York Teaching Hospital NHS
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Requesting and Interpreting Lab Tests

Alison Jones

Consultant in Clinical Biochemistry

- Focus on:
  - Tests / panels we would like to improve requesting / interpretation
  - Areas where we receive the most queries
  - The role of the Clinical Biochemist

https://tinyurl.com/YorkLabMed

- I won't be talking about (I am not an expert on):
  - ICE requesting (in any detail)
  - Lipids

Dr Deepak Chandrajay, Consultant in Metabolic Medicine
(deepak.chandrajay@york.nhs.uk, 01904 72 5855 / 5670)

- Focus on:
  - Tests / panels we would like to improve requesting / interpretation
  - Areas where we receive the most queries

- Troponin
- Ferritin and Iron Studies
- Thyroid Function Testing
- HbA1c and diabetes
- Paracetamol
- Other guidance

Troponin

- Measurement of troponin in Primary Care is rarely helpful
- Diagnosis of ACS requires clinical symptoms plus a rise and or fall in troponin level (i.e. more than one measurement)
- A negative troponin result cannot rule out ACS if the patient presents more than 12h after symptoms
- https://cks.nice.org.uk/
- The only reference to troponin in this Clinical Knowledge Summary is to guide the urgency of referral in patients who have chest pain >72h ago (Refer to Rapid Access Chest Pain Clinic)
- *If you must request troponin – agree a plan with the lab (Duty Biochemist), hospital (on-call Med Reg) and patient, in case of a positive result*

Directorate of Laboratory Medicine
Department of Clinical Biochemistry
Filename: CB-INF-GPTPT
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Troponin testing in Primary Care

Troponin is a cardiac structural protein released during myocyte injury. Two of its subunits can be measured to indicate myocardial damage: Troponin I and Troponin T. The labs at York and Scarborough provide **Troponin T**

DO NOT request troponin in Primary Care / Community:

- If the patient has suspected acute coronary syndrome (ACS) with chest pain >15 minutes duration – **dial 999**
- If the patient has had symptoms suggestive of ACS within the past 72h – **urgent assessment in ED required**
- If the chest pain is non-cardiac
- To diagnose angina

The Universal Definition of MI requires:
Rise or fall in cardiac troponin with 1 value above the 99th centile
AND *relevant ECG changes*
OR *symptoms of ischaemia*

The 99th centile for Troponin T is 14ng/L. This means that 99% of healthy individuals will have a Troponin T <14ng/L.

Troponin T results must be interpreted in light of the clinical presentation.

The laboratory will phone primary care Troponin T results >14ng/L to either GP surgery or GP out of hours service.

- **If hs Troponin T <5ng/L** ACS is excluded if >3hr post chest pain
- **If hs Troponin T 5-14ng/L** ACS is unlikely if >3hr post chest pain
- **If hs Troponin T 14-51ng/L** Discuss with cardiology/ambulatory care
- **If hs Troponin T >51ng/L** Further assessment in ED usually required

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Some Non-Cardiac causes of elevated hs TroponinT in the absence of an MI:
Pulmonary Embolism, Renal Failure, COPD, Diabetes, Acute neurological event, Drugs/Toxins
Non-acute elevations in hs Troponin T >14ng/L - seek Cardiology advice

Ferritin and Iron Studies

- Most ferritin requests due to (?)anaemia
- High ferritin and / or iron studies (iron / TSats) is an incidental finding
- Ferritin **alone** is sufficient to diagnose iron deficiency in most cases
  - Iron studies can be misleading – patient on iron (OTC), dietary influences
  - Persistently elevated ferritin and CRP with strong suspicion of iron deficiency – measure FASTING iron studies

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Elevated serum ferritin (CRP <5mg/L)

Check iron studies

Transferrin saturation >50%

Repeat on a fasting sample

FASTING transferrin saturation >50%

IRON OVERLOAD LIKELY

Send 2 x EDTA samples for Hereditary Haemochromatosis (HH) genotyping ***

2 x HH genes

Routine referral to gastroenterology

<2 x HH genes

Patient at low risk of significant iron overload in absence of other risk factors ****

Lab will often add this

Transferrin saturation <50%

IRON OVERLOAD EXCLUDED

Clinical assessment:
- Alcohol history
- Liver disease
- Metabolic syndrome (BMI, BP, DM2, lipids)
- Inflammatory conditions
- Malignancy
- Renal failure
- Thyrotoxicosis

