

“Have you got a minute?”

Interpreting blood results



30 November 2016

Thrombocytopenia

$<150 \times 10^9/L$

- **Decreased production** (disorders of bone marrow)- congenital or acquired (viral most common- e.g Herpes Simplex, EBV, CMV, HIV, Hepatitis- but also alcohol, aplastic anaemia, marrow infiltration, drugs/chemicals, megaloblastic anaemia, myelofibrosis)
- **Decreased platelet survival** (Immune: idiopathic thrombocytopenic purpura (ITP), SLE, drug induced, including heparin ; Thrombotic Thrombocytopenic Purpura (TTP); Hypersplenism; Haemolytic Uraemic Syndrome (HUS); Disseminated Intravascular Coagulation (DIC)
- (Dilutional)
- (Pregnancy)

- Incidental finding: Repeat FBC with blood film and differential, viral serology, B12/Folate, PT, aPTT, U&Es, TFTs
- Bone marrow >60 yrs (mainly to exclude dysplasia)/those with systemic symptoms/signs suggestive of haematological cancer
- If drug related, should recover by 5-7 days of stopping drug.
- **Degree of urgency of the referral to the haematologist with respect to the platelet count:**
 - **non-urgent referral** - platelet counts of $100-150 \times 10^9/L$ in a well patient
 - **fairly urgent referral** - $50-100 \times 10^9/L$
 - **urgent referral** - if platelet count $< 50 \times 10^9/L$, refer urgently and stop antiplatelets
- consider the clinical condition of the patient when considering referral - any degree of thrombocytopenia in an ill patient merits referral

Thrombocytosis and Thrombocythaemia

$>450 \times 10^9/L$

- Paradoxically, thrombosis and haemorrhage are main symptoms, is as much dependent on qualitative defects as much as their number
- Reactive thrombocytosis (>85% cases) vs essential thrombocythaemia (autonomous)
- Reactive causes include inflammation, infection, haemorrhage and iron deficiency- must be excluded before a diagnosis of essential thrombocythaemia.
- Any degree of persistent thrombocytosis, whether or not it fulfils the conventional criterion of being above $600 \times 10^9/L$, must be pursued for the possible diagnosis of essential thrombocythaemia.

- **Platelet count raised with nausea OR vomiting OR weight loss OR reflux OR dyspepsia OR upper abdominal pain, 55 and over** → think possible oesophageal or stomach cancer and consider 'non urgent OGD'.
- **Thrombocytosis, 40 and over** → Think possible lung cancer, and obtain CXR within 2 weeks.
- **Thrombocytosis with visible haematuria or vaginal discharge (unexplained) in women 55 and over** → Consider endometrial cancer and refer for direct access USS

B12 and Gastric Parietal Antibodies

- NICE CKS anaemia-B12 and folate deficiency
- When to test?
 - anaemia and unexplained neurological symptoms
- What to test?
 - FBC, B12, folate.
 - B12 normal range 211-911ng/L
- How helpful is the B12 level?
 - Measures total, not metabolically active vitamin B12.
 - Levels are not easily correlated with clinical symptoms, especially in elderly
- Low B12- why?
 - Check serum anti-intrinsic factor antibodies (pernicious anaemia)
 - Checking gastric parietal cell antibodies is no longer recommended
- What do I do now?
 - Treat folate deficiency
 - Neurological involvement- urgent advice from haematology
 - No neurological involvement
 - hydroxycobalamin 1mg IM alternate days for 2 weeks then maintenance
 - not diet related hydroxycobalamin 1mg IM 3 monthly for life
 - diet related oral cyanocobalamin 50-150 microgram OD or twice yearly 1mg IM hydroxycobalamin.
- Do I check it again?
 - FBC and reticulocyte count after 10 days of treatment and after 8 weeks.
 - Ongoing monitoring not usually needed.

