

# LAB RESULTS MADE EASY

Nazia Hussain

## UREA AND ELECTROLYTES

Na	136	mmol/L	(134-145)
K	6.1 H	mmol/L	(3.6-5.0)
Urea	4.2	mmol/L	(1.7-7.1)
Creatinine	101 H	umol/L	(45-84)
eGFR	52	mL/min/1.73m <sup>2</sup>	

## LIVER FUNCTION TEST

Tot. Bilirubin	10	umol/L	(0-22)
Total Protein	67	g/L	(63-82)
Albumin	40	g/L	(35-50)
Globulin	26	g/L	(21-35)
Alk. Phosph.	76	U/L	(38-126)
ALT	71 H	U/L	(0-50)

## Full blood count:

Wbc	4.8	10 <sup>9</sup> /L	(4.0-10.0)	
Rbc	5.33 H	10 <sup>12</sup> /L	(3.80-4.80)	
Hb	144	g/L	(120-150)	
Hct	0.445		(0.360-0.460)	
MCV	84	fL	(83-101)	
MCH	27.0	pg	(27.0-32.0)	
MCHC	324	g/L	(315-345)	
Platelets	365	10 <sup>9</sup> /L	(150-410)	
Neutrophils	2.46	10 <sup>9</sup> /L	(2.00-7.00)	Neutro
Lymphocytes	1.61	10 <sup>9</sup> /L	(1.00-3.00)	Lymph
Monocytes	0.49	10 <sup>9</sup> /L	(0.20-1.00)	Monocy
Eosinophils	0.17	10 <sup>9</sup> /L	(0.02-0.50)	Eosino
Basophils	0.06	10 <sup>9</sup> /L	(0.00-0.10)	Basoph
NRBC	0.00	10 <sup>9</sup> /L		



# LAB RESULTS MADE EASY

## **NAZIA HUSSAIN**

MBBCh, DRCOG, DCH, DFSRH, PG Cert in Medical Education  
General Practitioner, Aneurin Bevan University Health Board, NHS Wales

### **Consultant Editors:**

#### **NADIA EL-FARHAN**

Consultant Clinical Biochemist, Aneurin Bevan University Health Board, NHS Wales

#### **SARAH GODDARD**

Consultant Clinical Immunologist, University Hospitals of North Midlands

#### **CHRIS GREGORY**

Consultant Haematologist, Royal Albert Edward Infirmary, Wroughton,  
Wigan and Leigh Teaching Hospitals NHS Foundation Trust

#### **ELIZABETH KUBIAK**

Consultant Microbiologist, Aneurin Bevan University Health Board, NHS Wales

#### **SHALIKA PALANGASINGHE**

Consultant Microbiologist, Aneurin Bevan University Health Board, NHS Wales



**Scion**

---

© Scion Publishing Limited, 2025

ISBN 9781914961601

All rights, including for text and data mining (TDM), artificial intelligence (AI) training, and similar technologies, are reserved. No part of this book may be reproduced or transmitted, in any form or by any means, without permission.

A CIP catalogue record for this book is available from the British Library.

---

### **Scion Publishing Limited**

The Old Hayloft, Vantage Business Park, Bloxham Road, Banbury OX16 9UX, UK  
[www.scionpublishing.com](http://www.scionpublishing.com)

### **Important Note from the Publisher**

The information contained within this book was obtained by Scion Publishing Ltd from sources believed by us to be reliable. However, while every effort has been made to ensure its accuracy, no responsibility for loss or injury whatsoever occasioned to any person acting or refraining from action as a result of information contained herein can be accepted by the authors or publishers.

Readers are reminded that medicine is a constantly evolving science and while the authors and publishers have ensured that all dosages, applications and practices are based on current indications, there may be specific practices which differ between communities. You should always follow the guidelines laid down by the manufacturers of specific products and the relevant authorities in the country in which you are practising.

Although every effort has been made to ensure that all owners of copyright material have been acknowledged in this publication, we would be pleased to acknowledge in subsequent reprints or editions any omissions brought to our attention.

Registered names, trademarks, etc. used in this book, even when not marked as such, are not to be considered unprotected by law.

Typeset by Evolution Design & Digital Ltd (Kent)

Printed in the UK

Last digit is the print number: 10 9 8 7 6 5 4 3 2 1

# Contents

Preface	xii
Acknowledgements	xii
About the author and editors	xiii
Abbreviations	xiv
How to use this book	xvii

## Part I: ABNORMAL TEST RESULTS

### Chapter 1: Clinical biochemistry 3

#### ABNORMAL RESULTS

<b>1.1</b>	<b>Urea and electrolytes (U&amp;E)</b>	<b>6</b>
1.1.1	Renal function	6
	Acute kidney injury (AKI)	6
	Chronic kidney disease (CKD)	10
1.1.2	Sodium	15
	Hypernatraemia	15
	Hyponatraemia	18
1.1.3	Potassium	21
	Hyperkalaemia	21
	Hypokalaemia	24
1.1.4	Urea	27
	Raised urea	27
	Low urea	28
<b>1.2</b>	<b>Liver function tests</b>	<b>29</b>
	LFT pattern recognition	29
	Isolated raised bilirubin	30
	Hepatocellular	31
	Raised alkaline phosphatase (ALP)	32
	Albumin	32
	Bilirubin (total)	32
	Total protein	33
	Alanine aminotransferase (ALT)	33
	Aspartate aminotransferase (AST)	33
	Alkaline phosphatase (ALP)	33
	Gamma-glutamyl transferase (GGT)	34
	Prothrombin time (PT) and INR	34
<b>1.3</b>	<b>Bone profile</b>	<b>38</b>
1.3.1	Calcium	38
	Hypercalcaemia	38

---

	Hypocalcaemia	41
1.3.2	<b>Phosphate</b>	<b>44</b>
	High phosphate	44
	Low phosphate	46
1.3.3	<b>Magnesium</b>	<b>48</b>
	High magnesium	48
	Low magnesium	49
1.4	<b>Raised creatine kinase (CK)</b>	<b>52</b>
1.5	<b>Low vitamin D</b>	<b>56</b>
<b>TESTS</b>		
1.6	<b>Stool</b>	<b>60</b>
1.6.1	Faecal immunochemical test (FIT)	60
1.6.2	Faecal calprotectin (FC)	61
1.6.3	Faecal elastase	64
1.7	<b>Urine</b>	<b>64</b>
1.7.1	Urine albumin:creatinine ratio (ACR) and urine protein:creatinine ratio (PCR)	64
1.7.2	Urine dipstick	68
1.8	<b>Endocrine</b>	<b>73</b>
1.8.1	Thyroid function tests (TFT)	73
	Hyperthyroidism	73
	Hypothyroidism	79
1.8.2	9am cortisol	81
1.8.3	Parathyroid hormone (PTH)	83
1.8.4	Prolactin	85
1.9	<b>Cardiovascular</b>	<b>86</b>
1.9.1	Haemoglobin A1c (HbA1c)	86
1.9.2	Lipids	90
	Primary prevention	92
	Secondary prevention	93
	Triglycerides (TG)	93
	Familial hypercholesterolaemia (FH)	95
	Lipoprotein(a) [Lp(a)]	97
1.9.3	N-terminal pro-B-type natriuretic peptide (NT-pro-BNP)	97
1.10	<b>Liver screen</b>	<b>99</b>
1.10.1	Alpha-1 antitrypsin	99

1.10.2	Caeruloplasmin	100
<b>1.11</b>	<b>Men's health</b>	<b>101</b>
1.11.1	Male hormone profile	101
	Testosterone	102
	Follicle-stimulating hormone (FSH) and luteinising hormone (LH)	102
	Sex hormone-binding globulin (SHBG)	102
1.11.2	Prostate-specific antigen (PSA)	103
<b>1.12</b>	<b>Women's health</b>	<b>104</b>
1.12.1	Female hormone profile	104
	Follicle-stimulating hormone (FSH) and luteinising hormone (LH)	104
1.12.2	Oestradiol	107
1.12.3	Progesterone	108
1.12.4	Testosterone	109
	Testosterone	109
	Sex hormone-binding globulin (SHBG)	110
	Free androgen index (FAI)	111
1.12.5	Cancer antigen 125 (CA125)	112
1.12.6	Human chorionic gonadotrophin (hCG)	113

## Chapter 2: Haematology

115

### ABNORMAL RESULTS

<b>2.1</b>	<b>Full blood count</b>	<b>116</b>
2.1.1	Haemoglobin	116
	Low haemoglobin (anaemia)	116
	Iron-deficiency anaemia (IDA)	121
	Vitamin B12 deficiency	123
	Folate deficiency	126
	Raised haematocrit (erythrocytosis)	127
2.1.2	White cell count	129
	Low neutrophils (neutropenia)	129
	Low lymphocytes (lymphopenia)	131
	High white cell count (leucocytosis)	132
	High neutrophils (neutrophilia)	133
	High lymphocytes (lymphocytosis)	135
	High basophils (basophilia)	136
	High eosinophils (eosinophilia)	137
	High monocytes (monocytosis)	138

