
بسم الله الرحمن الرحیم

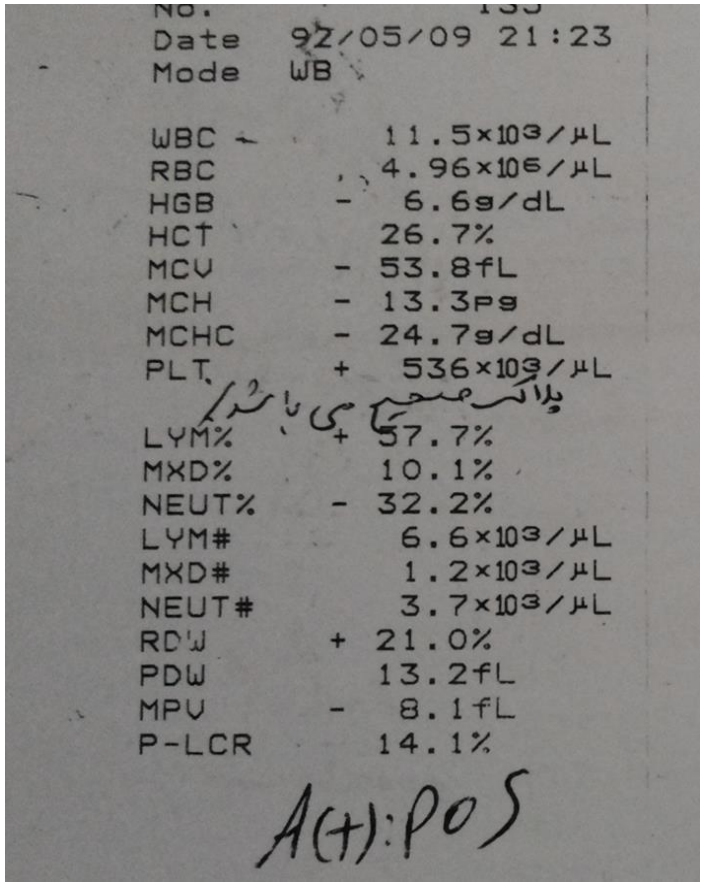
رویکرد بالینی به آنمی

Dr. B. Darbandi

Ped. Hematologist,Oncologist

GUMS

April 2022



پسر یک ساله ای با تابلوی گاستروآنتریت در بیمارستان بستری می شود.

آزمایشات وی عبارتند از:

۱ – در شرح حال گیری از این بیمار به چه نکاتی بایستی بیشتر توجه کرد ؟

۲ – برای رسیدن به تشخیص چه آزمایشاتی را درخواست بکنیم ؟

Anemia is a reduction in Hb, Hct, or RBC from 2SD below the mean for age and sex for the normal population

Table 1

Haemoglobin levels to diagnose anaemia at sea level (g/l)*

Population	Non -Anaemia*	Anaemia*		
		Mild[a]	Moderate	Severe
Children 6 - 59 months of age	110 or higher	100-109	70-99	lower than 70
Children 5 - 11 years of age	115 or higher	110-114	80-109	lower than 80
Children 12 - 14 years of age	120 or higher	110-119	80-109	lower than 80
Non-pregnant women (15 years of age and above)	120 or higher	110-119	80-109	lower than 80
Pregnant women	110 or higher	100-109	70-99	lower than 70
Men (15 years of age and above)	130 or higher	110-129	80-109	lower than 80

Box 9-1 Physiologic Classification of Anemia

1. Disorders of red cell production in which the rate of red cell production is less than expected for the degree of anemia
   a. Marrow failure
      - Aplastic anemia
        Congenital
        Acquired
      - Pure red cell aplasia
        Congenital
          Diamond-Blackfan syndrome
          Aase's syndrome
        Acquired
          Transient erythroblastopenia of childhood
          Human parvovirus B19 infection
      - Marrow replacement
        Malignancies
        Osteopetrosis
        Myelofibrosis
        Chronic renal disease
        Vitamin D deficiency
        Granulomatous infection
      - Pancreatic insufficiency–marrow hypoplasia syndrome
      - Fanconi's anemia

   b. Impaired erythropoietin production
      - Chronic renal disease
      - Hypothyroidism, hypopituitarism
      - Chronic inflammation
      - Protein malnutrition
      - Hemoglobin mutants with decreased affinity for oxygen

   c. Anemia of chronic disease
2. Disorders of erythroid maturation and ineffective erythropoiesis
   a. Abnormalities in cytoplasmic maturation
      - Iron deficiency
      - Thalassemia syndromes
      - Sideroblastic anemias
      - Lead poisoning

   b. Abnormalities in nuclear maturation
      - Vitamin B_{12} deficiency
      - Folic acid deficiency
      - Thiamine-responsive megaloblastic anemia
      - Hereditary abnormalities in folate metabolism
      - Orotic aciduria
      - Zinc-induced copper deficiency

   c. Congenital dyserythropoietic anemias (types I, II, III, IV)
   d. Erythropoietic protoporphyria
   e. Refractory sideroblastic anemia with vacuolization of marrow precursors and pancreatic dysfunction/deficiency
3. Hemolytic anemias
   a. Defects in hemoglobin
      - Structural mutants
      - Synthetic mutants (thalassemia syndromes)

   b. Defects in the red cell membrane
   c. Defects in red cell metabolism
   d. Antibody mediated
   e. Mechanical injury to the erythrocyte
   f. Thermal injury to the erythrocyte
   g. Oxidant-induced red cell injury
   h. Infectious agent–induced red cell injury
   i. Paroxysmal nocturnal hemoglobinuria
   j. Plasma lipid–induced abnormalities in the red cell membrane

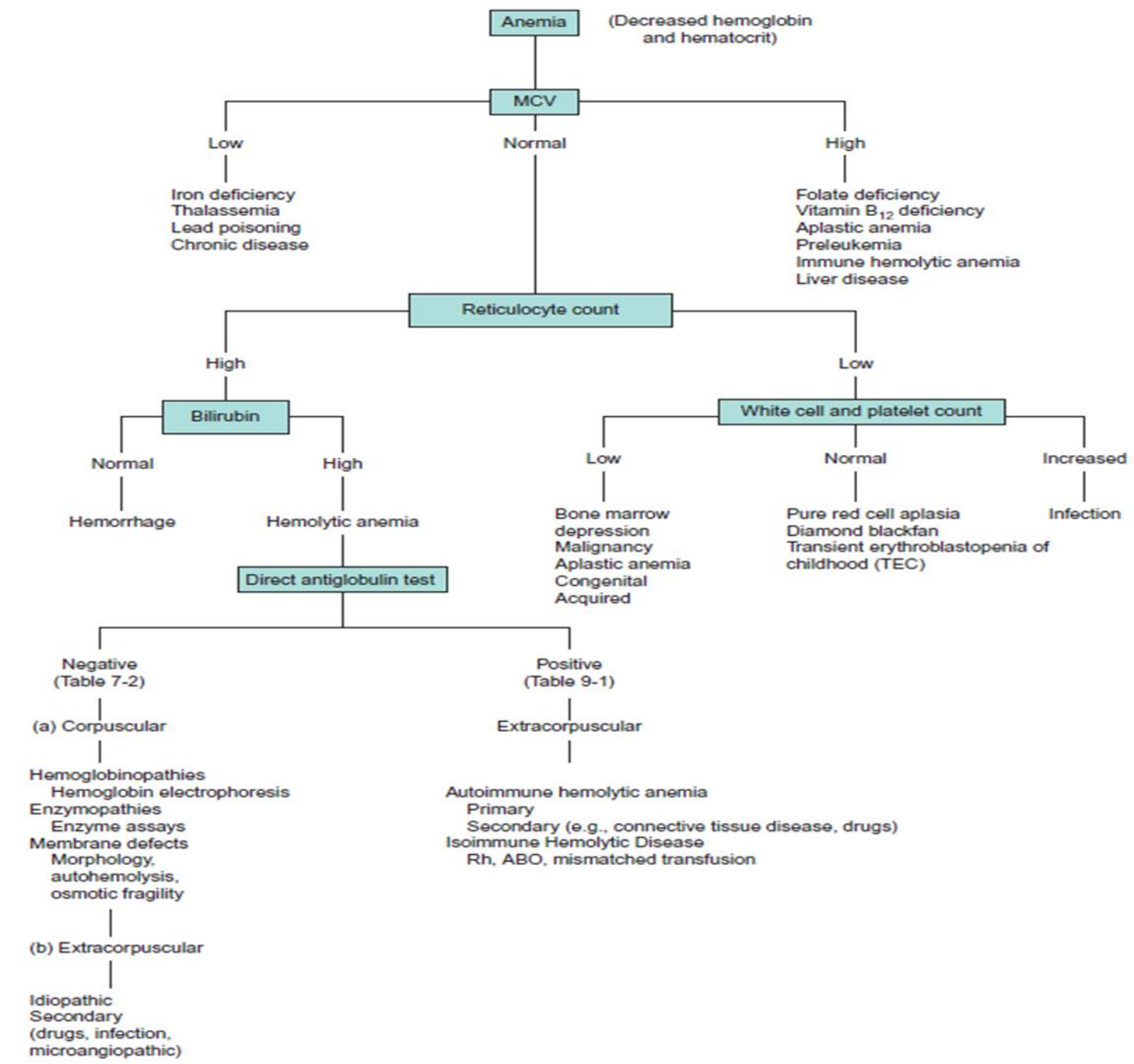


Figure 1-2 Approach to the Diagnosis of Anemia by MCV and Reticulocyte Count.

Historical Factors of Importance in Evaluating Patients with Anemia

- **Age** Nutritional **iron deficiency** is never responsible for anemia in term infants before 6 months of age

- **Gender** Consider X-linked disorders in males (**G6PD deficiency)**
- **Race** African Americans : Hb S, Hb C and a thalassemia
  Caucasians : β thalassemia
- **nutrition** cow's milk allergy : **IDA**
  Goats milk : **folate deficiency**

- **Ethnicity** **Thalassemia** syndromes and G6PD deficiency most common among patients of Mediterranean, Greeks and … origin. observed

Physical Findings as Clues to the Cause of Anemia

- **Petechiae, purpura** :

  AHA with thrombocytopenia,

  HUS, BM aplasia, BM infiltration

- **Jaundice** :

  HA, hepatitis

- **Spleen Enlargement** :

  HA, leukemia, lymphoma,

  portal hypertension

پسر یک ساله با آنمی میکروسیتیک

در شرح حال گیری از این بیمار به چه نکاتی بایستی بیشتر توجه کرد ؟

مصرف مکمل آهن

پاسخ **منفی** بود.

سابقه تالاسمی در خانواده

پدر بیمار بتا تالاسمی مینورو وضیعت مادر ازاین نظر نامعلوم بود.