Magnesium

- HypoMg is symptomatic $<0.5\text{mmol/L}$ (N- $0.7\text{-}1.1\text{mmol/L}$): muscular weakness, apathy, tremors, paraesthesia, tetany, vertical nystagmus, +ve Chvostek's and Trousseau's signs, seizures, atrial + ventricular arrhythmias
- HypoMg + HypoK(60% cases) + HypoCa+ Low PTH(Hungry bone Syndrome)
- Drugs: loop +thiazide diuretics, amphotericin B, aminoglycosides, cisplatin, ciclosporine, tacrolimus

PPI induced HypoMg (measure Mg prior starting PPI, while on treatment), returns to Normal in 1 week after stopping.

- *Magnaspartate* (magnesium aspartate dihydrate) –oral preparation is now licenced
- Most common side effect – diarrhoea
- *Magnesium Sulphate* is the anticonvulsant of choice for treatment of Pre-Eclampsia
- Food rich in Mg: avocado, spinach, chard, figs, pumpkin seeds, black beans, bananas, dark chocolate, almonds, yogurt, brown rice.



Liver function tests – the ‘asymptomatic’ pt

Bilirubin

Unconjugated, rise in reticulocytes:

Gilberts

Conjugated: liver disease, cholestasis

Obstructive: Biliary/ pancreatic disease

ALT/ AST:

Ratio helpful – AST \uparrow > ALT suggests cirrhosis, ALT \uparrow > AST in most chronic liver conditions

ALT more liver specific, but NB Myositis / Muscular dystrophy

ALP: use gamma GT to differentiate aetiology. Check hx/bloods for bone disease, CCF, coeliac, thyroid, NSAIDs, TCAs, allopurinol, COCP.

Gamma GT: raised in isolation is low risk for liver disease, even in the presence of known ETOH excess (but not specific for ETOH)

Isolated raised bilirubin \rightarrow check unconjugated, exclude haemolysis

Isolated raised gGT \rightarrow counsel re ETOH, if $<2x$ no further ix, refer if $>3x$

Raised ALT: Refer if > 120 , else recheck with HBA1C, hepatitis, caeruloplasmin, iron, autoimmune serology (in 1/12 if > 80 , in 3/12 if < 80)

Raised ALP \rightarrow check for non-liver causes (above), check for xsETOH, raised BMI, hepatotoxic drugs. If $<1.5/2x$ normal recheck in 4-6/12, If $>3x$ USS & antimitochondrial antibodies

Threshold for intervention: clinical context of alcohol, DM, BMI, hepatitis risk factors

■ Hepatitis B Serology

■ HBsAg : surface Ag

- - Indicates either acute infection or carrier of HBV if persists after 6m
- - These individuals are infectious to others
- - false positive in recent vaccination

■ Anti-HBs :

- - Indicates immunity to hepatitis B, from either exposure to the virus or vaccination

■ Anti-HBc : core Ab

- - Indicates that the person either has or had hepatitis B
- - develops after exposure to the hepatitis B virus and persists for life
- - not present in vaccinated patients

■ HBeAg : envelope Ag

- - acute stage of infection; indicates viral replication
- - is highly infectious to others.

Coeliac Serology

- ▶ Endomysial antibodies (EMA) and tissue Transglutaminase (tTG)
- ▶ EMA are IgA
 - If positive, likely coeliac
 - If negative, doesn't rule it out
- ▶ tTG are IgA or IgG
 - Therefore, the 1st line test suggested by NICE
- ▶ Only valid if the patient has ongoing symptoms and remains on a gluten diet for 6 weeks
 - Consider possibility if symptom free, and patient has autoimmune polyendocrine syndrome (e.g. T1Dm, Addisons, Autoimmune hepatitis, dermatitis herpetiformis).
 - Look at calcium, albumin, Hb, Folate
 - Vit B12 usually normal (terminal ileum sparing)
- ▶ Refer for Jejunal biopsy (Gold standard diagnosis)
 - If positive serology
 - If negative serology, but ongoing clinical suspicion
 - Must remain on gluten diet at least 6 weeks prior to endoscopy

