

Laboratory Testing

Sept 11, 2003

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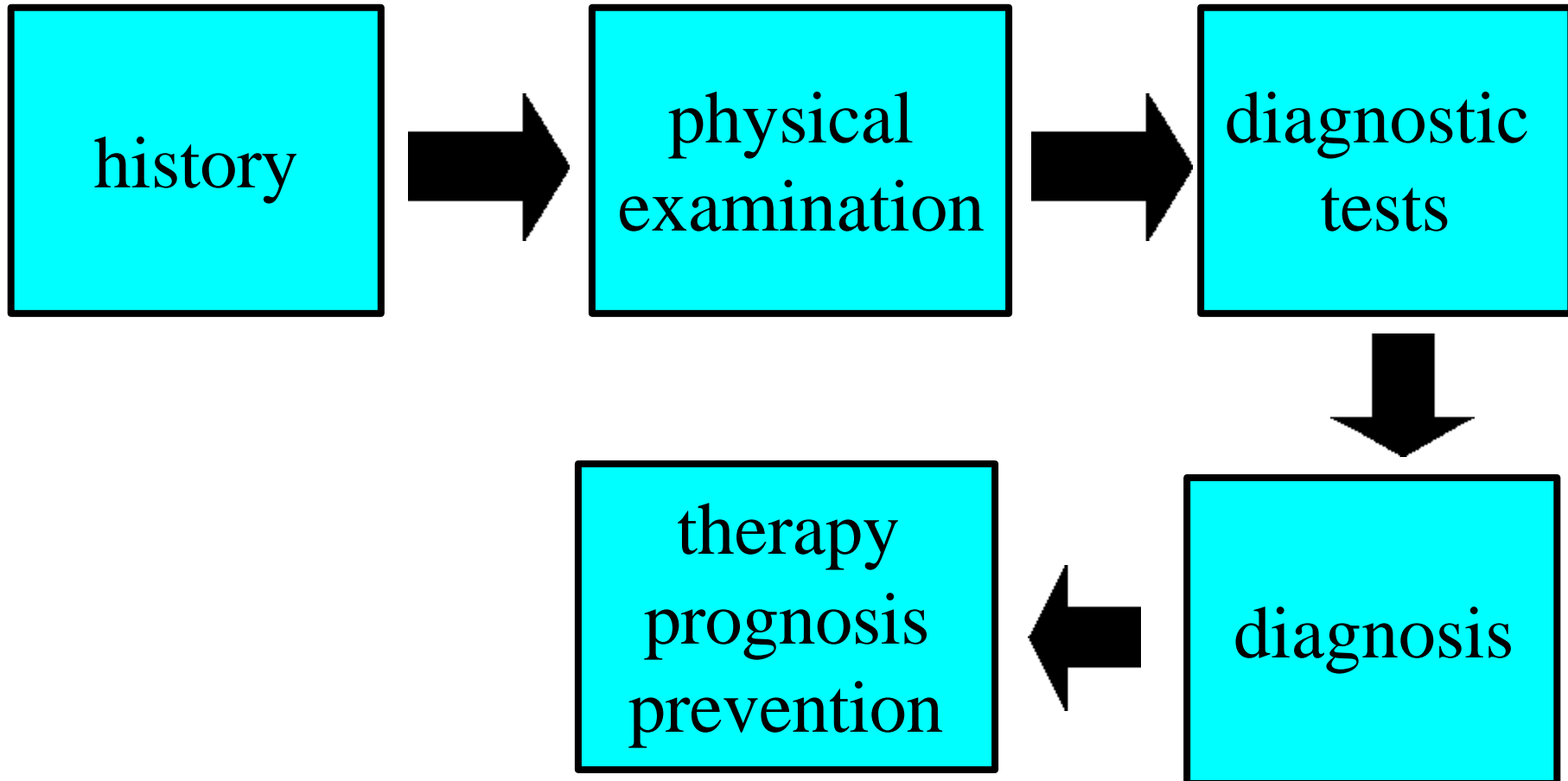


Objectives

- Role of Tests
- Define Gold Standard
- Reference Ranges
- Test Characteristics
- Review Tests



General Process of Medicine



Diagnostic Testing

- Advantages

- can assess parameters beyond the 5 senses
- laboratory data may be more valid than clinical data

- Disadvantages

- test results be incorrect
- test results may lead you in the wrong direction
- tests cost money
- tests may confer risk
- some diseases have no diagnostic test



Levels of Validity

- Gold Standard
- Non Gold Standard



Gold Standard

- The Gold Standard is the best test available for determining the presence or absence of a disease.

Gold Standard = 'reference standard'

- e.g: pulmonary angiogram for PE



Non-Gold Standard Test

- Non Gold Standard Tests are used to predict for the presence or absence of disease.