نکات مهم در معاینه بالینی :

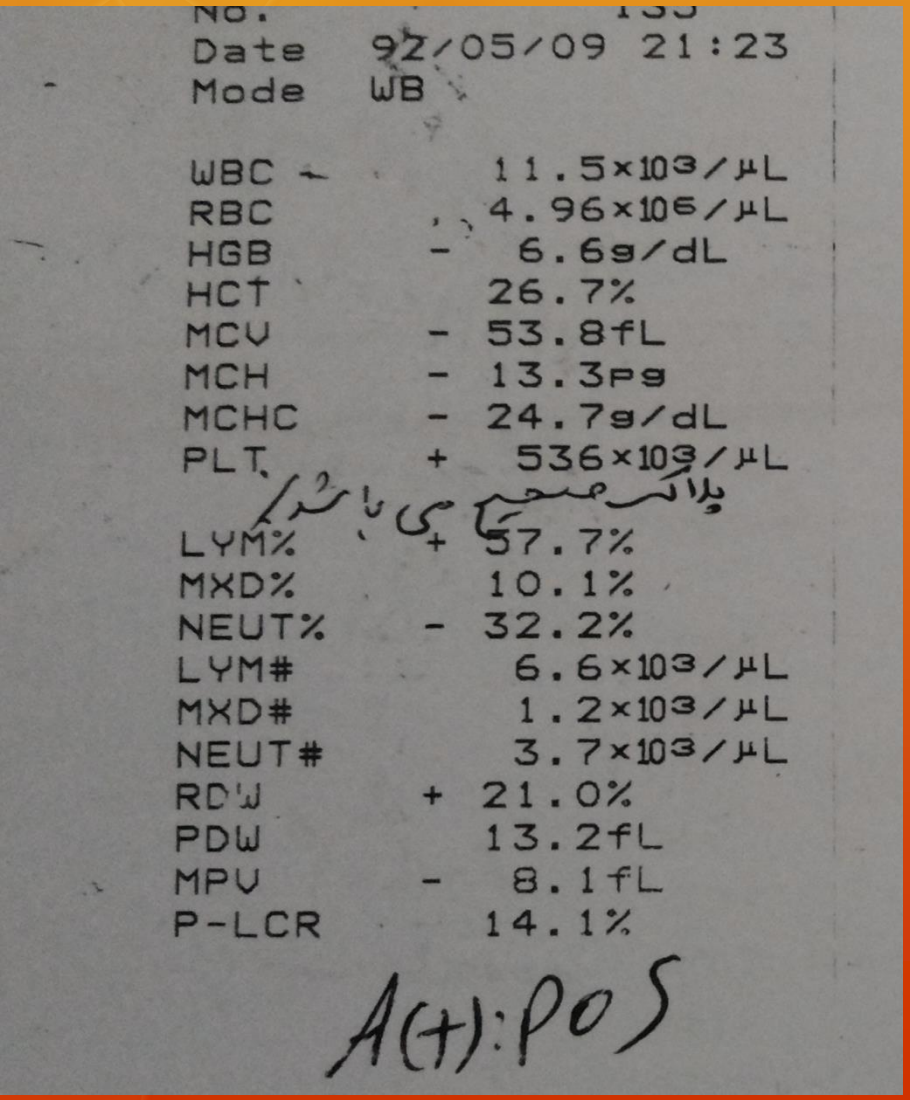
معیارها ی رشد

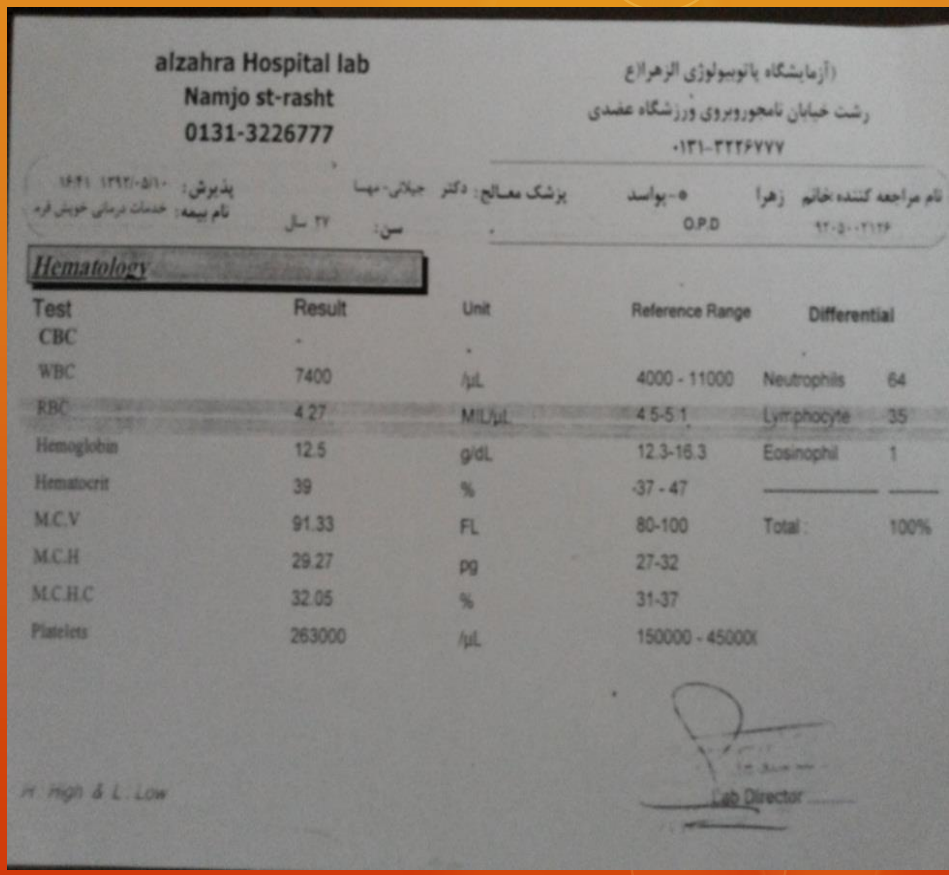
اندازه کبد و طحال

همگی نرمال بودند

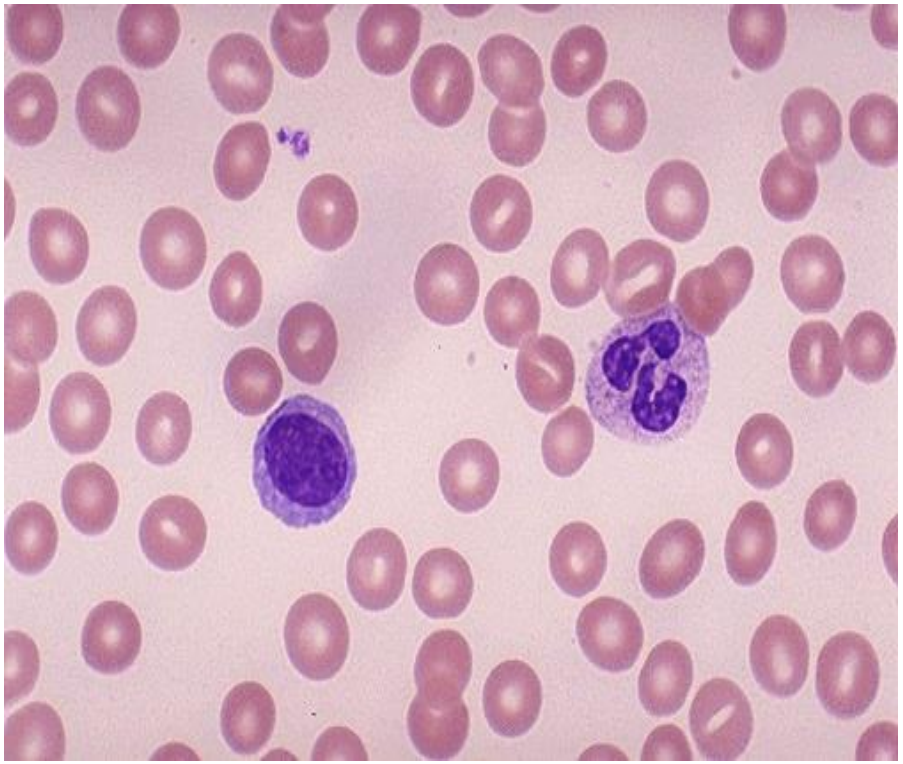
پسر یک ساله با آنمی میکروسیتیک

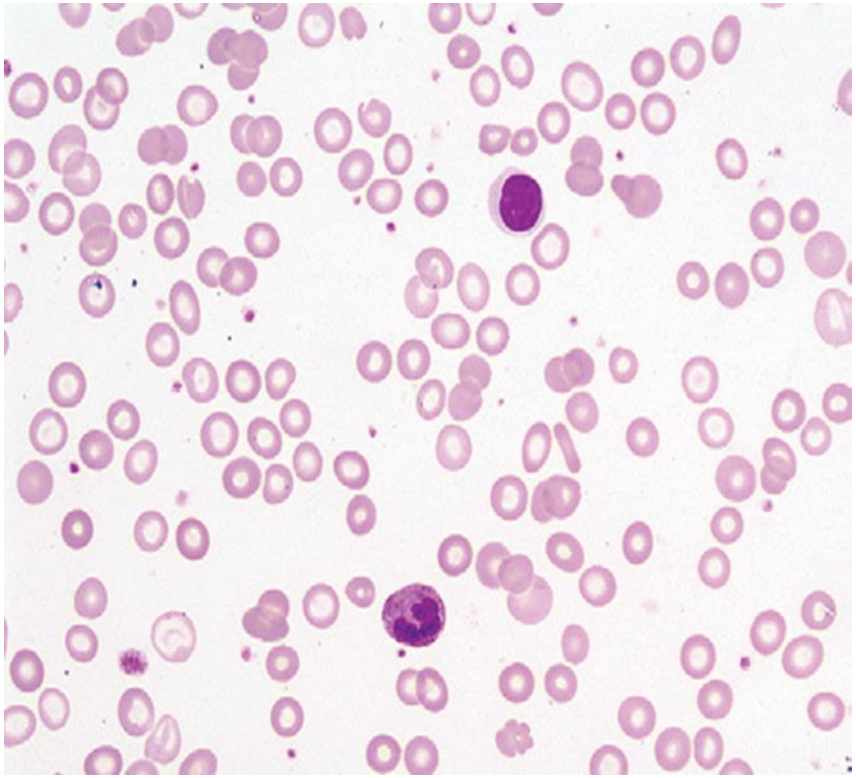
بررسی پدرو مادر





peripheral blood smear





پسر یک ساله با آنمی میکروسیتیک

- Hb electrophoresis :