Alpha 1 Anti Trypsin

- Glycoprotein produced in liver balances act of neutrophil elastase (made due to infection/inflammation/smoking)
- DEFICIENCY - molecule changed so can't leave liver, elastase can breakdown elastin unchecked leading to destruction of alveolar walls - emphysematous change. Liver disease results from congestion of A1AT
- Autosomal co-dominant on C14
- Heterozygous affected
- 1 in 3000-5000
- 5% of COPD - think of if young patient or severe disease
- LUNGS - SOB, wheeze, infections, usually 30s/40s & smokers onset 10 yrs earlier. LIVER - hepatitis, fibrosis, cirrhosis, failure.
- TESTS: serum levels, phenotype, CXR, lung function, CT scan, LFTs
- Family need testing
- TREAT: COPD/Liver, IV infusion but not NICE recommended

Amylase

- 3 or more times normal is diagnostic for acute pancreatitis >1000U/mL
- May be normal in severe pancreatitis (levels fall within 1st 24-48 hours)
- Lesser rises in cholecystitis, mesenteric infarction and GI perforation
- Will be elevated in renal failure as it is excreted renally
- Lipase more sensitive and specific- both pancreatic digestive enzymes
- FBC, U&E, CRP, calcium indicate prognosis
- LFTs- Raised bilirubin/ ALT suggests gallstones
- Hypocalcaemia common

D-Dimer

- Protein fragment detected in blood after blood clot degraded by fibrinolysis.
- Used in suspected DVT, PE, DIC
- Negative result rules out thrombosis
- Only use if low or moderate probability
- False positives: liver disease, high RF, inflammation, malignancy, trauma, pregnancy, surgery, age
- False negatives: taken too early/too late, anticoagulation, tube not sufficiently filled
- High results (>1000) associated with strong probability of malignancy
- If suspect DIC, also want to look at PT, APTT, fibrinogen, platelets

TFTs

TFTs check if:



- a. tiredness, depression
- b. on amiodarone or Lithium
- c. hypercholesterolemia
- d. AIO disease
- e. Turner's syndrome



- TSH – pituitary
- T4 and T3 (small amount)- thyroid
- T3 – majority created from T4 in peripheral tissues


Anti TPO-



1. Reflects destruction of thyroid cells
2. High likelihood to progression to myxoedema
3. Hashimoto

4 Main common diagnosis

• 1. TSH  T3,4 
Primary hypothyroidism

2. TSH  or normal T3,4 
Secondary hypothyroidism (replacement steroid Rx !)
Sick euthyroid sx (TSH may be normal, T3 very low)

3. TSH  T4 normal
Subclinical hypothyroidism or poor compliance

4. TSH  T3,4 
Hyperthyroidism
Different reference ranges= in pregnancy

Monitor

4-6 weeks after alteration of the dose

Monitor yearly

Different monitoring in pregnancy

Faecal calprotectin

What Is It?

- A zinc and calcium binding protein from neutrophils and monocytes
- A marker of neutrophil activity
- Measured in faeces is a marker of intestinal inflammation (ELISA, POCT)
- Stable up to 7 days
- Has a sensitivity and specificity for IBD of 93% and 96% respectively (spec 76% in children)

Conditions linked to

- IBD – (15–2574)
- IBS – (14-65)
- Malignancy
- Gastroenteritis
- Intestinal parasites
- NSAID use leading to erosion

Application and use in guidance

IBD vs IBS – NICE recommended test (NICE DG11)

Can significantly reduce invasive investigations for IBS and associated risks – ie perforation from colonoscopy (approx. 50%)

A more localised inflammatory marker than ESR or CRP

Suspected bowel malignancy

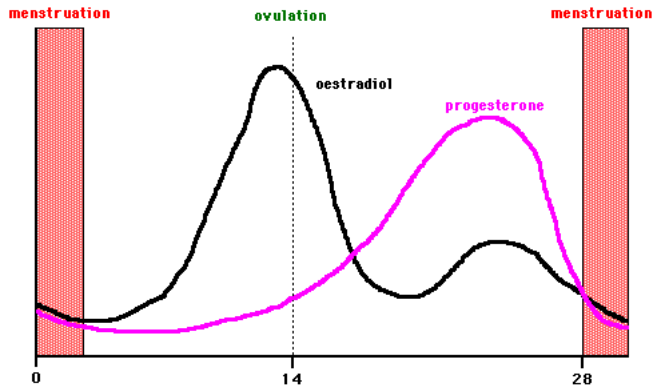
BMJ article in 2001 showed much more sensitive than FOB but less specific (79%, 72% vs 43%, 92%)

