The ABCs of the CBC

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Disclosures

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Objective

To develop an efficient approach to interpret the information contained in the CBC in assessing hematological and systemic diseases
Elements of the Complete Blood Count
Healthy 71 year old male

- **WBC**: 7.1×10⁹/L (4.5-11)
- **Hb**: 155 g/L (130-180)
- **Hct**: .455 (.4 -.52)
- **RBC**: 5.1×10¹²/L (4.4-5.9)
- **MCH**: 30.6 pg (26-34)
- **MCV**: 90 fL (80-98)
- **MCHC**: 340 g/L (320-365)
- **RDW**: 12 (11.4-14.4)
- **Plt**: 310×10⁹/L (140-440)
- **MPV**: 11 fL (10-14)
## Elements of the Complete Blood Count

Healthy 71 year old male

<table>
<thead>
<tr>
<th>Element</th>
<th>Value</th>
<th>Normal Range</th>
</tr>
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<tbody>
<tr>
<td>WBC</td>
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<td>310×10⁹/L (140-440)</td>
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</tr>
<tr>
<td>Neut</td>
<td>57.7% 4.1×10⁹/L</td>
<td></td>
</tr>
<tr>
<td>Lymph</td>
<td>33.8% 2.4×10⁹/L</td>
<td></td>
</tr>
<tr>
<td>Mono</td>
<td>5.6% 0.4×10⁹/L</td>
<td></td>
</tr>
<tr>
<td>Eos</td>
<td>1.4% 0.1×10⁹/L</td>
<td></td>
</tr>
<tr>
<td>Baso</td>
<td>1.4% 0.1×10⁹/L</td>
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</table>
Forgive the rant...

• Manitoba Health regulations prohibit the ordering of laboratory tests in panels
  • e.g. liver enzymes must be ordered separately:
    • AST, ALT, alk phos, GGT
• EVEN THOUGH all the CBC results are generated by the instrument automatically, MB Health does not permit private labs to report anything you didn’t order
• SO UNTIL WE CAN FIX THIS, please order Hb, WBC, platelets, red cell indices (ie. MCV), and auto diff every time. IT COSTS NO EXTRA
Peripheral Blood Smear - normal
Case 1: 44 y.o. man with fatigue and easy bruising

- WBC: 1.1×10^9/L
- Hb: 55 g/L
- RBC: 1.6×10^{12}/L
- Hct: 0.162
- MCV: 99 fL
- MCH: 33.7 pg
- MCHC: 340 g/L
- RDW: 12
- Plts: 13×10^9/L
Case 1: 44 y.o. man with fatigue and easy bruising

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- **Hct**: .162
- **MCV**: 99 fL
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- **MCHC**: 340 g/L
- **RDW**: 12
- **Plts**: 13×10⁹/L

This man may have:

A. AML
B. Aplastic anemia
C. CHOP chemotherapy 12 days earlier
D. Myelodysplastic syndrome
E. Multiple myeloma
F. Burkitt’s lymphoma
G. Alcohol?
H. Any of the above
Rule of thumb #1:

look at all the values in the CBC

In this case ...

Pattern = pancytopenia (WBC, Hgb, platelets all low)

Interpretation:
• Probable marrow disorder, toxicity or infiltration
• Of the list, the least likely would be chemotherapy. With acute myelosuppression, hemoglobin would fall more slowly
Which of the following would you do next?

• CT chest and abdomen
• Blood smear
• Bone marrow biopsy
• LFTs
• Serum protein electrophoresis
• B12 level
• ferritin
Case 1: 44 y.o. man with fatigue and easy bruising

What would you do next?

- Blood smear
- Bone marrow biopsy
- LFTs
- Serum protein electrophoresis
- B12 level
- Ferritin

**WBC** 1.1×10⁹/L  
**Hb** 55 g/L  
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**Hct** .162  
**MCV** 99 fL  
**MCH** 33.7 pg  
**MCHC** 340 g/L  
**RDW** 12  
**Plts** 13×10⁹/L
What if the blood film looks like this?

