# National minimum retesting intervals in pathology

# A final report detailing consensus recommendations for minimum retesting intervals for use in pathology

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| **Comments** | The original guidance on minimum retesting intervals in clinical biochemistry were put together under the auspics of the ACB in 2013. This version, incorporating other pathology disciplines, was coordinated by the RCPath.<br>While it is published in accordance with RCPath's publication policy, it should be regarded (and therefore the intellectual property) as a joint document between the RCPath and ACB. Both organisations, along with the IBMS, have formally endorsed its contents and hence their logos appear above.<br>In accordance with the College's pre-publications policy, this document was on the RCPath website for consultation from 18 September to 18 October 2015. Eighty-four items of feedback were received and the document was amended accordingly. Please email publications@rcpath.org to see members' responses and comments.<br>**Dr Lorna Williamson**<br>**Director of Publishing and Engagement** |

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# 1 Introduction

There is currently a drive in pathology to harmonise processes and remove unnecessary waste, thereby saving money. In addition, any intervention that acts to reduce waste and avoid unnecessary phlebotomy/booking appointment for the patient can only be seen as contributing to the optimisation of patient care. At a time when many laboratories and providers are implementing electronic requesting of laboratory tests, which allows the requestor and the laboratory to manage what is requested, there needs to be a solution to support this process based on the best available evidence. Similar initiatives have been reported including the work of the Pathology Harmony Group and the recent proposal to standardise test profiles.[1,2] How often a test should be repeated, if at all, should be based upon a number of criteria:

- the physiological properties
- biological half-life
- analytical aspects
- treatment and monitoring requirements
- established guidance.

This report proposes a set of consensus recommendations from the perspective of pathology and laboratory medicine.

## 1.1 What is a minimal retesting interval?

Minimal retesting intervals (MRI) are defined as the minimum time before a test should be repeated, based on the properties of the test and the clinical situation in which it is used**.**

## 1.2 Establishing MRIs

The original work on MRI was carried out with the support of the Association for Clinical Biochemistry and Laboratory Medicine (ACB) and was published in 2013.[3] It was prepared through the members of the Clinical Practice Section (CPS) of the ACB. This group represents the medically qualified practitioners in clinical biochemistry who are members of the ACB. The methodology is briefly described below.

A survey and a literature search was performed using a strategy previously used in this area.[4] However, little published evidence was identified on the use or production of MRIs in clinical practice.

The next phase of the project was the convening of small groups, made up of invited members of the CPS of the ACB, to investigate the evidence and existing guidelines and prepare recommendations in a number of work streams. The method used was an approach based on that used by Glaser *et al*, termed ‘the state of the art’.[5]

The evidence or source for these recommendations has been taken from a number of authorities such as the National Institute for Health and Clinical Excellence (NICE), NHS Clinical Knowledge Summaries (CKS) (formerly PRODIGY) and the Scottish Intercollegiate Guidelines Network (SIGN). The CKS are a reliable source of evidence-based information and practical 'know how' about the common conditions managed in primary care that were identified following a literature search and expert opinion strategy.

When the draft recommendations were completed, they were sent to an independent reviewer for assessment and comment.

The final stage of this project was a review of the prepared recommendations by a panel made up of representatives of the authors from each major region of the UK and invited

members from the ACB Executive. The recommendations were discussed and accepted by consensus. Where no evidence-based guidance existed, either in the literature or published guidance, recommendations were prepared based on the consensus opinion of the working group. The final document was then sent out for final consultation by the full membership of the CPS and the chairs of each ACB region, before submission to the ACB Executive.

A similar approach was used in the preparation of these pan-pathology recommendations.

It should be noted that only disciplines with anticipated MRI development are included in this draft.

### 1.3 Using minimum retesting intervals in practice

The recommendations presented in this document are intended to provide assistance in appropriately managing test requesting at all levels of the request cycle. They are intended to be used in a number of different scenarios, either delivered manually or via a laboratory/ remote requesting computer system. The following processes need to be in place to enable effective practice:

1. Education of requesters so that appropriate tests are requested at the right time and for the right patient.
2. Information on request cards or in pathology handbooks regarding when to repeat a test.
3. Delivery of prompts to remind the requester at point of requesting via remote/ward requesting software that a request is either too soon or inappropriate, with the facility to review previous results or ask questions. There should also be an option to record the reason for overriding a MRI.
4. Implementation of logic rules in the laboratory to remove or restrict requests based on previous patient data.

Any MRI being used must reflect not only the assay being used, but also how it is being used – thus the MRI must reflect the local protocol. It should also be implemented following full consultation with the users, ideally supported with an education package if required. It is important to understand the mechanism employed to restrict any test or its request so that it does not appear too restrictive. There must always be the option for the clinicians/requesters to override a rule if they feel that it is clinically appropriate to continue to request the test. How this is managed will reflect the way a test is requested locally. Ideally, there must be an opportunity for requestors to record their reason to override a rule and conversely to inform the requestor, at the earliest opportunity, why it has been rejected. The availability of previously reported laboratory results at or before the time of requesting a new test would greatly assist the requester in deciding whether a test was appropriate. To support this initiative, the availability of up-to-date clinical history from the requester or the patient's electronic patient record is of paramount importance so that prepared logic rules or MRIs can be correctly implemented. The implementation of electronic requesting of tests provides an opportunity to improve the quality of information received from the requester for the laboratory to use. When a profile is recommended, this refers to the standardised profile.[2] It may also be useful to allow the requester to request individual tests from a recognised profile so that only the required and necessary tests are performed. Limiting a test's use may also be achieved by restricting the requesting of a repeat test to a particular grade or level of staff, so that only those of an appropriate level may have access to a particular test.

If implementing the MRI into a laboratory information system or remote request system, the programmer must be aware of how the system counts time so that the correct unit is used.

### 1.4 Terms and conditions of use

These recommendations represent best practice in the opinion of the authors and have been reviewed through a consensus approach. However, new evidence at any time can invalidate these recommendations. No liability whatsoever can be taken as a result of using this information.

These recommendations should not be used in paediatric/neonatal patients unless specifically stated.

### 1.5 References


1. Berg J, Lane V. Pathology Harmony; a pragmatic and scientific approach to unfounded variation in the clinical laboratory. *Ann Clin Biochem* 2011;48:195–197.

2. Smellie WS, Association for Clinical Biochemistry's Clinical Practice Section. Time to harmonise common laboratory test profiles. *BMJ* 2012;344:e11693.

3. Lang T. *National Minimum Re-testing Interval Project: A final report detailing consensus recommendations for minimum retesting intervals for use in Clinical Biochemistry*. London: Association of Clinical Biochemistry and Laboratory Medicine, 2013.

4. Smellie WS, Finnigan DI, Wilson D, Freedman D, McNulty CA, Clark GJ. Methodology for constructing guidance. *J Clin Pathol* 2005;58:249–253.

5. Glaser EM. Using Behavioral Science Strategies for Defining the State-of-the-Art. *J App Behavioral Sci* 1980;16:79–92.

6. Brunton LL, Chabner BA, Knollman BC (eds). *Goodman and Gilman's The pharmacological basis of therapeutics (12th edition)*. New York: McGraw-Hill, 2011.

## 2 Abbreviations

| | |
|---|---|
| AACE | American Association of Clinical Endocrinologists |
| Ab | Antibody |
| ACB | Association for Clinical Biochemistry and Laboratory Medicine |
| AFB | Acid-fast bacilli |
| ALP | Alkaline phosphatase |
| AMPA | 2 Amino-3 (5-Methyl 3 Oxo-1,2 Oxazole 4 Yl) Propanoic Acid |
| ANA | Antinuclear antibody |
| ANCA | Antineutrophil cytoplasmic antibodies |
| APTT | Activated Partial Thromboplastin Time (APTT) |
| ASCO | American Society of Clinical Oncology |
| ASO | Antistreptolysin O |
| ATPOab | Anti-thyroid peroxidase antibodies |
| BCSH | British Committee for Standards in Haematology |
| BMI | Body mass index |
| BNF | British National Formulary |
| BSPGHAN | British Society of Paediatric Gastroenterology, Hepatology and Nutrition |
| BSH | British Society for Haematology |
| C3 | Complement component C3 |
| C4 | Complement component C4 |
| CA12.5 | Carbohydrate antigen 12.5 |
| CA15.3 | Carbohydrate 15.3 |
| CA 19.9 | Carbohydrate antigen 19.9 |
| CDC | Center for Disease Control |
| CCP | Cyclic citrullinated peptide antibody |
| CEA | Carcinoembryonic antigen |
| CFT | Complement fixation test |
| CG | Clinical Guideline |
| CHF | Congestive heart failure |
| CKD | Chronic kidney disease |
| CKS | Clinical Knowledge Summaries |
| CMV | Cytomegalovirus |
| CPS | Clinical Practice Section |
| EASL | European Association of the Study of the Liver |
| ED | Exposure day |
| e-GFR | Estimated glomerular filtration rate |
| EGTM | European Group on Tumour Markers |
| EP | Electrophoresis |
| ESR | Erythrocyte sedimentation rate |
| ESC | European of Society of Cardiology |
| FSH | Follicule stimulating hormone |
| FBC | Full blood count |
| FMH | Fetomaternal haemorrhage |
| fT3 | Free triiodothyronine |
| fT4 | Free thyroxine |
| GAD65 | Glutamic acid decarboxylase antibody |
| GAIN | Guidelines and Audit Implementation Network |
| GGT | Gamma-glutamyltransferase |
| GPC | Gastric parietal cell antibody |
| Hb | Haemoglobin |
| HBV | Hepatitis B virus |
| HCV | Hepatitis C virus |

| | |
|---|---|
| HIV | Human immunodeficiency virus |
| HSV | Herpes simplex virus |
| HVS | High vaginal swab |
| Ig | Immunoglobulin |
| IGF-1 | Insulin-like Growth Factor 1 |
| IHD | Ischaemic heart disease |
| INR | International normalised ratio |
| ITT | Immune tolerance therapy |
| ITU | Intensive treatment unit |
| IUCD | Intrauterine contraceptive device |
| IV | Intravenous |
| IVF | *In vitro* fertilisation |
| LCMS | Liquid chromatography mass spectrometry |
| LFT | Liver function tests |
| MAG | Myelin associated glycoprotein |
| MDRD | Modification of diet in renal disease |
| MMWR | Morbidity and Mortality Weekly Report |
| MOG | Myelin oligodendrocyte |
| MPO | Myeloperoxidase antibodies |
| MRI | Minimum retesting intervals |
| MRSA | Meticillin-resistant staphylococcus aureusis |
| MTC | Medullary thyroid carcinoma |
| MUSK | Muscle specific kinase |
| NA | Not applicable |
| NAAT | Nucleic acid amplification test |
| NICE | National Institute for Health and Clinical Excellence |
| NIH | Nationals Institute of Health |
| NMDA | N-methyl-d-aspartate |
| NPHS | National Public Health Service |
| PD | Peritoneal dialysis |
| Plt | Platelets |
| PR3 | Proteinase 3 antibodies |
| PT | Prothrombin time |
| RCOG | Royal College of Obstetricians and Gynaecologists |
| RCPath | The Royal College of Pathologists |
| RF | Rheumatoid factor |
| SAC | Specialty Advisory Committee of the RCPath |
| SIGN | Scottish Intercollegiate Guidelines Network |
| TB IFN | Tuberculosis interferon |
| TFT | Thyroid function tests |
| TPN | Total parenteral nutrition |
| TSH | Thyroid stimulating hormone |
| tTG | Tissue transglutaminase |
| U&E | Urea and electrolytes |
| UKMI | UK Medicines Information |
| UK-SMI | UK standards for microbiology investigations |
| VGCC | Voltage gated calcium channel |
| VGKC | Voltage gated potassium channel |
| VKA | Vitamin K antagonist |
| VZV | Varicella zoster virus |
| WCC | White cell count |

