NORTH LONDON PARTNERS in health and care
North Central London's sustainability and transformation partnership

NHS

STP Diagnostics UPDATED MAY 2019

Phases 1&2: Implementation of *Right Test Right Time*: an optimisation programme for GP direct-access pathology

1.0 Background

There is a great deal of unwarranted variation in the use of pathology based on the blood sciences (biochemistry, haematology, etc). The Carter review[1] estimated that perhaps a quarter of pathology requests are unnecessary.

The North Central London (NCL) CCGs are working together on an STP project focused on pathology optimisation in primary care. The project draws on work that has been done for the Choosing Wisely campaign, and is inspired by the significant efficiencies found by colleagues in other parts of London, and North Devon.

A clinical reference group of local lead clinical pathologists, hospital specialists and GPs has been established under the banner of 'Right Test, Right Time'. This group aims to develop common guidance and tools, available for local implementation. This includes the introduction of universal 'online' ordering systems, via T-Quest or SunQuest, to improve ease of ordering and the efficiency and accuracy of communication with the labs. With these systems, GPs will be able to view hospital test results, where these have been processed in the same laboratory.

The first change clinicians are likely to have seen is removal of the ESR request from the front page of the order form, although the test remains orderable if required via the search function. There will be a 'pop-up' of information about why CRP is generally a more useful test for acute inflammation, and the exceptions for when ESR might be preferred.

This guidance now includes two additional clinical areas agreed in April 2019 in addition to those in phase one (February 2019). These will give clinicians seeking to answer common diagnostic or monitoring questions and, where appropriate, a rational collection of tests available with one click. Further guidance about some tests will come from a limited range of additional 'pop-ups'.

There is no plan to reduce the availability of the current range of pathology tests that can be ordered in primary care. Where GPs wish to order additional tests or reduce test requests they may do so.

For a more detailed explanation of the plans for the group and guidance **please contact your local GP diagnostic lead:**

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[1] Report of the Second Phase of the Review of NHS Pathology Services in England, Lord Carter of Coles (2008)

2.0 Agreed guidance

NCL guidance has been developed in the following clinical areas:

- Inflammatory markers – ESR and CRP
- Vitamin D and PTH
- Diabetes
- Cardiology (including lipids)
- Nephrology (CKD)
- Tumour markers
- Hepatology
- Immunology
- Endocrinology

2.1 ESR

PLEASE CONSIDER NOT ROUTINELY TESTING ESR

CRP is the preferred biomarker of inflammation: its concentration rises earlier and changes more acutely than ESR.

The **exceptions** to this are to aid in the diagnosis, and monitoring response to therapy, of certain chronic conditions including temporal arteritis, polymyalgia rheumatica, multiple myeloma, systemic vasculitis and rheumatoid arthritis.

In primary care, it is unlikely that useful clinical information will be obtained by testing both ESR and CRP on the same sample. Do not request both CRP and ESR unless you can be sure doing so will benefit the patient.

Evidence:
https://bpac.org.nz/resources/other/audits/bpac_crp_audit_ww.pdf
http://www.choosingwisely.org/clinician-lists/american-society-clinical-pathology-erythrocyte-sedimentation-rate-for-acute-phase-inflammation"

2.2 Vitamin D

Routine monitoring of vitamin D levels is not required or recommended.

DO TEST:

1. Patients with bone disease such as osteomalacia or osteoporosis that is amenable to treatment with vitamin D

2. Patients about to start treatment with a potent antiresorptive agent (zoledronate or denosumab) or patients with Paget's disease, prior to use of a bisphosphonate

3. Patients with musculoskeletal symptoms (generalised bone or muscle pain, proximal myopathy) that may be attributable to vitamin D deficiency

4. When investigating abnormalities of corrected calcium levels, and for patients at risk of renal bone disease (CKD 4 and 5).

DO NOT TEST:

Asymptomatic high-risk individuals.

These patients should instead be offered lifestyle advice about sun exposure, diet and over the counter supplements.

Examples of risk factors for vitamin D-deficiency include:

- Reduced sunlight exposure
- Black or ethnic minority with darker skin
- Living in residential care, or prison
- Taking medications that affect vitamin D metabolism (such as phenobarbital, carbamazepine, phenytoin, valproate)
- Suspected malabsorption states e.g. IBD, coeliac disease, cystic fibrosis, previous gastric bypass surgery.

After vitamin D supplementation

Measure corrected calcium levels within 1 month of completing the loading regimen, in case primary hyperparathyroidism has been unmasked.

There is no need to measure PTH unless the calcium is abnormal (see PTH section 2.3, below).

Vitamin D levels should be retested 6 months after supplementation *only* if the cause of deficiency was malabsorption and this remains a concern.