  HbA : 90.3

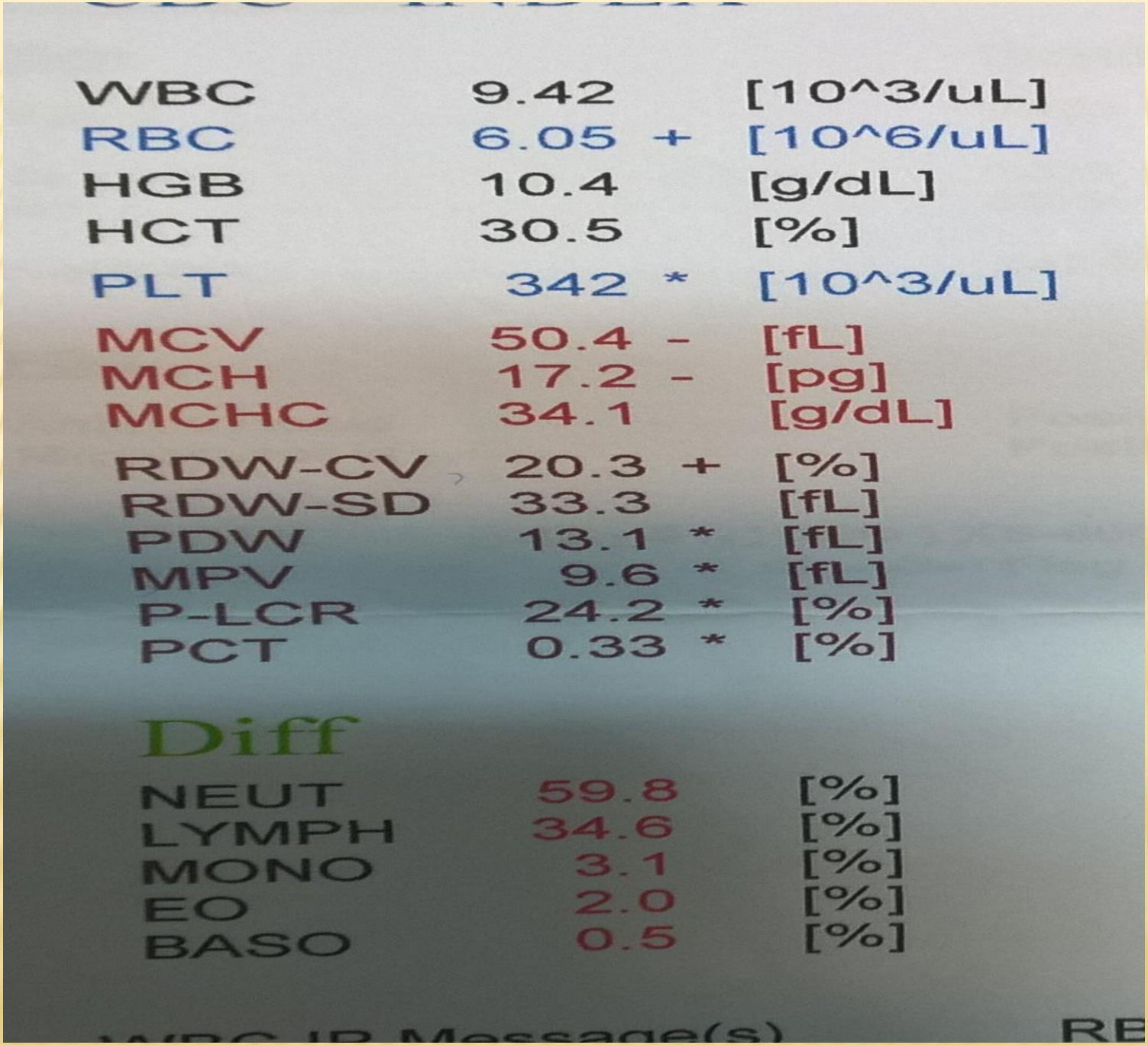
  HbF : 5.2%

  HbA_2 : 4.5%

- **Ferritin : 5**

تشخیص نهائی :

- بتا تالاسمی مینور همراه با آنمی فقر آهن



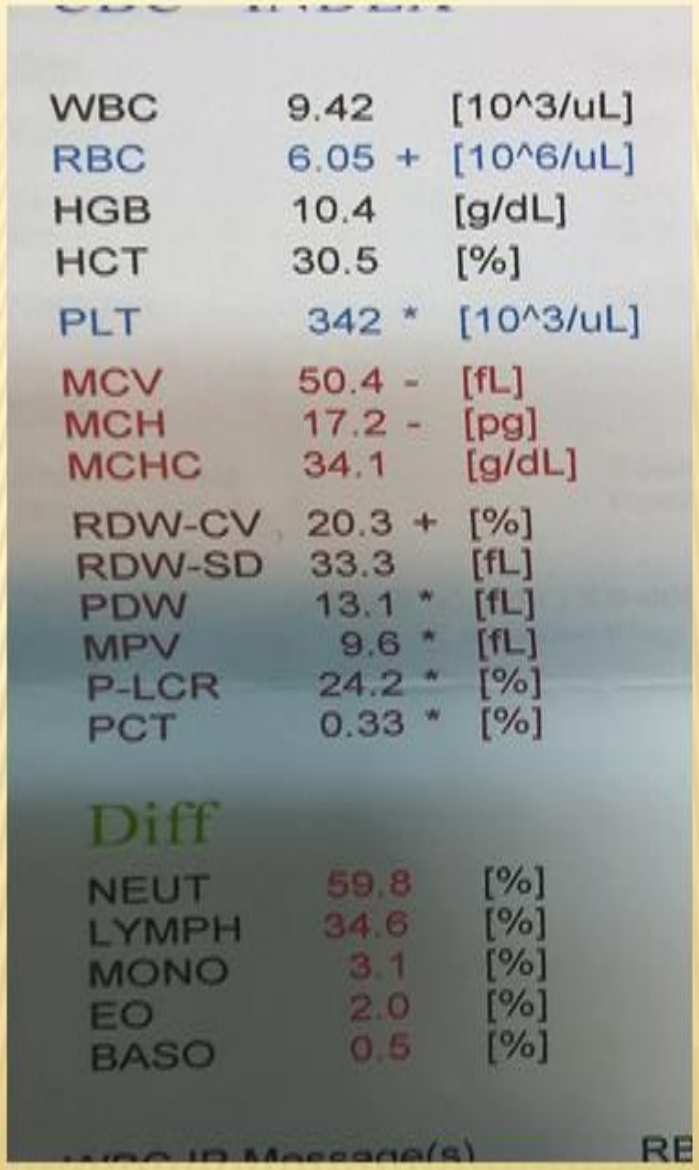
WBC	9.42		[10^3/uL]
RBC	6.05	+	[10^6/uL]
HGB	10.4		[g/dL]
HCT	30.5		[%]
PLT	342	*	[10^3/uL]
MCV	50.4	-	[fL]
MCH	17.2	-	[pg]
MCHC	34.1		[g/dL]
RDW-CV	20.3	+	[%]
RDW-SD	33.3		[fL]
PDW	13.1	*	[fL]
MPV	9.6	*	[fL]
P-LCR	24.2	*	[%]
PCT	0.33	*	[%]

Diff

NEUT	59.8	[%]
LYMPH	34.6	[%]
MONO	3.1	[%]
EO	2.0	[%]
BASO	0.5	[%]

TABLE 20-8 **Formulas for Differentiation of Thalassemia Trait from Iron Deficiency**

	Thalassemia Trait	Iron Deficiency
Mentzer index (552)*		
MCV/RBC	<13	>13
Shine and Lal (562)		
(MCV) 2 × MCH	<1530	>1530
England and Fraser (563)		
MCV − RBC −(5 × Hb) − 8.4	Negative values	Positive values

