

Requesting and Interpreting Lab Tests

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- 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

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- 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*

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:

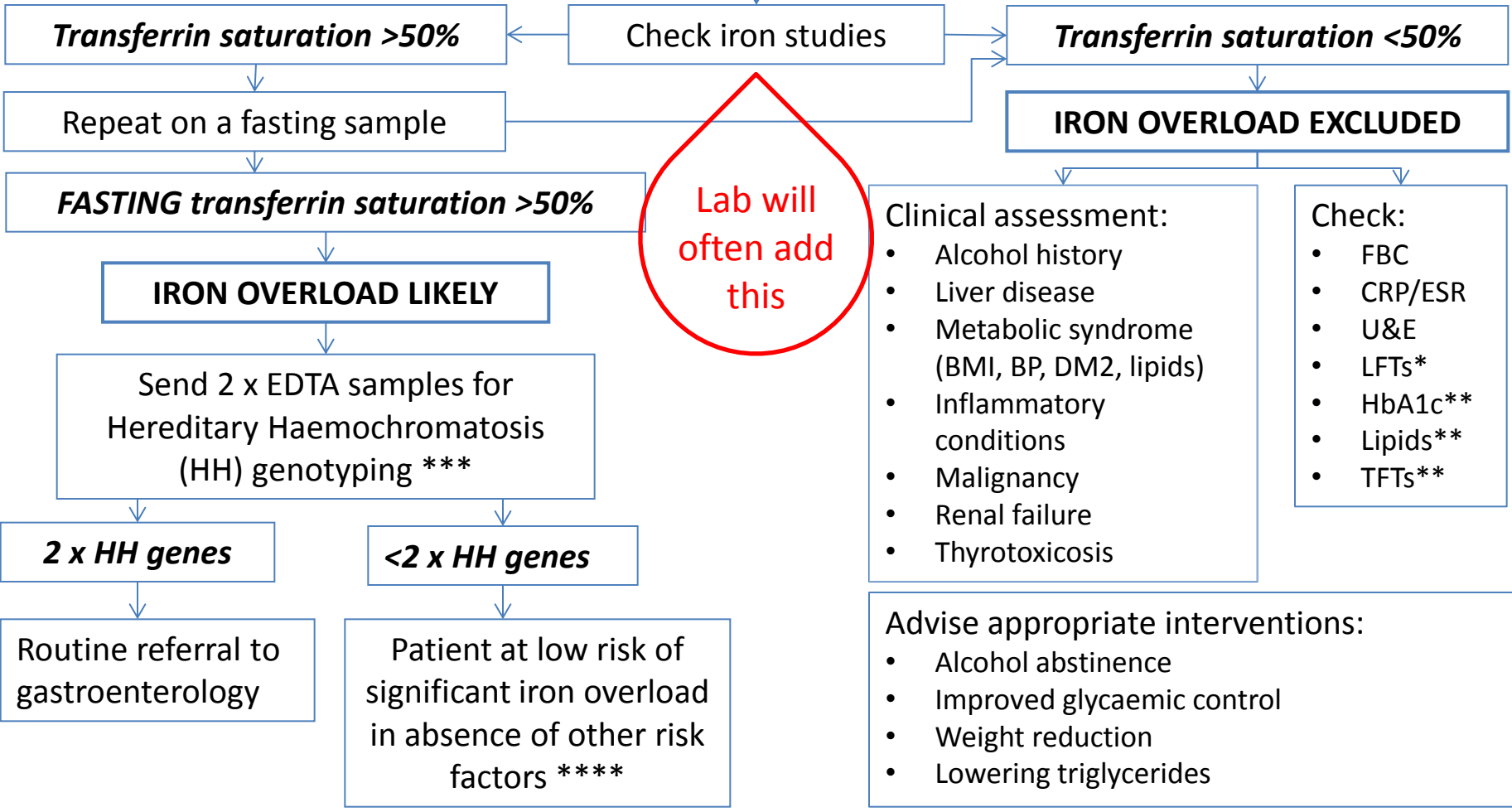
Pulmonary Embolism, Renal Failure, COPD, Diabetes, Acute neurological event, Drugs/Toxins

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

Elevated serum ferritin (CRP <5mg/L)



Lab will often add this

* 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, dyserythropoietic 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.”*

