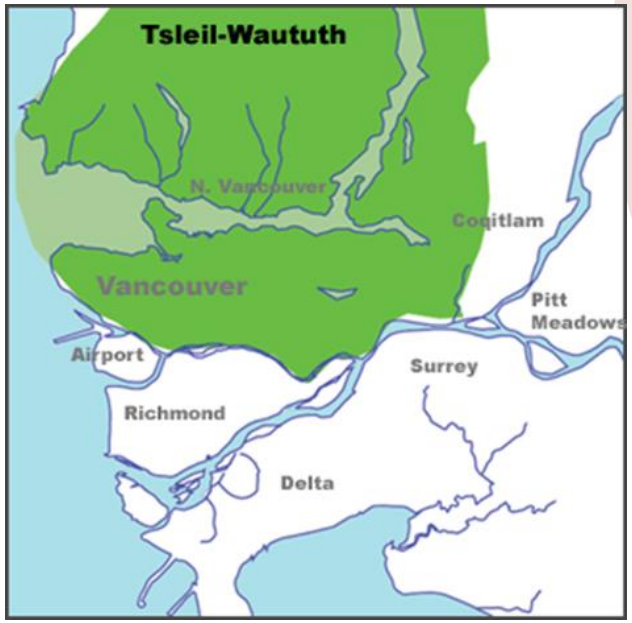
We would like to acknowledge that we are gathered today on the traditional territories of the Musqueam, Squamish and Tsleil-Waututh peoples.

Source: www.johomaps.net/na/canada/bc/vancouver/firstnations/firstnations.html



Managing commonly abnormal blood tests in primary care

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Speaker Fees: AstraZeneca, Bayer, Boehringer Ingelheim, Dexcom, Daiichi Sankyo, Grunenthal, Lilly, Menarini, Idorsia, Thornton & Ross, Boston Scientific

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Congress Attendance: Menarini, Daiichi Sankyo, Lilly, Bayer

Management of Acne in Primary Care

Medscape UK X Guidelines
Primary Care Hacks

Authors: Dr Catherine Fernando, Salaried GP, Haddington, East Lothian and GPwSI in Dermatology; Dr Kevin Fernando, GP Partner, North Berwick Health Centre; Content Advisor, Medscape Global and UK. Email: kfernando@webmd.net

Key Management Principles

1. **Counsel all patients on lifestyle factors that impact acne**
2. **Topical retinoids are a first-line treatment choice in all stages of acne, but must be introduced gradually**
3. **Skin of colour is more prone to scarring and hyperpigmentation so requires early, effective treatment**
4. **Be aware of certain drugs that can worsen acne**
5. **Practise antimicrobial stewardship**
6. **Conduct effective 12-week reviews**
7. **Early and effective referral is essential**
8. **Long-term complications should be considered**

See the table overleaf for a comprehensive overview of acne treatment options that can be prescribed in primary care

1. Lifestyle Factors[1–5]

Advise patients to:

- use a soap-free/'synthetic detergent' facial wash once or twice daily
- when using a moisturiser, choose a water-based, oil-free option
- avoid scrubs, astringents, and fragranced products that may irritate the skin
- avoid comedogenic/oil-based make-up and sunscreens
- avoid letting hair-styling products (oils, creams, mousses, gels) touch their face
- try to resist picking or squeezing spots, as this increases risk of scarring
- follow a healthy diet, as per the Eatwell guide.

Education is empowering. Signpost to the BAD's Acne Support website and acne PIL.

2. Initiating Topical Retinoids[2,3,6]

- **Topical retinoids are a first-line treatment choice in all stages of acne**
- **Start with a short-contact regimen** to ameliorate the irritant reaction:
  - e.g. apply a small amount to skin every 2nd or 3rd day and leave it on for 30–60 minutes before washing off
  - gradually build up frequency and then duration of application, to a target dose of once daily application overnight
- Concomitant daily use of a noncomedogenic moisturiser can lessen dryness and irritation.

3. Skin of Colour[2,4,7,8]

- **Skin of colour is more prone to scarring and hyperpigmentation**. Therefore, more aggressive, earlier treatment is warranted, with a lower threshold for referral to secondary care for consideration of isotretinoin therapy
- Topical agents, such as retinoids, benzoyl peroxide, and azelaic acid, may worsen hyperpigmentation due to their irritant effects on the skin. Conversely, when they are introduced gradually (see *2. Initiating Topical Retinoids*), these topical agents have the potential to improve hyperpigmentation
- Azelaic acid has a beneficial effect on post-inflammatory hyperpigmentation, so may be particularly beneficial for patients with skin of colour; NICE suggests preferentially using azelaic acid in addition to an oral antibiotic for the treatment of moderate-to-severe acne in those with skin of colour
- Sun avoidance and sun protection are important lifestyle factors that help to reduce the risk of hyperpigmentation.

4. Drugs That Can Worsen Acne[2,4,6,9,10]

- Progestogen-only contraception, including LARC
- Topical and oral corticosteroids, as well as anabolic steroids
- Testosterone therapy, e.g. for gender affirmation
- Lithium
- Ciclosporin
- Vitamins B6 and B12
- Herbal remedies containing oral iodine, e.g. sea kelp products.

5. Antimicrobial Stewardship[3,6]

DO NOT prescribe:

- a topical or oral antibiotic as sole treatment
- a combination of a topical antibiotic and an oral antibiotic
- any antibiotics continuously for more than 6 months, unless in exceptional circumstances.

6. The 12-Week Review[2,3,6]

- **Review all patients 12 weeks after a treatment regimen has been changed** (i.e. stepped up or down)
- For those whose acne has not responded to a course of topical treatment:
  - step up to a regimen that contains an oral antibiotic if acne is moderate to severe
  - offer a different topical treatment if acne is still mild to moderate
- After a 3-month course of treatment containing an oral antibiotic:
  - for those who are not responding to treatment, change to an alternative antibiotic and consider referral to secondary care (see *7. When to Refer*)
  - for those whose acne has improved but not cleared, consider an additional 3 months of this treatment regimen
  - for those who have achieved a good response, step down to maintenance therapy of a topical treatment and stop the antibiotic.

