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GIG CYMRU NHS WALES
Bwrdd Iechyd Prifysgol Caerdydd a'r Fro
Cardiff and Vale University Health Board

Issue 1
2017

# Laboratory Medicine Directorate

## Newsletter for Primary Care

**Inside this issue:**



## Allergy Testing

When patients have symptoms that might be due to allergy, the presence of allergy can often be confirmed by testing. The results of such tests help patient management as patients then know what they may need to avoid to minimise symptoms.

Skin-prick tests and blood tests can identify the allergens reacted to in most instances. The disadvantage of skin-prick tests is that referral to hospital is necessary, with attendant long waiting times to be seen the allergy clinic.

IgE (allergic) antibodies can be identified in a high proportion of people with allergy in 4 ml clotted blood sent to the laboratory requesting total IgE and specific IgE against the allergens suspected. For patients with symptoms from the eyes, nose or lungs the relevant specific allergens to request are those that are airborne. For people with symptoms consistently after eating particular foods the relevant specific allergens to request are those that are ingested. Thus the referral of patients to the allergy clinic, and the wait for confirmation of diagnosis can often be avoided by requesting:

| | |
|---|---|
| Patients with respiratory symptoms: | Total IgE & specific IgE against house dust mite, cat, dog, grass pollens, tree pollens and/or other aeroallergens according to the history |
| Patients with symptoms after food: | Total IgE & specific IgE against suspected foods identified by the patient or from the history (e.g. egg, milk, wheat, fish, peanut) |

More information, including around the false positive and false negative rates from allergy tests can be found in the following article: "Clinical Immunology Review Series: An approach to the use of the immunology laboratory in the diagnosis of clinical allergy." http://onlinelibrary.wiley.com/doi/10.1111/j.1365-2249.2008.03695.x/pdf

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# When (and not) to Measure PTH

Archie Cochrane was something of a local hero. He had many wise sayings, one of them became known as Cochrane's aphorism which stated:

'Before ordering a test decide what you will do with it if it is (1) positive or (2) negative. If both answers are the same, don't take the test.'

This wise saying is relevant across the realm of medicine, and we will see is especially true for the PTH story.

## Physiology

PTH is a peptide hormone secreted by the parathyroid glands. Its role is to increase calcium absorption from the gut and kidneys, and increase renal phosphate loss. Hypocalcaemia leads to a physiological increase in PTH secretion, while hypercalcaemia suppresses its secretion. In addition PTH increases mobilisation of calcium from bone and synthesis of vitamin D.

## Pathophysiology

Abnormal PTH values are often found in the context of primary abnormalities of vitamin D, calcium or kidney function. Alternatively stated, if there are no abnormalities in vitamin D, calcium or renal parameters, there would seem to be no indications to test PTH.

## The Problem

The problem arises when PTH is measured in the absence of any vitamin D, calcium or renal abnormality. This is often done perhaps as part of a 'health screening' or a battery of biochemical tests. We are then left with scenario of an elevated PTH 'in isolation'. This in itself is fairly meaningless and can have no relevance to the patient. Yet since it has been measured and has been found to be abnormal requires action. But if that action is to do nothing then perhaps we need reminding of Cochrane's aphorism here and question whether PTH should have been checked in the first instance?

**"Before ordering a test decide what you will do with it if it is:**
**(1) positive or**
**(2) Negative**

**If both answers are the same don't take the test."**

## 'Normocalcaemic hyperparathyroidism'

Historically primary hyperparathyroidism has seen three distinct eras:

- First there was the 'classical' *markedly clinical* primary hyperparathyroidism, when the patient presented with recurrent renal stones and marked hypercalcaemia (the 'textbook' picture).
- The second era saw the mildly hypercalcaemic patient who was asymptomatic or having *mild clinical* disease, needing assessment of end-organ damage and careful surveillance.
- The third era, which is now dawning upon us, is that of 'normocalcaemic hyperparathyroidism'. This entity is a *subclinical* disease and we are left with the problem of how to deal with this. Its prevalence is perhaps in the realm of 3%. This subclinical phase has only been identified as a PTH has been measured in the context of normal bone profile, renal profile and vitamin D.