# 3 Biochemistry recommendations

## 3.1 Renal (refers to the measurement of U&Es, unless otherwise stated)

| Ref | Clinical situation | Recommendation | Source |
|---|---|---|---|
| B-R1 | Normal follow up | A repeat would be indicated on clinical grounds if there were a significant change in the patient's condition which indicated that an acute renal (or other electrolyte-related problem) is developing | Consensus opinion of the relevant expert working group |
| B-R2 | Inpatient monitoring of a **stable** patient not on IV fluids | An inpatient with an admission sodium within the reference range should not have a repeat sodium within the average length of stay of 4 days | Consensus opinion of the relevant expert working group |
| B-R3 | Inpatient monitoring of a **stable** patient on IV fluids, adults as well as children | Daily monitoring of U&Es and glucose | Guidelines and Audit Implementation Network. *Hyponatraemia in adults (on or after 16th birthday).* GAIN, 2010. www.gain-ni.org/images/Uploads/Guidelines/Hyponatraemia_guideline.pdf |
| B-R4 | In symptomatic patients or following administering of hypertonic saline | Monitoring should be more frequent, i.e. every 2–4 hours | Guidelines and Audit Implementation Network. *Hyponatraemia in adults (on or after 16th birthday).* GAIN, 2010. www.gain-ni.org/images/Uploads/Guidelines/Hyponatraemia_guideline.pdf |
| B-R5 | Patient diagnosed with acute kidney injury | U&Es checked on admission and within 24 hours | UK Renal Association. *Clinical practice guideline, acute kidney injury, 5th edition.* Renal Association: Hampshire, 2011. www.renal.org/guidelines/modules/acute-kidney-injury |
| B-R6 | Monitoring of ACE inhibitors | Within 1 week of starting and 1 week after each dose titration. Then annually (unless required more frequently because of impaired renal function) | Clinical Knowledge Summary. *Hypertension – not diabetic*. NICE, 2014. cks.nice.org.uk/hypertension-not-diabetic |
| B-R7 | Diuretic therapy | Before the initiation of therapy and after 4 weeks, and then 6 monthly/yearly or more frequently in the elderly or in patients with renal disease, disorders affecting electrolyte status or those patients taking other drugs, e.g. corticosteroids, digoxin | Clinical Knowledge Summary. *Hypertension – not diabetic.* NICE, 2014. cks.nice.org.uk/hypertension-not-diabetic |

| Ref | Clinical situation | Recommendation | Source |
|---|---|---|---|
| B-R8 | Monitoring of potassium concentrations in patients receiving digoxin | 8 days after initiation or change in digoxin therapy and/or addition/subtraction of interacting drug.<br>Then annually if no change | North West Medicines Information Service. *Monitoring Drug Therapy*. Liverpool: UK Medicines Information, 2002.<br>Clinical Knowledge Summary. *Atrial fibrillation*. NICE, 2014. http://cks.nice.org.uk/atrial-fibrillation<br>Clinical Knowledge Summary. *Heart failure – chronic.* NICE, 2010. http://cks.nice.org.uk/heart-failure-chronic |
| B-R9 | Monitoring of potassium concentrations on patients receiving digoxin and diuretics | Regular monitoring | National Public Health Service for Wales. *Drug Monitoring: A Risk Management System, First Revision*. NPHS: Wales, 2008. |
| B-R10 | Aminosalicylates | In the elderly, every 3 months in first year, then every 6 months for next 4 years, then annually after that based on personal risk factors | Clinical Knowledge Summary. *Crohn's disease*. NICE, 2012. http://cks.nice.org.uk/crohns-disease#!prescribinginfo |
| B-R11 | Carbamazepine | 6 months | Clinical Knowledge Summary. *Crohn's disease.* NICE, 2012. http://cks.nice.org.uk/crohns-disease#!prescribinginfo |
| B-R12 | Anti-psychotics | 12 months | Clinical Knowledge Summary. *Bipolar disease*. NICE, 2012. http://cks.nice.org.uk/bipolar-disorder#!prescribinginfosub:1 |
| B-R13a | eGFR – MDRD – CKD | Repeat in 14 days if new finding of reduced GFR and/or confirmation of eGFR < 60 mL/min/1.73 $m^2$<br>*eGFR by MDRD not valid in AKI | NICE. *Chronic kidney disease in adults: assessment and management.* NICE, 2014. www.nice.org.uk/guidance/cg182 |
| B-R13b | eGFR – MDRD – Radiological procedures/contrast administration | eGFR or creatinine within previous 7 days in patients with acute illness or renal disease<br>eGFR for angiography: < 60 mL/min/1.73 $m^2$ should trigger local guidelines for contrast dosage<br>eGFR for Gadolinium: <30 mL/min/1.73 $m^2$ high risk agents contraindicated<br>eGFR 30–59 mL/min/1.73 $m^2$ lowest dose possible can be used and not repeated within 7 days | The Royal College of Radiologists. *Standards for intravascular contrast agent administration to adult patients (2nd ed).* London: Royal College of Radiologists, 2010. |

| Ref | Clinical situation | Recommendation | Source |
|---|---|---|---|
| B-R13c | eGFR – Cockcroft & Gault | For estimating chemotherapy and drug dosages. Within 24 hours unless rapidly changing creatinine concentrations or fluid balance | None (inferred from British National Formulary) |
| B-R13d | Iohexol GFR | 72 hours to avoid contamination (based on half-life of iohexol of 2 hours) | Krutzén E, Bäck SE, Nilsson-Ehle I, Nilsson-Ehle P. Plasma clearance of a new contrast agent, iohexol: a method for the assessment of glomerular filtration rate. *J Lab Clin Med* 1984;104:955–961. |

### 3.2 Bone (refers to the measurement of the bone profile, unless otherwise stated

| Ref | Clinical situation | Recommendation | Source |
|---|---|---|---|
| B-B1 | Non-acute setting unless there are other clinical indications | Testing at 3-month intervals | Consensus opinion of the relevant expert working group |
| B-B2 | Acute settings | Testing at 48-hour intervals | Consensus opinion of the relevant expert working group |
| B-B3 | Acute hypo/ hypercalcaemia, TPN and ITU patients | May require more frequent monitoring | Consensus opinion of the relevant expert working group |
| B-B4 | ALP and total protein in acute setting | Testing at weekly intervals. ALP may need checking more often, but probably only in the context of acute cholestatic changes. *See* Liver recommendations | Consensus opinion of the relevant expert working group |
| B-B5 | Vitamin D: no clinical signs and symptoms | Do not retest (whatever the result as there may be no indication to test in first place) | Consensus opinion of the relevant expert working group |
| B-B6 | Vitamin D: cholecalciferol or ergocalciferol therapy for whatever clinical indication, where baseline vitamin D concentration was adequate | Do not retest, unless otherwise clinically indicated, e.g. sick coeliac or Crohn's patient | Sattar N, Welsh P, Panarelli M, Forouhi NG.Increasing requests for vitamin D measurement: costly, confusing, and without credibility. *Lancet* 2012;379:95–96.<br>Sattar N, Welsh P, Panarelli M, Forouhi NG. Vitamin D testing — Authors' reply. *Lancet* 2012;379: 1700–1701. |

| Ref | Clinical situation | Recommendation | Source |
|---|---|---|---|
| B-B7 | Vitamin D: cholecalciferol or ergocalciferol therapy for whatever clinical indication, where baseline vitamin D concentration was low *and* where there is underlying disease that might impact negatively on absorption | Repeat after 3–6 months on recommended replacement dose | Consensus opinion of the relevant expert working group |
| B-B8 | Vitamin D: calcitriol or alphacalcidol therapy | Do not measure vitamin D | Consensus opinion of the relevant expert working group |

### 3.3 Liver (refers to the measurement of LFTs, unless otherwise stated)

| Ref | Clinical situation | Recommendation | Source |
|---|---|---|---|
| B-L1 | Non acute setting | Testing at 1–3-month intervals | Smellie S, Galloway M, McNulty S. *Primary Care and Laboratory Medicine, Frequently Asked Questions.* London: ACB Venture Publications, 2011. |
| B-L2 | Acute inpatient setting | Testing at 72 hour intervals in acute setting (apart from those in L4) | Consensus opinion of the relevant expert working group |
| B-L3 | GGT and conjugated bilirubin in acute setting | Testing at weekly intervals | Consensus opinion of the relevant expert working group |
| B-L4 | Acute poisoning (e.g. paracetamol), TPN, liver unit, acute liver injury and ITU patients | May require more frequent monitoring | Consensus opinion of the relevant expert working group |
| B-L5 | Neonatal jaundice | These recommendations must not be used in the management of neonatal jaundice | |

### 3.4 Lipids (refers to the measurement of lipid profile [non-fasting], unless otherwise stated)

| Ref | Clinical situation | Recommendation | Source |
|---|---|---|---|
| B-LP1 | LOW risk cases for IHD assessment | 3 years | Smellie WSA, Wilson D, McNulty CAM, Galloway MJ, Spickett GA, Finnigan DI *et al*. Best practice in primary care pathology: review 1. *J Clin Pathol* 2005;58:1016–1024 |
| B-LP2 | Higher risk cases for IHD assessment and those on stable treatment | 1 year | Consensus opinion of the relevant expert working group |
| B-LP3 | Initiating or changing therapies | 1–3 months | Consensus opinion of the relevant expert working group |
| B-LP4 | When assessing triglyceridaemia to see effects of changing diet and alcohol | 1 week | Consensus opinion of the relevant expert working group |
| B-LP5 | In patients on TPN or who have hypertriglyceridaemia-induced pancreatitis | 1 day | Consensus opinion of the relevant expert working group |

### 3.5 Endocrine related (for pregnancy-related endocrinology, *see* pregnancy)

| Ref | Clinical situation | Recommendation | Source |
|---|---|---|---|
| B-E1 | Thyroid function testing in healthy person in absence of any clinical symptoms | Three years | Consensus opinion of the relevant expert working group |
| B-E2 | Hyperthyroid - monitoring of treatment in Graves' disease | Follow up in first 1–2 months after radioactive iodine treatment for Graves' should include fT4 and total T3. If patient remains thyrotoxic then biochemical monitoring to continue at 4–6 week intervals<br>Following thyroidectomy for Graves' disease (and commencement of levothyroxine), serum TSH to be measured 6–8 weeks post-op | Bahn Chair RS, Burch HB, Cooper DS, Garber JR, Greenlee MC, Klein I *et al*. Hyperthyroidism and other causes of thyrotoxicosis: management guidelines of the American Thyroid Association and American Association of Clinical Endocrinologists. *Thyroid* 2011; 21:593–646. |

| Ref | Clinical situation | Recommendation | Source |
|---|---|---|---|
| B-E3 | Hyperthyroid - monitoring of treatment in toxic multinodular goitre and toxic adenoma | Follow up in first 1–2 months after radioactive iodine treatment for toxic multinodular goitre and toxic adenoma should include fT4 and total T3 and TSH. Should be repeated at 1–2 month intervals until stable results, and then annually thereafter<br>Following surgery for toxic multinodular goitre and start of thyroxine therapy, TSH should be measured 1–2 monthly until stable and annually thereafter<br>Following surgery for toxic adenoma TSH and fT4 concentrations should be measured 4–6 weeks post-op | Bahn Chair RS, Burch HB, Cooper DS, Garber JR, Greenlee MC, Klein I *et al*. Hyperthyroidism and other causes of thyrotoxicosis: management guidelines of the American Thyroid Association and American Association of Clinical Endocrinologists. *Thyroid* 2011; 21:593–646. |
| B-E4 | UK Thyroid guidelines | TFTs should be performed every 4–6 weeks for at least 6 months following radioiodine treatment. Once fT4 remains in ref range then frequency of testing should be reduced to annually. Life-long annual follow up is required<br>Indefinite surveillance required following radioiodine or thyroidectomy for the development of hypothyroidism or recurrence of hyperthyroidism. TFTs should be assessed 4–8 weeks post treatment then 3-monthly for up to one 1 year, then annually thereafter<br>TFTs should be performed every 4–6 weeks after commencing thionamides. Testing at 3-month intervals is recommended once maintenance dose achieved<br>In patients treated with 'block and replace', assess TSH and T4 at 4–6 wk intervals, then after a further 3 months once maintenance dose achieved, then 6-monthly thereafter. | Association for Clinical Biochemistry, British Thyroid Association and British Thyroid Foundation. UK guidelines for the use of thyroid function tests. London: Association for Clinical Biochemistry, British Thyroid Association, 2006. |

| Ref | Clinical situation | Recommendation | Source |
|---|---|---|---|
| B-E5 | Hypothyroidism – monitoring treatment | The minimum period to achieve stable concentrations after a change of dose of thyroxine is 2 months and TFTs should not normally be assessed before this period has elapsed<br>Patients stabilised on long-term thyroxine therapy should have serum TSH checked annually.<br>An annual fT4 should be performed in all patients with secondary hypothyroidism stabilised on thyroxine therapy | Association for Clinical Biochemistry, British Thyroid Association and British Thyroid Foundation. *UK guidelines for the use of thyroid function tests.* London: ACB, BTA, 2006. |
| B-E6 | Monitoring adult sub-clinical hyperthyroidism | If a serum TSH below ref range but >0.1 mU/L is found, then the measurement should be repeated 1–2 months later along with T4 and T3 after excluding non-thyroidal illness and drug interferences. This is contradicted later in the guidelines when the authors state that a 3–6 month repeat interval is appropriate unless the patient is elderly or has underlying vascular disease<br>If treatment not undertaken, then serum TSH should be measured in the long term every 6–12 months, with follow up with fT4 and fT3 and fT3 if serum TSH result is low | Association for Clinical Biochemistry, British Thyroid Association and British Thyroid Foundation. *UK guidelines for the use of thyroid function tests.* London: ACB, BTA, 2006. |
| B-E7 | Monitoring adult sub-clinical hypothyroidism | Patients with subclinical hypothyroidism should have the pattern confirmed within 3–6 months to exclude transient causes of elevated TSH<br>Subjects with subclinical hypothyroidism who are<br>ATPOab positive should have TSH and fT4 checked annually<br>Subjects with subclinical hypothyroidism who are ATPOab neg should have TSH and fT4 checked every 3 years | Association for Clinical Biochemistry, British Thyroid Association and British Thyroid Foundation.*UK guidelines for the use of thyroid function tests.* London: ACB, BTA, 2006. |

| Ref | Clinical situation | Recommendation | Source |
|---|---|---|---|
| B-E8 | Follow up of patients who have had differentiated (papillary and follicular) thyroid carcinoma and a total thyroidectomy and $^{131}$I ablation | TSH and fT4 should be measured as dose of levothyroxine increased (every 6 weeks) until the serum TSH is <0.1 mIU/L. Thereafter annually unless clinically indicated/pregnant<br><br>Samples for thyroglobulin (Tg) should not be collected sooner than 6 weeks post-thyroidectomy or $^{131}$I ablation/therapy. TSH, fT4/fT3 (whichever is being supplemented) and Tg autoantibodies (TgAb) should be requested when Tg is measured. If TgAb are detectable, measurement should be repeated every 6 months | British Thyroid Association, Royal College of Physicians. *Guidelines for the management of thyroid cancer (Perros P ed) 2nd edition.* Report of the Thyroid Cancer Guidelines Update Group. London: Royal College of Physicians, 2007 |
| B-E9 | Follow up of patients who have had medullary thyroid cancer and surgical resection | A baseline CEA and fasting calcitonin should be taken prior to operation. Postoperative samples should be measured no earlier than 10 days after thyroidectomy and plasma calcitonin concentrations are most informative 6 months after surgery<br><br>At least 4 measurements of calcitonin over a 2–3 year period can be taken to provide an accurate estimate of the calcitonin doubling time. CEA is elevated in approximately 30% of MTC patients, and in those patients CEA doubling time is comparably informative to calcitonin doubling time<br><br>Calcitonin monitoring should continue lifelong<br><br>TFTs should be measured as per guidance for hypothyroidism | British Thyroid Association, Royal College of Physicians. *Guidelines for the management of thyroid cancer (Perros P, ed) 2nd edition*. Report of the Thyroid Cancer Guidelines Update Group. London: Royal College of Physicians, 2007.<br><br>Giraud*et al*, Al Ghulzan A, Aupérin A, Leboulleux S, Chehboun A, Troalen F *et al*. Progression of medullary thyroid carcinoma: assessment with calcitonin and carcinoembryonic antigen doubling times. *Eur J Endocrinol* 2008;158: 239–246. |