7. When to Refer

Indications for Referral to Secondary Care[2–4,6,8]

- Acne that is leading to scarring or pigmentary change (risk is higher in people with skin of colour[2,4,8])
- Nodulocystic acne
- Acne fulminans (nodulocystic acne with associated systemic symptoms)—warrants urgent referral to the on-call hospital dermatology team, to be assessed within 24 hours
- Moderate-to-severe acne that has not responded to a completed course of treatment (12 weeks of an oral antibiotic plus topical therapy)
- Mild-to-moderate acne that has not responded to two completed courses of treatment (2 x 12 weeks of different oral antibiotics plus topical therapy)
- Severe psychological distress due to acne of any severity (also consider referral to mental health services).

Isotretinoin

Most patients referred to secondary care will be considered for **isotretinoin therapy**. Therefore, at the time of referral:[2,3,11]

- check LFTs, U&E, and fasting lipids
- prescribe contraception for female patients
- provide information on isotretinoin's risks and benefits, e.g. in a PIL.

Refer to the MHRA's regulatory guidance on isotretinoin referral and prescribing for further information.[11]

8. Long-Term Complications

Complication	Treatment Options
Hypertrophic scars	In primary care:[2,12,13] • Silicone gel/sheets • Potent topical steroids (cream, ointment, or fludroxycortide tape) or intradermal triamcinolone injections, for a trial of 2–3 months o monitor carefully for skin thinning and telangiectasia. In secondary care, NICE recommends glycolic acid peel and CO_2 laser treatment for acne-related scarring.[2] Pulsed dye laser is also available privately, within a specialised hospital department.[2]
Atrophic scars	Privately available:[2,12] • Ablative lasers combined with surgical techniques • Intradermal collagen or collagen-stimulating compounds • Other options for treating acne scars include skin needling, dermabrasion, chemical peels, scar revision, punch excision, and cryotherapy.
Hyperpigmentation	• Azelaic acid may be helpful in active acne and post-inflammatory hyperpigmentation[2,4,8] • Eucerin DermoPurifyer® creams and ointments for post-acne marks (non-NHS) may be of some benefit[2] • Chemical peels and laser therapy (only available privately).[4,14]

BAD=British Association of Dermatologists; **bd**=twice daily; **BNF**=British National Formulary; **COCP**=combined oral contraceptive pill; **eGFR**=estimated glomerular filtration rate; **FBC**=full blood count; **GPwSI**=GP With Special Interest; **HCP**=healthcare professional; **LARC**=long-acting reversible contraception; **LFT**=liver function test; **LNG**=levonorgestrel; **MHRA**=Medicines and Healthcare products Regulatory Agency; **od**=once daily; **PCDS**=Primary Care Dermatology Society; **PCOS**=polycystic ovary syndrome; **PIL**=patient information leaflet; **U&E**=urea and electrolytes; **VTE**=venous thromboembolism

Therapeutic Options for Acne in Primary Care[2–4,6,8,15–19]

- **Advise patients that any therapeutic option will take 6–8 weeks to work**
- **Arrange a review appointment at 3 months**
- **NB: topical retinoids, benzoyl peroxide, and oral antibiotics can all cause photosensitivity; benzoyl peroxide also bleaches hair and fabrics**
- **This table does not reflect management in patients aged <12 years, for whom requirements for investigation and treatment may differ.**

Therapeutic Option(s)		Prescribing Notes	Contraindications
Mild, Comedonal Acne			
Topical retinoid	Adapalene **or** trifarotene **or** fixed combination of topical adapalene and topical benzoyl peroxide	• Start with short-contact regimen.	• Pregnancy • Use with caution during breastfeeding.
Topical retinoid and topical antibiotic	Fixed combination of topical tretinoin and topical clindamycin	• Apply od in the evening • Start with short-contact regimen.	• Pregnancy • Breastfeeding • Perioral dermatitis, personal or family history of skin cancer, or rosacea.
Mild-to-Moderate Acne			
First line	Fixed combination of topical adapalene and topical benzoyl peroxide	• Apply od in the evening • Start with short-contact regimen.	• Pregnancy • Use with caution during breastfeeding.
Second line	Fixed combination of topical benzoyl peroxide and topical clindamycin	• Apply od in the evening • Start with short-contact regimen.	• Use with caution during pregnancy and breastfeeding.
	Fixed combination of topical tretinoin and topical erythromycin	• Apply od in the evening • Start with short-contact regimen.	• Pregnancy • Breastfeeding • Perioral dermatitis, personal or family history of skin cancer, or rosacea.
Third line (if combination products are not tolerated)	Adapalene **or** trifarotene	• Apply od in the evening • Start with short-contact regimen.	• Pregnancy • Use with caution during breastfeeding.
	Benzoyl peroxide	• Apply od in the evening • Start with short-contact regimen.	—
Moderate-to-Severe Acne			
First line	Fixed combination of topical adapalene and topical benzoyl peroxide **AND** doxycycline 100 mg od **or** lymecycline 408 mg od	• Apply topical component od in the evening • Start with short-contact regimen • Dose of oral tetracycline may be doubled to bd if there is partial response after 12 weeks.	• Pregnancy • Breastfeeding • Not for use in children aged <12 years.
	Topical azelaic acid **AND** doxycycline 100 mg od **or** lymecycline 408 mg od	• This option may be preferable in people with skin of colour to reduce hyperpigmentation secondary to inflammation[8,9] • Apply azelaic acid bd • Dose of oral tetracycline may be doubled to bd if there is partial response after 12 weeks.	• Pregnancy • Breastfeeding • Not for use in children aged <12 years.
Second line (if combination products are not tolerated)	Benzoyl peroxide **or** adapalene **or** trifarotene **AND** doxycycline 100 mg od **or** lymecycline 408 mg od	• Apply topical component od in the evening • Start with short-contact regimen • Dose of oral tetracycline may be doubled to bd if there is partial response after 12 weeks.	• Pregnancy • Breastfeeding • Not for use in children aged <12 years.
Third line (if the above tetracyclines are not tolerated or contraindicated)	Fixed combination of topical adapalene and topical benzoyl peroxide **or** benzoyl peroxide **or** adapalene **or** trifarotene **AND** clarithromycin 250–500 mg bd	• Apply topical component od in the evening • Start with short-contact regimen • Bacterial resistance to clarithromycin is high, but not as common as resistance to erythromycin.	• Topical retinoids should not be used in pregnancy, and used with caution during breastfeeding • The manufacturer advises avoiding use of clarithromycin in pregnancy and breastfeeding.
	Fixed combination of topical adapalene and topical benzoyl peroxide **or** benzoyl peroxide **or** adapalene **or** trifarotene **AND** trimethoprim 300 mg bd	• Start with short-contact regimen. For trimethoprim: • small risk of agranulocytosis or adverse cutaneous events • counsel patients and carers to seek medical help if they develop e.g. fever, sore throat, rash, purpura, bruising, bleeding, mouth ulcers • the BNF recommends monitoring FBC in long-term trimethoprim use.	• For trimethoprim: blood dyscrasias • Topical retinoids should not be used in pregnancy, and used with caution during breastfeeding • The manufacturer advises avoiding use of trimethoprim in pregnancy.
Alternative Options for Women With Acne			
COCP	Any 2nd-, 3rd-, or 4th-generation COCP	• Prescribe with reference to the UK Medical Eligibility Criteria.	
Licensed for treatment of refractory acne in PCOS	Co-cyprindiol (cyproterone acetate with ethinylestradiol)	• Prescribe with reference to the UK Medical Eligibility Criteria • 1.5–2x greater risk of VTE than LNG-containing contraception • Risk of VTE is greater when stopped and restarted • Small associated risk of meningioma.	