Check:
- FBC
- CRP/ESR
- U&E
- LFTs*
- HbA1c**
- Lipids**
- TFTs**

Advise appropriate interventions:
- Alcohol abstinence
- Improved glycaemic control
- Weight reduction
- Lowering triglycerides

* Abnormal LFTs: Consider viral hepatitis screening and / or abdominal US
** HbA1c, Lipids, TFTs: If clinically indicated / not checked in previous 12 months
*** Genetic testing: Ensure appropriate patient consent is obtained
**** Risk factors for secondary iron overload – multiple transfusions or iron infusions, chronic iron replacement, iron-loading anaemias (thalassaemia, chronic haemolytic anaemia, sideroblastic anaemia, dyserythropoeitic anaemia), chronic liver disease due to alcohol, Hepatitis B/C, NASH

References:
- Koperdanova M, O Cullis J. Interpreting raised serum ferritin levels. *BMJ* 2015; **351:** h3692
- Hazeldine S *et al.* Elevated serum ferritin: What GPs should know. *Aus Fam Phys* 2012; **41(12):** 945

Case Study – Tired

Mrs MC 72yo: SOB, Tires easily

- GP requested "usual panel" – including ferritin
  - Ferritin = 318ug/L (20 – 291)
  - Lab added iron studies – Transferrin Saturation = 75%

    Elevated ferritin and iron sat >50% - lab added comment:

"Consider sending fasting sample for iron saturation and 2 x EDTA samples for haemochromatosis gene analysis which will be processed if indicated. Consider requirement for patient consent for genetic testing."

- GP referred to gastro noting TATT (normally fit and well) and joint aches, with mildly raised ferritin and ALP.
- Gastro arranged liver screen due to raised ALP (prior to genotype results) – all NAD.

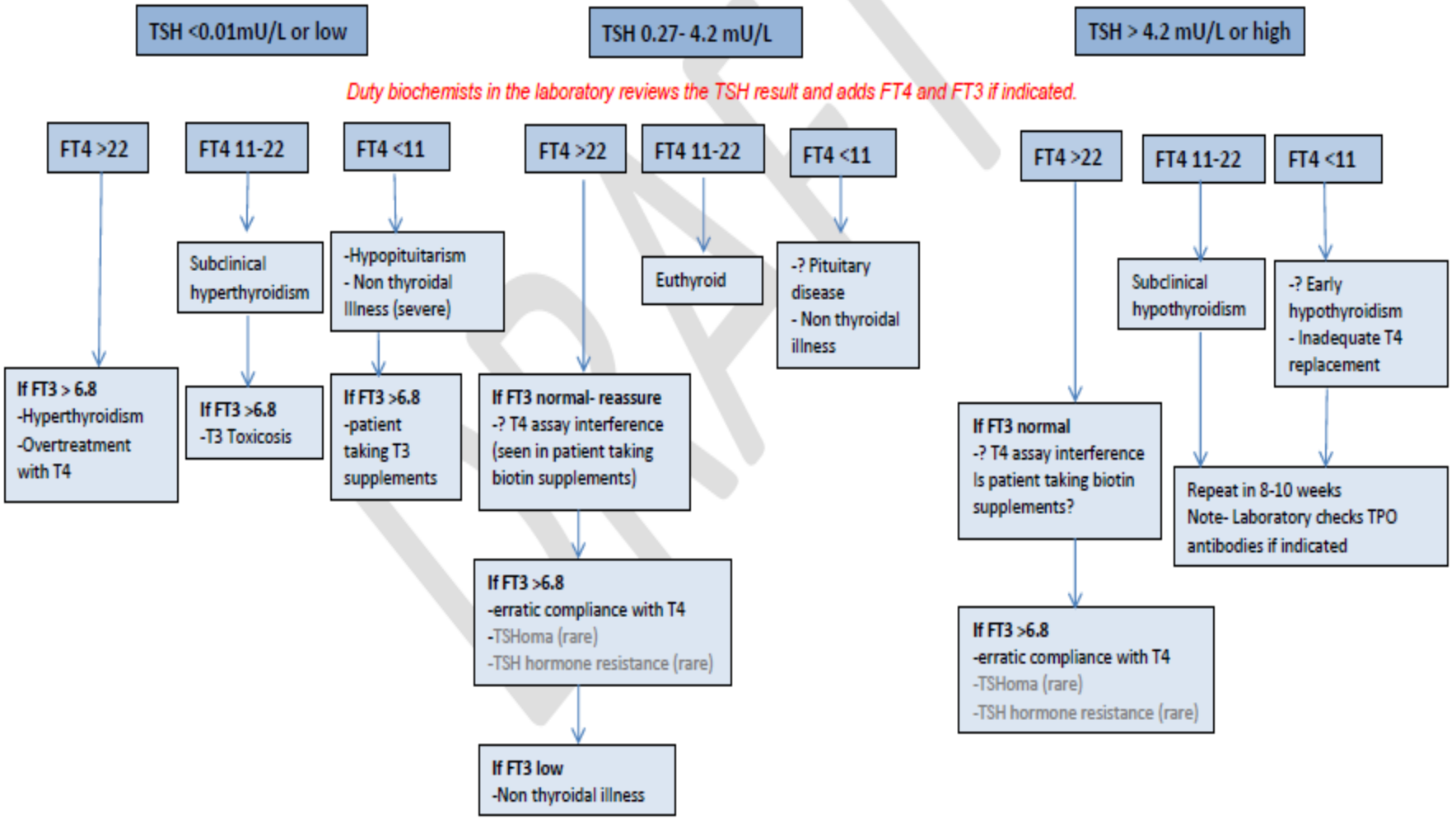
- Genetic testing confirmed C282Y homozygosity
- Commence venesection.
- Advise siblings to be screened.