Although normocalcaemic hyperparathyroidism is becoming increasingly recognised, there is still debate

about its existence, relevance and progression to overt clinical disease. The natural history is not fully known, although studies have suggested a progression of around 20% to hypercalcaemia at follow-up within 3-8 years, but these were generally in patients who were perhaps 'higher risk' anyway with evidence of end-organ involvement. Furthermore there are no robust studies that currently support any benefit of intervention in this group of patients, and thus Cochrane's words ring true here. In addition, it should be remembered that it is the hypercalcaemia that results in symptoms, not the increased PTH, and for that reason it is recommended that **PTH should not be checked in the context of a normal bone profile.**

## Chronic Kidney Disease

In patients with CKD, guidance for management of hyperparathyroidism does exist [1]. Vitamin D status and hyperphosphataemia evaluation is recommended for those with CKD Stages 3-5, with PTH monitoring to identify those who may benefit from calcitriol therapy.

## A Logical Question

**Is finding an elevated PTH in a normocalcaemic patient going to make any difference to management?**

Until we have more evidence that intervention will make any difference, the answer, on balance, has to be 'no'.

## How do I manage a patient with elevated PTH?

Although this article has aimed to reinforce the rationale of thinking twice before checking PTH in isolation, *if* a patient *is* found to have an 'increased PTH', a suggested algorithm based upon international consensus guidelines [2] has been produced to guide management, (Figure 1). This can also be found at the following link:
http://nww.cardiffandvale.wales.nhs.uk/pls/portal/docs/PAGE/CARDIFF_AND_VALE_INTRANET/TRUST_SERVICES_INDEX/ENDOCRINOLOGY_CP/OUTPATIENTS_REFERRALS/PRIMARY%

## Summary – when (and not) to measure PTH

PTH *should be* measured in the context of (a) an abnormal calcium result or (b) in renal disease (CKD 3-5). Otherwise we *would not* recommend its routine measurement.

### Key Points

- PTH should be measured in the context of an abnormal calcium
- There is no indication to test PTH in a patient with normocalcaemia unless in CKD stages 3-5
- PTH should not be checked as a cause of non-specific symptoms
- In the context of an increased PTH and normal calcium other causes must be excluded before a diagnosis of 'normocalcaemic hyperparathyroidism' is made
- The approach to managing normocalcaemic hyperparathyroidism is generally conservative until there is stronger evidence for intervention

## References:

1. KDIGO clinical practice guideline for the diagnosis, evaluation, prevention and treatment of Chronic Kidney Disease-Mineral and Bone Disorder (CKD-MBD). Kidney International 2009; **76:** S1-S130

2. Guidelines for the Management of Asymptomatic Primary Hyperparathyroidism: Summary Statement from the Fourth International Workshop. *JCEM* 2014; **99(10):** 3561-69.