Unlicensed in UK, but prescribed by dermatologists and GPwSI in dermatology	Spironolactone—50 mg od, increased to 200 mg od depending on response and tolerability	• May be prescribed with a topical therapy and instead of, or in addition to, antibiotics and hormonal therapy
		• Effective contraception essential
		• Check U&E prior to initiating therapy
		  o for women aged <45 years with normal renal function, no further monitoring is necessary
		  o if >45 years, impaired eGFR, or in another at-risk population, monitor 1 week after initiation, monthly for 3 months, every 3 months for 1 year, then 6-monthly.
			• Pregnancy
			• Addison's disease
			• Anuria
			• Hyperkalaemia.

Acne in Pregnancy			
Benzoyl peroxide od **or** fixed combination of topical benzoyl peroxide and topical clindamycin od **or** topical erythromycin 2% **or** azelaic acid bd		• Topical therapies are preferred during pregnancy • Erythromycin 500 mg bd may be considered if the benefits outweigh the risks, e.g. in scarring acne • Start topical retinoids and benzoyl peroxide formulations with short-contact regimen.	—

Table based on authors' interpretation of relevant guidance, BNF entries, and summaries of product characteristics. As always, take an individualised and holistic approach to the care of people living with acne.

@GLNS_Medscape @drkevinfernando medscape.co.uk/guidelines

For references, a list of useful resources, and to view this Hack online, go to: **medscape-uk.co/Hack-acne**

Last updated: June 2024

Lipid Management for the Primary and Secondary Prevention of Cardiovascular Disease

Medscape UK X Guidelines
Primary Care Hacks

Authors: Niraj Lakhani, Lead Clinical Pharmacist, Willows Health, and Primary Care Development Advisor for the Royal College of General Practitioners; Dr Kevin Fernando, GP Partner, North Berwick Health Centre and Content Advisor, Medscape Global and UK (email: kfernando@webmd.net)

Key Principles

1. **Review LDL-C and aim for levels as low as possible, as quickly as possible, for as long as possible**
2. **Healthy lifestyle changes can improve overall CV health and aid in achieving LDL-C targets, and should be reinforced at every person contact**
3. **Do not over-rely on QRISK3 and 10-year CV risk; calculating lifetime CV risk may offer a more holistic view of a person's life story**
4. **Consider tighter European LDL-C targets over the current, more lenient UK targets**
5. **Statins are safe and effective and should be utilised when indicated**
6. **Statin intolerance is rare, and should be approached appropriately**
7. **Raised triglycerides are a marker of residual CV risk that may warrant further lifestyle and pharmacological management**
8. **Lp(a) is an independent CV risk factor that, when raised, should act as a prompt to mitigate all other CV risk factors and review lifestyle choices**
9. **Combination LLT should be considered standard practice for high-risk and very high-risk individuals**
10. **Familial hypercholesterolaemia is underdiagnosed in primary care, and should be suspected in individuals with a total cholesterol >7.5 mmol/l.**

See the flowchart on the final page for a comprehensive lipid management pathway for primary care practitioners

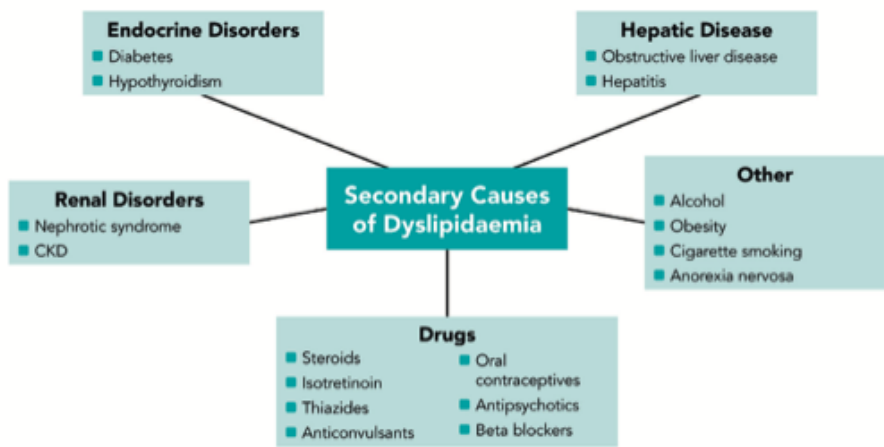
1. Overview of Lipid Management and Assessment

- The relationship between LDL-C levels and risk of major CV events is well established: **lower LDL-C translates into a lower risk of ASCVD, regardless of how it is achieved**[1–4]
  - evidence suggests that lowering LDL-C as quickly as possible and maintaining lower levels long-term significantly reduces risk of major CV events[1,3,4]
  - recent evidence also demonstrates that significant non-HDL-C reduction in the 2 months after an MI improves outcomes irrespective of baseline LDL-C, especially when sustained long-term[5]
- When reviewing cholesterol, focus on LDL-C or non-HDL-C rather than total cholesterol[1,6]—**the aim of therapy should be to lower LDL-C, to reduce the risk of ASCVD**
- NICE NG238 recommends a full lipid profile—including total cholesterol, HDL-C, LDL-C, and TGs—for comprehensive CV risk assessment.[6] **A fasting sample is not mandated**[1,6]
  - however, if lab results indicate a TG level >4.5 mmol/l or do not report an LDL-C due to high TGs, a retest should be conducted using a fasting blood sample[6]
- Although HDL-C has traditionally been viewed as protective, its exact role in CV health remains unclear and is still the subject of ongoing research[1,7]
  - Heart UK estimates that the protective effects of HDL-C reach a limit at around 1.4 mmol/l, with levels >2.3 mmol/l potentially increasing risk of ASCVD, especially in perimenopause/menopause[7]
- When reviewing a patient, it is essential to **identify and address secondary causes of dyslipidaemia and modifiable CV risk factors** (see Figure 1 and *2. Lifestyle Interventions*).[8,9]