| Ref | Clinical situation | Recommendation | Source |
|---|---|---|---|
| B-E10 | Anaplastic thyroid cancer | There is no need for any monitoring of thyroid function unless patient is on thyroid replacement, then as per hypothyroidism | British Thyroid Association, Royal College of Physicians. *Guidelines for the management of thyroid cancer (Perros P, ed) 2nd edition.* Report of the Thyroid Cancer Guidelines Update Group. London: Royal College of Physicians, 2007. |
| B-E11 | Progesterone | Testing weekly in patients with irregular cycle from day 21 until next menstrual period | NICE. *Fertility problems: assessment and treatment*. NICE, 2013. www.nice.org.uk/guidance/cg156 |
| B-E12 | FSH | Two tests 4–8 weeks apart in women with possible early or premature menopause | Goodman NF, Cobin RH, Ginzburg SB, Katz IA, Woode DE. American Association of Clinical Endocrinologists medical guidelines for clinical practice for the diagnosis and treatment of menopause. *Endocr Pract*. 2011;17(Suppl 6):1–25. |
| B-E13 | Patients with suspected drug-induced hyperprolactinaemia | Discontinue medication for 3 days and remeasure prolactin | Casanueva FF, Molitch ME, Schlechte JA, Abs R, Bonert V, Bronstein MD *et al*. Guidelines of the Pituitary Society for the diagnosis and management of prolactinomas. *Clin Endocrinol (Oxf)* 2006;65:265–273.<br>Melmed S, Casanueva FF, Hoffman AR, Kleinberg DL, Montori VM, Schlechte JA *et al*. Diagnosis and treatment of hyperprolactinemia: an Endocrine Society clinical practice guideline. *J Clin Endocrinol Metab* 2011;96:273–288. |
| B-E14 | Patients with hyperprolactinaemia commencing dopamine agonist therapy | Repeat prolactin measurement after 1 month to guide therapy | Melmed S, Casanueva FF, Hoffman AR, Kleinberg DL, Montori VM, Schlechte JA *et al.* Diagnosis and treatment of hyperprolactinemia: an Endocrine Society clinical practice guideline. *J Clin Endocrinol Metab.* 2011;96:273–288. |
| B-E15 | Diagnosis of male androgen deficiency | Repeat testosterone measurement to confirm diagnosis recommended | Bhasin S, Cunningham GR, Hayes FJ, Matsumoto AM, Snyder PJ, Swerdloff RS et al. Testosterone therapy in adult men with androgen deficiency syndromes endocrine society CG. J Clin Endocrinol Metab 2010;95:2536–2559. |

| Ref | Clinical situation | Recommendation | Source |
|---|---|---|---|
| B-E16 | Monitoring of patient with androgen deficiency on replacement therapy | Measure testosterone value 3–6 months after initiation of testosterone therapy<br>Measure testosterone every 3–4 months for first year<br>Measurement of prostate specific antigen (PSA). Please refer to TM7 | Bhasin S, Cunningham GR, Hayes FJ, Matsumoto AM, Snyder PJ, Swerdloff RS *et al*. Testosterone Therapy in Adult Men with Androgen Deficiency Syndromes Endocrine Society CG. *J Clin Endocrinol Metab* 2010;95:2536–2559.<br>Petak SM, Nankin HR, Spark RF, Swerdloff RS, Rodriguez-Rigau LJ. American Association of Clinical Endocrinologists Medical Guidelines for clinical practice for the evaluation and treatment of hypogonadism in adult male patients 2002 update. *Endocr Pract* 2002;8:440–456. |
| B-E17 | Female androgen excess | If measurement found to be raised by an immunoassay method, confirm measurement with a LCMS method: thereafter 1 year | Martin KA1, Chang RJ, Ehrmann DA, Ibanez L, Lobo RA, Rosenfield RL *et al*. Evaluation and treatment of hirsutism in premenopausal women: an endocrine society clinical practice guideline. *J Clin Endocrinol Metab* 2008;93:1105–1120.<br>Consensus opinion of the relevant expert working group |
| B-E18 | Oestradiol | No evidence, guideline or consensus exists for repeat frequency<br>For patients undergoing IVF samples may be taken daily<br>For patients receiving implant treatment a pre-implant value is checked to avoid tachy-phylaxis. Frequency depends on frequency of implant<br>For patients receiving implant treatment a pre-implant value is checked to avoid tachyphylaxis | |
| B-E19 | Growth hormone deficiency | IGF-1 is the most useful marker for monitoring and should be measured at least yearly. Assessment should be performed no sooner than 6 weeks following a dose change | Ho KK1; 2007 GH Deficiency Consensus Workshop Participants. Consensus guidelines for the diagnosis and treatment of adults with GH deficiency II: a statement of the GH Research Society in association with the European Society for Pediatric Endocrinol-ogy, Lawson Wilkins Society, European Society of Endocrinol-ogy, Japan Endocrine Society and Endocrine Society of Australia. *Europ J Endocrinol* 2007;157:695–700. |

| Ref | Clinical situation | Recommendation | Source |
|---|---|---|---|
| B-E20 | Acromegaly:<br>Post surgery<br><br>Medical therapy<br><br>Medical therapy using GH receptor antagonists<br>Post radiotherapy | <br>Measure both GH and IGF-1 at 3 months. If normal then at annual follow up<br>Measure both GH and IGF-1 at 3 months. If normal then at annual follow up<br>Measure only IGF-1 at 6-monthly intervals after dose titration. Monthly monitoring of LFTs for first 6 months<br>Measurement of GH and IGF-1 annually | Growth Hormone Research Society, Pituitary Society. Biochemical assessment and long-term monitoring in patients with acromegaly: statement from a joint consensus conference of Growth Hormone Research Society and Pituitary Society. *J Clin Endocrinol Metab* 2004;89:3099–3102. |
| B-E21 | Screening for diabetes in asymptomatic patients:<br>Adults <45 y with normal weight and no risk factor<br>Adults >45 y with normal weight (BMI <25 kg/m2) and no risk factor*<br>Adults >18 y with BMI ≥25 kg/m2 and 1 risk factor* | <br>Screening not recommended<br><br>3 years<br><br>3 years, if result is normal | American Diabetes Association. Clinical Practice Recommendations. Diabetes care 2012:35 (supplement 1).<br><br>* Risk[s] factors listed in Table 4 of this document |
| B-E22 | Diagnosing diabetes using HbA1C in an asymptomatic patient (not to be used in children or young adults) | Diagnosis should not be made on the basis of a single abnormal plasma glucose or HbA1C value. At least one additional HbA1C or plasma glucose test result with a value in the diabetic range is required within 2 weeks of initial measurement, either fasting, from random (casual) sample or from the oral glucose tolerance test (OGTT) | World Health Organisation. *Use of glycated haemoglobin (HbA1C) in the diagnosis of diabetes mellitus.* Geneva: WHO, 2011. www.who.int/diabetes/publications/diagnosis_diabetes2011/en/ |
| B-E23 | HbA1C monitoring of patients with type 2 diabetes | 2–6 monthly intervals (tailored to individual needs), until the blood glucose concentration is stable on unchanging therapy; use a measurement made at an interval of less than 3 months as an indicator of direction of change, rather than as a new steady state<br>6-monthly intervals once the blood glucose concentration and blood glucose lowering therapy are stable | NICE. *Type 2 diabetes*. NICE, 2008. www.nice.org.uk/guidance/CG66/resources |

### 3.6 Cardiac

| Ref | Clinical situation | Recommendation | Source |
|---|---|---|---|
| B-C1 | Using troponin (general) | MRI largely dependent on the assay being used and the clinical scenario. MRIs should be implemented according to the local protocol used | |
| | Acute coronary syndrome (ACS) | High sensitivity troponin assays will usually require several samples – with a second sample within 3 hours of presentation, the sensitivity for Myocardial infarction approaches 100% | Hamm CW, Bassand JP, Agewall S, Bax J, Boersma E, Bueno H *et al*. ESC Guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation. *Eur Heart J* 2011; 32:2999–3054. |
| | | For standard troponin assays - If the first blood sample for troponin is not elevated, a second sample should be obtained after 6–9 hours, and sometimes a third sample after 12–24 hours is required | Thygesen K, Mair J, Katus H, Plebani M, Venge P, Collinson P *et al*. Recommendations for the use of cardiac troponin measurement in acute cardiac care. *Eur Heart J* 2010;31:2197–2204. |
| | Cardiac surgery | Single measurement at 24 hours post surgery gives best correlation with outcome. Serial samples justified if clinical condition worsens and/or new ECG changes to assess ACS | Croal BL, Hillis GS, Gibson PH, Fazal MT, El-Shafei H, Gibson G *et al*. The relationship between post-operative cardiac troponin I levels and outcome from cardiac surgery. *Circulation* 2006; 114:1468–1475. |
| | Renal failure | Concentrations usually increased in chronic kidney disease (CKD) patients (especially using high sensitivity assays) – serial samples will be required if suspected ACS as above | Khan NA, Hemmelgarn BR, Tonelli M, Thompson CR, Levin A. Prognostic value of troponin T and I among asymptomatic patients with end-stage renal disease: a meta- analysis. *Circulation* 2005;112:3088–3096.<br><br>Consensus opinion of the relevant expert working group |
| B-C2 | Using BNP (NT-ProBNP)<br><br>Primary care (heart failure triage) | Should only be measured once unless there is a repeat episode of suspected heart failure with a change in clinical presentation and the diagnosis of heart failure has previously been excluded. Single time point use adequate for NICE guidance purposes | NICE. *Chronic heart failure: Management*. NICE, 2010. www.nice.org.uk/guidance/CG108 |

| Ref | Clinical situation | Recommendation | Source |
|---|---|---|---|
| B-C2 cont'd | Secondary care (acute 'short of breath' triage) | Should only be measured once per acute episode for diagnosis. Pre-discharge repeat measurement has prognostic significance but has not been shown to alter outcome | Consensus opinion of the relevant expert working group |
| | Therapeutic guidance in heart failure | Not yet accepted in guidelines | NICE. *Chronic heart failure: Management*. NICE, 2010. www.nice.org.uk/guidance/CG108 |

### 3.7 Gastrointestinal

| Ref | Clinical situation | Recommendation | Source |
|---|---|---|---|
| B-G1 | Coeliac serology in known adult patients on follow up | IgA tTG can be used to monitor response to a gluten-free diet. Retesting at 6–12 months depending on pre-treatment value | www.uptodate.com |
| B-G2 | Faecal elastase | Minimum retesting interval 6 months | Molinari I, Souare K, Lamireau T, Fayon M, Lemieux C, Cassaigne A *et al.* Fecal chymotrypsin and elastase-1 determination on one single stool collected at random: diagnostic value for exocrine pancreatic status. *Clin Biochem* 2004;37:758–763. |
| B-G3 | Faecal calprotectin | Minimum retesting interval 6 months | van Rheenen PF, Van de Vijver E, Fidler V. Faecal calprotectin for screening of patients with suspected inflammatory bowel disease: diagnostic meta-analysis. *BMJ* 2010;341:c3369. |
| B-G4 | Trace elements (copper, zinc, selenium) | Baseline then every 2–4 weeks depending upon results | NICE. *Nutrition support in adults: Oral nutrition support, enteral tube feeding and parenteral nutrition*. NICE, 2006. www.nice.org.uk/guidance/CG32 |
| B-G5 | Ferritin monitoring for haemochromatosis | EASL 2010 recommend retesting interval initially 3 months but test more frequently as ferritin approaches normal range. BCSH 2000 recommends monthly ferritin during venesection | European Association for the Study of the Liver. EASL Clinical Practice Guidelines for HFE Hemochromatosis. *J Hepatol* 2010;53:3–22.<br><br>British Committee for Standards in Haematology. *Guidelines on diagnosis and therapy – Genetic Haemochromatosis.* London: British Committee for Standards in Haematology, 2000. |

| Ref | Clinical situation | Recommendation | Source |
|---|---|---|---|
| B-G6 | Iron deficiency diagnosis | Repeat measurement not required unless doubt regarding diagnosis | Goddard AF, James MW, McIntyre AS, Scott BB; British Society of Gastroenterology. Guidelines for the management of iron deficiency anaemia. Gut 2011;60:1309–1316. |
| B-G7 | Iron profile/ferritin in patients on parenteral nutrition | Minimum retesting interval 3–6 months | NICE CG. Nutrition support in adults: Oral nutrition support, enteral tube feeding and parenteral nutrition. NICE, 2006. www.nice.org.uk/guidance/CG32 |
| B-G8 | Iron status in chronic kidney disease | Monitor iron status no earlier than 1 week after receiving IV iron and at intervals of 4 weeks to 3 months routinely | NICE CG. *Anaemia management in people with chronic kidney disease.* NICE, 2011. www.nice.org.uk/guidance/CG114 |
| B-G9 | Iron profile/ferritin in a normal patient | Minimum retesting interval 1 year | NICE CG. *Nutrition support in adults: Oral nutrition support, enteral tube feeding and parenteral nutrition*. NICE, 2006. www.nice.org.uk/guidance/CG32<br><br>Smellie WS, Forth J, Bareford D, Twomey P, Galloway MJ, Logan EC *et al*. Best practice in primary care pathology: review 3. *J Clin Pathol* 2006;59**:**781–789. |
| B-G10 | Monitoring vitamin B12 and folate deficiency | Repeat measurement of vitamin B12 and folate is unnecessary in patients with vitamin B12 and folate deficiency | Clinical Knowledge Summary. *Anaemia – B12 and folate deficiency*. NICE, 2014. http://cks.nice.org.uk/anaemia-b12-and-folate-deficiency |

For more guidance on the laboratory monitoring of patients on nutritional support, particularly parenteral nutrition and those receiving enteral or oral feeds who are metabolically unstable or at risk of refeeding syndrome, please refer to the NICE CG 32: *Nutrition support in adults*.