Inappropriate testing of vitamin D

Vitamin D is an extensively requested test, often for patients with non-specific symptoms such as tiredness, fatigue, malaise, exhaustion, 'off-legs', general decline, frailty, dizziness.

The results are rarely helpful and much less testing of vitamin D would not cause clinical harm.

Evidence and references:

NHS advice about healthy diet and supplements
Vitamin D and Bone Health: a practical guideline - National Osteoporosis Society
Vitamin D: supplement use in specific population groups - NICE
Vitamin D deficiency in adults - treatment and prevention – NICE CKS
Epilepsy - NICE CKS
Too much testing and treating? Clinical Medicine, Royal College of Physicians

2.3 PTH Testing

The appropriate indications for testing parathyroid hormone are:

1. Hypercalcaemia
   PTH high > refer to endocrinology
   PTH low > investigate for malignancy

2. Hypocalcaemia and normal vitamin D

3. CKD Stage 4 and 5
   PTH requested with calcium and vitamin D (usually only by low clearance clinic)

A **common inappropriate indication for testing PTH** is monitoring after vitamin D replacement. Only a serum calcium is needed, one month after high-dose vitamin D replacement. Request PTH only if the calcium level is abnormal.

Evidence and references
NICE CKS Hypercalcaemia
NICE CKS Chronic kidney disease

2.4 Diabetes

In order to monitor diabetes and its complications and associated conditions, including fatty liver, dyslipidaemia and thyroid problems, the following order sets have been developed.

Type 1 diabetes

Annual review

- U&Es, ALT[2], HBA1c, lipids, urine ACR, TSH[3]

Type 2 diabetes

New diagnosis

- U&Es, ALT, HBA1c, lipids, TSH, urine ACR

Annual review

- U&Es, ALT, HBA1c, lipids, urine ACR

Long-term use of metformin is associated with biochemical B12 deficiency. Consider measuring vitamin B12 levels in metformin-treated patients, especially if they have anaemia.

Hba1c and haemaglobinopathy
The NMUH measures HBA1c with a technique unaffected by common interferences such as haemoglobin variants. If this means of testing is not available, fructosamine levels can be used to monitor (but not diagnose) diabetes in patients with haemoglobinopathies.

Evidence and references
NICE Diabetes guidelines (2017)

[2] Where this is available to order as a single test. An AST will be automatically requested ('reflexed') if the ALT is abnormal to help diagnose fatty liver. Where this functionality is not available, the order set may trigger a full LFT panel.
[3] Where this is available to order as a single test. A free-T4 will be automatically requested ('reflexed') if the TSH is abnormal.

2.5 Cardiovascular disease

A series of test groups have been agreed to simplify pathology requesting for certain cardiovascular conditions at diagnosis and for the annual reviews of established CVD conditions including ischaemic heart disease, peripheral vascular disease, stroke, hypertension and heart failure.

Suspected heart failure diagnosis

- FBC, U&E, LFTs, NT-pro-BNP, lipids, HbA1c, TSH.

A urine dipstick should also be performed. Proceed to urine ACR if proteinuria is found.

Suspected hypertension

- U&Es, LFTs, HbA1c, lipids
- Urine dipstick, protein found → urine ACR

CVD annual review

- U&Es, HbA1c, lipids
- Urine dipstick, protein found → urine ACR

Starting statins (if none of these tests have been done in the last 3 months)

- U&Es, full lipid profile, ALT, HbA1c, TSH

Monitoring a statin at 3 and 12 months

- Lipid profile, ALT

If a 40% reduction in non-HDL cholesterol is achieved, there is no need to continue repeating the lipid profile in primary prevention.

Statins do not require liver enzyme monitoring if stable at 12 months unless clinically indicated.

Measuring lipids

To estimate cardiovascular risk a *standard* lipid profile (shown as 'lipids' in this document) is required. The total cholesterol and the HDL are measured. From this, the non-HDL cholesterol can be derived.

A *full* lipid profile, including triglycerides should be checked before starting lipid-lowering therapy. This does not need to be repeated after a normal result has been found once.

Patients do not need to fast for either test.

Evidence and references:

NICE hypertension guidelines (Nov 2016)
NICE heart failure guidelines (May 2018)
NICE Cardiovascular disease: risk assessment and reduction, including lipid modification (Sept 2016)

2.6 Nephrology test groups

CKD 3a (A1 or A2) Annual
- U&Es / eGFR, urine ACR

CKD 3a A3 / CKD 3b 6-monthly
- U&Es / eGFR, urine ACR

CKD 3b Annual
- U&Es / eGFR, urine ACR, FBC, lipids, HBA1c

For new onset CKD 3b, especially if there is proteinuria and raised calcium, please think of myeloma[4].

If anaemia is found, request haematinics. These can usually be obtained from the existing sample if requested within three days.