2.1.3	Platelets	139
	Low platelets (thrombocytopenia)	139
	High platelets (thrombocytosis)	141
<b>2.2</b>	<b>Reticulocytes</b>	<b>143</b>
<b>TESTS</b>		
<b>2.3</b>	<b>Immunoglobulins / serum protein electrophoresis / serum free light chains / urine Bence Jones proteins</b>	<b>144</b>
<b>2.4</b>	<b>Clotting tests</b>	<b>147</b>
<b>2.5</b>	<b>Blood film comments</b>	<b>149</b>
<b>2.6</b>	<b>Inflammatory markers: CRP/ESR/PV</b>	<b>150</b>
<b>2.7</b>	<b>Iron studies and ferritin</b>	<b>152</b>
2.7.1	Iron studies	152
2.7.2	Ferritin	154
<b>Chapter 3: Immunology and rheumatology</b>		<b>157</b>
<b>3.1</b>	<b>Immunology (autoantibodies)</b>	<b>158</b>
3.1.1	Statistics definitions	158
3.1.2	Antinuclear antibodies (ANA)	159
3.1.3	Cyclic citrullinated peptide antibodies (CCP)	160
3.1.4	Double-stranded DNA antibodies (dsDNA)	160
3.1.5	Endomysial antibodies (EMA)	160
3.1.6	Extractable nuclear antigen antibodies (ENA)	161
3.1.7	Gastric parietal cell antibodies	161
3.1.8	Intrinsic factor antibodies	162
3.1.9	Anti-mitochondrial antibodies (AMA)	162
3.1.10	Rheumatoid factor (RF)	162
3.1.11	Smooth muscle antibodies	163
3.1.12	Tissue transglutaminase (tTG) antibodies	163
3.1.13	Thyroid antibodies	163
	Thyroid peroxidase antibodies (TPO)	163
<b>3.2</b>	<b>Immunochemistry</b>	<b>164</b>
3.2.1	Serum immunoglobulins (Ig), protein electrophoresis	164
3.2.2	Total and specific IgE	167
<b>3.3</b>	<b>Rheumatology</b>	<b>168</b>
3.3.1	HLA-B27	168



3.3.2	Inflammatory markers: CRP, ESR, PV	169
3.3.3	Uric acid (urate)	170

## Chapter 4: Microbiology 171

<b>4.1</b>	<b>Microscopy, culture and sensitivity (MCS) tests</b>	<b>172</b>
4.1.1	Interpreting antibiotic sensitivity results	172
4.1.2	Nail clippings/scrapings MCS	173
4.1.3	Sputum MCS	175
4.1.4	Stool MCS	176
4.1.5	Urine MCS	181
4.1.6	Vaginal discharge MCS	186
<b>4.2</b>	<b>Specific testing</b>	<b>189</b>
4.2.1	Cervical screening and human papillomavirus (HPV)	189
4.2.2	Glandular fever	190
4.2.3	<i>Helicobacter pylori</i> ( <i>H. pylori</i> )	193
4.2.4	Hepatitis B	195
4.2.5	Hepatitis C	198
4.2.6	HIV	200
4.2.7	Lyme disease	202
4.2.8	Pregnancy and viral serology	203
	Chickenpox (varicella zoster virus, VZV)	204
	Measles	206
	Parvovirus B19	209
	Rubella	212
<b>4.3</b>	<b>List of notifiable diseases</b>	<b>214</b>

## Part II: REQUESTING INVESTIGATIONS

### Chapter 5: Clinical scenarios 217

Abnormal LFT (liver screen)	218	Diabetes: type 1	221
Anaemia	218	Diabetes: type 2	221
Antiphospholipid syndrome	219	Erectile dysfunction	221
Cardiovascular disease: PAD,		Fibromyalgia	222
angina, MI, stroke	219	Fungal nail infection	222
Coeliac disease	219	Giant cell arteritis (GCA)	222
Connective tissue disease	220	Gilbert's syndrome	223
Dementia	220	Glandular fever	223

Gout	223	Isolated raised ALP	228
<i>H. pylori</i> testing	223	Menopause	228
Haematuria	224	Myeloma	229
Haemochromatosis	224	Osteomalacia	229
Haemolytic anaemia	224	Osteoporosis	229
Heart failure	224	Pancytopenia	230
Hyper- / hypoparathyroidism	225	Pernicious anaemia	230
Hyperlipidaemia	225	Polycystic ovarian syndrome (PCOS)	231
Hypertension	225	Polymyalgia rheumatica (PMR)	231
Hyperthyroidism	226	Primary immunodeficiency	231
Hypoadrenalism	226	Restless legs syndrome	232
Hypopituitarism (female)	226	Sickle cell disease	232
Hypopituitarism (male)	226	Spondyloarthritis	232
Hypothyroidism	227	Suspected cancer	233
Infertility (female)	227	Thalassaemia	234
Infertility (male)	227	Thrombophilia	234
Inflammatory bowel disease (IBD)	227	Vasculitis	234
Irritable bowel syndrome (IBS)	228		

## Chapter 6: Signs and symptoms

235

Abdominal pain	236	Heavy menstrual bleeding	244
Acute confusion (delirium)	236	Hepatomegaly	244
Allergy	236	Hirsutism	244
Alopecia	237	Incontinence (female)	244
Altered bowel habit	237	Indigestion	245
Amenorrhoea (primary)	237	Inflammatory arthritis	245
Amenorrhoea (secondary)	237	Jaundice	246
Angular cheilitis	238	Leg ulcers	246
Ankle swelling	238	Loss of appetite	246
Back pain	238	Low libido (female)	246
Chest pain	239	Low libido (male)	247
Clubbing	239	Lower urinary tract symptoms	
Constipation	239	(LUTS) – male	247
Cough	240	Lymphadenopathy	247
Diarrhoea (acute)	240	Mouth ulcers	247
Diarrhoea (chronic)	240	Nausea and vomiting	248
Dizziness and syncope	241	Night sweats	248
Dyspareunia	241	Obesity	248
Dysphagia	241	Paget's disease	249
Easy bruising	242	Painful muscles	249
Excess sweating	242	Painful tongue (glossitis)	249
Galactorrhoea	242	Palpitations	249
Gynaecomastia	243	Pelvic pain (female)	249
Haematospermia	243	Penile discharge	250
Haemoptysis	243	Peripheral neuropathy	250

---

Polydipsia	250	Tinnitus	253
Pruritus (generalised)	250	Tired all the time (TATT)	253
Raynaud's phenomenon	251	Tremor	253
Rectal bleeding	251	Unexplained weight gain	254
Shortness of breath	251	Unexplained weight loss	254
Single joint pain	252	Urinary tract infection (female)	254
Sore throat	252	Urinary tract infection (male)	255
Splenomegaly	252	Urticaria	255
Steatorrhoea	252	Vaginal discharge	255
Index			257



Chapter 2

# Haematology

ABNORMAL RESULTS

<b>2.1</b>	<b>Full blood count</b>	<b>116</b>
2.1.1	Haemoglobin	116
	Low haemoglobin (anaemia)	116
	Iron-deficiency anaemia (IDA)	121
	Vitamin B12 deficiency	123
	Folate deficiency	126
	Raised haematocrit (erythrocytosis)	127
2.1.2	White cell count	129
	Low neutrophils (neutropenia)	129
	Low lymphocytes (lymphopenia)	131
	High white cell count (leucocytosis)	132
	High neutrophils (neutrophilia)	133
	High lymphocytes (lymphocytosis)	135
	High basophils (basophilia)	136
	High eosinophils (eosinophilia)	137
	High monocytes (monocytosis)	138
2.1.3	Platelets	139
	Low platelets (thrombocytopenia)	139
	High platelets (thrombocytosis)	141
<b>2.2</b>	<b>Reticulocytes</b>	<b>143</b>

TESTS

<b>2.3</b>	<b>Immunoglobulins / serum protein electrophoresis / serum free light chains / urine Bence Jones proteins</b>	<b>144</b>
<b>2.4</b>	<b>Clotting tests</b>	<b>147</b>
<b>2.5</b>	<b>Blood film comments</b>	<b>149</b>
<b>2.6</b>	<b>Inflammatory markers: CRP/ESR/PV</b>	<b>150</b>
<b>2.7</b>	<b>Iron studies and ferritin</b>	<b>152</b>
2.7.1	Iron studies	152
2.7.2	Ferritin	154

Follow your local reference ranges, clinical pathways, management and referral guidance. This guidance is not a substitute for individual clinical judgement. Reference ranges will vary according to the assay used by laboratories. Those provided are examples and may vary in your locality.

