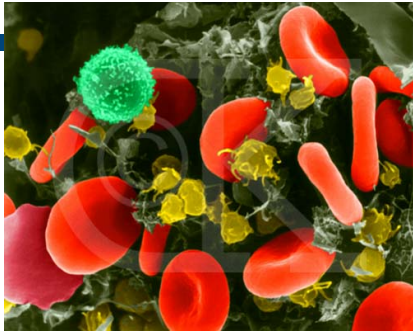


SO – YOU HAVE THIS THING

Now what do you have to learn?

Susan J. Leclair, Ph.D, CLS(NCA)
Chancellor Professor

Department of Medical Laboratory Science
University of Massachusetts
Dartmouth Massachusetts USA



ONCE UPON A TIME,

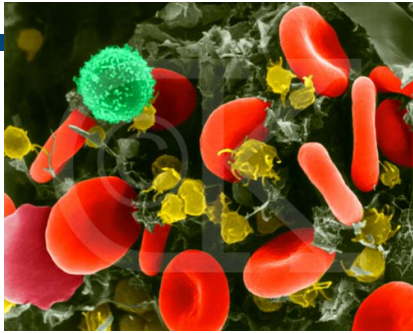
Physicians knew all the answers and patients believed them
Not so much anymore

Used to be

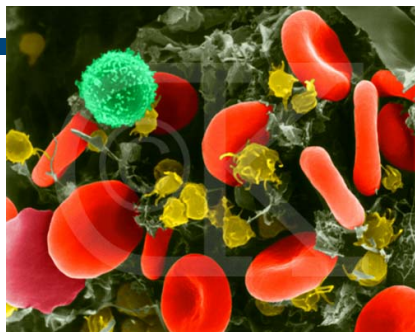
Get a diagnosis
Cry
Go to church, temple, etc.
Take the meds
Do what the physician says

Now a Days

Get a diagnosis
Cry
Go online & search
Go for the roots & berries
Argue – ask “why”



Physicians speak in medicalese and only rarely
in English
So
You have to learn medicalese.



IT TAKES TWO TO MISCOMMUNICATE

Patient Words

fine

not bad

I didn't tell him
because he didn't ask

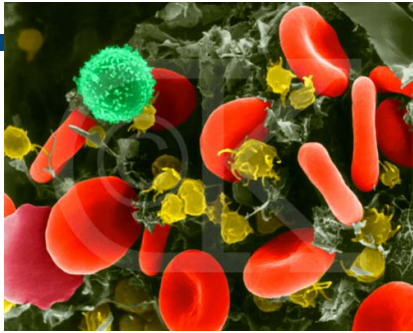
Translation

I don't want this to be bad so you won't mind if I skip a few salient details.

It really hurts like hell but I'm supposed to be brave (male)

It really hurts but I know no one pays attention to my complaining about pain so why tell (female)

You're the hot shot; go figure it out without telling you



IT TAKES TWO TO MISCOMMUNICATE

Physician Words

fine

Let's repeat it in
few weeks

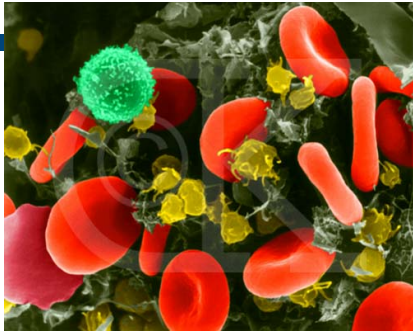
That is my job

Translations

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

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

I can't explain this in English



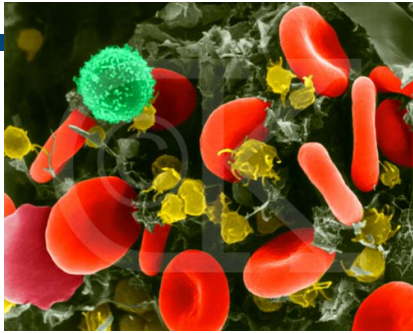
SOME TRANSLATIONS

What is Jak-Stat?

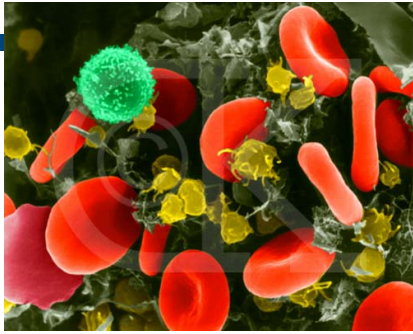
Original name – just another kinase

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.