### 3.8 Specific proteins

| Ref | Clinical situation | Recommendation | Source |
|---|---|---|---|
| B-SP1 | Paraproteins | Testing at 3-month intervals initially | Smellie WSA, Wilson D, McNulty CAM, Galloway MJ, Spickett GA, Finnigan DI *et al*. Best practice in primary care pathology: review 1. *J Clin Pathol* 2005;58:1016–1024. |
| B-SP2 | Patients with no features of plasma cell dyscrasia (e.g. anaemia, bone fracture or pain located in bone, suppression of other immune-globulin classes, renal impairment) and a band of <15 g/L | Annual serum protein electrophoresis and quantitation by densitometry without need for further immunofixation is recommended | Smellie WSA, Wilson D, McNulty CAM, Galloway MJ, Spickett GA, Finnigan DI *et al*. Best practice in primary care pathology: review 1. *J Clin Pathol* 2005;58:1016–1024. |
| B-SP3 | Monoclonal gammopathy of undetermined significance | 3-4 monthly within the first year of identification, then 6-12 monthly as long as no symptoms of progression. | UK Myeloma Forum and Nordic Myeloma Study Group: guideline for the investigation of newly detected M-proteins and the management of MGUS. Brit J Haemat 147; 22-42, 2009 |
| B-SP4 | Immunoglobulins | Patients on immunoglobulin replacement therapy must have trough IgG concentrations and liver function tests performed at least quarterly | UK Primary Immunodeficiency Network. *Standards of Care: CVID diagnosis and management (version 2).* Newcastle: UK Primary Immunodeficiency Network, 2011. www.ukpin.org.uk |
| B-SP5 | Immunoglobulins | For other purposes, testing at minimum interval of 6 months is recommended | Consensus opinion of the relevant expert working group |
| B-SP6 | Myeloma patients on active treatment | Local guidance and treatment regimes should be followed when requesting paraprotein concentrations for patients on active treatment | Consensus opinion of the relevant expert working group |
| B-SP7 | C-Reactive protein (CRP) | Not within a 24-hour period following an initial request with the exception of paediatric requests | Hutton HD, Drummond HS, Fryer AA. The rise and fall of C-reactive protein: managing demand within clinical biochemistry. *Ann Clin Biochem* 2009;46:155–158. |

| Ref | Clinical situation | Recommendation | Source |
|---|---|---|---|
| B-SP8 | Procalcitonin | 24 hour | Hochreiter M, Köhler T, Schweiger AM, Keck FS, Bein B, von Spiegel T *et al*. Procalcitonin to guide duration of antibiotic therapy in intensive care patients: a randomized prospective controlled trial. *Crit Care* 2009; 13:R83.<br>Seguela PE, Joram N, Romefort B, Manteau C, Orsonneau JL, Branger B *et al*. Procalcitonin as a marker of bacterial infection in children undergoing cardiac surgery with cardiopulmonary bypass. *Cardiol Young* 2011; 21:392–399. |

### 3.9 Tumour markers

| Ref | Clinical situation | Recommendation | Source |
|---|---|---|---|
| B-TM1 | α-Fetoprotein for hepatocellular carcinoma (HCC) surveillance: screening patients at high HCC risk | 6 months (UK) | Sturgeon CM, Duffy MJ, Hofmann BR, Lamerz R, Fritsche HA, Gaarenstroom K *et al*. National Academy of Clinical Biochemistry Laboratory Medicine Practice Guidelines for use of tumor markers in liver, bladder, cervical, and gastric cancers. *Clin Chem* 2010:56;e1–48. |
| B-TM2 | α-Fetoprotein for monitoring disease recurrence in HCC | 3–6 months | Sturgeon CM, Duffy MJ, Hofmann BR, Lamerz R, Fritsche HA, Gaarenstroom K *et al*. National Academy of Clinical Biochemistry Laboratory Medicine Practice Guidelines for use of tumor markers in liver, bladder, cervical, and gastric cancers. *Clin Chem* 2010:56;e1–48. |
| B-TM3 | Screening women with family history of ovarian cancer with CA125 | 12 months | Sturgeon CM, Duffy MJ, Stenman UH, Lilja H, Brünner N, Chan DW *et al*. National Academy of Clinical Biochemistry laboratory medicine practice guidelines for use of tumor markers in testicular, prostate, colorectal, breast, and ovarian cancers. *Clin Chem* 2008:54:e11–79. |

| Ref | Clinical situation | Recommendation | Source |
|---|---|---|---|
| B-TM4 | Using CA125 in diagnostic strategies | Retesting CA125 where imaging is negative within 1 month | NICE CG. *Ovarian cancer: The recognition and initial management*. NICE, 2011. www.nice.org.uk/guidance/CG122 |
| B-TM5 | Monitoring CA125 in disease recurrence | 1 month | Sturgeon CM, Duffy MJ, Stenman UH, Lilja H, Brünner N, Chan DW *et al*. National Academy of Clinical Biochemistry laboratory medicine practice guidelines for use of tumor markers in testicular, prostate, colorectal, breast, and ovarian cancers. *Clin Chem* 2008:54:e11–79. |
| B-TM7 | Monitoring disease recurrence with CA19.9 | 1 month | No available evidence.<br>All Wales Consensus Group |
| B-TM8 | PSA screening | When first result is raised, repeat once in 6 weeks to assess the trend | Prostate Cancer Risk management programme www.cancerscreening.nhs.uk/prostate/index.html |
| B-TM9 | Monitoring disease with PSA | Every 3 months for first 1–2 years.<br>Every 6 months for 2 years.<br>Annually thereafter | Smellie WS, Forth J, Sundar S, Kalu E, McNulty CA, Sherriff E *et al*. Best practice in primary care pathology: review 4. *J Clin Pathol* 2006:59;1116. |
| B-TM10 | Monitoring disease recurrence with CA15.3 | 2 months | Molina R, Barak V, van Dalen A, Duffy MJ, Einarsson R, Gion M *et al*. Tumor markers in breast cancer – European Group on Tumor Markers recommendations. *Tumour Biol* 2005;26;281–293. |
| B- TM11 | Serum β-HCG (tumour marker) | After evacuation of a molar pregnancy, hCG concentration should be monitored every week until normalisation then every month during the first year | Bidart JM, Thuillier F, Augereau C, Chalas J, Daver A, Jacob N *et al*. Kinetics of serum tumour marker concentrations and usefulness in clinical monitoring. *Clin Chem* 1999;45:1695–1707. |
| B-TM12 | Serum β-HCG (tumour marker) | After resection, prolonged marker half-life (>3 days for hCG) is a reliable indicator of residual tumour and a sig-nificant predictor of survival | |
| B- TM13 | Serum β-HCG (tumour marker) | If rate of change in tumour marker concentration changes velocity, an urgent repeat to confirm the result is reasonable | Sturgeon CM, Hoffman BR, Chan DW, Ch'ng SL, Hammond E, Hayes DF *et al*. National Academy of Clinical Biochemistry Laboratory Medicine Practice Guidelines use of tumour markers in clinical practice: quality requirements. *Clin Chem* 2008;54:1935–1939. |

### 3.10 Therapeutic drug monitoring

As drugs are xenobiotics, the time for significant change is based on the kinetics of absorption and clearance. Steady state concentrations on new dose regimens are normally established after five plasma half-lives have elapsed.

For drugs where over 30% of clearance is renal then dosing and half-life are reflected by the creatinine clearance calculated using the Cockcroft & Gault formula (eGFR is less reliable though widely used). Tables of half-lives for most drugs are given and referenced in Brunton *et al*.[6]

Some drugs induce their own metabolism, e.g. carbamazepine or can have hepatic clearance induced by another drug. Specific details need to be checked with the literature. Other xenobiotic interactions may significantly affect half-lives, e.g. smoking and clozapine.

Depending on the metabolic pathway an individual's pharmacogenetic phenotype may result in more rapid or much slower metabolism than the general population, so the half-lives will be shorter or longer respectively and the 5 half-life rule applies, but using a half-life specific to the individual.

As there are so many different combinations of interaction, the advice given above is a general guide and the specific classes discussed below are for high-level guidance.

| Ref | Clinical situation | Recommendation | Source |
|---|---|---|---|
| B-TD1 | Anticonvulsant drugs (carbamazepine, phenytoin) | Five half-lives after dosage change (4–5 days) during initial dose optimisation, **unless toxicity is suspected**. The kinetics of phenytoin are highly variable between individuals and when metabolism is saturated, a small dose change results in a disproportionate increase in plasma concentration. There is a significant risk of overdose and therefore when titrating dose changes check up to every 12 hours depending on clinical condition and therapy. This will be more frequent on iv therapy for status epilepticus.<br>Note: carbamazepine induces its own metabolism and concentrations should be confirmed 2–3 months after commencing therapy | Consensus opinion of the relevant expert working group |
| B-TD2 | Digoxin | 5 half-lives after dosage change (i.e. approx. 7 days) during initial dose optimisation, unless toxicity is suspected. When renal function has changed significantly recognise the proportionate decrease in clearance. In overdose situations, up to every 4 hours depending on clinical condition and therapy | Consensus opinion of the relevant expert working group. |

| Ref | Clinical situation | Recommendation | Source |
|---|---|---|---|
| B-TD3 | Aminoglycoside antibiotics (gentamicin, tobramycin) | Every 24 hours at start of therapy on high-dose parenteral regimes, less frequently when stable. Especially important in the elderly, patients with impaired renal function and those with cystic fibrosis. This only applies to once-daily dosing. If patient is on multiple doses per day, refer to local guidance | Consult local hospital guidelines |
| B-TD4 | Immuno-suppressive drugs (ciclosporin, tacrolimus, sirolimus) | Initially 3 per week after transplantation, less frequently when stable. Concentrations should also be checked when any medication with possible interactions is prescribed, the dosage is changed, the formulation is changed or when there is unexplained graft dysfunction | Baker R, Jardine A, Andrews P. *Post-operative Care of the Kidney Transplant Recipient*. Hampshire: The Renal Association, 2011 |
| B-TD5 | Theophylline | 5 half-lives after dosage change (i.e. approx. 2 days) during initial dose optimisation on oral regimes. Note smoking significantly reduces the half-life. Daily on IV aminophylline. In overdose situations requiring haemodialysis, every 4 hours | Consensus opinion of the relevant expert working group. |
| B-TD6 | Methotrexate (high dose IV) | 24 hours after completion of therapy then every 24 hours until plasma methotrexate is below cut-off concentration for toxicity (1 μmol/L at 48 hr or according to local protocol) | See product literature |
| B-TD7 | Lithium | Days 4–7 of treatment then every week until dosage has remained constant for 4 weeks, then every 3 months on stabilised regimes. Check concentration when preparation changed, when fluid intake changes or when interacting drugs are added/withdrawn. 100% renal clearance, so dependent on renal function. Up to every 4 hours in overdose situations requiring intensive therapy | British Medical Association, Royal Pharmaceutical Society of Great Britain, Edited by Joint Formulary Committee. *British National Formulary* (BNF) March 2012. London: Pharmaceutical Press, 2012. |
| B-TD 8 | Clozapine | Induces its own metabolism and is induced further by smoking. Approximately 4 days to reach new steady-state after dose change or smoking cessation with potentially fatal consequences due to the rapid increase to toxic concentrations | Consensus opinion of the relevant expert working group |

### 3.11 Occupational/toxicology

| Ref | Clinical situation | Recommendation | Source |
|---|---|---|---|
| B-O1 | Occupational lead exposure (chronic) | Initial blood lead concentration before commencing work or within 14 days of starting<br>Blood lead concentration monitoring performed at least every 12 months unless significantly exposed to metallic lead and its compounds, in which case the blood lead should be measured every three months<br>If the blood lead is ≥30 µg/dL in adult males (≥20 µg/dL in women of childbearing age) monitor at least every 6 months<br>If the blood lead is ≥40 µg/dL in adult males (≥25 µg/dL in women of childbearing age) monitor at least every 3 months<br>If the blood lead is ≥60 µg/dL in adult males (≥30 µg/dL in women of childbearing age) repeat measurement of blood lead within 2 weeks | Health and Safety Executive. *Control of lead at work 3rd edition.* HSE Books, 2002. |
| B-O2 | Acute lead poisoning in adults | If baseline blood lead concentration is <50 µg/dL, the patient is asymptomatic and not pregnant, repeat blood lead concentration after 2 weeks following removal from exposure<br>If baseline blood lead concentration is ≥50 µg/dL, monitor blood lead concentrations daily during chelation therapy and measure 24-hour urine lead excretion to assist in deciding the duration of treatment. Repeat the blood lead measurement 1 week after the end of chelation treatment | TOXBASE<br>www.toxbase.org |
| B-O3 | Acute lead poisoning in children | If baseline blood lead concentration is 10–50 µg/dL then repeat blood lead measurement in one month following removal from exposure<br>If baseline blood lead concentration is >50 µg/dL, monitor blood lead daily during chelation therapy and measure 24 hour urine lead excretion to assist in deciding the duration of therapy. Repeat the blood lead measurement 1 week after the end of treatment | TOXBASE<br>www.toxbase.org |

| Ref | Clinical situation | Recommendation | Source |
|---|---|---|---|
| B-O4 | Amphetamine toxicity | Retesting is not indicated in the same acute episode | Consensus opinion of the relevant expert working group |
| B-O5 | Benzodiazepine toxicity | Retesting is not indicated in the same acute episode | Consensus opinion of the relevant expert working group |
| B-O6 | Cocaine toxicity | Retesting is not indicated in the same acute episode | Consensus opinion of the relevant expert working group |
| B-O7 | Opiate toxicity including morphine, codeine and heroin | Retesting is not indicated in the same acute episode | Consensus opinion of the relevant expert working group |
| B-O8 | Opioid toxicity including methadone | Retesting is not indicated in the same acute episode | Consensus opinion of the relevant expert working group |