Totally Useless ↔ As Good as Gold

e.g. D-dimer, V/Q scan, Spiral CT for PE



Other Test Issues

Why we need non-Gold Std Tests

- Simple / minimal invasive / low cost
 - throat swab to assess pharyngitis
 - serum antibodies to hepatitis B
- Complex / invasive / expensive
 - open lung biopsy to assess a pulmonary nodule
 - coronary angiogram to assess angina



Reference Ranges

- What is the normal range for test?
- Sodium 135 - 145 mmol/L
- Potassium 3.5 - 5.0 mmol/L

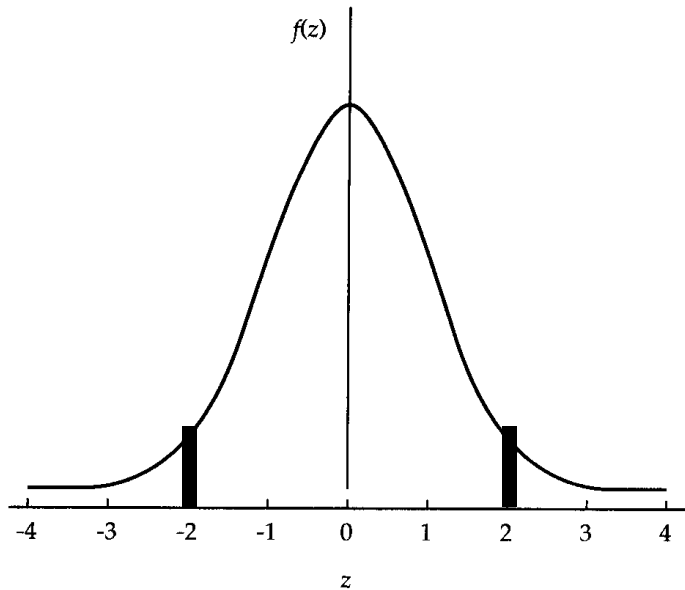


Reference Ranges

- What is the normal range for test?
- Hemoglobin 120 - 160 g/L
- Hemoglobin 100 - 120 g/L
- Calgary vs Saskatoon