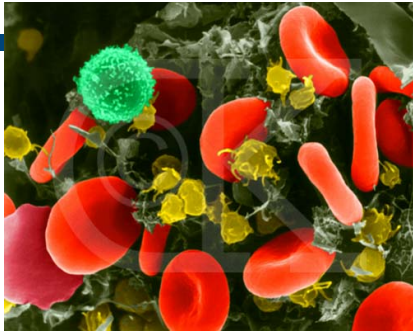
WHAT?????????



How does this sound:

JAK2 is a gene that turns on a series of actions that controls the production of blood cells and fibrocytes

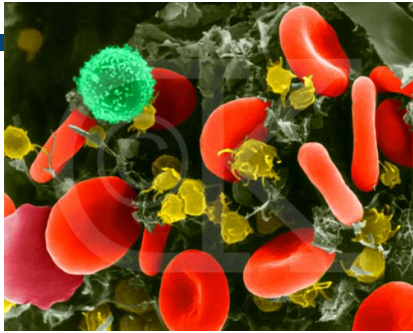
When abnormal, control is lost and excessive numbers of cells are produced



THE BALL IS IN YOUR COURT

Under normal physiological circumstances when a ligand (for example - EPO) binds with a receptor, a conformational change 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

????????



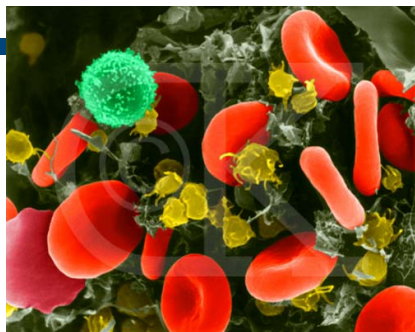
OR

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



ONE MORE LANGUAGE ISSUE

The US will not go along with the international system of concentration and values so

US really old

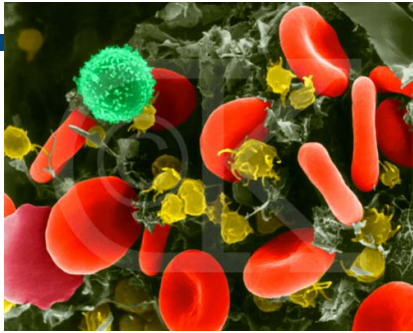
5,000 cells or 5K/cumm

US medium old

$5.0 \times 10^3 / \mu\text{L}$ or

Rest of world

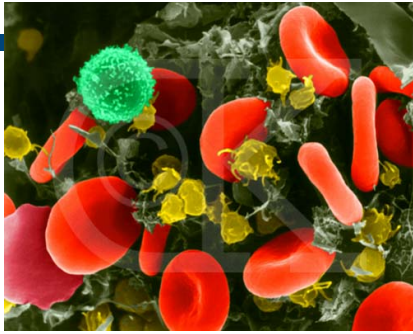
$5.0 \times 10^6 / \text{L}$



MY SPREADSHEET (OR MY “PRECIOUS”)

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 ever let anyone say to you that things cannot be connected.

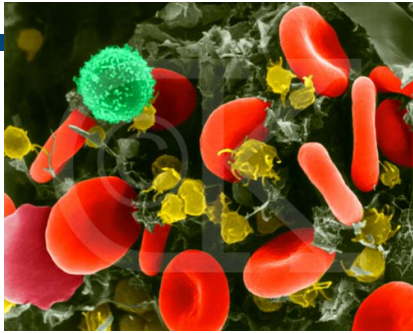


WBC

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 $3.0 \times 10^3/L$ is worthy of note



WBC DIFFERENTIAL

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

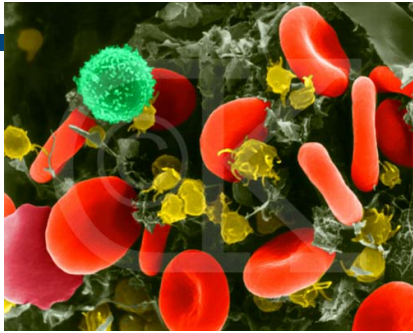
makes great comments about quality

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

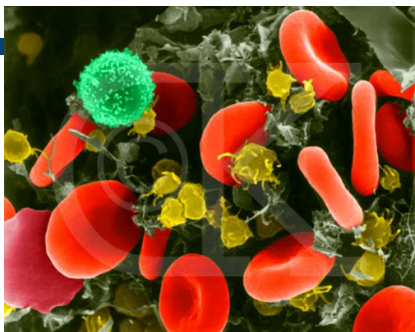
variable on quality but superb on quantity



