinogenolysis with prostate tumors, liver diseases, bleeding diathesis, consumptive coagulopathy, therapy – (fibrinolytic t., **thrombolytic t. with streptokinase**), hereditary bleeding disorders

Analyte	Age/Gender	Reference Range	SI Units	Note
Alpha-2-Antiplasmin		0.8–1.2		
		80–120	%	
		50–70	mg/l	

Antithrombin III

(AT III, syn: functional antithrombin III assay, AT III antigen assay, heparin co-factor, immunologic AT III, A-Th3, serine protease inhibitor) AT III is a plasma protein that inhibits thrombin by binding to its active site.
Function. AT III is the strongest/most important physiological serine coagulation protease inhibitor. The main AT III inhibitory effect goal are factor IIa (activated thrombin), and factor Xa; AT III has smaller inhibitory effect against factor XIa and XIIa, but is the only factor IXa inhibitor. AT III action is catalyzed by heparin. The heparin – antithrombin III complex will rapidly neutralize any thrombin that is generated by coagulation cascade activation. Homeostasis results from a balance between AT III and thrombin. AT III deficiency increases coagulation risk or tendency toward thrombosis. Platelets lysis releases PF 4 → inhibits AT III activity.
Production. Liver, vascular endothelium.
Test Purpose. 1) to evaluate thromboembolic disease conditions, 2) to evaluate hypercoagulable or fibrinogenolytic conditions and response to heparin, 3) to test for hereditary AT III deficiency, 4) thrombophilic conditions differential diagnosis, e.g. congenital or acquired AT III deficiency associated with severe cirrhosis, chronic liver failure, DIC, thrombolytic therapy, pulmonary embolism, nephrotic sy or postsurgical conditions.

Increased Values

vitamin K deficiency, acute hepatitis, hyperglobulinemia, **cholestasis, inflammatory diseases,** obstructive jaundice, **menstruation, kidney transplant** (recent), increased values of – (CRP, ESR, globulins), post-myocardial infarction

Interfering Factors: medicaments – (anabolic steroids, androgens, coumarins, oral contraceptives – containing progesterone, sodium warfarin)

Decreased Values

liver cirrhosis, hereditary antithrombin III deficiency, dialysis, diffuse venoocclusive disease, **pulmonary embolism,** enteropathy, partial hepatectomy, pregnancy induced hypertension, diseases – (**liver d.,** renal d.), **acute myocardial infarction, disseminated intravascular coagulopathy,** leukemia, malnutrition, tumours, **surgery, CNS surgery/trauma,** plasmapheresis, immature fetus, burns, **polytrauma, hepatic parenchyma lesions, preeclampsia,** increased AT III consumption, conditions – (**septic c.,** shock c.), severe blood loss, **nephrotic sy,** decreased AT III synthesis, **pregnancy** (3rd trimester), **liver transplant, thrombophlebitis, deep vein thrombosis,** increased AT III excretion, **chronic liver failure**

Interfering Factors: medicaments – (asparaginase, contraceptives containing estrogens, fibrinolytics, heparin, L-asparaginase)

Analyte	Age/Gender	Reference Range	SI Units	Note
Antithrombin III		0.8–1.2		
		80–120	%	
		180–300	mg/l	

Autohemolysis

Hemolysis: RBC breakdown and hemoglobin outflow from RBC into surrounding environment. Determined by the spontaneous hemolysis amount occurring in blood over 24–48 hour period under special laboratory conditions (ATP, glucose). Autohemolysis: RBC hemo-

lysis caused by RBC antibody production which are bound to RBC membrane as an immune system disorder result. Antibody types: warm, cold, bitermic. Autohemolysis causes are: a) congenital RBC inferiority (inner construction disorder, enzymatic set, or RBC hemoglobin), b) acquired RBC inferiority (RBC damaged by extraerythrocyte causes).
Test Purpose. 1) hemolysis level determination, 2) differential diagnosis of hemolytic anemias (congenital, acquired), paroxysmal nocturnal hemoglobinuria.

Decreased Values
congenital nonspherocytic hemolytic anemia (decreased less markedly), hereditary spherocytosis (decreased markedly)

Analyte	Age/Gender	Reference Range	SI Units	Note
Autohemolysis		2.5–5	% relat.	

Basophils

(bas) Granulocytic developmental stem cells with specific granules.
Function. Phagocytosis, fat metabolism, functionally similar to mastocytes. Contain heparin, histamine, serotonin, release chemotactic factors; involved with mast cells in immediate hypersensitivity reactions, have receptors for the complement C3, C5 components, and high affinity receptors for IgE. Binding of C3a and C5a or cross-linking of membrane bound IgE by allergens induces release 60–80% of the granules of both cell types. Tissue basophils receptors react with allergens and IgE to induce vasoactive mediators release. These factors cause contraction of endothelial cells and vasodilation of capillaries resulting in the redness, warmth and fluid accumulation in tissues characteristic of inflammation. Massive granule content release may evoke sudden death – anaphylactic shock.

Increased Values – basophilia, basophilic leukocytosis
chronic hemolytic anemia, hepatic cirrhosis, **hypothyroidism**, diseases – (**myeloproliferative d.**, chronic inflammatory d.), **ulcerative colitis**, leukemia – (**basophilic l.**, **chronic myelocytic l.**), **mastocytosis**, **myeloid metaplasia**, **morbilli**, **Hodgkin's disease**, myelofibrosis, **myxedema**, **nephrosis**, **polycythemia**, **polycythemia vera**, radiotherapy, recovery from infection, chronic sinusitis, **splenectomy**, allergic conditions – (inhalants, drug, food), **stress**, syndrome – (**myelodysplastic sy**, **nephrotic sy**), pregnancy, urticaria, **varicella**, variola, foreign protein injection, ionizing radiation

Interfering Factors: medicaments – (antithyroid preparations, contraceptives)

Decreased Values – basophilic leukopenia, basopenia
hemorrhagic conditions, **hyperthyroidism**, diseases – (**infectious d.**, **inflammatory d.**), myocardial infarction, prolonged steroid therapy, ovulation, reactions – (**acute allergic r.**, **hypersensitive r.**), **stress reactions**, **Cushing's sy**, **anaphylactic shock**, **urticaria**, bleeding peptic ulcer, **pregnancy**

Interfering Factors: medicaments – (ACTH, adrenaline, corticosteroids, progesterone)

Analyte	Age/Gender	Reference Range	SI Units	Note
Basophilic Granulocytes	Neonates	<3	%	
	Infants	<3	%	
	Adults	0–7	%	
		0–0.07		
		0–0.25	x 10^9/l	

Bleeding Time (Duke's Method)

(BT, syn: Duke's bleeding time, time of bleeding) Bleeding time is an interval between a standard cut/prick and bleeding stoppage; Duke's method is bleeding time after a 4th finger-tip prick. It is a primary hemostasis phase measure, platelet interaction with the blood vessel wall and hemostatic plug formation. Bleeding time duration depends upon the platelet quantity and quality, von Willebrand's factor, and the blood vessel walls ability to constrict.

Test Purpose. 1) to obtain information about normal or insufficient primary hemostatic plug formation, 2) to assess overall hemostatic function (platelet response to injury and functional vasoconstriction capacity), 3) to detect congenital and acquired platelet function disorders.

Bleeding Time (Ivy's Method)

An in vivo functional test for platelet and capillary function. Bleeding time is measured from standard forearm cut under standard pressure.

Test Purpose. 1) screening used to assess capillary function, platelet count and function, platelet ability to adhere to vessel wall and form a plug, 2) to assess overal platelet response to injury, 3) to assess functional capacity of vasoconstriction, 4) to detect congenital and acquired blood disorders, 5) to evaluate ecchymosis, spontaneous bruising and bleeding, bleeding tendency.

Increased Values – prolonged bleeding time

alcohol, amyloidosis, aplastic anemia, hepatic cirrhosis, coagulation factor defect/deficiency – (I, II, V, VII, VIII, IX, XI), congenital protein C or S deficiency, **capillary fragility, hemophilia, hypersplenism,** disease – (**Cushing's d.**, Henoch-Schönlein d., **hemolytic newborn d., von Willebrand's d.**), diseases – (**collagen vascular d., liver d.**, viral infectious d., myeloproliferative d.), ecchymosis, **primary/metastatic tumor bone marrow infiltration, disseminated intravascular coagulation** (DIC), **leukemia, Hodgkin's disease, Waldenström's macroglobulinemia,** parahemophilia, plasmocytoma (incl. multiple myeloma), disorders – (**platelet function d.**, blood vessel wall d.), preleukemia, **senile purpura,** scurvy, fibrinolytic states, syndrome – (**Bernard-Soulier sy,** Wiskott-Aldrich sy, myelodysplastic sy, Chédiak-Higashi sy, Hermansky-Pudlak sy, Ehlers-Danlos sy), hereditary teleangiectasia, massive transfusions, **Glanzmann's thrombasthenia, thrombocytoasthenia** (thrombasthenia), **thrombocytopathy, thrombocytopenia,** thrombocytosis, **uremia, vasculopathies,** failure – (**bone marrow f.**, renal f.), hemorrhagic conditions, deep intracerebral hemorrhage, hemorrhagic stroke

Interfering Factors: medicaments – (acetylsalicylic acid, allopurinol, aminocaproic acid, aminophylline, amitriptyline, amoxicillin, ampicillin, anticoagulants, antibiotics, antihistamines, antiinflammatory agents, asparaginase, azlocillin, beta-blockers, caffeine, calcium channel blockers, carbenicillin, cefoperazone, ceftizoxime, cephalosporins, chlorpromazine, clarithromycin, corticoids, dextran, dihydralazine, diltiazem, diuretics, ethanol, halothane, heparin, hydroxychloroquine, ibuprofen, imipramine, indomethacin, ketoprofen, lansoprazole, lipid-lowering drugs, meropenem, moxalactam, nafcillin, nandrolone, naproxen, nifedipine, nitrates, nitric oxide, nitrofurantoin, nitroglycerin, nonnarcotic analgesics, non-steroidal antiinflammatory drugs, nortriptyline, panthenol, penicillin, phenylbutazone, piperacillin, piroxicam, plicamycin, promethazine, propra-

nolol, prostacyclin, salicylates, streptodornase, streptokinase, sulfonamides, theophylline, thiazides, ticarcillin, tricyclic antidepressants, trifluoperazine, urokinase, valproic acid, warfarin)

Analyte	Age/Gender	Reference Range	SI Units	Note
Bleeding Time				
Ivy's		4–8	min	
Duke's		2–5	min	

Blood Culture

Test Purpose. 1) to establish the diagnosis in suspected septicemia, endocarditis, bacterial meningitis, pericarditis, septic arthritis, osteomyelitis, pyelonephritis, enteric fever, 2) to identify the causative organisms in severe pneumonia, postpartum fever, pelvic inflammatory disease, cannula sepsis, neonatal epiglottitis and sepsis.

Capillary Fragility Test

(syn: Rumpel–Leede positive pressure test, tourniquet test, negative pressure test) The infotest about primary phase hemostasis components (vascular wall and platelet condition). Test is used to demonstrate capillary fragility defects due to abnormalities in the capillary walls or thrombocytopenia by positive/negative pressure → forearm area petechiae are counted.
Test Purpose. 1) to assess the capillary wall fragility, 2) to identify platelet deficiency.

Positive

deficiency of – (factor VII, fibrinogen, prothrombin, vitamin K), diabetes mellitus with vascular complications, dysproteinemia, hypertension, chronic renal diseases, influenza, DIC, **von Willebrand's disease**, measles, polycythemia vera, purpura – (**senile p.**, **vascular p.**), scurvy, scarlet fever, **thrombasthenia**, thrombocytopathies, **thrombocytopenia**, vasculopathies

Interfering Factors: healthy persons, before menstruation, women over age 40

Analyte	Age/Gender	Reference Range	SI Units	Note
Capillary Fragility Test (Rumpel–Leede)		<10	*	*petechiae over 16 cm^2

Carboxyhemoglobin

(COHb) Carbon monoxide bound to Hb molecule (e.g. in intoxication) is irreverzible. Hb to CO affinity is 300-times higher when compared to O_2 afinity.
Test Purpose. Investigation of possible carbon monoxide exposure and poisoning. Toxicity relates more to inhibition of mitochondrial cytochrome respiration than to interference with blood oxygen transport.

Increased Values

CO poisoning, intestinal hemorrhage, following exercise, intestinal bacteria reactions, caloric reduction, hemolytic conditions

Interfering Factors: medicaments – (enflurane, halothane, isoflurane)

Analyte	Age/Gender	Reference Range	SI Units	Note
Carboxyhemoglobin	Non-smokers	<0.012		
	Smokers	<0.085		
	Lethal	>0.5		

Catalase in Erythrocytes

Catalase is iron containing hemin bound to protein by porphyrin circle, catalase is necessary for cell peroxide production. This enzyme is in all oxidative procedures performing cells.

Increased Values
beta-thalassemia minor

Decreased Values
acatalasemia, iron deficiency anemia

CD Antigens

(CD – cluster of differentiation) Lymphocytes, in the course of development from precursor cells into functionally mature forms, display a complex pattern of surface antigens, some of which are acquired at certain stages, while others are lost. The CD antigen nomenclature was introduced when it was found out that different monoclonal antibodies from different sources recognized identical antigens. Use of these antibodies also helps to delineate the biologic traits that distinguish normal immune and hematopoietic cells from their malignant counterparts, which is of fundamental importance in understanding hematological malignancies.

Cells of Inflammation

1) **circulating**: neutrophils, eosinophils, basophils, thrombocytes,
2) **tissue**: mastocytes, macrophages, endothelial cells.

Clot Retraction

(syn: clot retraction test, whole-blood clot retraction test) Blood clot investigation incubated in thermostat and the serum amount dislodged from blood clot is measured. In vitro testing is based on the fact that normally clotted whole blood will retract or recede from the container sides, resulting in transparent serum separation and contracted blood clot.
In vivo platelets play a major part in the clot retraction mechanism by active fibrin blood coagulum fibre shrinkage followed by wound edge contraction creating compact mass. It is the final definitive plug creation process. Clot retraction depends upon normal platelet function, contractile proteins in the platelet membrane (thrombostenin), magnesium, ATP and pyruvate kinase. It is also influenced by the hematocrit level, fibrinogen structure, and concentration.
Test Purpose. 1) to help in Glanzmann's thrombasthenia diagnosis, 2) to assess platelet function and fibrin structure in clot retraction induction.

Increased Values
severe anemia, hypofibrinogenemia

Decreased Values
erythrocytosis, hyperfibrinogenemia, **von Willebrand's disease, Waldenström's macroglobulinemia, thrombasthenia, Glanzmann's thrombasthenia, thrombocytopenia**

Analyte	Age/Gender	Reference Range	SI Units	Note
Clot Retraction		>0.88		
		>88	%	

Clotting Time (Lee-White)

(CT, ACT, syn: whole blood clotting time, coagulation time, activated coagulation time, activated clotting time, ground glass clotting time) Blood clot formation time in 37 °C.
Test Purpose. 1) it gives rough information about plasmatic prothrombin activator production (without thrombocytes), prothrombin to thrombin change, and fibrinogen to fibrin change influenced by this activator, 2) to monitor heparin effect during cardio-pulmonary bypass surgical procedures, 3) screening test for coagulation deficiencies, with special application to heparin effect monitoring, 4) to monitor heparin administration.

Increased Values – prolonged
anemia, coagulative factors deficiency – (II, V, VII, X, XII), **hemophilia A, B**, hypo/**afibrinogenemia**, von Willebrand's disease, **disseminated intravascular coagulation**, biliary ducts obstruction, vitamin K metabolism disorders, hepatic parenchyma injury

Interfering Factors: medicaments – (anticoagulative agents, coumarin, heparin, tetracyclines)

Analyte	Age/Gender	Reference Range	SI Units	Note
Clotting Time	37 °C	6–10	min	
Lee–White	20 °C	6–12	min	

Coagulation Tests – hemostasis

Vascular function and platelet function – primary hemostasis
- bleeding time, capillary fragility test/Rumpel–Leede test

Platelet function – primary hemostasis
- platelet adhesiveness, platelet aggregation, activated bleeding time, activated recalcification time, bleeding time, clotting time, platelet factor 3, prothrombin consumption, platelet count, recalcification time, clot retraction

Overall clotting ability
- activated partial thromboplastin time, fibrinogen, PT, TT

Internal coagulation system – contact phase (stage I hemostasis)
- activated clotting time, activated partial thromboplastin time, activated recalcification time, clotting time, prothrombin time, partial thromboplastin time, recalcification time, thromboplastin generation time

External coagulation system (stage II hemostasis)
- prothrombin time

Common coagulation phase (stage III hemostasis – 3rd coagulation phase)
- ethanol gelation test, fibrin stabilizing factor – (factor XIII), fibrinogen, protamine sulfate, thrombin time

Fibrinolytic process (stage IV hemostasis – fibrinolytic activity)
- euglobulin lysis time, ethanol gelation test, fibrin-degradation products, partial thromboplastin time, plasminogen, protamine sulfate, clot lysis test, thrombin time

Complete Blood Count

(CBC, syn: blood count, blood cell profile)
hemoglobin (Hb), hematocrit (HCT), erythrocytes (red blood cell (corpuscle) count, RBC), leukocytes (white blood cell count, WBC), thrombocytes (platelet count, PLT), differential white cell count, red blood cell indices – Wintrobe blood indices (mean corpuscular volume/MCV, mean corpuscular hemoglobin/MCH, mean corpuscular hemoglobin concentration/MCHC), microscopical stained cellular blood elements examination (film/peripheral blood smear)
Test Purpose. Differential diagnosis of anemias, polyglobulias, leukopenias, leukocytoses, thrombocytopenias, and thrombocytoses.

Cryofibrinogen

A test for one of the cold-precipitating plasma proteins in patients with cold intolerance.
Test Purpose. To evaluate coagulation disorders.

Increased Values – positive
pregnancy phlebitis, inflammatory diseases, neonatal infections, tumors, scleroderma
Interfering Factors: medicaments – (oral contraceptives)

Analyte	Age/Gender	Reference Range	SI Units	Note
Cryofibrinogen		<60	mg/l	

Differential White Cell Count

(syn: differential, leukogram, blood smear, smear evaluation, white blood cell slide differential, differential WBC count, leukocyte differential, manual differential) Differential gives the WBC category percentage in a particular blood sample obtained microscopically from stained blood smear or from native blood using a blood cell computer.
Test Purpose. 1) to evaluate the body's capacity to resist and overcome infection, 2) to detect and identify various leukemia types, 3) to determine infection degree and severity, 4) to detect allergic reactions, 5) to assess allergic reaction severity.
Leukocytes types
- **basophilic granulocytes** = basophils
- **eosinophilic granulocytes** = eosinophils
- **lymphocytes**
- **monocytes**
- **mononuclear leucocytes** = lymphocytes + monocytes
- **neutrophilic segmented granulocytes** = segmented neutrophils

- **neutrophilic sticks** = band neutrophils
- **plasmocytes**
- **polymorphonuclear leukocytes** = neutrophils + eosinophils + basophils = granulocytes

Analyte	Age/Gender	Reference Range	SI Units	Note
Leukogram				
Granulocytes				
neutrophilic sticks	Adults	3–5	%	
		0.03–0.05		
		0.6–1.2	x 10^9/l	
neutrophilic g.	Neonates	<65	%	
	Infants	<25	%	
	Adults	47–79	%	
		0.47–0.79		
		2.5–5.6	x 10^9/l	
eosinophilic g.	Neonates	<3	%	
	Infants	<3	%	
	Adults	1–7	%	
		0,01–0.07		
		0.03–0.25	x 10^9/l	
basophilic g.	Neonates	<0.75	%	
	Infants	<0.25	%	
	Adults	0–2	%	
		0–0.02		
		0<0.03	x 10^9/l	
Monocytes	Neonates	<8	%	
	Infants	<10	%	
	Adults	2–11	%	
		0.02–0.11		
		0.15–0.58	x 10^9/l	
Lymphocytes	Neonates	<22	%	
	Infants	<60	%	
	Adults	12–40	%	
		0.12–0.40		
		1.2–3.1	x 10^9/l	
Plasmocytes	Neonates	<0.25	%	
	Infants	<0.5	%	

D-Dimers

(syn: fragment D-dimer, fibrin degradation fragment) D-dimers are fibrin derivatives (DD-fragments with preserved cross covalent bonds in the D-domain area; produced in stabilized blood fibrin coagulum creation) produced during fibrinolysis by plasmin effect onto fibrin coagulum. They are a terminal stabilized fibrin degradation product. The fragment D-dimer assesses both thrombin and plasmin activity. This fragment is formed after thrombin converts fibrinogen to fibrin; factor XIIIa stabilizes it to a clot, and plasmin lyses the clot. **Test Purpose.** 1) screening test for deep-vein thrombosis detection, embolism, bleeding conditions, liver diseases, malignant tumors and differential diagnosis, 2) to evaluate acute myocardial infarction, unstable angina pectoris and disseminated intravascular coagulation.

Increased Values
arthritis, unstable pectoral angina, cellulitis, **pulmonary embolism, fibrinolysis primary/secondary,** false-positive values – (high rheumatoid factors titers), diseases – (inflammatory d., infectious d.), acute myocardial infarction, **disseminated intravascular coagulation, vaso-occlusive sickle cell anemia crisis, thrombolytic/defibrination therapy with tissue plasminogen activator, tumors, surgery** (within 2 days), severe trauma, pneumonia, pregnancy (3rd trimester), **arterial thromboembolism, deep-vein thrombosis,** failure – (renal f., liver f., cardiac f.)

Analyte	Age/Gender	Reference Range	SI Units	Note
D-dimers		0.2–0.4	µg/ml	

2,3-Diphosphoglycerate

(syn: 2,3-DPG in erythrocytes) 2,3-DPG is a RBC enzyme that controls oxygen transport to the tissues. Enzyme deficiency results in RBC oxygen dissociation curve alterations controlling oxygen release to the tissues. An increase in 2,3-DPG decreases the hemoglobin oxygen binding capacity → increased oxygen amount is released and becomes available to tissues at lower oxygen tensions. The oxygen red cells affinity is inversely proportional to 2,3-DPG concentration.
Test Purpose. Enzyme hemolytic anemias differential diagnosis.

Increased Values
anemia, hepatic cirrhosis, pyruvate kinase deficiency, **cystic fibrosis with pulmonary involvement, hyperthyroidism, hypoxia, obstructive lung disease,** diseases – **(lung d., heart d., congenital cyanotic heart d.), after vigorous exercise conditions,** thyrotoxicosis, **uremia, high altitudes, chronic renal failure**

Decreased Values
acidosis, inherited genetic defects, deficiency – (phosphofructokinase d., hexokinase d.), **hemoglobin C diseases,** banked blood, polycythemia, respiratory distress sy

Interfering Factors: medicaments – (acetanilid, adriamycin, amylnitrite, isosorbide dinitrate, nalidixic acid, niridazole, nitrofurantoin, phenazopyridine, primaquine, sulfacetamide, sulfamethoxazole, sulfanilamide, sulfapyridine, sulfasalazine)

Eosinophil Cationic Protein

(ECP) ECP is an eosinophil granule-derived protein which is released during activation of eosinophils. Assay of ECP is claimed to assist in monitoring bronchial inflammation in acute asthma, serving as an index of disease severity and as an adjunct to quantitation of the reponse to bronchial provocation.
Test Purpose. To determine in vivo eosinophil activity.

Increased Values
bronchial asthma

Eosinophils

(eos, eo) Granulocytic developmental stem cells with a two-lobed nucleus and moderately large granules.

Function. Eosinophils are active in later inflammation stages.Active in allergic reactions and parasitic infections (ability to damage certain helminth parasites) via cationic proteins (major basic protein – MBP; eosinophil-derived neurotoxin – EDN; eosinophil cationic protein – ECP; eosinophil peroxidase – EPO). Eosinophils bear receptors for IgG, complement components C3, C5 and low-affinity receptors for IgE. Involved in chemotaxis and antigen–antibody complex engulfment.Eosinophils release enzymes that are able to inactivate biologically active substances (histamine). This is important in type I hypersensitivity reactions. Involved in detoxication processes (against chemical mediators, in hypersensitive reactions, in tissue lesion, in fibrin deposit removal). Eosinophil circulation half-time is about 12–18 hours and 3–10 days in tissues.

Increased Values – eosinophilia, eosinophilic leukocytosis

allergy – (**medicamentous a.**, milk protein a., **food a.**), **amebiasis, pernicious anemia, rheumatoid arthritis, ascariasis, aspergillosis, bronchial asthma, atopy, brucellosis, eosinophilic cellulitis**, hepatic cirrhosis, **excessive exercise**, IgA deficiency, dermatitis – (exfoliative d., **herpetiformis d.**), dermatomyositis, peritoneal dialysis, **eczema, Löffler's endocarditis**, protein losing enteropathy, **erythema multiforme**, eosinophilic fasciitis, **eosinophilic gastroenteritis**, acute hemolysis, cholestatic hepatitis, hay fever (pollinosis), **adrenal hypofunction**, hypopituitarism, serum sickness, diseases – (**allergic d., autoimmune d.**, collagen-vascular d., inflammatory bowel d., gastrointestinal d., **dermatologic d., myeloproliferative d., parasitic d., professional pulmonary d., connective tissue d.**, chronic inflammatory d.), infectious diseases – (bacterial i. d., **fungal i. d.**, viral i. d.), Pneumocystis carinii infection, **eosinophilic pulmonary infiltrate**, colitis ulcerosa, acute hemorrhage, leukemia – (**eosinophilic l., chronic granulocytic l., chronic myelocytic l.**), **systemic lupus erythematosus**, lymphogranulomatosis, **non-Hodgkin's lymphoma, Addison's disease, Hodgkin's disease**, malaria, tumour metastases – (kidney, lungs, gastrointestinal tract), infectious mononucleosis, tumours of – (colon, bone, uterus, melanoma, pancreas, lung, ovary), thymic disorders, interstitial nephritis, tumor necrosis, **graft rejection** (graft-versus-host disease), intestinal parasites, **pemphigus**, pityriasis rubra, pneumonia – (chlamydial p., eosinophilic p.), **polyarteritis nodosa**, polycythemia, **psoriasis, radiotherapy**, tropical eosinophilia, drug hypersensitivity reaction, **hyperimmune reactions, sarcoidosis, scleroderma, splenectomy, scabies**, syndrome – (**angioneurotic sy**, Dressler's sy, **eosinophilia-myalgia sy**, Goodpasture's sy, Wiskott-Aldrich sy, **hypereosinophilic sy**), **scarlet fever, toxocarosis**, toxoplasmosis, **trichinosis**, trichuriasis, tropical eosinophilia, **tuberculosis**, urticaria, vasculitis, ionizing radiation

Interfering Factors: medicaments – (acarbose, acetylsalicylic acid, ajmaline, aldesleukin, allopurinol, aminosalicylic acid, amoxapine, amoxicillin, amphotericin B, ampicillin, antithymocyte globulin, aztreonam, bacitracin, beclomethasone, captopril, carbamazepine, carbenicillin, carisoprodol, cefalexin, cefalotin, cefamandole, cefazolin, cefoperazone, cefoxitin, cefradine, ceftazidime, ceftizoxime, ceftriaxone, cephalosporins, chloral hydrate, chloramphenicol, chlorpromazine, chlorpropamide, chlorprothixene, chlortetracycline, clindamycin, clofibrate, clometacin, clomipramine, codeine, dacarbazine, dapsone, demeclocycline, desipramine, digitalis, digitoxin, disulfiram, doxepin, doxycycline, enflurane, erythromycin, ethosuximide, etretinate, fenofibrate, flavoxate, fluconazole, flunisolide, fluorides, fluphenazine, flurbiprofen, fluticasone, fomepizole, fosphenytoin, gemfibrozil, glibenclamide, gold salts, halothane, imipramine, indomethacin, inter-

ferons, isoniazid, iodides, kanamycin, lamotrigine, levofloxacin, lomefloxacin, loracarbef, mebendazole, mephenytoin, meprobamate, mercaptopurine, meropenem, methotrexate, methyldopa, methysergide, meticillin, mezlocillin, minocycline, modafinil, montelukast, moxifloxacin, nalidixic acid, naproxen, nevirapine, nitrofurantoin, nomifensine, nortriptyline, oxacillin, oxcarbazepine, papaverine, penicillamine, penicillins, perphenazine, phenazopyridine, phenothiazines, phenytoin, piperacillin, potassium iodide, probucol, procainamide, procarbazine, prochlorperazine, promethazine, protriptyline, ranitidine, rifampicin, streptokinase, sulfadoxine, sulfafurazole, sulfamethoxazole, sulfasalazine, sulfonamides, sulindac, tetracyclines, thioridazine, thiothixene, ticlopidine, tocainide, triamterene, trifluoperazine, trifluperidol, verapamil, viomycin)

Decreased Values – eosinopenia, eosinophilic leukopenia

anoxia, aplastic/pernicious anemia, cold environment, hemodialysed patients, Löffler's endocarditis, hypersplenism, diseases – (**severe bacterial infectious d.**, severe viral infectious d., **inflammatory d.**), hormone secreting tumors, Hodgkin's disease, infectious mononucleosis, myocardial infarction, tumours, surgery, **morbilli**, pancytopenia, polyarteritis nodosa, **burns**, sarcoidosis, seizure conditions, splenectomy, states after radiation, **stress**, syndrome – (**Cushing's sy**, Löffler's sy), shock, **typhoid fever**, **trauma**, congestive heart failure

Interfering Factors: intermenstrual period, medicaments – (ACTH, adrenaline, aminophyllin, amphotericin B, cefuroxime, corticosteroids, cortisone, glucocorticoids, gold salts, histamine, hydrocortisone, nortriptyline, prednisone, thyroxine)

Analyte	Age/Gender	Reference Range	SI Units	Note
Eosinophilic Granulocytes	Neonates	<3	%	
	Infants	<3	%	
	Adults	1–7	%	
		0.01–0.07		
		0.03–0.25	x 10^9/l	

Erythrocyte Sedimentation Rate

(ESR, FW, SR, syn: Fahraeus–Westergren, sed rate test) Complex RBC sedimentation process in unclotted blood sample based on equable blood plasma RBC division which depends on RBC movement and suspension plasma stability. ESR consists of three phases: a) early period (slow RBC decrease, nearly according to Stockes' formula), b) RBC agglomeration (faster RBC conglomerates fall), c) resistance/packing stage, when RBC in close contact decrease slowly. ESR means RBC settling rate in the unclotted blood sample in milimeters which is measured between fluid column top and settled RBC column top in a specific period. Test is based on the fact that inflammatory and necrotic processes cause an alteration in blood proteins and result in red blood cells aggregation, making them heavier and more likely to fall rapidly. A highly non-specific screening test (high sensitivity, low specificity). Normal ESR cannot be used to exclude organic disease. ESR depends on RBCs size/specific concentration, and blood plasma specific concentration/viscosity, as well as earth gravitation acceleration (Stockes' formula). ESR rises >24 hours after inflammation onset and symptoms, gradually returns to normal until 4 weeks after resolution. Factors influencing ESR: 1) plasma factors (fibrinogen concentration, globulin concentration, serum cholesterol), 2) red cell factors (red cell surface area – microcytes sediment more slowly than macrocytes).

