

Folate and vitamin B₁₂ Assessment (243 points)

Note: Clinical values are reported to **one decimal place**; please report your final calculations accordingly. Must show calculations and units for full credit.

(1) Folate/folic acid deficiency anemia can be characterized by: (2 points)

- a) **High MCV and normal MCHC**
- b) normal MCV and low MCHC
- c) Low MCH and high Hct
- d) a and b only
- e) none of the above

(2) Lab tests/indices and specific clinical terms are used to both define the presence of anemia as well as provide morphological characteristics of blood cells which can then be used in ascribing or narrowing down possible cause(s) of the anemia. Match the test/indice or clinical term listed at left to the statements on the right. Note – each indice or term may have more than one letter match. (23 points)

RDW < B, I, U >	A. measure of the ave. size (ave. volume) of a RBC in the sample B. indice may be significantly influenced by any change in cell size
Poikilocytosis < M >	C. measure of the concentration of hemoglobin in whole blood D. a value used to establish clinical presence of anemia
Chromicity < L >	E. would be influenced by significant hemolysis of a blood sample F. value for the proportion of whole blood that are RBCs
Macrocytosis < N >	G. will ultimately always be altered in anemia H. indice for the ave. hemoglobin conc. per unit volume RBCs
MCHC < E, H >	I. measure of the size variation in a sample population of RBCs J. indicates that there are abnormal gases within the blood sample
Hemoglobin (HgB) < C, D, E, G >	K. indice for the ave. HgB amount in an ave. RBC L. term/value indicating the color intensity of RBCs
Microcytosis < R >	M. indicates there is variation in cell shape within a blood sample N. indicates the ave. RBC is abnormally large (>100 fL)
Anisocytosis < U >	O. is never observed or never changes with anemia P. indicates the presence of different HgB sub-types in the RBCs
MCV < B, D, E, F >	Q. refers to the presence of lysed cells within the blood sample R. indicates the ave. RBC is abnormally small (<80 fL)
Hematocrit (Hct) < B, D, E, F >	S. Term indicates an abnormal number of white blood cells T. indicates that the ave. RBC is of normal size (80-100 fL)
MCH < B, E, K, L >	U. indicates a variation in cell sizes within a blood sample

(3) Just over 2 weeks ago (15 days ago), a 38 yr. old male subject presented with complaints of “tiredness” and that he “fatigues easily” with any simple exertion. At that time a blood sample was taken his CBC values were: RBCs = 3.94×10^{12} cells/L Hct = 41.6% HgB = 10.3 g/dL (25 points)

Based on these values, was he anemic? (Yes / No) (1 pt)

Based on: Low Hct / **Low HgB** / neither (both Normal) (1 pt) (1 pt) Severity = **Mild**

Using the values listed above, what were his values for: [Show calculations, 6 points]

$$\text{MCV} = (0.416) / (3.94 \times 10^{12}) \\ = 105.6 \text{ fL}$$

$$\text{MCH} = [(10.3 \text{ g/dL}) / (3.94 \times 10^{12})] \times 10 \\ = 26.1 \text{ pg}$$

$$\text{MCHC} = (10.3 \text{ g/dL}) / (0.416) \\ = 24.8 \text{ g/dL}$$

RBC Morphology (circle ALL that apply): microcytic / normocytic / **macrocytic**
[1 pt.each] **hypochromic** / **normochromic** / hyperchromic

In reviewing his health history, you learn that he is a habitual 2 pack/day smoker. Which of the indices could be affected by this? (Circle only those that could be affected) (5 points)

Hct HgB MCV MCH MCHC **All could be affected**

He also reported that he started on a new diet about 2 months ago. Additional blood work just completed provided the following values:

Serum Folate = 5.8 nmol/L

RBC Folate = 253 nmol/L

In addition, results indicate significant elevations in his serum methylmalonic acid concentration.

Based on the older and most recent information and data, describe and discuss his current folate and B12 status – including any/all contributing factors. (9 points)

High MCV, low serum folate and low RBC folate indicates that he is folate deficiency. Also, high MCV and high MMA indicate he is vitamin B12 deficiency. His Hct value, 41.6%, is normal and HgB value (10.3g/dL) is little lower than normal range.