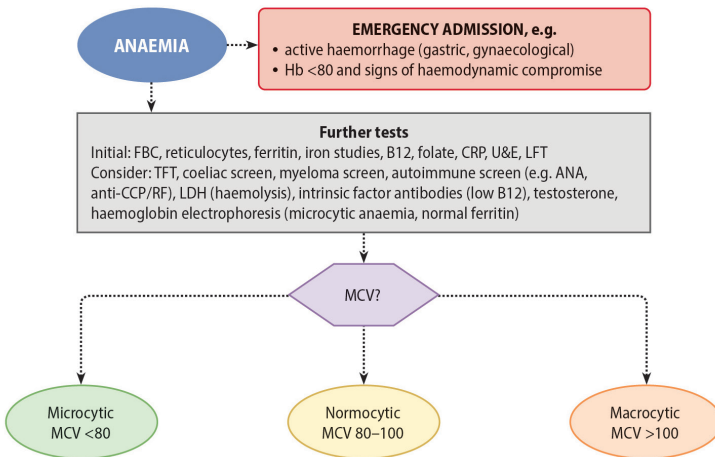
# 2.1 Full blood count

## 2.1.1 Haemoglobin

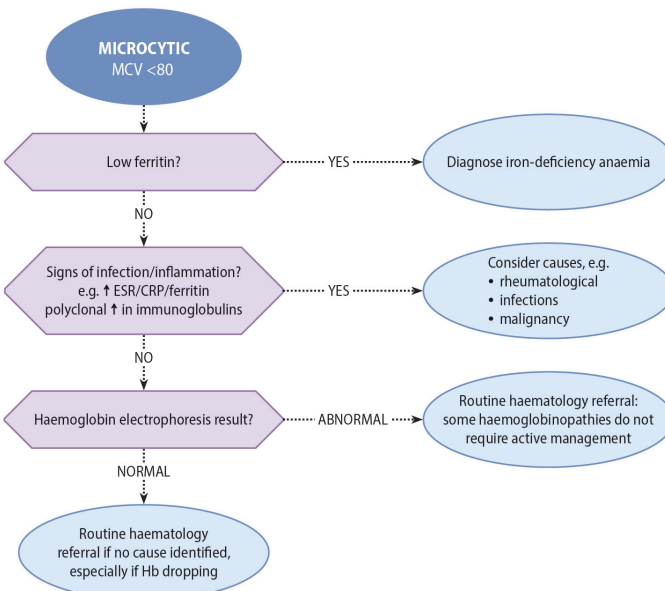
**Low haemoglobin (anaemia) ( $\delta$  Hb  $<130$  g/L;  $\text{♀}$  Hb  $<115$  g/L)**

Normal range:  $\delta$  130–180 g/L;  $\text{♀}$  115–165 g/L

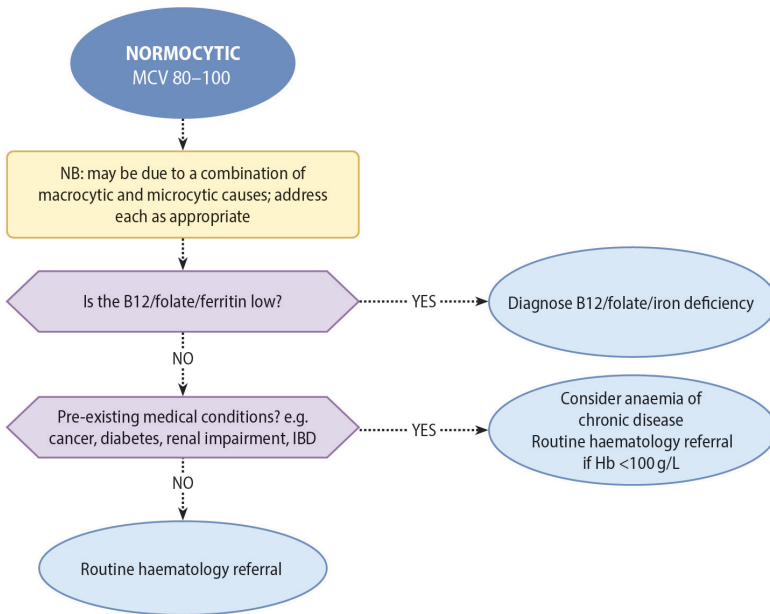
MCV: 80–100 fL



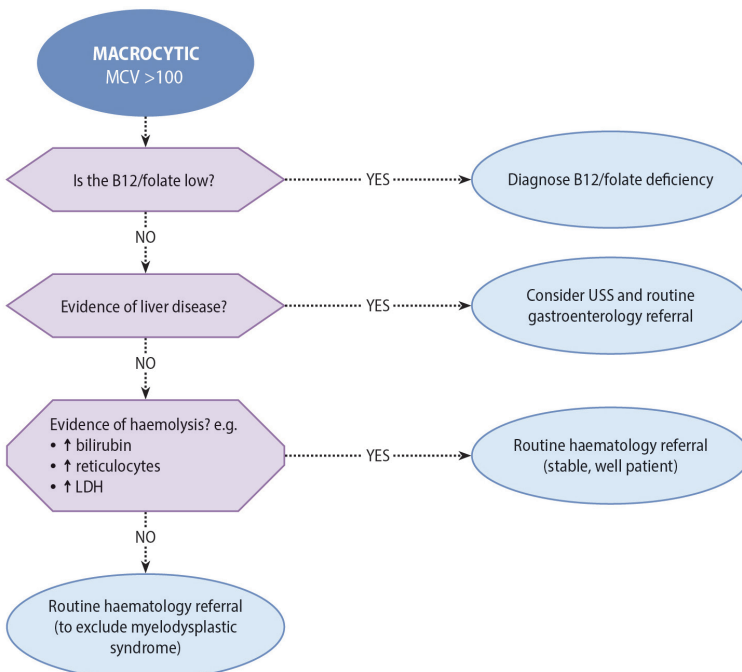
## Microcytic anaemia (MCV <80 fL)



## Normocytic anaemia (MCV 80–100 fL)



## Macrocytic anaemia (MCV >100 fL)



### Background

- Anaemia can be multifactorial: note a combination of causes may result in a mixed picture
- The MCV is a useful starting point to guide further investigation

### Causes

#### Microcytic anaemia (MCV <80 fL)

- Iron-deficiency anaemia (IDA)
- Inflammation or infection
- Haemoglobinopathies, e.g. thalassaemia, sickle cell disease

#### Normocytic anaemia (MCV 80–100 fL)

- Mixed haematinic deficiency, e.g. iron and B12 deficiency
- Anaemia of chronic disease, e.g. renal impairment, diabetes, ↓ testosterone
- Malignancy
- Acute blood loss

#### Macrocytic anaemia (MCV >100 fL)

- ↓ B12
- ↓ folate
- Alcohol excess
- Liver disease
- Hypothyroidism
- Medication, e.g. hydroxycarbamide, methotrexate
- Pregnancy
- Haemolysis
- Bone marrow disorder, e.g. myelodysplasia

### History and examination

- Bleeding history
- Chronic disease history, e.g. renal failure, liver disease, inflammatory bowel disease (IBD)
- Ethnicity
- Family history (FHx), e.g. of bleeding disorder



- Lifestyle review, e.g. diet, alcohol
- Medication, e.g. non-steroidal anti-inflammatory drugs (NSAIDs), steroids
- Significant past medical history e.g. gastritis, fibroids
- Symptoms and signs of anaemia, e.g. shortness of breath, fatigue, dizziness, pallor, jaundice, koilonychia, angular cheilosis, glossitis, alopecia
- Symptoms and signs of recurrent infections, ulcers, recent viral illness, autoimmune or connective tissue disorders
- Symptoms and signs of malignancy, e.g. bowel symptoms, post-menopausal bleeding, haemoptysis, lymphadenopathy and hepatosplenomegaly, 'B symptoms' (fever, drenching night sweats, weight loss >10% in previous 6 months), weight loss

### Investigations

- Initial:
  - full blood count (FBC) repeat
  - reticulocytes
  - ferritin, iron studies
  - B12, folate
  - CRP
  - U&E, liver function test (LFT)
- Consider:
  - thyroid function test (TFT)
  - coeliac screen
  - myeloma screen
  - lactate dehydrogenase (LDH) (haemolysis)
  - intrinsic factor antibodies (low B12, if not had previously and no known GI surgery that could cause malabsorption)
  - autoimmune screen, e.g. ANA, anti-CCP/RF (as per local guidance)
  - testosterone
  - haemoglobin electrophoresis (if microcytic anaemia, normal ferritin levels and not previously checked)
  - urine dip (for blood)
  - stool parasites (if relevant travel history and/or eosinophilia)
  - faecal immunochemical test (FIT): offer to all with IDA, or age ≥60 and non-IDA
  - liver ultrasound scan (USS) (liver disease)
  - pelvis USS: women age ≥55 with anaemia and visible haematuria (endometrial cancer)
  - routine oesophagogastrroduodenoscopy (OGD): age ≥55 with anaemia and upper abdominal pain (oesophageal or stomach cancer)