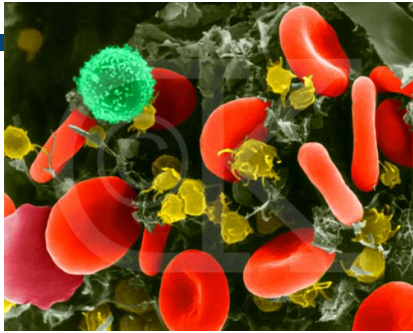
WBC

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



Date	WBC	ANC
	Ref. interval	Ref. interval
	Value	Value



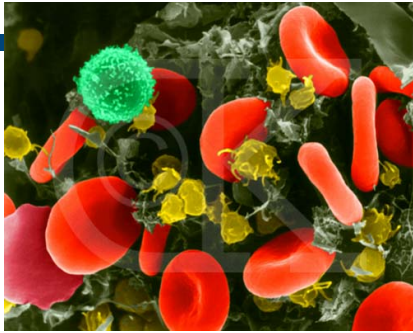
HEMOGLOBIN

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

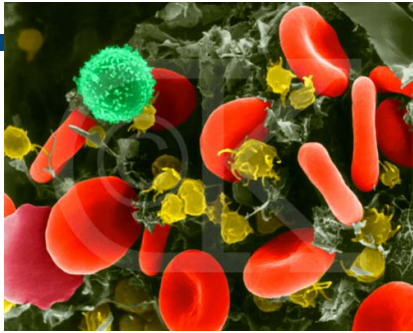
Hemoglobin – varies by gender, age and altitude

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 O_2
- usually need transfusions



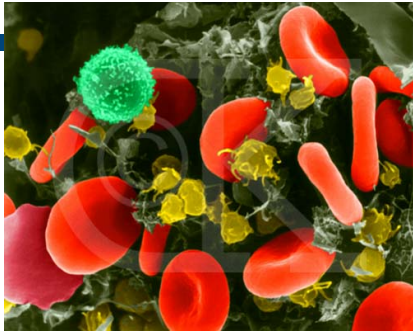
HEMOGLOBIN

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

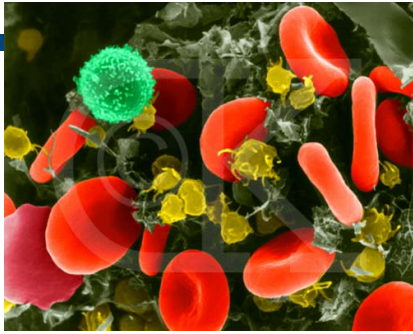


HEMATOCRIT

Hematocrit (HCT)

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

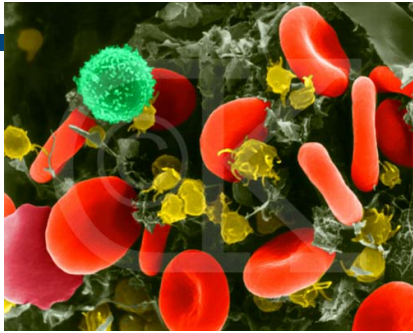
now – we don't perform it. We calculate it so not as accurate or reliable



HEMATOCRIT

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.

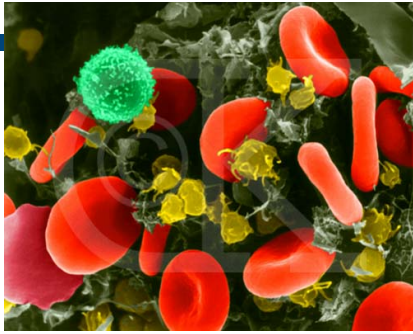


HEMATOCRIT

Hematocrit

only makes sense if all the cells are the same size but as the RDW increases and the MCV decreases, it gets fuzzier.

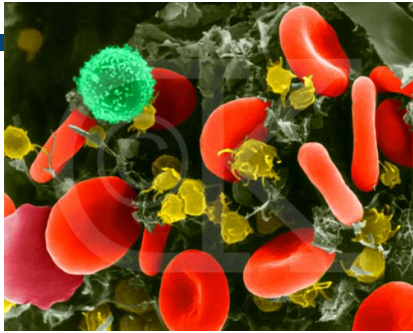
When the RDW is greater than 20, the hematocrit is invalid so using the hemoglobin values is most consistent.



HEMOGLOBIN

How do you decrease viscosity?

