So – you have this thing

Now what do you have to learn?

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Physicians knew all the answers and patients believed them. Not so much anymore.

<table>
<thead>
<tr>
<th>Used to be</th>
<th>Now a Days</th>
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<tbody>
<tr>
<td>Get a diagnosis</td>
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<tr>
<td>Cry</td>
<td>Cry</td>
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<tr>
<td>Go to church, temple, etc.</td>
<td>Go online &amp; search</td>
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<tr>
<td>Take the meds</td>
<td>Go for the roots &amp; berries</td>
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<tr>
<td>Do what the physician says</td>
<td>Argue – ask “why”</td>
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Physicians speak in medicales and only rarely in English

So

You have to learn medicales.
<table>
<thead>
<tr>
<th>Patient Words</th>
<th>Translation</th>
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<tbody>
<tr>
<td>fine</td>
<td>I don’t want this to be bad so you won’t mind if I skip a few salient details.</td>
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<tr>
<td>not bad</td>
<td>It really hurts like hell but I’m supposed to be brave (male)</td>
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<tr>
<td></td>
<td>It really hurts but I know no one pays attention to my complaining about pain so why tell (female)</td>
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<tr>
<td>I didn’t tell him</td>
<td>You’re the hot shot; go figure it out without telling you</td>
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<tr>
<td>because he didn’t ask</td>
<td></td>
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It takes two to miscommunicate

Physician Words
fine

Translations
It is not a surprise to me so I don’t have to explain why to you.

Let’s repeat it in a few weeks

I am not sure why this is here so let’s hope it goes away

That is my job

I can’t explain this in English
What is Jak-Stat?

Original name – just another kinase

The Janus kinase-signal transducer and activator of transcription (JAK-STAT) pathway mediates signaling by cytokines, which control survival, proliferation and differentiation of several cell types.

Constitutive JAK activation leads to persistent activation of STAT transcription factors.
WHAT????????
How does this sound:

JAK2 is a gene that turns on a series of actions that controls the production of blood cells and fibrocytes. When abnormal, control is lost and excessive numbers of cells are produced.
Under normal physiological circumstances when a ligand (for example - EPO) binds with a receptor, a conformational changes occurs. The JAK2 protein then makes contact with the cytoplasm domain of the receptor where it catalyzes tyrosine phosphorylation. This leads to the activation of signal transducers and transcription (STAT) molecules.
Erythropoietin chemically binds to a receptor controlled by JAK2. When the two are bound together, the cell becomes committed to making red blood cells.

If less erythropoietin, fewer cells should be made.

BUT – with the JAK2 (V617F) mutation, the STAT enzymes are always on, causing more cells to be made regardless of the amount of EPO. Over time, the mutation will cause damage to the platelets, granulocytes, and fibrocytes.
The US will not go along with the international system of concentration and values so

US really old 5,000 cells or 5K/cumm
US medium old 5.0x10³/µL or
Rest of world 5.0x10⁶/L
WBC – total number of white blood cells

- can bounce around within a +/- 3.0 range
- can double the neutrophils/granulocytes if fever, exercise, emotional stress, etc. are present
- suppressed by lots of cardiac meds such as ACE inhibitors (ex. Lisinopril) so don’t every let anyone say to you that things cannot be connected.
As MPN’s progress, the white cell count will wander erratically higher.

Clinical significance is hard to define since it can bounce so easily.

If out of the reference interval ~greater than 3.0x10^3/L is worthy of note.
Two different ways to describe the different white blood cells you see

a. percentage
   older form of differential
   identify the first 100 cells you see
   makes great comments about quality
   both an increase in one cell or a decrease in another cell line can look the same

b. absolute
   identifies between 10,000–50,000 cells
   variable on quality but superb on quantity
Follow the granulocytes/neutrophils for they are controlled by the same cell (common myeloid progenitor cell) as the red cells.

No immature forms should be seen although a once in a while an intermediate form (metamyelocyte) can be tolerated.
<table>
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<tr>
<th>Date</th>
<th>WBC</th>
<th>ANC</th>
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<tr>
<td></td>
<td>Ref. interval</td>
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<td>Value</td>
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You can count RBCs but no one takes that value seriously any more. There are better tests.

Hemoglobin – concentration of oxygen carrying protein
- can quantify the hemoglobin that has oxygen and the hemoglobins that do not (carboxyhemoglobin) or can not (carboxyhemoglobin)

remains consistent regardless of cell size
Hemoglobin – varies by gender, age and altitude

**Signs and symptoms of anemia**
- Around 10.0 g/ml (or 100 g/L in Canada)
- Pallor, shortness of breath, fatigue, etc

**Below 8g/dL or 80g/L (Canadian)**
- Damages organs due to lack of O₂
- Usually need transfusions
Hemoglobin – issues in over production

More cells make the blood more viscous (jello™ with a lot of fruit as opposed to clear jello™)

Over 15g in males and 14 g. in women

a. increased blood pressure – kidney damage and/or CVAs
b. increased cardiac stress – heart attack
c. increased fragility in blood vessels
d. best indicator of phlebotomy need
Hematocrit (HCT)

once upon a time – most accurate test in the clinical laboratory

now – we don’t perform it. We calculate it so not as accurate or reliable
Hematocrit is calculated from the MCV (average Red cell size) calculated.

If you know the average size of the cells, then you simply multiply the MCV by the RBC count and you get the hematocrit.
Hematocrit only makes sense if all the cells are the same size but as the RDW increases and the MCV decreases, it gets fuzzier.

When the RDW is greater than 20, the hematocrit is invalid so using the hemoglobin values is most consistent.
HEMOGLOBIN

How do you decrease viscosity?

1. lower the RBC absolute number
easiest method – phlebotomy

2. make them smaller
make them iron deficient
Hemoglobin

But wait (as the TV ads say)

if you phlebotomize someone, you make them iron deficient so, for a short time only, you can get damaged cells that are smaller and will not live as long AND you get an increase in smaller platelets!
Hemoglobin values will be lower in the evening (as much as 1 g/mL) probably due to changing levels of hydration, so try to have the blood specimen collection at the same time each time.
Chemistry values

Uric acid – waste product of nuclear metabolism
The more cell activity, the greater the number of waste products that must be cleared by the kidney

Too much – gout, kidney damage, joint pain

Keep your diet consistent – high protein meals increase uric acid concentration
Chemistry

LD (lactate dehydrogenase) – almost every cell in the body has this enzyme. When the cell is damaged/dies, the enzyme is released into the blood stream.

Increases in this suggest increased damage but you can’t use this when on meds.
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<th>PLT</th>
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Liver function studies
LD, bilirubin, alkaline phosphatase, ALT, GGT

- Bilirubin – either liver damage or hemolysis
- Alkaline phosphatase – bone, GI tract, liver damage
- ALT – enzyme found only in liver cells
- GGT – another enzyme from the liver but 1
  aspirin can cause it to increase
Probably not

If hemolysis - reticulocyte count

If loss of immune function proteins esp. immunoglobulins

serum protein electrophoresis

or immunoelectrophoresis
For the anal-retentive

That is anal retentive

With the hyphen

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<th>Retic count</th>
<th>Bilirubin</th>
<th>Protein</th>
<th>Just in case</th>
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