“Peripheral blood smear reveals abundant nucleated red blood cells, and marked left shift including myelocytes, promyelocytes and blasts”
Rule of thumb #2

The peripheral smear can add a large amount of information in setting of:

• Pancytopenia
• Hemolytic anemia
• Marrow failure anemia
• Thrombocytopenia

• Peripheral smear is NOT useful in microcytic anemias (unless there is some other cytopenia or other problem going on).
Case 2

23 year old woman, feeling well

WBC  7.1 x 10^9/L
Hb   86 g/L (130-180)
Hct  0.29 (0.40-0.52)
MCH  21.3 pg
RDW 17 (11.4-14.4)
Plts 440 x 10^9/L

RBC  4.1 x 10^{12}/L (4.4-5.9)
MCV  71 fL (80-98)
MCHC 300 g/L (320-365)

This woman is most likely to have:
A. Thalassemia trait
B. Anemia of chronic disease
C. Iron deficiency
D. Aplastic anemia
Rule of thumb #3

Pay attention to the MCV

All microcytic anemias are caused by impaired hemoglobin synthesis:
• Iron deficiency
• Thalassemia
• Anemia of inflammation (due to iron sequestration => hypoferremia)
• Congenital sideroblastic anemia (for the zebra-lovers among you)
What investigation will you do now?

1. Serum Ferritin
2. Serum iron and TIBC
3. Hemoglobin electrophoresis
4. CRP
5. Referral for gastroscopy and colonoscopy
Case 3

23 year old woman, feeling well

WBC $7.1 \times 10^9$/L
Hb 116 g/L (130-180)
Hct .39 (0.40-0.52)
MCH 21.3 pg
RDW 15 (11.4-14.4)
Plts $240 \times 10^9$/L
RBC $5.4 \times 10^{12}$/L (4.4-5.9)
MCV 69 fL (80-98)
MCHC 300 g/L (320-365)

This woman is most likely to have:
A. Thalassemia trait
B. Anemia of chronic disease
C. Iron deficiency
D. Aplastic anemia
Rule of thumb #4

Pay attention to the RBC count (concentration)

A microcytic anemia with elevated RBC can be due to:
• Polycythemia with iron deficiency
• Thalassemia
Another common feature of iron deficiency anemia is that the platelet count is often elevated or high-normal
What investigation will you do now?

1. Serum Ferritin
2. Serum iron and TIBC
3. Hemoglobin electrophoresis
4. Review previous blood counts in eChart
5. Referral for gastroscopy and colonoscopy
Rule of thumb #5

The best biopsy is a chart biopsy

• The evolution of hematological variables tells a lot about what pathology is involved
• For example the microcytosis in thalassemia trait does not vary, while iron deficiency does
• A previously normal MCV rules out thalassemia trait as effectively – and much more cheaply – than specialized tests
Case 4

63 year old woman complains of fatigue, and stiff shoulders in the mornings. A CBC a year earlier was normal.

<table>
<thead>
<tr>
<th>Test</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>WBC</td>
<td>8.1 x 10^9/L</td>
</tr>
<tr>
<td>Hb</td>
<td>103 g/L</td>
</tr>
<tr>
<td>RBC</td>
<td>4.14 x 10^{12}/L</td>
</tr>
<tr>
<td>Hct</td>
<td>.33</td>
</tr>
<tr>
<td>MCV</td>
<td>80.3 fL</td>
</tr>
<tr>
<td>MCH</td>
<td>24.9 pg</td>
</tr>
<tr>
<td>RDW</td>
<td>14</td>
</tr>
<tr>
<td>Plts</td>
<td>403 x 10^9/L</td>
</tr>
</tbody>
</table>

This woman is most likely to have:

A. Thalassemia trait
B. Anemia of chronic disease
C. Iron deficiency
D. Myelodysplastic syndrome
## Case 4

<table>
<thead>
<tr>
<th>Iron Deficiency Anemia</th>
<th>Anemia of inflammation or chronic disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>Decreased serum iron</td>
<td>Decreased serum iron</td>
</tr>
<tr>
<td>Increased TIBC (=transferrin)</td>
<td>Decreased TIBC (=transferrin)</td>
</tr>
<tr>
<td>Decreased ferritin</td>
<td>Increased ferritin</td>
</tr>
<tr>
<td>Decreased marrow storage iron</td>
<td>Increased marrow iron in macrophages</td>
</tr>
</tbody>
</table>
Rule of thumb #6 (of sorts...)