However, his serum folate and RBC folate indicate he is folate deficiency. His low HgB and macrocytic MCV show he is folate deficiency anemia.

Smoking increases Hct and HgB, decrease serum & RBC folate concentration, and RBC folate is long-term. Although serum folate is short-term, he is still in deficiency range.

(4) A 27 yr. old female has recently (1 week ago) returned after spending 20 months in the Swiss Alps. She has returned early from her assignment, complaining of stress, fatigue and weight loss, and during the last several months, had increased her smoking to about 2 packs per day (up from less than 1 pack per day before she left). As part of her monitoring, the following data have been collected: (33 points)

	<u>HgB (g/dl)</u>	<u>RBC# ($\times 10^{12}$)</u>	<u>MCV [\pm SD] (fL)</u>	<u>Serum Folate (nmol/L)</u>
24 months ago (prior to going abroad)	13.6	4.41	91.3 [11.22]	20.4
16 weeks ago	12.4	4.07	96.8 [15.64]	7.6
8 weeks ago	10.4	3.72	100.4 [15.13]	6.3
4 weeks ago	8.2	3.44	108.7 [14.88]	5.1

Current 7.9 3.38 110.3 [13.52] 10.5

What were her Hct values at the indicated time points? (10 pts)

$$\begin{aligned}
 24 \text{ mo. ago} &= [(91.3\text{fL}) \times (4.41 \times 10^{12})] / 10 = \mathbf{40.3\%} & 16 \text{ wks ago} &= [(96.8\text{fL}) \times (4.07 \times 10^{12})] / 10 = \mathbf{39.4\%} \\
 8 \text{ wks. ago} &= [(100.4\text{fL}) \times (3.72 \times 10^{12})] / 10 = \mathbf{37.3\%} & 4 \text{ wks ago} &= [(108.7\text{fL}) \times (3.44 \times 10^{12})] / 10 = \mathbf{37.4\%} \\
 \text{Current} &= [(110.3\text{fL}) \times (3.38 \times 10^{12})] / 10 = \mathbf{37.3\%}
 \end{aligned}$$

Is she currently anemic? (**Yes** / No) (1 pt) Based on: low Hct / **low HgB** / both normal (1 pt)

(1 pt) Severity = **Severe**

$$\begin{aligned}
 (7.9\text{g/dL} \times 10) / (3.38 \times 10^{12}) &= 23.4 \text{ pg} \\
 (7.9\text{g/dL}) / (0.373) &= 21.2 \text{ g/dL}
 \end{aligned}$$

Describe her current RBC Morphology (circle all that apply):

microcytic / normocytic / **macrocytic**
hypochromic / normochromic / hyperchromic

What were her RDW values at the indicated time points (10 Points)

$$\begin{aligned}
 24 \text{ mo. ago} &= (11.22 \times 100) / 91.3\text{fL} = \mathbf{12.3\%} & 16 \text{ wks ago} &= (15.64 \times 100) / 96.8\text{fL} = \mathbf{16.2\%} \\
 8 \text{ wks. ago} &= (15.13 \times 100) / 100.4\text{fL} = \mathbf{15.1\%} & 4 \text{ wks ago} &= (14.88 \times 100) / 108.7\text{fL} = \mathbf{13.7\%} \\
 \text{Current} &= (13.52 \times 100) / 110.3\text{fL} = \mathbf{12.3\%}
 \end{aligned}$$

Evaluate her current status taking into account all factors (8 points) (You may attach extra paper if you need more space.)

Her serum folate continuously decreased because she had increased smoking to about 2 packs per day. Increased smoking will also increase Hct and HgB, and decrease serum folate and RBC folate. Her MCV is gradually increased as serum folate decreases due to folate deficiency. The ability of cells dividing less results decrease number of RBC and increase size of RBC.