## Referral

### Emergency admission

- Acutely unwell, e.g. active haemorrhage, Hb <80 and haemodynamic compromise
- ↓ B12/folate with neurological symptoms (hypokalaemia can develop during initial replacement of severe B12 deficiency)
- Unexplained progressive symptomatic anaemia
- Sickle cell crisis, e.g. severe pain, acute chest syndrome, stroke, priapism

### Urgent suspected cancer

- Suspected malignancy (relevant specialty)
- Suspected haematological malignancy (haematology), e.g.
  - abnormal blood film, e.g. leucoerythroblastic picture (presence of immature white cells and nucleated red blood cells)
  - anaemia with accompanying cytopenia but normal B12, folate and ferritin
  - associated hepatosplenomegaly, lymphadenopathy

### Routine outpatient

- Persistent unexplained anaemia with Hb ≤100 g/L (haematology)
- Unresponsive to or unable to tolerate corrective therapy (relevant specialty)
- Anaemia of chronic disease (relevant specialty as needed)
- Renal anaemia (nephrology)
- Persistent unexplained MCV >105 (haematology)
- Interpreting haemoglobin electrophoresis results; not all haemoglobinopathies need active management, e.g. beta thalassaemia trait, sickle cell trait and alpha thalassaemia trait (haematology)
- Suspected haemolysis (haematology)

### Advice & Guidance

- Diagnostic uncertainty (relevant specialty)

## GP management tips

- Consider interval monitoring of patients who are elderly/frail with a mild, unexplained, asymptomatic anaemia (Hb >100 g/L) following exclusion of reversible causes
- Uncomplicated B12 or folate deficiency does not require referral
- IDA is generally not managed by haematology
- Haemoglobinopathy screening: document testing result clearly (no need for repeat testing)

## Iron-deficiency anaemia (IDA)

### Background

- Defined as ↓ red blood cell production due to ↓ body iron stores
- Blood findings: ↓ haemoglobin, ↓ MCV, serum ferritin level <30 µg/L, ↓ transferrin saturation
- Blood film: microcytic, hypochromic red cells, pencil cells and thrombocytosis
- Interpreting ferritin levels
  - ferritin is the most specific test for iron deficiency in the absence of inflammation
  - the lower limit of normal for most labs is between 15 and 30 µg/L
    - ferritin <15 µg/L is indicative of absent iron stores (specificity 0.99)
    - ferritin <30 µg/L is indicative of low body iron stores
  - ferritin is an acute phase protein, so apparently normal levels may occur with iron deficiency in the context of an inflammatory disease process
  - a cut-off of 45 µg/L has been suggested as providing the optimal trade-off between sensitivity and specificity for iron deficiency in practice (specificity of 0.92); figures below this may warrant consideration of GI investigation, especially in the context of a chronic inflammatory process with anaemia
  - a value >150 µg/L is unlikely to occur with absolute iron deficiency, even in the presence of inflammation

### Causes

- Blood loss, e.g. gastrointestinal, gynaecological or urological, blood donor
- Poor dietary iron intake, e.g. vegetarian
- Malabsorption, e.g. coeliac, gastrectomy
- Increased requirements, e.g. myeloproliferative neoplasms
- Pregnancy
- Medication, e.g. aspirin, NSAIDs, selective serotonin reuptake inhibitors (SSRIs), clopidogrel, corticosteroids, long-term PPI

### Investigations

- Initial tests
  - FBC, ferritin, iron studies, B12, folate, coeliac screen, ESR/CRP, reticulocytes
  - FIT
  - urine dip (for blood)
- Consider:
  - stool parasite (if relevant travel history and/or eosinophilia)

### Referral

IDA is generally not managed by haematology

### Emergency admission

- Acutely unwell, e.g. active haemorrhage, Hb <80 and haemodynamic compromise
- Unexplained progressive symptomatic anaemia

### Urgent suspected cancer

- Suspected malignancy (relevant specialty)
  - FIT result of  $\geq 10$   $\mu\text{g}$  Hb/g faeces (colorectal)
  - post-menopausal bleeding in women age  $\geq 55$  (gynaecology; endometrial cancer)
  - post-menopausal bleeding in women age  $< 55$  (consider gynaecology referral; endometrial cancer)

### Urgent outpatient (gastroenterology)

NB: check local referral protocols if meets urgent suspected cancer pathway criteria

- Men and post-menopausal women with newly diagnosed IDA unless they have overt non-GI bleeding
  - men with Hb  $< 120$  g/L and post-menopausal women with Hb  $< 100$  g/L should be investigated more urgently, as lower levels of Hb suggest more serious disease (consider urgent suspected cancer referral)
- All people age  $\geq 50$  with marked anaemia, or a significant FHx of colorectal carcinoma, even if coeliac disease is found
- Premenopausal women if they are age  $< 50$  and have colonic symptoms, a strong FHx (two affected 1st-degree relatives or just one 1st-degree relative affected before the age of 50) of GI cancer, persistent IDA despite treatment, or if they do not menstruate, e.g. hysterectomy

### Routine outpatient

- Unable to tolerate corrective therapy, for possible IV iron therapy (gastroenterology)
- Unresponsive to initial therapy, i.e. Hb increase  $< 20$  g/L after 4 weeks, or develops anaemia again without an obvious underlying cause (gastroenterology)
- Positive coeliac screen (gastroenterology)
- Menorrhagia unresponsive to medical management (gynaecology)

### GP management tips

- Do not wait for investigations to be carried out before prescribing iron supplements, e.g. one tablet daily of oral ferrous sulfate/fumarate/gluconate, unless colonoscopy imminent
- If not tolerated, reduce the dose to one tablet on alternate days, or consider alternative oral preparations, e.g. oral ferric maltol
- Monitor to ensure adequate response to treatment:
  - recheck FBC in the first 4 weeks of treatment: Hb should rise by about 20 g/L
  - if there is a response, check FBC at 2–4 months to ensure Hb has normalised
  - continue iron treatment for a further 3 months to replenish stores, then stop
  - monitor FBC periodically, e.g. every 6 months
  - if Hb drops below normal, prescribe iron supplements
- Further investigation is only necessary if Hb cannot be maintained this way or if there is any evidence of an active undiagnosed pathology, e.g.
  - ongoing weight loss
  - chronic unexplained diarrhoea

- persistently ↑ inflammatory markers
- persistence or recurrence of IDA
- Consider ongoing prophylactic iron (e.g. 200 mg ferrous sulfate daily), monitoring FBC every 6–12 months, in those at particular risk of IDA, e.g.
  - recurring anaemia in elderly and further tests are not indicated or appropriate
  - plant-based diets
  - malabsorption, e.g. coeliac disease, gastrectomy
  - menorrhagia
- Iron turns the stool black, so melaena may be difficult to report once iron treatment is started
- Advise food sources rich in iron:
  - red meats (beef, lamb and pork) and offal
  - fish and poultry
  - plant-based sources: pulses and legumes (e.g. beans, peas and lentils), dark green vegetables (e.g. spinach, kale and broccoli), nuts and seeds
  - some foods are fortified with iron, e.g. all UK-sold bread (except wholemeal) must be fortified; many breakfast cereals are also fortified
  - absorption is enhanced with animal protein foods and vitamin C, but reduced by bran-containing cereals and tannins in tea and coffee
- Iron deficiency without anaemia
  - before iron-deficiency anaemia develops, there is an initial phase where body iron stores are depleted, resulting in low ferritin levels with a normal Hb concentration
  - the prevalence of significant underlying GI pathology, especially malignancy, is low
  - thus, in the absence of other pointers, GI investigation generally is not warranted in premenopausal women; the cause is likely to be menstrual blood loss and/or recent pregnancy
  - the threshold for investigation of iron deficiency without anaemia should be low in men, postmenopausal women, and those with GI symptoms or a FHx of GI pathology

## Vitamin B12 deficiency (<180 ng/L: confirmed deficiency)

### Background

- Blood findings: macrocytic anaemia with megaloblastic changes (hyper-segmented neutrophils on blood film)
- There is no gold standard test for measuring vitamin B12 deficiency, but the likelihood of deficiency can be determined by measuring serum cobalamin (total B12)
  - a serum cobalamin of <200 ng/L is sensitive enough to diagnose 97% with vitamin B12 deficiency
- NICE recommends these thresholds to interpret test results (serum cobalamin):
  - <180 ng/L            confirmed deficiency
  - 180–350 ng/L      possible deficiency
  - >350 ng/L          unlikely deficiency

### Causes

- Poor absorption, e.g. pernicious anaemia, gastrectomy, IBD
- Medication, e.g. PPI, H<sub>2</sub> receptor antagonists, colchicine, metformin, oral contraceptive pill (OCP), recreational nitrous oxide use
- Dietary, e.g. malnutrition, vegan diet