Anemia of inflammation is most often normocytic or borderline microcytic, but hypochromic

- Inflammatory (mainly through IL-6) increases levels of hepcidin, and hepcidin causes sequestration of iron in macrophages, lowering serum iron, thus starving erythroid progenitors

- Since red cells last ~100 days, microcytosis takes months to occur (though reticulopenia occurs quickly).
Case 5

78 year old man complains of shortness of breath with walking, and stumbles often

WBC 3.7 x 10^9/L
Hb 70 g/L  RBC 1.58 x 10^{12}/L
Hct .20  MCV 130 fL
MCH 44.2 pg  MCHC 340 g/L
RDW 19
Plts 103 x 10^9/L

Which test(s) would be most useful?
A. Serum folate
B. Serum B12
C. Reticulocyte count
D. Blood smear
E. A look at the DPIN
Rule of thumb #7

MCV very high = megaloblastic anemia: check B12 and DPIN

Differential diagnosis
• B12 deficiency
• Folate deficiency, outside North America
• Antimetabolite drug therapy
  • Hydroxyurea, AZT, azathioprine, MTX

Neutrophils show hypersegmentation
All cell lines will go down but anemia is most pronounced
Case 6

67 year old woman who is pale and jaundiced

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>WBC</td>
<td>$4.7 \times 10^9/L$</td>
</tr>
<tr>
<td>Hb</td>
<td>97 g/L</td>
</tr>
<tr>
<td>Hct</td>
<td>.29</td>
</tr>
<tr>
<td>MCH</td>
<td>35.6 pg</td>
</tr>
<tr>
<td>RBC</td>
<td>$2.85 \times 10^{12}/L$</td>
</tr>
<tr>
<td>MCV</td>
<td>104 fL</td>
</tr>
<tr>
<td>MCHC</td>
<td>340 g/L</td>
</tr>
<tr>
<td>RDW</td>
<td>15</td>
</tr>
<tr>
<td>Plts</td>
<td>$203 \times 10^9/L$</td>
</tr>
</tbody>
</table>

What is the difference diagnosis here?
Rule of thumb #8

Mild macrocytosis has a broader differential diagnosis

- Early megaloblastic anemia
- Hemolysis (because reticulocytes are large)
- Myelodysplasia
- Liver disease (not necessarily anemic)
- Alcohol
- Some cases of myeloma, aplastic anemia, etc
- Hypothyroidism is on this list in some text books, but I’ve never seen it
Case 6

67 year old woman who is pale and jaundiced

WBC 4.7 x 10^9/L  
Hb 97 g/L  
RBC 2.85 x 10^{12}/L  
Hct .29  
MCV 104 fL  
MCH 35.6 pg  
MCHC 340 g/L  
RDW 15  
Plts 203 x 10^9/L

Which test(s) would be most useful?
A. Bone marrow  
B. Serum B12  
C. Reticulocyte count  
D. Blood smear  
E. Liver enzymes
Case 7

37 year old woman who is pale and jaundiced

WBC 6.7 x 10⁹/L
Hb 67 g/L
Hct .20
MCH 31.8 pg
RDW 16
Plts 303 x 10⁹/L

RBC 2.85 x 10¹²/L
MCV 95 fL
MCHC 340 g/L

Which test(s) would be most useful?
A. Bone marrow
B. Serum B12
C. Reticulocyte count
D. Blood smear
E. Liver enzymes
Rule of thumb #9

In normocytic anemia (and mildly macrocytic anemia), check the reticulocyte count AND get a blood smear

- Retic count distinguishes hemolytic from hypoproliferative anemias
- Blood smear sheds information about the specific process
Case 7

37 year old woman who is pale and jaundiced

WBC 6.7 x 10^9/L
Hb 67 g/L
Hct .20
MCH 31.8 pg
RDW 16
Plts 303 x 10^9/L
Retics 330 x 10^9/L