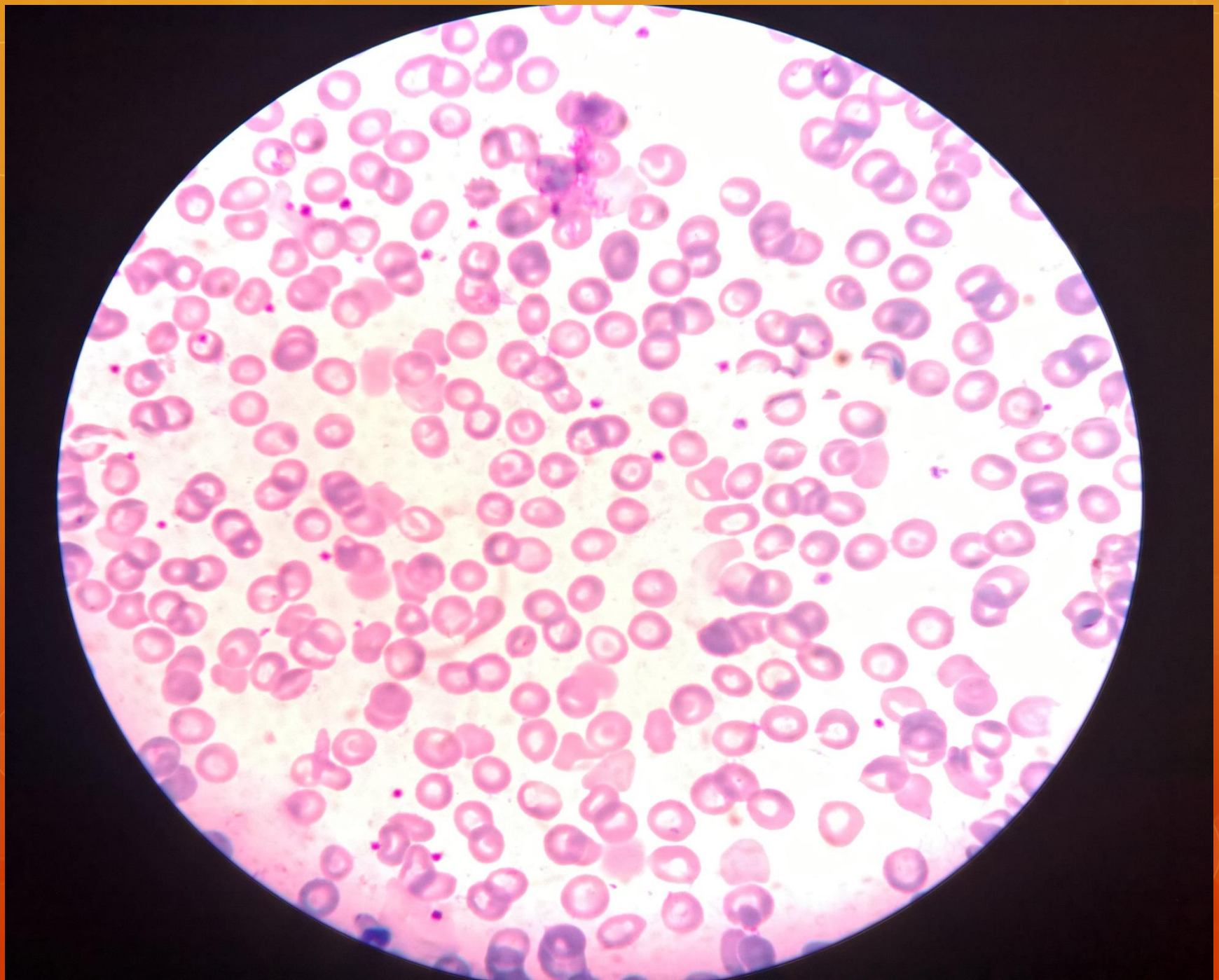


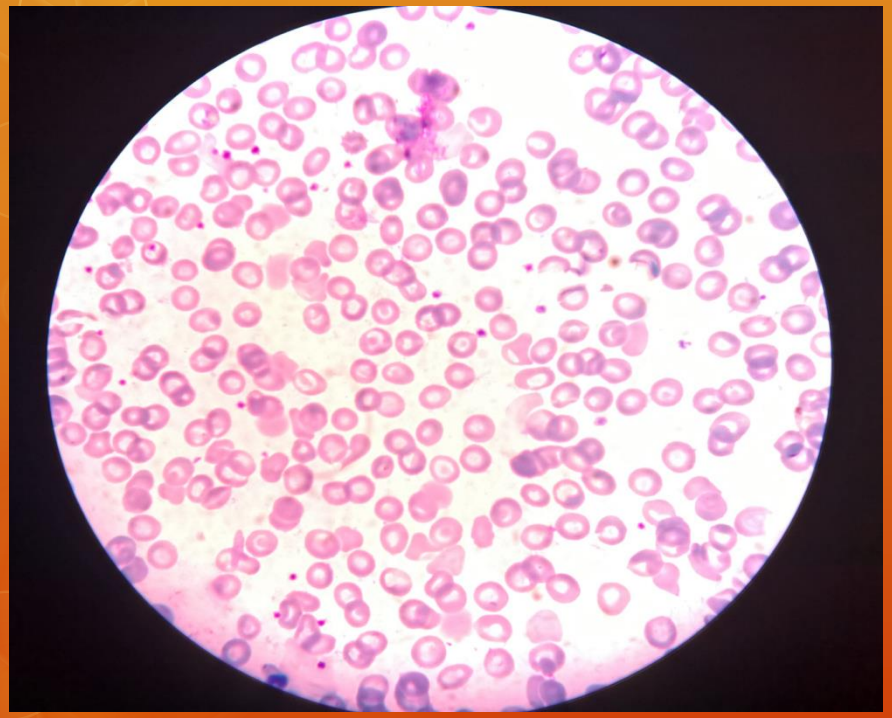
WBC	9.42	[10^3/uL]
RBC	6.05 +	[10^6/uL]
HGB	10.4	[g/dL]
HCT	30.5	[%]
PLT	342 *	[10^3/uL]
MCV	50.4 -	[fL]
MCH	17.2 -	[pg]
MCHC	34.1	[g/dL]
RDW-CV	20.3 +	[%]
RDW-SD	33.3	[fL]
PDW	13.1 *	[fL]
MPV	9.6 *	[fL]
P-LCR	24.2 *	[%]
PCT	0.33 *	[%]

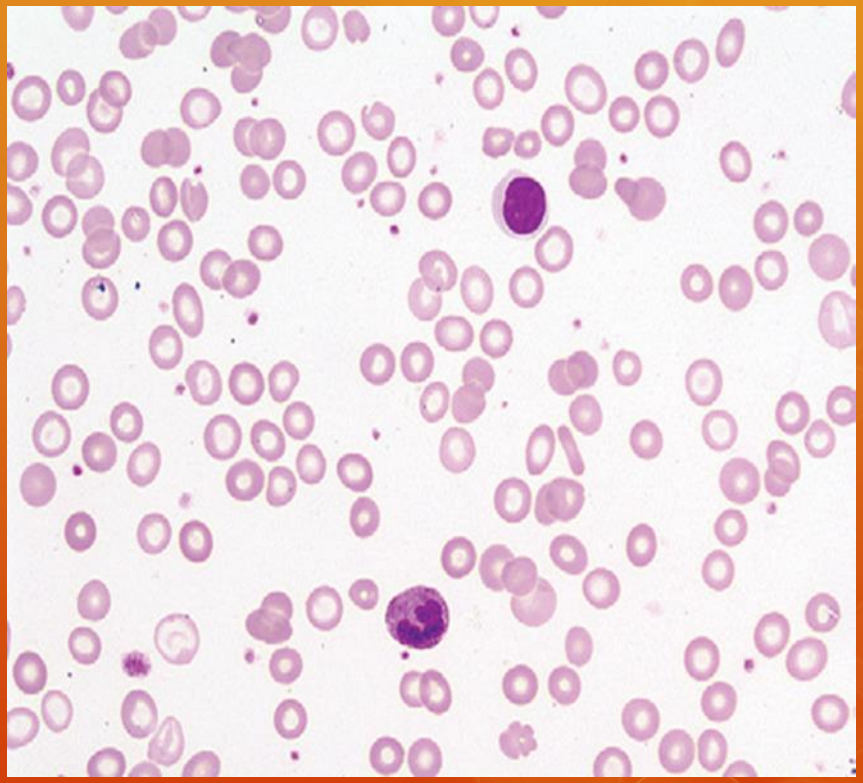
Diff

NEUT	59.8	[%]
LYMPH	34.6	[%]
MONO	3.1	[%]
EO	2.0	[%]
BASO	0.5	[%]

- MCV/RBC : 50.4/6.05 = 8.33
- MCV-RBC-(5×Hb)-8.4 = -16.05







Hematology

Test	Flag	Result	Unit
Direct Coombs - Neonate		Negative	
CBC		-	
WBC	H	20200	/µL
RBC	L	1.64	MIL/µL
Hemoglobin	L	5.0	g/dL
Hematocrit	L	15.6	%
M.C.V		95.12	FL
M.C.H		30.49	pg
M.C.H.C		32.05	%
Platelets		416000	/µL
Hypochromia		Mild	
Anisocytosis		1+	
Poikilocytosis		Mild	
RDW	H	15.8	%
Reticulocyte		3.3	%
BG & Rh		(B)	
Rh		Positive	
G6PD		Severely decreased	

Biochemistry

Test	Flag	Result	Unit
BUN		21	mg/dl
Creatinine		0.5	mg/dl
Sodium Na		137	mEq/L
Potassium K		4.8	mEq/L
Bilirubin Total	H	5.8	mg/dl
Bilirubin Direct	H	0.5	mg/dl
SGOT (AST)	H	82*	IU/L
SGPT (ALT)		16	IU/L

H : High & L : Low

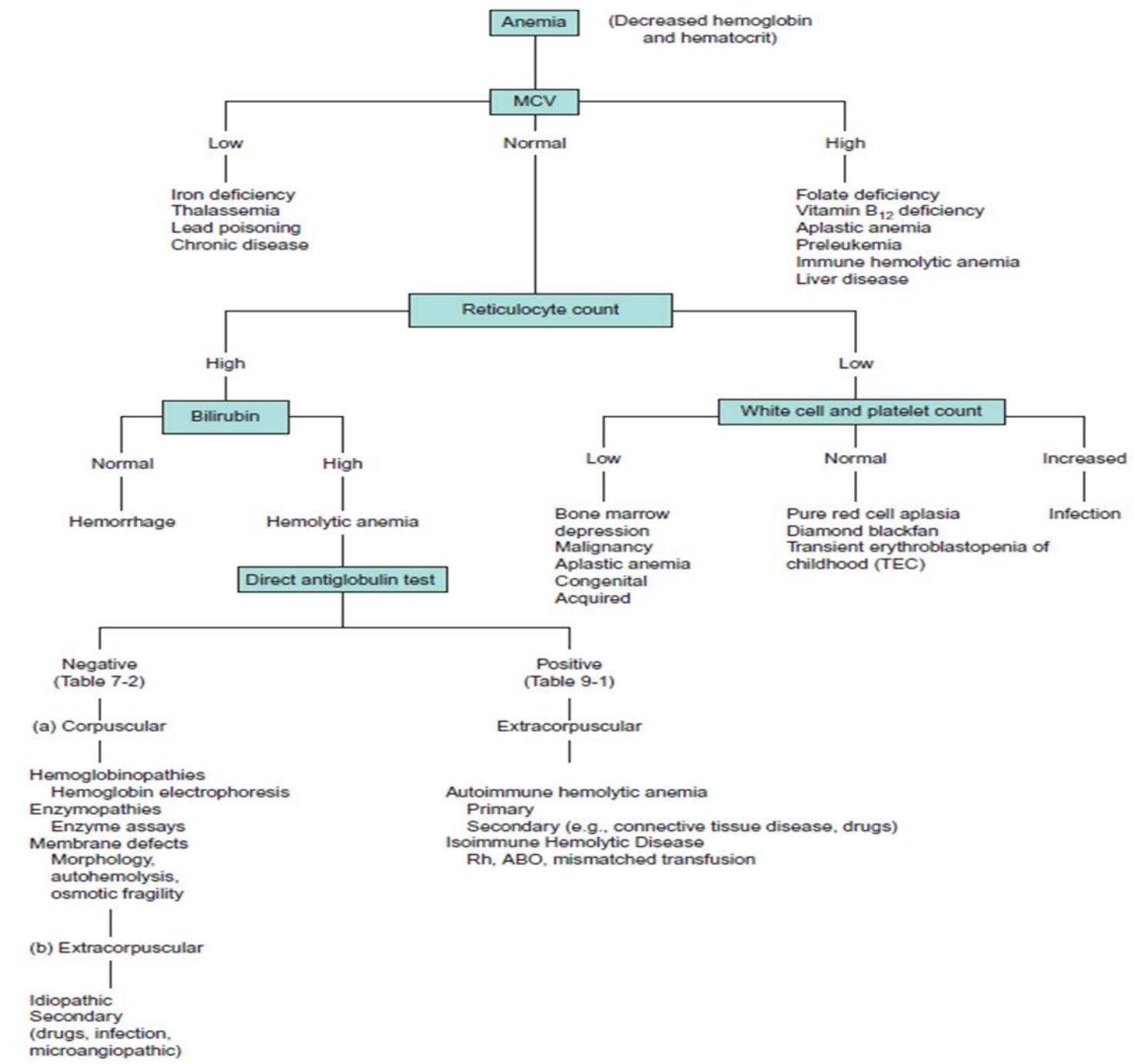


Figure 1-2 Approach to the Diagnosis of Anemia by MCV and Reticulocyte Count.

دانشگاه علوم پزشکی و خدمات بهداشتی درمانی استان گیلان

برگ شرح حال و معاینه بدنی
MEDICAL HISTORY & PHYSICAL EXAMINATION SHEET

۳۰-۷۴-۰۷

Attending Physician: پزشک معالج: دکتر دربندی	Ward: بخش: خون Room: اتاق: Bed: تخت:	Name: نام: علیرضا	Family Name: نام خانوادگی: [redacted]
Date of Admission: تاریخ پذیرش: ۹۱/۲/۳۱		Date of Birth: تاریخ تولد: ۷ ماهه	Father's Name: نام پدر: [illegible]

Chief Complaint: شکایت اصلی بیمار:

CC = [illegible] به دنبال مصرف باقالا

History of Peresent Illness: تاریخچه بیماری فعلی:

PI = شیرخوار ۷ ماهه که از حدود ۱ ماه پیش به دنبال مصرف باقالا توسط مادر [illegible] شده

استفراغ ⊖ [illegible] ⊕ تب ⊕ تعریق ⊕

PMH = [illegible] / [illegible] C/S / واکسیناسیون کامل / ترم

[illegible]

Past Disease History: تاریخچه بیماریهای قبلی:

Family History: [illegible]

[illegible]