Test Purpose. 1) to monitor inflammatory or malignant diseases, 2) to aid detection and diagnosis of occult disease, such as TB, tissue necrosis, or connective tissue diseases, rheumatic conditions, 3) to monitor disease course or activity and treatment, 4) may help grade severity in emergency setting.

Increased Values

- **↑ 100 mm/1st hour**: autoimmune hemolytic anemia, liver cirrhosis, hemolytic-uremic sy, chronic myelogenous leukemia, collagenosis, dermatomyositis, giant-cell arteritis, rheumatoid arthritis, endocarditis, phlegmon, hemoblastosis, rheumatic fever, cholecystitis, systemic lupus erythematosus, malaria, Hodgkin's disease, Waldenström's disease, tumours, nephrosis, osteomyelitis, peritonitis, plasmocytoma (incl. multiple myeloma), polyarthritis, polymyalgia rheumatica, renal diseases, pyelitis, pyelonephritis, sepsis, nephrotic sy, vasculitis, chronic granulomatous disease
- **↑ 50 mm**: severe anemia, liver cirrhosis, glomerulonephritis – (acute g., chronic g.), lupoid hepatitis, infectious hepatitis, hemodilution, hyperfibrinogenemia, hypergammaglobulinemia, hypothyroidism, diseases – (bacterial infectious d., renal d., chronic hepatic d., inflammatory bowel d.), cardiac infarction (increase at 12–48 hrs, peaking at 4th–5th d., decrease at 1–4 months), acute heavy metal poisoning, cachexia (advanced), Henoch–Schönlein purpura, Mediterranean fever, collagenoses, leptospirosis, leukemia, lymphoma, metastatic tumours, pleuritis, pneumonia, polyarteritis nodosa, polymyalgia rheumatica, toxic liver disorders, necrotic states, sarcoidosis, infantile cortical hyperostosis, scleroderma, syphilis, pregnancy, thrombophlebitis, thyroiditis, cat scratch disease, primary atypical pneumonia, systemic fungal infections, acute pancreatitis, burn injury, drug hypersensitivity reaction
- **↓ 50 mm**: anemia, diabetes mellitus, leucemia, menses, undernutrition, postoperative states, pregnancy (2nd, 3rd trimester), tuberculosis

  Interfering Factors: ↓ 50 mm: acanthocytosis, macrocytosis, hypercholesterolemia, hyperfibrinogenemia, hyperglobulinemia, poikilocytosis, medicaments – (acetylsalicylic acid, allopurinol, clometacin, cyclosporine, dextran, globulin, heparin, hydralazine, methyldopa, methysergide, naproxen, nitrofurantoin, nomifensine, oral contraceptives, penicillamine, phenylbutazone, procainamide, retinol, theophylline, thiabendazole, trifluperidol, vitamin A, zimeldine)

Decreased Values

afibrinogenemia, acanthocytosis, HbC disease, alkalosis, sickle-cell anemia, angina pectoris, disseminated intravascular coagulation, exsicosis, hemoconcentration, hyperalbuminemia, hyperglycemia, severe plasma hyperviscosity, hypofibrinogenemia, obstructive icterus, cachexia, cardiac insufficiency, poisoning by – (CO, phosphorus), cryoproteinemia, leukocytosis, macroglobulinemia, microcytosis, infectious mononucleosis, massive hepatic necrosis, poikilocytosis, polycythemia, polycythemia vera, polyglobulia, defibrination sy, shock – (allergic s., anaphylactic s.), spherocytosis, old blood specimen, congestive heart failure

Interfering Factors: medicaments – (ACTH, adrenal steroids, amphotericin B, calcium, cardiotonics, cortisone, quinine, salicylates)

Analyte	Age/Gender	Reference Range	SI Units	Note
Erythrocyte Sedimentation Rate	3 m–13 y	12–24	mm	
	Adults M	5–10	mm	
	F	10–20	mm	

Erythrocyte Survival

Test Purpose. To confirm decreased RBC survival.

Increased Values
thalassemia minor

Decreased Values
anemia – (idiopathic acquired hemolytic a., sickle cell a., pernicious a., megaloblastic a., congenital nonspherocytic hemolytic a., hereditary spherocytosis), elliptocytosis with hemolysis, HbC disease, paroxysmal nocturnal hemoglobinuria, chronic lymphatic leukemia, pregnancy, uremia

Erythrocytes

(RBC, syn: red blood cells, red blood cell count, red blood corpuscle count) RBC are biconcave disc shape cells without nuclei, characterized by red color caused by hemoglobin. They do only glycolysis, they have no mitochondria.
Function. O_2 transport from the lungs to the body tissues + transfer CO_2 from the tissues to the lungs through the hemoglobin. They also function in acid-base balance. They continually produce lactate, which is continually excreted out of the RBC, in exchange for OH^- coming in.
Production. Formed in the red bone marrow (ribs, sternum, vertebrae, pelvis) = erythropoietin effect erythropoiesis from clone cells. In O_2 decrease a renal hormone erythropoietin stimulates RBC production.
Test Purpose. 1) to provide data for calculating MCV and MCH that reveals RBC size and Hb content, 2) to support other hematological tests for diagnosing anemia or polycythemia.

- **Peripheral blood smear** (syn. stained red cell examination/film, smear evaluation, stained blood film, blood smear, red blood cell morphology, RBC smear): used for evaluation of changes in numbers or morphology of red cells, white cells and platelets. Blood film examination clarifies abnormalities detected by automated hematology instruments and guides further investigation.
- **Physiologic**: normochromic normocytes
- **Acanthocytes → acanthocytosis** (irregularly spiculated surface, spur cells): **abetalipoproteinemia**, alcoholic cirrhosis with hemolysis, hepatic necrosis, asplenia, **pyruvate kinase deficiency**, liver diseases, postsplenectomy sy, irreversibly abnormal membrane lipid content, uremia, infantile pyknocytosis
- **Anisocytes → anisocytosis** (variable size, simultaneous macrocytes and microcytes occurrence): severe anemia, deficiency of – (folic acid, vitamin B_{12}, iron), reticulocytosis, transfusing normal blood into microcytic or macrocytic cell population
- **Anisochromia** (different RBC staining caused by non-equal RBC Hb content)
- **Anulocytes → anulocytosis** (erythrocytes deficient in hemoglobin which is localized in the erythrocyte periphery): anemia – (hypochromic a. , severe sideropenic a.)
- **Echinocytes → echinocytosis** (syn. crenated cells, burr cells, regularly spiculated cell surface): anemia, reversible membrane lipid content abnormalities, bile acids abnormalities, pyruvate kinase deficiency, high plasma free fatty acids, gastrointestinal bleeding, hypophosphatemia, hypomagnesemia, medicaments – (barbiturates, salicylates), gastric tumors, uremia, peptic ulcer

- **Elliptocytes → elliptocytosis** (syn: ovalocytes, oval cells, oval/sickle shaped): anemia – (hemolytic a., megaloblastic a., **hereditary ovalocytosis – elliptocytosis, sickle cell a.**, refractory normoblastic a., sideropenic a., **thalassemia**), iron deficiency, myelofibrosis
- **Hyperchromic** (hyperchromasia, more colored): anemia – (macrocytic a., spherocytic a.), concentrated hemoglobin (usually caused by dehydration)
- **Hypochromic** (enlarged pallor area, RBC are insufficiently hemoglobinised): **iron deficiency, cardiac diseases**, heme synthesis disorder, **thalassemia**
- **Macrocytes** (↑ 8.5 µm) → **macrocytosis**: alcoholism, anemia – (**aplastic a., hemolytic a., macrocyte a., megaloblastic a., pernicious a., postsplenectomic a.**, sideroblastic a.), deficiency of – (folic acid, vitamin B_{12}), smoking, interfering factors – electronic cell sizing artifact – (cold agglutinins, severe hypoglycemia, hyponatremia, stored blood), **hypothyroidism**, diseases – (myeloproliferative d., **chronic hepatic d., chronic lung d.**), obstructive icterus, **leukemia**, medicaments – (alcohol, chemotherapeutics, hydroxyurea, immunosuppressives, zidovudine), myxedema, tumors, **newborn, plasmocytoma** (incl. multiple myeloma), **reticulocytosis secondary to increased erythropoiesis, myelodysplastic sy**, pregnancy, old age
- **Megalocytes** (10–16 µm) → **megalocytosis**: megaloblastic anemia, folate/vitamin B_{12} deficiency, chemotherapy, myeloproliferative diseases
- **Microcytes** (<6.5 µm) → **microcytosis**: anemia – (a. of chronic disease, sickle cell a., **spherocytic a., sideropenic a., thalassemia**), **hemoglobinopathies**, tumours, nephritis, increased iron consumption, chronic hemorrhage conditions, polycythemia vera, toxic chronic diseases effects on bone marrow, tuberculosis
- **Microspherocytes** (small, round): autoimmune hemolytic anemia, hemolysis, hereditary spherocytosis
- **Normocytes** (biconcave disc): physiologically
- **Poikilocytes → poikilocytosis** (variations in shape, irregular shape): anemia – (sickle cell a., pernicious a., severe a.), extramedullary hematopoiesis, microangiopathic hemolysis, leukemias, post-transfusion reaction, marrow stress of any cause
- **Polychromasia** (RBC with blue or gray-violet color in the partially basophilic cytoplasm): hemolytic anemia, increased young RBC outflow – (tumor metastases to bone marrow, newborn, polycythemia), increased erythropoiesis, increased reticulocytopoiesis
- **Pyknocytes → pyknocytosis** (distorted/contracted/spiculed): hemolytic anemia, newborn
- **Schistocytes → schistocytosis** (syn. helmet cell, burr cell, fragmented RBC with bizarre shape, triangular or spiral, helmet-shaped): hemolytic anemia, eclampsia, glomerulonephritis, giant hemangioma, hemoglobinuria, hemolytic-uremic sy, **microangiopathic hemolysis, malignant hypertension, artificial/prosthetic heart valves, disseminated intravascular coagulation** (DIC), **metastatic tumors**, normal newborn, severe burns, thalassemia, **thrombotic thrombocytopenic purpura**, renal graft rejection, severe valvular heart diseases, snakebite, increased intravascular mechanical trauma, uremia, **vasculitis**
- **Sickle cells** (syn. drepanocytes, ERCs that assume a crescent or sickle shape due to some abnormal hemoglobins, half-moon shape): anemia – (hemolytic a., **sickle cell a.**, thalassemia), hemoglobinopathies (HbI, HbC)
- **Siderocytes → siderocytosis**: anemia – (chronic hemolytic a., pernicious a., hereditary spherocytosis, thalassemia), hemochromatosis, lead poisoning, newborn, polycythemia vera, post-splenectomy
- **Spherocytes → spherocytosis** (smaller, round, cells with no central pallor, biconcave shape loss): anemia – (**congenital hemolytic a., acquired immunohemolytic a., hereditary spherocytosis**), accelerated red blood cell destruction by reticuloendothelial sys-

tem, acute alcoholism, hemoglobin C disease, severe burn injury, hemolytic transfusion reactions, severe hypophosphatemia, acute oxidant injury (hexose monophosphate shunt defect), Clostridium Welchii septicemia, recent blood transfusion

- **Stomacytes → stomatocytosis** (syn. stomatocytes, slit-like central pallor area in erythrocyte): **acute alcoholism**, diseases – (cardiovascular d., hepatobiliary d.), hemolytic anemia, Rh null disease, medicaments – (phenothiazines), liver diseases, tumors, **hereditary stomatocytosis**
- **Target cells → leptocytosis** (syn. leptocytes, codocytes, hypochromic cells, dark peripheral hemoglobin rim and dark central ring, often microcytic): decreased lecithin-cholesterol acyltransferase activity, anemia – (hypochromic a., sickle cell a., sideropenic a., **thalassemia**), severe iron deficiency, hemoglobinopathies – (HbC, HbD, HbE, HbS), **liver diseases**, obstructive icterus (jaundice), hemoglobin C and S presence, lead intoxication, **splenectomy**
- **Tear-shaped** (dacrocytes, dacryocytes, drop-shaped RBCs, often microcytic): anemia – (myelophthisic a., severe hemolytic a.), erythroleukemia, **extramedullary erythropoiesis**, marrow infiltration with tumor, **myelofibrosis**, **thalassemia**
- **RBC intracellular structures:**
  - **basophilic stippling** – basophilic RNA – (**hemolytic anemia**, **megaloblastic anemia**, **pernicious anemia**, arsenic poisoning, sideroblastic anemia, **lead poisoning**, **leukemia**, **reticulocytosis**, **thalassemia**), unstable hemoglobin, increased erythropoiesis,
  - **Heinz bodies** – insoluble oxidatively denatured Hb masses and the end-product of oxidative degradation of Hb – (**hemolytic anemia**, **G6PD deficiency**, **hemoglobinopathies**, acute hemolytic crisis, **methemoglobinemia**, **drug-induced RBC injury**, **following splenectomy**, **severe oxidative stress**, excessive globin-chain production, **thalassemia**, intoxication), medicaments – (analgesics, antimalarials, antipyretics, furazolidine, nalidixic acid, nitrofurans, phenazopyridine, phenylhydrazine, primaquine, procarbazine, sulfacetamide, sulfamethoxazole, sulfapyridine, sulfonamides, tolbutamide, large vitamin K doses),
  - **Howell–Jolly bodies** (nuclear remnants) – nuclear DNA fragments – (**hemolytic anemia**, **megaloblastic anemia**, **intense erythrocyte production**, **postsplenectomy**, vitamin B_{12} deficiency, hyposplenism, thalassemia, folic acid deficiency),
  - **nucleus – nucleated red blood cells**, nucleated RBC – (marrow-occupying neoplasm or fibrotic tissue in: **myeloma**, **leukemia**, **erythroleukemia**), (physiologic response to RBC deficiency in: **hemolytic anemias**, **sickle cell crisis**, **transfusion reaction**, **erythroblastosis fetalis**), (physiologic response to hypoxemia in: **congenital heart disease**, **congestive heart failure**), **"normal" for infants blood**, tumors – (**breast t.**, **lung t.**, **prostate t.**, **thyroid t.**), disease – (**Niemann-Pick d.**, **Gaucher's d.**, **Hodgkin's d.**), **osteopetrosis**, **Hand-Schüller-Christian sy**, plasmocytoma (incl. multiple myeloma), **leukemoid reaction**, **thrombotic thrombocytopenic purpura**, **miliary tuberculosis**, agnogenic myeloid metaplasia with myelofibrosis
  - **parasitized RBCs** – (malarial stippling, Bartonella parasites)
  - **siderotic granules** (Pappenheimer bodies) – iron-containing granules – (after splenectomy, iron-overload sy, sideroblastic anemia, thalassemia, lead poisoning, pyridoxine-un-/responsive anemias)

Increased Values – erythrocytosis

cryptogenic fibrosing alveolitis, anaphylaxis (capillary leak syndromes), **cor pulmonale**, **renal cysts**, deficiency of – (**2,3-DP-glycerate**, salt), **dehydration**, long-term hemodialysis, enteropathy, familial erythrocytosis, CO exposure, **smoking**, **diarrhea**, **hydronephrosis**, alveolar hypoventilation, diseases – (neuromuscular d., **hypoxic pulmonary d.**, **cyanotic congenital heart d.**, renal d.), **carboxyhemoglobinemia**, diabetic hyperosmolar coma, methemoglobinemia, tumours – (pheochromocytoma, uterus t., cerebellum t., adrenal t., **kidney**

t., liver t., lung t., ovary t.), **secondary response to hypoxia, polycythemia due to plasma volume contraction, polycythemia vera, polyglobulia,** burns, chronic osmoregulation disorders, **increased erythropoietin production, cardiovascular right-to-left shunt,** low-output cardiac states, **renal artery stenosis,** blood loss due to hemolysis/hemorrhage, **physical/psychic stress,** syndrome – (sleep apnea sy, **Bartter's sy,** Cushing's sy, hypoventilation sy, nephrotic sy, pickwickian sy), **renal transplantation, high altitude,** vomiting, **chronic congestive heart failure**

Interfering Factors: medicaments – (androgens, corticosteroids, diuretics, gentamicin, methyldopa, methyltestosterone, testosterone)

Decreased Values – erythrocytopenia

amyloidosis, anemia – (**hereditary nonspherocytic hemolytic a., sickle cell a., pernicious a., hereditary spherocytosis, thalassemia, a. from dietary deficiency of – iron, vitamin B_6, B_{12}, folic acid**), **subacute endocarditis,** erythropoietin deficiency, erythroleukemia, **hemoglobinopathies, acquired paroxysmal nocturnal hemoglobinuria, hemolysis,** viral hepatitis, **rheumatic fever, hyperhydration,** hypothyroidism, diseases – (bone marrow d., chronic renal d., **rheumatic d., chronic inflammatory d.**), infectious diseases – (fungal i. d., viral i. d.), intoxication by – (arsenic, benzene, copper, lead), **hemorrhage, leukemia,** systemic lupus erythematosus, malnutrition, mastocytosis, myelofibrosis, Addison's disease, Gaucher's disease, **Hodgkin's disease,** infectious mononucleosis, **myelofibrosis, tumors, plasmocytoma** (incl. multiple myeloma), **radiation, sepsis,** Fanconi's sy, **pregnancy,** transfusion reaction, tuberculosis, failure – (**bone marrow f., renal f.**)

Interfering Factors: medicaments – (antiarthritic preparations, antibiotics, antidepressants, antidiabetics, antiinflammatory drugs, antihistamine preparations, anticonvulsants, antineoplastics, antithyroid preparations, chloramphenicol, diphenylhydantoin, methotrexate, penicillin, phenacetin, quinidine, quinine)

Analyte	Age/Gender	Reference Range	SI Units	Note
Erythrocytes	Neonates	4.5–5.6 *		
	3 m–13 y	3.8–5.0 *		* x 10^{12}/l
	Adults M	4.6–5.5 *		
	Adults F	4.2–5.0 *		

Erythrocytic Folate

Since serum folate values fluctuate significantly with diet, measurement of red cell folate is a better measure of tissue folate stores. Attention to clinical setting is important since a normal red cell folate level can be found in a rapidly developing folic acid deficiency such as the stress of pregnancy. Test is used to detect folate deficiency and monitor therapy with folate.

Erythrocytic Indices

(syn: Wintrobe red cell indices, blood indices) Erythrocytic indices derived from RBC parameters inform about RBC size and blood stain, calculated from hemoglobin, RBC count, and hematocrit values.

- **MCV** – mean corpuscular volume
- **MCH** – mean corpuscular hemoglobin
- **MCHC** – mean corpuscular hemoglobin concentration

Erythrocytic Protoporphyrin

(FEP, syn: free erythrocyte protoporphyrin, RBC protoporphyrin) It is a heme pre-step in biosynthesis created by oxidation from protoporphyrinogen and protoporphyrin oxidase action. Free erythrocyte protoporphyrin expresses the noncomplexed, nonheme protoporphyrin amount in red cells. Increased lead absorption is reported in the presence of iron deficiency.

Test Purpose. 1) to aid in congenital/acquired erythropoietic porphyrias diagnosis, 2) to help confirm diagnosis of disorders affecting red blood cell activity, 3) to screen for lead poisoning, iron deficiency and iron deficiency anemia, 4) to monitor chronic industrial exposure to lead.

Increased Values

anemia – (severe hemolytic a., **a. of chronic disease, sideroblastic a., iron-deficiency a.**), diseases – (infectious d., chronic d.), increased erythropoiesis, **lead poisoning, chronic industrial exposure, lead intoxication porphyria, erythropoietic protoporphyria**

Decreased Values

anemia – (thalasemia minor, pyridoxine-responsive a.)

Erythropoietin

(EPO)

Production. EPO is a glycoprotein hormone produced principally by the kidney (renal cortex peritubular cells). The liver is the major extrarenal production site and accounts for about 10% of EPO in adults. EPO synthesis is governed by mild mechanisms where the peripheral oxygen saturation and hemoglobin concentration play an important feed-back regulatory role; their decrease leads to EPO synthesis increase. It is released in response to renal hypoxia (tissue oxygen delivery reduction).

Function. Major stimuli for erythropoiesis effecting erythroid clone cells (erythroid progenitors proliferation and maturation) and accelerating erythropoiesis in bone marrow. EPO concentrations are relatively low in healthy persons. In some anemias, e.g. aplastic, EPO production regulation is not impaired; it leads to high EPO levels (up 1000 x higher). EPO kinetics in hemorrhage and acute hypoxic conditions is in hours. Basal EPO concentration determination is an important EPO therapy condition. During renal anemias evaluation (the most frequent EPO therapy indication) it is needed to take into consideration: 1) renal tissue decrease during ageing and by synthesis place number diminution, 2) metabolic synthesis influence by toxic, uremic and inhibitory substances, 3) chronic renal insufficiency patients have lowered endogenous EPO marrow answer, 4) less quality synthesis by RBC, 5) possible increased blood loss caused by examination, dialysis, and hemorrhage. Lowest levels are in early afternoon, increase to peak around midnight. Within-day variation is 60%.

Test Purpose. 1) to aid in anemia and polycythemia diagnosis, 2) to aid in malignant tumors diagnosis/therapy, 3) to detect erythropoietin abuse by athletes, 4) to monitor erythropoietin therapy in chronic renal failure.

Increased Values

AIDS, cryptogenic fibrosing alveolitis, anemia – (**aplastic a., hemolytic a.**), exercise, chronic iron deficiency, high-altitude hypoxia, chronic obstructive pulmonary disease, tumors – (testicular t., breast t.), erythropoietin-producing tumors – (**pheochromocytoma, cerebel-**

lar hemangioblastoma, hepatoma, hemangiosarcoma, leiomyoma, renal adenocarcinoma, meningioma, **nephroblastoma**), myelodysplasia, **polycystic renal disease, secondary polycythemia, kidney transplant rejection**, following moderate normal individual bleeding, athletes using EPO as doping, **pregnancy**

Interfering Factors: medicaments – (anabolic steroids)

Decreased Values

congenital erythropoietin absence, AIDS, rheumatoid arthritis, chronic disease anemia in – (**malignancy, chronic inflammation**), decreased renal function, **starvation**, hypogonadism, hypocorticism, **hypopituitarism, hypothyroidism, severe renal diseases**, plasmocytoma (incl. multiple myeloma), tumors, **polycythemia vera, renal tissue loss**, bone marrow transplant, autonomic neuropathy, nephrotic sy, **renal failure**

Interfering Factors: high plasma viscosity, medicaments – (ACE inhibitors, amphotericin B, beta-adrenergic blockers, enalapril, estrogens)

Analyte	Age/Gender	Reference Range	SI Units	Note
Erythropoietin		6–20	mU/ml	See ref.
		25–125	mU/ml	ranges note

Ethanol Gelation Test

(syn: ethanol gel) Screening test which identifies abnormal exaggerated intravascular coagulation activation. Test detects fibrin monomers by gelification with ethanol.

Test Purpose. 1) dissolved plasma fibrin monomer amount evaluation, 2) information about abnormal intravascular blood coagulation (e.g. DIC).

Positive Values

pulmonary embolism, phlebothrombosis, disseminated intravascular coagulation

Euglobulin Lysis Time

(syn: whole blood clot lysis, euglobulin clot lysis, euglobulin lysis) Euglobulins are precipitated proteins coming from acidified dilute plasma. The euglobulin plasma fraction contains fibrinogen, plasminogen, and plasminogen plasma activators, but only antiplasmin traces. Thrombin added to the euglobulin solution converts fibrinogen to fibrin and activates plasminogen. Fibrinolytic activity evaluation which measures fibrin coagulum lysis time of clotted plasma endoglobulin fraction (fibrinogen, prothrombin, fibrinolytic enzymes). The fibrinolytic system normally breaks down small fibrin deposits. When this system is abnormally overactive, as in primary fibrinolysis, any fibrin clot formed will be dissolved immediately that results in a bleeding tendency. Usually, fibrin formed in the euglobulin plasma fraction is very rapidly dissolved by plasmin (fibrinolysin). The time measured from clot formation to clot lysis is referred to as the euglobulin lysis time. These tests are generally not practical, since it is difficult to determine whether fibrinolysis has occurred through a primary mechanism specifically activating the fibrinolytic pathway, or through secondary intravascular coagulation with secondary fibrinolytic activation.

Test Purpose. 1) to assess the fibrinolytic system, 2) to detect abnormal fibrinolytic states, 3) to monitor streptokinase/urokinase therapy, 4) to investigate possible acquired bleeding disorders.

Increased Values – (increased, prolonged lysis time, shortened, decreased fibrinolysis) hypoxia, **diabetes mellitus, disseminated intravascular coagulation,** fibrinolytic system insufficiency, **premature infants,** pyrogen reactions, **incompatible blood transfusion**

Interfering Factors: hyperventilation

Decreased Values – (decreased, shortened lysis time, prolonged, increased fibrinolysis) **amniotic fluid embolism, primary fibrinolysis,** extracorporeal circulation, **liver cirrhosis,** fetal death, **thrombolytic therapy** (streptokinase, urokinase), **obstetric complications, antepartum hemorrhage,** hereditary deficiency of fibrinogen, **leukemia, mola hydatidosa,** plasminogen rich organs surgery – (uterus, pancreas, lungs, prostate, heart), **septic abortion, shock conditions,** trauma – (acute t., **extensive vascular t.**), tumours of – (pancreas, **prostate**), **thrombocytopenic purpura,** first 48 hours after surgery, systemic fibrinolytic states

Interfering Factors: arterial blood, **elder people, physical exercise, normal newborns, obesity, postmenopause,** medicaments – (ACTH, alteplase, anistreplase, asparaginase, dextran, clofibrate, steroids, streptokinase, urokinase)

Analyte	Age/Gender	Reference Range	SI Units	Note
Euglobulin Lysis Time		10–18	hrs	

Ferritin

(see ferritin in blood-plasma-serum parameters chapter) (iron hydroxide + protein part → apoferritin). Ferritin is an alpha-1-globulin, tumor marker, and acute phase reactant. Ferritin is the major, water-soluble iron storage protein.