Reference Ranges

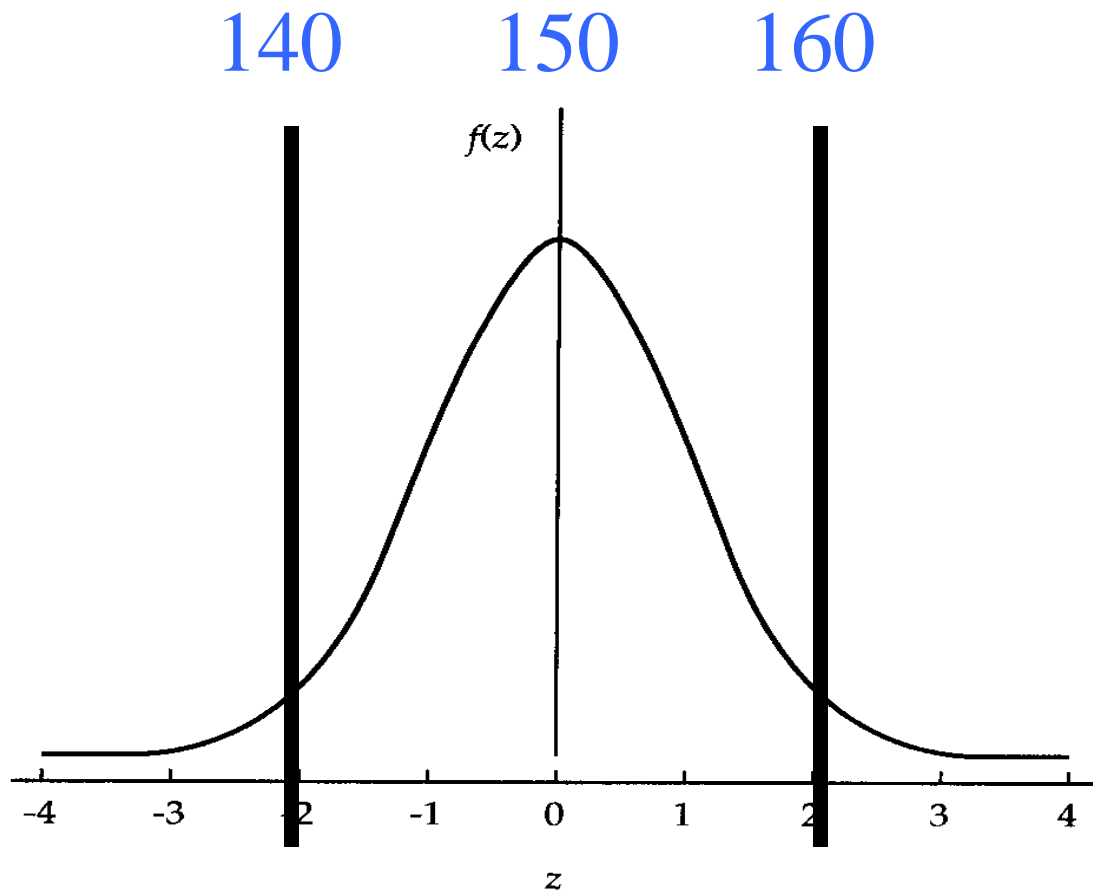


The standard normal curve for which $\mu = 0$ and $\sigma = 1$

Normal includes
2 Standard
Deviations
from average
value
95% of normal
population



Reference Range includes 95% & excludes 5% of normals



The standard normal curve for which $\mu = 0$ and $\sigma = 1$



Probability of Abnormal Test

- For every 20 independent tests ordered on a normal healthy person, 1 will return abnormal by statistical chance alone!



Diagnostic Testing Issues

- Test Characteristics
 - sensitivity
 - specificity
 - positive predictive value
 - negative predictive value



		DISEASE	
		Present	Absent
TEST	Positive	TRUE POSITIVE	FALSE POSITIVE
	Negative	FALSE NEGATIVE	TRUE NEGATIVE



Sensitivity

- Probability that test is positive given that disease is present.

$$P (T+ | D+)$$



Sensitivity

		DISEASE (PE)		
		Present	Absent	
TEST (V/Q scan)	Positive	TRUE POSITIVE a = 80	FALSE POSITIVE b = 20	a + b = 100
	Negative	FALSE NEGATIVE c = 10	TRUE NEGATIVE d = 90	c + d = 100
		a + c = 90	b + d = 110	a+b+c+d = 200

$$80 / (80 + 10) = 88.9\%$$



Specificity

- Probability that test is negative given that disease is absent.

$$P(T- | D-)$$



Specificity

		DISEASE (PE)		
		Present	Absent	
TEST (V/Q scan)	Positive	TRUE POSITIVE a = 80	FALSE POSITIVE b = 20	a + b = 100
	Negative	FALSE NEGATIVE c = 10	TRUE NEGATIVE d = 90	c + d = 100
		a + c = 90	b + d = 110	a+b+c+d = 200

$$90 / (90 + 20) = 81.8\%$$



Positive Predictive Value

- Probability that disease is present given that the test was positive.

$$P(D+ | T+)$$



Positive Predictive Value

		DISEASE (PE)		
		Present	Absent	
TEST (V/Q scan)	Positive	TRUE POSITIVE a = 80	FALSE POSITIVE b = 20	a + b = 100
	Negative	FALSE	TRUE	0
				200

$80 / (80 + 20) = 80.0\%$



Negative Predictive Value

- Probability that disease is absent given that the test was negative.

$$P(D- | T-)$$



Negative Predictive Value

		DISEASE (PE)		
		Present	Absent	
TEST (V/Q scan)	Positive	TRUE POSITIVE a = 80	FALSE POSITIVE b = 20	a + b = 100
	Negative	FALSE NEGATIVE c = 10	TRUE NEGATIVE d = 90	c + d = 100
		a + c = 90	b + d = 110	a+b+c+d = 200

$$90 / (90 + 10) = 90.0\%$$



Test Characteristic Issues

- **Highly Sensitive Tests:**
 - tend to be less invasive, less risky, less costly
 - best for screening programs
 - best for ruling out disease: “SNOUT”



Test Characteristic Issues

- Highly Specific Tests:
 - tend to be more invasive, more risky, more costly
 - best for confirming (ruling in) disease: “SPIN”



Likelihood Ratio

		DISEASE (PE)		
		Present	Absent	
TEST (V/Q scan)	Positive	TRUE POSITIVE a = 80	FALSE POSITIVE b = 20	a + b = 100
	Negative	FALSE NEGATIVE c = 10	TRUE NEGATIVE d = 90	c + d = 100
		a + c = 90	b + d = 110	a+b+c+d = 200

$$(80 / 90) / (20 / 100) = 4.89$$



Utility of (Positive) Likelihood Ratios

- Likelihood ratios express how many times more likely a test result is to be found in diseased, compared to nondiseased, people.
- The likelihood ratio can also be applied to the prevalence of disease to generate a post-test probability of disease.