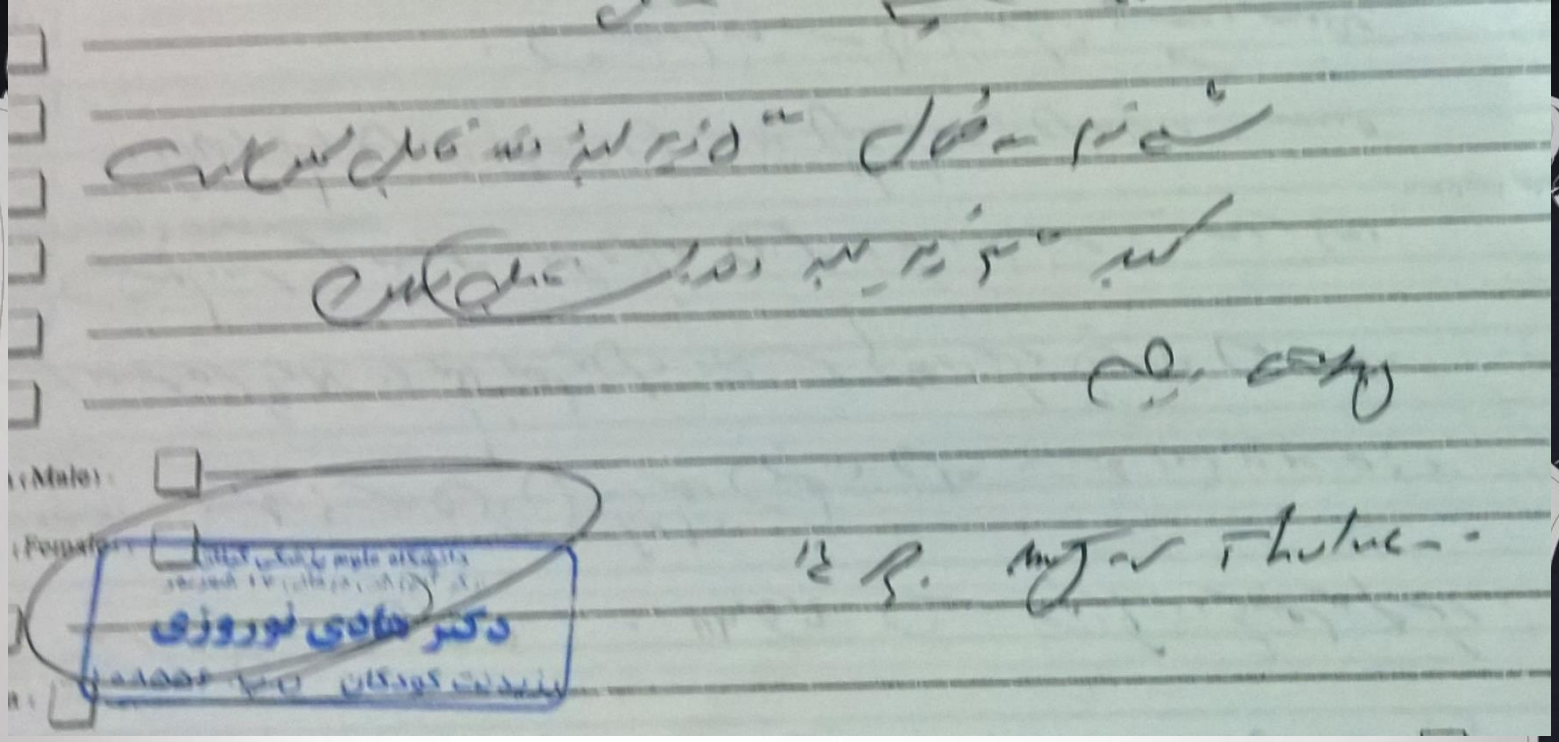
[illegible]

Physical Examination & Clinical Investigation: معاینه فیزیکی و بررسی های بالینی:

- [ ] Skin: [illegible]
- [ ] Skull: [illegible]
- [ ] Ear: [illegible]

Please Complete the Back of the Sheet. لطفاً پشت صفحه را تکمیل کنید.

برگ شرح حال و معاینه بدنی


(Male)
(Female)
دکتر هادی نوروزی

Hematology

Test	Flag	Result
Direct Coombs		Negative
CBC		
WBC		27400 True WBC
RBC		2.97
Hemoglobin		6.4
Hematocrit		20.5
M.C.V		69.02
M.C.H		21.55
M.C.H.C		31.22
Platelets		336
Hypochromia		2+
Anisocytosis		2+
Poikilocytosis		2+
Nucleated RBC		18 %
Schistocytes		Few
Reticulocyte		5.3 % (RI: 2.4 & RP
ESR 1st hr		4
Blood Group		O +
Rh		Positive
G6PD		Normal

API

Biochemistry

Test	Flag	Result
BUN		6.5
Creatinine		0.4
Blood Sugar		90
Sodium,Na	L	134

آزمایش معالج دکتر بهرام دریادی

تاریخ : ۹۱/۰۳/۲۱ 90667 : شماره فاکتور F / سن : ۲۲ سال جنس :

Blood Hematology

*Test		Result	Units	Reference Range
W.B.C		7000	/cumm	4000-11000
R.B.C	H	6.17	mil/cumm	M : 4.50-5.90 F : 4.20-5.10
Hb		11.6	g/dL	M: 13.5-17.5 F: 12.0-16.0
Hct		37.7	%	M : 41.5-50.4 F: 35.9-44.6
M.C.V	L	61.1	fL	78.0-100
M.C.H	L	18.8	pg	26.0-34.0
M.C.H.C		30.8	g/dL	31.0-37.0
Platelet		353000	/cumm	150000-450000
Anisocytosis		+		
Hypochromia		+		
Poikilocytosis		+		
Microcytosis		+		
Basophilic Stippling		+		

Hb ELECTROPHORESIS

Hb A1	L	94.6	%	95-98
Hb F		0.0	%	Adult : 0-2 90% of Infants: 6 Months <8% 1yr <5% 1-2yr <3%
Hb A2	H	5.5	%	1.5-3.5

Note L :Low H :High

Blood Biochemistry

Test	Result	Units	Refe
Ferritin	70.9	ng/mL	Fem Male 2-5 6 m

× نام بیمار: آقای [redacted] سن: ۳۰ سال

تاریخ پذیرش: ۹۱/۰۳/۲۰ تاریخ جواب: ۹۱/۰۳/۲۲

Hematology

*Test		Result	Units	Referen
W.B.C		8910	/Cumm	4400 -
R.B.C		5.33	Mil/Cumm	M: 4.5 - F: 4.5 -
Hb		10.4	g/dl	M: 14 - F: 12.3
Hct		31.5	%	M: 41.5 F: 35.9
M.C.V	L	59.1	fL	80 - 100
M.C.H	L	19.5	pg	27 - 32
M.C.H.C		33.0	%	31-37
Platelets		164000	/Cumm	150000
RDW	H	16.4	%	11.6 - 1

Peripheral Blood Smear

Anisopoikilocytosis	(+)
Hypochromia	(+)
Eliptocytes	Mild
Schistocytes	Mild
Tear drops	Mild

Hemoglobin Electerophoresis

Hb A		93.2	%	95 - 98
Hb F		1.1		Adult: 0
Hb A2	H	5.7	%	1.5 - 3.5

Note L :Low H :High

Special Blood Biochemistry

Test	Result		Units
Ferritin	121	(RIA)	ng/ml

نام بیمار: کودک [redacted]

سن: ۷ ماه

تاریخ پذیرش: ۹۱/۰۳/۰۱

تاریخ جواب: ۹۱/۰۳/۰۴

Hematology

*Test		Result	Units	Reference Range
R.B.C		2.96	Mil/Cumm	M: 4.5 - 5.9 F: 4.5 - 5.1
Hb		5.6	g/dl	M: 14 - 17.5 F: 12.3 - 15.3
Hct		19.7	%	M: 41.5 - 50.4 F: 35.9 - 44.6
M.C.V	L	66.6	fL	80 - 100
M.C.H	L	18.9	pg	27 - 32
M.C.H.C	L	28.4	%	31-37

Hemoglobin Electerophoresis

Hb A	L	6.7	%	95 - 98
Hb F	H	90.8		Adult: 0.1 - 2
Hb A2		2.5	%	1.5 - 3.5

Note L :Low H :High
- The sample is not collected in this lab.

Special Blood Biochemistry

Test	Result		Units	Refe
Ferritin	158 *	(CLIA)	ng/ml	1 mo 2 - 5 6 mo Adul Adul

Note * :Checked
- CLIA : Chemiluminescent immunoassay

S.Hoda M.D. R.Shahbaz M.D. M.Habibzadeh M.D.

E-1307

نام بیمار: خ [redacted] بهرام دربندی

سن :۱۷سال

تاریخ پذیرش:۰۰/۰۷/۱۸

تاریخ جواب: ۰۰/۰۷/۱۹

Hematology

*Test		Result	Units	Reference Range
W.B.C	H	12400 *	/Cumm	4400 - 11000
R.B.C		3.28	Mil/Cumm	M: 4.5 - 5.9 F: 4.5 - 5.1
Hb		10.8	g/dl	M: 14 - 17.5 F: 12.3 - 15.3
Hct		29.9	%	M: 41.5 - 50.4 F: 35.9 - 44.6
M.C.V		91.2	fL	80 - 100
M.C.H		32.9	pg	27 - 32
M.C.H.C		36.1	%	31-37
Platelets		367000	/Cumm	150000 - 450000
RDW		20.1	%	11.6 - 14.6

Differential

Neutrophils
Lymphocytes
Eosinophil
Monocyte

Total: 100

Peripheral Blood Smear

Anisocytosis	(+)		
Hypochromia	Mild		
Reticulocyte	6.9	%	
Retic. Production Ind (RPI)	2.6	%	>3% indicates active erythropoiesis

Note H :High

General Biochemistry

Test		Result	Units	Reference Range
Bilirubin Total	H	9.54 *	mg/dl	0.1 - 1.2
Bilirubin Direct		0.49 *	mg/dl	up to 0.5
LDH		499	IU/L	225 - 500

Note H :High * :Checked

M.Habibzadeh M.D. A.Mesbah M.D. E.Kord Mostafapour M.D.