Evidence and references:
NICE CKD (2014)
NCL CKD Pathway guidance

2.7 Tumour markers

Tumour markers usually perform badly as diagnostic or screening tests. In particular, false reassurance can be obtained by tests that may have poor sensitivity.

These tests will be removed from the standard lists available by electronic ordering systems, but since they are an important part of surveillance, they can be arranged on request.

The RTRT group has agreed that the *only* tumour markers expected to be requested by GPs are:

- CA-125 (ovarian)
- PSA (prostate)
- Serum protein and urine (Bence Jones protein) electrophoresis (myeloma screen)

B-HCG can be requested as a pregnancy test.

2.8 Hepatology test groups

Order sets for use in the event of abnormal liver function tests and suspected viral hepatitis.

This information does not replace the detailed pathways that are available to guide clinicians on the management of abnormal LFTs.

Case finding hepatitis B and C
- Hb Surface Ag, HCV Ab

[4] Myeloma UK Diagnostic Pathway

Hepatitis B surface Ag positive

- FBC, INR, LFT (including AST), HBV viral load, Hepatitis C Ab, Hepatitis D Ab, HIV, AFP

Hepatitis C Ab positive

FBC, INR, LFT, AST, TFT, HCV viral load, HCV genotype, Hepatitis B sAg, HIV

Extended LFT Screen (ALT repeated after 1 month is still raised)

FBC, INR, LFT (including GGT and AST), HB sAg, HCV Ab, autoantibodies, ferritin/iron studies, caeruloplasmin (only for patients <40yr), immunoglobulins, alpha-1 antitrypsin

ALT>300: an acute hepatitis screen

Hepatitis A IgM
Hepatitis B core antibody, IgM
Hepatitis B surface Ag
Hep C Ab

} Acute hepatitis screen

Liver autoantibodies, immunoglobulins, FBC, LFT, AST, GGT

Consider also drug induced injury

Fatty liver on ultrasound

- FBC, LFT, AST
- Calculate Fib-4
  Fib-4 > 3.25 → high risk of advanced fibrosis → refer to secondary care.

If ELF test is available

- Fib-4 1.3-3.25 → Request ELF test

For fatty liver (aka NASH):

- ELF > 9.8 → High risk of advanced fibrosis → refer to secondary care.

For those drinking harmful amounts of alcohol and at risk of fibrosis:

- ELF > 10.5 → High risk → refer to secondary care.

If low risk of fibrosis, repeat LFTs and calculate Fib-4 annually.

Evidence and references:
Aligns with NCL liver pathways and NICE guidance.
Fib-4 calculator: https://gps.camdenccg.nhs.uk/fib-4-calculator

2.9 Immunology testing in primary care

2.9.1 Immunodeficiency

Repeated bacterial infections (≥4 infections in one year), particularly with encapsulated organisms, may suggest antibody or complement deficiency.

Useful initial investigations are IgG, IgA and IgM levels, C3 and C4.

2.9.2 Allergy

An allergy-focused clinical history is essential to the diagnosis of allergy and in many cases no blood testing is required in primary care.

The review group has decided not to provide allergy testing order sets.

Children should not be subjected to blanket IgE testing looking for a possible cause of their symptoms. Children can be referred to the paediatric allergy clinic for skin prick tests +/- specific IgE tests if this is required to help make a diagnosis.

Further guidance on diagnosis and assessment of allergy can be found in the references below.

2.9.3 Rheumatology autoimmune antibody testing

Autoimmune rheumatological testing **should only be done** in the context of a patient where there is a higher clinical suspicion.

Do not use these tests as 'screens': If an autoimmune condition is likely, specific autoantibody tests can help to narrow a differential diagnosis but are not essential for referral.

Refer patients early if they have a history or examination findings consistent with inflammatory rheumatological condition.

Early Inflamatory Arthritis (EIA):

- CRP, Rheumatoid Factor, Anti-cyclic citrullinated peptide antibodies (CCP)

Anti-cyclic citrullinated peptide (anti-CCP):

- High specificity, low sensitivity (a negative result does **not exclude disease)**
- Presence early in disease
- Identifies those at higher risk for more severe disease

Rheumatoid factor:

- Cannot be used to exclude RA, 32% of patients who go on to develop RA have a negative RhF result when first testing.
- Poor sensitivity: It is detectable in 15% of the population without RA following chronic inflammation or infection, and in the elderly.

ANA:

- ANA is positive in 98% of patients with SLE and systemic sclerosis and 80% with Sjogren's disease.
- ANA testing in low pre-test probability of rheumatological disease is likely to result in high numbers of false positive results. ANA has been found to be positive in low-titre in up to 15% of the healthy population.
- Poor specificity: A negative result should not rule out a specialist referral if CTD is suspected on clinical grounds.