### 3.12 Pregnancy related

| Ref | Clinical situation | Recommendation | Source |
|---|---|---|---|
| B-P1 | Urine βHCG (pregnancy) | Urine pregnancy test can be repeated at 3 days after a negative result or approx 28 days after period commences | Manufacturer's instructions |
| B-P2 | Serum βHCG (pregnancy) | Serum βHCG test: do not repeat if positive. Repeat after 3 days if negative and no menstrual period has occurred | Serum HCG doubling time = 1.5–2 days |
| B-P3 | Serum βHCG (ectopic pregnancy) | 48-hour repeat interval | *Ectopic pregnancy and miscarriage: diagnosis and initial management*. NICE guidelines CG154 |
| B-P4 | Serum βHCG (tumour marker) | After evacuation of a molar pregnancy, the βhCG concentration should be monitored every week until normalisation and then every month during the first year | Bidart JM, Thuillier F, Augereau C, Chalas J, Daver A, Jacob N *et al*. Kinetics of serum tumor marker concentrations and usefulness in clinical monitoring. *Clin Chem* 1999;45:1695–1707. |
| B-P5 | LFTs in obstetric cholestasis | Once obstetric cholestasis is diagnosed, it is reasonable to measure LFTs weekly until delivery.<br>Postnatally, LFTs should be deferred for at least 10 days | Royal College of Obstetricians and Gynaecologists. *Obstetric Cholestasis: Green-top Guideline No 43.* London: Royal College of Obstetricians and Gynaecologists, 2011. |

| Ref | Clinical situation | Recommendation | Source |
|---|---|---|---|
| B-P6 | Women with persistent pruritus and normal biochemistry | LFTs repeated every 1–2 weeks | Royal College of Obstetricians and Gynaecologists. *Obstetric Cholestasis: Green-top Guideline No. 43.* London: Royal College of Obstetricians and Gynaecologists, 2011. |
| B-P8 | Measurement of urate in pre-eclampsia | Awaiting expert advice whilst not admitted: twice-weekly urate | No evidence but reflects the practice of tertiary centre of excellent |
| B-P9 | Urine protein in pre-eclampsia | At each antenatal visit to screen for pre-eclampsia<br>Once diagnosed do not repeat quantification of proteinuria<br>However, daily urine protein recommended in severe hypertension | NICE CG. *Antenatal care for uncomplicated pregnancies*. NICE, 2008. www.nice.org.uk/guidance/cg62<br>NICE CG. *Hypertension in pregnancy: diagnosis and management*. NICE, 2010. www.nice.org.uk/guidance/cg107 |
| B-P10 | LFT/renal in pre-emclampsia | At least daily when the results are abnormal but more often if the clinical condition<br>If mild hypertension* then perform tests twice weekly.<br>If moderate hypertension* then perform tests three times a week<br>If severe hypertension* then perform tests three times a week<br>* See source guidelines for definitions of hypertension | Royal College of Obstetricians and Gynaecologists. *Severe Pre-eclampsia/Eclampsia, Management: Green-top Guideline No 10A.* London: RCOG, 2006.<br>NICE CG. *Hypertension in pregnancy: diagnosis and management*. NICE, 2010. www.nice.org.uk/guidance/cg107 |
| B-P11 | Pregnant women – monitoring of thyrotoxicosis treatment (UK) | In women taking anti-thyroid drugs, TFTs should be performed prior to conception, at time of diagnosis of pregnancy or at antenatal booking<br>Newly diagnosed hyperthyroid patients require monthly testing during pregnancy until stabilised.<br>Pregnant women receiving anti-thyroid drugs should be tested frequently (perhaps monthly) | Association for Clinical Biochemistry, British Thyroid Association and British Thyroid Foundation. *UK guidelines for the use of thyroid function tests.* London: ACB, BTA, 2006. |
| B-P12 | Pregnant women – monitoring thyrotoxicosis treatment (USA) | It is recommended that women treated with anti-thyroid drugs in pregnancy, fT4 and TSH should be monitored approximately every 2–6 weeks | Stagnaro-Green A, Abalovich M, Alexander E, Azizi F, Mestman J, Negro R *et al*. Guidelines of the American Thyroid Association for the diagnosis and management of thyroid disease during pregnancy and postpartum. *Thyroid* 2011;21:1081–1125. |

| Ref | Clinical situation | Recommendation | Source |
|---|---|---|---|
| B-P13 | Pregnant women – monitoring thyroxine replacement therapy | Both TSH and fT4 (and fT3 if TSH below detection limit) should be measured to assess thyroid status and monitor thyroxine therapy in pregnancy<br>The thyroid status of hypothyroid patients should be checked with TSH and fT4 during each trimester. Measurement of T3 is not appropriate<br>The following TFT test sequence is recommended by the UK guidelines [ii]:<br>• before conception<br>• at time of diagnosis of pregnancy<br>• at antenatal booking<br>• at least once in second and third trimesters and again after delivery<br>Newly diagnosed hypothyroid patient to be tested every 4–6 weeks until stabilised | Association for Clinical Biochemistry, British Thyroid Association and British Thyroid Foundation. *UK guidelines for the use of thyroid function tests.* London: Association for Clinical Biochemistry, British Thyroid Association, 2006. |
| B-P14 | Pregnancy sub-clinical hypothyroidism | Women with subclinical hypothyroidism who are not initially treated should be monitored for progression to overt hypothyroidism with serum fT4 and TSH every 4 weeks until 16–20 weeks gestation and at least once between 26–32 weeks<br>(Euthyroid women (not receiving LT4) who are antithyroid antibody positive should be monitored during pregnancy – with serum fT4 and TSH every 4 weeks until 16–20 weeks gestation and at least once between 26–32 weeks) | Stagnaro-Greenet A, Abalovich M, Alexander E, Azizi F, Mestman J, Negro R,*et al*. Guidelines of the American Thyroid Association for the diagnosis and management of thyroid disease during pregnancy and postpartum. *Thyroid* 2011; 21:1081–1125. |
| B-P15 | Women with diabetes who are planning to become pregnant | Monthly<br>measurement of $HbA_{1C}$ | NICE CG. *Diabetes in pregnancy: Management of diabetes and its complications from pre-conception to the postnatal period*. NICE, 2008. www.nice.org.uk/guidance/cg63 |
| B-P16 | Assessing glycaemic control using HbA1c in pregnancy | $HbA_{1C}$ should not be used routinely for assessing glycaemic control in the second and third trimesters of pregnancy | NICE CG. *Diabetes in pregnancy: Management of diabetes and its complications from pre-conception to the postnatal period.* NICE, 2008. www.nice.org.uk/guidance/cg63 |

### 3.13 Paediatric related

| Ref | Clinical situation | Recommendation | Source |
|---|---|---|---|
| B-CH1 | $HbA_{1C}$ monitoring in children and young people with type 1 diabetes | 2 months | NICE. *Type 1 diabetes: Diagnosis and management of type 1 diabetes in children and young people*. NICE, 2004. www.nice.org.uk/guidance/CG15 |
| B-CH2 | Coeliac serology in known paediatric patients on follow up | Testing at 6 months in children | Murch S, Jenkins H, Auth M, Bremner R, Butt a, France S *et al*. Joint ESPGHAN and Coeliac UK guidelines for the diagnosis and management of coeliac disease in children. *Arch Dis Child* 2013; 98:806–811. |

# 4 Haematology recommendations

## 4.1 Haematology general

| Ref | Clinical situation | Recommendation | Source |
|---|---|---|---|
| **Full blood count (FBC) refers to the measurement of Hb, WCC and Plt count unless otherwise stated** | | | |
| H-FBC1 | Normal follow up | A repeat would be indicated on clinical grounds if there were a significant change in that patients condition | Consensus of the haematology working group |
| H-FBC2 | Inpatient monitoring of a stable patient | An inpatient with a normal admission FBC should not have a repeat within the average length of stay of 4 days | Consensus of the haematology working group |
| H-FBC3 | Inpatient monitoring of an unstable patient who is not actively bleeding or a patient receiving cytotoxic drugs | Not usually required more than once daily | Consensus of the haematology working group |
| H-FBC4 | Patients with major bleeding | Repeat interval should be determined by the clinical situation. Should be repeated at least every hour in massive haemorrhage | Association of Anaesthetists of Great Britain and Ireland, Thomas D, Wee M, Clyburn P, Walker I, Brohi K *et al*. Blood transfusion and the anaes-thetist: management of massive haemorrhage. *Anaesthesia* 2010;65:1153–1161. |
| H-FBC5 | Pregnant on haematinic supplements (iron, folate, B12) | Repeat after at least 14 days | British Committee for Standards in Haematology. *UK Guidelines on the management of iron deficiency in pregnancy*. London: BCSH, 2011. |
| H-FBC6 | Routine pregnancy monitoring | At booking, 28 weeks and postpartum | NICE. *Antenatal care for uncomplicated pregnancies*. NICE, 2008. www.nice.org.uk/guidance/cg62<br>British Committee for Standards in Haematology. *UK Guidelines on the management of iron deficiency in pregnancy*. London: BCSH, 2011. |
| H-FBC7 | Immune thrombocytopenia in pregnancy | Every 4 weeks and then every 2 weeks after 28 weeks | British Committee for Standards in Haematology. *UK Guidelines on the management of iron deficiency in pregnancy*. London: BCSH, 2011. |

| Ref | Clinical situation | Recommendation | Source |
|---|---|---|---|
| H-FBC8 | Hypertensive disorders of pregnancy*<br><br>*FBC in combination with renal and liver function | Once only if moderate antenatal gestational hypertension (<160/110) without proteinuria. Weekly if severe gestational hypertension. Twice weekly if mild antenatal hypertension with pre-eclampsia, three times weekly if moderate to severe. As clinically indicated in peripartum period (may require multiple repeats over 24 hours) and then repeat 48 hours after delivery/step down from critical care and stop monitoring if normal values | NICE CG. *Hypertension in pregnancy: diagnosis and management*. NICE, 2010. www.nice.org.uk/guidance/CG107 |
| H-FBC9 | Inpatients with suspected platel*et al*loantibodies or receiving HLA matched platelets | A repeat 1 hour after completion of platelet transfusion | |
| H-FBC10 | Patients with anaemia of chronic kidney disease | Every 2–4 weeks in the induction phase of ESA therapy and every 1–3 months in the maintenance phase of ESA therapy | NICE CG. *Anaemia management in people with chronic kidney disease*. NICE, 2011. www.nice.org.uk/guidance/CG114 |
| **Erythrocyte sedimentation rate (ESR)** | | | |
| H-ESR1 | Temporal arteritis/ polymyalgia rheumatica | Every 3 months following first month of treatment | Dasgupta B, Borg FA, Hassan N, Barraclough K, Bourke B, Fulcher J *et al*. BSR and BHPR guidelines for the management of polymyalgia rheumatica. *Rheumatology (Oxford).* 2010;49:186–190. |
| H-ESR2 | Rheumatoid arthritis | Every month until treatment has controlled the disease (NICE CG79 recommends use of CRP) | NICE CG. Rheumatoid arthritis: The management of rheumatoid arthritis in adults. NICE, 2009. www.nice.org.uk/guidance/CG79 |

### 4.2 Haematology coagulation

Basic clotting screen (CS) refers to the combined measurement of PT and APTT unless otherwise stated.