(5) You are monitoring a 53 yr. old male who began taking a drug with known Folate antagonist (“antifolate”) properties 8 weeks ago and is now half way through his treatment regimen. (21 points)

His current lab values are:

$$\begin{aligned}
 \text{MCV} &= 103.7 \text{ fL (SD} = 16.3 \text{ fL)} & \text{RBC\#} &= 3.94 \times 10^{12} & \text{MCH} &= 32.6 \text{ pg.} \\
 \text{Serum Folate} &= 6.5 \text{ nmol/L} & \text{RBC Folate} &= 210.3 \text{ nmol/L}
 \end{aligned}$$

Based on these values, complete the questions below (show calculations and units)

(2 pt) What is his Hct value?
 $(103.7 \times 10^{-15}) \times (3.94 \times 10^{12})$
 $= \mathbf{40.9\%}$

(2 pt) What is his HgB value?
 $[(32.6 \times 10^{12}) \times (3.94 \times 10^{12})] / 10$
 $= \mathbf{12.8 \text{ g/dL}}$

(2 pt) What is his MCHC value?
 $[(32.6\text{pg}) / (103.7 \text{ fL})] \times 100$
 $= \mathbf{31.4\%}$

(2 pt) What is his RDW value?
 $[(16.3 \times 100) / 103.7 \text{ fL}]$
 $= \mathbf{15.7\%}$

(2 points) Describe his current RBC Morphology (circle all that apply):

microcytic / normocytic / **macrocytic**
hypochromic / **normochromic** / hyperchromic

Is he currently anemic? (**Yes** / No) (1 pt) Based on: **low Hct** / **low HgB** / both normal (1 pt)

Is there evidence that he has been compliant in taking the medication with anti-folate properties? (4 pts)

Both serum folate and RBC folate indicate folate deficiency. The value for Hct and HgB are both lower than the normal range, which shows macrocytic morphology (long-term) is caused by folate deficiency. Also, serum and RBC folate concentrations are low due to decreased number of RBC and increase size of RBC.

Given that his treatment is scheduled to continue for 9 more weeks, should an RBC synthesis stimulating drug (eg. Erythropoietin / 'Procrit') be prescribed (briefly discuss why / why not)? (5 pts)

Yes, RBC synthesis stimulating drug should be prescribe. His RBC value is 3.94×10^{12} , which is lower than the normal range, $4.7 \times 10^{12} - 6.1 \times 10^{12}$. Both Hct and HgB are low, which also indicates anemia. Symptoms of anemia are muscle weakness, sleepiness, dizziness, and more. Continuing medication would further decrease folate and RBC, therefore Procrit is needed for his treatment.

(6) Data sets for 3 adult non-pregnant females is presented below. Match the data set to the most logical corresponding nutritional situation as listed below. (9 points)

Data set 1: MCV = 97.6 fL HgB = 11.8 g/dL MMA = 71 nmol/L (3 pt) Situation = **C**

RBC Folate = 256 nmol/L HoloTC = 43 pmol/L ser Folate = 5.9 nmol/L Hcyst = 17 mmol/L

Data set 2: MCV = 97.8 fL HgB = 11.8 g/dL MMA = 277 nmol/L (3 pt) Situation = **A**

RBC Folate = 256 nmol/L HoloTC = 30 pmol/L ser Folate = 7.9 nmol/L Hcyst = 17 mmol/L

Data set 3: MCV = 103.4 fL HgB = 11.8 g/dL MMA = 71 nmol/L (3 pt) Situation = **B**

RBC Folate = 378 nmol/L HoloTC = 43 pmol/L ser Folate = 11.4 nmol/L Hcyst = 11 mmol/L

Situation **A** = Early B₁₂ Deficiency

Situation **B** = Recovering from Folate Deficiency Anemia

Situation **C** = Early Folate Deficiency

Situation **D** = Early B₁₂ Depletion

(7) 3 non-pregnant 35 yr.old female subjects have the following identical blood data (13 points)

RBC conc. = 4.0×10^{12} /L MCV = 85 fL HgB = 13.1 g/dL Hct = 38% RDW = 11.8%

Unique aspects for each subject are:

Subj. A: ser Folate = 7-8 nmol/L; RBC Folate = 340 nmol/L; (+) Antibodies against IF; smokes

Subj. B: ser Folate = 11-14 nmol/L; RBC Folate = 420 nmol/L; Kidney disease

Subj. C: ser Folate = 10-12 nmol/L; RBC Folate = 380 nmol/L; takes asthma medication

All 3 are about to start an experimental Folate deficient diet. Given the above information, answer and briefly discuss the following questions:

Which subject would you predict to display abnormal RBC indices and/or display clinical Anemia first?