Production. Reticuloendothelial system (liver, spleen, bone marrow, kidney). Ferritin, which is circulating in blood, is a serum ferritin (glycated ferritin, considered as normal secretory cells product) and tissue ferritin mixture, which is released from damaged cells. Ferritin creates complexes with other proteins in blood, e.g. alpha-2-macroglobulin.

Analyte	Age/Gender	Reference Range	SI Units	Note
Ferritin	M	30–310	ng/ml	
	F	22–180	ng/ml	

Fetal Hemoglobin

(HbF, syn: hemoglobin F, alkali-resistant hemoglobin) Fetal hemoglobin is normal hemoglobin manufactured in the fetal/infant RBCs and composes 50 to 90% of the newborn hemoglobin. This hemoglobin type disappears from circulation during the 1st year. The remaining hemoglobin portion in the newborn is made up of adult type hemoglobin A1 and A2.

Test Purpose. 1) to state HbF percentage, 2) differential diagnosis of hemolytic anemias (sickle-cell, beta thalassemia) and hereditary disorders (elliptocytosis, hereditary HbF persistence).

Increased Values

anemia – (**aplastic a., sickle cell a., pernicious a.,** chronic infection a., blood loss a., megaloblastic a., spherocytic a., sideroblastic a., **heterozygous/homozygous beta-thalassemia**), elliptocytosis, erythroleukemia, benign monoclonal gammopathies, paroxysmal nocturnal

hemoglobinuria, hyperthyroidism, diseases – (hemoglobin H d., myeloproliferative d., chronic renal d.), infants who are small for gestational age, fetomaternal hemorrhage, leukemia – (**acute/chronic l.**, juvenile chronic myeloid l.), **hydatidiform mole**, plasmocytoma (incl. multiple myeloma), cancer with marrow metastases, **hereditary HbF persistence**, erythropoietic porphyria, pregnancy, **trisomy D**, Down sy, chronic renal failure

Decreased Values
hemolytic anemia in the newborn

Analyte	Age/Gender	Reference Range	SI Units	Note
Hemoglobin F	1 d	0.62–0.92		
	5 d	0.65–0.88		
	3 w	0.55–0.85		
	6–9 w	0.31–0.75		
	3–4 m	0.02–0.59		
	6 m	0.02–0.09		
	Adults	<0.02		

Fibrin Degradation Products

(FDP, FDPs, syn: fibrin/fibrinogen split products – FSPs, fibrin breakdown products – FBP, fibrinogen degradation products) Fibrin/fibrinogen split products by plasmin during fibrinolysis. Test is used in consumptive coagulopathy degree determination. When plasma acts to dissolve fibrin blood clots FDPs (X, D, E, Y) are formed. Split products have an anticoagulant action and inhibit clotting when there is an product excess. Tests for FDP are done on serum; since FDPs do not coagulate, they remain in the serum after fibrinogen is removed through clotting. Normal serum contains neither fibrinogen nor FDP → there is nothing present to react with antifibrinogen antibodies.
Test Purpose. 1) to detect fibrin degradation products in the circulation, 2) to help determine presence and approximate hyperfibrinolytic condition severity that may result in primary fibrinogenolysis or hypercoagulability, 3) to help determine the disseminated intravascular coagulation diagnosis, 4) to determine thrombolytic condition in thrombolytic therapy patients.

Increased Values
alcoholic cirrhosis, pulmonary embolism, primary/secondary fibrinolysis, hypoxia, diseases – (**infectious d., renal d., liver d., congenital heart d.**), **myocardial infarction, disseminated intravascular coagulation** (DIC), obstetric complications – (**abruptio placentae, intrauterine fetal death, preeclampsia**), coma due to hypnotics, **acute leukemia, fibrinolytic therapy**, tumors, surgery of the – (**thorax, heart**), polycythemia vera, **burns**, renal injury, **transplant rejection, sepsis, portocaval shunt, thromboembolic states**, pregnancy (3rd trimester), blood transfusion – (incompatible b. t., **massive b. t.**), renal transplantation, **venous thrombosis**, exercise, anxiety, stress conditions, sunstroke, trauma, following Cesarean birth

Interfering Factors: medicaments – (barbiturates, heparin, streptokinase, tissue plasminogen activator, urokinase)

Analyte	Age/Gender	Reference Range	SI Units	Note
Fibrin Degradation Products		<5	mg/ml	

Analyte	Age/Gender	Reference Range	SI Units	Note
		<10	mg/ml	See ref. ranges note

Fibrinogen

(F I, syn: factor I, fibrinogen level) Factor I in hemocoagulation. Protein fibrin precursor needed for fibrin fibre production and definitive coagulant plug creation. Substrate for thrombin which splits 3-chain fibrinogen molecules to fibrin monomers, they are connecting (polymerization) by hydrogen bonds → this leads to unstable fibrin net creation. Fibrinogen is not present in serum. Activity is destroyed during coagulation process. Protective acute phase protein (reactant) produced by the liver. Fibrinogen is characterized with genetic polymorphism; as an inflammatory protein it increases with 24–48 hrs latency. Synthesis is decreased during liver diseases. It is involved in platelet aggregation processes, determines some blood attributes, and via interaction with vascular wall has a direct relation to thrombosis and atherosclerosis origin. It is assumed, that it plays a key role in ischemic heart disease origin and development.

Test Purpose. 1) to aid in the diagnosis of suspected clotting or bleeding disorders caused by fibrinogen abnormalities (congenital/acquired a/hypo/dysfibrinogenemia) and liver diseases, 2) to identify disseminated intravascular coagulation (DIC) and fibrinolytic activity, 3) to estimate ischemic heart disease and cerebrovascular disorders, peripheral angiopathy risks and prognoses, 4) to aid in the diagnosis of inflammatory disorders and neoplastic conditions, 5) to aid in the diagnosis of unexplained high ESR, 6) to monitor disease activity.

Increased Values – hyperfibrinogenemia

rheumatoid arthritis, **atherosclerosis**, diabetes mellitus, **smoking**, **glomerulonephritis**, hepatitis, rheumatic fever, hypertension, **coronary artery disease**, diseases – (**cerebrovascular d.**, **acute infectious d.**, **acute/chronic inflammatory d.**), **myocardial infarction**, compensated disseminated intravascular coagulation (DIC), collagenosis, leukemia, fibrinolytic treatment, non-specific pulmonary malignant tumours marker, menstruation, bone metastases, tumours – (bronchial t., pancreatic t., **plasmocytoma** (incl. multiple myeloma), nephrosis, **tissue necrosis**, obesity, biliary ways obstruction, paraproteinemia, pleuritis, pneumopathies, pneumonia, polyarthritis, burns, hypercoagulative disorders, septicemia, conditions – (hemorrhagic c., postsurgery c.), **stress**, nephrotic sy, pregnancy (3rd trimester), tuberculosis, trauma, uremia

Interfering Factors: elderly people, medicaments – (acetylsalicylic acid, estrogens, nandrolone, oral contraceptives, oxymetholone)

Decreased Values – hypofibrinogenemia

abruption/ablation of placenta, **afibrinogenemia**, hepatic cirrhosis, **dysfibrinogenemia**, **acute hepatic dystrophy**, eclampsia, amniotic fluid embolism, **primary/secondary fibrinolysis**, **hypofibrinogenemia**, severe infections with septicemia, **acute/chronic hepatic diseases with insufficiency**, acute inflammatory diseases, obstructive icterus, phosphorus poisoning, **cachexia**, **DIC**, leukemia – (acute l., myeloid l.), thrombolytic treatment by – (streptokinase, urokinase), meningococcal meningitis, prostate tumour metastases, tumors of – (**bone marrow**, **pancreas**, **lung**, **prostate**), nephrosis, polycythemia vera, **severe surgery**, spontaneous abortion, defibrination sy, shock, pregnancy, **large blood transfusion**, typhoid fever, **trauma**

Interfering Factors: medicaments – (anabolic steroids, androgens, antiepileptics, asparaginase, dextran, heparin – in high concentrations, oral contraceptives, metformin, phenobarbital, streptokinase, testosterone, valproic acid)

Analyte	Age/Gender	Reference Range	SI Units	Note
Fibrinogen (Factor I)	Neonates	1.25–3.0	g/l	
	Adults	1.5–3.5	g/l	
		4.0–10.0	µmol/l	

Fibrinopeptide A

(FPA) Thrombin fibrinogen to fibrin conversion is associated with peptides (A, B) release. Reflects active intravascular blood clotting as in subclinical disseminated intravascular coagulation. Fibrinogenesis marker.

Increased Values

pulmonary emboli, early leukemia treatment phase, DIC, leukemic patients at time of initial diagnosis or during relapse after remission, **deep-vein thrombosis**

Decreased Values

clinical leukemia remission after chemotherapy

Analyte	Age/Gender	Reference Range	SI Units	Note
Fibrinopeptide A		<3	ng/ml	

Folic Acid

(syn: folate) Active folic acid form = folinic acid. It is a pteridine, para-aminobenzoic acid and glutamic acid derivative. One of water soluble B vitamin group. Food folates are polyglutamates that are broken down by intestinal mucosal conjugase enzymes to a more soluble monoglutamates before absorption. This folate form circulates in the plasma freely or loosely bound to albumin, rapidly entering the tissues. To utilize liver folate stores, it is necessary to excrete into the bile and reabsorb the matter by jejunum – enterohepatic circulation.
Function. Necessary for normal red and white blood cells function, and important for the cellular genes and DNA production. Folic acid is a part of the coenzymes involved in purine and thymine synthesis, pyrimidine DNA methylation reactions, conversion of homocystine to methionine, conversion of serine and glycine, degradation of histidine; it plays a key role in cell growth and reproduction. Tetrahydrofolic acid is an active folic acid form serving as a co-factor in monocarbon radicals metabolism. It transfers activated formic acid and activated formaldehyde. Folate absorption depends on normal intestinal mucosa functioning.
Occurrence. Fresh green vegetables, fruits, beans, nuts, liver, kidney. It is stored in the liver. Highest values are in winter, lower are in summer.
Test Purpose. 1) questionable deficiency in conditions like megaloblastic anemias, undernutrition, malabsorption sy (celiac disease, conditions after intestine resection), alcoholism, neurological diseases, 2) to assess folate stores in pregnancy, 3) long term therapy monitoring with antiepileptics (mainly phenytoin), antibiotics, and cytostatics, 4) dialyzed patient monitoring, 5) dermatological disease diagnosis (e.g. psoriasis).

Increased Values

vitamin B_{12} deficiency, blood transfusion, distal small bowel disease, **inadequate folate intake**, blind loop sy, **vegetarianism**

Interfering Factors: medicaments – (metformin, phenformin)

Decreased Values

amyloidosis, alcoholism, anemia – (**hemolytic a.,** macrocytic a., megaloblastic a., **pernicious a., sideroblastic a.,** hereditary spherocytic a., thalassemia), nutritional megaloblastic anemia in – (infants, **infectious diseases**), **anorexia nervosa, coeliac disease,** hepatic cirrhosis, vitamin B_{12}/C deficiency, **dermatitis herpetiformis,** exfoliative dermatitis, diabetes mellitus, diabetic enteropathy, smoking, **partial gastrectomy, hemodialysis/peritoneal dialysis, chronic hemolysis,** paroxysmal nocturnal hemoglobinuria, hepatoma, **starvation,** infant diarrhea, homocystinuria, **hyperthyroidism,** hypothyroidism, diseases – (infant infectious d., **exfoliative skin d.,** myeloproliferative d.), liver disease connected with – (**alcoholism,** malabsorption sy), lactation, **leukemia, lymphoma, elder people, folate malabsorption, malnutrition, Crohn's disease, Whipple's disease, tumours, prematurity, insufficient folic acid intake, psoriasis, extensive intestinal resection,** scleroderma, **sprue,** febrile states, idiopathic steatorrhea, **pregnancy,** taeniasis, **excessive folate utilization by the body, protracted cardiac failure**

Interfering Factors: infancy, medicaments – (acetylsalicylic acid, alcohol, aminopterin, aminosalicylic acid, ampicillin, antiepileptics, anticonvulsants, antimalarials, azulfadine, barbiturates, carbamazepine, chloramphenicol, cycloserine, erythromycin, estrogens, ethanol, isoniazid, metformin, methotrexate, nitrofurantoin, oral contraceptives, penicillin, pentamidine, phenobarbital, phenytoin, primidone, pyrimethamine, sulfasalazine, tetracyclines, triamterene, trimethoprim, valproic acid)

Analyte	Age/Gender	Reference Range	SI Units	Note
Folic Acid	Neonates	15.9–72.4	nmol/l	See ref.
	F + M	4.1–38	nmol/l	ranges note
		>4.3	nmol/l	

Galactokinase in RBC

Test Purpose. 1) to investigate increased levels of galactose, 2) to investigate a juvenile onset cataract.

Decreased Values

cataract, **galactosemia,** genetic galactokinase deficiency

Galactose-1-Phosphate in RBC

Test Purpose. 1) to investigate a neonate with suspected galactosuria, 2) to help in diagnosis of galactosemia in a baby with a positive neonatal screening test, 3) to help in diagnosis of classical galactosemia, 4) dietary monitoring of patients with galactosemia.

Increased Values

galactosemia

Glucose-6-Phosphate Dehydrogenase in RBC

(G6PD) G6PD is a red cell X-linked inheritance enzyme important to maintain reduced RBC proteins (reduced glutathione form, G-SH). Enzyme is involved in RBC saccharide NADPH metabolism production. In G6PD deficiency, NADPH is not produced, effecting protective glutathione function loss and hemolytic disorders.

Test Purpose. RBC metabolic disorders and hemolytic anemias differential diagnosis.

Increased Values
anemia – (megaloblastic a., pernicious a.), hyperthyroidism, myocardial infarction, hepatic coma, idiopathic thrombocytopenic purpura, chronic blood loss

Decreased Values
congenital nonspherocytic anemia, G6PD deficiency

Analyte	Age/Gender	Reference Range	SI Units	Note
Glucose-6-Phosphate Dehydrogenase in RBC		0.22–0.52	*	*mU/mol Hb
		0.10–0.23	**	**nU/10^6 RBC

Glutathione in RBC

(syn: reduced glutathione in erythrocytes) RBC tripeptide is created from amino acid glycine, cystine and glutamic acid by enzyme glutathione synthase.
Function. Reduced RBC glutathione protects: a) enzyme and coenzyme – SH group against oxidation, b) membrane lipids against peroxidation, an enzyme involved in methemoglobin (Fe^{3+}) to hemoglobin (Fe^{2+}) reduction.
Test Purpose. RBC metabolism disorders and hemolytic anemias differential diagnosis.

Increased Values
pyrimidine-5'-nucleotidase deficiency, myelofibrosis

Decreased Values
strenuous exercise, deficiency of – (G6PD, gamma-glutamylsynthetase), diabetes mellitus, lead exposure

Glutathione Peroxidase in RBC

As a hexose-monophosphate shunt and glutathione cycle portion, enzyme is involved in RBC oxidative glycolysis (selenium-metalloenzyme which catalyzes hydrogen peroxide to water conversion).
Test Purpose. RBC metabolism disorders and hemolytic anemias differential diagnosis.

Increased Values
G6PD deficiency, acute lymphocytic leukemia, polyunsaturated fatty acids supplementation, alpha-thalassemia

Decreased Values
anemia – (sickle cell a., iron deficiency a.), selenium deficiency, lead exposure

Glutathione Reductase in RBC

(GR) Red cell enzyme. Its activity is chiefly a riboflavin nutrition state reflection.

Increased Values
strenuous exercise, G6PD deficiency, diabetes mellitus
Interfering Factors: medicaments – (nicotinic acid)

Decreased Values
anemia – (congenital nonspherocytic hemolytic a., hypoplastic a., alpha-thalassemia a.), Gaucher's disease, oligophrenia, pancytopenia, thrombocytopenia

Glycated Hemoglobin

(HbA_{1c}, HbAc, GHb, GHB, syn: glycohemoglobin, glycosylated hemoglobin, glycogenous hemoglobin, fast hemoglobin) Reaction product between glucose and N-terminal HbA valine. Glycohemoglobin is a minor hemoglobin (A_1 component). A_1 components (A_{1a}, A_{1b}, A_{1c}) which make up approximately 4–8% of the total hemoglobin are glycosylated. Blood glucose bound to hemoglobin is stored by the erythrocytes. Glycosylation is irreversible. GHb amount depends on the glucose amount available in the bloodstream over the RBC's 120-day life span. Because old RBCs are constantly being destroyed while new are being formed, GHb value determination reflects the average blood sugar level for the 100 to 120-day period before the test. With more glucose exposure there is greater GHb percentage. One important test advantage is that the sample can be drawn at any time, because it is not affected by short-term variations (food intake, exercise, stress, hypoglycemic agents, patient cooperation).
Test Purpose. 1) to assess diabetes mellitus control, 2) to check unstable IDDM and gestation DM therapies, 3) permanent hyperglycemia diagnosis.

Increased Values
alcohol, anemia – (sickle-cell a., thalassemia, **iron deficiency a.**), rheumatoid arthritis, iron deficiency, diabetes mellitus – (newly diagnosed d.m., **non-insulin dependent d.m.**, **insulin dependent d. m.**, d. m. in pregnancy, poorly controlled diabetic patient), pheochromocytoma, cystic pancreatic fibrosis, fructosuria, galactosemia, **hemodialysis**, false elevated values – (when the RBC life span is lengthened – as in thalassemia), **chronic hyperglycemia**, intoxi-cation by – (lead, opiates), hyperlipoproteinemia, diseases – (d. with abnormal hemoglobin, d. with shortened survival erythrocyte rate), chronic renal insufficiency, diabetic neuropathy, tumours, **splenectomy**, **stress**, Cushing's syndrome, **chronic renal failure**
Interfering Factors: TAG increase, medicaments – (hydrochlorothiazide, morphine, oral contraceptives, propranolol, salicylates)

Decreased Values
anemia – (**hemolytic a.**, congenital spherocytosis, **sickle cell a.**), shortened RBC life span (HbS, HbC, HbD presence), dialysis, phlebotomy, transfusion, acute caloric restriction, chronic blood loss, **pregnancy**, **chronic renal failure**
Interfering Factors: medicaments – (galactose, salicylate, vitamin C, vitamin E)

Analyte	Age/Gender	Reference Range	SI Units	Note
Hemoglobin, Glycated (HbA_{1c})	Normal	0.036–0.058 0.042–0.063 0.050–0.080 0.050–0.080 0.033–0.056		See ref. ranges note

Analyte	Age/Gender	Reference Range	SI Units	Note
		0.044–0.057		
	Good compensation	0.06–0.07		
	Insufficient compensation	>0.08		

Haptoglobin

(Hp, HPT, syn: hemoglobin binding protein) Hemoglobin metabolism acute phase protein and antioxidative system portion, it is characterized with genetic polymorphism with three phenotypes (1-1, 2-1, 2-2). Phenotype 2-2 is an ischemic heart disease risk indicator. There are other haptoglobin subtypes used in forensic medicine.

Production. Transport glycoprotein (alpha-2-globulin) is synthesized in the liver.

Function. Protein carrier of released hemoglobin = irreversible free Hb binding mainly through the Hb and haptoglobin globin alpha-chain. Haptoglobin-hemoglobin complex is taken from circulation and catabolized by spleen and liver reticuloendothelial tissue phagocytic cells, thus ensuring iron and amino acid salvage. Haptoglobin concentration is inversely related to the hemolysis level. Hemoglobin-haptoglobin complexes preserve iron stores. Once the haptoglobin binding capacity has been exceeded, free Hb appears in the plasma. Since free Hb is a small molecule, it can be excreted in the urine. Hemoglobinemia and hemoglobinuria occur when the haptoglobin capacity for binding hemoglobin dimers is saturated.

Test Purpose. 1) to serve as an hemolysis index, 2) to distinguish between hemoglobin and myoglobin in plasma, as haptoglobin binds with free hemoglobin but does not bind with myoglobin, 3) to investigate hemolytic transfusion reactions, 4) to establish paternity proof, using genetic haptoglobin structure variations, 5) diagnosis of hemolytic anemia, 6) diagnosis of inflammatory disorders.

Increased Values – hyperhaptoglobinemia

amyloidosis, aplastic anemia, **rheumatoid arthritis**, dermatomyositis, **tissue destruction**, **diabetes mellitus**, **acute rheumatic fever**, diseases – (**arterial d.**, granulomatous d., **acute/chronic infectious d.**, **acute/chronic inflammatory d.**), **cardiac infarction**, **collagenoses**, **colitis ulcerosa** (ulcerative colitis), **systemic lupus erythematosus**, **Hodgkin's disease**, lymphosarcoma, **tumours**, **nephritis**, nephrosis, **biliary ways obstruction**, **burns**, **pyelonephritis**, trauma, necrosis of tissue, scurvy, stress, pregnancy, **nephrotic sy**, **peptic ulcer**

Interfering Factors: medicaments – (anabolic steroids, androgens, estrogens, fluoxymesterone, metandienone, methyltestosterone, nandrolone, oxymetholone)

Decreased Values – hypohaptoglobinemia

anemia – (**hemolytic a.**, **autoimmune hemolytic a.**, sickle-cell a., **megaloblastic a.**, **hereditary spherocytosis**, **thalassemia**), **liver cirrhosis**, G6PD deficiency, subacute bacterial endocarditis, **fetal erythroblastosis**, **hematoma**, paroxysmal nocturnal hemoglobinuria, intravascular hemolysis – (autoantibodies, immunohemolytic i. h. = cool autoantibodies + thermic autoantibodies, infectious i. h., medicamentous i. h., mechanical i. h.), chronic hepatitis, **hypertension**, **prosthetic heart valves**, **liver diseases**, **systemic lupus erythematosus**, chronic lymphadenosis, **malaria**, infectious mononucleosis, pancytopenia, **liver parenchyma disorders**, **thrombotic thrombocytopenic purpura**, **transfusion reactions**, malabsorption sy, **contact sports**, pregnancy, **uremia**, **congenital ahaptoglobinemia**

Interfering Factors: medicaments – (aminosalicylic acid, asparaginase, chlorpromazine, cisplatin, cortisone, dapsone, dextran, diphenhydramine, estrogens, furazolidine, indomethacin, isoniazid, methyldopa, nitrofurantoin, oral contraceptives, quinidine, streptomycin, sulfasalazine, tamoxifen, testosterone)

Analyte	Age/Gender	Reference Range	SI Units	Note
Haptoglobin	Adults	0.5–3.3	g/l	
	Hp 1–1	0.7–2.3	g/l	
	Hp 2–1	0.9–3.6	g/l	
	Hp 2–2	0.6–2.9	g/l	

Hematocrit

(Hct, HCT, Crit, PCV, syn: packed cell volume, packed red cell volume) Cellular blood constituent percentage in the total blood volume.
Test Purpose. 1) to aid in diagnosis of polycythemia, anemia or abnormal hydration conditions, 2) to aid in red cell indices calculation: mean corpuscular volume, mean corpuscular hemoglobin concentration, and mean corpuscular hemoglobin.

Increased Values

dehydration – (**hypotonic d., isotonic d.**), **eclampsia, erythrocytosis, hemoconcentration, diarrhea, congenital heart disease, surgery, polycythemia, polycythemia vera, polyglobulia, burns, shock, trauma, living in high altitudes**, profound diuresis

Interfering Factors: medicaments – (androgens, nandrolone, oral contraceptives, spironolactone)

Decreased Values

anemia, rheumatoid arthritis, hepatic cirrhosis, idiopathic/infectious enterocolitis, hyperhydration – (hypertonic h., isotonic h.), **hyperthyroidism**, prosthetic heart valves, **hemorrhage** (recovery stage after acute h.), **leukemia**, malabsorption – (folic acid m., vitamin B_{12} m., iron m.), **malnutrition, Hodgkin's disease, plasmocytoma** (incl. multiple myeloma), burns, reaction to infectious/chemicals agents/medicaments, **hemolytic conditions, pregnancy**, incompatible blood transfusion, bone marrow failure due to – (radiation, toxins, fibrosis, tumor), transfusion reaction

Interfering Factors: medicaments – (amphotericin B, azathioprine, cefalotin, chloramphenicol, chlorphenamine, hydralazine, ibuprofen, methyldopa, penicillin)

Analyte	Age/Gender	Reference Range	SI Units	Note
Hematocrit	Neonates	0.44–0.62		
	3 m–13 y	0.31–0.43		
	Adults M	0.42–0.52		
	Adults F	0.37–0.47		

Hemoglobin

(Hb, Hgb) Hb concentration is a measure of the total Hb peripheral blood amount. Red blood stain consists from hem (ferroprotoporphyrin complex) and globin (tetramer molecule composed from 4 globin chains). Hemoglobin proportion in adults: HbA (97% of total Hb, 2 alpha and 2 beta globin chains), HbA2 (2.5% of total Hb, 2 alpha and 2 delta globin chains), HbF (0.5%).

Production. Hemoglobin is produced by nucleated immature red blood cells.
Function. Main erythrocyte component, vehicle for O_2 and CO_2 transportation. Serves as one of primary extracellular fluid buffer substance, maintains acid-base balance by a process called chloride shift. The clinical test implications closely parallel those of the RBC count. Factors affecting hemoglobin oxygen affinity: 1) increased oxygen affinity: alkalosis (Bohr effect), ↓ RBC 2,3-DPG, ↓ temperature, carboxyhemoglobinemia, high-affinity hemoglobinopathies, 2) decreased oxygen affinity: acidosis (Bohr effect), ↑ RBC 2,3-DPG, ↑ temperature, hemoglobinopathies.
Test Purpose. 1) to measure anemia, polycythemia, blood loss severity and to monitor therapy response, 2) to obtain data for calculating mean corpuscular hemoglobin and mean corpuscular hemoglobin concentrations.

Increased Values

stroke, **dehydration**, encephalitis, **hemoconcentration**, diarrhea, **chronic obstructive pulmonary disease**, diseases – (**mitral valve d.**, **pulmonary d.**, **congenital heart d.**), tumours, **physical exertion**, intestinal obstruction, **polycythemia**, **polyglobulia**, burns, environment – (cold e., **high altitude e.**), loss of – (ions, body fluids), **symptomatic polyglobulia**, **congestive heart failure**, endocrine caused increase – (adrenaline, parathormone)

Interfering Factors: medicaments – (adrenaline, gentamicin, glucocorticoids, hydralazine, oral contraceptives, methyldopa, pilocarpine)

Decreased Values

anemia – (**sickle cell a.**, thalassemia), rheumatoid arthritis, **hepatic cirrhosis**, deficiency of – (copper, iron), **glomerulonephritis**, hemoblastoses, **hemoglobinopathies**, paroxysmal nocturnal hemoglobinuria, **hyperhydration**, **hyperthyroidism**, adrenal hypofunction, artificial heart valves, diseases – (infectious d., acute renal d., chronic liver d., systemic d., acute inflammatory d.), **renal insufficiency**, chronic intoxication by – (benzene, copper, lead), carcinomatosis, leukemia, **systemic lupus erythematosus**, lymphoma, Crohn's disease, Hodgkin's disease, excess of – (ions, water), tumours, renal cortical necrosis, undernutrition, severe burns, X-rays therapy, reaction to chemicals/infectious agents/medicaments, **sarcoidosis**, splenectomy, splenomegaly, **hyper-IgM sy**, conditions – (**hemolytic c.**, **hemorrhagic c.**), **pregnancy**, incompatible blood transfusion, typhoid fever

Interfering Factors: medicaments – (acetazolamide, acetylsalicylic acid, ACTH, aminosalicylic acid, amphetamine, amiodarone, amitriptyline, amphotericin B, ampicillin, antibiotics, antiepileptics, antineoplastic drugs, asparaginase, azapropazone, azathioprine, barbiturates, busulfan, captopril, carbimazole, cefalexin, cephalosporins, cefalotin, cefoxitin, cefuroxime, chlorambucil, chloramphenicol, chloroquine, chlorothiazide, chlorphenamine, chlorpromazine, chlorpropamide, chlortalidone, cholestyramine, cimetidine, cisplatin, clindamycin, cyclofenil, cyclophosphamide, cyclosporine, dactinomycin, dapsone, desipramine, diazepam, digitoxin, diclofenac, doxycycline, erythromycin, estrogens, ethanol, ethosuximide, fenoprofen, fluorouracil, gold salts, griseofulvin, hydralazine, ibuprofen, indomethacin, isoniazid, latamoxef, levodopa, mebendazole, mepacrine, mephenytoin, meprobamate, metamizole, metformin, methotrexate, meticillin, methyldopa, miconazole, nafcillin, naproxen, nomifensine, oral contraceptives, oxyphenbutazone, paracetamol, penicillamine, penicillin, phenacetin, phenazone, phenothiazines, phenylbutazone, phenytoin, probenecid, procainamide, procarbazine, propranolol, pyrazinamide, pyrimethamine, quinidine, rifampicin, streptomycin, sulfafurazole, sulfamethizole, sulfamethoxazole, sulfasalazine, sulfonylureas, sulindac, sulfonamides, tamoxifen, tetracyclines, thioridazine, thioguanine, tobramycin, tolazoline, tolbutamide, trimethadione, trimethoprim, valproic acid, vinblastine)

Analyte	Age/Gender	Reference Range	SI Units	Note
Hemoglobin	Neonates	145–225	g/l	
	2 m	90–140	g/l	
	6–18 y	115–155	g/l	
	Adults M	130–160	g/l	
	Adults F	120–160	g/l	
Hemoglobin, Free		0.01–0.05	g/l	

Hemoglobin A2

(HbA2) Hemoglobin A2 (2 alpha and 2 delta globin chains) is a minor normal adult blood component. HbA2 levels have special application to the diagnosis of beta-thalassemia trait, which may be present even though peripheral blood smear is normal.
Test Purpose. 1) to evaluate a HbA2 percentage from total Hb, 2) hemolytic anemias differential diagnosis, 3) to aid in the diagnosis of hemoglobinopathies and thalassemias.