### Investigations

- Initial tests
  - FBC, B12, folate, coeliac screen
  - intrinsic factor antibodies (if not had previously and no known GI surgery that could cause malabsorption)
- Consider:
  - LFT, TFT (non-megaloblastic causes of macrocytosis)
  - ferritin, iron studies (exclude concurrent deficiency)

### Referral

Uncomplicated B12 deficiency does not require referral to haematology

### Emergency admission

- ↓ B12 with neurological symptoms (treatment can cause hypokalaemia so requires regular monitoring)

### Urgent suspected cancer

- Known pernicious anaemia and a suspicion of gastric cancer (gastroenterology)
- Suspected blood malignancy (haematology)

### Routine outpatient

- Suspected malabsorption, IBD, positive coeliac screen (gastroenterology)
- Nutritional advice (dietitian)
- Cause of deficiency unclear after investigations, not responding to treatment, MCV >105 (haematology)

### Advice & Guidance

- Recreational nitrous oxide use requires different tests: serum methylmalonic acid (MMA) can be used as the initial test, or plasma homocysteine (secondary care tests)

### GP management tips

- Medication-induced or nitrous oxide-related B12 deficiency:
  - offer either intramuscular (IM) or oral B12 replacement while using medication
  - review if the medication can be stopped; encourage stopping nitrous oxide use
  - review B12 replacement if stopped and deficiency symptoms have resolved
- Suspected dietary cause:
  - review dietary B12 intake and consider oral B12 replacement. B12 sources:

- meat, egg and dairy products
  - B12-fortified plant foods: yeast extract, fortified plant-based drinks and alternatives to yogurt and most fortified breakfast cereals
- review OTC vitamin use
  - oral supplement should contain at least one of the following: cyanocobalamin, methylcobalamin or adenosylcobalamin
- review concurrent causes of possible B12 deficiency
- consider IM B12 injections instead of oral if:
  - concurrent condition which may affect quality of life, e.g. ataxia or anaemia
  - concerns about oral treatment concordance, e.g. frailty, cognitive impairment
- Cause unknown:
  - offer B12 replacement, considering oral versus IM replacement and review response
- If hydroxocobalamin injection is necessary, initially administer 1 mg IM three times a week for 2 weeks
- The maintenance dose depends on whether the deficiency is diet-related or not
  - if not thought to be diet-related:
    - give hydroxocobalamin 1 mg IM every 2–3 months for life
    - alternatively, consider daily large oral doses (500–1000 µg)
  - if thought to be diet-related
    - oral cyanocobalamin tablets 50–150 µg OD between meals
    - alternatively twice-yearly hydroxocobalamin 1 mg IM
    - in vegans, treatment may need to be lifelong, whereas in other people with dietary deficiency replacement, treatment can be stopped once the B12 levels have corrected and diet has improved
- Monitoring response; check FBC and reticulocytes:
  - within 7–10 days of starting treatment
    - a ↑ in Hb and ↑ in reticulocyte count above the normal range indicates treatment is working
  - after 8 weeks of treatment (FBC, reticulocytes)
    - blood counts and MCV should have normalised
    - measure ferritin/iron studies and folate to ensure other deficiencies not masked
- Measuring cobalamin levels is unhelpful as levels increase with treatment regardless of how effective it is, and retesting is not usually required; however, cobalamin can be:
  - measured 1–2 months after starting treatment if there is no response
  - rechecked if a lack of treatment compliance is suspected, anaemia recurs, or neurological symptoms do not improve or progress
- Neurological recovery may take time: improvement begins within 1 week and complete resolution usually occurs between 6 and 12 weeks

## Folate deficiency (<3 µg/L)

### Background

- Blood findings: macrocytic anaemia, megaloblastic changes (hyper-segmented neutrophils)
- There is no clear consensus on the level of serum folate that indicates deficiency. Conventionally, a serum folate <3 µg/L is used as a guideline, as the risk of megaloblastic anaemia greatly increases below this level

### Causes

- Malabsorption, e.g. coeliac disease, surgery, IBD
- Dietary, e.g. malnutrition, vegan diet, excess alcohol
- Medication, e.g. nitrofurantoin, trimethoprim, anticonvulsants, sulfasalazine, methotrexate
- Increased requirements
  - pregnancy
  - malignancy
  - blood disorders, e.g. haemolytic anaemia, sickle cell anaemia
  - inflammatory diseases, e.g. TB
  - exfoliative skin diseases
- Excessive urinary excretion, e.g. heart failure, liver disease, renal disease

### Investigations

- Initial tests
  - FBC, B12, folate, coeliac screen
- Consider:
  - LFT, TFT (non-megaloblastic causes of macrocytosis)
  - ferritin, iron studies (exclude concurrent deficiency)

### Referral

Uncomplicated folate deficiency does not require referral to haematology

### Emergency admission

- ↓ folate with neurological symptoms

### Urgent suspected cancer

- Suspected blood malignancy (haematology)

### Routine outpatient

- Suspected malabsorption, IBD, positive coeliac screen (gastroenterology)
- Nutritional advice (dietitian)
- Cause of deficiency unclear after investigations, not responding to treatment, MCV >105 (haematology)



### GP management tips

- Ensure B12 levels are normal or replaced **before** treating to avoid development of sub-acute combined degeneration of the cord
- Dietary sources: asparagus, broccoli, brown rice, brussels sprouts, chickpeas, peas
- Prescribe oral folic acid 5 mg daily for 4 months; may be required for longer (even for life) if the underlying cause of deficiency is persistent
- Monitoring response; check FBC and reticulocytes:
  - within 7–10 days of starting treatment
    - a  $\uparrow$  in Hb and  $\uparrow$  in reticulocyte count above the normal range indicates treatment is working
  - after 8 weeks of treatment (FBC, reticulocytes)
    - blood counts and MCV should have normalised
  - on completion of folic acid treatment to confirm response

### Raised haematocrit (erythrocytosis)

Normal ranges: ♂ 0.40–0.52 L/L (40–52%); ♀ 0.37–0.48 L/L (37–48%)

### Background

- Raised haematocrit can be due to  $\uparrow$  haemoglobin (true erythrocytosis) or  $\downarrow$  plasma volume (apparent erythrocytosis)
- The term 'polycythaemia' should be reserved for overproduction of red cells due to a bone marrow problem, e.g. polycythaemia rubra vera

### Causes

- Primary erythrocytosis
  - polycythaemia rubra vera (97% have *JAK2* gene mutation)
- Secondary erythrocytosis
  - congenital (rare)
  - acquired
    - hypoxia from respiratory or cardiac disease
    - medication, e.g. testosterone, anabolic steroids
    - lifestyle, e.g. obesity, alcohol excess, smoking, hypertension
  - abnormal erythropoietin production
    - renal issues
    - tumour, e.g. fibroids, hepatocellular and renal cell carcinoma
- Apparent erythrocytosis
  - dehydration
  - medication, e.g. diuretics

### History and examination

- Aquagenic pruritus (itching after getting body wet)

- Symptoms of hyperviscosity, e.g. headaches, visual disturbances, neurological symptoms, weakness
- Examination: oxygen saturations, blood pressure, BMI

### Investigations

- Initial:
  - full blood count (FBC) (uncuffed sample, minimum interval 1 week, non-fasted)
  - blood film
  - U&E, LFT, bone profile
  - HbA1c
  - ferritin/iron studies (iron deficiency can mask the degree of erythrocytosis)
  - urine dip (exclude renal issues, e.g. proteinuria, haematuria)
- Consider:
  - chest X-ray (CXR), spirometry (suspected respiratory cause)
  - USS abdomen

### Referral

#### Emergency admission

- ↑ haematocrit ( $\delta >0.52$ ,  $\text{♀} >0.48$ ) and symptoms of hyperviscosity

#### Urgent outpatient

- New extreme ↑ haematocrit ( $\delta >0.60$ ,  $\text{♀} >0.56$ ) in the absence of congenital cyanotic heart disease (haematology)
- ↑ haematocrit ( $\delta >0.52$ ,  $\text{♀} >0.48$ ) in association with recent (last 3 months) arterial or venous thrombosis (including DVT/PE, CVA/TIA, MI/unstable angina, PVD) (haematology)

#### Routine outpatient

- Persistent unexplained ↑ haematocrit ( $\delta >0.52$ ,  $\text{♀} >0.48$ ) (two tests >6 weeks apart) (haematology)
- ↑ haematocrit, but ↓ MCV or ferritin: could be iron-deficient polycythaemia vera; do not give iron therapy in this situation as it will worsen the erythrocytosis (haematology)
- Suspected hypoxic respiratory disease (respiratory)
- Suspected heart failure (cardiology)