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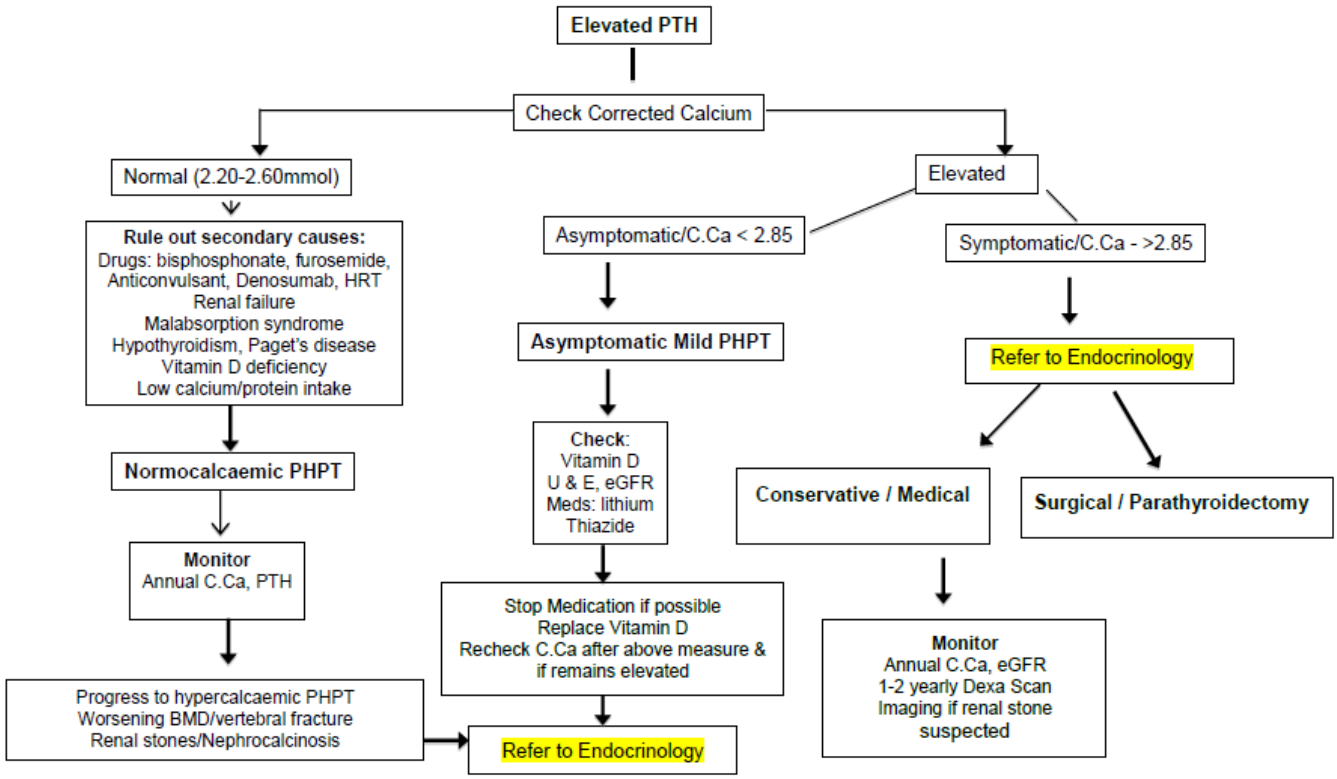
Reference: Bilezikian JP *et al.* Guidelines for the Management of Asymptomatic Primary Hyperparathyroidism: Summary Statement from the Fourth International Workshop. *JCEM* 2014; 99(10): 3561-69.