Increased Values
megaloblastic anemia, beta-thalassemia, hyperthyroidism

Decreased Values
anemia – (sideroblastic a., alpha-thalassemia), **untreated iron deficiency, erythroleukemia, HbH disease**

Hemoglobin S

(HbS) Pathological Hb characterized with glutamic acid to valine change in the beta-globin chain 6th position. Hemoglobin S becomes more viscous, precipitating or bonding to cause sickle red cells. The abnormally shaped cells are unable to pass freely through the capillary system, this results in increased blood viscosity and sluggish circulation.
Test Purpose. 1) sickle cell anemia diagnosis, 2) hemolytic anemias differential diagnosis.

Increased Values – positive
sickle-cell anemia

Decreased Values
false negative values – (protein abnormalities, infants before 3 months, polycythemia)

Hemopexin

(Hx, Hpx) Hemopexin is a weak acute phase reactant. This polymorphic protein is synthesized by hepatocytes. Metheme is oxidized heme hemoglobin without globin and the hemopexin binds heme/metheme with high affinity after hemoglobin breakdown. The complex is cleared from the circulation by the liver, while the hemoglobin-haptoglobin complex is cleared by the reticuloendothelial system. Free carrier returns to the circulation and binds hematin from the methemalbumin complex. Hemopexin also binds other porphyrins. Once processed in the liver, the heme-hemopexin complex releases/returns hemopexin to the circulation; haptoglobin is destroyed once complexed with hemoglobin. Beta-migrating globulin hemopexin binds the heme released by hemoglobin degradation. By this means small

iron atom porphyrin molecules are protected from urine excretion, thereby preserving body iron stores. Hemoglobin agents bonding to protein carriers protect body against renal impairment by excess Hb excretion.
Test Purpose. Hemolysis diagnosis.

Increased Values
diabetes mellitus, melanoma

Decreased Values
liver cirrhosis, malnutrition, intense hemolytic processes, nephrotic syndrome

Analyte	Age/Gender	Reference Range	SI Units	Note
Hemopexin	Total	0.50–3.3	g/l	
	fenotype 1–1	0.70–2.3	g/l	
	fenotype 2–1	0.90–3.6	g/l	
	fenotype 2–2	0.60–2.9	g/l	

Heparin Co-Factor II

(HC II) With dermatan sulphate plasmatic protein HC II inhibits thrombin selectively by creating a complex. Its activity is multiplied by heparin.
Test Purpose. 1) thrombotic conditions differential diagnosis, 2) inborn HC II defect identification.

Analyte	Age/Gender	Reference Range	SI Units	Note
Heparin Co-Factor II		90–105	mg/l	

Human Hematopoietic Growth Factors

- **SCF** (stem cell factor) – increases all hematopoietic cell type production, production of gonadal cells, mast cells, melanocytes.
  Production. Fibroblasts, hepatocytes, stromal cells, epithelial/endothelial cells.
- **IL-3** – increases neutrophil, monocyte, eosinophil, erythrocyte and basophil production.
  Production. T-lymphocytes.
- **IL-5** – increases eosinophil production.
  Production. T-lymphocytes
- **IL-11** – increases all hematopoietic progenitor and platelet production.
  Production. Stromal cells, fibroblasts.
- **GM-CSF** – increases neutrophil, dendritic cell, monocyte, eosinophil production.
  Production. T-lymphocytes, endothelial cells, fibroblasts, monocytes.
- **G-CSF** – increases neutrophil production.
  Production. Monocytes, fibroblasts.
- **M-CSF** – increases placental trophoblast cell and monocyte production.
  Production. Monocytes, fibroblasts, lymphocytes, epithelial/endothelial cells.
- **EPO** – increases erythrocyte production.
  Production. Kidney cells.
- **TPO** – increases platelet production.
  Production. Kidney, liver.

Left Side Shift

More neutrophilic sticks and metamyelocytes in peripheral blood smear (younger cells, juvenile neutrophils, immature neutrophil forms). Regenerative response indicator used in differential diagnosis of primary hemathological diseases and reactive blood stain changes.
Occurrence. Acidosis, actinomycosis, amebiasis, acute appendicitis, acute/chronic pelvic inflammatory disease, arthritis – (gonococcal a., suppurative a.), aspergillosis, balanitis, bartonellosis, blastomycosis, cellulitis, chronic pituitary adrenocortical insufficiency, dermatomyositis, diverticulitis, excessive hemolysis, thoracic empyema, chemotherapeutics, choledocholithiasis, cholera, diphtheria, diseases – (Chagas d., legionnaires' d., Lyme d.), disseminated intravascular coagulation, ulcerative colitis, echinococcosis, endometritis, epiglottitis, erysipelas, hantavirus infection, bacterial infections, acute hemorrhage, suppurative hidradenitis, chronic neutropenia in children, intoxications, leptospirosis, leukemia, listeriosis, lung anthrax, malaria, sepsis (toxemia), uremia, abscess – (brain a., breast a., kidney a., perinephric renal a., perianal a., gingival a., alveolar a., liver a., lung a., omentum a., pancreas a., parotid gland a., peritonsillar a., prostate a., scrotum a., spinal epidural a., spleen a., stomach a., subphrenic a., tonsil a., tubo-ovarian a.), acute myocarditis, bronchiectasis, diabetic ketoacidosis, acute/chronic sinusitis, acute/subacute bacterial endocarditis, purulent pericarditis, intestine perforation, acute fatty liver of pregnancy, puerperal infection, pyopneumothorax, pyoureter, cholangitis, cholecystitis, osteomyelitis, enterocolitis – (acute pseudomembranous e., necrotizing e.), acute epididymitis, peritonitis, pharyngitis, gonorrheal proctitis, pneumonia – (aspiration p., Hemophilus influenzae p., mycoplasmal p., acute interstitial p., tularemic p., Klebsiella p., staphylococcal p., streptococcal p., pneumococcal p.), polycythemia vera, acute prostatitis, oophoritis, acute pyelonephritis, toxoplasmosis, scarlet fever, herpes simplex infection in newborn, mesenteric venous thrombosis, meningitis – (bacterial m., meningococcal m., pneumococcal m.), shigellosis, rheumatic fever, septic shock

Leukocyte Antibodies

In recipient's blood, a positive result indicates presence of leukoagglutinins, identifying the transfusion reaction as a reaction to these antibodies. In donor's blood, a positive result indicates presence of leukoagglutinins.
Test Purpose. 1) to detect leukoagglutinins in blood recipeints who develop transfusion reactions, 2) to detect leukoagglutinins in blood donors after transfusion causes a reaction.

Increased Values
transfusion reactions
Interfering Factors: i.v. contrast media, medicaments – (dextran)

Leukocytes

(WBC, syn: white blood cell count, WBC count, leukocyte count, total white count, white cell count, leucocytes) Leukocytes are colorless globe-shaped cells produced in bone marrow that always contain a nucleus. Peripheral blood smear (stained blood film, differential count, leucogram).
Function. To fight against infection, to defend the body against foreign organisms invasion by phagocytosis and transport/distribute antibodies in the immune response.

Production. Granulocytes, monocytes and lymphocytes are formed in the red bone marrow. Lymphocytes mature in the lymphatic tissue (spleen, thymus, tonsils).
Test Purpose. 1) to determine infection or inflammation, 2) to determine need for further tests, such as the WBC differential or bone marrow biopsy, 3) to monitor response to chemotherapy or radiation therapy.

- **Leukocyte division**
  - **basophils (basophilic segments)**: blood dyscrasia, myeloproliferative diseases
  - **eosinophils (eosinophilic segments)**: parasitic diseases, allergic disorders
  - **lymphocytes**: viral infections – (varicella, infectious mononucleosis, morbilli, rubella)
  - **monocytes**: severe infections
  - **neutrophils (neutrophilic sticks and neutrophilic segments)**: diseases – (bacterial infectious d., inflammatory d.), stress
  - **agranulocytes – mononuclears (monocytes, lymphocytes)**
  - **phagocytes** (microphages – granulocytes) + (macrophages – monocytes, histiocytes)
  - **immunocytes** (lymphocytes – B-lymphocytes, T-lymphocytes, NK-cells) + (plasma cells)
- **Leukocyte findings**
  - **toxic granulation of neutrophils and metamyelocytes**: bacterial infections
  - **atypical lymphocytes**: viral infections
  - **giant cytoplasmic granules**: Chediak–Higashi sy
  - **bilobed neutrophils**: Pelger–Huet anomaly
  - **hypersegmented neutrophils**: pernicious anemia, folate deficiency, myeloproliferative diseases
  - **myeloblasts, promyelocytes, myelocytes**: leukemia – (acute myeloblastic l., acute promyelocytic l., chronic myelocytic l.), myelofibrosis, polycythemia vera
  - **large granular lymphocytes**: T-gamma proliferative disease (natural killer cells)
  - **lymphoblasts**: leukemia – (acute lymphoblastic l., prolymphocytic l., chronic lymphocytic l.), malignant lymphoma, infectious mononucleosis
  - **plasmablasts**: plasmocytoma (incl. multiple myeloma)

Increased Values – leukocytosis

abortion – (**spontaneous a.**, **threatened a.**, **septic a.**, **missed a.**), **placental abruption**, **abscess**, **acidosis**, actinomycosis, allergy to – (mold, dust), dissecting aortic aneurysm, **amyloidosis**, **amebiasis**, anemia – (pernicious a., **sickle cells a.**, **acute posthemorrhagic/posthemolytic a.**), anesthesia, **appendicitis**, **severe anoxia**, lung anthrax, arteritis – (**giant cell a.**, **Takayasu's a.**), aspergillosis, pulmonary atelectasis, arthritis – (**rheumatoid a.**, gonococcal a., **suppurative a.**, psoriatic a., meningococcal a., syphilitic a., tuberculous a., viral a.), ascariasis, bronchial asthma, **balanitis**, bartonellosis, arachnid bite, neurogenic atonic bladder, **bronchitis**, beryllosis, **blastomycosis**, bronchiectasis, **bronchiolitis**, **subacromial bursitis**, **dehydratation**, cellulitis, **hepatic cirrhosis**, chronic bilateral obstructive uropathy, benign ovarian cyst, dermatitis herpetiformis, dermatomyositis, **acute gout**, diphtheria, **diverticulitis**, echinococcosis, **eclampsia**, embolism – (systemic arterial e., air e., cerebral e., **pulmonary e.**, coronary e., amniotic fluid e., fat e., paradoxical e., renal artery e.), acute disseminated encephalomyelitis, **endometritis**, enterocolitis – (**acute pseudomembranous e.**, **necrotizing e.**, **tuberculous e.**), tropical eosinophilia, **acute epididymitis**, **epiglottitis**, **erysipelas**, **erythema nodosum**, **HIV infection**, emotional disturbance, **thoracic empyema**, encephalitis – (St. Louis e., **herpes e.**, cytomegalovirus e.), **endocarditis**, **pharyngitis**, fasciitis – (**necrotizing f.**, **eosinophilic f.**), fascioliasis, **Q fever**, **rheumatic fever**, smoking, cystic fibrosis, **gangrene**, viral gastroenteritis, granulomatosis – (lymphomatoid g., **Churg–Strauss g.**, **Wegener's g.**), hepatitis – (**alcoholic h.**, chemical-induced h., viral h.), **febris rheumatica**, hidradenitis sup-

purativa, **malignant hyperthermia**, chloroma, **cholangitis**, **cholecystitis**, **choledocholithiasis**, **cholera**, **chorioamnionitis**, **lymphocytic choriomeningitis**, **syphilitic chorioretinitis**, immunodeficiency disorders, acute chorea, disease – (**legionnaire's d.**, cat-scratch d., Caroli's d., silo-filler d., Hodgkin's d., Wilson's d., **Still's d.**, Chagas d., **Lyme d.**, Crohn's d., **chronic granulomatous d.**, Brill-Zinsser d., Whipple's d., IgM heavy chain d.), diseases – (allergic d., endocrine d., **bacterial infectious d.**, **chronic infectious d.**, **parasitic i. d.**, **fungal i. d.**, rickettsial i. d., **myeloproliferative d.**, **inflammatory d.**), **cardiac infarction** (increase at 6–12 hrs, decrease at 3–7 d.), infarction – (**liver i.**, **spleen i.**, **omentum i.**, **kidney i.**), insufficiency – (acute adrenocortical i., chronic pituitary adrenocortical i.), poisoning by – (chemicals, metals, medicaments, arsenic, benzene, beryllium, carbon monoxide, carbon tetrachloride, **ethylene glycol**, **venoms**, heavy metals, lead, mercury, nicotine, nickel, phosphorus, thallium, turpentine), **gonorrhea**, **diabetic ketoacidosis**, **pulmonary candidiasis**, disseminated intravascular coagulation, **coccidioidomycosis**, colitis – (**ulcerative c.**, **granulomatous c.**), coma – (**diabetic c.**, **uremic c.**, non-ketotic hyperosmolar c.), hereditary coproporphyria, cryptococcosis, **leptospirosis**, **listeriosis**, **acute/chronic leukemia**, **chronic lymphocytic leukemia**, **chronic myelocytic leukemia**, **progressive multifocal leukoencephalopathy**, **mesenteric lymphadenitis**, lupus erythematosus systemicus, **lymphangitis**, **lymphogranuloma venereum**, **lymphoma**, **Burkitt's lymphoma**, Waldenström's macroglobulinemia, **malaria**, **mastoiditis**, melioidosis, meningitis – (**pneumococcal m.**, aseptic m., **bacterial m.**, **meningococcal m.**, Listeria m., Mollaret's m., tuberculous m.), **menstruation**, **tumor metastases**, **infectious mononucleosis**, **mumps**, **myelitis**, **acute myocarditis**, infectious myringitis, myelosclerosis, systemic mycosis, **myositis**, tumours of – (**bone**, **breast**, **colorectum**, esophagus, kidney, pancreas, liver, melanoma, gastrointestinal tract, lungs, stomach), **physical exertion**, nausea, necrosis – (**hepatic n.**, **tissue n.**), lupus nephritis, **newborn**, **neonates with Down sy**, nocardiosis, response to – (**pain**, cold, **massage**, sunlight), **orchitis**, ornithosis, **osteomyelitis**, **pancreatitis**, paracoccidioidomycosis, paroxysmal nocturnal hemoglobinuria, **fatty liver**, **acute fatty liver of pregnancy**, **pelvic inflammatory disease**, bullous pemphigoid, **intestine perforation**, **pericarditis**, **periostosis**, **peritonitis**, pityriasis rosea, **pneumonia**, pneumomediastinum, **pertussis**, **plasmocytoma** (incl. multiple myeloma), **drug induced interstitial pneumonitis**, **polyarteritis nodosa**, polycythemia, **polycythemia vera**, **polymyositis**, **pre-eclampsia**, **premature labor**, **burns**, porphyria – (acute intermittent p., erythropoietic protoporphyria, erythropoietic p.), epidemic hemorrhagic fever, **prostatitis**, purpura – (**thrombocytopenic p.**, Henoch–Schoenlein p.), **pyelonephritis**, **pyoderma gangrenosum**, **pyometra**, **pyopneumothorax**, **pyoureter**, **rabies**, **radiotherapy**, reaction – (**leukemoid r.**, **transfusion r.**), **leukemic reticuloendotheliosis**, **schistosomiasis**, silicotuberculosis, conditions – (allergic c., comatose c., **hemolytic c.**, febrile c., hypersensitivity c., **acute hemorrhagic c.**, convulsive c., **c. after surgery**, post splenectomy c. – early, **posthemorrhagic c.**, **septic c.**, **stress c.**, **shock c.**), heat stroke, **electric shock**, **ectopic pregnancy**, **ruptured tubal pregnancy**, paroxysmal tachycardia, **pregnancy**, **miliary tuberculosis**, **uremia**, **vasculitis**, **acute/**chronic **sinusitis**, **toxic megacolon**, vomiting, ultraviolet irradiation, viral infectious diseases – (herpes zoster, poliomyelitis, **chicken pox**, measles, smallpox), **elderly people**, **otitis media**, ischemic damage to – (**extremities**, **abdominal viscera**, **heart**), pseudogout, **scarlet fever**, **shigellosis**, **syphilis**, **salpingitis**, **tonsillitis**, toxoplasmosis, **thrombangitis obliterans**, thrombocytemia – (**primary t.**, hemorrhagic t.), **thrombosis**, **thrombophlebitis**, **thyroiditis**, thyrotoxicosis, **trauma**, trichinosis, chronic morphine addiction, trypanosomiasis, **tularemia**, typhoid fever, typhus – (epidemic t., endemic t.), urticaria, **gonorrheal urethritis**, syndrome – (Waterhouse–Friederichsen sy, Sheehan's sy, Guillain–Barré sy, Mikulicz sy, hypereosinophilic sy, eosinophiliamyalgia sy, carcinoid sy, **Kawasaki sy**, **toxic shock sy**, **Cushing's sy**), occlusion of internal carotid artery, small intestine volvulus, **penetrating duodenal/gastric** ulcer, retinal artery occlusion, **puerperal infection**, ovary torsion, **acute/**chronic renal failure, acute liver failure, familial mediterranean fever

Interfering Factors: medicaments – (ACTH, adrenaline, aldesleukin, allopurinol, amphotericin B, ampicillin, atropine, azathioprine, carbamazepine, chlorambucil, chloroform, chloroquine, chlorpromazine, codeine, corticosteroids, dexmedetomidine, ethanol, ether, filgrastim, fluorouracil, fluphenazine, fosphenytoin, haloperidol, halothane, levodopa, lithium, mefloquine, melphalan, mycophenolate, naproxen, nitrofurantoin, norepinephrine, omeprazole, oral contraceptives, penicillamine, perphenazine, phenytoin, pilocarpine, piroxicam, prednisone, prochlorperazine, promethazine, quinidine, quinine, sargramostim, strychnine, sulfasalazine, sulfonamides, thioridazine, thiothixene, tretinoin, trifluoperazine, verteporfin)

Decreased Values – leukopenia

septic abortion, metabolic acidosis, **hereditary orotic aciduria**, **agranulocytosis**, **AIDS**, alcoholism, amebiasis, anaphylaxis, anemia – (aplastic a., megaloblastic a., pernicious a., hereditary spherocytosis, iron deficiency a., myelophthisic a., pyridoxine-responsive a.), **anorexia nervosa**, congenital red cell dysplasia, arthritis – (rheumatoid a., parvovirus a.), aspergillosis – (allergic pulmonary a., invasive a.), babesiosis, brucellosis, diabetes mellitus, diverticulitis, eclampsia, encephalitis – (herpes e., echo-encephalitis), epidemic myalgic encephalomyelitis, non-bacterial endocarditis, exanthema subitum, hemoglobinuria – (paroxysmal nocturnal h., paroxysmal h. following exercise), inhibited hemopoiesis, hepatitis – (infectious h., alcoholic h., acute h. type A, acute h. type B, chronic active h. B, acute h. type D, acute h. type E, autoimmune h.), herpes zoster, malignant histiocytosis, **histoplasmosis**, fever – (Dengue f., Colorado tick f., West Nile f., **yellow f.**, Rocky Mountain spotted f., epidemic hemorrhagic f., Q f., lassa f.), primary hyperparathyroidism, **hypersplenism**, hypopituitarism, disease – (legionnaires' d., Gaucher's d., Wilson's d., **Brill-Zinsser d.**, heavy chain d., light chain d., Letterer-Siwe d., graft-versus-host d.), diseases – (**autoimmune d.**, **liver d.**, spleen d.), infectious diseases – (protozoan i. d., **rickettsial i. d.**), viral infectious diseases – (**influenza**, varicella, measles, morbilli, parainfluenza, poliomyelitis, rubella), **immune mediated marrow suppression**, intoxication by – (acetaminophen, alcohol, **arsenic**, benzene, phenytoin, toluene), kala-azar, disseminated intravascular coagulopathy, **collagenoses**, leishmaniasis, leptospirosis, leukemia – (acute monocytic l., promyelocytic l., megakaryocytic l., acute lymphoblastic l., acute myeloblastic l., leukemic reticuloendotheliosis), **systemic lupus erythematosus**, angioimmunoblastic lymphadenopathy, intestinal lymphangiectasia, familial erythrophagocytic lymphohistiocytosis, **Waldenström's macroglobulinemia**, malaria, infantile malnutrition, systemic mastocytosis, **infectious mononucleosis**, mycosis fungoides, primary myelofibrosis, tumors – (small cell lung t., Hodgkin's d., neuroblastoma, rhabdomyosarcoma, thymoma), lupus nephritis, neutropenia – (**familial n.**, **idiopathic n.**, cyclic n.), ornithosis, panmyelopathy, paratyphus, parotitis, peritonitis, plasmocytoma (incl. multiple myeloma), pneumonia – (pneumococcal p., Klebsiella p., staphylococcal p., viral p.), bone marrow injuries – (**metastases**, **tumours**, **fibrosis**, **failure**), psittacosis, idiopathic thrombocytopenic purpura, **radiotherapy**, **sarcoidosis**, **septic conditions** (advanced), septic shock, neonatal sepsis, schistosomiasis, shigellosis, chronic congestive splenomegaly, hepatic steatosis, bone marrow suppression by – (heavy metals, medicaments), syndrome – (Felty's sy, **Chediak-Higashi sy**, myelodysplastic sy, preleukemic sy, Hand-Schueller-Christian sy, **Sjögren's sy**), toxoplasmosis, portal vein thrombosis, **miliary tuberculosis**, **tularemia**, **typhoid fever**, typhus – (endemic t., **epidemic t.**), radiation

Interfering Factors: prolonged rest, ageing, medicaments – (acetaminophen, acetazolamide, acetohexamide, acetylsalicylic acid, aciclovir, ajmaline, aldesleukin, allopurinol, amiloride, aminocaproic acid, aminoglutethimide, amlodipine, amoxapine, amoxicillin, amphotericin B, ampicillin, antazoline, antibiotics, antiepileptics, anticonvulsants, antihistamines, antimetabolites, antithymocyte globulin, arsenic, asparaginase, atenolol, azathioprine, barbiturates, benazepril, benzylpenicillin, bexarotene, bisoprolol, bume-

tanide, busulfan, candesartan, capecitabine, captopril, carbamazepine, carbidopa, carbimazole, carboplatin, carbutamide, carmustine, cefaclor, cefadroxil, cefalexin, cefalotin, cefamandole, cefazolin, cefdinir, cefixime, cefoperazone, cefotaxime, cefoxitin, cefprozil, cefradine, ceftazidime, ceftizoxime, ceftriaxone, cefuroxime, cephalosporins, chloral hydrate, chlorambucil, chloramphenicol, chlordiazepoxide, chloroquine, chlorothiazide, chlorphenamine, chlorpromazine, chlorpropamide, chlorprothixene, chlortetracycline, chlortalidone, cimetidine, cisplatin, cladribine, clofibrate, clomipramine, clozapine, cloxacillin, codeine, colchicine, corticosteroids, cyclophosphamide, cyclosporine, cysteamine, cytarabine, cytostatics, dacarbazine, dactinomycin, dapsone, daunorubicin, denileukin, desipramine, dexrazoxane, diazepam, diazoxide, dicloxacillin, didanosine, digitoxin, disopyramide, docetaxel, doxepin, doxorubicin, doxycycline, enalapril, epirubicin, erythromycin, estramustine, estrogens, ethanol, ethosuximide, ethotoin, etidronate, etoposide, felbamate, fenofibrate, flavoxate, floxuridine, flucytosine, fludarabine, fluorouracil, fluphenazine, flurbiprofen, fosinopril, fosphenytoin, furazolidine, furosemide, gabapentin, gatifloxacin, gemfibrozil, gemtuzumab, glipizide, glyburide, gold salts, grepafloxacin, haloperidol, heparin, hydralazine, hydrochlorothiazide, hydroxyurea, ibuprofen, idarubicin, ifosfamide, imipenem, imipramine, indomethacin, interferon alfa-2a, interferon alfa-2b, interferon alfa-n1, interferon alfa-n3, interferon alfacon-1, interferon beta-1b, irinotecan, isoniazid, lamotrigine, lansoprazole, leflunomide, leuprolide, levamisole, levetiracetam, levodopa, levofloxacin, levomepromazine, lomustine, loracarbef, mebendazole, mechlorethamine, meloxicam, melperone, melphalan, mepacrine, mephenytoin, meprobamate, mercaptopurine, meropenem, metamizole, metaxalone, methimazole, methocarbamol, methotrexate, meticillin, metolazone, metronidazole, mexiletine, mezlocillin, mitomycin, mitoxantrone, moxifloxacin, mycophenolate, nafcillin, nalidixic acid, naproxen, nitrofurantoin, nitrous oxide, nortriptyline, oral contraceptives, oxacillin, oxaprozin, oxyphenbutazone, paclitaxel, pamidronate, pantoprazole, paramethadione, penicillamine, penicillins, pentamidine, pentazocine, pentostatin, perindopril, perphenazine, phenazone, phenobarbital, phenothiazines, phenylbutazone, phenytoin, piperacillin, plicamycin, primaquine, primidone, probenecid, procainamide, procarbazine, prochlorperazine, promazine, promethazine, propylthiouracil, protriptyline, pyrimethamine, quinidine, rabeprazole, ranitidine, rifampicin, rifapentine, rituximab, samarium-153, silver sulfadiazine, sirolimus, sparfloxacin, streptomycin, streptozocin, strontium-89 chloride, sulfadiazine, sulfafurazole, sulfamethizole, sulfamethoxazole, sulfasalazine, sulfonamides, sulfones, sulfonylureas, sulindac, sultiame, tamoxifen, temozolomide, teniposide, thiazides, thioguanine, thioridazine, thiotepa, thiothixene, tobramycin, tocainide, tolazamide, tolazoline, tolbutamide, tolmetin, topiramate, topotecan, trastuzumab, trifluoperazine, trimethadione, trimethoprim, trovofloxacin, thyrostatics, valproic acid, valrubicin, vancomycin, verteporfin, vinblastine, vincristine, vinorelbine, warfarin, zalcitabine, zimeldine, zinc salts)

Analyte	Age/Gender	Reference Range	SI Units	Note
Leukocytes	Neonates	15–20*		*x 10^9/l
	Adults	4.1–10.9*		

Lipoxins

(LX) Eicosanoids formed from arachidonic acid (lipoxygenase interaction products). Lipoxin A4 (LXA4) effects: neutrophil chemotaxis, neutrophil chemokinesis, NK-cell activity inhibition, arteriolar dilatation, leukotriene antagonist, thromboxane 2 and PGI2 release,

bronchial smooth muscle contraction, activates polymorphonuclears, stimulates prostaglandin (PG) formation. Lipoxin B4 (LXB4) effects: NK-cell activity inhibition, vasoconstriction, bronchial smooth muscle contraction.