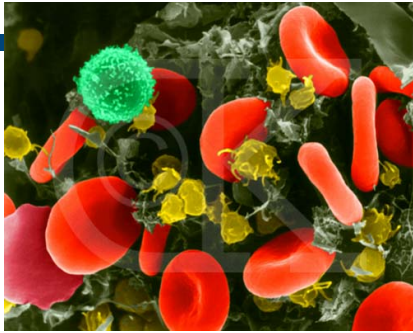
1. lower the RBC absolute number
easiest method – phlebotomy
2. make them smaller
make them iron deficient



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!

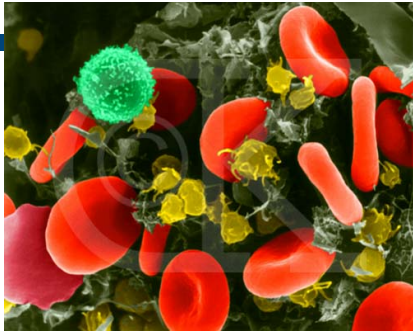


YOUR OWN SPREADSHEET

Should look like this

DATE	WBC	ANC	HGB	MCV	MCH	RDW	PLT
	Ref. interval	Ref. interval	Ref. interval	Ref. interval	Ref. interval	Ref. interval	Ref. interval
	Value	Value	Value	Value	Value	Value	Value

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.



IF YOU HAVE TIME

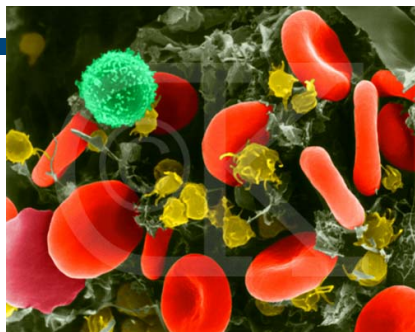
Chemistry values

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

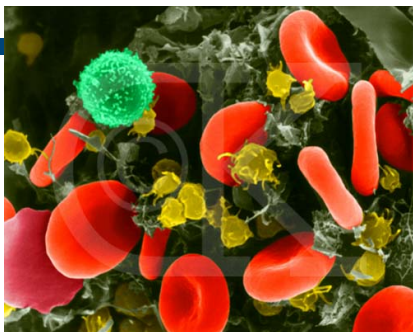
Keep your diet consistent – high protein meals increase uric acid concentration



CHEMISTRY

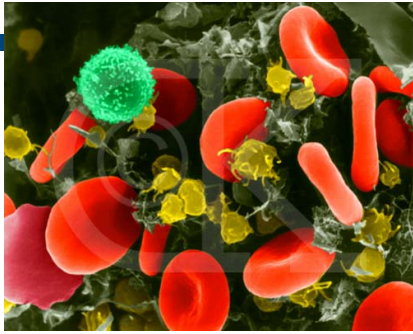
LD (lactate dehydrogenase) – almost every cell in the body has this enzyme. When the cell is damaged/dies, the enzyme is released into the blood stream

Increases in this suggest increased damage but you can't use this when on meds.



SO

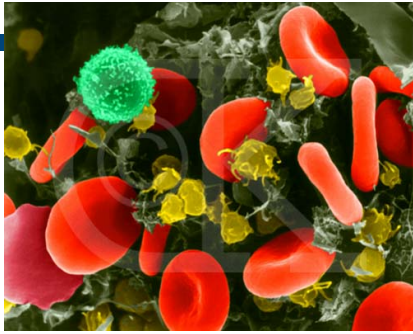
WBC	ALC	ANC	HGB	MCV	RDW	PLT	Uric Acid	LD (LDH)
Ref. interval	Ref. interval	Ref. interval	Ref. interval	Ref. interval	Ref. interval	Ref. interval	Ref. interval	Ref. interval
Variation	Variation	Variation	Variation	Variation	Variation	variation	Variation	variation



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	



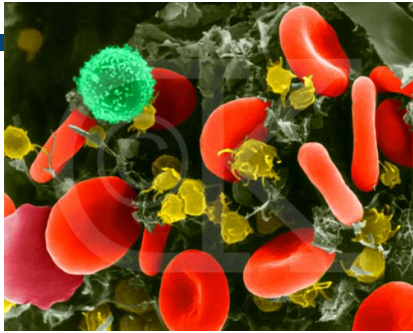
IS THAT ALL??????

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

WBC	ALC	ANC	HGB	MCV	RDW	PLT	Uric Acid	LD (LDH)	Retic count	Bilirubin	Protein	Just in case
Ref. interval	Ref. interval	Ref. interval	Ref. interval	Ref. interval	Ref. interval	Ref. interval	Ref. interval	Ref. interval	Ref. interval	Ref. interval	Ref. Interval	
variation	variation	variation	variation	variation	variation	variation	variation	variation	variation	variation	variation	variation