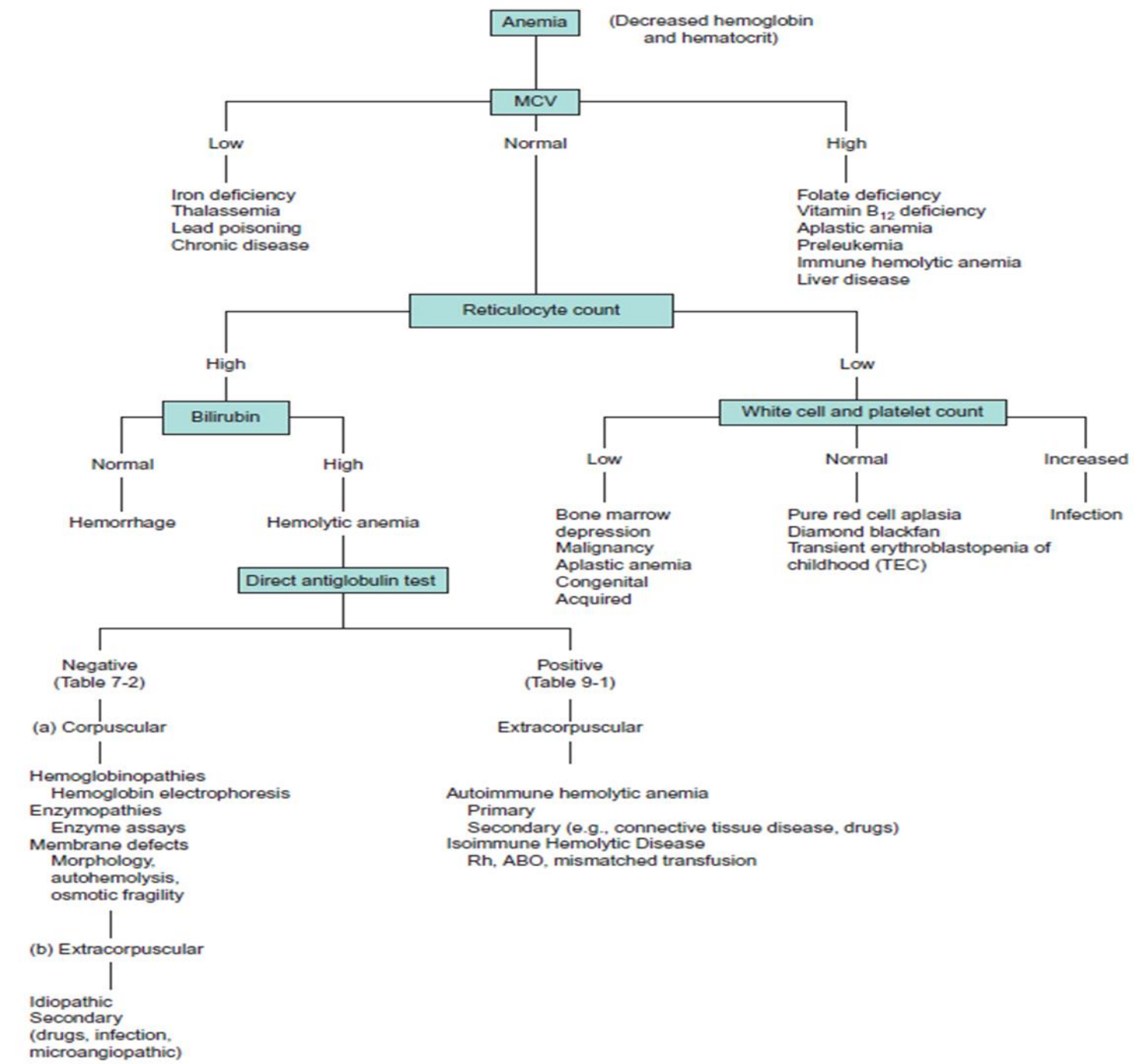
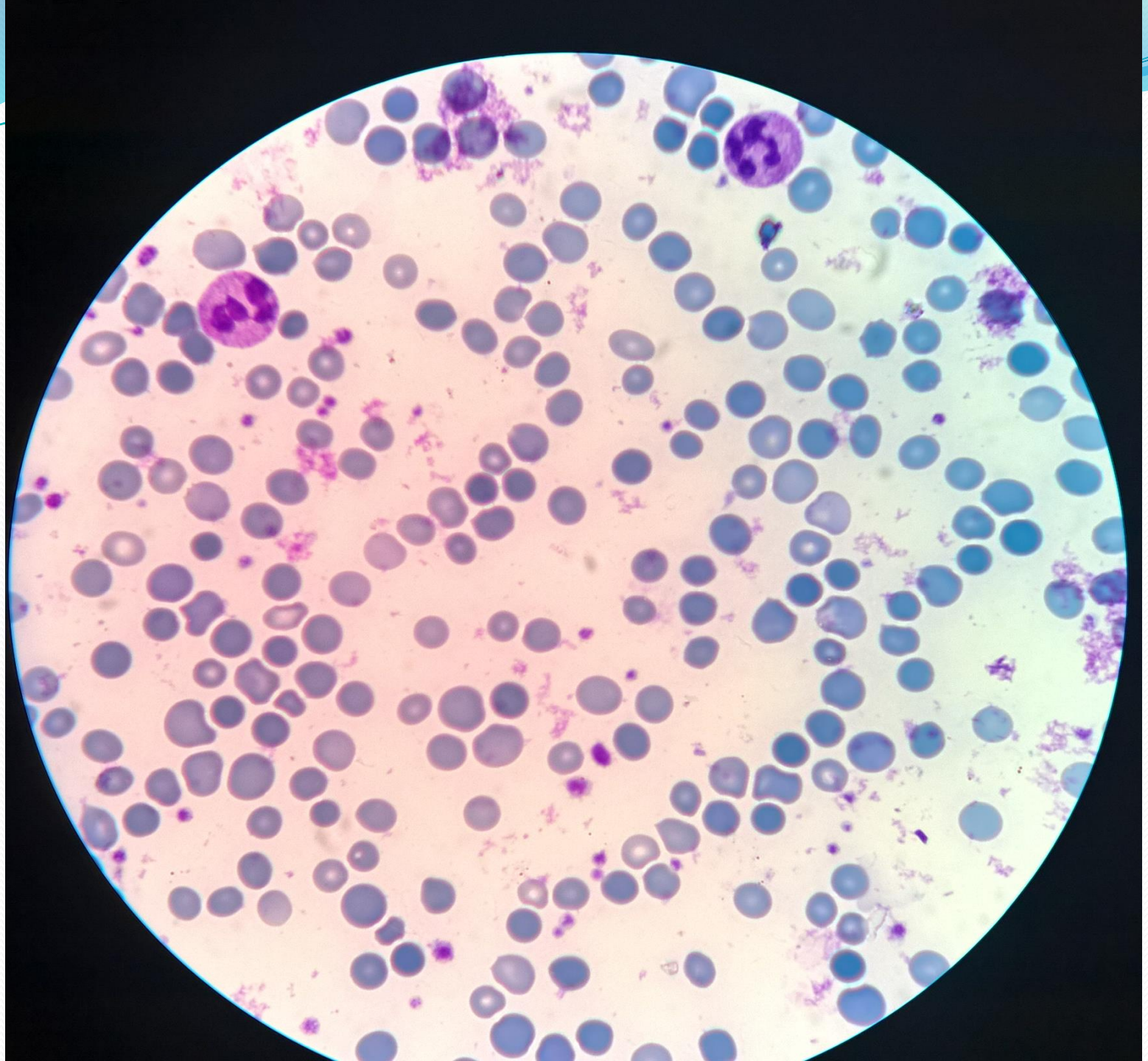
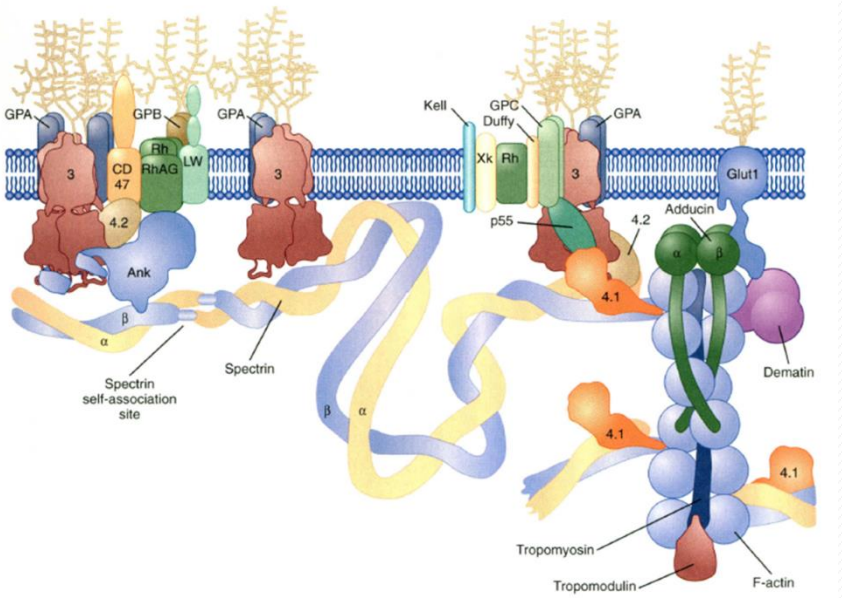
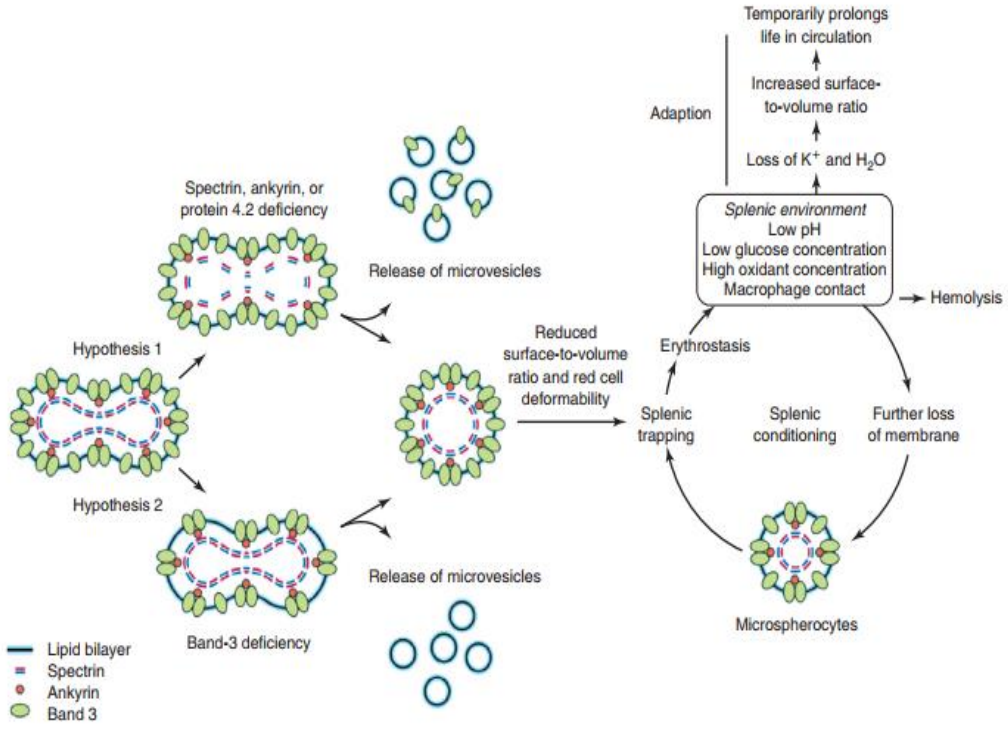


Figure 1-2 Approach to the Diagnosis of Anemia by MCV and Reticulocyte Count.