(1 pt) Subject: **A** (12 pts) Why?

A has lowest serum and RBC folate deficiency. Smoking decreases serum and RBC folate concentration. (+) Antibodies against IF affect absorption of vitamin B12. Folate deficiency results in increase RBC size and decrease in number of cells.

B and C have higher serum and RBC folate deficiency than A.

(8) Data for 6 patients is presented below: (24 points)

Patient (gender) (%)	s Folate (nmol/L)	RBC Folate (nmol/L)	Homocys (mmol/L)	HgB (g/dL)	MCV (fL)	HoloTC (pmol/L)	s B ₁₂ (pmol/L)	s MMA (pmol/L)	RDW (nmol/L)
Al (m)	5.7	307	14.8	14.2	93.7	43	357	104	13.4
Bert (m)	12.5	368	18.3	8.2	108.6	29	123	284	13.4
Nan (F)	16.8	353	8.4	9.4	103.2	44	298	86	19.2
Mark (m)	5.8	258	17.2	13.6	96.1	44	306	93	15.8
Jill (preg)	13.2	398	7.6	8.6	84.5	42	322	124	12.1
Lucy (F)	9.1	318	12.4	13.4	91.8	32	187	237	12.2

Possible diagnosis:

Early depletion/depletion stage (Folate)	Early depletion/depletion stage (B ₁₂)
Early Deficiency stage (Folate)	Early Deficiency stage (B ₁₂)
Anemia from Folate deficiency	Anemia from B ₁₂ deficiency
Recovering from Folate Deficiency Anemia	Recovering from B ₁₂ Deficiency Anemia
Moderately Anemic (but NOT from Folate or B ₁₂ deficiency)	

Based on all the above data, write the “most consistent” diagnosis (choose from diagnosis listed above) with respect to their lab values next to the patient name. Also, indicate whether each patient should have the following tests done. (24 Points)

Patient	Diagnosis (from choices above)	Test for Intrinsic-Factor Antibodies (IF-Abs) Yes or No	Test for Renal (Kidney) Function Yes or No
Al (m)	Early depletion (Folate)	NO	No
Bert (m)	Anemia from B12 deficiency	YES	YES
Nan (F)	Recovering from folate; Deficiency anemia	NO	NO
Mark (m)	Early deficiency stage (Folate)	YES	YES
Jill (Preg)	Moderately Anemic	NO	NO

Lucy (F)	Early depletion (B12)	YES	YES
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Finally, one of the 3 patients is vitamin B₁₂ deficient. Who is it? **Bert** (2 pts)

(9) You are monitoring the progress of 3 patients (Bill, Greg, and Joan). Joan is suffering from a chronic folate deficiency anemia, Bill is recovering from surgery after a traumatic motorcycle accident, while Greg is being monitored following the accidental, prolonged ingestion (over a 5 week period) of a potent Folate antagonist almost 2 months ago. (29 points)

You have the data sets below. Unfortunately, the patient codes were not attached. Based on these data sets, deduce which describes the condition and thus identify the likely patient for that data set.

Data set A: HgB = 12.3g/dL Hct = 40.3% RBC# = 4.02×10^{12} RDW = 19.5%

(1 pt) $MCV = (0.403) / (4.02 \times 10^{12}) = 100.2 \text{ fL}$ (1 pt) $MCHC = (12.3\text{g/dL}) / 0.403 = 30.5\%$

(3 pts) Anemia (**yes** / no) Based on: **low Hct** / **low HgB** / both normal

RBC Morphology (circle all that apply): microcytic / normocytic / **macrocytic** (1 pt)
hypochromic / **normochromic** / hyperchromic (1 pt)

Serum Folate = 13.3 nmol/L
Serum MMA = 87 nmol/L

RBC Folate = 337 nmol/L
Serum Hcyst = 12.7 nmol/L

(2 pts) Probable patient = **Greg**

Data set B: HgB = 9.2g/dL Hct = 30.4% RBC# = 2.81×10^{12} RDW = 16.3%

(1 pt) $MCV = 0.304 / (2.81 \times 10^{12}) = 108.2 \text{ fL}$ (1 pt) $MCHC = (9.2 \text{ g/dL}) / 0.304 = 30.3\%$