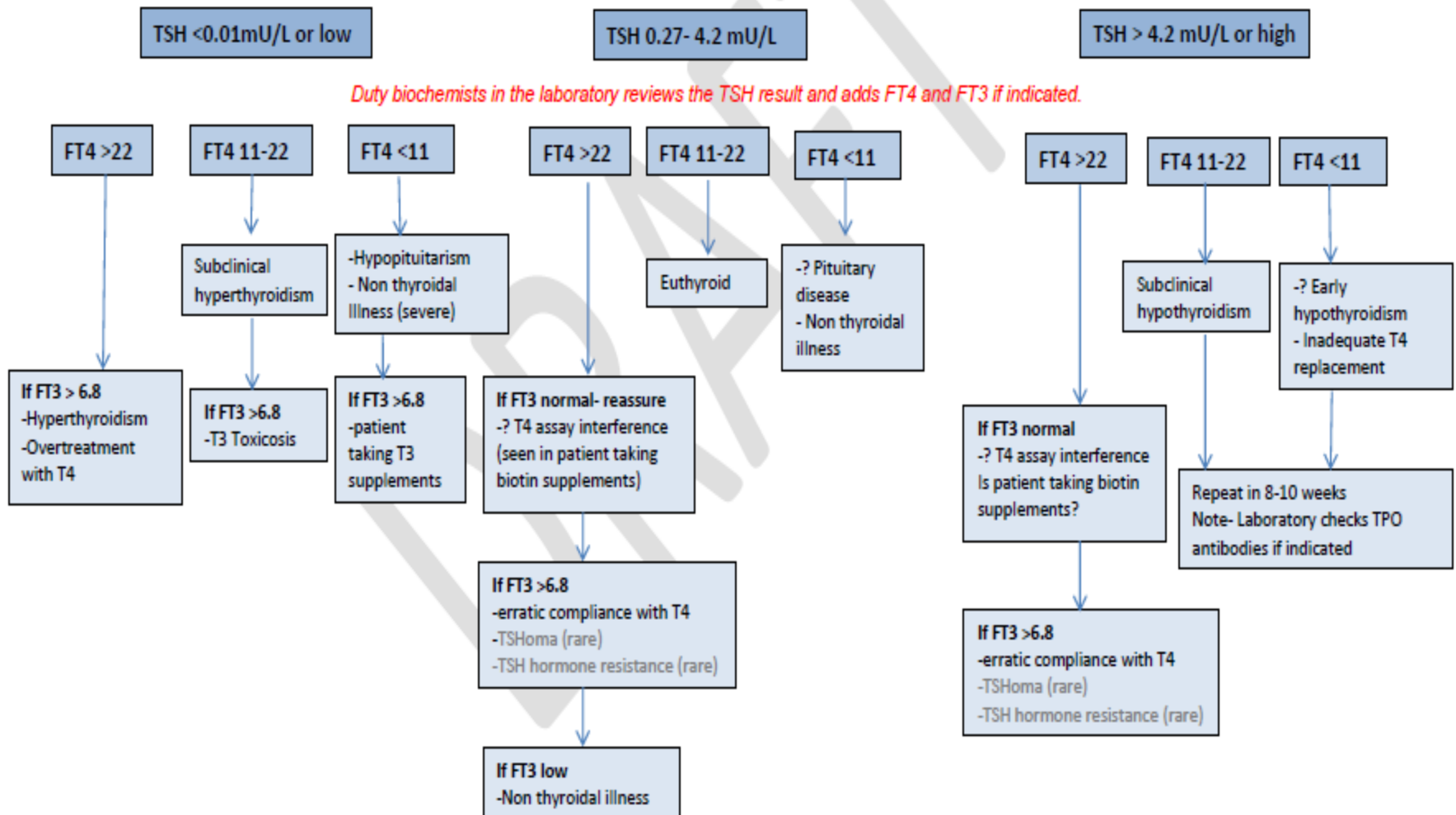
- GP referred to gastro noting TATT (normally fit and well) and joint aches, with mildly raised ferritin and ALP.
- Gastro arranged liver screen due to raised ALP (prior to genotype results) – all NAD.
- Genetic testing confirmed C282Y homozygosity
- Commence venesection.
- Advise siblings to be screened.