Anti-ENA tests (Ro,La, Sm, RNP, Scl70, CENP, Jo1, Ku, Mi2):

- **Usually used in secondary care only –** these should not be requested directly, but will be added to the ANA test profile if indicated by the diagnostic laboratory.
- Used to aid diagnosis and differentiation of various CTD.
- Poor sensitivity: Cannot be used as a rule out test for CTD.

Evidence and References:

- Diagnosis and assessment of food allergy in children and young people in primary care and community settings. Clinical Guidelines, CG116 – Issued February 2011. https://www.nice.org.uk/guidance/cg116
- NICE Guidance CG134: Anaphylaxis. December 2011. https://www.nice.org.uk/guidance/cg134
- EAACI Food Allergy and Anaphylaxis Guidelines for consultation – published 2017 http://www.eaaci.org/resources/guidelines/faa-guidelines.html
- Rheumatoid arthritis in adults, NICE guidelines, July 2018
- Anti-CCP antibody testing as a diagnostic and prognostic tool in rheumatoid arthritis. QJM. 2007 Apr;100(4):193-201.
- Christian D. Mallen, Toby Helliwell & Ian C. Scott (2018) How can primary care physicians enhance the early diagnosis of rheumatic diseases?, Expert Review of Clinical Immunology, 14:3, 171-173, DOI: 10.1080/1744666X.2018.1429919
- Specialist immunologist ad rheumatology clinical advice from Dr. Matthew Buckland (Royal Free Hospital), Dr Magdalena Dziadzio (UCLH), Dr Jeffrey Lee (Barnet General Hospital).

2.10 Endocrinology pathology testing in primary care

Infertility pre-referral (Female)

- FSH
- LH
- Oestradiol

} Day 2-4 of a 28 day cycle

- Progesterone (Measure it 7 days before expected period i.e. on day 21 of a 28 day cycle or day 28 of a 35 day cycle)
- Rubella Ab,
- FBC
- HIV Ab
- Hepatitis B surface Ag
- Hepatitis C Ab
- Haemoglobinopathy screen

Chlamydia (self swab)

If **irregular cycles** add:

- Prolactin, TSH, testosterone, SHBG and US pelvis

Depending on the timing of menstrual periods, serum progesterone may need to be measured later (for example on day 28 of a 35-day cycle) to confirm ovulation, and repeated weekly thereafter until the next menstrual cycle starts.

Suspected PCOS
If not already done as part of investigating abnormal periods, consider:

- FSH, LH, TSH, testosterone, SHBG and HBA1c
- Refer adults for ultrasound scan to look for the classic picture of polycystic ovaries (unless the diagnosis of PCOS is obvious on clinical and biochemical grounds).

Erectile dysfunction

- HBA1c, standard Lipids, U&E

Consider PSA testing if >40 years of age
Consider SHBG / testosterone (If testosterone <12, please check FSH, LH, TSH, prolactin, FBC)

Oligomenorrhoea / Secondary amenorrhoea

- TSH, FSH, LH, oestradiol, testosterone, prolactin

Please refer to the pathway which can be found here:
http://gps.camdenccg.nhs.uk/pathways/secondary-amenorrhoea-or-oligomenorrhoea

Osteoporosis (secondary causes screen)*

- FBC, ESR, serum protein electrophoresis, calcium, phosphate, LFT, U&E, TSH and coeliac screen

*Secondary causes of osteoporosis are present in 30% of women and 55% of men with vertebral crush fractures

In men with vertebral fractures, serum testosterone should be measured to exclude hypogonadism

In primary osteoporosis, *no blood tests are needed*.

Consider this order set when an underlying disease affecting bone metabolism is suspected.

Tired All The Time (TATT) **No bundle on system**
Testing should only be carried out if tiredness has persisted for 1 month or longer and there is no obvious lifestyle reason apparent. Consider:

- FBC, CRP, LFTs, U&E, TSH, HBA1c and coeliac screen

Evidence and References:

- Tiredness/fatigue in adults - NICE CKS
  - https://cks.nice.org.uk/tirednessfatigue-in-adults
- Infertility pathways (RCOG National Guidance and NICE 156)
- Barnet CCG Gynaecology pathway
- NICE CKS PCOS guidance
- NCL Urology pathway
- Interpreting raised serum prolactin results
  - BMJ 2014;348:g3207

- Testing for secondary causes of osteoporosis
  - BMJ 2010; 341 doi: https://doi.org/10.1136/bmj.c6959 (Published 16 December 2010)
- Endocrinology NCL consultant clinical expert group:
  - Dr Bernard Khoo, Royal Free Hospital
  - Dr Helen Simpson, UCLH
  - Dr Karen Anthony, Whittington Hospital
  - Dr Michela Rossi, Whittington Hospital