Probability of Disease

- Pre-test probability of disease
- Post-test probability of disease





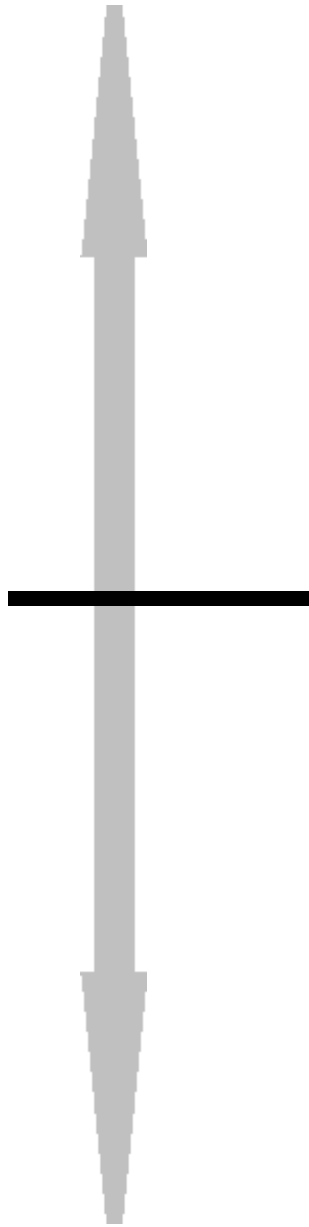
hypoxemia
polycythemia
rubra vera

Hemoglobin

iron, B12 def
sickle cell
hemorrhage
chronic disease
bone marrow



hematocrit



hypoxemia
polycythemia
rubra vera

iron, B12 def
sickle cell
hemorrhage
chronic disease
bone marrow



hypoxemia
polycythemia
rubra vera

RBC count



iron, B12 def
sickle cell
hemorrhage
chronic disease
bone marrow



hypoxemia
polycythemia
rubra vera

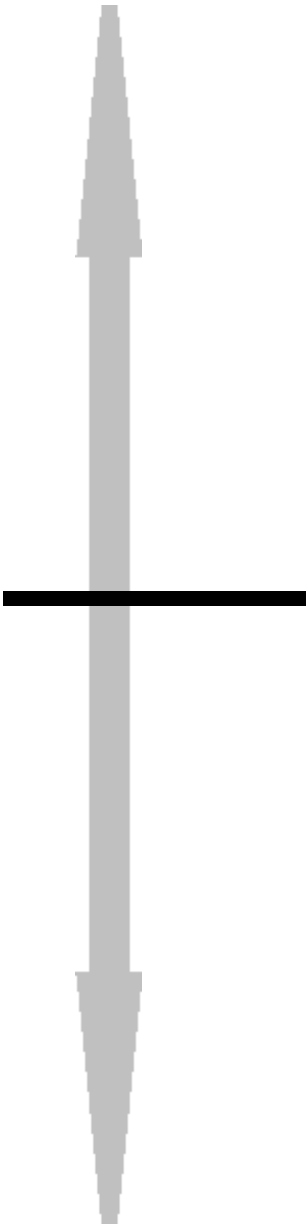
RBC count



iron, B12 def
sickle cell
hemorrhage
chronic disease
bone marrow



MCV

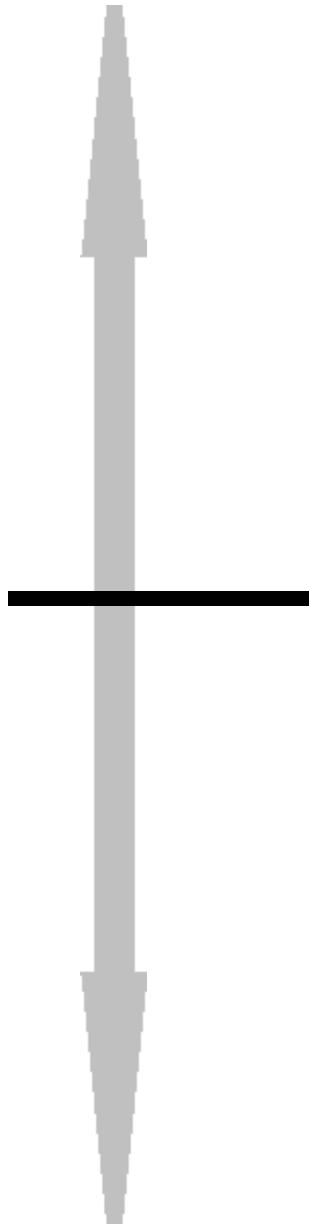


B-12 deficiency
folate deficiency
AZT, sepra
liver disease