Lymphocytes

(lym, T-lymphocytes + B-lymphocytes + non-T-, non-B-lymphocytes) Lymphocytes belong to a heterogenous leukocyte group created from mother stem cells in the bone marrow; they mature to progenitor lymphatic cells. Bone marrow and thymus are primary lymphatic tissues. B-/T-lymphocytes and NK-cells pass from bone marrow to blood circulation → lymphatic tissue and organs (secondary lymphatic tissues). Lymphocytes reproduce and are released into blood stream with proper stimulation (recirculation). Their primary function is to interact with antigens and mount an immune response. The latter may be: 1) antibody humoral production form, 2) cell mediated with lymphokines lymphocyte elaboration or 3) cytotoxic with cytotoxic killer lymphocyte production. **T-lymphocytes** (about 70% of lymphocytes) – migrate from bone marrow to the thymus → processed by the thymic epithelial cell hormone → transformed into immunocompetent cells: 1) **T_H-helper** lymphocytes 55% (enhance B-cells and macrophage activity, bearing the surface antigen $CD4^+$). T_H-1 subpopulation produces IL-2, TNF-beta, IFN-gamma, T_H-2 subpopulation produces IL-4, 5, 6, 10, 13; T_H-lymphocytes support antibody production (humoral, antibody immunity); 2) **T_S – suppressor** lymphocytes (carry $CD8^+$ surface antigen and inhibit other immune system cell activity); 3) **T_C – cytotoxic** lymphocytes (killers, carrying the $CD8^+$ surface antigen that are responsible for killing cells that express foreign antigens); 4) **T_D** - delayed hypersensitivity lymphocytes. T-cells distribution: a) $CD4^+$ (peripheral blood 35–60%, lymph nodes 35–60%, spleen 20–90%, thymus cortex 90%, thymus marrow 60–80%), b) $CD8^+$ (peripheral blood 20–30%, lymph nodes 20–40%, spleen 10–80%, thymus cortex 90%, thymus marrow 20–40%). **B-lymphocytes** (about 25%) – from the bone marrow-derived stem cell → transformed into plasma cells (plasmocytes). B-cells distribution: peripheral blood 15–30%, lymph nodes 70–95%, spleen 0–40%, thymus 0–10%.

Function of T-lymphocytes. Responsible for specific cell-mediated immunity, delayed hypersensitivity – cellular immune response, immunodefense against parasitic/intracellular microorganisms (acidfast bacteria, viral infections, fungal infections, protozoan infections), graft rejection reactions.

Function of B-lymphocytes. Responsible for humoral immunity and antibody production – serum immunoglobulins (specific antibody immunity) → protect against staphylococcus, streptococcus, hemophilus, pneumococcus reinfection. Neutralize viruses to prevent initial infection. Act as barriers along gastrointestinal and respiratory passages. Initiate microorganisms killing by macrophages and other cells bearing Fc receptors. Cause vasoactive amines secretion from mast cells and basophils. Active lyse autologous origin cells or engage in antigen-antibody complex diseases. Interfere with T-killer cell activity by directly/indirectly blocking the reaction. Immediate humoral immune response (primary immune response). Secondary (anamnestic, booster) immune response. Antibody synthesis is inhibited by T_S-cells. **NK-cells** (natural killer cells, 3–5 %) are responsible for nonspecific cell and antitumor immunity.

Serum lymphocyte suppression factors. a) proteins – albumin, immunoregulatory globulin, pregnancy associated globulins, alpha-1-acid glycoprotein, CRP, SAA, AFP, alpha globulins in inflammatory diseases, chronic infectious diseases, cancer, LDL-C, HLA antibodies, antigen-antibody complexes, T-cell antibodies, b) hormones – glucocorticoids, progesterone, estrogens, androgens, prostaglandins, c) drugs – ouabain, acetylsalicylic acid, chloroquine, d) others – interferon, cytokines, cyclic nucleotides.

Test Purpose. 1) to aid in primary and secondary immunodeficiency diseases diagnosis, 2) to distinguish benign from malignant lymphocytic proliferative diseases, 3) to monitor therapy response (antibiotics, chemotherapeutics), 4) to help in inflammatory disease diagnosis, mainly viral, 5) monitoring HIV infected pediatric/adult patients.

Increased Values – lymphocytosis, lymphocytic leukocytosis
anemia – (aplastic a., hereditary elliptocytosis, hereditary spherocytic hemolytic a., thalassemia major), angiostrongyliasis, syphilitic aortitis, arthritis – (rheumatoid a., syphilitic a., viral a.), **brucellosis**, dermatitis, dermatitis herpetiformis, dermatomyositis, encephalitis – (e. lethargica, herpes e.), enterocolitis – (tuberculous a.), viral exanthemas, heat exhaustion, mycoplasmal pharyngitis, acute hepatitis – (type A, type B, type D, type E), histoplasmosis, hyperthyroidism, **decreased adrenal function** (hypoadrenalism), **cytomegalovirus infection**, lymphocytic choriomeningitis, syphilitic chorioretinits, disease – (**Addison's d.**, **Hodgkin's d.**, heavy chain d., Graves' d., Chagas' d., Crohn's d.), diseases – (**autoimmune d.**, upper respiratory way d.), infectious diseases – (**acute/chronic i. d.**, **chronic bacterial i. d.**), viral infectious diseases – (**parotitis**, **pertussis**, smallpox, **rubella**, varicella, **rubeola**), insufficiency – (chronic pituitary adrenocortical i., acute adrenocortical i.), intoxication by – (arsenicals, lead, tetrachlorethane), **ulcerative colitis**, progressive multifocal leukoencephalopathy, immunoblastic lymphadenopathy, infectious lymphocytosis – (**mycoplasmatic i. l.**, **rickettsial i. l.**), leukemia – (**acute/chronic lymphatic l.**, **chronic lymphocytic l.**, hairy cell l., monoblastic l., plasma cell l.), systemic lupus erythematosus, mesenteric lymphadenitis, lymphogranuloma venereum, **lymphosarcoma**, non-Hodgkin's lymphoma, malaria, meningitis – (aseptic m., tuberculous m.), **infectious mononucleosis**, mumps, tumors – (breast t., stomach t., uterine cervix t.), **neutropenia**, mumps orchitis, osteopetrosis, tuberculous pericarditis, graft rejection, **plasmocytoma** (incl. multiple myeloma), pneumonia – (**viral p.**, mycoplasmal p.), **polyarteritis nodosa**, **idiopathic thrombocytopenic purpura**, serum sickness, scleroderma, silicotuberculosis, stress, syndrome – (chronic fatigue sy, preleukemic sy, DiGeorge sy), **syphilis**, **toxoplasmosis**, trypanosomiasis, pituitary dwarfism, **tuberculosis**, typhoid fever, **thyrotoxicosis**, vasculitis, **Waldenström's macroglobulinemia**, acute liver failure

Interfering Factors: children (up to 5 years), high altitudes, medicaments – (p-aminosalicylic acid, chlorphenamine, dexamethasone, diphenylhydantoin, epinephrine, griseofulvin, interferon alfacon-1, isoprenaline, norepinephrine, oxacillin, phenothiazines, phenytoin, salbutamol, sulfonamides)

Increased Values of CD4+/CD8+ ratio
rheumatoid arthritis, primary biliary cirrhosis, atopic dermatitis, IDDM, systemic lupus erythematosus without kidney impairment, psoriasis

Decreased Values – lymphopenia, lymphocytopenia, lymphocytic leukopenia
AIDS (acquired immunodeficiency syndrome), antithymocyte antibodies, **aplastic anemia**, **bone marrow aplasia/suppression**, lymphocyte destruction by – (**antilymphocytic globulin**, **cytostatic chemotherapy**, **ionization**), thoracic duct drainage, hemodialysed patients, malignant histiocytosis, **hypogammaglobulinemia**, diseases – (**collagen vascular d.**, **immunodeficiency d.**, cardiac d.), acute myocardial infarction, **renal insufficiency**, **severe cachexia**, cardiomyopathy, **leukemia**, **systemic lupus erythematosus**, intestinal lymphangiectasia, intestinal lymphangitis, irradiation therapy, lymphogranuloma, **Whipple's disease**, malignant histiocytosis, multiple sclerosis, **myasthenia gravis**, mycosis fungoides, tumors – (pituitary gland t., Burkitt's lymphoma, lymphomas, **Hodgkin's disease**, thymoma), constrictive pericarditis, burns, alkylating agents, radiotherapy, reticular dysgenesis associated with aleukocytosis, **sarcoidosis**, conditions – (**malabsorption c.**, **septic c.**), **severe combined immunodeficiency disorders** (SCID), stress – (physical s., psychic s.), syndrome – (**ataxia–teleangi-**

ectasia sy, Cushing's sy, DiGeorge sy, Nezelof's sy, Guillain–Barré sy, lymphoproliferative sy linked to X-chromosome, **postradiation sy, Wiskott–Aldrich sy**), tuberculosis – (**miliary t.**, t. of lymphatic nodes – advanced), trauma, uremia, failure – (**renal f., congestive heart f.**), Waldenström's macroglobulinemia

Interfering Factors: medicaments – (abacavir, ACTH, aldesleukin, alemtuzumab, antilymphocyte antibodies, capecitabine, chlorambucil, cladribine, corticosteroids, cyclosporine, denileukin, dexamethasone, gemtuzumab, hydrocortisone, immunosuppressives, irinotecan, kava kava, lithium, methotrexate, pamidronate, phenytoin, prednisone, rifapentine, steroids)

Decreased Values of CD4+/CD8+ ratio

systemic lupus erythematosus with kidney impairment, viral infectious diseases – (AIDS, cytomegalovirus v. i. d., herpetic v. i. d., measles), myelodysplastic diseases, infectious mononucleosis, burns, graft-versus-host reaction, vigorous exercise

Decreased Values of T-Lymphocytes CD3

bronchial asthma, cytostatics, eczema, irradiation disease, diseases – (atopic d., autoimmune d., chronic liver d., gastrointestinal tract d.), infectious diseases – (candidiasis, parasitic i. d., Pneumocystis carinii), viral infectious diseases – (herpetic v. i. d., influenza, morbilli, rubella), infectious mononucleosis, tumors, burns, postsurgery conditions

Analyte	Age/Gender	Reference Range	SI Units	Note
Lymphocytes	Neonates	<22	%	
	Infants	<60	%	
	Adults	12–40	%	
		0.12–0.40		
		1.2–3.1	x 10^9/l	
Lymphocytic Surface Markers (T-cells)				
	CD3	0.84–3.06 *		*x 10^9 cells/l
		0.57–0.85		
	CD4	0.49–1.74 *		
		0.30–0.61		
	CD8	0.18–1.17 *		
		0.12–0.42		
	CD4/CD8	0.86–5.00		

Mastocytes

(syn: mast cells) Mastocytes are lymphoreticular character cells with a small nucleus and dark-violet granules in cytoplasma which are water-soluble. Mastocyte granules are replete with substances (mediators, heparin and histamine mainly) that have the capacity to regulate microcirculation, leading to changes in vascular permeability. Their products influence cell traffic in/out of tissues, activate neural pathways and may severely constrict the airway smooth muscles. Thus massive mast cell and basophil products release mediate a violent hypersensitive immediate-type life-threatening reaction known as anaphylaxis. Mast cell mediators: a) preformed and eluted are histamine, eosinophil chemotactic factors, neutrophil chemotactic factors, superoxide, arylsulfatase A, elastase, hexosaminidase, glucosidase, galactosidase, kallikrein-like enzyme, interleukins 3, 4, 5, 6, 8, interferon gamma, and tumor

necrosis factor alpha, b) preformed and granule associated are tryptase, carboxypeptidase, superoxide dismutase, catalase, arylsulfatase B, c) newly generated: leukotrienes LTC4, LTD4, LTE4, platelet-activating factor, and prostaglandins (PGD2).
Test Purpose. 1) to help in bone marrow suppression diagnosis, 2) to help in chronic inflammatory disorder diagnosis, 3) to confirm mastocytosis.

Increased Values – mastocytosis
macroglobulinemia, **mastocytosis**, bone marrow suppression

Mean Corpuscular Hemoglobin

(MCH) Auxiliary index obtained by multiplying blood hemoglobin concentration by ten and dividing by the red blood cell count (Hb:RBC) as an expression of the hemoglobin amount/ weight per single red blood cell.
Test Purpose. To aid in diagnosis and classification of anemias.

Increased Values (relatively)
macrocytic anemia, newborns, infants
Interfering Factors: severe leukocytosis, cold agglutinins, in vivo hemolysis, monoclonal proteins, lipemia, medicaments – (ethanol)

Decreased Values
anemia – (**hypochromic a.**, **microcytic a.**, a. in infectious disease, sideroblastic a., sideropenic a., thalassemia)

Analyte	Age/Gender	Reference Range	SI Units	Note
Mean Corpuscular Hemoglobin				
	Neonates	0.48–0.57	fmol	
	<2m	0.40–0.53	fmol	
	2 m–2 y	0.35–0.48	fmol	
	2 y–6 y	0.37–0.47	fmol	
	6 y–12 y	0.39–0.51	fmol	
	12–18 y	0.39–0.54	fmol	
	Adults	0.40–0.53	fmol	
		27–34	pg	

Mean Corpuscular Hemoglobin Concentration

(MCHC) Auxiliary index obtained by dividing blood hemoglobin concentration by the hematocrit (Hb:HCT). The average hemoglobin concentration in single erythrocyte is conventionally expressed in percentage. When values are decreased, the cell has a hemoglobin deficiency and is said to be hypochromic; when values are normal, the anemia is said normochromic (normocytic), and when values are increased anemia is hyperchromic.
Test Purpose. To aid in anemias diagnosis and classification.

Increased Values (relatively)
anemia – (**hereditary spherocytosis**, pernicious a., **sickle cell anemia**), newborns, infants
Interfering Factors: cold agglutinins, severe lipemia, medicaments – (heparin, oral contraceptives)

Decreased Values

anemia – (**hypochromic a.**, macrocytic a., a. in infectious diseases, pyridoxine-responsive a., sideroblastic a., **sideropenic a.**, **thalassemia**, chronic blood loss a., **iron deficiency a.**), hemoglobinopathies

Interfering Factors: severe leukocytosis

Analyte	Age/Gender	Reference Range	SI Units	Note
Mean Corpuscular Hemoglobin Concentration	Neonates	4.65–5.58	*	*mmol Hb/l
	<2m	4.50–5.74	*	RBC
	2 m–2 y	4.65–5.58	*	
	2 y–18 y	4.81–5.74	*	
	Adults	4.84–5.74	*	
		30–35	g/dl	

Mean Corpuscular Volume

(MCV) Average single RBC volume is obtained by multiplying the HCT by 1 000 and dividing by the red cell count. When the MCV is increased, RBC is said to be abnormally large – macrocytic, when the MCV value is decreased RBC is said to be abnormally small – microcytic. RBC are normo-/micro-/macrocytic.

Test Purpose. To aid diagnosis and classification of anemias.

Increased Values

alcoholism, anemia – (**aplastic a.**, hemolytic a., macrocytic a. in hepatic diseases, megaloblastic a., **pernicious a.**, sideroblastic a., myelophthisic a.), deficiency – (**folate d.**, **vitamin B_{12} d.**), smoking, **hypothyroidism**, celiac disease, **liver diseases**, tumors – (stomach t.), **reticulocytosis**, sprue, myelofibrosis, conditions – (posthemorrhagic c., postsplenectomy c.), **myelodysplatic sy**, marrow suppression/aplasia, orotic aciduria, pregnancy, women after menopause, newborns, infants

Interfering Factors: cold agglutinins, severe leukocytosis, hyperglycemia, medicaments – (aminosalicylic acid, anticonvulsants, azathioprine, carbamazepine, colchicine, cyclophosphamide, ethanol, ethotoin, hydroxyurea, isoniazid, metformin, methotrexate, neomycin, oral contraceptives, phenacetin, phenobarbital, phenytoin, primidone, pyrimethamine, sulfamethoxazole, sulfasalazine, triamterene, trimethoprim, zidovudine)

Decreased Values

anemia – (hypochromic a., microcytic a., **a. of chronic disease**, a. in infectious diseases, hereditary spherocytosis, **sideroblastic a.**, **sideropenic a.**, **thalassemia**, pyridoxine-responsive a., a. from chronic blood loss), **hemoglobinopathies**, hyperthyroidism, hemorrhage, tumors, posttraumatic splenectomy, blood transfusion, chronic renal failure, lead poisoning

Interfering Factors: in vitro hemolysis

Analyte	Age/Gender	Reference Range	SI Units	Note
Mean Corpuscular Volume	1–3 d	95–121	fl	
	6 m–2 y	70–86	fl	
	6 y–12 y	77–95	fl	
	12 y–18 y	78–100	fl	
	Adults	80–94	fl	

Mean Platelet Volume

(MPV) Mean platelet volume means an average single PLT volume. With intense thrombopoietin stimulation, higher ploidy megakaryocytes proportion increases. These megakaryocytes produce larger PLT and thus elevate the PLT volume. MPV varies with total PLT production.
Test Purpose. Information about thrombocytopoiesis activity.

Increased Values
megaloblastic anemia, **May-Hegglin anomaly**, diabetes mellitus with retinopathy, hyperthyroidism, prosthetic heart valve, splenectomy, rheumatic heart disease, diseases – (**myeloproliferative d., valvular heart d.**), disseminated intravascular coagulation, acute/chronic myelogenic leukemia, systemic lupus erythematosus, idiopathic thrombocytopenic purpura in remission, **Bernard-Soulier sy**, vasculitis, massive hemorrhage

Decreased Values
anemia – (**aplastic a.**, megaloblastic a.), **hypersplenism, chemotherapy-induced myelosuppression, Wiskott-Aldrich sy**

Analyte	Age/Gender	Reference Range	SI Units	Note
Mean Platele Volume		7.8–11.0	fl	

Methemalbumin

(syn: Fairley's pigment, methem, hematin) Residual hematin overlaps transport protein hemopexin capacity, binds temporarily to albumin, and creates in large RBC breakdown. Methemalbumin (hematin bound to serum albumin) is formed in plasma during intravascular hemolysis when haptoglobin is depleted. Free metheme may be bound to other transport conservation proteins, hemopexin and transported to the liver for further catabolism. Oxidized heme is bound to hemopexin or to albumin (methemalbumin). Complex with albumin is retained in kidney until hemopexin from liver hematin releases. Methemalbumin remains stable in the plasma until more hemopexin is synthesized to activate transport molecules; hemopexin binds hematin from methemalbumin complex. Therefore, methemalbumin is more indicative of a chronic intravascular hemolysis.
Test Purpose. Sensitive chronic intravascular hemolysis indicator.

Increased Values – methemalbuminemia
hemoglobinuria – (paroxysmal cold h. – PCH, paroxysmal nocturnal h. – PNH), intravascular hemolysis, hemolytic newborn disease, falciparum malaria, acute hemorrhagic pancreatitis, hemolytic posttransfusion reaction

Methemoglobin

(MHb, MetHb, syn: hemiglobin) Blood stain in which the heme ferrous iron form has been ferric oxidized; it is incapable of combining with and transporting oxygen (oxygen and iron cannot combine). Reverse hemoglobin binding can be done via two reduction systems: NADH-methemoglobin reductase and NADPH-reduced glutathione. Methemoglobin causes

oxyhemoglobin dissociation curve shift to the left. When high MetHb concentration is produced in the RBC, it reduces the RBC capacity to combine with oxygen → anoxia and cyanosis result.

Test Purpose. 1) acquired hemolytic anemia differential diagnosis, 2) to investigate unexplained central cyanosis, 3) to assess possible oxidant drug hemolysis.

Increased Values – methemoglobinemia

NADH-MetHb reductase deficiency, paroxysmal hemoglobinuria, **HbM hemoglobinopathy**, black water fever, clostridial infection, poisoning by – (aminoaromatic derivatives, aniline, dyes, nitrobenzene), hereditary methemoglobinemia, radiation

Interfering Factors: increased water/food nitrates, smoking, ionizing radiation, medicaments – (acetaminophen, acetanilid, amyl nitrite, benzocaine, chlorates, chloroquine, dapsone, isoniazid, isosorbide dinitrate, isosorbide mononitrate, lidocaine, local anesthetics, metoclopramide, nitrates, nitric oxide, nitrites, nitrofurantoin, nitroglycerin, nitroprusside, phenacetin, phenazone, phenazopyridine, phenytoin, potassium chlorate, prilocaine, primaquine, sulfamethoxazole, sulfasalazine, sulfonamides, trimethoprim)

Analyte	Age/Gender	Reference Range	SI Units	Note
Methemoglobin		9.3–37.2	µmol/l	
	Infants	0.004–0.0115		
	Children	<0.02		
	Adults	<0.008		
	Smokers	<0.02		

Monocytes

(mono, syn: monomorphonuclear monocytes) Belong to heterogenous leukocyte group, created in the bone marrow from common monocyte and granulocyte stem cells (CFU-GM). Monocytes are washed to blood stream → enter into tissue → change to free/bound macrophages → become MPS portion (mononuclear phagocytic system) → differentiate to specific tissue macrophages.

Function. Immunodefense cells, macrophage system → enter the tissues to become the macrophages (e.g. histiocytes, liver Kuppfer's cells, spleen and lymph node sinusoidal macrophages, peritoneal macrophages, macrophages that line the pulmonary air spaces). They are particularly active and evident in subacute/chronic inflammations. Kill/phagocytize/remove injured/dead cells, microorganisms, insoluble particles, antigens. By phagocytosed material breakdown to antigen peptides → surface monocyte receptors bind antigen peptides to HLA system molecules and expose them to T-lymphocytes. Monocytes interact with antigen-antibody-complement complexes to promote phagocytosis. Antiviral agent production – interferon. They are responsible for antigen recognition and processing → presenting to responsive T- and B-lymphocytes → participate in immune reactions (T-lymphocytes proliferation induction) → initiate both cell-mediated and humoral immune responses. Monocytes have an antitumorous activity. Participate in hemopoiesis (growth factors production – extrarenal erythropoietin, inhibition factors production – prostaglandins). They secrete various soluble, biologically active substances: enzymes – (lysozyme, neutral proteases, plasminogen activator, collagenase, elastase, angiotensin convertase), acid hydrolases – (lipases, ribonucleases, glycosidases, phosphatases), vitamin D, arachidonic acid metabolites, complement components – (C1, 2, 3, 4, 5, properdin), binding proteins – (transferrin, transcobalamin II, fibronectin), monokines (e.g. interleukin 1, 6, 8, 10, 12), IFN-alpha, IFN-beta, GM-CSF, M-CSF, G-CSF, TNF-alpha, PDGF, PAF, TGF-beta, angiogenesis factors, factors B, D, I, H, coagulation factors (V, VII, IX, X, prothrombin, thromboplastin). Ligands bound

by macrophage surface receptors: a) opsonins – complement components (C3, C4), immunoglobulins, carbohydrates and carbohydrate-binding proteins, b) chemotactic factors – oligopeptides, complement components (C5a), thrombin, fibrin, c) hormones and other mediators – insulin, histamine, epinephrine, calcitonin, parathyroid hormone, somatomedins, d) growth factors and cytokines – colony-stimulating factors (GM-CSF, M-CSF), interleukins (IL-1, 3, 6, 10), interferons (alpha, beta, gamma), tumor necrosis factors, transforming growth factor beta, e) miscellaneous – transferrin, lactoferrin, modified low-density lipoproteins, fibronectin. Tissue/other macrophages: 1) lung macrophages (alveolar) → phagocytose and retain dust particles, 2) liver macrophages (Kuppfer cells) → phagocytose iron excess and bile stains, 3) spleen macrophages → phagocytose disintegrated RBCs, 4) connective tissue macrophages (histiocytes), 5) bone marrow macrophages/precursors, 6) skin and tissue macrophages, 7) lymph node macrophages, 8) CNS macrophages (microglia), 9) blood – monocytes, 10) synovium – type A synovial cells, 11) bone – osteoclasts, 12) pleural cavity – pleural macrophages, 13) chronic inflammatory exudate – exudate macrophages, 14) peritoneal cavity – peritoneal macrophages.

Increased Values – monocytosis, monocytic leukocytosis

anemia, arteritis temporalis, **rheumatoid arthritis, brucellosis, bacterial endocarditis,** hepatitis, malignant histiocytosis, cytomegalovirus infection, diseases – (collagen vascular d., **acute/chronic infectious d., viral infectious d., myeloproliferative d.**), myocardial infarction in remission, protozoal and rickettsial diseases – (kala-azar, malaria, toxoplasmosis, trypanosomiasis, epidemic typhus, Rocky Mountain spotted fever), inflammatory bowel disease, chemical poisoning, collagenoses, **colitis ulcerosa,** leprosy, leukemia – (**monocytic l.,** myeloid l., acute/chronic myelomonocytic l.), radiation therapy, **systemic lupus erythematosus,** lymphogranuloma, **infectious mononucleosis,** tumours – (**Hodgkin's lymphoma,** non-Hodgkin's lymphoma, mammary gland t., ovarian t., stomach t.), disease – (**Crohn's d.,** Gaucher's d., Niemann–Pick d.), chronic idiopathic neutropenia, myeloid metaplasia, newborn, parotitis, plasmocytoma (incl. multiple myeloma), **polyarteritis nodosa,** polycythemia vera, thrombocytopenic purpura, **salmonellosis, sarcoidosis, postsplenectomy conditions,** sprue, **syphilis, myelodysplastic sy, tuberculosis,** bone marrow suppression

Interfering Factors: medicaments – (griseofulvin, prednisone)

Decreased Values – monocytopenia, monocytic leukopenia

anemia – (aplastic a., lymphocytic a.), acute infectious diseases, leukemia – (acute myelogenous l., **hairy cell l.**), stress

Interfering Factors: medicaments – (glucocorticoids, glucose, immunosuppressives, prednisone)

Analyte	Age/Gender	Reference Range	SI Units	Note
Monocytes	Neonates	<8	%	
	Infants	<10	%	
	Adults	2–11	%	
		0.02–0.11		
		0.15–0.58	x 10^9/l	

Neutrophil Alkaline Phosphatase

(LAP, NAP, syn: leukocyte alkaline phosphatase, combined esterase) A constituent in mature granulocyte granules.

Test Purpose. 1) to examine the alkaline phosphatase in neutrophils, 2) differential diagnosis of myeloproliferative diseases (chronic myelocytic leukemia versus leukemoid reaction), 3) helpful parameter in acute leukemia and paroxysmal nocturnal hemoglobinuria diagnosis, 4) to aid in the evaluation of polycythemia vera, myelofibrosis with myeloid metaplasia.

Increased Values

agranulocytosis, **aplastic anemia, liver cirrhosis**, cardiac cirrhosis, hairy cell leukemia, myeloproliferative diseases, bacterial infectious diseases, thrombocytopenia infections, **obstructive jaundice**, reactive leukocytosis, neutrophilia, acute/chronic lymphoblastic leukemia, **Hodgkin's disease, myelofibrosis**, myeloid metaplasia, plasmocytoma (incl. multiple myeloma), **polycythemia vera, leukemoid reactions**, conditions – (**postoperative c., stress c.**), syndrome – (Down sy, Klinefelter's sy), **pregnancy**, essential thrombocytemia

Interfering Factors: medicaments – (corticosteroids, oral contraceptives)

Decreased Values

anemia – (aplastic a., pernicious a., sickle cell a., sideroblastic a.), hepatic cirrhosis, diabetes mellitus, progressive muscular dystrophy, gout, granulocytopenia, **paroxysmal nocturnal hemoglobinuria, hereditary hypophosphatasia**, diseases – (infectious d., collagen d.), leukemia – (**acute/chronic granulocytic l., acute monocytic l., acute myeloblastic l., chronic myelogenous l.**), infectious mononucleosis, **idiopathic thrombocytopenic purpura**, sarcoidosis, syndrome – (nephrotic sy, nephrotic sy), congestive heart failure

Analyte	Age/Gender	Reference Range	SI Units	Note
Neutrophil Alkaline Phosphatase		<0.02 0.16–0.83		See ref. ranges note

Neutrophils

(neu, Pans, Segos, Ploys, syn: segmented neutrophils, polymorphonuclear neutrophils) Neutrophils are cells belonging to the leukocyte group created in bone marrow. Their mother cell is GFU-GM. Neutrophil sticks alive in blood stream only few hours before returning to tissues → disintegration.

Function. Responsible for primary non-specific defense (with NK-cells) against microbial invasion through phagocytosis. They are equipped with specific properties: a) WBC adhesion to endothelium, b) movement and chemotaxia, c) phagocytosis and degranulation, d) microorganism killing. Neutrophils are acute inflammation cells and bear surface receptors for IgA, IgG and complement components. Neutrophil antimicrobial systems: low pH, lysozyme, lactoferrin, defensin, cathepsin G, peroxide, superoxide radical, hydroxyl radical, singlet oxygen, myeloperoxidase, defensin.

Test Purpose. 1) to aid in inflammatory processes and intoxication diagnosis, 2) myeloproliferative diseases differential diagnosis, 3) to aid in myocardial infarction diagnosis, 4) leukopenia differential diagnosis.