GPA
GPB
GPA
Kell
GPC
Duffy
GPA
3
CD
47
Rh
RhAG
LW
3
Xk
Rh
3
Glut1
4.2
p55
4.2
Adducin
Ank
α
β
4.1
β
α
Spectrin
self-association
site
Spectrin
Dematin
4.1
4.1
Tropomyosin
Tropomodulin
F-actin


Temporarily prolongs
life in circulation
Adaption
Increased surface-
to-volume ratio
Loss of K+ and H2O
Splenic environment
Low pH
Low glucose concentration
High oxidant concentration
Macrophage contact
Hemolysis
Spectrin, ankyrin, or
protein 4.2 deficiency
Release of microvesicles
Hypothesis 1
Reduced
surface-to-volume
ratio and red cell
deformability
Erythrostasis
Splenic
trapping
Splenic
conditioning
Further loss
of membrane
Hypothesis 2
Release of microvesicles
Band-3 deficiency
Microspherocytes
Lipid bilayer
Spectrin
Ankyrin
Band 3

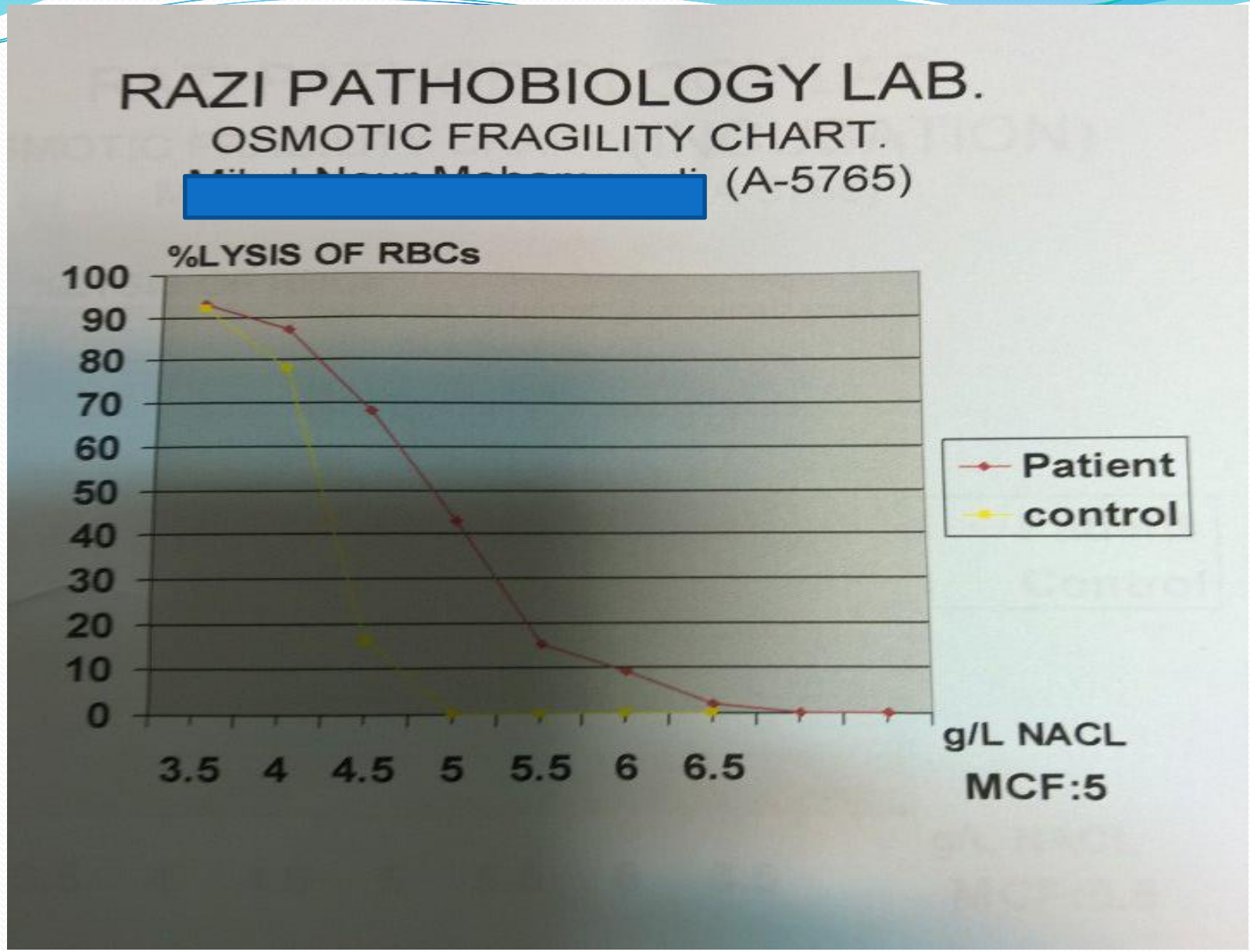

RAZI PATHOBIOLOGY LAB.
OSMOTIC FRAGILITY CHART.
(A-5765)
%LYSIS OF RBCs
100
90
80
70
60
50
40
30
20
10
0
3.5
4
4.5
5
5.5
6
6.5
Patient
control
g/L NACL
MCF:5

Table 485.2 Clinical and Laboratory Classification of Hereditary Spherocytosis

	NORMAL	MILD SPHEROCYTOSIS	MODERATE SPHEROCYTOSIS	MODERATELY SEVERE SPHEROCYTOSIS	SEVERE SPHEROCYTOSIS*
Inheritance	—	Autosomal dominant	Autosomal dominant, de novo mutation	Autosomal dominant, de novo mutation	Autosomal recessive
Proportion of hereditary spherocytosis cases	—	≈20–30%	≈60–70%	≈10%	<5%
Hemoglobin (Hb, g/dL)†	11.5-16‡	10.5-15	8-12	6-8	<6
Reticulocytes (%)†	0.5-1.5	1.5-6	≥6	≥10	≥10
Bilirubin (mg/dL)†,§	0-1	0.5-2	≥2	≥2	≥3
Peripheral smear*	Normal	Mild spherocytosis	Spherocytosis	Spherocytosis	Spherocytosis ± poikilocytosis
Osmotic fragility (fresh)	Normal	Normal or slightly increased	Increased	Increased	Greatly increased
Osmotic fragility (incubated)	Normal	Usually increased	Increased	Increased	Greatly increased
MCHC (g/dL)[5]	32-36	34-37	34-38	35-39	
RDW (%)[5]	11-14	12-19	16-23	20-30	
Hb/MCHC*	0.38-0.41	0.35-0.40	0.29-0.33	0.18-0.28	
Hb/RDW[5]	0.95-1.05	0.7-1.0	0.48-0.74	0.16-0.35	
Serum transferrin receptor (nmol/L)[5]	18-25	30-65	80-125	100-150	
Erythropoietin (mIU/mL)[5]	7-16	9-30	25-90	30-300	
Membrane protein patterns (SDS-PAGE)¶	—	"Normal"# Slight ↓ spectrin Slight ↓ spectrin and ankyrin Slight ↓ band 3 and 4.2 Absent protein 4.2 and ↓ CD47	↓ Spectrin ↓ Spectrin and ankyrin ↓ Band 3 and protein 4.2 Absent protein 4.2 and ↓ CD47	↓ Spectrin ↓ Spectrin and ankyrin ↓ Band 3 and protein 4.2	↓↓ Spectrin ↓↓ Spectrin and ankyrin ↓↓ Band 3 and protein 4.2**
Transfusions	—	No	Sometimes required in infancy or with aplastic crisis	Occasionally with crises	Regular*
Splenectomy	—	Rarely, partial splenectomy††	Sometimes; consider partial splenectomy	Usually (6-9 yr)	Yes (>3 yr)

Chief Complaint: عدم تعادل :شکایت اصلی بیمار

Pt بیمار پسر ۱۲ ساله که از حدود ۷ روز قبل دچار عدم تعادل شده است که مادرش متوجه [illegible]

[illegible] بیمار با کمک [illegible] به بیمارستان مراجعه کرد. بیمار سابقه چنین علائمی را در حدود یک سال

History of Percent illness: تاریخچه بیماری فعلی: قبل نیز داشته است که [illegible]

بیمار [illegible] شدید بوده است و [illegible] ۲ [illegible]

[illegible]

Current Drugtherapy & Other Addiction: داروهای در حال مصرف و سایر اعتیادات

HTN : [illegible] Pale (+) اسهال شدید (−) CAP (−) خشونت صدا (−) زمین خوردن (+)

نام بیمار: **رضا [redacted]** سن : ۱۳ سال بیمه: تامین اجتماعی نام بخش :اورژانس – اتاق اول (– (R تاریخ انجام ۱۳۹۵/۰۷/۰۲

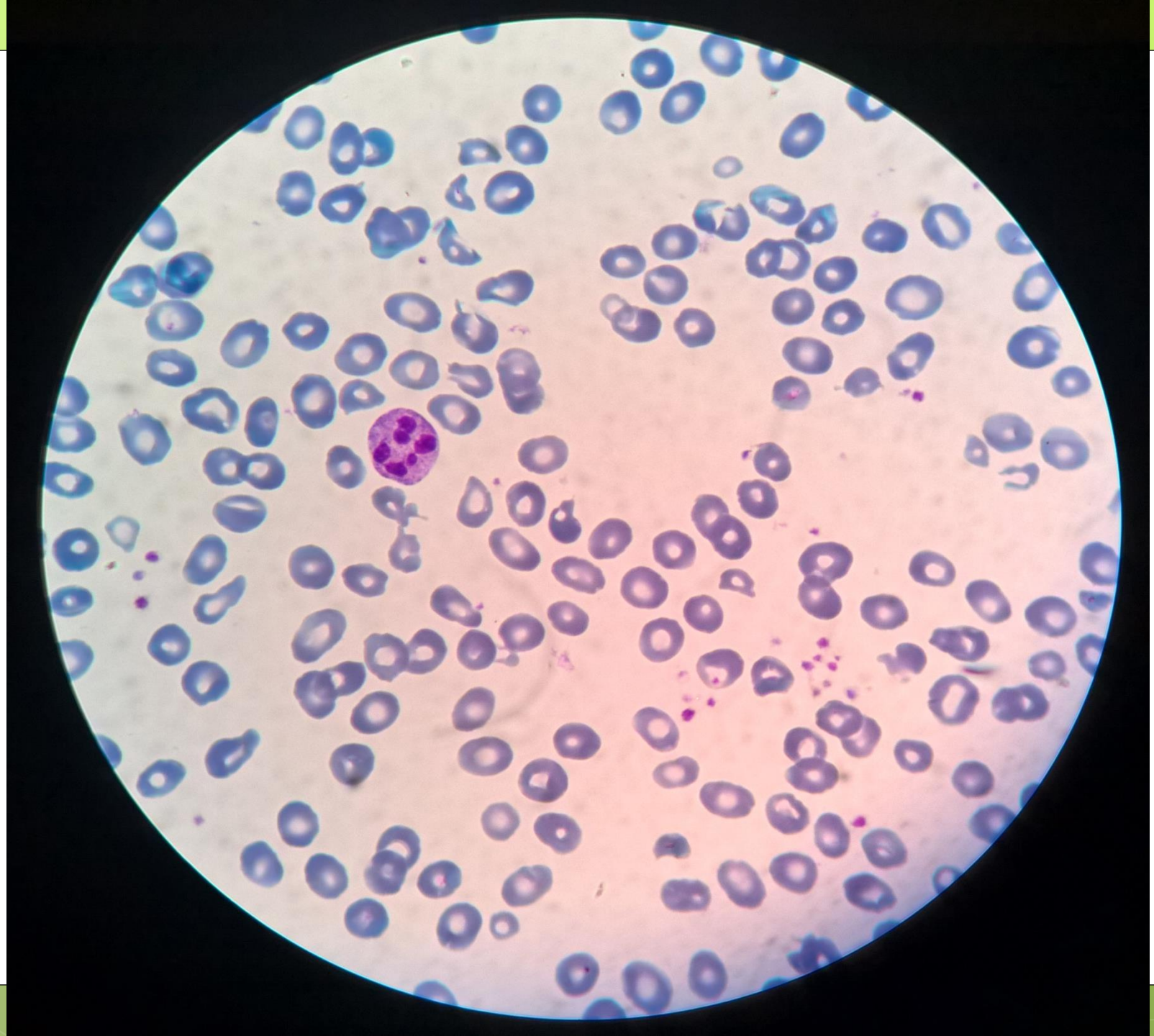
شماره : ۹۵۰۴۰۰۰۱۷۹ شماره پرونده : ۰۹-۹۲-۳۹ شماره سریال : ۹۵۰۰۲۶۶۲ **پزشک معالج:** دکتر صنعتی آگاه دکتر فینا