BJGP article Feb 2016 showed that in suspected cases the NPV of 97% could save about 28% of 2ww referrals for suspected colorectal Ca

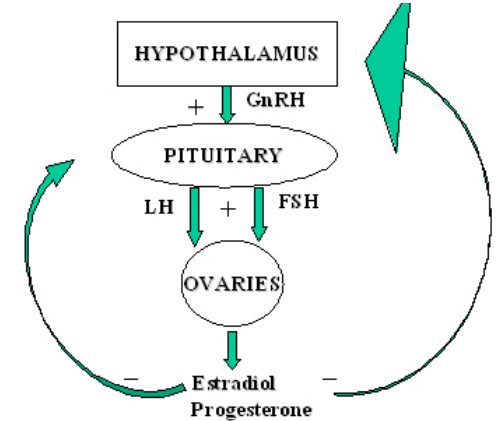
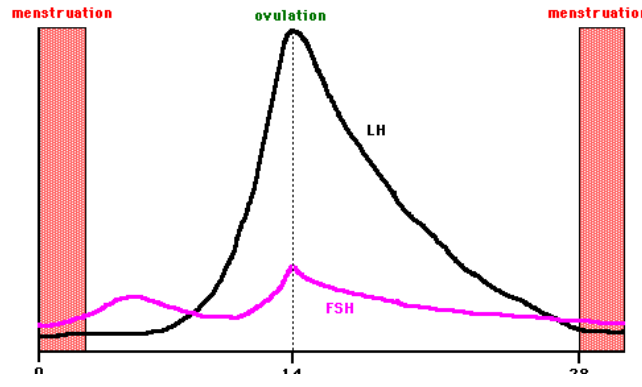
...If in doubt can repeat

Progesterone, FSH/LH

Uestradiol & progesterone in the menstrual cycle



FSH & LH in the normal menstrual cycle



FSH/LH: measure in first 4 days of cycle. Progesterone 7 days prior to period

1. Menstrual irregularities - Premature menopause suspected <45 years (High FSH >30 and high LH), PCOS (LH >10, FSH normal)

2. Infertility - Primary gonadal failure v pituitary cause, ovulation

3. Pituitary gland dysfunction

4. Pubertal/growth problems

FSH/LH: **high** in primary gonadal failure, testicular injury precocious puberty; **low** in secondary gonadal failure, anorexia, starvation, drugs

Remember:

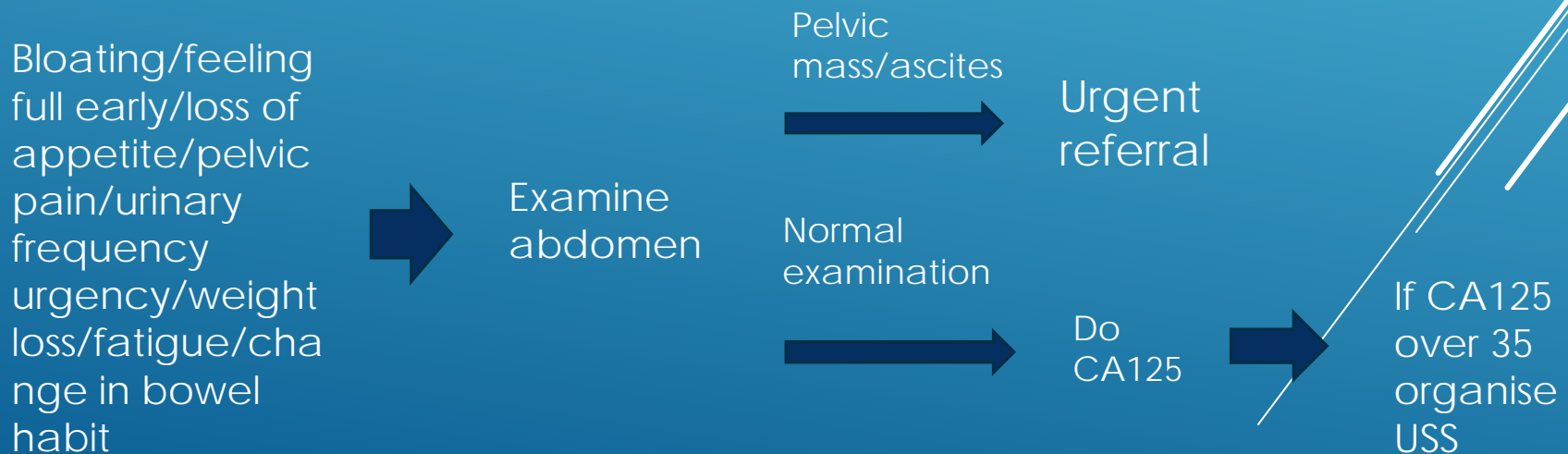
Uninterpretable on COCP. Not advised to confirm menopause >45years unless >50y + on progesterone only contraceptive and amenorrhoeic.