2. Lifestyle Interventions

- Lifestyle interventions are fundamental in managing CV risk and cholesterol levels, and in promoting overall CV health over and above cholesterol[1,6]
- Heart UK advises the following as key strategies:
  - maintaining a balanced, heart-healthy diet[11]
  - regular physical activity (adults should aim for ≥150 minutes of moderate-intensity activity or ≥75 minutes of intense activity every week—if they can do more, that's even better)[12]
  - smoking cessation[13]
  - maintaining a healthy weight[14]
- Heart UK has published a helpful guide explaining how to carry out a quick dietary assessment and provide tailored dietary advice based on the person's responses
- Although lifestyle changes can lower LDL-C, the reduction may be modest, typically around 20%[15]
  - therefore, it is important not to delay medical treatment, especially in individuals at higher risk of CVD.

Figure 1: Secondary Causes of Dyslipidaemia[9,10]



3. Risk Estimation

- Although QRISK3[16] is a valuable tool for estimating 10-year CV risk, it should not be solely relied upon,[6] especially in younger people with CV risk factors or those with risk factors that accumulate over time—**early intervention is key to prevention of CVD**
  - **NICE NG238 recommends assessing both short-term CV risk (with QRISK3) and lifetime CV risk** for a more comprehensive assessment that informs discussions of CV risk; this helps to identify people with a high lifetime risk even if their short-term risk appears low[6]
    - risk assessments can be carried out in those as young as 25 years[6,16]
  - lifetime CV risk can be assessed using tools such as QRISK3-lifetime[6,17]
  - do not depend exclusively on QRISK3 to determine whether to start statins[6]
- A more pragmatic approach may be to gauge risk based on the individual's age and the number of LTCs they have, alongside any CV risk calculations—for example, an under-40-year-old living with multiple LTCs or CV risk factors is likely to have a high lifetime risk and therefore benefit from early intervention, independent of any risk calculation
- According to NICE guidance, QRISK3 should **not** be used in certain groups, including people:[6]
  - with FH or another form of genetic dyslipidaemia
  - with pre-existing CVD
  - aged ≥85 years
  - with CKD (stages 3–5)
  - with T1D, for whom specific guidance is applied regardless of QRISK3
- Furthermore, QRISK3 may **underestimate** risk in certain groups, including people:[6]
  - who have recently stopped smoking
  - living with HIV
  - living with severe mental illness
  - already taking medicines to treat CV risk factors
  - taking medicines that can cause dyslipidaemia, such as immunosuppressant drugs
  - living with autoimmune disorders and other systemic inflammatory disorders.

Use of Liraglutide, Semaglutide, and Tirzepatide for Adults Living With Overweight and Obesity

Medscape UK X Guidelines
Primary Care Hacks

Authors: Dr Kevin Fernando, GP Partner, North Berwick Health Centre and Content Advisor, Medscape Global and UK (email: kfernando@webmd.net); Dr Eimear Darcy, GP Partner, Grange Family Practice Omagh

Incretin Therapy	Indication	Standard Dose Escalation Schedule (in Weeks)									Further Considerations (see also *Prescribing Considerations and Special Precautions for Use*)
		1	2	3	4	5–8	9–12	13–16	17–20	21–24	
Liraglutide (Saxenda®)[3,4]	Weight management, as an adjunct to a reduced-calorie diet and increased physical activity in adults with an initial BMI of: • ≥30 kg/m², or • 27–30 kg/m² in the presence of ≥1 weight-related comorbidity.[A],[B]	0.6 mg (od)[C]	1.2 mg (od)[C]	1.8 mg (od)[C]	2.4 mg (od)[C]	3.0 mg (od)[C]					• No dose adjustment is required according to age, but therapeutic experience is limited in patients aged ≥75 years and use is not recommended in these patients • No dose adjustment is required in mild/moderate renal impairment (CrCl ≥30 ml/min) or mild/moderate hepatic impairment • Avoid in severe renal impairment (CrCl <30 ml/min), including ESRD • Not recommended in patients with severe hepatic impairment; should be used cautiously in mild/moderate hepatic impairment.
Semaglutide (Wegovy®▼)[5–8]	Weight management, as an adjunct to a reduced-calorie diet and increased physical activity in adults with an initial BMI of: • ≥30 kg/m², or • 27–30 kg/m² in the presence of ≥1 weight-related comorbidity.[A],[D] To reduce the risk of major adverse CV events in adults with established CVD and BMI ≥27 kg/m²,[A] as an adjunct to a reduced-calorie diet and increased physical activity.	0.25 mg (once weekly)				0.5 mg (once weekly)	1.0 mg (once weekly)	1.7 mg (once weekly)	2.4 mg (once weekly)[E]		• No dose adjustment is required according to age, but there is limited therapeutic experience in patients aged ≥85 years • No dose adjustment is required in mild/moderate/severe renal impairment; avoid in ESRD (eGFR <15 ml/min/1.73 m²) • No dose adjustment is required in hepatic impairment; exercise caution when prescribing in severe hepatic impairment.
Tirzepatide (Mounjaro®▼)[9,10]	Weight management, as an adjunct to a reduced-calorie diet and increased physical activity in adults with an initial BMI of: • ≥30 kg/m², or • 27–30 kg/m² in the presence of ≥1 weight-related comorbidity.[A],[F]	2.5 mg (once weekly)				5 mg (once weekly)	7.5 mg (once weekly)[G]	10 mg (once weekly)[G]	12.5 mg (once weekly)[G]	15 mg (once weekly)[G]	• No dose adjustment is required according to age, but there are limited data available for patients aged ≥85 years • No dose adjustment is required in renal impairment (including ESRD) • No dose adjustment is required in hepatic impairment; exercise caution when prescribing in severe hepatic impairment.