(3 pts) Anemia (**yes** / no) based on: **low Hct** / **low HgB** / both normal

RBC Morphology (circle all that apply): microcytic / normocytic / **macrocytic** (1 pt)
hypochromic / **normochromic** / hyperchromic (1 pt)

Serum Folate = 4.7 nmol/L
Serum MMA = 293 nmol/L

RBC Folate = 194 nmol/L
Serum Hcyst = 19.3 nmol/L

(2 pts) Probable patient = **Joan**

Data set C: HgB = 10.7g/dL Hct = 31.4% RBC# = 3.92×10^{12} RDW = 12.7%

(1 pt) $MCV = 0.314 / (3.92 \times 10^{12}) = 80.1 \text{ fL}$ (1 pt) $MCHC = 10.7\text{g/dL} / 0.314 = 34.1\%$

(3 ptS) Anemia (**yes** / no) based on: **low Hct** / **low HgB** / both normal

RBC Morphology (circle all that apply): microcytic / **normocytic** / macrocytic (1 pt)
hypochromic / **normochromic** / hyperchromic (1 pt)

Ser Folate = 15.3 nmol/L RBC Folate = 457 nmol/L ser MMA = 71 nmol/L ser Hcyst = 7.4 nmol/L
(2 pts) Probable patient = **Bill**

(10) The 3 women below are part of a study examining a new, strict diet. At the start of the study, the following data was collected for each woman:

	Hct (%)	HgB (g/dL)	RDW (%)	MCV (fL)	(nmol/L) RBC Folate	(nmol/L) Ser. Folate	(16 points) (mmol/L) Ser Homocyst.
Sally	41	13.6	12.7	92	394	15.2	11.2
Hillary	45	13.2	11.6	87	423	19.4	6.8
Louise	43	15.4	11.3	82	408	13.2	7.7

The following data was collected on Day 60 of the diet trial:

	Hct (%)	HgB (g/dL)	RDW (%)	MCV (fL)	(nmol/L) RBC Folate	(nmol/L) Ser. Folate	(mmol/L) Ser Homocyst.
Sally	37	12.3	16.6	99	343	12.5	17.8
Hillary	42	12.2	14.8	96	384	12.1	9.7
Louise	37	13.4	15.7	94	341	16.3	13.4

Describe any problem or risk of this new diet (4 pts)

This new diet decreased folate concentration, Hct, and HgB. Also, it increased MCV, which indicate macrocytic morphology and folate deficiency anemia.

Based on the data, which woman (if any) would you expect to become anemic first? (1 pt)

Sally

Why? (Provide data to substantiate your answer) (3 pts)

Sally would become anemic first because she has the lowest Hct and HgB value. Also, her RBC folate concentration is low, which indicates long-term status.

Diet histories indicate that one of the women may have had marginal B₁₂ status at the start of the study and that inadequate (low) B₁₂ intake has likely persisted through this 60 day time. Based on the data, which woman is most likely to be the one with chronic, inadequate B₁₂? (1 pt)

Sally

Why? (3 pts)

Sally is most likely to be the one with chronic, inadequate B12 because her Ser Homocyst concentration is highest compare to others concentration. Ser Homocyst concentrate indicates low folate or low B12.

The technician doing the sample analysis informs you that one of the day 60 serum samples had evidence of hemolysis, but is not sure which patient sample it was. Based on the above, whose day 60 sample is the most likely to have hemolysis? (1 pt)

Louise

Why? (3 pts)

Louise is most likely to have hemolysis because her hemolysis will decrease Hct. Her Hct value is reduced the most compare to other's Hct value. Also, hemolysis increases serum folate.