reticulocytosis

iron deficiency
thallasemia
sickle cell



MCHC



iron deficiency





transfusion
recent blood loss
and new
production
chemo

no too low

RDW



inflammation
essential
thrombocytosis
iron deficiency

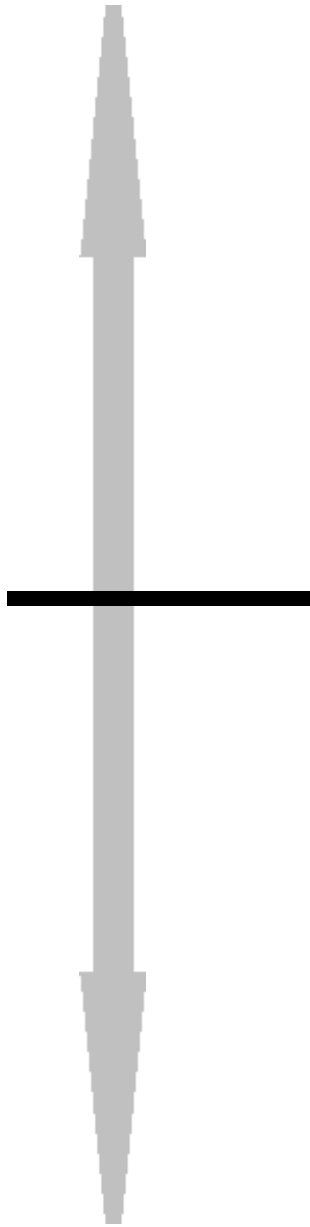
PLT count



ITP
TTP
Clumping
Marrow disease



WBC



infection
inflammation
leukemia

sepsis
bone marrow dx
chemo
hypersplenism
lupus





infection
inflammation
steroids

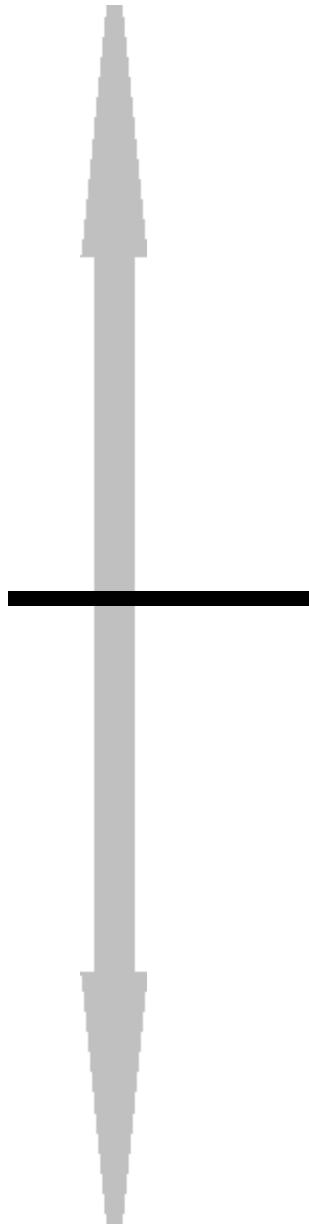
Neutrophils

bone marrow dx
sepsis
chemo
autoimmune



allergy
parasites
Addison's
disease

eosinophils



diabetes

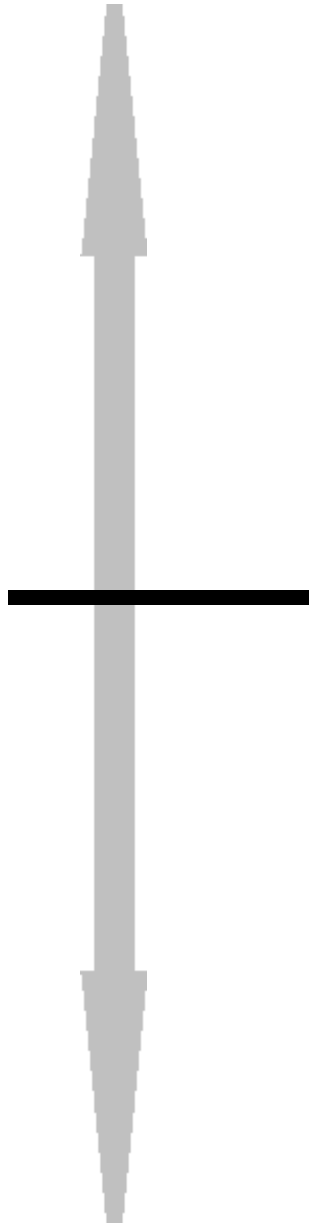
random > 11.1

fasting > 7.0

hypoglycemia

normal

Glucose



insufficient water
diabetes insipidus

sodium