Footnotes

[A] **NICE recommends lower BMI thresholds (usually, reduced by 2.5 kg/m²) for people of South Asian, Chinese, other Asian, Middle Eastern, Black African, or African–Caribbean family backgrounds**[4,7,10]

[B] NICE TA664[4] recommends liraglutide for overweight or obesity if it is prescribed by a specialist, multidisciplinary, tier-3 weight-management service and is provided according to the commercial arrangement for the drug. NICE recommends provision in patients with all of the following: a BMI of ≥35 kg/m²; nondiabetic hyperglycaemia (HbA_{1c} of 42–47 mmol/mol or fasting plasma glucose of 5.5–6.9 mmol/l); and high risk of CVD, based on risk factors.[4] After 12 weeks of treatment with the 3.0 mg/day dose, treatment should be discontinued if patients have not lost ≥5% of their initial bodyweight[3]

[C] If escalation to the next dose is not tolerated for 2 weeks consecutively, consider discontinuing treatment[3]

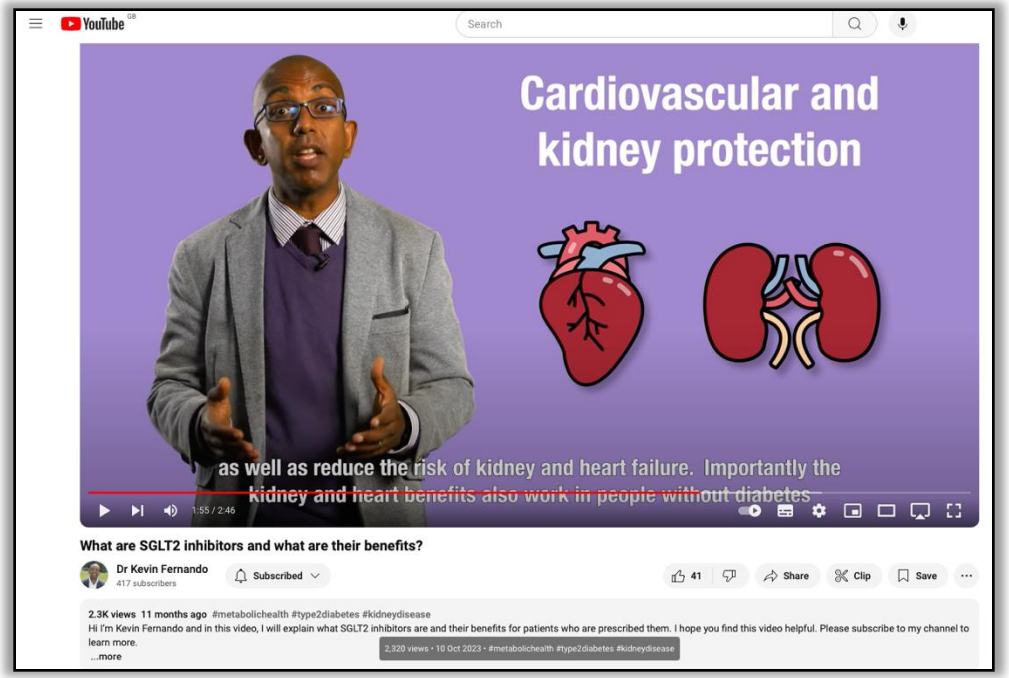
[D] NICE TA875[7] recommends semaglutide if it is used for a maximum of 2 years, is prescribed within a specialist weight-management service providing multidisciplinary management, and is provided according to the commercial arrangement for the drug; NICE recommends provision in patients with ≥1 weight-related comorbidity and either a BMI ≥35 kg/m² or a BMI of 30–34.9 kg/m² if the patient meets the criteria for referral to specialist weight-management services in NICE NG246;[11],[A] if weight loss is <5% of initial weight after 6 months of treatment, consider stopping semaglutide;[7] as the SELECT trial has demonstrated CV benefits of semaglutide irrespective of weight loss, it may be worth considering continuation independent of weight loss when used for CV indications[8]

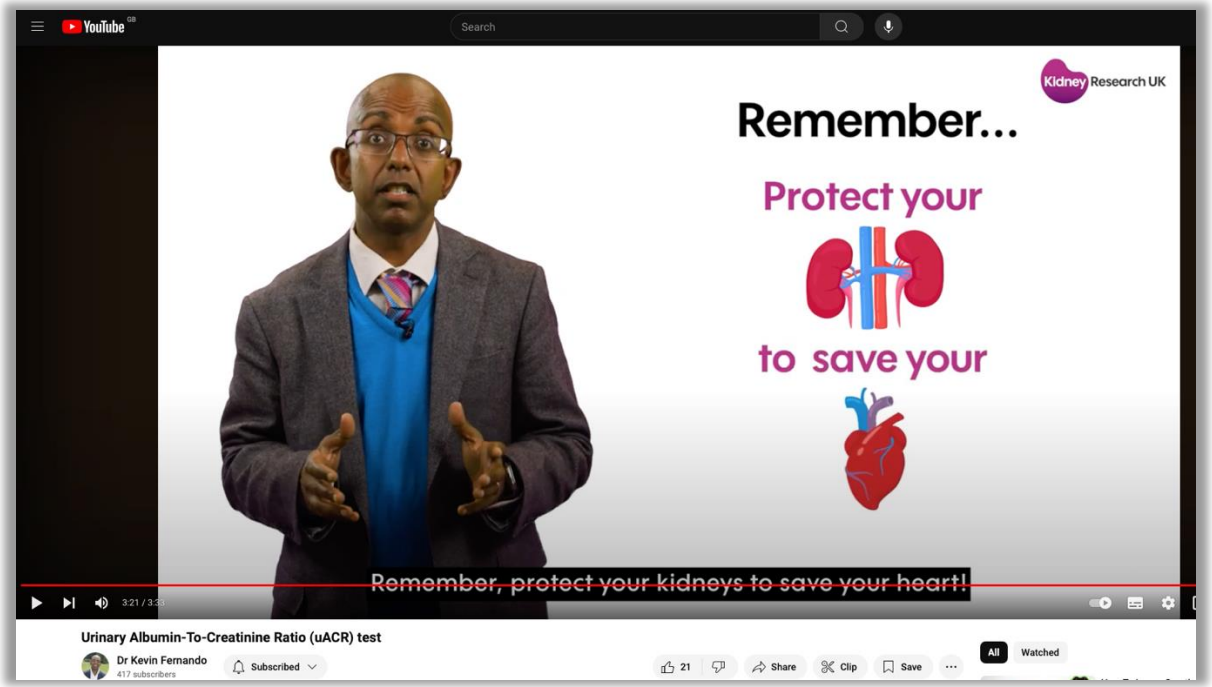
[E] If semaglutide is not tolerated at 2.4 mg, maintain at 1.7 mg for 4 more weeks then re-escalate afterwards[6]