Outcome - Haemochromatosis

- After 6 months, good symptomatic response to venesection re aches and lethargy.
- After 12 months, frequency of venesection reduced from fortnightly to monthly.
- After 2 years, venesection able to be stopped.
- Brother also tested and found to be affected – similar symptoms (tiredness and joint pains, ferritin = 598, iron sat = 66%)

Thyroid Function Tests

- TSH-only is the recommended first line test
  - FT4 and FT3 can be requested by a specific search
  - *Consulted with over 40 GPs and ACPs*
- Duty Biochemist reviews all abnormal TFTs and comments / adds further tests if indicated (please provide relevant clinical details)
- Lab software rejects repeat requests within 21 days (please provide relevant clinical details)



** High dose biotin supplements can interfere with TSH and FT4 measurement (⇩TSH and ⇧FT4)

HbA1c

- **Screening for diabetes:**
- **With symptoms** (e.g. polyuria, polydipsia and unexplained weight loss) plus one laboratory measure of hyperglycaemia:
  - HbA1c >47 mmol/mol
  - Random venous plasma glucose concentration ≥ 11.1 mmol/l
  - Fasting plasma glucose concentration ≥ 7.0 mmol/l

- **With no symptoms:**
  - Two 'diabetic range' lab tests on ***separate days***
  - If the second HbA1c sample is <48mmol/mol (6.5%) the person should be treated as at high risk of diabetes and the test should be repeated in 6 months, or sooner if symptoms develop

HbA1c cannot be used for the diagnosis of diabetes if:

RAPID CHANGES IN GLUCOSE METABOLISM:

- ALL children and young people
- Patients of any age suspected of having Type 1 diabetes
- Patients with symptoms of diabetes for less than 2 months
- Patients at high risk who are acutely ill (e.g. those requiring hospital admission)
- Patients taking medication that may cause rapid glucose rise e.g. steroids, antipsychotics
- Patients with acute pancreatic damage, including pancreatic surgery
- In pregnancy

FACTORS THAT INFLUENCE HBA1C FORMATION AND / OR MEASUREMENT

HbA1c

	Increased HbA1c	Decreased HbA1c
ERYTHROPOIESIS	⇩ Erythropoiesis (Iron, B12 deficiency)	⇧ Erythropoiesis (Iron, B12, EPO administration) Reticulocytosis Chronic liver disease
ALTERED Hb	Haemoglobinopathies – may increase or decrease	
GLYCATION	Alcoholism Chronic renal failure Acidosis	Aspirin Vitamin C and E Alkalosis
ERYTHROCYTE DESTRUCTION	⇧ Erythrocyte life span (splenectomy)	⇩ Erythrocyte life span (Hb'opathies, splenomegaly, RA, anti-retrovirals, ribavirin, dapsone)

- **Diagnose** diabetes using glucose measurements

Use of Glycatated Haemoglobin (HbA1c) in the Diagnosis of Diabetes Mellitus, WHO 2011

- **Monitor** diabetes using HbA1c (standard treatment targets may not apply) or fructosamine (glycated albumin)

Case Study

Contacted by endocrinologist regarding inconsistent HbA1c results.
Could this be due to a variant haemoglobin?