CA125 Serum tumour marker

Reference range <35
= normal

- Elevated in 80% of patients with advanced ovarian cancer
- However may be normal in 50% of early stage ovarian cancer i.e. not sensitive
- Also may be raised in pancreatic, gastric, colonic and breast carcinoma as well as benign ovarian cysts, PID, ascites, endometriosis i.e. not specific

Uses: 1. Investigation of symptoms suggestive of ovarian cancer
2. Monitoring disease progression/response to treatment in ovarian cancer



Testosterone

Testosterone level.	Male	Female	Both.
↓	Delayed puberty. Klinefelter's syndrome, Kallmann's syndrome, myotonic dystrophy). ED, Infertility. Primary (Balls) / Secondary (Brain) hypogonadism. "Male Menopause"	Menopause.	Hypothalamic/pituitary disorders.
↑	Preconscious puberty. Testicular tumours. End organ insensitivity.	Infertility. PCOS Hirsutism. Ovarian tumours.	CAH. Adrenal tumours.

Late onset Hypogonadism "Male menopause".

- Decline in Testosterone levels of around 2%/year from 30-40 years.
- Symptoms: Loss of libido, Erectile dysfunction, decreased morning erections, Obesity, Sarcopenia, Low bone mass, Depressive thoughts, Fatigue, Loss of body hair, Hot flushes, Loss of vigour.
- Associated conditions: TIIDM, Obesity, Pituitary disease, ESRF, COPD, HIV, #, Medications (corticosteroids, opiates).
- Measure Early morning and fasting, on two separate occasions. Measure the free testosterone level if borderline result (8-12 nmol/L), or known SHBG abnormality. Analyse LH serum levels to differentiate between primary and secondary forms of hypogonadism.
- Screen for concomitant osteoporosis.

<http://uroweb.org/guideline/male-hypogonadism/?type=pocket-guidelines>

SHBG (sex hormone binding globulin)

A total testosterone test determines the overall quantity of testosterone, that is bound and unbound testosterone.

In many cases, this is sufficient to evaluate excess or deficient testosterone production (e.g. infertility, decreased sex drive, and erectile dysfunction in men or infertility, irregular menstrual periods, and excess facial and body hair in women).

Bound testosterone is carried by SHBG, a protein in the blood. In this form, it is inactive. Unbound testosterone is free in the blood and is active. Total testosterone is a summation of these.

SHBG is measured when your total testosterone results do not seem to be consistent with clinical signs and symptoms of excess or deficiency. In these case, the SHBG levels are abnormal and the likely cause of signs and symptoms.

A high SHBG level means that, likely less free testosterone is available to the tissues than is indicated by the total testosterone test. A low SHBG level means that more of the total testosterone is bioavailable and not bound to SHBG. These may be in more keeping with the clinical signs.

Estrodiol is another sex hormone carried in the blood.