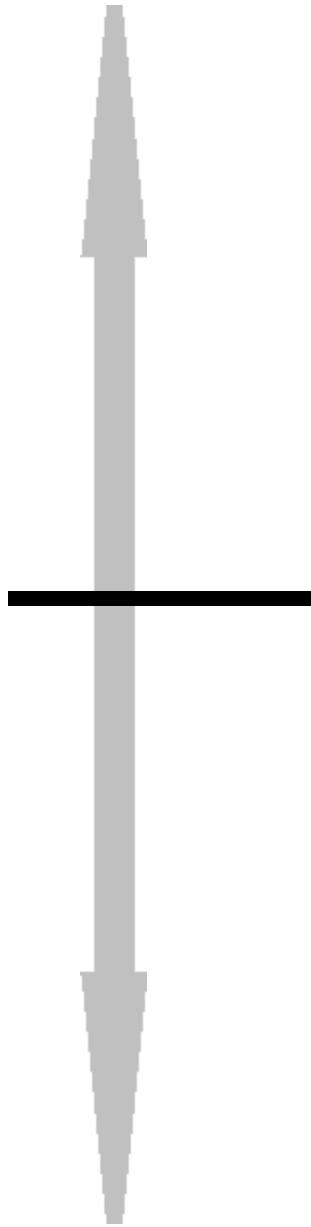


CHF, kidney, liver dx
SIADH

hypothyroid / addisons
thiazide diuretics
too much water

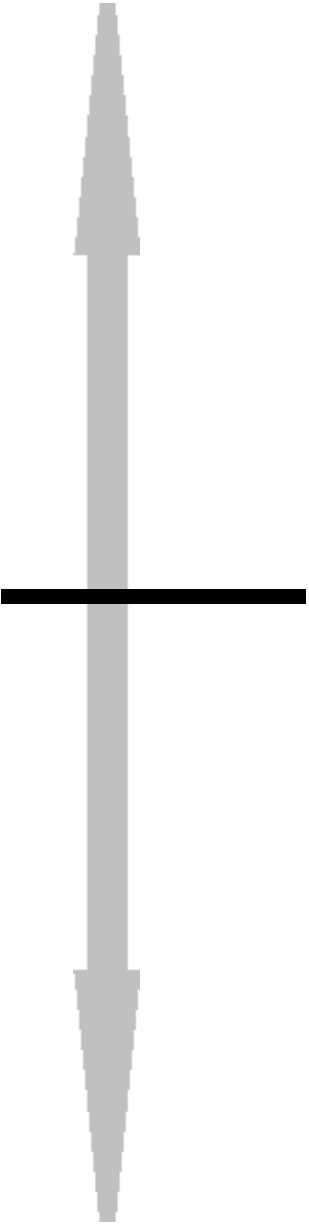


potassium



renal failure
excess intake
high WBC, PLT
hemolysis
some diuretics
other diuretics
diarrhea
vomiting
renal diseases





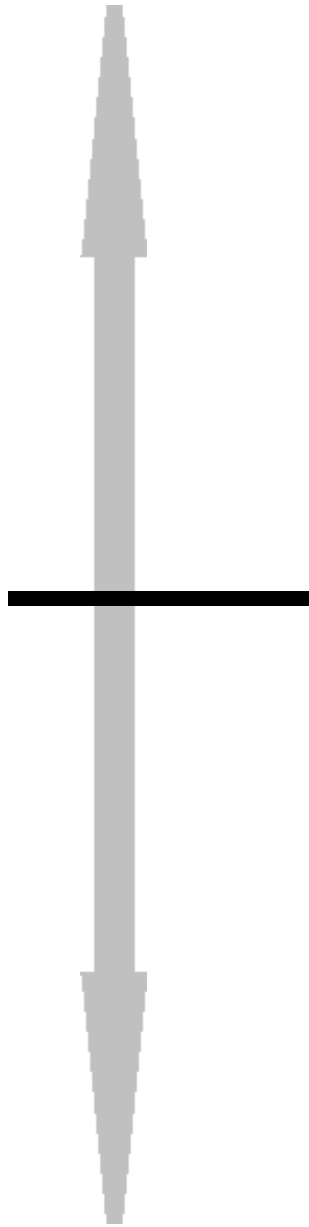
steroids
diuretics
bicarb IV

CO₂ content

acidosis
DKA, lactate
normal saline



calcium



malignancy

hyper-parathyroidism

increased intake / vit D

bed rest, fracture

[correct for albumin]

post-op

parathyroidectomy

pancreatitis



ALT



hepatitis
shock liver
muscle damage
drugs
fatty liver
toxemia

0 - 60 (no low)



ALP



obstruction to bile flow
gallstones
intrahepatic disease
bone diseases
lactation
pregnancy

