York Teaching Hospital NHS
NHS Foundation Trust

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/ - Chest Pain
- 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*

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

Directorate of Laboratory Medicine
Department of Clinical Biochemistry
Filename: CB-INF-HIGHFERRITIN
Version: 1.0
Date of issue: July 2017

York Teaching Hospital NHS
NHS Foundation Trust

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 routine bloods – 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

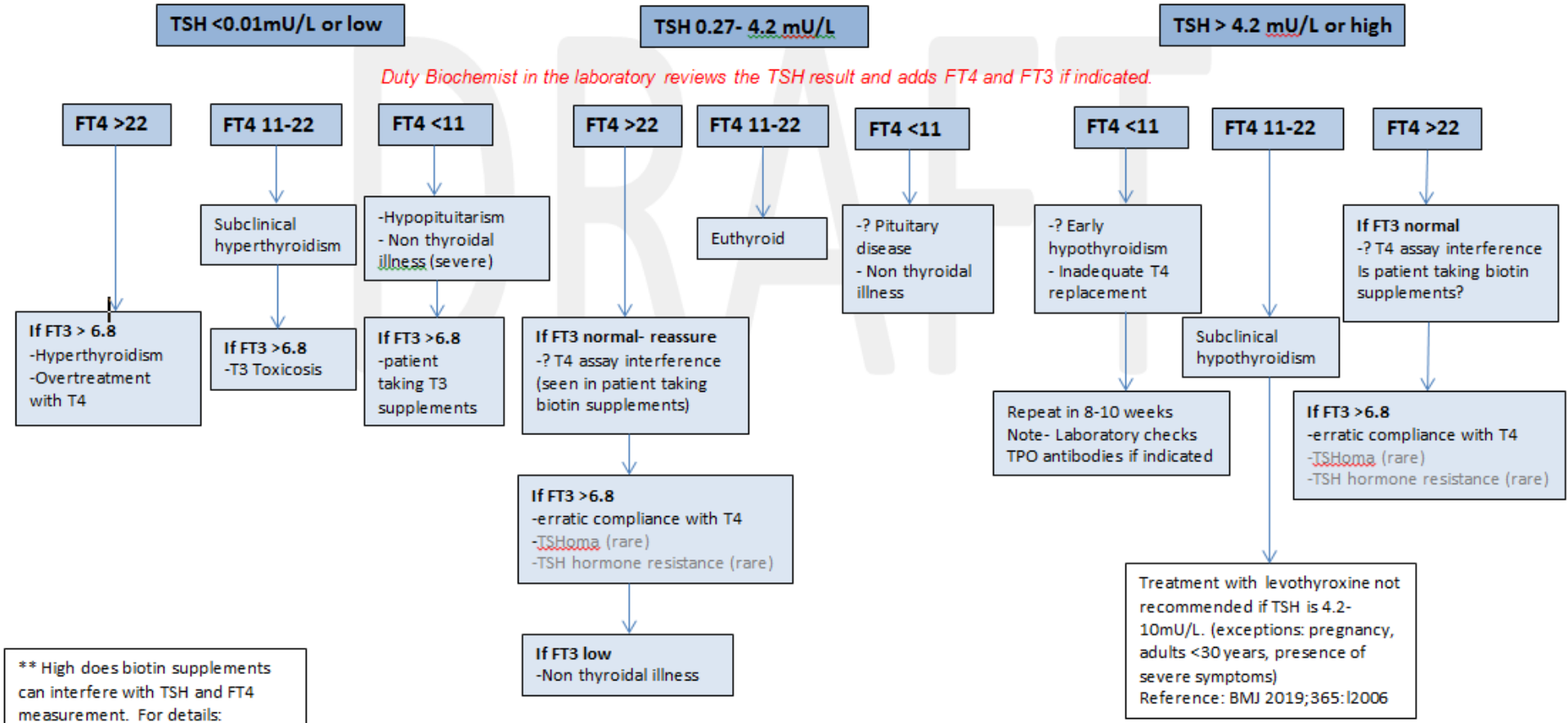
- After 6 months, good symptomatic response to venesection re aches and lethargy.
- After 12 months, frequency of venesection reduced from fortnightly to monthly.
- After 2 years, venesection able to be stopped.
- Brother also tested and found to be affected – similar symptoms (tiredness and joint pains,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

Interpretation of thyroid function test results.

(This pathway is not appropriate if the patient is pregnant or if taking amiodarone/lithium).