High SHBG : liver disease, hyperthyroidism, anorexia, and oestrogen use

Low SHBG: obesity, hypthyroidism, cushing's disease, androgen use



All you ever wanted to know about : PSA

- PCRMP - Prostate Cancer Risk management program for over 50s
- Benefits, limitations, Risks
- Key Statistics
- Whom to offer PSA
- other conditions causing raised PSA
- Preparing for the test
- Range :
 - 40-49=2 or higher
 - 50-59=3 or higher
 - 60-69=4 or higher
 - 70-75=5 or higher
- What happens next – normal, slightly raised, raised, very high
- Good to know
 - FAQ and patient trade offs : Decision Aid (patient.co.uk)
 - NHS Shared Decision Making (sdm.rightcare.nhs.uk)



Angiotensin Converting Enzyme

- Part of R-A-A system to regulate blood pressure
- Mainly found in lung vascular endothelial cells
- Normal levels: 0-57 units/L
- Sarcoidosis is a chronic inflammatory condition where non-caseating granulomas form, >90% involves lungs
- Sensitivity 57%, specificity 90%, PPV 90%, NPV 60%
- Elevated ACE also found in several other systemic conditions, also in 5% healthy population
- Initially used for monitoring disease activity but now thought to be of limited value

Troponin

- Cardiac ischaemia
- Important to establish a rise or fall (as per third universal definition of MI) – at first assessment and 6 hours later (if using highly sensitive assay)
 - Tropl <17ng/L = no cardiac damage
 - Tropl 17-56ng/L = repeat in 6 hours
 - Tropl >56 = evolving MI, repeat in 6 hours
- Tropl elevated for 5 days, TropT for 7-10 days
- Stable troponin – consider alternative to cardiac ischaemia (highly sensitive assays are more sensitive but less specific)
- Non-ischaemic causes: PE, sepsis, heart failure, renal failure, SAH, tachycardia/arrhythmia, COPD, myocarditis

NT-proBNP

1. **What is it:**
 - a. NT-proBNP and BNP are biologically active form of ProBNP (brain natriuretic peptides).
 - b. Hormones released from ventricles in heart disease or increased load on the ventricles.

2. **Use: To exclude heart failure and aid diagnosis of heart failure.**
 - a. Either BNP or NT-proBNP can be used, depending on local availability.
 - b. Normal levels virtually excludes the diagnosis of heart failure (beware false negatives)
 - c. Raised levels more than 95% specificity and 98% sensitivity for HF diagnosis
 - d. Raised levels correlate with severity
 - e. Decreases with effective treatment

3. **Interpretation: NICE referral guidelines**
 - a. **NT-ProBNP >2000 pg/mL = 2 week wait referral to Cardiology**
 - b. **NT-proBNP 400-2000 pg/mL = Refer to cardio within 6 weeks**
 - c. Normal Levels <400 pg/mL = HF unlikely. Refer if clinical suspicion of HF and conditions that may cause false negative result.

4. **Limitations: NT-proBNP:**
 - a. Reduced by:
 - i. BMI > 35
 - ii. Drug: ACE-I, AIIIRA, Beta blockers
 - b. Increased by:
 - i. Age
 - ii. Female gender
 - iii. Other cardiac conditions e.g. LVH/MI
 - iv. Respiratory conditions e.g. COPD, pulmonary HTN
 - v. Sepsis
 - vi. Liver cirrhosis
 - vii. CKD
 - viii. Diabetes Mellitus

5. **Other tests to consider alongside it:** CXR, ECG, Bloods (TFTs, LFTs, Hb1AC, U+Es).
Echo (arranged by specialists)

Folate (aka Folic Acid/Vit B9) 2-20ng/dl

Plasma folate VS RedBloodCell folate (used for diagnosis once plasma levels low)

CAUSES:



Diet (overcooked food)
Alcohol use
Age (advanced)
Malabsorption (IBD...)
↑folate demand
Medications



Pernicious anaemia
Vegetarian diet
Vitamin B12 deficiency

FOLATE in PREGNANCY:

400mcg for all
5mg if Hx NTD, Coeliac,
DM, Obesity, Sickle,
Epileptic meds

CONSEQUENCES:

Macrocytic anaemia
Neural tube defects
Increase methotrexate toxicity

DIET SOURCES:

Meats/egg
Legumes
Starches
Fruit&veg (green, banana,
orange, peach)

TREATMENT:

Folic Acid supplement.
?Vit B12 supplement