Increased Values – neutrophilia, neutrocytosis, neutrophilic leukocytosis

acidosis, anemia – (pernicious a., **acute posthemorrhagic/posthemolytic a.**), **anoxia**, appendicitis, **rheumatoid arthritis**, hepatic cirrhosis, dermatitis, diphtheria, diverticulitis, **gout**, eclampsia, endocarditis, exposure to extreme heat/cold, gangrene, **rheumatic fever**, diseases – (**myeloproliferative d., inflammatory d.**), infectious diseases – (**bacterial i. d., parasitic i. d., fungal i. d.**, rickettsial i. d.), viral infectious diseases – (herpes zoster, poliomyelitis, chicken

pox, smallpox), **myocardial infarction**, intoxication by – (arsenic, benzene, carbon monoxide, ethylene glycol, venoms, heavy metals, lead, mercury, turpentine), disseminated intravascular coagulation, **diabetic/uremic coma**, gonorrhea, leukemia – (granulocytic l., chronic myelogenic l., **myelocytic l.**), **elderly people**, myelosclerosis, **myositis**, tumours – (bone marrow t., lymphoma, melanoma, liver t., gastrointestinal tract t.), **physical exertion** (physical exercise), **newborn, neonates with Down sy**, osteomyelitis, otitis media, **polycythemia vera, burns**, ischemic damage to – (extremities, abdominal viscera, heart), hemolytic transfusion reactions, salpingitis, septicemia, conditions – (allergic c., **hemolytic c.**, hemorrhagic c., **c. after surgery**, shock c.), **stress, Cushing's sy, electric shock**, pregnancy, **primary thrombocytemia, thrombosis, miliary tuberculosis, thyroiditis**, thyrotoxicosis, **trauma**, uremia, **vasculitis**, vomiting, chronic morphine addiction

Interfering Factors: medicaments – (ACTH, adrenaline, chlorpropamide, corticoids, cortisone, dexamethasone, digitalis, erythromycin, glucocorticoids, heparin, histamine, hydrocortisone, lithium, norepinephrine, potassium chlorate, prednisone, procainamide, quinidine, sulfonamides, vaccines)

Decreased Values – neutropenia, neutrophilic leukopenia

agranulocytosis, acromegaly, **AIDS, aleukia**, alcoholism, anemia – (**aplastic a., megaloblastic a., myelophthisic a., pernicious a., iron deficiency a.**), anorexia nervosa, apergillosis, autoimmune neutropenia, autoimmune panleukopenia, bone radiation therapy, rheumatoid arthritis, **brucellosis**, hepatic cirrhosis, **congenital dysgranulopoietic neutropenia**, copper deficiency, cytomegalovirus infection, familiary neutropenia – (**benign f. n., severe f. n.**), severe folic acid or vitamin B_{12} deficiency, erythropoietin administration in children, renal dialysis, **paroxysmal nocturnal hemoglobinuria**, chronic active hepatitis, **infectious hepatitis**, hepatitis – (type B, type E), histoplasmosis, hypersensitivity, hypersplenism, portal hypertension, hyperthyroidism, hypopituitarism, hypothyroidism, diseases – (endocrine d., **severe infectious d.**, blood d., liver d., protozoal d., **acute viral infectious d.**), **influenza**, insufficiency – (chronic pituitary adrenocortical i., chronic primary adrenocortical i.), intravenous immunoglobulins injection in children, kala-azar, **varicella** (chickenpox), toxic agents, leukemia – (**acute lymphoblastic l., monocytic l.**), **systemic lupus erythematosus, lymphomas, Addison's disease**, m. haemolyticus neonatorum, malaria, malnutrition, **mucormycosis**, myelokathexia, myelofibrosis, myelophthisis, **infectious mononucleosis**, neuroblastoma, **tumors/metastases, idiopathic neutropenia**, extracorporeal circulation (heart-lung machines), **measles, newborn alloimmune neutropenia**, neutropenia associated with agammaglobulinemia linked to X-chromosome, neutropenia associated with LGL-leukemia, newborn asphyxia, paratyphoid, **mumps** (parotitis), extracorporeal oxygenation, parvoviruses infection, **pneumonia, poliomyelitis**, polyarteritis nodosa, pre-leukemia, pulmonary microcirculation disorders, **radiotherapy**, rickettsial infections, **rubella**, scleroderma, septic conditions, neonatal sepsis, **splenomegaly**, drug-induced marrow suppression – (allopurinol, aminopyrine, antibiotics, oral antidiabetics, antineoplastic drugs, nonsteroid antirheumatics, azathioprine, cimetidine, phenothiazines, phenylbutazone, phenytoin, chloramphenicol, chlorothiazides, ibuprofen, isoniazid, carbamazepine, co-trimoxazol, propylthiouracil, sulfasalazine, sulfonamides, tolbutamide, gold), syndrome – (Blackfan-Diamond sy, Felty's sy, Chediak-Higashi sy, **hyper-IgM sy**, lazy leukocytes sy, Pearson's sy, Schwachmann's sy), **anaphylactoid shock**, trypanosomiasis, **tuberculosis, tularemia**, thyrotoxicosis, **typhoid fever**, inborn error of amino acid metabolism

Interfering Factors: medicaments – (acetaminophen, acetazolamide, acetylsalicylic acid, ajmaline, alemtuzumab, allopurinol, alprenolol, altretamine, amiloride, aminoglutethimide, aminophenazone, aminosalicylic acid, amiodarone, amoxicillin, ampicillin, aprin-

dine, asparaginase, auranofin, azathioprine, benzylpenicillin, busulfan, candesartan, capecitabine, captopril, carbamazepine, carbenicillin, carbimazole, carboplatin, carmustine, cefaclor, cefadroxil, cefalexin, cefalotin, cefamandole, cefazolin, cefoperazone, cefotamine, cefotaxime, cefotetan, cefoxitin, cefprozil, cefradine, ceftazidime, ceftizoxime, ceftriaxone, cefuroxime, cephalosporins, chlorambucil, chloramphenicol, chlordiazepoxide, chloroquine, chlorothiazide, chlorpromazine, chlorpropamide, chlortalidone, cidofovir, cimetidine, cisplatin, cladribine, clindamycin, clomipramine, cloxacillin, clozapine, cyclophosphamide, cytarabine, dacarbazine, dactinomycin, dapsone, daunorubicin, demeclocycline, desipramine, diazepam, diazoxide, dicloxacillin, didanosine, diltiazem, diphenylhydantoin, disopyramide, docetaxel, doxorubicin, doxycycline, enalapril, epirubicin, ethacrynic acid, ethosuximide, etoposide, fenoprofen, floxuridine, flucytosine, fludarabine, fluorouracil, fluphenazine, fomivirsen, foscarnet, fosphenytoin, furosemide, ganciclovir, gemcitabine, gemtuzumab, gentamicin, gold salts, griseofulvin, haloperidol, hydralazine, hydrochlorothiazide, hydroxychloroquine, hydroxyurea, ibuprofen, idarubicin, ifosfamide, imipenem, imipramine, indomethacin, interferon alfa-2a, interferon alfa-2b, interferon alfa-n1, interferon beta-1b, interferon gamma-1b, irinotecan, isoniazid, isotretinoin, itraconazole, lamivudine, lansoprazole, levamisole, levetiracetam, levodopa, lincomycin, lomustine, mebendazole, mechlorethamine, melphalan, meprobamate, mercaptopurine, metamizole, methazolamide, methimazole, methotrexate, methysergide, meticillin, metronidazole, methyldopa, methylthiouracil, mezlocillin, minocycline, mirtazapine, mitomycin, mitoxantrone, mycophenolate, nafcillin, naproxen, nevirapine, nitrofurantoin, novobiocin, olanzapine, omeprazole, oxacillin, oxyphenbutazone, paclitaxel, paracetamol, penicillamine, penicillins, pentazocine, pentazoline, pentostatin, perindopril, phenacemide, phenacetin, phenazone, phenothiazines, phenylbutazone, phenytoin, piperacillin, plicamycin, primidone, procainamide, procarbazine, prochlorperazine, promazine, propranolol, propylthiouracil, pyrimethamine, quinidine, quinine, ranitidine, retinol, rifabutin, rifampicin, rifapentine, rituximab, saquinavir, spironolactone, stavudine, streptomycin, streptozocin, strontium-89, sulfafurazole, sulfamethoxazole, sulfapyridine, sulfasalazine, sulfathiazole, sulfisoxazole, sulfonamides, sulindac, tamoxifen, temozolomide, teniposide, terbinafine, tetracyclines, thalidomide, thiamazole, thiamphenicol, thiazides, thiethylperazine, thioridazine, thiotepa, ticlopidine, tocainide, tolbutamide, topotecan, trandolapril, trimethadione, trimethoprim, trimetrexate, valrubicin, vancomycin, vinblastine, vinorelbine, zalcitabine, zidovudine, zinc salts, zomepirac)

Analyte	Age/Gender	Reference Range	SI Units	Note
Granulocytes				
neutrophilic sticks	Adults	3–5	%	
		0.03–0.05		
		0.6–1.2	x 10^9/l	
neutrophilic g.	Neonates	<65	%	
	Infants	<25	%	
	Adults	47–79	%	
	Adults	0.47–0.79		
		2.5–5.6	x 10^9/l	

Osmotic Resistance of Erythrocytes

(OF, syn: osmotic fragility, red cell fragility, erythrocyte fragility) The osmotic fragility test measures the susceptibility or RBC resistance to osmotic stress. By exposing erythrocytes to a hypotonic sodium chloride solution → the cell swells → erythrocytes rupture → hemolysis. Spherocytic RBCs, with a decreased surface-to-volume ratio, have a limited capacity to expand in hypotonic solutions, and thus lyse at a lesser osmotic stress level than do normal biconcave RBCs. Conversely, target cells, with a high surface to volume ratio, have an increased capacity to expand in hypotonic solutions, and have decreased susceptibility to osmotic lysis. Erythrocytes which burst in higher salt concentration have higher fragility; those that burst in lower salt concentration have decreased fragility. In healthy persons, unincubated blood RBC hemolysis begins at 0.45–0.50% sodium chloride and is complete by 0.35 % sodium chloride.
Test Purpose. 1) to aid in hereditary spherocytosis diagnosis, 2) to supplement stained cell examination to detect morphologic red cell abnormalities, 3) to evaluate hemolytic anemia and immune hemolytic conditions.

Increased osmotic resistance – decreased fragility, low fragility (<0.3% NaCl)
anemia – (**sickle-cell a.**, **thalassemia**, **iron deficiency a.**, megaloblastic a.), **hemoglobinopathies**, **liver diseases**, **obstructive icterus**, leptocytosis associated with – (iron deficiency anemia, asplenia, liver diseases, reticulocytosis), early infancy, polycythemia vera, **splenectomy**

Decreased osmotic resistance – increased fragility, high fragility (>0.5% NaCl)
anemia – (**autoimmune hemolytic a.**, familial hemolytic a., hereditary nonspherocytic hemolytic a., **acquired hemolytic a.**, **hereditary spherocytosis**), liver cirrhosis, infectious diseases – (malaria, syphilis, tuberculosis), severe pyruvate kinase deficiency, hereditary elliptocytosis, hemolytic newborn disease (erythroblastosis fetalis), hemolytic disease caused by Rh incompatibility, hemolytic icterus, **chemical/drug poisoning**, malignant lymphoma, leukemia, pregnancy, tumors, **burns**

Analyte	Age/Gender	Reference Range	SI Units	Note
Osmotic Resistance of Erythrocytes				
In 20 °C	Min	0.44–0.40		
	Max	0.32–0.30		
In 37 °C	Min	0.75–0.70		
	Max	0.40–0.30		

Pancytopenia

All blood cell counts decrease (red blood cells, white blood cells, platelets). Pancytopenia evaluation is used in bone marrow suppression differential diagnosis (aplastic anemia, myelodysplastic sy), pernicious anemia, osteomyelofibrosis and immunity disorders.

- **Central causes**: anemia – (**aplastic a.**, **megaloblastic a.**), vitamin B_{12}/folate deficiency, viral hepatitis, cytomegalovirus infection, infectious diseases, Epstein–Barr virus infection, primary bone marrow infiltration, medicaments – (chemotherapeutics, chloramphenicol, phenylbutazone), leukemia – (**acute l.**, hairy cell l.), lymphomas, Hodgkin's

disease, **myelofibrosis** (myelosclerosis), tumours, **plasmocytoma** (incl. multiple myeloma), osteopetrosis, parvoviruses, irradiation, **myelodysplastic syndrome**, tuberculosis, bone marrow inhibition

- **Peripheral causes:** AIDS, anorexia nervosa, rheumatoid arthritis, hepatic cirrhosis, hemodilution, **paroxysmal nocturnal hemoglobinuria**, hypersplenism, autoimmune diseases, kala-azar, chronic myelogenic leukemia, **systemic lupus erythematosus**, malaria, infectious mononucleosis, **Gaucher's disease**, Niemann–Pick disease, tumors, splenic/portal vein obstruction, Felty's sy, elevated right-sided heart pressure, tuberculosis

Partial Thromboplastin Time

(PTT, APTT, syn: activated partial thromboplastin time) APTT informs about intrinsic/common hemocoagulation activation pathway plasmatic factors initiated by negatively charged surface factor XII interaction. PTT evaluates factors I, II, V, VIII, IX, X, XI, XII, prekallikrein and high-molecular weight kininogen. Factor VII is not required for the PTT because it bypasses the extrinsic system. Sensitive screening test for internal (intrinsic) coagulation system and stage II clotting mechanism disorder detection. This test is performed on a citrated blood specimen. The PTT is more sensitive for detecting minor common pathway deficiencies than the prothrombin time.

Test Purpose. 1) to aid in preoperative screening of bleeding tendencies, 2) to screen for congenital/acquired coagulation deficiencies (clotting factors VIII, IX, X, XI, XII, prekallikrein and high molecular weight kininogen), 3) to monitor heparin therapy, 4) to screen for factor VIII, IX, XI inhibitors, 5) to determine lupus anticoagulant presence, 6) disseminated intravascular coagulation diagnosis, 7) differential diagnosis of thrombotic complications, 8) to detect classical hemophilia A, 9) to detect the presence of dysfibrinogenemia, liver failure, congenital hypofibrinogenemia.

Increased Values – prolonged PTT

amyloidosis, pyogenic liver abscess, **lupus anticoagulant**, **rheumatoid arthritis**, **liver cirrhosis**, primary/secondary biliary cirrhosis, chronic glomerulonephritis, **dysfibrinogenemia**, coagulant factors defects/deficiency – (prekallikrein, II, V, VIII, IX, X, XI, XII), **vitamin K deficiency**, glycogen storage disease – (type IV, VI), hemophilia – (**A, B**), hemochromatosis – (secondary h., idiopathic h.), **hyperfibrinolysis**, **hypofibrinogenemia**, **liver diseases**, hepatic coma, **disseminated intravascular coagulation**, leishmaniasis, **leukemia**, drug induced lupus erythematosus, systemic lupus erythematosus, malabsorption, malaria, disease – (**von Willebrand's d.**, Wilson's d.), fatty liver, drug reactions, hemorrhagic shock, syndrome – (Reye's sy, hepatorenal sy), massive blood transfusion, repeated plasma transfusions, tuberculosis, liver failure, congenital deficiency of Fitzgerald factor and high molecular weight kininogen, fibrin degradation products, typhoid fever, intoxication by – (**acetaminophen**, **coumarin**, **heparin**)

Interfering Factors: lipemia, positive rheumatoid factor, medicaments – (acetaminophen, antihistamines, anistreplase, argatroban, ascorbic acid, asparaginase, azlocillin, chlorpromazine, digitalis, heparin, oral anticoagulants, penicillin, phenothiazines, phenytoin, protamine, salicylates, tetracyclines, thrombolytics, valproic acid, warfarin)

Decreased Values – shortened PTT

early stage of disseminated intravascular coagulation, acute hemorrhage, polycythemia vera, **tumours**

Interfering Factors: medicaments – (oral contraceptives)

Analyte	Age/Gender	Reference Range	SI Units	Note
Partial Thromboplastin Time				
standard		60–85	s	
Activated Partial Thromboplastin Time (APTT)	Children	<90	s	
	Adults	25–35	s	

Phagocytes

Function. 1) chemotaxis, 2) phagocytosis – (direct, mediated by opsonines), 3) killing – (intracellular – non/dependent, extracellular – direct, mediated by antibody), 4) secretion – (monokines – IL-1, TNF-2).
Neutrophils, eosinophils, basophils, monocytes, tissue macrophages – (Kupffer's hepatic cells, alveolar macrophages, neuroglia).

Analyte	Age/Gender	Reference Range	SI Units	Note
Phagocytosis (NBT-test)	spontaneous ph.	0.60–0.80		
	stimulated ph.	0.80–1.00		

Phosphofructokinase in RBC

(PFK) Enzyme involved in RBC metabolism (anaerobic glycolysis) with fructose-6-phosphate to fructose-1,6-diphosphate change.
Test Purpose. RBC metabolic disorders and hemolytic anemias differential diagnosis.

Decreased Values
severe muscle dysfunction (type VII glycogen storage disease)

Plasmatic Coagulation Factors

Protein character factors involved in blood coagulation in the 2nd (plasmatic) coagulation phase, functioning as enzymes after activation.

- **Factor I**
  (syn: fibrinogen, F I). See fibrinogen.
- **Factor II**
  (F II, syn: prothrombin) Glycoprotein (alpha-1-globulin), vitamin K dependent, serine protease, when activated by catalytic prothrombin complex action (enzyme factor Xa, Va, Ca^{2+}, PF3, phospholipid tissue thromboplastin component) → thrombin (enzyme) production. Besides main substrate fibrinogen later thrombin activates factor V, VIII, XIII and platelets. Thrombin changes fibrinogen to fibrin. It adsorbs to $Al(OH)_3$, $BaSO_4$, $Ca_3(PO_4)_2$.

Production. Hepatocyte in liver reticuloendothelial system. Retains its potency in stored blood or plasma and remains in serum in trace amounts after plasma clotting.
Test Purpose. 1) differential diagnosis of thrombophilic conditions, 2) to aid in hepatic lesion stage assessment.

Increased Values – hyperprothrombinemia
hypercoagulation conditions
Interfering Factors: medicaments – (estrogens, oral contraceptives)

Decreased Values – hypoprothrombinemia
vitamin K impaired absorption, anemia – (aplastic a., pernicious a.), lupus anticoagulant, **congenital deficiency of factor II, vitamin K deficiency**, gastrocolic fistula, gastroenteritis, **hereditary hypoprothrombinemia, liver diseases**, leucemia, newborns, biliary ducts obstruction, plasmocytoma, hepatic parenchyma injury, fat malabsorption, liver cirrhosis
Interfering Factors: medicaments – (anabolic steroids, androgens, antibiotics, coumarin anticoagulants, heparin, latamoxef, paracetamol, salicylates, warfarin)

Analyte	Age/Gender	Reference Range	SI Units	Note
factor II		<100	mg/l	
		0.7–1.2		
		70–120	%	
		0.6–1.40	µmol/l	
		0.5–1.5	kU/l	
		60–150	AU	

Factor III
(F III, syn: tissue factor, thrombokinase, tissue thromboplastin) External coagulation way factor, injured tissue product (co-factor), with two components: a) lipoprotein component (tissue factor) for thrombin activation by F VII to VIIa activation, b) phospholipid component (tissue phospholipid), a prothrombinase complex component in the prothrombin to thrombin change. Clotting pathway: extrinsic system only.
Production. Thromboplastic activity in most tissues, especially active tissues are brain, lung and placenta.

Factor IV
(F IV, syn: calcium ions)
Function. Factor IX and X co-factor. Calcium ions are involved in hemostasis as a coagulation factor activation co-factor in all coagulation cascade stages except contact phase and fibrinogen to fibrin change. They are not in stabilized plasma, but are in serum. They are involved in the prothrombin to thrombin change. Anticoagulants (citrate, oxalate, ethylene diaminetetraacetic acid – EDTA) chelate calcium and anticoagulate blood, thus calcium is unable to participate in coagulation. See also blood calcium.

Factor V
(F V, syn: proaccelerin, platelet phospholipids and calcium ions, unstable factor, labile factor, Ac globulin, plasma accelerator globulin) Factor V is a glycoprotein.
Function. Activated proaccelerin form is a factor Xa co-factor, involved in the prothrombin to thrombin change. Platelet factor V is present in granules of platelets and is necessary to the binding of Xa to the platelet surface. Activated factor V–Va is a prothrombin converting complex component; proaccelerin is labile. It is involved in plasmin activation. The molecular characterization of Va, in particular identification of the structural determinants responsible for accelearation of prothrombin activation and those that bind to phospholipid surfaces have been described.
Production. Liver – hepatocytes, megakaryocytes, reticuloendothelial system histiocytes. F V is converted in the plasma from a single chain to a two chain molecule under the influence of thrombin activation. Activity is destroyed during coagulation process. F V is absent in serum.

Increased Values – hyperproaccelerinemia

Interfering Factors: medicaments – (antiepileptics, estrogens, oral contraceptives)

Decreased Values – hypoproaccelerinemia

lupus anticoagulant, **congenital factor V deficiency, hereditary hypoproaccelerinemia, liver diseases, disseminated intravascular coagulation** (DIC), massive blood transfusion, liver cirrhosis, primary fibrinolysis

Interfering Factors: medicaments – (anabolic steroids, androgens, antibiotics, asparaginase, dextran, heparin, methyltestosterone, salicylates)

Analyte	Age/Gender	Reference Range	SI Units	Note
factor V		<10	mg/l	
		0.7–1.2		
		70–120	%	
		0.6–1.40	µmol/l	
		0.5–2.0	kU/l	
		60–150	AU	

Factor VII

(F VII, SPCA, syn: proconvertin, coenzyme, proconvertin stable factor, autoprothrombin I, serum prothrombin conversion accelerator) Vitamin K dependent glycoprotein, serine protease, external coagulation pathway factor, the only factor in factor X activation. Factor VII is directly activated by tissue thromboplastin lipoprotein component to VIIa. Active F VIIa form is a F X to F Xa change and F IX to F IXa catalyst. Clotting pathway: extrinsic system only.

Production. Liver – hepatocytes. Retains its potency in stored stabilized blood or plasma and remains present in serum after plasma has clotted. It adsorbs to $Al(OH)_3$, $BaSO_4$, $Ca_3(PO_4)_2$. It is the first clotting factor decreasing after vitamin K antagonists administration, e.g. oral anticoagulants.

Test Purpose. 1) differential diagnosis of inborn/acquired hypoproconvertinemia, 2) aids in liver dysfunction assessment and vitamin K deficiency.

Increased Values – hyperproconvertinemia

atherosclerosis

Interfering Factors: medicaments – (estrogens, oral contraceptives)

Decreased Values – hypoproconvertinemia

lupus anticoagulant, deficiency – (**congenital factor VII d., vitamin K d.**), **hemorrhagic newborn disease, liver diseases, kwashiorkor**, fat malabsorption

Interfering Factors: medicaments – (acetylsalicylic acid, anabolic steroids, androgens, antibiotics, coumarin anticoagulants, dextran, heparin, latamoxef, methyltestosterone, paracetamol, salicylates, tocopherol, warfarin)

Analyte	Age/Gender	Reference Range	SI Units	Note
factor VII		<0.5	mg/l	
		0.7–1.3		
		70–130	%	
		0.7–1.30	µmol/l	
		65–135	AU	

Factor VIII

(F VIII, AHG A, AHF A, syn: antihemophilic globulin A, antihemophilic factor A) Factor X and Xa activation co-factor by factor IXa. Clotting pathway: intrinsic system only. Factor VIII is an acute-phase reactant. Factor VIII deficiency is the most common hereditary bleeding disorder.

Production. Possibly liver – hepatocytes, possibly endothelial cells and megakaryocytes. Activity destroyed during coagulation process. Absent in serum; F VIII is labile, disappearing fairly rapidly from refrigerated plasma.

Test Purpose. Differential diagnosis of inborn/acquired hemorrhagic disorders.

Increased Values

atherosclerotic vascular disease, **congenital factor VIII deficiency, hyperthyroidism,** hypoglycemia, disease – (**coronary heart d., thromboembolic d.**), disseminated intravascular coagulation, diseases – (liver d., **acute inflammatory d.**), **macroglobulinemia, plasmocytoma** (incl. multiple myeloma), secondary fibrinolysis, **sudden coumarin therapy cessation, postoperative states,** Cushing's sy, **pregnancy** (3rd trimester), acute deep venous thrombosis

Interfering Factors: medicaments – (epinephrine, oral contraceptives)

Decreased Values

lupus anticoagulant, **hemophilia A,** disseminated intravascular coagulation, **von Willebrand's disease, antibodies to factor VIII,** massive blood transfusion

Interfering Factors: plasminogen activators, medicaments – (heparin, streptokinase)

Analyte	Age/Gender	Reference Range	SI Units	Note
factor VIII		<0.15	mg/l	
		0.6–1.5		
		60–150	%	
		0.5–2.0	µmol/l	
		60–145	AU	
factor VIII antigen		0.7–1.5		
		50–200	AU	

Factor IX

(F IX, syn: Christmas factor, antihemophilic globulin B – AHG B, antihemophilic factor B – AHF B, plasma thromboplastin component – PTC, autoprothrombin II, Christmas disease factor) Serine protease, vitamin K dependent single chain glycoprotein, a coagulation protein. It is about 18% carbohydrate, its complete amino acid sequence has been determined. Factor IX is activated to the F IXa by F XIa, tissue factor substance and calcium. Active F IXa form catalyzes F X to F Xa with F VIIIa as a co-factor. Clotting pathway: intrinsic system only.

Production. Liver – hepatocytes. Retains its potency in stored blood or plasma and remains in serum after the plasma has clotted; it is stable and adsorbable.

Test Purpose. 1) differential diagnosis of inborn/acquired hemorrhagic diseases, 2) liver dysfunction condition assessment.

Increased Values

Interfering Factors: medicaments – (epinephrine, estrogens, oral contraceptives)

Decreased Values

congenital deficiency of factor IX, lupus anticoagulant, **decompensated hepatic cirrhosis**, **vitamin K deficiency**, **hemophilia B**, **liver diseases**, Gaucher's disease, **newborns**, **nephrotic sy**, fat malabsorption

Interfering Factors: plasminogen activators, medicaments – (dextran, dicumarol, heparin, streptokinase, tocopherol, warfarin)

Analyte	Age/Gender	Reference Range	SI Units	Note
factor IX		<4	mg/l	
		0.6–1.5		
		60–150	%	
		0.6–1.40	µmol/l	
		60–140	AU	

Factor X

(F X, syn: Stuart–Prower factor, Stuart factor) Stable protease, vitamın K dependent glycoproteın. Its actıve form F Xa is directly involved in prothrombin (II) to thrombin (IIa) change with F Va, Ca^{2+} and PF 3 as co-factors. F X is involved in F VII to F VIIa change. Common coagulation pathway factor.

Production. Liver – hepatocytes.Retains potency in stabilized stored blood or plasma and remains in serum after plasma has clotted; it is adsorbable.

Test Purpose. 1) low-molecular weight heparin therapy monitoring, 2) differential diagnosis of hemorrhagic diathesis.

Increased Values

pregnancy

Interfering Factors: medicaments – (antiepileptics, estrogens, oral contraceptives)

Decreased Values

lupus anticoagulant, **congenital factor X deficiency**, fat malabsorption, liver disease, vitamin K deficiency

Interfering Factors: medicaments – (anabolic steroids, androgens, antibiotics, heparin, methyltestosterone, salicylates, tocopherol, warfarin)

Analyte	Age/Gender	Reference Range	SI Units	Note
factor X		<10	mg/l	
		0.7–1.3		
		70–130	%	
		0.7–1.30	µmol/l	
		60–130	AU	

Factor XI

(F XI, syn: Rosenthal's factor, plasma thromboplastin antecedent – PTA, antıhemophilic factor C – AHF C) Plasmatic thromboplastin precursor, serine protease, a coagulation glycoprotein. Circulates in the plasma as a dimer, the two chains are held by disulfide bonds. Factor XI (to XIa) is activated by factor XIIa and the dimer is broken into two chains. Activation of F XI requires surfaces (usually phospholipid) and presence of prekallikrein and HMWK. Structural organization of the complete factor XI gene has been descrıbed. Activated form F XIa is involved with F VIIa in F IX to F IXa change. Clotting pathway: intrinsic system only.

Production. Liver – hepatocytes. Present in serum.
Test Purpose. 1) differential diagnosis of hemorhagic conditions, 2) F XI deficiency diagnosis.