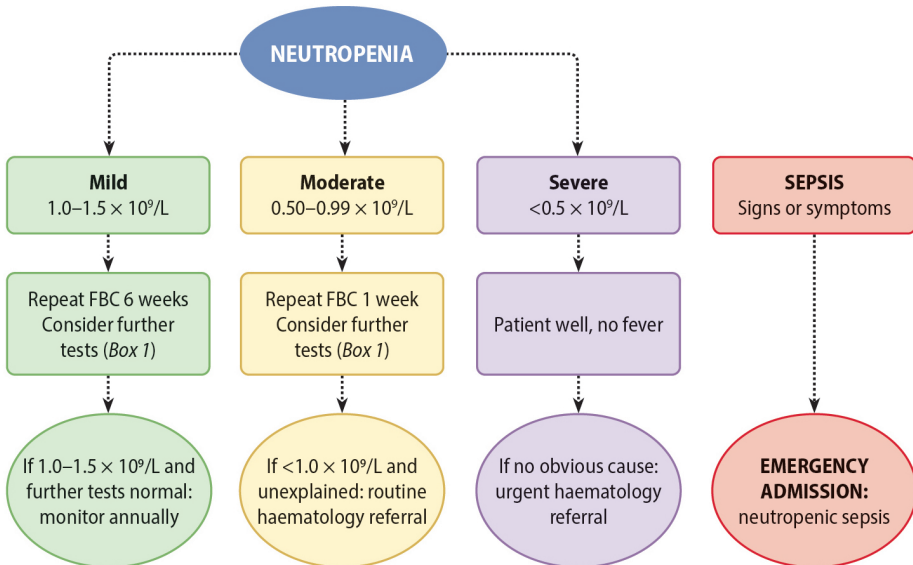
### GP management tips

- Cardiovascular risk factors (including hyperlipidaemia, smoking, hypertension and diabetes) should be managed in all with erythrocytosis of any cause

## 2.1.2 White cell count

### Low neutrophils (neutropenia) (neutrophils $<1.5 \times 10^9/L$ )

Normal range:  $1.5\text{--}8.0 \times 10^9/L$



#### Box 1 Further tests

Initial: Blood film, LFT, TFT, B12, folate

Consider: Autoimmune screen (e.g. ANA, anti-CCP/RF), myeloma screen, HIV, hepatitis B & C

### Background

- Neutropenia secondary to chemotherapy should be referred for acute oncology review: neutropenic sepsis is a medical emergency
- There is ↑ risk of more serious infection when  $<1.0 \times 10^9/L$ , and especially when  $<0.5 \times 10^9/L$

### Causes

- Medication, e.g. carbimazole, clozapine, clotrimazole, chemotherapy, phenytoin
- Viral infections, e.g. Epstein–Barr virus (EBV), hepatitis B and C, HIV (may take weeks to resolve)
- Sepsis
- Autoimmune disease, e.g. rheumatoid arthritis (RA), systemic lupus erythematosus (SLE)
- ↓ B12 or ↓ folate

- Ethnic variations, e.g. people of African or Middle Eastern descent frequently have a constitutional neutropenia, usually  $>1.0 \times 10^9/L$ , that is of no clinical consequence. This is a diagnosis of exclusion after ruling out other causes and seeing a persistent ↓ count without increased risk of infection
- Hypersplenism
- Thyroid dysfunction
- Nutritional deficiencies, e.g. anorexia nervosa
- Bone marrow issues, e.g. myelodysplasia, aplastic anaemia, acute leukaemia, myeloma

### History and examination

- Having chemotherapy or causative medications?
- Baseline observations, including temperature (sepsis signs)
  - NB: temperature may be low or affected by concurrent medication, e.g. steroids

### Investigations

- Initial:
  - blood film
  - B12, folate
  - LFT, TFT
- Consider:
  - autoimmune screen, e.g. ANA, anti-CCP/RF (as per local guidance)
  - myeloma screen
  - HIV, hepatitis B and C

### Referral

#### Emergency admission

- Neutrophil  $<0.5 \times 10^9/L$  and sepsis
- Unwell patient with **any** severity of neutropenia

#### Urgent suspected cancer

- Suspected blood malignancy, e.g. associated cytopenia, hepatosplenomegaly, lymphadenopathy (haematology)

#### Urgent outpatient

- Neutrophil  $<0.5 \times 10^9/L$ , but systemically well (significant risk of infection) (haematology)

#### Routine outpatient

- Persistently unexplained neutropenia  $<1.0 \times 10^9/L$  (two tests  $>6$  weeks apart) (haematology)

**Low lymphocytes (lymphopenia) (lymphocyte count  $<1.5 \times 10^9/L$ )**

Normal range:  $1.5\text{--}5.0 \times 10^9/L$

**Background**

- Grading of severity:
  - mild:  $1.0\text{--}1.5 \times 10^9/L$
  - moderate:  $0.50\text{--}0.99 \times 10^9/L$
  - severe:  $<0.5 \times 10^9/L$
- Lymphopenia is a common, non-specific and often transient finding which increases in frequency with older age and comorbidities
- It is more often of no pathological significance: however, HIV infection is commonly associated with lymphopenia
- Rarely associated with haematological conditions, but can be observed in lymphoproliferative disorders

**Causes**

- Increasing age
- Infection, e.g. acute or chronic (HIV, hepatitis B and C, TB)
- Medication, e.g. steroids, immunosuppressants, chemotherapy, methotrexate, azathioprine
- Systemic disorders, e.g. autoimmune disease, IBD, sarcoidosis
- Malignancy, e.g. lymphoproliferative disorders, solid organ malignancies
- Stress, e.g. exercise, malnutrition, alcohol, surgery, radiotherapy
- Chronic disease, e.g. cardiac failure, renal failure
- Primary immunodeficiency

**History and examination**

- Examine for lymphadenopathy and hepatosplenomegaly
- Ask about B symptoms
- Symptoms and signs of recurrent infections, ulcers, recent viral illness, autoimmune or connective tissue disorders

**Investigations**

- Initial:
  - blood film
  - B12, folate
  - U&E, LFT
- Consider:
  - myeloma screen
  - autoimmune screen, e.g. ANA, anti-CCP/RF (as per local guidance)
  - HIV, hepatitis B and C

### Referral

#### Urgent suspected cancer

- Suspected malignancy (relevant specialty)

#### Urgent outpatient

- Severe lymphopenia ( $<0.5 \times 10^9/L$ ), as may predispose to opportunistic infections, e.g. *Pneumocystis pneumonia*, oesophageal candidiasis, herpes zoster (haematology)

#### Routine outpatient

- Diagnostic uncertainty with persistent moderate lymphopenia  $>6$  months (haematology)
- Lymphopenia with recurrent infections and HIV negative, consider immunodeficiency issue and checking immunoglobulins (immunology)
- Suspected autoimmune disease (rheumatology)

### GP management tips

- Mild lymphopenia ( $1.0\text{--}1.5 \times 10^9/L$ ), well patient: no further action
- Well patient, age  $>70$  and lymphocytes  $>0.5 \times 10^9/L$ : no further action
- Moderate lymphopenia ( $0.50\text{--}0.99 \times 10^9/L$ ), well patient:
  - consider further investigations
  - if no cause identified, repeat FBC at 6 months
    - if no change in count and patient remains well, no need to investigate further
    - consider routine haematology referral if there are any changes/concerns

### High white cell count (leucocytosis) (white cell count $>11 \times 10^9/L$ )

Normal range:  $3.6\text{--}11.0 \times 10^9/L$

### Background

- The differential is wide-ranging, from a normal reaction to infection to haematological malignancies

### Causes

- Infection (especially bacterial)
- Inflammation
- Stress events, e.g. trauma, MI
- Malignancy, e.g. haematological or solid tumour
- Autoimmune disease
- Smoking (minor non-specific leucocytosis or neutrophilia is often seen)

### History and examination

- Examine for lymphadenopathy and hepatosplenomegaly
- Ask about B symptoms
- Symptoms and signs of infection, autoimmune or connective tissue disorders

### Investigations

- Initial:
  - assess white cell count (WCC) differential (if lymphocytosis and neutrophilia present, reactive cause is more likely)
  - blood film
  - ESR/CRP
- Consider:
  - autoimmune screen, e.g. ANA, anti-CCP/RF (as per local guidance)
  - HIV, hepatitis B and C

### Referral

#### Emergency admission

- New suspected acute leukaemia (likely to be contacted by lab about the result)
- New suspected chronic myeloid leukaemia (CML) with WCC  $>100 \times 10^9/L$  or hyperviscosity symptoms (likely to be contacted by lab about the result)
- Acutely unwell patient, e.g. with severe infection / sepsis

#### Urgent suspected cancer

- New CML without emergency admission criteria (haematology)
- Age  $\geq 60$  and  $\uparrow$  WCC with unexplained non-visible haematuria (bladder cancer, urology)
- Suspected malignancy (relevant specialty)

#### Urgent outpatient

- Unexplained leucocytosis with WCC  $>50 \times 10^9/L$  (haematology)