| Ref | Clinical situation | Recommendation | Source |
|---|---|---|---|
| H-CS1 | Patients with major bleeding | Repeat interval should be determined by the clinical situation. Should be repeated at least every hour in massive haemorrhage | Association of Anaesthetists of Great Britain and Ireland, Thomas D, Wee M, Clyburn P, Walker I, Brohi K *et al*. Blood transfusion and the anaesthetist: management of massive haemorrhage. *Anaesthesia* 2010;65: 1153–1161. |
| H-CS2 | Patients with acute coagulopathy | Usually no more than daily if not receiving coagulation factors and no active bleeding | Consensus of the haematology working group |
| **Prothrombin time (PT) expressed as time in seconds or as a ratio with normal** | | | |
| H-PT1 | Patients with chronic liver disease | Every 3 months if otherwise stable | Consensus of the haematology working group |
| **International normalised ratio (INR)** | | | |
| H-INR1 | Patients being initiated on vitamin K antagonist (VKA) | No more than once daily | Consensus of the haematology working group |
| H-INR2 | Unstable inpatient on VKA | No more than once daily | Consensus of the haematology working group |
| H-INR3 | Stable outpatient on VKA | Usually no more than once weekly and up to 12 weeks when very stable | Consensus of the haematology working group |
| H-INR4 | Patient requiring urgent reversal of VKA (or to treat any acquired deficiency of vitamin K dependent coagulation factors) with vitamin K | Repeat only after at least 6 hours following IV dose and the following day after an oral dose | Consensus of the haematology working group |
| H-INR5 | Patient requiring urgent reversal of VKA with a 4 factor PCC | Repeat within an hour of administration | Consensus of the haematology working group |

| Ref | Clinical situation | Recommendation | Source |
|---|---|---|---|
| **Activated partial thromboplastin time (APTT) expressed as time in seconds and/or as a ratio with normal** | | | |
| H-APTT1 | Patient receiving intravenous infusion of unfractionated heparin | Repeat 6 hours after dose adjustment (2 hours if previous APTT ratio >5.0) and daily when APTT in the target range | Raschke RA, Reilly BM, Guidry JR, Fontana JR, Srinivas S. The weight-based heparin dosing nomogram compared with a "standard care" nomogram. *Ann Intern Med* 1993;119:874–881. |
| H-APTT2 | Patients receiving intravenous infusion of a parenteral direct thrombin inhibitor (Bivalirudin, Argatroban) | Repeat 2 hours after each dose adjustment then daily when in the target range | Summary of Product Characteristics |
| **Clauss fibrinogen assay** | | | |
| H-F1 | Patients with acute coagulopathy | Usually no more than daily if not receiving coagulation factors and no active bleeding | Consensus of the haematology working group |
| H-F2 | Patients with major bleeding | Repeat interval should be determined by the clinical situation. Should be repeated at least every hour in massive haemorrhage | Association of Anaesthetists of Great Britain and Ireland, Thomas D, Wee M, Clyburn P, Walker I, Brohi K *et al*. Blood transfusion and the anaesthetist: management of massive haemorrhage. *Anaesthesia* 2010;65: 1153–1161. |
| **Anti-Xa assay** | | | |
| H-Anti-Xa1 | Patient on therapeutic dose of LMWH with significant renal impairment, extreme weight, pregnancy or other indication for measurement | At least 3 days after initiation or dose adjustment then no more than once weekly if the dose is unchanged | Consensus of the haematology working group |
| **Lupus anticoagulant screen (LA)** | | | |
| H-LA1 | Investigation of suspected antiphospholipid syndrome | Repeat after 12 weeks if abnormal | Keeling D, Mackie I, Moore GW, Greer IA, Greaves M; British Committee for Standards in Haematology. Guidelines on the investigation and management of antiphospholipid syndrome. *Br J Haematol* 2012;157:47–58. |

| Ref | Clinical situation | Recommendation | Source |
|---|---|---|---|
| H-LA2 | Investigation for antiphospholipid syndrome after completion of anticoagulation | At least 7 days after stopping anticoagulation | |
| **Coagulation factor assay (CFA). Refers to the measurement of antigen and/or activity of a coagulation factor (procoagulant or anticoagulant)** | | | |
| H-CF1 | A patient under investigation for suspected coagulation factor deficiency | An abnormal result can be repeated for confirmation at a clinically appropriate interval | Consensus of the haematology working group |
| H-CF2 | A patient receiving coagulation factor replacement therapy | An assay immediately before and up to 60 minutes after administration and then as clinically indicated, usually no more than once daily (either trough, peak or both) | Consensus of the haematology working group |
| **Coagulation factor inhibitor testing including the use of a Bethesda assay or equivalent, other inhibitor screens, ELISA or trough factor measurement** | | | |
| H-CFI1 | Surveillance in patients with severe haemophilia A or B | After every 3rd factor exposure day (ED) or every 3 months (whichever is sooner) until 20 ED then every 3–6 months until 150 ED (then 1–2 times per year in severe haemophilia A only) | Collins PW, Chalmers E, Hart DP, Liesner R, Rangarajan S, Talks K *et al*. Diagnosis and treatment of factor VIII and IX inhibitors in congenital haemophilia (4th ed). UK Haemophilia Centre Doctors Organization.*Br J Haematol* 2013;160:153–170. |
| H-CFI2 | Surveillance after change of factor concentrate in severe haemophilia A | Before the change and then twice in the first 6 months after the change | |
| H-CFI3 | Surveillance in patients with moderate or mild haemophilia A | Annually if exposed to factor concentrate or after intensive exposure (>5ED) or surgery | |
| H-CFI3 | Monitoring of immune tolerance therapy (ITT) during treatment | Monthly | |
| H-CFI4 | After completion of successful ITT | Monthly for 6 months then every 2 months for up to a year | |
| H-CFI5 | Monitoring patients with newly diagnosed acquired coagulation factor inhibitor | Monthly until 6 months after remission | Consensus of haematology working group<br>W Collins P, Chalmers E, Hart D, Jennings I, Liesner R, Rangarajan S *et al*. Diagnosis and management of acquired coagulation inhibitors: a guideline from UKHCDO. *Br J Haematol* 2013;162: 758–773. |

### 4.3 Haematology transfusion (general and screening group in PBLC)

| Ref | Clinical situation | Recommendation | Source |
|---|---|---|---|
| **Blood group and antibody screen** | | | |
| H-BGAS1 | A first time patient prior to transfusion | A second sample can be requested prior to the planned procedure/transfusion | British Committee for Standards in Haematology, Milkins C, Berryman J, Cantwell C, Elliott C, Haggas R *et al*. Guidelines for pre-transfusion compatibility procedures in blood transfusion laboratories. British Committee for Standards in Haematology. *Transfus Med* 2013;23:3–35. |
| H-BGAS2 | A patient who has not had a transfusion or pregnancy within the previous 3 months | The original sample can be valid for up to 3 months | |
| H-BGAS3 | A patient who has had a transfusion or pregnancy within the previous 3 months | The original sample is valid for up to 3 days | |
| H-BGAS4 | A pregnant women who requires blood on standby for obstetric emergencies (e.g. placenta praevia) | A sample may be considered valid for up to 7 days | |
| H-BGAS5 | A chronically transfused patient with no red cell alloantibodies | A sample may be considered valid for up to 7 days after individual risk assessment | |
| H-BGAS6 | A pregnant women over 20 weeks gestation who has anti-D, -C or -K antibodies | Repeat with quantification every 4 weeks until 28 weeks and then every 2 weeks until delivery | Gooch A, Parker J, Wray J, Qureshi H. *Guideline for blood grouping and antibody testing in pregnancy*. London: British Committee for Standards in Haematology, 2006. |

| Ref | Clinical situation | Recommendation | Source |
|---|---|---|---|
| **Estimation of fetomaternal haemorrhage (FMH)**<br>**Refers to the measurement of FMH by Kleihauer and/or flow cytometry** | | | |
| H-FMH 1 | An antenatal sensitising event in an RhD negative women after 20 weeks gestation who is at risk of developing RhD antibodies | Repeat for each new sensitising event unless there is an ongoing sensitising event (e.g. intermittent uterine bleeding) then repeat no more frequently than every 2 weeks | BCSH guideline for the use of anti-D immunoglobulin for the prevention of haemolytic disease of the fetus and newborn. *Transfus Med* 2014;24:8–20. |
| H-FMH2 | If FMH >4 ml in RhD negative women after 20 weeks gestation who are at risk of developing RhD antibodies (RhD positive baby or fetal RhD status unknown) | Repeat 48 hours after IV anti-D or 72 hours after IM anti-D and repeat process until no detectable fetal cells | BCSH guideline for the use of anti-D immunoglobulin for the prevention of haemolytic disease of the fetus and newborn. *Transfus Med* 2014;24:8–20. |
| H-FMH3 | After cell salvage in RhD negative women | Check 30–45 minutes after reinfusion of salvaged cells then as per FMH1 | |

## 5 Immunology recommendations

If no source is quoted, then the recommendation is based on the response from the RCPath's SAC for Immunology.

| Ref | Test | Recommendation | Source |
|---|---|---|---|
| I-1 | A3 ganglionic receptor antibody | Repeat testing of limited value – frequency to be determined by clinical context | |
| I-2 | Acetyl choline receptor antibody | Frequency determined by clinical context – every 6 months while on treatment | |
| I-3 | Adrenal cortex antibody | Repeat testing of limited value – frequency to be determined by clinical context | |
| I-4 | aPL Ab | Repeat testing once diagnosis is confirmed is of limited value | |
| I-5 | Alpha-1 antitrypsin genotype | Not routinely required | |
| I-6 | AMPA receptor antibody | Repeat testing of limited value – frequency to be determined by clinical context | |
| I-7 | Anti nuclear antibody (HEP2) | Once diagnosis of SLE is established, repeat testing is of limited value | |
| I-8 | Aquaporin 4 antibodies (NMO) CSF | Repeat testing guided by clinical context and only allowed if Oxford clinical questionnaire completed | |
| I-9 | Aquaporin 4 antibodies (NMO) Serum | Repeat testing guided by clinical context and only allowed if Oxford clinical questionnaire completed | |
| I-10 | Basal ganglia antibody | Repeat testing of limited value – frequency to be determined by clinical context | |
| I-11 | Beta 2 microglobulin | Repeat testing of limited value – frequency to be determined by clinical context | |
| I-12 | Beta2-glycoprotein I antibody | Repeat testing once diagnosis is confirmed is of limited value | |
| I-13 | C3/4 | 90 days, earlier frequency of testing maybe required in exceptional cases | Consensus of surveyed labs |
| I-14 | C3 nephritic factor | Not routinely required if positive<br>Only allowed if C3 below reference range | |
| I-15 | Cardiac muscle antibody | Not routinely required | |
| I-16 | Cardiolipin antibody | Repeat testing once diagnosis is confirmed is of limited value | |

| Ref | Test | Recommendation | Source |
|---|---|---|---|
| I-17 | CCP | Most centres offer only to rheumatologists (NICE CG79).LL | Consensus of surveyed labs |
| I-18 | CD62 ligand shedding | Discuss with lab | |
| I-19 | Complement C1q | Repeat testing of limited value – frequency to be determined by clinical context | Tarzi MD, Hickey A, Förster T, Mohammadi M, Longhurst HJ. An evaluation of tests used for the diagnosis and monitoring of C1 inhibitor deficiency: normal serum C4 does not exclude hereditary angio-oedema. *Clin Exp Immunol* 2007; 149:513–516. |
| I-20 | Complement 1 inhibitor immunochemical | Only once to confirm; repeat testing limited to exceptional cases<br>Generally only performed if C4 is low or with compatible clinical information. | |
| I-21 | Complement AP100 | Only once to confirm<br>Only allowed with compatible clinical information | |
| I-22 | Complement C2 | Only once to confirm<br>Only allowed with compatible clinical information | |
| I-23 | Complement CH100 | Only once to confirm<br>Only allowed with compatible clinical information | |
| I-24 | Complement Factor B | Only once to confirm<br>Only allowed with compatible clinical information | |
| I-25 | Complement Factor H | Only allowed with compatible clinical information | |
| I-26 | CSF Oligoclonal | Repeat testing of limited value – frequency to be determined by clinical context | |
| I-27 | Cryoglobulin screen | Repeat testing of limited value – frequency to be determined by clinical context | |
| I-28 | Cryoglobulin type | Repeat testing of limited value – frequency to be determined by clinical context | |
| I-29 | DNA(ds)antibody elisa | Every 3–6 months while on treatment | |
| I-30 | Endomysial antibody (IgA) | Not routinely required Only for confirmation of Ttg positives | |
| I-31 | Endomysial antibody (IgG) | Only for patients with complete IgA deficiency | |

| Ref | Test | Recommendation | Source |
|---|---|---|---|
| I-32 | Extractable nuclear antigens (ENA) RNP Sm Ro La Scl Jo1 and centromere | Repeat testing of limited value – frequency to be determined by clinical context | |
| I-33 | GABA receptor antibody | Repeat testing of limited value – frequency to be determined by clinical context | |
| I-34 | GAD 65 antibody | Not routinely required | |
| I-35 | Ganglioside GD1b antibody | Not routinely required | |
| I-36 | Ganglioside GM1 antibody | Not routinely required | |
| I-37 | Ganglioside GQ1b antibody | Not routinely required | |
| I-38 | GBM antibody | Every 3–6 months while on treatment | |
| I-39 | Glycine receptor antibody | Repeat testing of limited value – frequency to be determined by clinical context | |
| I-40 | Haemophilus influenza b (Hib) antibody | Repeat testing to assess response to test immunisation - serial monitoring of limited value | |
| I-41 | Histone antibody | Not routinely required | |
| I-42 | IA2 antibody | Not routinely required | |
| I-43 | IgA low level | Not routinely required | |
| I-44 | IgE | Not routinely required | |
| I-45 | IgG low level | Not routinely required | |
| I-46 | IgG subclasses (1,2,3,4) | Not routinely required | |
| I-47 | IgG4 | Repeat testing of limited value – frequency to be determined by clinical context | |
| I-48 | Insulin antibody | Not routinely required | |
| I-49 | Intrinsic factor antibody | Not routinely required | Khan S, Del-Duca C, Fenton E, Holding S, Hirst J, Doré PC *et al*. Limited value of testing for intrinsic factor antibodies with negative gastric parietal cell antibodies in pernicious anaemia. *J Clin Path* 2009;62:439–441. |
| I-50 | Islet cell antibody | Not routinely required | |
| I-51 | Liver antibody line blot, including M2(PDH) | Not routinely required | |
| I-52 | Liver autoantibodies | Repeat testing of limited value – frequency to be determined by clinical context | |
| I-53 | Lymphocyte phenotype CD3,4,8,19,56 | Discuss with lab | |