**Primary Hyperparathyroidism (PHPT) Protocol (Version 1, Nov 2016)**

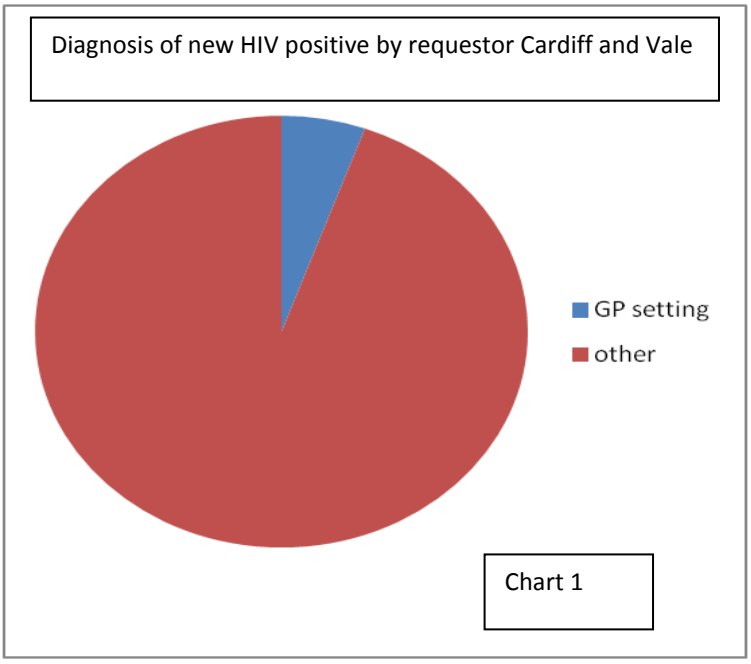


# Never Too Old for an HIV Test

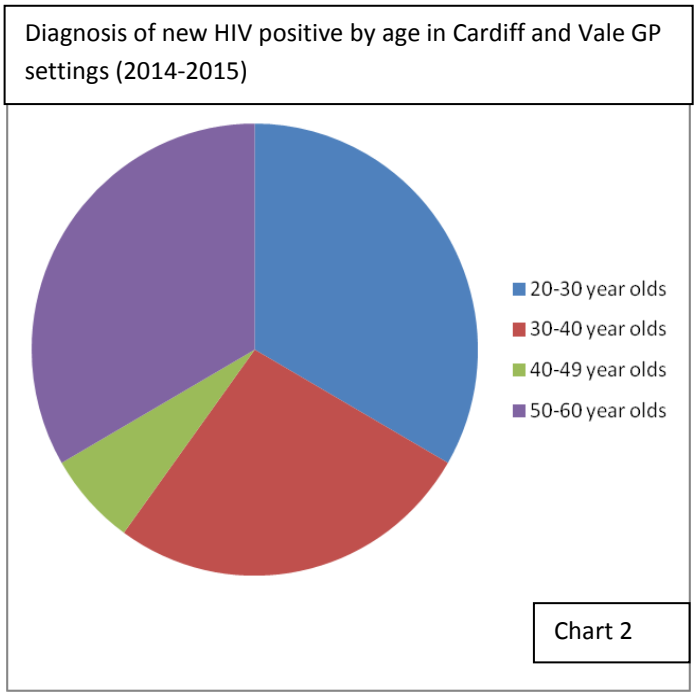
British HIV Association (BHIVA) UK National HIV Guidelines 2008 provide information about when to consider performing an HIV test. This is a useful document that is easily accessible on the internet and handy to refer to when thinking about which patients should be tested. It also provides helpful guidance around consenting patients for the test, and information about follow-up if the test is positive. BHIVA's summary is:

- HIV is now a treatable medical condition and the majority of those living with the virus remain fit and well on treatment.
- Despite this a significant number of people in the United Kingdom are unaware of their HIV infection and remain at risk to their own health and of passing their virus unwittingly on to others.
- Late diagnosis is the most important factor associated with HIV-related morbidity and mortality in the UK.
- Patients should therefore be offered and encouraged to accept HIV testing in a wider range of settings than is currently the case.
- Patients with specific indicator conditions should be routinely recommended to have an HIV test.
- All doctors, nurses and midwives should be able to obtain informed consent for an HIV test in the same way that they currently do for any other medical investigation.

Over the past 2 years, 518 patients in Cardiff and Vale area were diagnosed with new HIV infections. Forty-one of these patients were diagnosed in Primary Care. See chart 1.




Of particular interest, in one year (2014-15), one third of patients who had tested positive in Primary Care were in the 50-60 year old age group. See Chart 2. There was the same proportion of positive patients in the 20-30 year age group. It is important to remember HIV can present at any age in any patient who has risk factors, or who presents with an unusual infection or clinical indicator disease. For additional interest, the age range of the 655 newly diagnosed HIV positive patients within all Cardiff and Vale settings in that period was 21-79 years; 15% of patients were 50 years old and above; and 3 of the patients were aged 73-79 years old.




An HIV test can be requested on a blood sample using a purple virology form. If the test is positive, the GP is telephoned by the laboratory. A confirmatory sample and referral to Integrated sexual health (ISH clinic) or Infectious diseases are discussed to ensure appropriate patient follow-up.

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For any queries contact the Virology Department at UHW on 029 2074 2178

## Using CRP Testing to Support Clinical Decisions in Primary Care

Guidance has recently been published by an expert group (a sub-group of the Antimicrobial Delivery Plan task and finish group Delivery Theme 2: Optimising prescribing practice) on the use of point of care (POCT) C reactive protein (CRP) in primary care in certain defined clinical settings. The full guidance is available to download on http://www.gpone.wales.nhs.uk/prescribing

The guidance provides advice for general practitioners wishing to undertake CRP to support their clinical decisions in antibiotic prescribing. A brief summary is available below:

CRP is an acute phase protein that rises in the blood stream non-specifically in response to inflammation. Liver failure can impair the production of CRP and chronic inflammatory conditions can result in persistently elevated levels. CRP levels can become elevated in response to viral infections, but generally rise to higher levels in bacterial infections, especially severe bacterial infections.

The main role that CRP POCT is likely to have in general practice is in guiding antibiotic prescribing decisions. It is not a replacement for clinical decision making and results should be interpreted in the context of the clinical assessment. In general, it will not add much to clinical decision making in situations where the pre-test probability of bacterial infection is very low or very high, but may help resolve uncertainty where there is an intermediate, or uncertain, risk of bacterial infection. It can also be used as a tool to help you in the dialogue you have with your patient around the need for antibiotics.

Your decision as a practice as to whether investing in this technology is warranted must thus be based on an understanding of your overall antibiotic stewardship, the case mix of your population and the instances of uncertainty you face regarding bacterial infections within your daily practice.