#### Routine outpatient

- Unexplained persistent raised levels (two tests  $>6$  weeks apart) (haematology)
  - WCC:  $>20 \times 10^9/L$
  - neutrophilia:  $>15 \times 10^9/L$
  - lymphocytes:  $>5 \times 10^9/L$
  - eosinophilia:  $>1.5 \times 10^9/L$
  - monocytosis:  $>1 \times 10^9/L$
  - basophilia:  $>0.2 \times 10^9/L$

### High neutrophils (neutrophilia) (neutrophils $>8 \times 10^9/L$ )

Normal range:  $1.5\text{--}8.0 \times 10^9/L$

### Background

- Usually a reactive phenomenon
- It is unusual for a reactive neutrophilia to be above  $100 \times 10^9/L$

### Causes

- Infection (especially bacterial)
- Inflammation
- Stress events, e.g. trauma, myocardial infarction (MI)
- Medication, e.g. steroids, lithium
- Pregnancy
- Smoking (minor non-specific leucocytosis or neutrophilia is often seen)
- Hyposplenism
- Autoimmune disease
- Malignancy, e.g. haematological or solid tumour

### History and examination

- Examine for lymphadenopathy and hepatosplenomegaly
- Ask about B symptoms
- Symptoms and signs of infection, autoimmune or connective tissue disorders
- Travel history

### Investigations

- Initial:
  - blood film
  - CRP/ESR
  - U&E, LFT
- Consider:
  - autoimmune screen, e.g. ANA, anti-CCP/RF (as per local guidance)
  - prostate-specific antigen (PSA)

### Referral

#### Emergency admission

- Acutely unwell patient, e.g. with severe infection/sepsis
- New suspected CML with WCC  $>100 \times 10^9/L$  or hyperviscosity symptoms (likely to be contacted by lab about the result)

#### Urgent suspected cancer

- Suspected haematological malignancy, e.g. abnormal blood film, splenomegaly (haematology)
- Suspected malignancy (relevant specialty)

#### Urgent outpatient

- Unexplained inflammatory process (relevant specialty)



### Routine outpatient

- Unexplained persistent neutrophilia  $>15 \times 10^9/\text{L}$  (two tests  $>6$  weeks apart) (haematology)

### High lymphocytes (lymphocytosis) (lymphocytes $>5 \times 10^9/\text{L}$ )

Normal range:  $1.5\text{--}5.0 \times 10^9/\text{L}$

#### Background

- Usually a reactive phenomenon, but it is important to check a blood film

#### Causes

- Infection, especially viral, e.g. EBV; bacterial, e.g. tuberculosis (TB) (common)
- Chronic lymphocytic leukaemia (CLL): characterised by chronic lymphocytosis, often asymptomatic in its early stages
- Smoking
- Post-splenectomy
- Autoimmune, e.g. RA

#### History and examination

- Examine for lymphadenopathy and hepatosplenomegaly
- Ask about B symptoms
- Symptoms and signs of infection, autoimmune or connective tissue disorders
- Travel history

#### Investigations

- Initial:
  - blood film
  - FBC repeat 6 weeks if suspected viral cause (likely to be transient)
- Consider:
  - glandular fever screen
  - autoimmune screen, e.g. ANA, anti-CCP/RF (as per local guidance)

#### Referral

### Emergency admission

- Acutely unwell patient, e.g. with severe infection / sepsis

### Urgent suspected cancer

- Suspected haematological malignancy, e.g. abnormal blood film, splenomegaly (haematology)
- Progressive lymphadenopathy (relevant specialty depending upon location)

### Urgent outpatient

- Lymphocytosis  $>30 \times 10^9/L$  (haematology)

### Routine outpatient

- Persistent unexplained lymphocytes  $>5 \times 10^9/L$  (two tests  $>6$  weeks apart), otherwise well (haematology)

## High basophils (basophilia) ( $>0.2 \times 10^9/L$ )

Normal range:  $0.0-0.2 \times 10^9/L$

### Background

- Reactive causes are rare: if persistent, particularly  $>0.4 \times 10^9/L$ , this strongly suggests a myeloproliferative neoplasm

### Causes

- Myeloproliferative neoplasms, e.g. CML, myelofibrosis
- Autoimmune, e.g. IBD, hypothyroidism
- Acute illness
- Allergy
- Hyposplenism

### History and examination

- Examine for lymphadenopathy and hepatosplenomegaly
- Ask about B symptoms
- Symptoms and signs of infection, autoimmune or connective tissue disorders

### Investigations

- Initial:
  - blood film
  - ESR/CRP
  - TFT

### Referral

### Urgent suspected cancer

- Suspected haematological malignancy, e.g. abnormal blood film, splenomegaly (haematology)

### Routine outpatient

- Unexplained persistent basophilia  $>0.2 \times 10^9/L$  (two tests  $>6$  weeks apart) (haematology)

## High eosinophils (eosinophilia) ( $>0.5 \times 10^9/L$ )

Normal range:  $0.04\text{--}0.50 \times 10^9/L$

### Background

- Eosinophils play a part in allergic, parasitic and malignant disease processes, as well as tissue repair and remodelling
- Hypereosinophilia:
  - defined as eosinophils  $>1.5 \times 10^9/L$  persisting for  $>6$  months with no obvious cause
  - associated with signs of organ dysfunction:
    - cardiovascular: chest pain, heart failure, venous thromboembolism (VTE)
    - respiratory: dyspnoea, cough and wheeze
    - neurological: cerebrovascular accident (CVA), peripheral neuropathy
    - gastrointestinal: dysphagia, treatment-refractory gastro-oesophageal reflux disease (GORD)

### Causes

- Atopy, allergy, e.g. asthma, eczema, rhinitis
- Infections, e.g. parasites, fungal, HIV
- Medication, e.g. angiotensin-converting enzyme inhibitors (ACEi), penicillin, anti-epileptics, proton pump inhibitors (PPIs)
- Gastrointestinal, e.g. chronic pancreatitis, IBD, coeliac
- Respiratory, e.g. asthma, sarcoidosis
- Malignancy, e.g. solid tumours, Hodgkin lymphoma, T-cell non-Hodgkin lymphoma, CML
- Hyposplenism
- Autoimmune, e.g. SLE, RA
- Dermatological, e.g. pemphigoid
- Adrenal insufficiency

### History and examination

- Examine for lymphadenopathy and hepatosplenomegaly
- Ask about B symptoms
- Symptoms and signs of infection, autoimmune or connective tissue disorders
- Travel history

### Investigations

- Initial:
  - FBC, blood film
  - ESR/CRP
  - vitamin B12 ( $\uparrow$  may point to a myeloid disorder)
  - U&E, LFT, bone profile
  - coeliac screen

- Consider:
  - for those with systemic symptoms or persistent eosinophilia  $>1.5 \times 10^9/L$ , test for causes and evaluate organ damage:
    - autoimmune screen, e.g. ANA, anti-CCP/RF (as per local guidance)
    - parasite investigations, e.g. stool ova cysts, appropriate serology tests
    - CXR: if respiratory symptoms
    - amylase: pancreatic issues
    - hepatitis B and C, HIV

### Referral

#### Emergency admission

- Acutely unwell patient, e.g. with severe infection, or end organ damage

#### Urgent suspected cancer

- Suspected haematological malignancy, e.g. abnormal blood film, splenomegaly (haematology)
- Suspected malignancy (relevant specialty)

#### Urgent outpatient

- Eosinophils  $>5 \times 10^9/L$  without obvious secondary cause (haematology)
- Eosinophils  $>1.5 \times 10^9/L$  with suspected end organ damage (haematology)

#### Routine outpatient

- Unexplained persistent eosinophilia  $>1.5 \times 10^9/L$  (two tests  $>6$  weeks apart), otherwise well (haematology)
- Diagnostic uncertainty (relevant specialty)
- Significant travel history and unsure about appropriate testing (microbiology/infectious diseases)

### GP management tips

- For well patients with eosinophilia  $0.5\text{--}1.5 \times 10^9/L$ , further testing may not be indicated
- Unprovoked DVT/PE may be a manifestation of end organ damage

### High monocytes (monocytosis)

Normal range:  $0.2\text{--}1.0 \times 10^9/L$

### Background

- This is frequently transient
- Persistent count  $>1.0 \times 10^9/L$  for  $>12$  months may represent a myeloproliferative disorder (chronic myelomonocytic leukaemia – CMML)

### Causes

- Smoking (common cause of mild monocytosis)
- Infections, e.g. TB, malaria
- Autoimmune and inflammatory diseases, e.g. sarcoidosis, RA
- Stress response, e.g. post MI
- Hyposplenism
- CMML (chronic, incurable disorder of varying severity)
- Malignancy

### History and examination

- Examine for lymphadenopathy and hepatosplenomegaly
- Ask about B symptoms
- Symptoms and signs of infection, autoimmune or connective tissue disorders

### Investigations

- Initial:
  - blood film
  - ESR/CRP
  - U&E, LFT, bone profile
- Consider:
  - autoimmune screen, e.g. ANA, anti-CCP/RF (as per local guidance)