Outcome - Haemochromatosis

- After 6 months, good symptomatic response to venesection reaches 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)

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

- **Diagnose** diabetes using glucose measurements
- **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 dapson

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

Paracetamol

Refer to BNF – Emergency treatment of poisoning

ACUTE OVERDOSE (>75mg/kg)

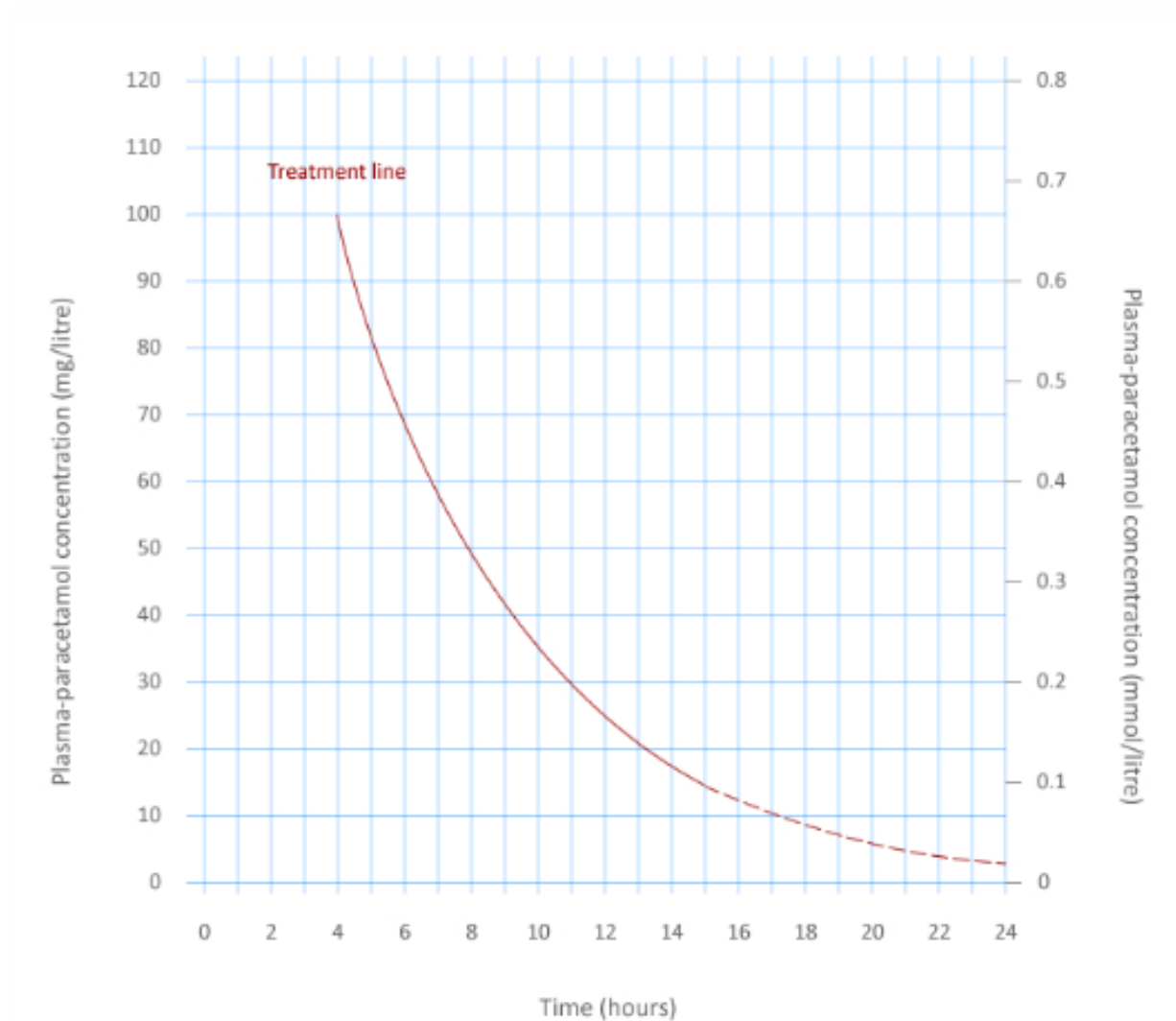
- <4h ago – send straight to ED. Don't take bloods.

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

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 = 47.5 nmol/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?