Increased Values
Interfering Factors: medicaments – (epinephrine, oral contraceptives)

Decreased Values
lupus anticoagulant, **congenital factor XI deficiency**, **paroxysmal nocturnal hemoglobinuria**, diseases – (**liver d.**, **congenital heart d.**), **intestinal vitamin K malabsorption**, newborns
Interfering Factors: plasminogen activators, medicaments – (dextran, heparin, streptokinase)

Analyte	Age/Gender	Reference Range	SI Units	Note
factor XI		2–7	mg/l	
		0.6–1.4		
		60–140	%	
		0.6–1.40	µmol/l	
		65–135	AU	

Factor XII

(F XII, syn: Hageman's factor, factor of contact, contact factor) Plasmatic coagulation factor, serine protease which can be activated via active surfaces (in vivo: exposed subendothelium, activated platelet surface, some fatty acids, bacterial endotoxin, in vitro: a) glass, caolin, b) proteolytic activation – plasmin, kallikrein, trypsin). F XII to F XIIa activation starts F XI to F XIa change and gradual step-activation of other plasmatic factors; so-called intrinsic clotting pathway. Factor XII is the first protein adsorbed to negatively charged surfaces (collagen fibers, platelet membranes and other tissue surfaces) after endothelial damage. With XII to XIIa activation (by kallikrein), there is interaction with prekallikrein, HMWK and XIIa fragments in a complex circular reinforcement loop where activation also occurs in fibrinolytic system (plasminogen), complement system (C1), and vasoactive system (kinin pathway, HMWK to bradykinin activation). Clotting pathway: intrinsic system only.
Production. Liver – hepatocytes. Present in serum.
Test Purpose. 1) differential diagnosis of hemorrhagic diathesis and thrombotic conditions, 2) to identify F XII defect.

Increased Values
physical exercise
Interfering Factors: medicaments – (epinephrine, oral contraceptives)

Decreased Values
lupus anticoagulant, **congenital factor XII deficiency**, newborns, thrombophilic states, **nephrotic sy**, pregnancy
Interfering Factors: plasminogen activators, medicaments – (captopril, heparin, streptokinase)

Analyte	Age/Gender	Reference Range	SI Units	Note
factor XII		27–45	mg/l	
		0.6–1.4		
		60–140	%	

Analyte	Age/Gender	Reference Range	SI Units	Note
		0.6–1.40	µmol/l	
		65–150	AU	

■ **Factor XIII**
(F XIII, FSF, syn: fibrin stabilizing factor, fibrinoligase, Laki-Lorand factor) Transglutaminase. Activated factor XIII (by thrombin) stabilizes fibrin unstable monomer conversion to polymerized fibrin and a fibrin coagulum (in calcium presence, it causes covalent fibrin gamma-chain molecule cross-linkage → stable insoluble definite clot, making it resistant to the lytic action of plasmin). Factor XIII also promotes the cross-linking of alpha-2-antiplasmin to fibrin, increasing the resistance to fibrin degradation.
Production. Liver – hepatocyte, megakaryocytes or platelets. Activity destroyed during coagulation process. F XIII is stable in stabilized plasma; only a small rest remains in serum.
Test Purpose. 1) screening test for F XIII decreased values, 2) differential diagnosis of hemorrhagic diathesis, 3) to aid in keloid scar creation differentiation and wound healing disorders, 4) F XIII deficiency identification.

Decreased Values
agammaglobulinemia, anemia – (sickle cell a., pernicious a.), hyperfibrinogenemia, liver diseases, lead poisoning, plasmocytoma, Henoch-Schönlein purpura, postoperative states, pregnancy

Analyte	Age/Gender	Reference Range	SI Units	Note
factor XIII				
(fibrin stabilizing		<10	mg/l	
factor)		0.6–1.5		
		60–150	%	
		20–50	U/l	
		1–2	AU	

■ **Plasmatic Prekallikrein**
(syn: Fletcher's factor, prekallikrein assay) Serine protease that functions as factor XIIa co-factor in F XI to F XIa activation during the contact coagulation cascade phase. Prekallikrein is a coagulation protein involved in the bradykinin generation (vasoactive peptide) and one of the major factors required for contact activation (others are Hageman's factor and high-molecular weight kininogen). Clotting pathway: intrinsic system only. Fletcher's factor deficiency is associated with a clotting defect without bleeding. This factor is normally deficient in newborns.
Production. Liver.

Decreased Values
hereditary prekallikrein deficiency, severe liver diseases, nephrotic sy, uremia

Analyte	Age/Gender	Reference Range	SI Units	Note
prekallikrein		<50	mg/l	

■ **High-molecular Weight Kininogen**
(HMW-K, syn: Williams-Fitzgerald-Flaujeace factor) Plasmatic kininogen, contact factor, co-factor. It functions as factor XIIa co-factor in F XI to F XIa activation during the contact phase in coagulation cascade. HMWK is a protein required for bradykinin generation (a vasoactive peptide). Clotting pathway: intrinsic system only.

Production. Liver.

Decreased Values
hereditary HMW-K deficiency, acute myocardial infarction

Analyte	Age/Gender	Reference Range	SI Units	Note
High-Molecular Weight Kininogen		<60	mg/ml	

Plasmin

(syn: fibrinolysin) Plasmin is an effector fibrinolytic system enzyme; plasmin functions in fibrinolysis and fibrinogenolysis as well as in activated complement cascade. Plasmin inhibitors include: A2MG, alpha-2 plasmin inhibitor, AAT, antithrombin III.
Test Purpose. 1) plasmin deficiency identification, 2) fibrinolysis disorders differential diagnosis.

Increased Values
metastatic prostatic tumors, **intrauterine fetal death**
Interfering Factors: medicaments – (oral contraceptives)

Plasminogen

(PMG, Pgn, syn: profibrinolysin) PMG is beta-2-globulin converted to plasmin by plasminogen activators (tPA, uPA).
Function. Plasminogen is inactive plasmin precursor having the ability to dissolve formed fibrin clots (fibrinolysis), fibrinogen, fibrin monomers, and factor II. It is useful parameter during streptokinase therapy; activates factor XII, factor VII, and induces platelet aggregation.
Test Purpose. 1) to assess fibrinolysis, 2) to detect congenital/acquired fibrinolytic disorders, 3) to monitor thrombolytic therapy, 4) to evaluate DIC.

Increased Values
exercise, **eclampsia**, inflammatory diseases, metastatic prostatic tumors, **intrauterine fetal death**, **pregnancy** (3rd trimester), arterial/venous clotting
Interfering Factors: medicaments – (anabolic steroids, estrogens, ethanol, oral contraceptives)

Decreased Values
primary fibrinolysis, diabetic patients with thrombosis, Behcet's disease, liver cirrhosis, congenital deficiency of plasminogen, premature neonates, newborns, neonatal hyaline membrane disease, **liver diseases**, **disseminated intravascular coagulation** (DIC), pre/eclampsia, **hyperfibrinolytic states**
Interfering Factors: medicaments – (streptokinase, urokinase)

Analyte	Age/Gender	Reference Range	SI Units	Note
Plasminogen		0.8–1.50		
		80–150	%	
		0.06–0.25	g/l	

Plasminogen Activator Inhibitor

(PAI, tPAi) Single chain plasma glycoprotein produced by different cells (endothelial cells, hepatocytes, fibroblasts), PAI-1 is stored in endothelial cells and platelet alpha-granules. It plays an important role in fibrinolysis regulation. It is a potent tissue-type (tPA) plasminogen activator inhibitor and urokinase/urokinase-type (uPA) plasminogen activator by stechiometric complex creation. PAI functions as a serine protease inhibitor and acute phase reactant. PAI-2 is synthesized by macrophages. Higher values are in the morning.
Test Purpose. 1) to evaluate deep vein thrombosis, myocardial infarction and postoperative thrombosis risk, 2) non-specific endothelial cell injury indicator.

Increased Values
atherosclerosis, diabetes mellitus, embolism, hyperlipoproteinemia, hypertriacylglycerolemia, disease – (**coronary artery d.**, hypertonic d.), infectious diseases, liver diseases, **myocardial infarction, tumors**, obesity, sepsis, **after surgery conditions**, preeclampsia, trauma, pregnancy (3rd trimester), **deep vein thrombosis**

Interfering Factors: pregnancy

Decreased Values
inborn PAI-1 deficiency connected with bleeding conditions

Interfering Factors: medicaments – (anabolic steroids)

Analyte	Age/Gender	Reference Range	SI Units	Note
Plasminogen Activator Inhibitor		<10	AU/ml	
		0.6–3.5	U/ml	

Plasmocytes

Plasmocytes are differentiated secretory lymphocytic B-stem cells which originate in lymphocyte with antigen contact.
Function. Antibody secretion in immune body response.
Test Purpose. 1) differential diagnosis of reactive plasmocytoses, 2) generalized plasmocytoma identification.

Increased Values – plasmocytosis
aplastic anemia, bone marrow aplasia, rheumatoid arthritis, liver cirrhosis, diseases – (acute/chronic infectious d., chronic renal d., liver d.), leukemia – (**plasma-cell l.**, chronic lymphytic l.), Hodgkin's disease, systemic lupus erythematosus, malaria, infectious mononucleosis, benign lymphocytic meningitis, rubella, measles, tumours – (liver t., kidney t., breast t., prostate t.), **plasmocytoma** (incl. multiple myeloma), rheumatism, syphilis, trichinosis, **tuberculosis**, varicella

Decreased Values – plasmocytopenia
inborn/acquired immunoglobulin decrease

Analyte	Age/Gender	Reference Range	SI Units	Note
Plasmocytes	Neonates	<0.25	%	
	Infants	<0.5	%	

Platelet-Activating Factor

(PAF) Allergic reaction mediator.
Production. Neutrophils, eosinophils, basophils, mast cells, monocytes, platelets, endothelial cells, renal medullary epithelial cells, glomerular mesangial cells.
Function. Platelet activation, amine secretion, neutrophil activation, enzyme release, prostaglandins and thromboxanes production by platelets.Increases vascular permeability and plasma extravasation. Mimics physiological and intravascular IgE-mediated human systemic anaphylaxis sequelae. Potent eosinophils/neutrophils chemotactic attraction/activation. Prolongs increase in bronchial hyperresponsiveness (bronchoconstriction). Hypotension, decreased cardiac output, vasoconstriction. Arachidonic acid release and eicosanoid production. Host cells and tissues damage.

Increased Values
atherosclerosis

Platelet Adhesion

(syn: platelet adhesiveness, platelet retention) Platelet are able to adhere to the damaged vessel surface, vascular wall collagen, through subendothelial structures (collagen is the most potent adhesion activator), physical factors (blood viscosity, platelet count, blood flow speed), plasmatic proteins (von Willebrand's factor is the most important) and platelet activation. Platelet adhesion is the first step of primary hemostatic plug production.
Test Purpose. 1) to evaluate platelet function, 2) to aid in von Willebrand's disease, Glanzmann's thrombasthenia, Bernard–Soulier syndrome diagnosis.

Increased Values
atherosclerosis, **diabetes mellitus**, homocystinuria, hyperfibrinogenemia, hyperlipidemia, ischemic heart disease, acute infections, increased factor VII levels, tumours, burns, sclerosis multiplex, after surgery, trauma

Interfering Factors: elder people, diurnal variations, physical exertion, medicaments – (oral contraceptives)

Decreased Values
platelet defects, glycogenoses (glycogen storage disease), diseases – (myeloproliferative d., congenital heart d.), **von Willebrand's disease, Bernard-Soulier sy, Glanzmann's thrombasthenia**, uremia

Interfering Factors: medicaments – (acetylsalicylic acid)

Analyte	Age/Gender	Reference Range	SI Units	Note
Platelet Adhesion		44.5–53.5		See ref.
		27.4–36.6		ranges note

Platelet Aggregation

Platelet aggregation and sticking is an important step in primary hemostatic plug production with acute blood vessel endothelium damage. Reciprocal platelet aggregation binding is mediated preferably by fibrinogen, which creates the linkage between neighbouring plate-

let membranes by receptor connection place created by specific membrane glycoproteins complex (GP IIb, GP IIIa). Many factors are involved in aggregation, e.g. thromboxane (TXA2), thrombin, epinephrine, platelet activating factor (PAF), collagen, arachidonic acid, ADP. Platelets have surface-binding sites for adenosine diphosphate (ADP), a natural biologically active platelet aggregating substance.
Test Purpose. 1) to assess platelet aggregation, 2) diagnosis/differential diagnosis of congenital/acquired platelet bleeding disorders, and other bleeding disorders (von Willebrand's disease, Glanzmann's disease, Bernard–Soulier sy, Raynaud's phenomenon), 3) to determine storage pool or platelet granule defects, 4) to determine an aspirin-like defect or defect of prostaglandin pathway.

Increased Values – shortened aggregation
diabetes mellitus, **smoking, hemolysis, familial hyperlipoproteinemia** (type II), thromboembolic disease, cardiovascular system diseases, von Willebrand's disease (type IIB), myocardial infarction, stress

Interfering Factors: hyperbilirubinemia, hyperlipidemia, blood storage temperature, medicaments – (heparin, oral contraceptives)

Decreased Values – prolonged aggregation
afibrinogenemia, albinism, pernicious anemia, May–Hegglin anomaly, recent aortocoronary/dialysis bypass, liver cirrhosis, connective tissue defects, vitamin B_{12} deficiency, dysproteinemias, hypothyroidism, **von Willebrand's disease**, diseases – (**myeloproliferative d., liver d.**), **acute leukemia, systemic lupus erythematosus, infectious mononucleosis**, narcotics – (cocaine, marijuana), antiplatelet antibodies, polycythemia vera, idiopathic thrombocytopenic purpura, syndrome – (**Bernard–Soulier sy**, Chediak–Higashi sy, **Wiskott–Aldrich sy**), **Glanzmann's thrombasthenia**, thrombocytopenia, **uremia**

Interfering Factors: medicaments – (acetylsalicylic acid, antibiotics, antihistamines, azlocillin, captopril, carbenicillin, chlordiazepoxide, chloroquine, chlorpromazine, clofibrate, corticosteroids, dextran, diazepam, diclofenac, dipyridamole, diuretics, furosemide, gentamicin, heparin, ibuprofen, indomethacin, ketoprofen, mezlocillin, nifedipine, nitrofurantoin, penicillin, phenothiazines, phentolamine, phenylbutazone, piperacillin, promethazine, propranolol, prostaglandin E1, pyridinol, pyrimidine, sulfinpyrazol, theophylline, tricyclic antidepressants, volatile general anesthetics, warfarin)

Analyte	Age/Gender	Reference Range	SI Units	Note
Platelet Aggregation		>0.60		

Platelet Antibodies

(PLA, syn: antiplatelet antibody, platelet-bound antibodies, platelet-specific antibodies, platelet-associated antibodies) Immune-mediated platelet destruction may be caused by autoantibodies directed against antigens located on the platelet membrane. To antibodies belong: a) autoantibodies, e.g. in infectious diseases, medicament influences, and lymphoproliferative diseases, b) allo-antibodies, e.g. in incompatible blood transfusion, and in bone marrow transplantation. Antibodies directed to platelets will cause early platelets destruction and subsequent thrombocytopenia.
Test Purpose. 1) to detect the antibodies that destroy platelets, 2) to diagnose and follow immune thrombocytopenia conditions, 3) to detect causes of clinical refractoriness to platelet transfusions.

Increased Values – positive

paroxysmal hemoglobinuria, diseases – (**autoimmune d., lymphoproliferative d.**), **disseminated intravascular coagulation, systemic lupus erythematosus, Hodgkin's disease**, purpura – (**idiopathic thrombocytopenic p., posttransfusion p.**), **sepsis, neonatal thrombocytopenia, recovery from chemotherapy**

Interfering Factors: medicaments – (acetaminophen, antabuse, cephalosporins, chlorothiazide, chlorpropamide, digoxin, heparin, oral hypoglycemic agents, penicillin, phenobarbital, quinidine, salicylates, gold salts, organic arsenicals)

Platelet-Associated Immunoglobulin G

Increased Values

immune-complex diseases, systemic lupus erythematosus, plasmocytoma (incl. multiple myeloma), acute/chronic immune thrombocytopenic purpura, septic thrombocytopenia

Platelet Factor 4

(PF 4, syn: endothelial cell growth inhibitor, heparin neutralizing protein) Specific thrombocytic protein composed of four identical subunits. It is synthesized in megakaryocytes and platelets. PF 4 is released from platelet alpha-granules after stimulation (platelet activation) in conjunction with proteoglycan. The synthesis of PF4 is enhanced by IL-1. It is stored in endothelial cells and not present in urine. PF4 is found also in mast cell granules and on the endothelium of human umbilical veins, but not arteries. It is chemotactic for inflammatory cells such as neutrophils and monocytes. It activates neutrophils and induces their degranulation. PF4 has a half-life in plasma less than 3 minutes, and its rapid clearance appears to be a function of binding to the vascular endothelium. Once bound to the endothelium, PF4 can be released by heparin in a time-dependent manner. It neutralizes the anticoagulatory activity of heparin sulfate in the extracellular matrix of endothelial cells. It inhibits local antithrombin III activity and thus promotes coagulation. It stimulates the activity of leukocyte elastase and inhibits collagenases. PF4 accelerates the generation of blood clots at the sites of injuries and initiates many cellular processes of wound healing. It may be useful in the treatment of tumors due to its marked anti-angiogenic activity. PF4 may be implicated in pathological and physiological processes of bone and has been found to inhibit the growth of human osteoblast-like osteosarcoma cells. Recombinant PF4 efficiently reverses heparin anticoagulation without adverse effects of heparin-protamine complexes and may be an appropriate substitute for protamine sulfate in patients undergoing cardiovascular surgery and other procedures that require heparin anticoagulation. It has been suggested that PF4 mRNA expression should be a marker of mature megakaryoblasts and that its expression in megakaryoblastic leukemia may indicate that a patient will have long survival and a good response to chemotherapy.

Test Purpose. Platelet activation indicator and an index of platelet aggregation and thromboembolic risk.

Increased Values

angina pectoris, diabetes mellitus, pulmonary embolism, diseases – (vascular d., infectious d., renal d., chronic cardiac d., thrombotic d., inflammatory d.), myocardial infarction, insufficiency – (pulmonary i., heart i.), tumors, extracorporal circulation, polycythemia vera, conditions – (c. after heart prostheses implantation, postsurgery c., shock c.)

Analyte	Age/Gender	Reference Range	SI Units	Note
Platelet Factor 4		<15	µg/l	

Platelet Serotonin

Test is used for carcinoid syndrome diagnostics.

Increased Values

oat cell carcinoma of lung, multiple endocrine neoplasia (types I and II), islet cell tumors of pancreas, medullary carcinoma of the thyroid, **carcinoid sy**

Platelet-Specific Alloantibodies

Increased Values – positive

purpura – (post-transfusion p., idiopathic thrombocytopenic p.), neonatal alloimmune thrombocytopenia

Platelets

(PLT, syn: thrombocytes, platelet count, thrombocyte estimation, thrombocyte count) Platelets are the smallest individual blood cells.
Function. Involved in primary hemostasis (blood coagulation/clotting), vascular integrity, vasoconstriction, adhesion and aggregation activity in primary platelet hemostatic plug formation that occludes small vessel breaks or obturates vessel by blood clot in pathological conditions (thrombogenesis) + stores/transports/releases vasoactive amines, platelet factor 3 and thromboxane A2. Platelets influence right endothelium cell function; they are involved in plasma coagulation factor activation and have phagocytic activity.
Production. In bone marrow by peripheral megakaryocyte cytoplasm cleavage during megakaryocytopoiesis and thrombocytopoiesis, 2/3 are in circulating blood, 1/3 in the spleen.
Production agonists. a) strong a.: thrombin, collagen, PGs, endoperoxides, TXA2, PAF, b) mild a.: ADP, epinephrine, vasopressin and serotonin.
Production antagonists. PGI2, PGD2, EDRF.
Platelet activating agents. a) indirect: collagen, b) direct: thrombin, epinephrine, ADP, TXA2.
Platelet inflammation mediators. Serotonin, ADP, ATP, histamine, fibrinogen, factor Va/VII, platelet factor 4, von Willebrand's factor, B-lysine, protease, cathepsin A, collagenase, elastase, PAF, TXA2, TGF-beta, galactosyl-transferase, P-selectin, PDGF, reactive oxygen products, glycoprotein Ib, thrombospondin.
Test Purpose. 1) to evaluate platelet production 2) to assess chemotherapy or radiation therapy platelet production effects, 3) to diagnose and monitor severe thrombocytosis or thrombocytopenia, 4) to confirm visual platelet number estimation and morphology from a stained blood film, 5) to evaluate, diagnose and/or follow up bleeding disorders, idiopathic thrombocytopenic purpura, disseminated intravascular coagulation, leukemia states, 6) to investigate purpura, petechiae, 7) to evaluate response to platelet transfusions, steroid or other therapy.

Platelet morphology. Megathrombocytes (platelet >2.5 μ): accelerated platelet production, compensation for increased platelet destruction, vitamin B_{12} deficiency, myeloproliferative diseases, Bernard–Soulier syndrome

Increased Values – thrombocytosis, thrombocytemia

anemia – (hemolytic a., **posthemorrhagic a.**, **sideropenic a.**), rheumatoid arthritis, asphyxia, celiac disease, **hepatic cirrhosis**, **strenuous exercise**, **iron deficiency**, acute rheumatic fever, hemophilia, diseases – (autoimmune d., **myeloproliferative d.**, rheumatic d., heart d., **inflammatory d.**), **acute/chronic infectious diseases**, colitis ulcerosa (ulcerative colitis), **acute hemorrhage**, collagenoses, leukemia – (chronic granulocytic l., megakaryocyte l., **chronic myelogenous l.**), treatment of – (folate deficiency, vitamin B_{12} deficiency), lymphomas, Hodgkin's disease, Whipple's disease, **myelofibrosis with myeloid metaplasia**, **tumours**, **surgery**, **osteomyelitis**, **chronic pancreatitis**, **polycythemia**, **polycythemia vera**, **high altitudes**, conditions – (after surgery c., postpartum c., after blood loss c.), **splenectomy**, **stress**, pregnancy, **essential thrombocytemia**, **reactive thrombocytosis**, **tuberculosis**, **trauma**, recovery from – (bone marrow suppression, bleeding episode, thrombocytopenia), postpartum

Interfering Factors: medicaments – (ceftazidime, ceftizoxime, ceftriaxone, cephalosporins, cytotoxic medicaments, enoxaparin, epinephrine, estrogens, glucocorticoids, isotretinoin, lithium, meropenem, methadone, metoprolol, miconazole, oral contraceptives, penicillamine, propranolol, rifampicin, ticlopidine, tocopherol, tolazamide)

Decreased Values – thrombocytopenia

AIDS, **alcoholism**, alloimmunization, **anaphylaxis**, anemia – (**aplastic a.**, dyserythropoietic a., autoimmune hemolytic a., **hemolytic a.**, microangiopathic hemolytic a., **megaloblastic a.**, pernicious a., iron deficiency a.), anesthesia, cold environment, **May–Hegglin anomaly**, **hepatic cirrhosis**, deficiency of – (folate, vitamin B_{12}, iron), eczematous dermatitis, eclampsia, **tumor emboli in microcirculation**, **erythroblastosis fetalis**, hyperbaric exposure, **hemangioma**, **paroxysmal nocturnal hemoglobinuria** (PNH), histoplasmosis, **hypersplenism**, hyperthyroidism, **chemotherapy**, **heart valve prostheses**, diseases – (hepatic d., cyanotic congenital heart d.), infectious diseases – (bacterial i. d., protozoan i. d., rickettsial i. d., **viral i. d.**), marrow infiltration (leukemia, lymphoma, fibrosis), intoxication by – (benzene, benzol, organic chemicals), isoimmunization, **disseminated intravascular coagulation**, **collagenoses**, post-delivery complications, leukemia – (acute/**chronic lymphocytic**/myeloid l., hairy cell l.), **lymphoma**, malaria, bone marrow metastases, microangiopathies, **Gaucher's disease**, **myelofibrosis** (myelosclerosis), myelophthisis, atrial myxoma, **tumors**, extracorporeal circulation, **pancytopenia in bone marrow failure**, **plasmocytoma** (incl. multiple myeloma), pneumonia, preeclampsia, purpura – (neonatal p., **posttransfusion p.**, **idiopathic thrombocytopenic p.**, **thrombotic thrombocytopenic p.**), **radiation**, **radiotherapy**, neonatal rubella, **sepsis**, spleen diseases – (congestive s. d., infectious s. d., tumorous s. d.), **splenomegaly**, **allergic conditions**, syndrome – (**aplastic sy**, Alport's sy, **Bernard-Soulier sy**, **adult respiratory distress sy** – ARDS, Ehlers-Danlos sy, Evans' sy, **Fanconi's sy**, Felty's sy, **hyper-IgM sy**, **hemolytic-uremic sy**, Hermansky-Pudlak sy, Chédiak-Higashi sy, **myelodysplastic sy**, **Wiskott-Aldrich sy**, thrombocytopenia – absent radius bones sy), toxoplasmosis, transfusion – (**massive blood t.**, exchange t.), grafts, Glanzmann's thrombasthenia, thrombocytopenia – (**idiopathic t.**, **isoimmune neonatal t.**, **secondary t.**, **t. in HIV positivity**), drug induced thrombocytemia, immune thrombocytopenia – (lymphoproliferative i. t., **i. t. in systemic lupus erythematosus**), renal vein thrombosis, brain injury, **uremia**, vasculitis, heart bypass, failure – (renal f., congestive heart f.), fetal – maternal ABO incompatibility, bleeding conditions

Interfering Factors: medicaments – (abciximab, acetaminophen, acetazolamide, acetylsalicylic acid, aciclovir, ajmaline, aldesleukin, alemtuzumab, allopurinol, alprenolol, altretamine, aminophenazone, aminocaproic acid, aminosalicylic acid, amiodarone, amlodipine, amoxapine, amoxicillin, amphotericin B, ampicillin, amrinone, antazoline, antiepileptics, antihemophilic factor VIII, antihistamines, antirheumatics, antithymocyte globulin, apronal, ardeparin, asparaginase, atenolol, auranofin, aurothioglucose, azapropazone, azathioprine, barbiturates, benazepril, benoxaprofen, betamethasone, bisoprolol, H_2-blocking agents, bumetanide, busulfan, candesartan, capecitabine, captopril, carbamazepine, carbenicillin, carbidopa, carboplatin, carbutamide, carmustine, carvedilol, cefalexin, cefalotin, cefamandole, cefazolin, cefixime, cefoxitin, ceftizoxime, cephalosporins, chlorambucil, chloramphenicol, chloroquine, chlorothiazide, chlorphenamine, chlorpromazine, chlorpropamide, chlorprothixene, chlortalidone, cimetidine, cisplatin, cladribine, clindamycin, clometacin, clomipramine, clonazepam, clopamide, codeine, colchicine, cortisone, cotrimoxazole, cyclosporine, cyclophosphamide, cytarabine, cytostatics, dacarbazine, dactinomycin, dalteparin, danaparoid, daunorubicin, denileukin, desipramine, dexamethasone, dexrazoxane, diamorphine, diazepam, diazoxide, dicloxacillin, diflunisal, digitalis, digitoxin, digoxin, diltiazem, diphenylhydantoin, diuretics, enalapril, enoxaparin, epirubicin, erythromycin, estramustine, estrogens, ethacrynic acid, ethambutol, ethanol, ethosuximide, etoposide, felbamate, fenofibrate, fenoprofen, floxuridine, fluconazole, flucytosine, fludarabine, fluorouracil, fluphenazine, flurbiprofen, fomivirsen, fosphenytoin, furosemide, ganciclovir, gatifloxacin, glutethimide, gold salts, heparin, hydantoines, hydralazine, hydrochlorothiazide, hydroxyurea, ibuprofen, idarubicin, ifosfamide, imipenem, imipramine, inamrinone, indomethacin, interferon alfa-2a, interferon alfa-2b, interferon alfa-n1, interferon alfacon-1, irbesartan, irinotecan, isocarboxazid, isoniazid, isoprenaline, isotretinoin, kava kava, lamivudine, lamotrigine, lansoprazole, latamoxef, leflunomide, levamisole, levodopa, linezolid, lomustine, loracarbef, loxapine, measles/mumps/rubella vaccines, mebendazole, mechlorethamine, mefloquine, meloxicam, melphalan, meperidine, meprobamate, mercaptopurine, mercurial diuretics, meropenem, metamizole, methicillin, methimazole, methotrexate, methyldopa, methylprednisolone, mexiletine, miconazole, milrinone, minoxidil, mitomycin, mitoxantrone, moricizine, moxifloxacin, mycophenolate, myelosuppressives, nafcillin, nalidixic acid, nimodipine, nitrofurantoin, nitroglycerin, nortriptyline, omeprazole, oral contraceptives, oxacillin, oxaprozin, oxprenolol, oxyphenbutazone, paclitaxel, pantoprazole, paracetamol, penicillins, penicillamine, pentamidine, pentobarbital, pentosan, pentostatin, perphenazine, pethidine, phenacetin, phenazone, phenobarbital, phenothiazines, phenylbutazone, phenytoin, piroxicam, plicamycin, potassium iodide, prednisolone, prednisone, primidone, probucol, procainamide, procarbazine, propylthiouracil, pyrazinamide, pyrimethamine, quinidine, quinine, rabeprazole, ranitidine, reserpine, rifabutin, rifampicin, rituximab, salbutamol, salicylates, samarium-153, saquinavir, secobarbital, silver sulfadiazine, sirolimus, sparfloxacin, stavudine, stilbol, streptomycin, streptozocin, strontium-89 chloride, sulfadiazine, sulfamethizole, sulfamethoxazole, sulfasalazine, sulfizoxazole, sulfonamides, sulfonylureas, sulindac, tamoxifen, temozolomide, teniposide, terbinafine, tetracyclines, thiazide diuretics, thiethylperazine, thioguanine, thioridazine, thiotepa, thiothixene, ticarcillin, ticlopidine, tirofiban, tobramycin, tocainide, tolazamide, tolazoline, tolbutamide, topotecan, trandolapril, triamcinolone, triamterene, trifluoperazine, trimethadione, trimethoprim, trimetrexate, trovafloxacin, vancomycin, valproic acid, velaciclovir, verapamil, vinblastine, vincristine, vinorelbine, zidovudine, zimeldine)

Analyte	Age/Gender	Reference Range	SI Units	Note
Platelets	Neonates	290–350*		*x 10^9/l
	Adults	130–370*		

Porphobilinogen Deaminase

(U-I-S, syn: uroporphyrinogen I synthase/cosynthetase, erythrocyte uroporphyrinogen I synthase, uroporphyrinogen decarboxylase) This enzyme converts porphobilinogen to uroporphyrinogen I; the enzyme is necessary for the RBC to produce heme which catalyzes 4 porphobilinogen molecules condensation → linear tetrapyrrole, hydroxymethylbilane creation. Enzyme is in RBC, fibroblasts, lymphocytes, liver cells and amniotic fluid cells.
Test Purpose. 1) acute intermittent porphyria carriers screening, 2) differential diagnosis of acute intermittent porphyria when compared to variegate porphyria.