NICE guidelines on diagnosis and management of pneumonia in adults recommend that POCT CRP should be considered for people with symptoms of lower respiratory tract infection in primary care if a diagnosis is unclear after clinical assessment.

## Interpreting the Results – Figure 1 CRP Algorithm (see overleaf)

The majority of patients will have a low (less than 20 mg/l) CRP level and can be reassured that the risk of serious infection, and the chance of having an infection that will benefit from antibiotic treatment, are minimal. Patients with high CRP values that are being managed in the community should be informed that their blood test indicates that their body is responding to something, and that this is likely to be a bacterial infection. They should be treated with antibiotics and given safety-netting information, including what should prompt them to seek a further assessment.

Patients with a CRP value in the intermediate range need to be assessed and a decision made about antibiotic treatment. It is important to inform the patient that although you have not identified any clear indicator of pneumonia, their blood test shows that their body is responding to something, and that this could be a bacterial infection. It is important to give them good safety-netting advice, and if you decide to give them a delayed (back-up) prescription then it is important to give clear advice about what should prompt them to collect and use the prescription. This is not a replacement for safety-netting advice, as people with features of more severe illness should be re-assessed rather than just starting to take antibiotics. It is important to ensure that the patient is supported in this and leaflets such as “treating your infection” may help. **Patients who do not have evidence of bacterial infection should not be prescribed antibiotics.**

## Quality Assurance

It is essential the POCT CRP undergoes the appropriate level of quality assurance. This will require collaboration with your local hospital POCT department for advice on the most appropriate device, developing operating protocols on how the test is used, and ensuring all users are trained and have documented competency. This will extend to ensuring records of internal quality control, External Quality Assurance (EQA), clinical audit and electronic storage of results in patient records.

These requirements and processes are covered in detail in the Welsh Scientific Advisory Committee (WSAC) Policy on the management of POCT and at http://nww.poctmatters.wales.nhs.uk/home

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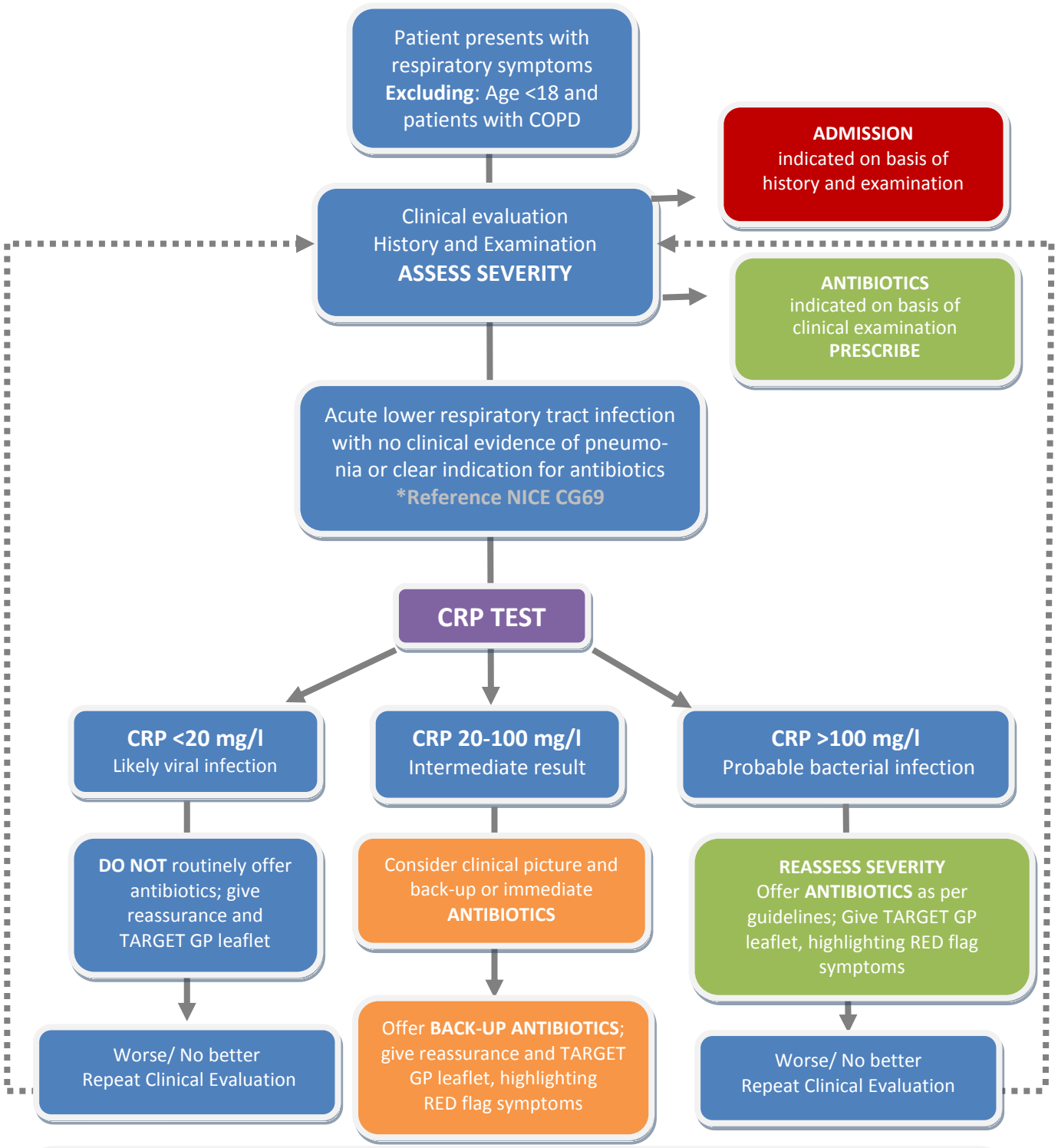
# CRP POCT Algorithm