** 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 there are:

RAPID CHANGES IN GLUCOSE METABOLISM:

- ALL children, young people and 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 (RBC formation)	⇩ Erythropoiesis (Iron, B12 deficiency)	⇧ Erythropoiesis (Iron, B12, EPO administration) Reticulocytosis Chronic liver disease
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)
ALTERED Hb	Haemoglobinopathies – may increase or decrease	

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

- **Diagnose** diabetes using glucose measurements
- **Monitor** diabetes using HbA1c (if effect on Hb over time is consistent, e.g. variant Hb) 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 – 10 x 500mg tabs / 65kg adult)

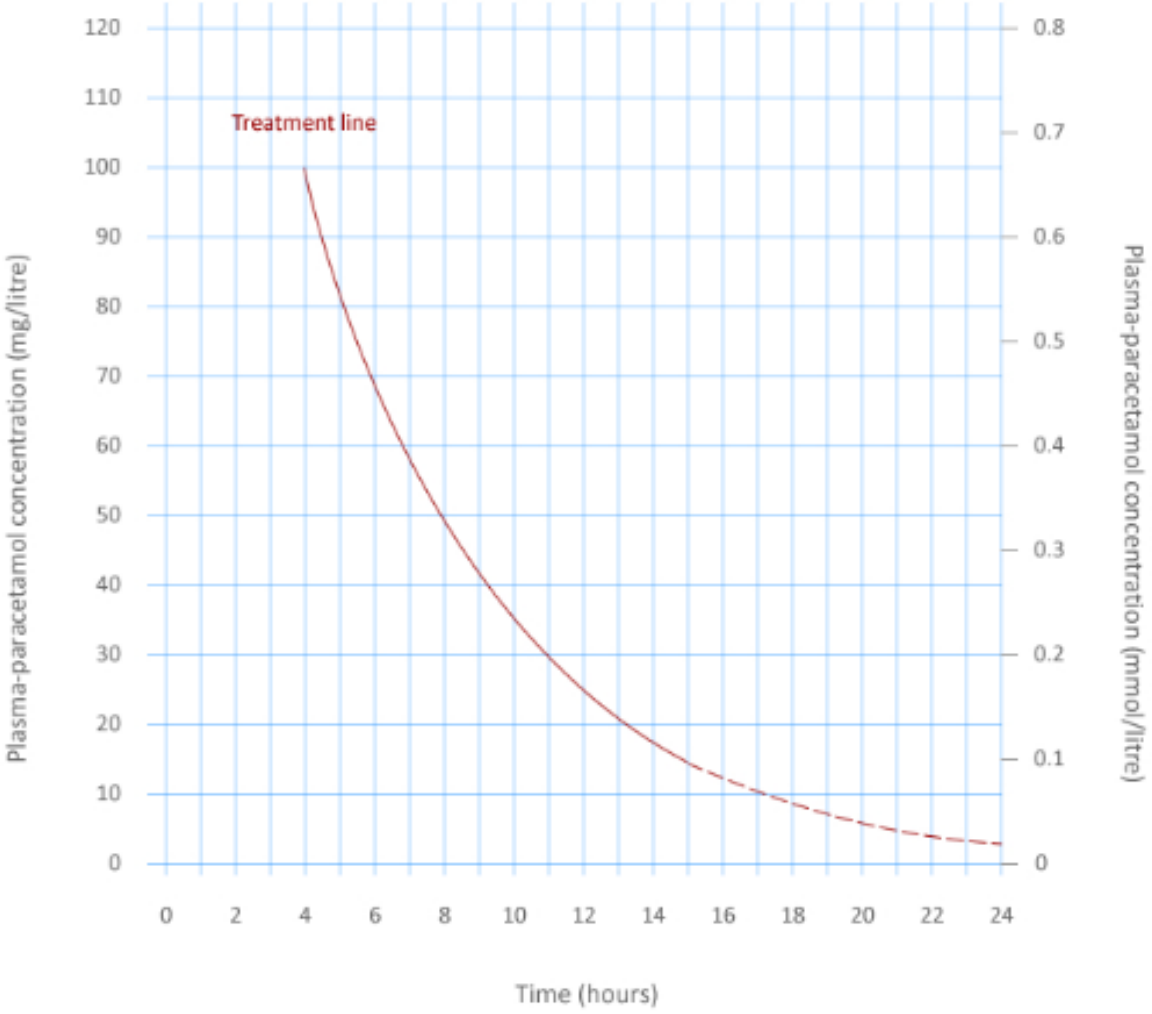
- <4h ago – send straight to ED. Don't take bloods.

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

- 4-24h ago and >150mg/kg – (20 x 500mg tabs / 65kg adult) - 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) – 20 tabs

- 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 for chronic heart failure
- Hyperkalaemia – investigation and management
  - eGFR-only request available in ICE
- Elevated Creatine Kinase (CK)
- Screening for Cushing's Syndrome
- Faecal Calprotectin
- FSH and the menopause
- Paraproteins – Management in Primary Care
- Elevated Prolactin
- Therapeutic Drugs
- Troponin in Primary Care
- Requesting Zinc levels

New guidance – due this month

- *B12, folate and ferritin*
- *Requesting and Interpreting Thyroid Function Tests*
- *Hyponatraemia – In progress*

https://tinyurl.com/BiochemInfo

What would you like to see?

York Teaching Hospital NHS
NHS Foundation Trust

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
- Email for non-clinical, non-urgent queries: yhs.tr-Biochemist@nhs.net

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?