Decreased Values
acute intermittent porphyria (AIP)

Porphobilinogen Synthase

(PBG-S, syn: DALA dehydratase)

Decreased Values
inborn PBG-S defect, plumboporphyria, **lead exposure, lead intoxication**

Potassium in RBC

Increased Values
congestive heart failure

Decreased Values
hyperaldosteronism, long-standing diuretic therapy

Prostacyclin

(6-keto-PG-F1a, PGI2) Prostacyclin is the main arachidonic acid product in vascular tissue (endothelial cells).
Function. Strong hypotensive agent in vascular beds vasodilation, including the pulmonary and cerebral circulation. Prostacyclin is the most potent endogenic platelet aggregation inhibitor; blocks fibrinogen ADP-induced bond to activated platelets; it is the most potent natural vascular wall antiaggregation principle.

Increased Values
dysmenorrhea, Graves' disease, tumors of – (prostate, breast), congestive heart failure

Decreased Values
atherosclerosis, diabetes mellitus, hypertension, conditions – (hypercoagulability c., thrombotic c.)

Protein C

(PC, syn: protein C antigen) Glycoprotein depending on vitamin K.
Production. By the liver.
Function. When activated, inhibits hemocoagulation. PC is a major key coagulation cascade co-factor, factors Va/VIIIa inhibitor in complex with protein S. Thrombomodulin is a protein C activation potentiator, an endothelial cell co-factor, and important to potentiate proteins C and S in thromboembolism prevention. It has both profibrinolytic and anticoagulant properties.
Test Purpose. 1) to investigate the otherwise unexplained thrombosis causes and to establish inheritance patterns, 2) to help the diagnostic evaluation for hypercoagulability.

Increased Values

nephrotic sy

Interfering Factors: medicaments – (oral contraceptives, stanozolol)

Decreased Values

biliary obstruction, deficiency – **(inborn protein C d., vitamin K d.)**, diseases – (autoimmune d., **severe liver d.**), **consumptional coagulopathy, liver parenchyma lesion**, malabsorption, tumors, **surgery**, gram-negative sepsis, **adult respiratory distress sy** (ARDS), nephrotic sy, **pregnancy, deep venous thrombosis**

Interfering Factors: elder people, medicaments – (coumarin, L-asparaginase, oral contraceptives, warfarin)

Analyte	Age/Gender	Reference Range	SI Units	Note
Protein C		70–130	%	
		0.70–1.30		
		3–6	mg/l	

Protein S

A glycoprotein depending on vitamin K. A plasma factor essential for prevention of thrombosis, partly due to its activity as cofactor for the plasma anticoagulant protease-activated protein C.
Production. Synthesized by the liver.
Function. Coagulation inhibitor. Free protein S form as a protein C co-factor in stechiometric complex with activated protein C and inactivated F V leads to acceleration of F Va and F VIIIa inactivation. Protein S linked to C_{4b}-BP (C_{4b} binding protein) has no anticoagulation activity. The unbound fraction circulates in the plasma as the active form.

Decreased Values

biliary obstruction, deficiency – (congenital d. of protein S, **vitamin K d.**), diseases – (autoimmune d., **liver d.**), **disseminated intravascular coagulation**, malabsorption, surgery, diabetic nepropathy, acute-phase reaction, chronic renal failure, gram-negative sepsis, syndrome – (adult respiratory distress sy (ARDS), **nephrotic sy**, antiphospholipid sy), coumarin induced skin necrosis, **pregnancy, deep venous thrombosis**

Interfering Factors: newborns, medicaments – (L-asparaginase, coumarin, oral contraceptives)

Analyte	Age/Gender	Reference Range	SI Units	Note
Protein S		70–140	%	
		0.70–1.40		
		418–600	mg/l	

Prothrombin Fragment 1+2

(F 1+2, syn: prothrombin fragment F1.2) Prothrombin fragment 1+2 is released by prothrombinase from prothrombin during thrombin formation, thus it is a prothrombin activation fragment.
Test Purpose. 1) to study hypercoagulable conditions, 2) to assess thrombotic risks, 3) to monitor anticoagulant therapy, 4) to assess patients with active and/or progressive thrombosis.

Increased Values
severe liver diseases, leukemia, postmyocardial infarction, **thrombosis**

Decreased Values
Interfering Factors: medicaments – (anticoagulants, antithrombin III)

Analyte	Age/Gender	Reference Range	SI Units	Note
Prothrombin Fragment 1+2		0.4–1.1	nmol/l	

Prothrombin Time

(PT, syn: Quick time, Quick test, Quick prothrombin time, thromboplastin time, pro time) PT measures the extrinsic coagulation cascade portion initiated by factor VII and tissue factor interaction. Stage II hemostasis evaluation (factors I, II, V, VII, IX, X). PT reagents are tissue thromboplastin and ionized calcium.
Test Purpose. 1) to provide overall extrinsic coagulation factors V, VII and X, prothrombin and fibrinogen evaluation, 2) to monitor oral anticoagulant therapy response, 3) screening test for vitamin K deficiency diagnosis, 4) disseminated intravascular coagulation diagnosis, 5) to diagnose factors II, V and X inhibitors, 6) to screen for hemostatic disorders involving fibrin formation, 7) to detect congenital deficiencies of factors II, V, VII, X.

Increased Values – >120% (1.2 INR), shortened PT
high fat diet, hypercoagulability, metastatic tumors, thrombophlebitis, **vitamin K supplementation**

Interfering Factors: medicaments – (anabolic steroids, antacids, antibiotics, barbiturates, chloral hydrate, cholestyramine, carbamazepine, clofibrate, diphenhydramine, digitalis, estrogens, glutethimide, griseofulvin, nafcillin, oral contraceptives – estrogen, rifampicin, salicylates – low dose, sulfonamides)

Decreased Values – <80% (0.8 INR), prolonged PT
afibrinogenemia, alcoholism, **impaired vitamin K intestinal absorption, liver cirrhosis, amyloidosis, vitamin K deficiency**, diverticulitis, hepatitis – (acute h. type A, **acute h. type B**, chronic active h. B, acute h. type E, cholestatic h., drug induced h., autoimmune h., acute

h. type D, **alcoholic h., chemical induced h.**), **hyperfibrinolysis, dysfibrinogenemia, hypervitaminosis A, hypofibrinogenemia**, idiopathic familial hypoprothrombinemia, **acute/chronic hepatic diseases**, renal insufficiency, intoxication by – (**salicylate, heparin, coumarin**), jaundice – (obstructive j., cholestatic j.), **disseminated intravascular coagulation** (DIC), ulcerative colitis, hepatic coma, passive congestion of liver, **systemic lupus erythematosus**, malnutrition, Crohn's disease, metastatic liver tumors, coagulant factors deficiency – (**I, II, V, VII, IX, X**), **biliary ducts obstruction, antibodies against coagulant factors**, scurvy, sprue, Reye's sy, premature infants, fistulas, steatorrhea, steatohepatitis, celiac disease, chronic diarrhea, acute liver failure, heat exhaustion

Interfering Factors: alcohol, diarrhea, vomiting, medicaments – (acetaminophen, acetylsalicylic acid – large doses, allopurinol, aminosalicylic acid, amiodarone, antacids, anabolic steroids, anistreplase, antibiotics, antihistamine, asparaginase, barbiturates, beta-lactam antibiotics, carbenicillin, cefalotin, cefoperazone, cefotetan, cefradine, ceftizoxime, ceftriaxone, cephalosporins, chloral hydrate, chloramphenicol, chlorpromazine, cholestyramine, cimetidine, clofibrate, colchicine, colestipol, coumarines, cyclophosphamide, diazoxide, diphenylhydantoin, disulfiram, erythromycin, estrogens, ethacrynic acid, ethylalcohol, fluconazole, glucagon, glutethimide, griseofulvin, halothane, heparin, heptabarbital, ibuprofen, indomethacin, interferon alpha-2b, ketoconazole, laxatives, loracarbef, MAO-inhibitors, mefenamic acid, meprobamate, mercaptopurine, methimazole, methotrexate, methyldopa, metronidazole, neomycin, niacin, nortriptyline, oral anticoagulants, oral contraceptives, phenylbutazone, phenytoin, plicamycin, propylthiouracil, pyrazinamide, quinidine, quinine, salicylates, sulfinpyrazone, sulfonamides, tamoxifen, theophylline, thiazides, ticarcillin, thyroid hormones, tolazamide, tolbutamide, tolmetin, vitamin E – large doses, warfarin)

Analyte	Age/Gender	Reference Range	SI Units	Note
Prothrombin Time		12–15	s	
		0.8–1.2	(INR)	
		80–120	%	

Pyrimidine-5′-Nucleotidase in RBC

(P-5'-NT, syn: pyrimidine-5'-nucleotide nucleotidase)

Decreased Values

anemia – (autosomal recessive hemolytic a., beta thalassemia), pyrimidine-5'-nucleotidase deficiency, occupational lead exposure, severe lead poisoning

Pyruvate Kinase

(PK, syn: pyruvate kinase assay) Red cell enzyme, takes part in the phosphoenolpyruvate to pyruvate anaerobic glucose metabolism.

Test Purpose. 1) to differentiate PK-deficient hemolytic anemia from other congenital hemolytic anemias or from acquired hemolytic anemia, 2) to detect PK deficiency in asymptomatic heterozygous inheritance.

Increased Values

Duchene's muscular dystrophy, muscular diseases, myocardial infarction, physical exercise

Decreased Values

congenital inherited nonspherocytic hemolytic anemia, anemias, aplasias, **pyruvate kinase deficiency**, metabolic liver diseases, leukemia, medicaments, myelodysplastic sy

Red Cell Distribution Width

(RDW) Main RBC population width in histogram by MCV. RDW measures size variability of RBC population.

Test Purpose. 1) information about the RBC anisocytosis stage, 2) to evaluate anemia, 3) to differentiate iron deficiency anemia from other microcytic anemias.

Increased Values

alcoholism, anemia – (megaloblastic a., immune hemolytic a., a. of chronic disease, myelodysplastic a., myelophthisic a., nutritional a., sickle cell a., sideroblastic a., sideropenic a., homozygous thalassemias), deficiency – (G6PD d., folate d., vitamin B_{12} d.), liver diseases, RBC fragmentation, HbH presence

Interfering Factors: cold agglutinins, hyperglycemia, chronic lymphocytic leukemia, post red cell transfusion

Analyte	Age/Gender	Reference Range	SI Units	Note
Red Cell Distribution Width (index)		12.8–15.2		

Red Cell Mass Volume

(RCV) Total volume of body RBCs. At hematocrit values between 0.20 and 0.55, a linear relationship exists between HCT and RCV.

Test Purpose. 1) conditions with changed total blood volume without plasma to RBC ratio change (simple hypervolemia), 2) to evaluate untrue anemia in polyplasmia and splenomegalia, 3) to evaluate polyglobulia as a dehydration result or hypervolemia „anemia", 4) to help in polycythemia vera diagnosis.

Increased Values

diseases – (pulmonary d., congenital cardiac d.), carboxyhemoglobinemia, methemoglobinemia, newborn infants with HCT ↑ 0.55, tumors – (cerebellar hemangioma, hepatoma, uterine leiomyomas, kidney t.), polycythemia vera, right-left cardiac shunt, pregnancy, high altitude

Decreased Values

anemia, pheochromocytoma, starvation, chronic infectious diseases, acute/chronic hemorrhage, obesity, bed rest, radiation, old age

Reptilase Time

Test giving information about qualitative/quantitative fibrinogen changes. Reptilase is a thrombin-like enzyme derived from Bothrops atrox venom that is not inhibited by heparin. It acts on fibrinogen to cleave fibrinopeptide A, leading to clottable fibrin monomer formation.

Test Purpose. 1) differential diagnosis of hypo/dysfibrinogenemias, 2) fibrin polymerization disorders differential diagnosis, 3) to examine heparinized patient fibrinogen changes, 4) to investigate patients with prolonged thrombin time.

Increased Values – prolonged reptilase time
a/dys/hypofibrinogenemia, primary systemic amyloidosis, Waldenström's macroglobulinemia, plasmocytoma (incl. multiple myeloma)

Interfering Factors: paraproteins, medicaments – (anistreplase)

Analyte	Age/Gender	Reference Range	SI Units	Note
Reptilase Time		15–22	s	

Reticulocyte Hemoglobin Content

Test Purpose. 1) to help in diagnosis of iron deficiency and iron-deficiency anemia, 2) to monitor the response to iron therapy in iron-deficiency anemia.

Decreased Values
anemia – (iron deficiency a., thalassemia), iron deficiency

Reticulocytes

(syn: reticulocyte count) Young, immature, erythrocyte non-nucleated cells series formed in the bone marrow, the last developmental erythropoiesis stage before the mature erythrocyte. Reticulocyte contains original structure remnants of some organels (ribosomes, endoplasmic reticulum) in cytoplasm after nucleus expelling; therefore, reticulocyte can still synthesize hemoglobin. The test is underutilized, especially when one considers it is at a pivotal decision making conjuncture. The reticulotyte production index will indicate whether one is working with a hyperproliferative or nonproliferative anemia, and thus what testing should be subsequently ordered.
Test Purpose. 1) to aid in distinguishing between hypoproliferative and hyperproliferative anemias, 2) to help assess blood loss, bone marrow response to anemia and anemia therapy response, 3) to evaluate erythropoietic activity.

Increased Values – reticulocytosis
abetalipoproteinemia, anemia – (**hemolytic a.**, **sickle cell a.**, hereditary spherocytosis, thalassemia major, thalassemia minor, hereditary elliptocytosis, autoimmune hemolytic anemia, G6PD hemolytic a., pyruvate kinase deficiency hemolytic a., myelophthisic a., microangiopathic a.), babesiosis, bartonellosis, cirrhosis – (liver c., primary biliary c.), deficiency – (factor I, V, VII, VIII, IX, X, XI, vitamin E d.), **erythroblastosis fetalis**, **erythroleukemia**, hemoglobinopathy, hemoglobinuria – (paroxysmal nocturnal h., paroxysmal cold h., paroxysmal post-exercise h.), sickle cell crisis, acute hemolysis, hepatitis – (acute h. type A, acute h. type B, acute h. type D, acute h. type E), chronic hemorrhage, hypersplenism, **chronic hypoxemia**, disease – (hemoglobin C d., hemoglobin H d., Gaucher's d., von Willebrand's d., Hodgkin's d.), **acute hemorrhage** (3 to 4 days later), **leukemia**, lymphocytic lymphoma, malaria, specific anemia treatment – (**megaloblastic a.**, **iron deficiency a.**), endocardial myxoma, nephropathy – (sickle cell n., chronic lead n.), metastatic tumors, post-anemia treatment – (folate supplementation, iron supplementation, vitamin B_{12} supplementation),

poisoning by – (arsenic, lead), **polycythemia vera**, thrombocytopenic thrombotic purpura, leukemoid reaction, scurvy, **splenectomy**, **hemolytic states**, syndrome – (hemolytic uremic sy, tropical splenomegaly sy), **pregnancy**

Interfering Factors: medicaments – (ACTH, captopril, chlorphenamine, cisplatin, hydralazine, methyldopa, paracetamol, phenazone, quinidine, sulfasalazine)

Decreased Values – reticulocytopenia

alcoholism, anemia – (**aplastic a.**, **megaloblastic a.**, **a. of chronic disease**, **sideroblastic a.**, **thalassemia**, macrocytic a., microcytic a., **folic acid deficiency a.**, **iron deficiency a.**, vitamin B_{12} deficiency a.), **untreated pernicious anemia**, **hepatic cirrhosis**, hypofunction – (**anterior pituitary h.**, **adrenocortical h.**), diseases – (endocrine d., liver d., **chronic infectious d.**, renal d.), **bone marrow infiltration**, bone marrow suppression – (sepsis, chemotherapy/radiotherapy), **aplastic crisis in hemolytic anemia**, polycythemia vera, blood transfusion, bone marrow replacement, **radiotherapy**, **myxedema**, myelodysplastic sy, **marrow failure**

Interfering Factors: medicaments – (chloramphenicol, dactinomycin, methotrexate, vinblastine)

Analyte	Age/Gender	Reference Range	SI Units	Note
Reticulocytes	Neonates	0.02–0.06*		*x 10^{12}/l
		0.100–0.300		
	Adults	0.025–0.075*		
		0.005–0.015		

Right Side Shift

Hypersegmented, multilobulated neutrophils, polymorphonuclear cells, older cells in peripheral blood smear. Used in differential diagnosis of liver diseases, pernicious and megaloblastic anemias.

Occurrence. Anemia – (megaloblastic a., pernicious a.), gangrene, hemolysis, liver diseases, medicaments and chemicals – (ACTH, arsenic, benzene, digitalis, venoms, potassium chlorate, mercury, sulfonamides), myocardial infarction, tumours – (bone marrow t., liver t., gastrointestinal tract t.), burns, hemolytic transfusion reactions, after surgery conditions

Sulfhemoglobin

Sulfhemoglobin is a green monochrome formed through oxidative sulfation of 1 or 2 heme from 4 heme hemoglobin groups. It cannot be reduced to Hb (bond is irreversible) but it may be oxidized further and will contribute to Heinz bodies formation in some instances. Generally it is very stable in blood and is lost from the circulation only with erythrocytes breakdown. It is incapable of carrying oxygen and shifts the P50 to the right.

Test Purpose. To assess possible drugs exposure.

Increased Values – sulfhemoglobinemia

chronic constipation

Interfering Factors: medicaments – (acetylsalicylic acid, nitrates, nitrites, phenacetin, sulfides, sulfonamides)

Analyte	Age/Gender	Reference Range	SI Units	Note
Sulfhemoglobin		negat.		

Terminal Deoxynucleotidyl Transferase

(TdT, syn: terminal transferase) Nuclear enzyme which is important in lymphocyte differentiaton with immature and less mature cellular forms.
Occurrence. Thymocytes, precursor cells of lymphocytes in bone marrow.
Test Purpose. 1) acute leukemia differential diagnosis, 2) acute lymphatic leukemia type determination.

Increased Values
active acute lymphoblastic leukemia, chronic myelogenous leukemia in blast crisis, **lymphomas**, neuroblastoma, idiopathic thrombocytopenic purpura

Thrombin Time

(TT, TCT, syn: thrombin clotting time, fibrin time, thrombin-fibrindex) The test is affected by the fibrinogen/plasmin concentrations and quality, FDP, and antithrombotic agents. Performed on citrated blood specimens; the test measures the time needed for plasma to clot (first fibrin fibre creation time) in the laboratory after calcium and thrombin are added – (fibrinogen → fibrin). TT is a test for the presence of sufficient amount of functional (clottable) fibrinogen. The test evaluates thrombin–fibrinogen interaction, bypassing the extrinsic and intrinsic pathways and assessing the terminal common pathway order (as a component of plasmatic coagulation).
Test Purpose. 1) to detect fibrinogen deficiency or defect, 2) to aid in disseminated intravascular coagulation and hepatic disease diagnosis and monitoring, 3) to monitor heparin, fibrinolytic or thrombolytic agent treatment effectiveness.

Increased Values – prolonged TT
afibrinogenemia, increased antithrombin activity, **dysfibrinogenemia**, hyperbilirubinemia, **hypofibrinogenemia**, diseases – (**liver d.**, inflammatory d.), **DIC**, systemic lupus erythematosus, paraproteinemia, plasmocytoma (incl. myeloma multiforme), polycythemia vera, pregnancy, systemic hyperfibrinolysis, **uremia**

Interfering Factors: fibrin degradation products, fibrinogen, medicaments – (anistreplase, asparaginase, heparin, streptokinase, thrombolytics, urokinase)

Analyte	Age/Gender	Reference Range	SI Units	Note
Thrombin Time		18–22	s	

Beta-Thromboglobulin

(beta-TG) Beta-thromboglobulin is a specific platelet protein containing 4 identical subunits in PLT alpha-granules and released after stimulation (e.g. ADP, collagen, immune complexes, thrombin). It is synthesized in the cells as a biologically inactive precursor called platelet basic protein (PBP). Beta-TG is a platelet-specific protein released with PLT aggregation. It inhibits prostacyclin secretion (PGI2), a locally active anticoagulant modulating intravascular coagulation. Beta-TG is a strong chemoattractant for fibroblasts and is weakly chemotactic for neutrophils. It stimulates mitogenesis, extracellular matrix synthesis, glucose metabolism and plasminogen activator synthesis.

Test Purpose. 1) to evaluate prothrombotic conditions/hypercoagulability, 2) to aid in disseminated intravascular coagulation diagnosis, 3) to differentiate DIC from primary lysis, 4) to assess PLT hyperreactivity, 5) to evaluate the thrombolytic regimen effects (e.g. vascular occlusive disease, heart failure, coronary atherosclerosis).

Increased Values
atherosclerosis, diabetes mellitus, disseminated intravascular coagulation, acute myocardial infarction, systemic lupus erythematosus, tumors, vascular wall injury, preeclampsia, vulgar psoriasis, conditions – (c. after heart prostheses implantation, c. after surgery, thromboembolic c.), nephrotic sy, deep-vein thrombosis

Analyte	Age/Gender	Reference Range	SI Units	Note
Beta-Thrombo-Globulin		10–35	µg/l	

Thrombomodulin

(TM, syn: endothelial co-factor) Thrombomodulin is endothelial cell thrombin receptor. The thrombin-thrombomodulin complex activates protein C (anticoagulant influence). TM is an anticoagulant protein co-factor modulating thrombin specificity for receptor and activating the central enzyme protein C; involved in factor Va, VIIIa, and fibrinogen inactivation. Plasma thrombomodulin fragments reflect endothelial cell injury. TM activates platelets by thrombin and inhibits thrombin via antithrombin III.
Test Purpose. Endothelial cell damage assessment.

Increased Values
atherosclerosis, diabetes mellitus, diabetic microangiopathy, **endothelial injury**, ischemic heart disease, DIC, systemic lupus erythematosus, tumors, endothelial cell injury, thrombotic thrombocytopenic purpura, adult respiratory distress syndrome (ARDS), pulmonary thromboembolism, thrombosis, failure – (renal f., acute hepatic f.), **vasculitis**

Decreased Values
smoking, primary pulmonary hypertension

Thrombopoietin

(TPO, MGDF, c-mpl-ligand) TPO is highly glycated protein; the terminal portion is identical with erythropoietin.
Function. Main thrombopoiesis regulator involved in CD 34+ cell differentiation to megakaryocyte line; increases aggregation to many inductors: ADP, epinephrine, thrombin, and collagen; involved in platelet alpha-granule degradation with thrombin cooperation.
Production. Kidney, liver, spleen, and bone marrow.

Thromboxane A2

(TXA2) Belongs to the prostaglandins, synthesized from platelet arachidonic acid where its release has an opposite effect to prostacyclin. Allergic reactions mediator.

Function. Microvasculature constriction (arterial smooth muscle), bronchodilation. TXA2 stimulates platelet aggregation; it is the last prostaglandin metabolism stage in activated platelets; increases neutrophil adhesion. It has a very short half-life (about 30 s) and is rapidly converted to an inactive metabolite thromboxane B2.

Analyte	Age/Gender	Reference Range	SI Units	Note
Thromboxane B2		18–91	pg/ml	

Tissue Plasminogen Activator

(tPA) Plasma serine protease proteins stored in endothelial cells are released to blood circulation after stimulation. Initiates fibrinolytic process by plasminogen to plasmin transformation. Two tPA forms (tissue and vascular) are structurally identical but immunologically unlike uPA (urokinase) and scuPA precursor (single chain urokinase PA type).
Test Purpose. Endothelial cell injury marker.

Increased Values

atherosclerosis, inborn hyperfibrinolysis, diabetes mellitus, severe liver diseases, myocardial infarction, conditions – (septic c., shock c.)

Interfering Factors: physical exertion, venous stasis, stress, elder age, medicaments – (antidiuretic hormone)

Decreased Values

fibrinolysis insufficiency

Total Blood Volume (TBV)

Sum of plasma volume plus red cell volume, small leukocyte and platelet volume.
Test Purpose. 1) information about blood volume condition changes, where the total blood volume changes without plasma to RBC ratio change (simple hypervolemia with normal hemogram), excessive plasma volume increase (polyplasmia with false anemia), RBC distribution change (false anemia in splenomegaly), in other conditions (e.g. dehydration polyglobulia, fluid retention „anemia", true polycythemia evidence), where direct total circulating RBC and plasma volume determination is needed, 2) to evaluate the blood volume change level.

Increased Values

acidosis, severe starvation, overhydration, diseases – (pulmonary d., congenital cardiac d.), renal insufficiency, recumbent posture, polycythemia vera, primary/secondary erythrocytosis, athletes, pregnancy, thyrotoxicosis, vasodilatation, cardiac failure

Decreased Values

severe anemias, chronic azotemia, physical exercise, salt deficiency, dehydration, diabetes mellitus, exposure to cold, pheochromocytoma, starvation, diarrhea, chronic infections, hemorrhage, recumbent posture, obesity, burns, prolonged bed rest, prolonged standing, old age, vomiting

Von Willebrand's Factor

(vWF) High-molecular plasma glycoprotein present physiologically in low concentrations. It is produced in endothelial cells and platelets, and stored in endothelial cells (Weibel–Paladie bodies), released after activation or endothelial cell damage.
Function. It is a coagulatory F VIII: C carrier circulating in blood as a complex, and playing an important role in primary hemostasis as platelet adhesion to endothelium mediator. Factor deficiency results in prolonged bleeding time.
Test Purpose. 1) hemorrhagic diatheses differential diagnosis, 2) von Willebrand's disease identification, 3) endothelial cell damage indicator.

Increased Values

rheumatoid arthritis, atherosclerosis, **diabetes mellitus**, smoking, hyperlipidemia, hypercholesterolemia, disease – (hypertonic d., **ischemic heart d.**), diseases – (renal d., **connective tissue d.**, liver d., **inflammatory d.**), **myocardial infarction**, **tumors**, vascular endothelium damage, arteriosclerosis obliterans, conditions – (febrile c., postsurgery c.), **vasculitides**

Interfering Factors: blood group "O" carriers, stress, pregnancy, medicaments – (oral contraceptives)

Decreased Values

von Willebrand's disease

Analyte	Age/Gender	Reference Range	SI Units	Note
von Willebrand's Factor		<8	mg/l	
		0.6–1.5	IU/ml	