| Ref | Test | Recommendation | Source |
|---|---|---|---|
| I-54 | Leucocyte adhesion molecules | Discuss with lab | |
| I-55 | Lymphocyte phenotyping extended panel | Discuss with lab | |
| I-56 | Mast cell tryptase | Three samples over a 24 hr period for assessment of anaphylaxis; Repeat testing may be required in mastocytosis – frequency to be determined by clinical context | NICE guidelines (CG 134) |
| I-57 | MPO ANCA | On treatment: 6 months<br>Off treatment: annually | British Society for Rheumatology Guidelines 2014 |
| I-58 | Muscle specific kinase antibody(MUSK) | Repeat testing of limited value – frequency to be determined by clinical context | |
| I-59 | Myelin associated glycoprotein antibody (MAG) | Repeat testing of limited value – frequency to be determined by clinical context | |
| I-60 | Myelin oligodendrocyte (MOG) ab | Not routinely required | |
| I-61 | Myositis antibody profile | Repeat testing of limited value – frequency to be determined by clinical context | |
| I-62 | Neutrophil cytoplasmic antibody(ANCA) | On treatment: 6 months<br>Off treatment: annually | British Society for Rheumatology Guidelines 2014 |
| I-63 | Neutrophil oxidative burst | Discuss with lab | |
| I-64 | N-methyl D-aspartate receptor antibody (NMDA) CSF | Repeat testing of limited value – frequency to be determined by clinical context | |
| I-65 | N-methyl D-aspartate receptor antibody (NMDA) (NMDA) serum | Repeat testing of limited value – frequency to be determined by clinical context | |
| I-66 | Ovarian antibody | Not routinely required | |
| I-67 | Paraneoplastic antibody profile | Not routinely required | |
| I-68 | Paraprotein (monolonal band) quantitation | 3 months | |
| I-69 | Paraprotein serum gel fix | | |
| I-70 | Parathyroid antibody | Not routinely required | |
| I-71 | Parietal cell antibody | Not routinely required | |
| I-72 | Pemphigoid antibody | On treatment: 6 months<br>Off treatment: annually | |
| I-73 | Pemphigus antibody | On treatment: 6 months<br>Off treatment: annually | |
| I-74 | Phospholipase A2 receptor antibody | Repeat testing of limited value – frequency to be determined by clinical context | |
| I-75 | Pituitary antibody | Not routinely required | |

| Ref | Test | Recommendation | Source |
|---|---|---|---|
| I-76 | PR3 ANCA | On treatment: 6 months<br>Off treatment: annually | British Society for Rheumatology Guidelines 2014 |
| I-77 | Protein (serum) electrophoresis | 3 months | Smellie WSA, Wilson D, McNulty CAM, Galloway MJ, Spickett GA, Finnigan DI *et al*. Best practice in primary care pathology: review 1. *J Clin Pathol* 2005;58: 1016–1024 |
| I-78 | Protein (serum) electrophoresis | Annually for MGUS | Smellie WSA, Wilson D, McNulty CAM, Galloway MJ, Spickett GA, Finnigan DI *et al*. Best practice in primary care pathology: review 1. *J Clin Pathol* 2005;58:1016–1024 |
| I-79 | Quantiferon TB IFN gamma | Discuss with lab | |
| I-80 | Rheumatoid factor | Not routinely required | |
| I-81 | Scleroderma antibody profile | Repeat testing of limited value – frequency to be determined by clinical context | |
| I-82 | Serotype Specific APA | Repeat testing to assess response to test immunisation - serial monitoring of limited value | |
| I-83 | Serum amyloid A | Repeat testing of limited value – frequency to be determined by clinical context | |
| I-84 | Serum free light chains | Where possible local guidance and treatment regimes should be followed when requesting paraprotein concentrations for patients on active treatment. If no local advice or treatment regimes then 3 months – only for diagnosis/monitoring of amyloidosis, non-secretory myeloma and light chain only myeloma | |
| I-85 | Serum immunofixation | Not unless change in serum electrophoresis.<br>Not performed as follow up to electrophoresis unless for remission confirmation | |
| I-86 | Skeletal (striated) muscle antibody | Not routinely required<br>Comment on ordering that imaging is superior for thymoma investigation | |
| I-87 | Specific IgE | Not routinely required | |

| Ref | Test | Recommendation | Source |
|---|---|---|---|
| I-88 | Submaxillary gland antibody | Never | |
| I-89 | Tetanus Ab | Repeat testing to assess response to test immunisation - serial monitoring of limited value | Consensus of surveyed labs |
| I-90 | tIgE | Repeat testing of limited value – frequency to be determined by clinical context | Consensus of surveyed labs |
| I-91 | Thyroid peroxidase antibody | Not routinely required | |
| I-92 | T Lymphocyte subset CD3,4,8 | Discuss with lab | |
| I-93 | TTg IgA antibody | IgA tTG can be used to monitor response to a gluten-free diet. Retesting at 6–12 months depending on pre-treatment value | www.uptodate.com |
| I-94 | TTg IgG antibody | Re-testing at 6-12 months Only in IgA deficient patients | |
| I-95 | Urine electrophoresis | Not routinely required | |
| I-96 | Urine free light chain quant | Repeat testing of limited value – frequency to be determined by clinical context | |
| I-97 | Voltage gated calcium channel antibody (VGCC) | Repeat testing of limited value – frequency to be determined by clinical context | |
| I-98 | Voltage gated potassium channel antibody (VGKC) CSF | Repeat testing of limited value – frequency to be determined by clinical context | |
| I-99 | Voltage gated potassium channel antibody (VGKC) Serum | Repeat testing of limited value – frequency to be determined by clinical context | |

# 6 Microbiology recommendations

## 6.1 General microbiology

All recommendations in this area of pathology were based on consensus expert peer opinion.

| Ref | Clinical situation | Recommendation |
|---|---|---|
| M-1 | AFB microscopy and culture | NA |
| M-2 | Antrum washings | 7 days |
| M-3 | ASO titre | 14 days |
| M-4 | Aspirates and fluids from sterile sites | NA |
| M-5 | Blood culture | NA |
| M-6 | Blood cultures | NA |
| M-7 | Borrelia burgdorferi (Lyme) | 14 days |
| M-8 | Bronchoalveolar lavage | 3 days |
| M-9 | Bronchoalveolar lavage | 3 days |
| M-10 | Cerebrospinal fluid (CSF) | NA |
| M-11 | Chlamydia/GC NAAT | NA |
| M-12 | Complement Fixation Test (CFT) | 14 days |
| M-13 | Cough swab | 7 days |
| M-14 | CSF for molecular investigation, e.g. Meningococcus | NA |
| M-15 | CSF microscopy and culture | NA |
| M-16 | Drug monitoring: Glycopeptides; Vancomycin, Teicoplanin, etc | 24 hours |
| M-17 | Drug monitoring: Aminoglycosides; Gentamicin, Amikacin, etc. This only applies to once-daily dosing. If patient is on multiple doses per day please refer to local guidance. | 24 hours |
| M-18 | Ear swab | 7 days |
| M-19 | Ear/nose and throat swab | 7 days |
| M-20 | EDTA blood for Meningococcal infection | 7 days |
| M-21 | Endocervical swab | NA |
| M-22 | Eye swab | 7 days |
| M-23 | Faeces – C.difficile<br><br>*GDH positive/toxin negative | Dependent on result:<br>Confirmed positive = 28 days<br>Equivocal* = 24 hours<br>Negative = 24 hours |
| M-24 | Faeces – ova, cysts and parasites | 24 hours |
| M-25 | Faeces – routine | 7 days |
| M-26 | Genital swab (GC only) | NA |
| M-27 | Genital swab microscopy and culture | NA |
| M-28 | Helicobacter pylori – negative | 28 days |

| Ref | Clinical situation | Recommendation |
|---|---|---|
| M-29 | Helicobacter pylori – positive serology | Never |
| M-29 | High vaginal swab (HVS) | NA |
| M-30 | Intrauterine contraceptive device (IUCD) | NA |
| M-31 | IUCD for actinomyces | NA |
| M-32 | Joint fluids, microscopy and culture | NA |
| M-33 | Legionella pneumophila Sgp1 antigen | 7 days |
| M-34 | Mouth swab | 7 days |
| M-35 | MRSA Screen | 7 days |
| M-36 | Mycoplasma | 14 days |
| M-37 | Nasal swab | 7 days |
| M-38 | Nasopharyngeal aspirate | 7 days |
| M-39 | Non-directed bronchial lavage | 3 days |
| M-40 | PD fluids, microscopy and culture | NA |
| M-41 | Peritoneal fluid | NA |
| M-42 | Pernasal swab (for pertussis) | NA |
| M-43 | Pernasal swabs | 7 days |
| M-44 | Pleural effusion/Chest fluids | NA |
| M-45 | Pleural fluid | NA |
| M-46 | Pneumocystis jirovecii (DIF) | NA |
| M-47 | Pus swab | 3 days |
| M-48 | Pus/exudate | NA |
| M-49 | Seminal fluid | 28 days |
| M-50 | Skin, nail and hair for mycology | 3 months |
| M-51 | Sputum | 3 days |
| M-52 | Syphilis | 14 days |
| M-53 | Throat swab | Dependent on result:<br>Positive = 7 days<br>Negative = 3 days |
| M-54 | Tissue/bone microscopy and culture | NA |
| M-55 | Tissues and biopsies | NA |
| M-56 | Toxoplasma IgG screen negative | 7 days |
| M-57 | Toxoplasma IgG screen positive | Never |
| M-58 | Tuberculosis | NA |
| M-59 | Urethral swab | NA |
| M-60 | Urine for tuberculosis | NA |
| M-61 | Urine, microscopy and culture | 3 days |
| M-62 | Wound and ulcer swab | 7 days |

### 6.2 Fungal recommendations

Recommendations made based on consensus expert peer opinion with supporting references

| Ref | Clinical situation | Recommendation | Source |
|---|---|---|---|
| *Aspergillus* galactomannan (GM) (Bio-Rad Platelia *Aspergillus* ELISA) | Serial screening for blood GM in high-risk haematology patients*:<br>• single negative sample can be used to exclude invasive aspergillosis (IA)<br>• rwo consecutive positive samples (or same sample retested) provide good positive predictive value<br>• reduction of the GM index during the first 2 weeks of antifungal therapy is a reliable predictor of treatment response | Twice weekly | Maertens J, Verhaegen J, Lagrou K *et al*. Screening for circulating galactomannan as a noninvasive diagnostic tool for invasive aspergillosis in prolonged neutropenic patients and stem cell transplantation recipients: a prospective validation. *Blood* 2001,97:1604–1610.<br>Furfaro E, Mikulska M, Miletich F *et al*. Galactomannan: testing the same sample twice? *Transpl Infect Dis* 2012;14:E38–E39.<br>Leeflang MM, Debets-Ossenkopp YJ, Vissers CE *et al*. Galactomannan detection for invasive aspergillosis in immunocompromized patients (Review). *The Cochrane Collaboration* 2008, issue 4.<br>Chai LYA, Kullberg BJ, Johnson EM *et al*. Early serum galactomannan trend as a predictor of outcome of invasive aspergillosis. *J Clin Microbiol* 2012;50(7):2330.<br>Nouer SA, Nucci M, Kumar NS *et al*. Earlier response assessment in invasive aspergillosis based on the kinetics of serum aspergillus galactomannan: proposal for a new definition. *Clin Infect Dis* 2011;53:671–676.<br>Bergeron A, Porcher R, Menotti J *et al*. Prospective evaluation of clinical and biological markers to predict the outcome of invasive pulmonary aspergillosis in hematological patients. *J Clin Microbiol* 2012;50:823.<br>Schelenz S, Barnes RA, Barton RC *et al*. British Society for Medical Mycology |

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| | | | best practice recommendations for the diagnosis of serious fungal diseases. *Lancet Infect Dis* 2015;15:461–474. doi: 10.1016/S1473–3099(15)70006-X. Epub 2015 Mar 12. Review. |
| β-1-3-*D*-glucan (BDG) (Fungitell, Associates of Cape Cod Inc.) | Screening for severely ill ICU patients and patients with haemato-logical malignancies and post allogeneic hematopoietic stem cell transplants:<br>• single negative sample can be used to exclude invasive fungal infection (IFI)<br>• repeatedly positive BDG results may be used as supportive evidence for the presence of an IFI | Twice weekly | Eggimann P, Marchetti O. Is (1→3)-β-D-glucan the missing link from bedside assessment to pre-emptive therapy of invasive candidiasis? *Crit Care* 2011;15:1017. doi: 10.1186/cc10544.<br>Cuenca-Estrella M, Verweij PE, Arendrup MC *et al*. ESCMID* guideline for the diagnosis and management of Candida diseases 2012: diagnostic procedures. *Clin Microbiol Infect* 2012 Dec;18 Suppl 7:9–18. doi: 10.1111/1469–0691.12038.<br>Hammarström H, Kondori N, Friman V, Wennerås C. How to interpret serum levels of beta-glucan for the diagnosis of invasive fungal infections in adult high-risk hematology patients: optimal cut-off levels and confounding factors. *Eur J Clin Microbiol Infect Dis* 2015;34(5):917–925.<br>Schelenz S, Barnes RA, Barton RC, Cleverley JR, Lucas SB, Kibbler CC, Denning DW; British Society for Medical Mycology. British Society for Medical Mycology best practice recommendations for the diagnosis of serious fungal diseases. *Lancet Infect Dis* 2015;15(4):461–74. doi: 10.1016/S1473–3099(15)70006-X. Epub 2015 Mar 12. Review. |

*Neutropaenic patients and allogeneic stem cell transplantation recipients during the early engraftment phase, who are not on mould-active antifungal prophylaxis or treatment.