No too low



obstruction to bile flow
any liver process
1-2 drinks

GGT

No too low



liver failure

ammonia



liver disease

hemolysis

rhadomyolysis

MI

LDH



pancreatitis
bowel infarction

lipase

no too low



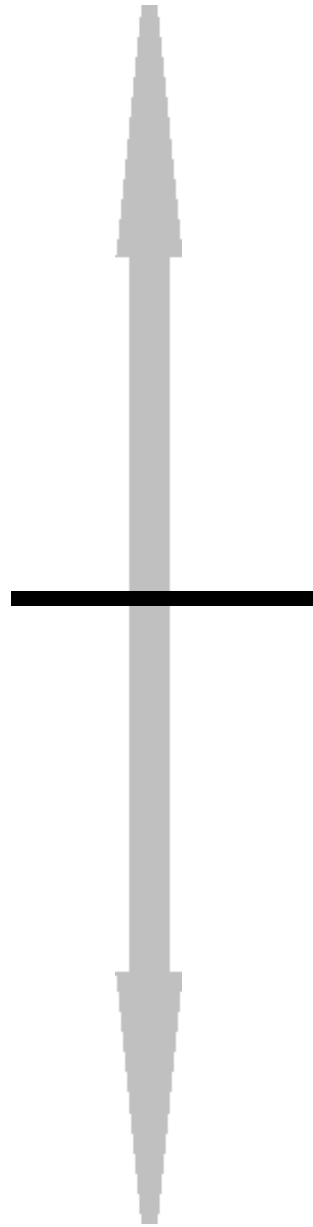
pancreatitis
parotid gland dx
mumps

amylase

no too low



renal failure

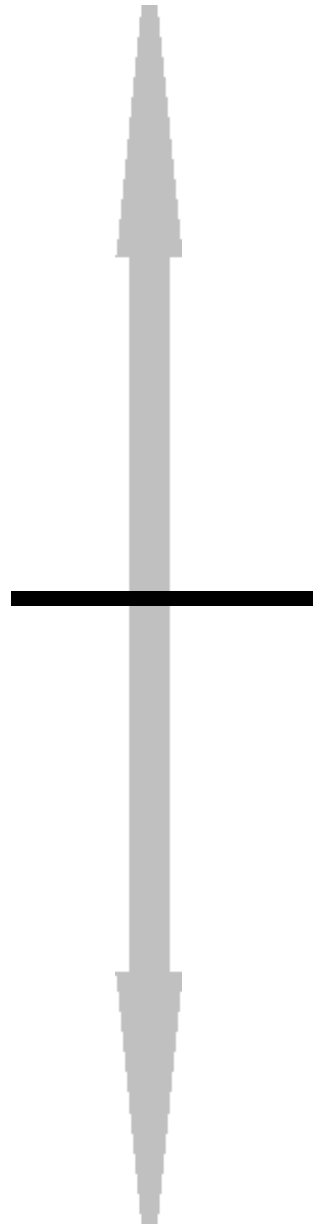


creatinine

early nephropathy in DM
low muscle mass



renal failure
upper GI bleed



urea

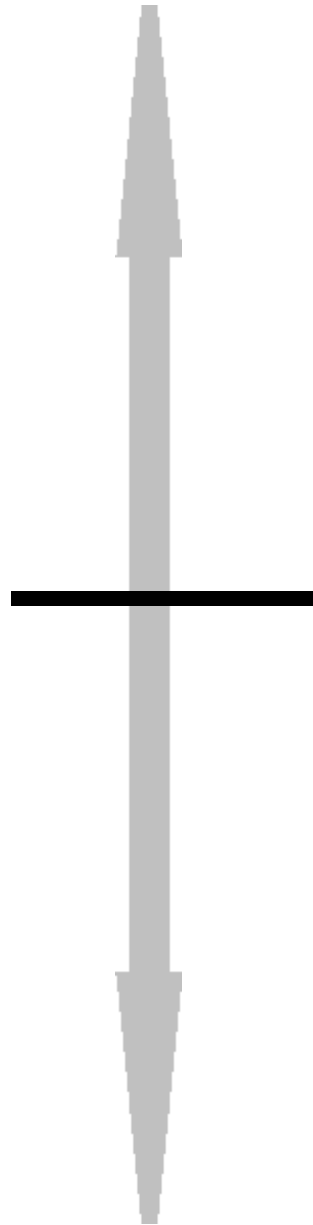


Hypothyroidism

Hyperthyroidism

Pituitary failure

TSH

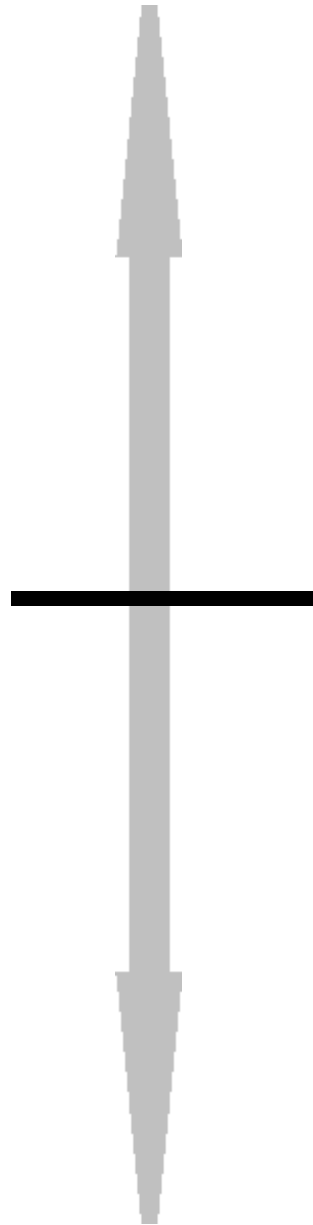


hyperthyroidism

may not be accurate in
ill health

hypothyroidism

T4





Hashimoto's thyroiditis
Grave's disease
Normal Population

Antithyroid Ab

- anti-thyroglobulin
- anti-thyroid peroxidase

No too low



ANA



SLE

MCTD

advancing age

alcoholism

normal in 3% (false +)

no too low



rheumatoid arthritis

normal (false +)

Rheum Factor



Ankylosing spondylitis
normal (false +)

HLA-B27 Ag





inflammation e.g.
temporal arteritis
PMR

infection