*__NICE CG69 Section 1.7 'Respiratory Tract Infections (self-limiting): prescribing antibiotics'__: An immediate prescription and/or further appropriate investigation and management should only be offered to patients in the following situations: **If the patient** is systemically unwell: **If the patient** has symptoms and signs suggestive of serious illness and/or complications (particularly pneumonia, mastoiditis, peritonsillar abscess, peritonsillar cellulitis, intraorbital and intracranial complications): **If the patient** is at high risk of serious complications because of pre-existing co-morbidity. This includes patients with significant heart, lung, renal, liver or neuromuscular disease, immunosuppression, cystic fibrosis, and young children born prematurely: If the patient is >65 years with acute cough and two or more of the following criteria, or older than 80 years with acute cough and one or more of the following criteria:

(1) Hospitalisation in previous year (2) Type 1 or type 2 diabetes (3) History of congestive heart failure (4) Current use of glucocorticoids.

**For these patients, the no antibiotic prescribing strategy and the back-up antibiotic strategy SHOULD NOT be considered.**

# And Finally..

## Did You Know?

If patient demographic and location barcodes are of poor print quality or out of alignment, Specimen Reception are unable to scan the information. This results in a manual transcription of data with the potential for delays, transcription error and reports being returned to the incorrect clinical location. Can you please check and maintain your barcode printers?

For statin monitoring alone routine annual liver function monitoring is not recommended.
ALT measurement is adequate (NICE CVD guideline):

- Before starting statin
- Within 3 months of starting and
- At 12 months, but not again unless clinically indicated.

In Cardiff and Vale simply write 'ALT' on the blood form and DO NOT tick 'LFT'

There are two thyroid related tick boxes on the biochemistry request form.

**DO**- Tick the TSH only box on blood request form

- To monitor primary hypothyroid patients (stable on levothyroxine). This leads to a 'TSH only' workflow within the laboratory and depending on the TSH concentration set automated interpretative comments may be added to the report.

**DON'T**-Tick the TSH only box on blood request form when both Free T4 & TSH are required.

In the following situations Thyroid Function (which comprises FreeT4 & TSH) should be selected:

- Patients being tested for the first time i.e. diagnostic testing
- Pregnancy
- Monitoring levothyroxine replacement in patients with secondary hypothyroidism (hypopituitarism)
- Monitoring patients on levothyroxine replacement for the treatment of differentiated thyroid cancer
- Monitoring treatment of patients with hyperthyroidism

## Contact Us:

Laboratory Medicine would welcome your suggestions for service improvements. If you use any of our services and you have an idea about how we can improve, please email: lisa.griffiths3@wales.nhs.uk

**For feedback and comments on the newsletter in general, please contact either:**

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