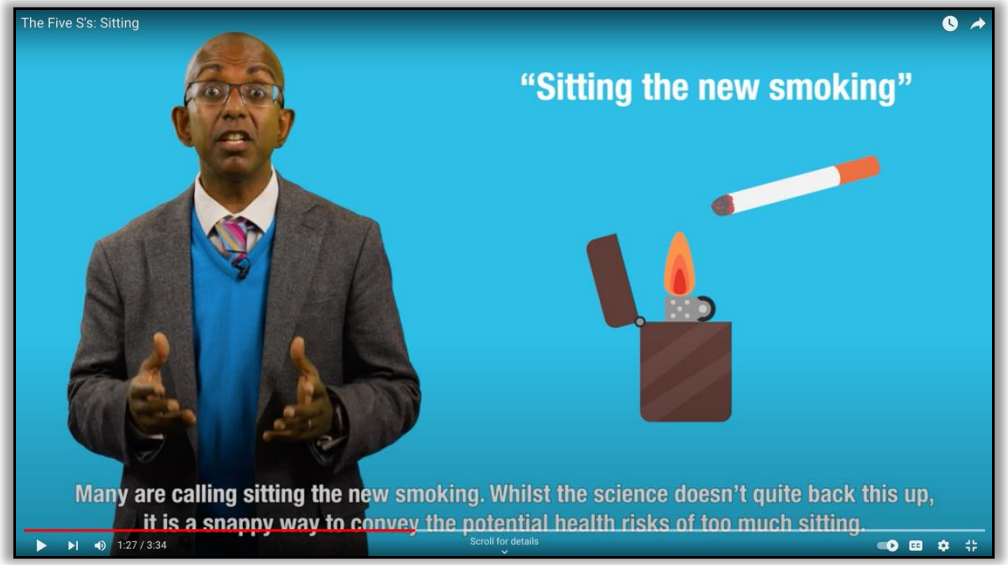
[F] NICE TA1026[10] recommends prescribing tirzepatide for adults with a BMI of ≥35 kg/m² and ≥1 weight-related comorbidity;[A] if weight loss is <5% of initial weight after 6 months of treatment, consider stopping tirzepatide

[G] Individualise tirzepatide above 5 mg depending on individual treatment goals, increasing dose by 2.5 mg after ≥4 weeks at current dose; 5 mg, 10 mg, and 15 mg are the recommended maintenance doses.[9]

This table is based on the authors' interpretation of summaries of product characteristics and relevant guidance. HCPs are asked to report all suspected adverse drug reactions to products with a Black Triangle symbol (▼) through the Yellow Card Scheme: yellowcard.mhra.gov.uk.







YouTube @DrKevinFernando

Talking Points

- Management of abnormal liver blood tests in primary care
- Use of CRP & ESR in primary care
- Management of neutropenias and lymphopenias in primary care

Cara

Age	52
History	Found to have fatty liver on USS for suspected cholecystitis
BP	148/92 mmHg
Lipid profile (mmol/l)	TC 6.3 TRG 4.9 HDL 0.8 Unable to calculate LDL-C
BMI & Weight	33 kg/m² Waist 88cm
LFTs (U/L)	ALT 62 (10-50), AST 63 (8-50), ALP 85 (40-125) GGT 65 (5-55) Bili 17 (3-21)
HbA1c	45 mmol/mol
eGFR	>60 mL/min/1.73m²
Medications	Nil
Social History	Tattoo artist, non-smoker, social alcohol

What is the likely cause of her abnormal LFTs?

1. Chronic HCV infection
2. MASLD
3. MetALD (metabolic alcohol-related liver disease)
4. Hepatocellular carcinoma
5. Something else?

What is your next step with respect to her LFTs?

1. Lifestyle advice – weight loss & alcohol consumption
2. Check targeted liver screen
3. Refer hepatology
4. Check FIB-4 score
5. Refer liver elastography e.g., FibroScan
6. Repeat 4 weeks…

What is MASLD?

- NAFLD is now termed **M**etabolic Dysfunction **A**ssociated **S**teatotic **L**iver **D**isease
  - MASLD encompasses individuals who have **hepatic steatosis** and at least **1 cardiometabolic risk factor:**
    - BMI≥25 (23 if high-risk ethnic group) or waist circumference >94 cm  (>90cm if high-risk ethnic group) or >80 cm  (all ethnicities)
    - HbA1c 42-47mmol/mol or established T2D
    - Blood pressure ≥130/85 or antihypertensive drug treatment
    - Plasma triglycerides ≥1.70mmol/L or lipid-lowering treatment
    - Plasma HDL-C ≤1.0mmol/L or lipid-lowering treatment

- **MASH** replaces NASH
- **MetALD** describes individuals with MASLD who consume above recommended amounts of alcohol per week i.e. combined aetiology
- **MASLD is primarily a metabolic disease**; it is the liver's manifestation of the metabolic syndrome (MetS)

Abnormal liver blood tests

- Mildly abnormal LFTs are very common!
  - Degree of abnormality does not always correlate with disease severity
  - LFTs often checked for unexplained or non-specific symptoms
    - 1:5 will have abnormal LFTs & most of these individuals will not have significant liver disease
  - BALLETS study BMJ Open 2013 BMJ Open
    - n=1290 from primary care with abnormal LFTs and without known liver disease
    - Only 2.5% (n=32) of people with abnormal LFTs had a specific disease of the liver
      - 40% of whole cohort had ”fatty liver” on USS
      - 8 malignancies found
      - Repeating entire LFT panel in 1 month is ineffective!
      - ALT & ALP most associated with significant liver disease
      - GGT had a very high false positive rate but was sensitive to alcohol intake
      - **Liver disease is rare among those with abnormal LFTs in primary care**
  - So, worth having a heuristic at hand to identify those with modifiable liver disease

Abnormal liver blood tests: Key Points

- LFTs may be normal even in advanced liver disease & are frequently abnormal in the absence of liver disease
  - Interpreting LFTs in isolation may be ineffective in diagnosing or excluding liver disease

- Liver enzymes are a poor guide to the development of alcohol-related liver disease (ARLD)
  - But, if elevated, can be useful in promoting behaviour change
  - ARLD is not limited to those who are dependent on alcohol; the risk of liver disease doubles for any given alcohol intake if BMI>35

- Look for:
  - Predominant pattern of enzyme alteration (hepatocellular vs cholestatic)
  - Magnitude of abnormality <3x ULN, >3-10x ULN, >10x ULN
  - Rate of change over time

When to consider checking LFTs:

- Non-specific symptoms suggestive of liver disease e.g. anorexia, fatigue or nausea

- Evidence of chronic liver disease e.g. symptoms or signs of cirrhosis, portal hypertension or liver failure such as ascites, peripheral oedema, spider naevi and hepatosplenomegaly

- Conditions associated with a risk of developing liver disease e.g. other autoimmune disease, IBD (10% risk of PSC)

- Use of hepatotoxic drugs e.g. DMARDs, terbinafine NB statins
- FH of liver diseases e.g. haemochromatosis, Wilson's disease
- Alcohol misuse though poor guide to development of ARLD but can motivate behaviour change. GGT best predictor of mortality
- Risk factors for viral hepatitis

Interpreting liver blood tests

- ALT is predominantly liver-specific enzyme & is a sensitive marker of hepatocyte injury or death e.g. viral hepatitis
  - Varies with age, sex, ethnicity, BMI, illness & exercise

- AST is not as liver-specific (present in cardiac, smooth & skeletal muscle) but is a more sensitive marker of liver injury particularly alcohol
  - In children, checking CK can be helpful to determine whether isolated rise in AST is due to an underlying skeletal muscle disorder e.g. muscular dystrophy

- Isolated GGT difficult to interpret as present in liver, intestines, kidneys, pancreas & prostate (but not bone) & raised by multiple factors:
  - Alcohol, obesity & several drugs
  - Best role is for establishing likely origin of an elevated ALP – bone or liver
  - Despite low specificity, GGT is one of the best predictors of mortality in established liver disease

Interpreting liver blood tests

- ALP predominantly liver enzyme but also found in bone, intestine, kidneys, WBCs. ALP higher in childhood & pregnancy
  - ALP elevated in cholestatic liver disease, bone disease, hepatic congestion due to right-sided HF
  - If raised ALP worth checking GGT – if GGT normal think "bone", if GGT high think "liver"
    - Also, ALP electrophoresis can be used to differentiate
  - Consider checking AMA if persistently ↑ isolated ALP >200 of liver origin to exclude PBC

- Isolated raised bilirubin (unconjugated, usually not >70) often due to Gilbert's syndrome but exclude haemolysis (consider blood film, reticulocytes, LDH)
  - Raised conjugated bilirubin seen in HPB obstruction, hepatitis from any cause or advanced cirrhosis

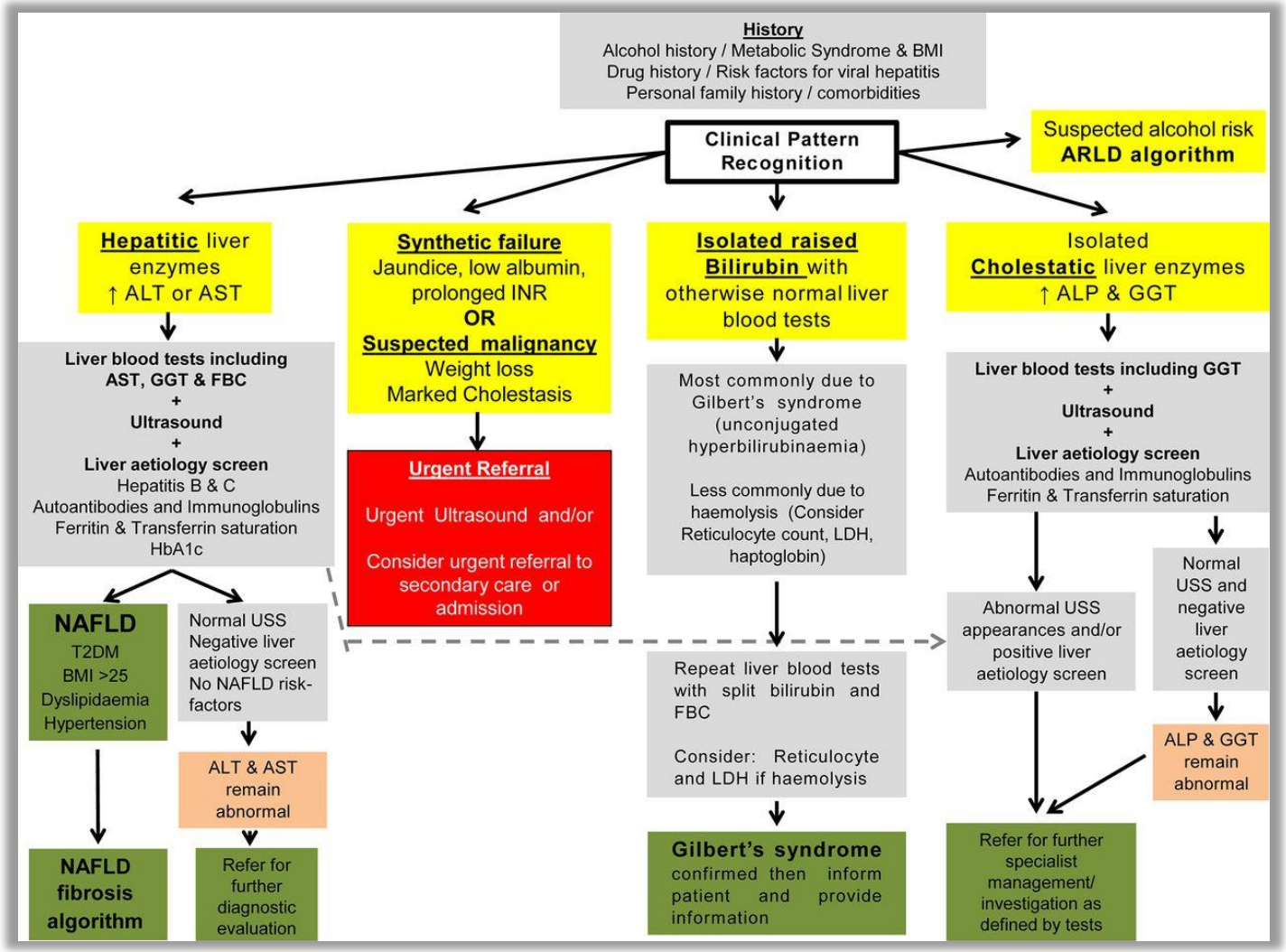
Interpreting liver blood tests

- Albumin is a protein synthesised by the liver and is a sensitive marker of liver synthetic function
  - Albumin may also be reduced in other clinical scenarios e.g. sepsis, systemic inflammatory disorders, nephrotic syndrome, HF, malabsorption and GI protein loss

- Clotting factors are synthesised in the liver and if significant liver damage (usually >70%) production is reduced and PT or INR can be prolonged
  - Prolonged PT or INR can also be caused by vitamin K deficiency in fat malabsorption & chronic cholestasis

- Platelet reduction is an indicator of advanced liver disease usually due to splenic enlargement secondary to portal hypertension
- LDH is not specific to liver (also heart & muscle) but is typically elevated in liver diseases associated with haemolysis, solid tumours, lymphomas & viral hepatitis

Response to abnormal liver blood tests.