myeloma
cancer
clots
MI



ESR

CRP



inflammation e.g.
temporal arteritis
PMR

infection
myeloma
cancer
clots
MI



prostate cancer

benign prostate
hypertrophy

prostatitis

dig rectal exam?

PSA



ovarian cancer

CA-125



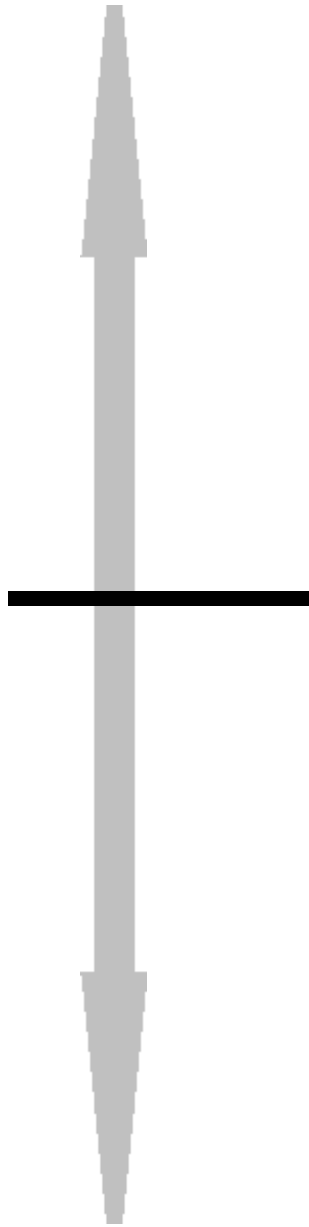
adenocarcinoma
pancreas
stomach
gi tract

CA-19 9



hepatoma
testicular cancer

Alpha-feto-
protein



Down's pregnancy



ovarian cancer

CA-125



D-dimer



PE

DVT

infection

inflammation

surgery

trauma

pregnancy

normal



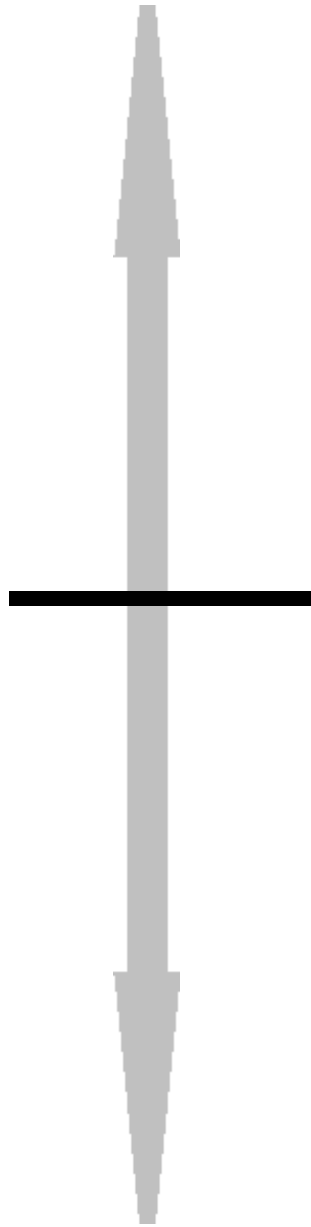
Normal response

Prednisone use

Adrenal insufficiency



cortisol



PTT



hemophilia A

heparins

++ warfarin effect

SLE

liver failure



warfarin

liver failure

prolonged antibiotics

vitamin K deficiency

INR



serum protein
electrophoresis

looks for protein spike
myeloma
waldenstrom's
macroglobulinemia
MGUS



Immunoglobulins



Selective deficiency



Hepatitis C infection

(90% do not clear)

Hep C Ab



Active Hep B infection



Hep B sAg



Prev hep B vaccination
Prev hep B infection
(cleared)

Hep B sAb