(11) You are involved with a 57 yr. old female patient who presented 2 weeks ago with complaints symptomatic for anemia. At that time, blood tests were done as indicated in the table below. Current, follow-up blood test data is also presented. Calculate and insert the blood indice data in the table, and answer the questions that follow. (40 points)

Indice	2 wks ago	Current		Indice	2 wks ago	Current
RBC # ($\times 10^{12}/L$)	3.22	3.29		MCV (fL)	103.7	99.1
HgB (g/dL)	9.2	9.0		MCH (pg)	28.6	27.4
Hct (%)	33.4	32.6		MCHC (g/dL)	27.5	27.6
RDW (%)	16.3	16.4				

(3 pts) 2 wks ago: Anemia (**yes** / no) based on: **low Hct** / **low HgB** / both normal

RBC Morphology: (microcytic / normocytic / **macrocytic**) (1 pt)

(**hypochromic** / **normochromic** / hyperchromic) (1 pt)

(3 pts) Currently: Anemia (**yes** / no) based on: **low Hct** / **low HgB** / both normal

RBC Morphology: (microcytic / **normocytic** / macrocytic) (1 pt)

(**hypochromic** / **normochromic** / hyperchromic) (1 pt)

Blood tests evaluating Folate and vit.B₁₂ were done 2 weeks ago. At that time, she was prescribed daily, oral tablets for BOTH Folate and vit. B₁₂. She is adamant that she has been taking the daily supplements exactly as prescribed. Her 2 week old and current Folate and vit.B₁₂ data are provided below. Fill-in the evaluative data and answer the questions that follow. (8 Points)

Test	2 wks ago	Status	Current	Status
Ser. Folate (nmol/L)	10.7	Depletion	18.4	Normal
RBC Folate (nmol/L)	203	Deficiency	224	Deficiency
tHcy (mmol/L)	17.7	Deficiency	16.8	Deficiency
Ser. B ₁₂ (pmol/L)	126	Deficiency	129	Deficiency

What is the evidence that she has been compliant in taking the supplements (as she claims)? (4 pts)

After taking daily supplements, her serum folate greatly increased. Currently, her serum folate status became normal. Her RBC folate and Ser. B12 also increased and tHcy decreased.

What is your overall interpretation of her condition AND your plan for further TESTS and course of action? (6 pts)

Although her daily supplements increased serum folate to normal range, RBC folate, tHcy and Ser. B12 are deficiency that still needs to be improved. Further test, such as schilling test and Antibody test can be used to measure B12 absorption, or treatment with B12 injection. Also, continuous monitoring is necessary.

- (12) In evaluating values and indices during the progression leading to folate deficiency anemia in an adult male, which of the following sequences is/are correct? (2 pts)
- a) low folate intake **g** decrease serum folate **g** decreased RBC folate **g** an RDW = 17.7%
 - b) a prolonged RBC folate concentration of 260 nmol/L would lead to an elevated MCV
 - c) acute renal failure as well as liver disease would result in further decreases in serum Folate
 - d) all of the above
 - e) **a and b only**
- (13) Which of the following is/are consistent with Folate deficiency anemia in an adult female? (2 pts)
- a) an MCV = 106 fL and a Hct = 30%
 - b) an MCV = 108 fL and a HgB value = 11.2 g/dL
 - c) a serum folate concentration = 5.2 nmol/L and an RBC Folate conc. = 213 nmol/L
 - d) **all of the above**
 - e) a and b only
- (14) Concerning the inter-relationships and distinctions between folate and vitamin B₁₂, which of the following statements is/are true? (2 pts)
- a) a lack or low amount of B₁₂ can result in a functional folate deficiency because the folate becomes metabolically “trapped” in an inactive form
 - b) the anemia blood cell indices resulting from either a folate or B₁₂ deficiency can present identically
 - c) measurement of methylmalonic acid can establish that B₁₂ is the main (primary) nutrient underlying the deficiency if the MMA level is <100 pmol/L
 - d) all of the above
 - e) **a and b only**
- (15) Results from a blood smear analysis state a finding of anisocytosis with hypochromacia. Based on these observations, which of the following indice values would you expect? (2 pts)
- a) an RDW of 25.2% with an MCHC = 38 g/dL
 - b) an MCV = 78 fL and HgB = 10 g/dL
 - c) **an RDW of 20.4% with an MCHC = 27 g/dl**
 - d) a and b only
 - e) none of the above