No indication of variant haemoglobin on HbA1c analyser

	HbA1c	Glucose	Fructosamine
01/02/16	125		
25/07/16	53		
06/01/17		15.5	
26/04/17	54		
17/10/17			
15/06/18	38		
14/11/18	27		
18/12/18	53	35.5	964 *

Fructosamine of 964 predicts an HbA1c of 181-195 mmol/mol!!

Review of clinic letters in CPD indicates patient is on dapsone

HbA1c is contraindicated in patients on dapsone as it can oxidise Hb to MetHb and cause haemolysis.

Unnikrishnan R, *et al*. Unexpectedly low HbA1c levels in two diabetic patients following dapsone use. *Indian J Endocrinol Metab*. 2012; 16(4): 658-659

Paracetamol

Refer to BNF – Emergency treatment of poisoning

ACUTE OVERDOSE (>75mg/kg)

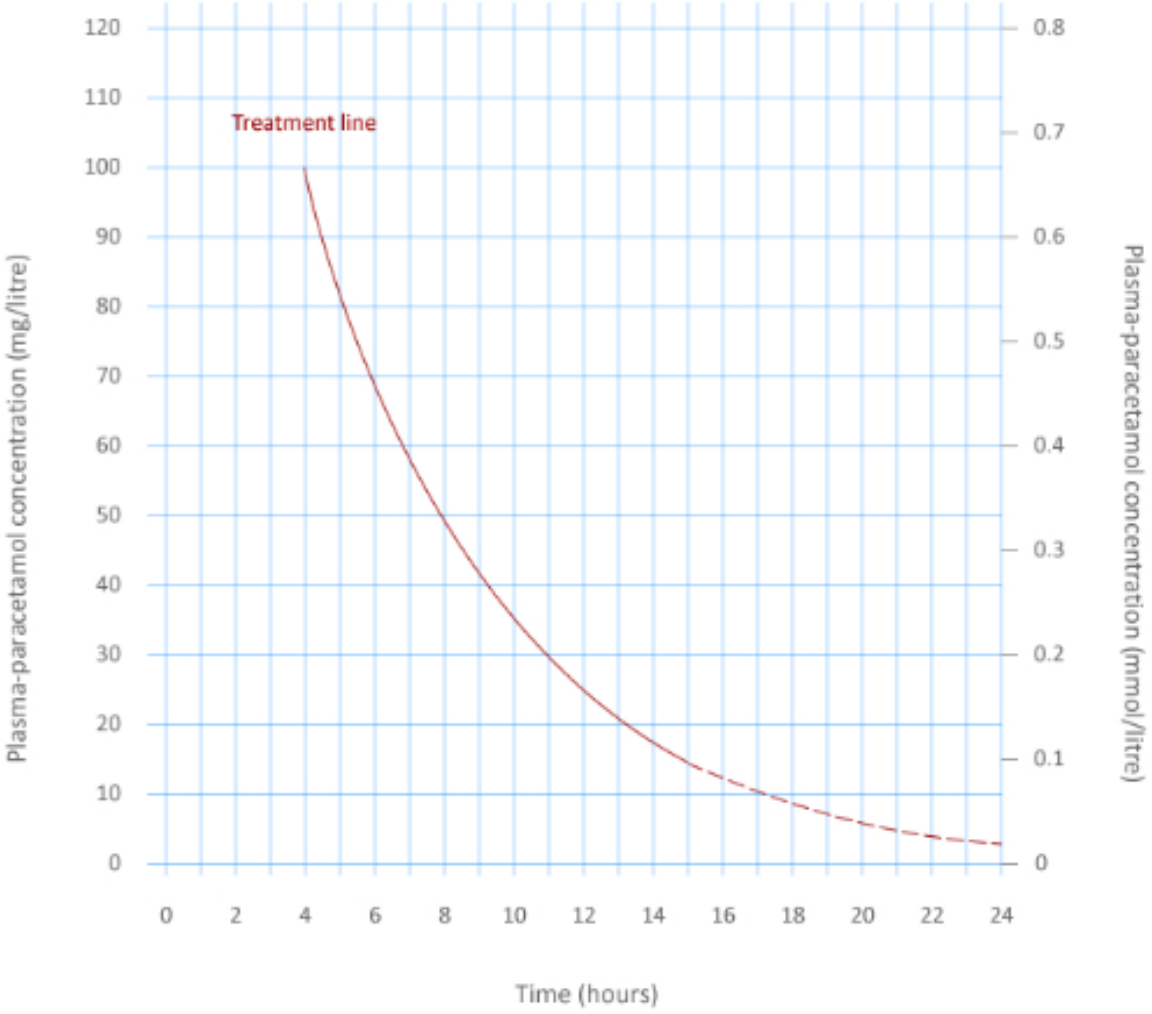
- <4h ago – send straight to ED. Don't take bloods.