# 7 Virology recommendations

If no source is quoted, then the recommendation is based on the response from the RCPath's SAC for Virology

## 7.1 Congenital/perinatal bloodborne viral infection – testing in asymptomatic infants

| Ref | Clinical situation | Recommendation | Source |
|---|---|---|---|
| V-1 | Maternal infection with HIV | Test infant blood (EDTA):<br>HIV DNA (proviral DNA) PCR within 48 hours of birth and/or HIV RNA PCR within 48 hours of birth, repeat HIV RNA PCR at 6 weeks (ie 2 weeks after cessation of prophylaxis),<br>repeat HIV RNA PCR at 12 weeks (ie 2 months after cessation of prophylaxis)<br>Test infant blood (clotted):<br>anti-HIV antigen/antibody – at 18 months | Taylor GP1, Clayden P, Dhar J, Gandhi K, Gilleece Y, Harding K *et al*. British HIV Association guidelines for the management of HIV infection in pregnant women 2012. *HIV Medicine* 2012;13 (Suppl. 2):87–157. |
| V-2 | Maternal infection with hepatitis B | Test infant blood (clotted) or infant blood (dried blood spot):<br>Hepatitis B surface antigen at 12 months (or later at conclusion of prophylaxis if vaccine course delayed beyond 12 months) | Hepatitis B: chapter 18. *Immunisation against Infectious Diseases* 'The Green Book'. Public Health England, 2013. |
| V-3 | Maternal infection with hepatitis C | Test infant blood (EDTA), blood (clotted), blood (dried blood spot):<br>Hepatitis C RNA PCR at 2–3 months, repeat HCV RNA PCR at 6 months (no further PCR follow up if negative)<br><br>Test infant blood (clotted or dried blood spot):<br>Anti-HCV antibody at 12–18 months (no further follow up if negative) | Public Health England. *UK Standards for Microbiological Investigations V8: Vertical and Perinatal Transmission of Hepatitis C*. PHE, 2014. www.gov.uk/government/publications/smi-v-8-vertical-hcv-transmission |

## 7.2 Congenital viral infection

| Ref | Clinical situation | Recommendation | Source |
|---|---|---|---|
| V-4 | Suspected congenital infection | PCR for:<br>• CMV (urine, saliva or blood which is less sensitive) within 3 weeks of birth. No need to repeat<br>• toxoplasma, (blood, throat swab, nose swab, lesions)<br>• HSV(blood, throat swab, nose swab, lesions)<br>• rubella(blood, throat swab, nose swab, lesions)<br>• syphilis(blood, throat swab, nose swab, lesions) | Kadambari S, Williams EJ, Luck S, Griffiths PD, Sharland M. Evidence based management guidelines for the detection and treatment of congenital CMV. *Early Hum Dev* 2011;87: 723–728. |
| V-5 | Suspected congenital infection | IgM antibody (within 3 weeks of birth). No need to repeat except syphilis repeat at 6 weeks | BASHH UK National Guidelines on Management of Syphilis 2015. www.bashh.org/documents/syphilis%20Guideline%20v%2010.pdf |
| V-6 | Suspected congenital infection | IgG antibody – if negative no need to repeat | |
| V-7 | Maternal infection with syphili | PCR (exudates, lesions, nasal discharge) with maternal and neonate paired serology | BASHH UK National Guidelines on Management of Syphilis 2015. www.bashh.org/documents/syphilis%20Guideline%20v%2010.pdf |

## 7.3 Viral encephalitis investigation

| Ref | Clinical situation | Recommendation | Source |
|---|---|---|---|
| V-8 | Encephalitis | Test CSF for HSV, VZV, enterovirus nucleic acid by PCR as soon as possible<br>Negative CSF PCRs – repeat HSV, VZV, enterovirus PCRs in 48 hours, unless other cause has been identified, consider additional PCRs | Solomon T, Michael BD, Smith PE, Sanderson F, Davies NW, Hart IJ *et al*. Management of suspected viral encephalitis in adults – Association of British Neurologists and British Infection Association National Guidelines. *J Infect* 2012; 64:347–373. |
| V-9 | Herpes simplex encephalitis management | Test CSF for HSV DNA by PCR after 14 days treatment (immunocompetent)<br><br>If negative, consider repeat test 3–7 days later<br>Test CSF for HSV DNA by PCR after 21 days immunosuppressed | Solomon T, Michael BD, Smith PE, Sanderson F, Davies NW, Hart IJ *et al*. Management of suspected viral encephalitis in adults – Association of British Neurologists and British Infection Association National Guidelines. *J Infect* 2012; 64:347–373. |

### 7.4 Respiratory tract infection

| Ref | Clinical situation | Recommendation | Source |
|---|---|---|---|
| V-10 | Respiratory virus infection or respiratory bacterial infection with mycoplasma, chlamydia/ chlamydophila, | Samples investigated for respiratory virus infections must be tested by PCR testing where possible.<br>Serological testing for atypical pneumonia is generally carried out by complement fixation test, if available<br>Test blood (clotted) collected >10 days after first blood in parallel with previous sample to available range of antigens for mycoplasma, chlamydia/ chlamydophila, Q fever | |
| | Q fever | Test clotted blood for IgG phase 2 and IgM soon after onset<br>Test clotted blood in parallel with blood 7–14 days later<br>Test clotted blood at 6 months for C.burnetii IgA and phase 1 IgG to exclude chronic infection | Anderson A, Bijlmer H, Fournier PE, Graves S, Hartzell J, Kersh GJ *et al*. Diagnosis and management of Q fever – United States 2013: *Recommendations from CDC and the Q Fever Working Group. MMWR Recomm Rep* 2013;29:1–30. |

### 7.5 Renal testing

| Ref | Clinical situation | Recommendation | Source |
|---|---|---|---|
| V-11 | Renal failure – dialysis screen, UK dialysis only | Test HIV antigen/antibody, HCV antibody, antigen/antibody or antigen, HBsAg pre-dialysis | Public Health England. *UK Standards for Microbiology Investigations V 10: Bloodborne virus testing in dialysis patients*. PHE, 2014. www.gov.uk/government/ publications/ smi-v-10-bloodborne-virus-testing- in-dialysis-patients |
| V-12 | | Test HIV 3 monthly (if risk factors) | Public Health England. *UK Standards for Microbiology Investigations V 10: Bloodborne virus testing in dialysis patients*. PHE, 2014. www.gov.uk/government/ publications/ smi-v-10-bloodborne-virus-testing- in-dialysis-patients |
| V-13 | | Test HCV 3 monthly | Public Health England. *UK Standards for Microbiology Investigations V 10: Bloodborne virus testing in dialysis patients*. PHE, 2014. www.gov.uk/government/ publications/ smi-v-10-bloodborne-virus-testing- in-dialysis-patients |
| V-14 | | Test HBsAg 1-3 monthly | Public Health England. *UK Standards for Microbiology Investigations V 10: Bloodborne virus testing in dialysis patients*. PHE, 2014. www.gov.uk/government/ publications/ smi-v-10-bloodborne-virus-testing- in-dialysis-patients |
| V-15 | Renal failure – dialysis abroad (Also refer to DoH guidance on BBV testing following dialysis abroad) | Test HCV NAAT or HCV antigen or HCV antigen/antibody every 2 weeks for 3 months | Renal Association; expert opinion |
| V-16 | | Test HBsAg or HBV NAAT every 2 weeks for 3 months | Renal Association. *Blood Borne Virus Infection*. Hampshire: Renal Association, 2009. |
| V-17 | | Test HIV antigen/antibody every 2 weeks for 3 months | Renal Association. *Blood Borne Virus Infection*. Hampshire: Renal Association, 2009. |
| V-18 | Renal failure – dialysis but HBsAg negative and known anti-HBs response to vaccine >100 mIU/mL | Test HBsAg yearly | Renal Association. *Blood Borne Virus Infection*. Hampshire: Renal Association, 2009. |

### 7.6 Post-exposure to bloodborne viruses

| Ref | Clinical situation | Recommendation | Source |
|---|---|---|---|
| V-19 | Potential significant exposure to HBsAg positive material, hepatitis B susceptible | Collect baseline blood for storage.<br>Test HBsAg at 3 months<br>Test HBsAg, anti-HBc at 6 months<br>Test anti-HBs 1–2 months after vaccine course | |
| V-20 | Potential significant exposure to HIV positive material but no post-exposure prophylaxis given | Test for HIV antigen/antibody at 12 weeks after cessation of post-exposure prophylaxis, no further test required (DoH) but note that patients attending for HIV testing who identify a specific risk occurring less than 4 weeks previously should not be made to wait before HIV testing as doing so may miss an opportunity to diagnose HIV infection (and in particular acute HIV infection during which a person is highly infectious). They should be offered a fourth generation laboratory HIV test and be advised to repeat it when 4 weeks have elapsed from the time of the last exposure. A negative result on a fourth generation test performed at 4 weeks post-exposure and 4–6 weeks post-prophylaxis is highly likely to exclude HIV infection. A further test at 8 weeks post-exposure need only be considered following an event assessed as carrying a high risk of infection (BASHH). | DoH. HIV post-exposure prophylaxis Guidance from the UK Chief Medical Officers' Expert Advisory Group on AIDS. Department of Health, 2008.<br>www.gov.uk/government/news/hiv-post-exposure-prophylaxis-guidance-from-the-uk-chief-medical-officers-expert-advisory-group-on-aids<br><br>BASHH/EAGA statement on HIV window period<br>www.bashh.org/BASHH/Guidelines/Guidelines/BASHH/Guidelines/Guidelines.aspx |

| Ref | Clinical situation | Recommendation | Source |
|---|---|---|---|
| V-21 | Potential significant exposure to HIV positive material and postexposure prophylaxis given | Test for HIV antigen/antibody at 12 weeks after cessation of postexposure prophylaxis, no further test required (DH) but note that patients attending for HIV testing who identify a specific risk occurring less than 4 weeks previously should not be made to wait before HIV testing as doing so may miss an opportunity to diagnose HIV infection (and in particular acute HIV infection during which a person is highly infectious). They should be offered a fourth generation laboratory HIV test and be advised to repeat it when 4 weeks have elapsed from the time of the last exposure. A negative result on a fourth generation test performed at 4 weeks post-exposure and 4-6 weeks post-prophylaxis is highly likely to exclude HIV infection. A further test at 8 weeks post-exposure need only be considered following an event assessed as carrying a high risk of infection (BASHH). | DoH. HIV post-exposure prophylaxis<br>Guidance from the UK<br>Chief Medical Officers' Expert<br>Advisory Group on AIDS. Department of Health, 2008.<br>www.gov.uk/government/news/hiv-post-exposure-prophylaxis-guidance-from-the-uk-chief-medical-officers-expert-advisory-group-on-aids<br><br>BASHH/EAGA statement on HIV window period<br>www.bashh.org/BASHH/Guidelines/Guidelines/BASHH/Guidelines/Guidelines.aspx |
| V-22 | Potential significant exposure to HCV positive material | Test at 6 weeks and 12 weeks by HCV NAAT<br>If negative test at 12 and 24 weeks with HCV antibody | Ramsay ME. Guidance on the investigation and management of occupational exposure to hepatitis C. *Commun Dis Public Health* 1999;2:258–262. |

# 8 Cellular pathology recommendations

All recommendations in this area of pathology were based on consensus expert peer opinion.

Letters in parenthesis refer to recommendation number.

## 8.1 General aspects of laboratory practice

a) It is not helpful to specify minimum retesting intervals for the majority of cellular pathology specimens, which tend to be unique to a particular clinical episode. The areas where repeat sampling/re-biopsy or laboratory testing may be considered are detailed in sections 2 and 3. (CP-1)

b) Where a diagnosis has been confidently established on pre-operative biopsies, is it usually not necessary to confirm the immunohistochemical phenotype or molecular genetic changes on resection specimens. More specific guidance on retesting may be found in the RCPath's datasets for cancer histopathology reports and tissue pathways (https://www.rcpath.org/resource-library-homepage/publications/cancer-datasets.html). (CP-2)

c) No specific implications or roles have been identified for minimum retesting intervals in neuropathology or the non-forensic autopsy. (CP-3)

## 8.2 Exfoliative and fine needle aspiration cytology

a) For patients whose tissues are sampled as part of national screening programmes, the sampling interval for asymptomatic patients will be determined by the programme. The investigation of symptoms or clinical abnormalities should be investigated as appropriate and is out with the screening service. (CP-4)

b) When considering the appropriate tests to request, the negative predictive value should be considered. Some tests, such as urine or nipple discharge cytology, are recognised as having a low negative predictive value and thus cannot be used to exclude significant disease. Repeating such tests does not provide further reassurance or negate previous equivocal results. (CP-5)

c) Repeatedly sending samples when a definitive diagnosis (e.g. positive for specific tumour type) has been established is a waste of resources. A repeat sample may be necessary if an initial specimen does not provide sufficient information for clinical management. (CP-6)

d) Cytological surveillance of asymptomatic patients following malignant disease (e.g. urine specimens as follow up for urothelial carcinoma) should not be performed more frequently than annually. The development of symptoms should be investigated as appropriate. (CP-7)

## 8.3 Histopathology

a) In general, biopsies are taken for specific clinical indications. A repeat biopsy may be necessary if an initial biopsy does not provide sufficient information for clinical management. (CP-8)

b) When clinical features or disease progression do not fit with a previously established diagnosis then review of previous biopsy material should be undertaken before considering a repeat biopsy. (CP-9)

c) Where patients are undergoing regular clinical review, e.g. endoscopies for Barrett's, inflammatory bowel disease, repeated biopsies may be required to monitor response to treatment or to detect progressive disease at an early stage. (CP-10)

d) Rebiopsy in chronic renal disease – an annual (for example) biopsy is recommended for monitoring and should not be repeated more frequently unless clinically indicated. (CP-11)

e) Repeat liver biopsies are only done by protocol for disease progression monitoring, e.g. post-transplant hep C, or if the initial sample is insufficient for diagnosis. (CP-12)

## 9 Contributors

Many people were involved in the preparation and/or the review of recommendations for minimal retesting intervals in pathology. The leads of the project would like to acknowledge all the work of the panel members in particular in contributing to the preparation of this document.

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