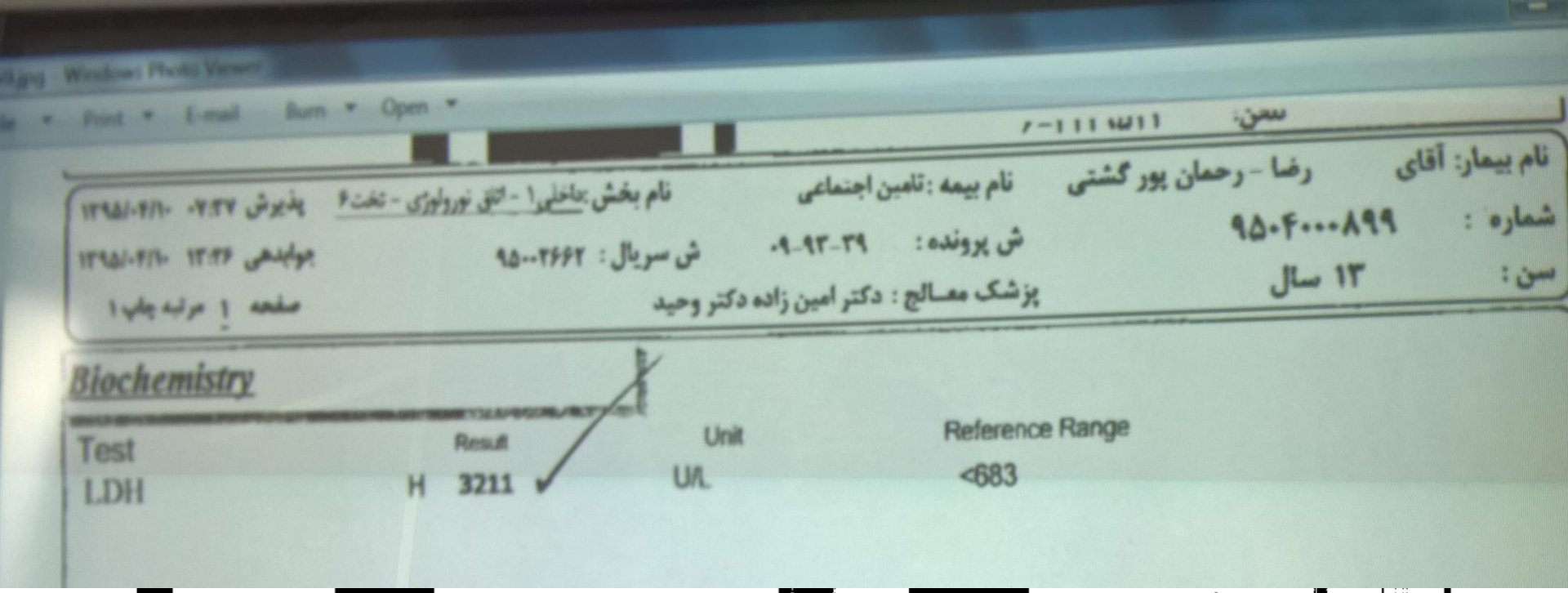
Hematology

Test		Result	Unit	Reference Range	Differential	
C						
BC		4400	/µL	4000 - 11000	Neutrophils	56
RC	L	2.36	MIL/µL	4.5-5.9	Lymphocyte	39
Hemoglobin	L	9.7	g/dL	11.5 - 14.5	Monocyte	2
Hematocrit	L	26.9	%	33 - 43	Eosinophil	3
MCV	H	113.98	FL	80-100	----------	----------
MCH	H	41.10	pg	27-32	Total	100%
MCHC		36.06	%	31-37		
Platelets		197000	/µL	150000 - 450000		
Hypochromia		Mild				
Anisocytosis		1+				
Poikilocytosis		Mild				
RDW	H	18.1	%	11.6 _ 14.6		
ESR 1st Hr		6	mm/hr	1-20		

Biochemistry

Test	Flag	Result	Unit	Reference Range
Blood Sugar		95	mg/dl	40 - 120
BUN		6	mg/dl	6 - 23
Creatinine		0.5	mg/dl	Infant : 5 - 18 Adult : 0.6 - 1.5 Infant : 0.2 - 0.4 Child : 0.3 - 0.7
Sodium,Na		137	mEq/L	135 - 145
Potassium,K		3.9	mEq/L	3.5 - 5.5
Calcium		8.6	mg/dl	8.6 - 10.3
Phosphor		4	mg/dl	Adult : 2.5 - 5.0 Child : 4.0 - 7.0
SGOT (AST)		28	IU/L	Up to 37
SGPT (ALT)		25	IU/L	Up to 40
Alkaline Phosphatase		315	U/L	180-1200
CPK		45	U/L	24 - 195





نام بیمار: آقای رضا - رحمان پور گشتی نام بیمه :تامین اجتماعی نام بخش :داخلی۱ - اتاق نورولوژی - تخت۶ پذیرش ۱۳۹۵/۰۴/۱۰ ۰۷:۳۷

شماره : ۹۵۰۴۰۰۰۸۹۹ ش پرونده : ۰۹-۹۳-۳۹ ش سریال : ۹۵۰۰۲۶۶۲ جوابدهی ۱۳۹۵/۰۴/۱۰ ۱۳:۴۶

سن : ۱۳ سال پزشک معالج : دکتر امین زاده دکتر وحید صفحه ۱ مرتبه چاپ ۱

Biochemistry

Test	Result	Unit	Reference Range
LDH	H 3211	U/L	<683

نام بیمار: آقای رضا - رحمان پور گشتی نام بیمه :تامین اجتماعی نام بخش :داخلی۱ - اتاق نورولوژی - تخت۶ پذیرش ۱۳۹۵/۰۴/۰۶ ۱۳:۴۷

شماره : ۹۵۰۴۰۰۰۵۳۱ ش پرونده : ۰۹-۹۳-۳۹ ش سریال : ۹۵۰۰۲۶۶۲ جوابدهی ۱۳۹۵/۰۴/۰۹ ۰۸:۰۰

سن : ۱۳ سال پزشک معالج : دکتر امین زاده دکتر وحید صفحه ۱ مرتبه چاپ ۱

Specific biochemistry

Test	Result	Unit	Reference Range
Vitamin B12	<83	pg/mL	<120 :deficient 120-160 :Borderline 160-950 :Normal

Megaloblastic anemia

- **Introduction**

  Megaloblastic anemias result from impaired DNA synthesis in hematopoietic cells and are characterized by macrocytosis with marked variation in the size and shape of RBCs, low reticulocyte count, hypersegmented neutrophils, and pancytopenia.

  Megaloblastic changes in the marrow include hypercellular marrow with an erythroid predominance, presence of giant pronormoblasts and metamyelocytes.
- Elevated LDH, elevated unconjugated bilirubin, low haptoglobin, may be seen.
- In more than 95% of cases, megaloblastic anemia is a result of folate and vitamin B12 deficiency

Megaloblastic anemia

- **Causes of vitamin B12 deficiency**
- inadequate intake

  nutritional deficiency(maternal dietary deficiency either during pregnancy or while breastfeeding, has had previous gastric bypass surgery or short gut syndrome)

Megaloblastic anemia

- **Causes of vitamin B12 deficiency**
- **defective absorption**

Congenital intrinsic factor deficiency
Juvenile pernicious anemia
Gastric mucosal disease, gastritis, gastric atrophy (i.e., Helicobacter pylori),
gastrectomy
Failure of absorption in small intestine
Defective cobalamin transport by enterocytes
Intestinal failure/resection
Celiac disease
Infection: HIV infection, parasites (Giardia lamblia, Diphyllobothrium latum, Plasmodium falciparum, and Strongyloides stercoralis)

Megaloblastic anemia

- **Causes of vitamin B12 deficiency**
- Defective transport

  Congenital TC II deficiency

  Transient deficiency of TC II

  Partial deficiency of TC I, haptocorrin deficiency
- defective metabolism.

Congenital

Adenosylcobalamin deficiency

Deficiency of methylmalonyl-CoA mutase

Combined adenosylcobalamin, methylcobalamin deficiencies:

Acquired

Liver disease

Protein malnutrition (kwashiorkor, marasmus)

Drugs associated with impaired absorption and/or utilization of vitamin B12 (e.g.salicylic acid, colchicine, neomycin, ethanol, oral contraceptive agents, and metformin)

Megaloblastic anemia

- **Clinical features of cobalamin deficiency**
- pallor, lethargy, fatigue, anorexia, sore red tongue and glossitis, and diarrhea.
- unexplained anemias, or cytopenias.
- Infants may show signs of developmental delay, weakness, irritability, and loss of developmental milestones, particularly motor development (head control, sitting); athetoid movements, hypotonia, and loss of reflexes occur.
- Older children may develop subacute combined degeneration of the spinal cord, resulting in signs of degeneration of the posterior and lateral columns with associated peripheral nerve loss. Loss of vibration and position sense with an ataxic gait and positive Romberg's sign. Paresthesia in the hands or feet,difficulty in walking and/or use of the hands may occur due to peripheral neuropathy.
- MRI findings include increased signals on T2-weighted images of the spinal cord, brain atrophy, and retarded myelination.
- Increased risk of vascular thrombosis due to hyperhomocysteinemia may occur.

Megaloblastic anemia

- **Diagnosis of cobalamin deficiency**
- a. Hemoglobin: anemia with inappropriately low absolute reticulocyte count.
- b. Red cell indices: MCV increased for age
- 2. White blood cell: leukopenia
- 3. Platelet count: moderately reduced
- 4. Blood smear: neutrophils show hypersegmentation); RBCs show macrocytes and macro-ovalocytes;anisocytosis, poikilocytosis with teardrop cells, presence of Cabot rings, HowellJolly bodies,

Megaloblastic anemia

- **Bone marrow:** megaloblastic appearance

- Markers of ineffective erythropoiesis:
  increased levels LDH, indirect bilirubin, ferritin, serum iron, transferrin saturation, and low serum haptoglobin

- Serum vitamin B12 level: not most sensitive diagnostic test hough levels <80 pg/mL almost always indicative of vitamin B12 deficiency (normal values 200-800 pg/mL).
- Homocysteine: nonspecific but elevated in vitamin B12 deficiency

Megaloblastic anemia

- Methylmalonic acid: more specific test for cobalamin deficiency.
- Elevated levels more sensitive to functional B12 deficiency.
- detailed dietary and GI history

assessing for factors that may affect gastric acidity or absorption.

- Laboratory evaluations
- assessment of serum methylmalonic acid, homocystein serum B12 levels,

GI evaluation may include assessment for parietal cell antibodies and/or endoscopy.

Megaloblastic anemia

Treatment

- Prevention: In conditions such as autoimmune gastritis, ileal resection prophylactic vitamin B12 should be prescribed.
- Active treatmen:
- daily doses of cyanocobalamin (25-100 µg) in either oral, intramuscular, or deep subcutaneous.

  After a week of daily dosing, weekly dosing may be given followed by transition to monthly doses.
- maintenance therapy can be started with monthly intramuscular injections in doses between 200- 1000-µg cyanocobalamin.


NODY.IR