Blood levels are helpful 4-15h post dose but may best be taken in ED

- 4-24h ago and >150mg/kg - send straight to ED.
- 4-24h ago and < 150mg/kg - take blood to check paracetamol level. Phone Duty Biochemist to make aware, agree a plan with patient (esp. if result will be phoned to Yorkshire Doctors)

Liver damage is maximal 3-4 days after overdose – do not hesitate to refer, even in the absence of early symptoms

Paracetamol treatment line



Paracetamol

THERAPEUTIC EXCESS (>150mg/kg in 24h)

- Send to ED unless:
  - >24h since last dose AND
  - Patient is asymptomatic AND
  - Plasma paracetamol is undetectable

    Phone Duty Biochemist to make aware, agree a plan with patient (esp. if result will be phoned to Yorkshire Doctors)
  - AND LFTs, creatinine and INR are normal
- Consider THERAPEUTIC EXCESS at 75-150mg/kg if concerning clinical / biochemical features present

Other Guidance

- Allergy testing
- BNP – *Updated version **live** this month*
- Hyperkalaemia – ***New** guidance **live** this month*
  - ***CKD-EPI** reporting and **eGFR-only** requests **live** this month (20th)*
- Elevated Creatine Kinase (CK)
- Screening for Cushing's Syndrome
- Faecal Calprotectin
- FSH and the menopause
- Paraproteins – Management in Primary Care
- Prolactin – *Updated guidance due this month*
- Therapeutic Drugs
- Thyroid Function Tests – ***New** guidance due this month*
- Requesting Zinc levels

https://tinyurl.com/BiochemInfo

What would you like to see?

The Duty Biochemist

- Consultant (or consultant-supervised) Clinical Biochemist / Chemical Pathologist
- Mon-Fri, 0900h-1700h, on 01904 72 6366 (or via Lab Enquiries: 72 6802)
- On-call consultant, via switchboard, outside of these hours

Clinical Authorisation

- 3 consultants – FRCPath - 1 GMC registered, 2 Clinical Scientists
- 2 juniors – FRCPath in progress
- 1 trainee – Healthcare Scientist training programme (3 year)

- Results filtered by a series of rules based on absolute values, changes from previous, location, age.
- See all results phoned by BioMedical Scientist (BMS) lab staff but many more – for commenting / less urgent communication
- Identify unusual patterns, unexplained changes, unexpected findings. Comment or phone – depending on urgency, and clinical information available to us

- Some examples……

Assay interference

- GP Diabetes review – routine bloods including Vitamin D
- Level measured in lab = >375 nmol/L
- D/w GP – patient not on supplements

- Referred for measurement by an alternative method (mass spec)
  - Vit D = 47.5nmol/L

Secondary causes

Case 1

50yo male – GP request: Clinical details erectile dysfunction, NHS healthcheck

- Chol = 7.7 (⇧)
  - Lab added TSH = >150 (⇧⇧)
- Treated with T4. TSH fell to within normal limits after 3 months.
- Unfortunately, lipids haven't been re-checked.

Case 2

63y female – GP request: No clinical details

- "Usual panel" including calcium and PTH
  - PTH = 11.2 pmol/L (1.1 – 6.9) (⇧)
  - Serum ACal = 2.34mmol/L (✓), eGFR = 78
- Lab added Vitamin D = <30nmol/L (⇩⇩)

Duty Biochemist – here to help

- What does this result mean?
- What test should I request to diagnose / rule out Cushing's?
- What is the significance of the urine drug screen results?
- How do I investigate ?Diabetes Insipidus?
- What's the significance of an isolated low ALP?
- Why wasn't this high potassium telephoned? (pseudohyperK)
- Why hasn't my test been processed?
- *How do I manage abnormal lipids in my patient?*
- What's the significance of a raised SHBG?