Which test(s) would be most useful?
A. Direct bilirubin
B. Total bilirubin
C. Haptoglobin
D. Blood smear
E. LDH
Rule of thumb #10

(*Especially) if reticulocyte count is elevated, check LDH, direct & total bilirubin, and haptoglobin
- Can be useful for normocytic anemia without a discernable cause)

Elevated retic count can be due to:
- Hemolysis
- Recover from
  - Acute blood loss
  - Nutrient deficiency (iron, B12)
  - Myelosuppression
Case 8

23 year old woman complains of bruising

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>WBC</td>
<td>6.7 x 10⁹/L</td>
</tr>
<tr>
<td>Hb</td>
<td>130 g/L</td>
</tr>
<tr>
<td>Hct</td>
<td>.38</td>
</tr>
<tr>
<td>RBC</td>
<td>4.1 x 10¹²/L</td>
</tr>
<tr>
<td>MCV</td>
<td>90 fL</td>
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</tr>
<tr>
<td>RDW</td>
<td>13</td>
</tr>
<tr>
<td>Plts</td>
<td>3 x 10⁹/L</td>
</tr>
</tbody>
</table>

What is the differential?

What do you want to know?
A. LDH
B. Retic count
C. Recent new medications
D. Blood smear
Rule of thumb #11

In severe, isolated thrombocytopenia, first
• Rule out platelet clumping
  (pseudothrombocytopenia)

Then consider
• Medications including tonic water
  • (p.s....its never the medication)
• ITP
Case 9

23 year old woman complains of bruising

WBC  6.7 x 10⁹/L
Hb   83 g/L   RBC  2.71 x 10¹²/L
Hct  .24    MCV  90 fL
MCH 30.6 pg  MCHC 340 g/L
RDW 15
Plts 43 x 10⁹/L

What do you want to know?
A. LDH
B. Retic count
C. Recent new medications
D. Blood smear
E. Creatinine
Rule of thumb #12

When platelets and hemoglobin are both low, consider:

- Microangiopathy (TTP, HUS)
- Rule out by blood film
- Thrombocytopenia-exacerbated bleeding with acute blood loss
Case 10

58 year old man complains of bruising

WBC 3.7 x 10⁹/L  
Hb 143 g/L 
Hct .43 
MCH 33.8 pg 
RDW 15 
Plts 83 x 10⁹/L 

What could be going on here??

What would you like to do?
Case 10

58 year old man complains of bruising

WBC  3.7 x 10^9/L  
Hb   143 g/L       
Hct  .43           
MCH  33.8 pg       
RDW  15            
Plts 83 x 10^9/L   

RBC  4.23 x 10^{12}/L  
MCV  102 fL           
MCHC 331 g/L

What do you want to know?
A. Medical History (?infection)  
B. Physical exam!  
C. Medications  
D. Liver enzymes and INR  
E. Blood smear
Rule of thumb #13

When platelets and WBC are both moderately low, think about hypersplenism
Objective

To develop an efficient approach to interpret the information contained in the CBC in assessing hematological and systemic diseases
Take Home Messages

1. Awesome medical diagnoses (not just hematologic ones) can be made just starting with the CBC

2. Order all components of the CBC, all of the time

3. Rid yourself of the MCH (and MCHC for the most part) and consider the algorithm provided

4. Focus on absolute values and not percents (%)
Questions?

rzarychanski@cancercare.mb.ca
Donald.houston@umanitoba.ca
1. A 23 year old Nigerian man has the following CBC:

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<tr>
<td>Hb</td>
<td>96 g/L</td>
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<tr>
<td>RBC</td>
<td>4.5×10¹²/L</td>
</tr>
<tr>
<td>Hct</td>
<td>.32</td>
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<tr>
<td>MCV</td>
<td>71 fL</td>
</tr>
<tr>
<td>MCH</td>
<td>21.3 pg</td>
</tr>
<tr>
<td>MCHC</td>
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<tr>
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<td>14.5</td>
</tr>
<tr>
<td>Plts</td>
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What is the likely diagnosis?

A. Thalassemia  
B. Iron deficiency  
C. ITP  
D. TTP  
E. There must be more than one diagnosis
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