### Referral

#### Urgent suspected cancer

- Suspected haematological malignancy, e.g. abnormal blood film, splenomegaly (haematology)

#### Urgent outpatient

- Persistent monocytosis  $>5 \times 10^9/L$  (two tests  $>6$  weeks apart) (haematology)
- Monocytosis ( $1.0\text{--}5.0 \times 10^9/L$ ) with other cytopenia (haematology)

#### Routine outpatient

- Persistent monocytosis ( $1.0\text{--}5.0 \times 10^9/L$ ) (two tests  $>6$  weeks apart), otherwise well (haematology)

## 2.1.3 Platelets

### Low platelets (thrombocytopenia) (platelets $<150 \times 10^9/L$ )

Normal range:  $150\text{--}450 \times 10^9/L$



## Chapter 5

# Clinical scenarios

Abnormal LFT (liver screen)	218	Hypoadrenalism	226
Anaemia	218	Hypopituitarism (female)	226
Antiphospholipid syndrome	219	Hypopituitarism (male)	226
Cardiovascular disease: PAD, angina, MI, stroke	219	Hypothyroidism	227
Coeliac disease	219	Infertility (female)	227
Connective tissue disease	220	Infertility (male)	227
Dementia	220	Inflammatory bowel disease (IBD)	227
Diabetes: type 1	221	Irritable bowel syndrome (IBS)	228
Diabetes: type 2	221	Isolated raised ALP	228
Erectile dysfunction	221	Menopause	228
Fibromyalgia	222	Myeloma	229
Fungal nail infection	222	Osteomalacia	229
Giant cell arteritis (GCA)	222	Osteoporosis	229
Gilbert's syndrome	223	Pancytopenia	230
Glandular fever	223	Pernicious anaemia	230
Gout	223	Polycystic ovarian syndrome (PCOS)	231
<i>H. pylori</i> testing	223	Polymyalgia rheumatica (PMR)	231
Haematuria	224	Primary immunodeficiency	231
Haemochromatosis	224	Restless legs syndrome	232
Haemolytic anaemia	224	Sickle cell disease	232
Heart failure	224	Spondyloarthritis	232
Hyper- / hypoparathyroidism	225	Suspected cancer	233
Hyperlipidaemia	225	Thalassaemia	234
Hypertension	225	Thrombophilia	234
Hyperthyroidism	226	Vasculitis	234

## Abnormal LFT (liver screen)

### Initial

- Hepatitis B and C
- Liver autoantibodies (anti-mitochondrial antibody, anti-smooth muscle antibody, antinuclear antibody)
- Immunoglobulins
- Ferritin and transferrin saturation (iron studies)
- USS liver

### Consider

- FBC
- Coagulation
- U&E
- TFT
- HbA1c, lipids
- Coeliac screen
- Acute hepatitis: hep A, hep E, CMV, EBV
- HIV
- CK
- Serum caeruloplasmin (checking for Wilson's disease if age <40)
- Alpha-1-antitrypsin deficiency (if there is a positive FHx or associated respiratory symptoms)
- Fibrosis risk assessment if non-alcoholic fatty liver disease (NAFLD) confirmed on USS (check local protocols)

## Anaemia

### Initial

- FBC
- Reticulocytes
- Ferritin, iron studies
- B12, folate
- CRP
- U&E, LFT

### Consider

- TFT
- Coeliac screen
- Myeloma screen
- LDH (haemolysis)
- Intrinsic factor antibodies (low B12, if not had previously and no known GI surgery that could cause malabsorption)



- Autoimmune screen, e.g. ANA, anti-CCP / RF (as per local guidance)
- Testosterone
- Haemoglobin electrophoresis (if microcytic anaemia, normal ferritin levels and not previously checked)
- Urine dipstick (haematuria)
- Stool parasites (if relevant travel history and/or eosinophilia)
- FIT: offer to all with IDA, or age  $\geq 60$  and non-IDA (colorectal cancer)
- Liver USS (liver disease)
- Pelvis USS: women age  $\geq 55$  with anaemia and visible haematuria (endometrial cancer)
- Routine OGD: age  $\geq 55$  with anaemia and upper abdominal pain (oesophageal or stomach cancer)

See also Pernicious anaemia

## Antiphospholipid syndrome

Antiphospholipid syndrome is diagnosed in a patient with venous and/or arterial thrombosis and/or defined pregnancy morbidity who has persistent antiphospholipid antibodies.

- **Not** a primary care diagnosis: secondary care will likely initiate specialist review when seeing patients with thrombotic complications
- Seek specialist review if suspected, e.g.
  - VTE in the absence of major provoking factors
  - arterial thrombosis in patients aged  $<50$  without clear risk factors
  - history of SLE or other autoimmune disease developing thrombosis or pregnancy complications
  - recurrent miscarriage ( $>3$ )

## Cardiovascular disease: PAD, angina, MI, stroke

### Initial

- FBC
- U&E, LFT
- HbA1c, lipids

## Coeliac disease

### Initial

- Coeliac serology:
  - 1st-line: total IgA and IgA tissue transglutaminase (tTG)
  - 2nd-line: IgA endomysial antibodies (EMA) if IgA tTG testing is unavailable or IgA tTG is weakly positive
  - if IgA deficient (total IgA  $<0.07$  g/L): IgG EMA, IgG deamidated gliadin peptide (DGP) or IgG tTG can be checked

## Chapter 6

# Signs and symptoms

Abdominal pain	236	Low libido (female)	246
Acute confusion (delirium)	236	Low libido (male)	247
Allergy	236	Lower urinary tract symptoms	
Alopecia	237	(LUTS) – male	247
Altered bowel habit	237	Lymphadenopathy	247
Amenorrhoea (primary)	237	Mouth ulcers	247
Amenorrhoea (secondary)	237	Nausea and vomiting	248
Angular cheilitis	238	Night sweats	248
Ankle swelling	238	Obesity	248
Back pain	238	Paget's disease	249
Chest pain	239	Painful muscles	249
Clubbing	239	Painful tongue (glossitis)	249
Constipation	239	Palpitations	249
Cough	240	Pelvic pain (female)	249
Diarrhoea (acute)	240	Penile discharge	250
Diarrhoea (chronic)	240	Peripheral neuropathy	250
Dizziness and syncope	241	Polydipsia	250
Dyspareunia	241	Pruritus (generalised)	250
Dysphagia	241	Raynaud's phenomenon	251
Easy bruising	242	Rectal bleeding	251
Excess sweating	242	Shortness of breath	251
Galactorrhoea	242	Single joint pain	252
Gynaecomastia	243	Sore throat	252
Haematospermia	243	Splenomegaly	252
Haemoptysis	243	Steatorrhoea	252
Heavy menstrual bleeding	244	Tinnitus	253
Hepatomegaly	244	Tired all the time (TATT)	253
Hirsutism	244	Tremor	253
Incontinence (female)	244	Unexplained weight gain	254
Indigestion	245	Unexplained weight loss	254
Inflammatory arthritis	245	Urinary tract infection (female)	254
Jaundice	246	Urinary tract infection (male)	255
Leg ulcers	246	Urticaria	255
Loss of appetite	246	Vaginal discharge	255

Follow your local reference ranges, clinical pathways, management and referral guidance. This guidance is not a substitute for individual clinical judgement. Reference ranges will vary according to the assay used by laboratories. Those provided are examples and may vary in your locality.

## Abdominal pain

### Initial

- FBC
- CRP
- U&E, LFT, bone profile
- HbA1c/glucose

### Consider

- CA125
- PSA
- Urine pregnancy test
- Urine dipstick ± MCS
- STI screen
- Stool MCS
- FIT
- Faecal calprotectin
- *H. pylori* testing

## Acute confusion (delirium)

### Consider

- FBC
- ESR, CRP
- Folate, B12
- U&E, LFT, bone profile
- TFT
- HbA1c/glucose
- Urine dipstick ± MCS

## Allergy

This is primarily a clinical diagnosis: tests are used to help confirm or refute a diagnosis. Follow appropriate local testing and referral procedures. Note, there are no tests for food intolerance.

### Consider

- Specific IgE testing: to support clinical diagnosis in suspected IgE-mediated allergies
- Check total IgE when testing specific IgE

## Alopecia

### Consider

- FBC
- Ferritin
- TFT
- Skin scrapings and hair samples for fungal MCS

## Altered bowel habit

### Initial

- FBC
- U&E, LFT, bone profile
- ESR/CRP
- Coeliac screen

### Consider

- TFT
- CA125
- Faecal calprotectin
- Stool MCS, including *C. difficile* toxin
- FIT

## Amenorrhoea (primary)

### Initial (likely to be investigated by secondary care)

- Urine pregnancy test
- Prolactin
- TFT
- FSH, LH
- Oestradiol
- Total testosterone
- Coeliac screen
- USS pelvis

## Amenorrhoea (secondary)

### Initial

- Urine pregnancy test
- Prolactin
- TFT