Philip N Newsome et al. Gut 2018;67:6-19

GUT

Cara

Age	52
History	Found to have fatty liver on USS for suspected cholecystitis
BP	148/92 mmHg
Lipid profile (mmol/l)	TC 6.3 TRG 4.9 HDL 0.8 Unable to calculate LDL-C
BMI & Weight	33 kg/m² Waist 88cm
LFTs (U/L)	ALT 62 (10-50), AST 63 (8-50), ALP 85 (40-125) GGT 65 (5-55) Bili 17 (3-21)
HbA1c	45 mmol/mol
eGFR	>60 mL/min/1.73m²
Medications	Nil
Social History	Tattoo artist, non-smoker, social alcohol

What is the likely cause of her abnormal LFTs?

MASLD

What is your next step with respect to her LFTs?

Lifestyle advice – weight loss & alcohol consumption

Targeted liver screen

FIB-4 score 2.08: intermediate risk for fibrosis. Refer hepatology for 2nd line non-invasive testing e.g. ELF, FibroTest or Fibroscan

Actively manage features of MetS

Interpreting Liver Blood Tests in Primary Care

Medscape UK X Guidelines
Primary Care Hacks

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LBTs have traditionally been referred to as liver function tests (LFTs). However, typical LBTs include measurement of both hepatobiliary enzymes (e.g. ALT and AST) and markers of liver function (e.g. albumin and clotting factors).[1,2] Additionally, many individuals with abnormal LBTs have normal liver function.[1,2] Therefore, to avoid confusion and over-investigation, 'LBT' is now the preferred terminology.[1,2]

Key Messages

1. **Standard LBTs usually comprise ALT, AST, ALP, GGT, total bilirubin, and serum albumin**
2. **Abnormal LBTs are very common in primary care!**
3. **LBTs should only be checked when specifically indicated by the clinical situation**
4. **Interpretation of abnormal LBTs should be individualised and in clinical context**
5. **Abnormal LBTs are likely to remain abnormal on repeat testing**
6. **Common patterns of abnormal LBTs are often more helpful than individual markers**
7. **GGT is useful in determining whether raised ALP is of bone or liver origin**
8. **Isolated raised bilirubin is commonly caused by Gilbert's syndrome, but haemolysis should be excluded**
9. **Always consider a possible pharmacological cause for abnormal LBTs**
10. **Liver enzymes are a poor guide to the development of ALD.**

1. Commonly Requested LBTs[1,3–9]

Test	Notes
ALT	• ALT level varies with age, gender, ethnicity, BMI, illness, and exercise • Recent consensus suggests that the current ULN for ALT is too low; updated EASL–EASD–EASO guidance on MASLD[11] suggests that an individual has elevated ALT if >33 U/l in males and >25 U/l in females (usual normal range 10–50 U/l in both men and women).
AST	• Not as liver-specific as ALT; however, in ALD, AST is a more sensitive marker of liver injury than ALT • May be elevated in MI or myositis • The **De Ritis/AST:ALT ratio** may be useful in elevated aminotransferase levels, as most causes of liver injury are associated with a greater increase in ALT than AST. As a general guide: o **AST:ALT <1** (i.e. AST<ALT) is suggestive of MASLD, chronic viral hepatitis B or C, or acute hepatocellular injury o **AST:ALT ≥2** is associated with ALD, cirrhosis (e.g. in MASH), drug-induced liver injury, and primary liver malignancy o **AST:ALT ≥5** warrants suspicion of possible extrahepatic causes (e.g. MI, myositis), particularly if ALT levels are normal.
ALP	• ALP is elevated in **cholestatic liver disease** (e.g. PBC, drug-induced liver injury), **extrahepatic biliary obstruction** (e.g. gallstones, pancreatic cancer), **bone disease** (e.g. bony metastases, vitamin D deficiency, Paget's disease, bone fractures), **renal osteodystrophy**, and **hepatic congestion caused by right-sided HF** • ALP is also higher in pregnancy because of placental production, and in adolescence because of increased bone turnover.
GGT	• **Raised by multiple factors**, particularly excessive alcohol consumption, obesity, and various drugs (e.g. paracetamol. phenytoin, sodium valproate) • Mild elevations are nonspecific, and isolated increases rarely indicate liver disease • Can also be raised in a range of nonhepatic conditions (e.g. COPD or CKD), and for several weeks after acute MI • Despite its low specificity for liver disease, **GGT is one of the best predictors of mortality in those with established liver disease** • **GGT is useful in determining whether raised ALP is of bone or liver origin** (see *7. Interpreting Raised ALP*).
Bilirubin	• Initial testing usually reports **total bilirubin** (including both unconjugated and conjugated fractions) • **Unconjugated hyperbilirubinaemia** is increased primarily in **Gilbert's syndrome and RBC breakdown (i.e. haemolysis)** (see *8. Isolated Raised Bilirubin*) • **Conjugated hyperbilirubinaemia** is usually caused by **impaired liver processing or bile flow**, e.g. from hepatitis, drug-induced cholestasis, or biliary obstruction (e.g. by gallstones or malignancy).
Albumin	• Serum albumin is a **marker of synthetic liver function**; levels are usually reduced in liver failure but may still be normal in severe acute liver damage, as the half-life of albumin in plasma is around 20 days • Levels are also reduced in sepsis, malnutrition, systemic inflammatory disorders, malabsorption, nephrotic syndrome, GI protein loss, acute infection, and HF (all subtypes) • In the absence of other abnormal LBTs, low serum albumin is unlikely to be of liver origin.
PT and INR	• In the presence of significant liver injury (usually >70% loss of synthetic function), production is reduced and PT prolonged/INR raised • Prolonged PT/raised INR can also be caused by warfarin therapy, or by vitamin K deficiency in fat malabsorption or chronic cholestasis • In the presence of otherwise normal LBTs, prolonged PT is unlikely to be of liver origin.

Platelet reduction is also an indicator of advanced liver disease; this is the result of a multifactorial mechanism involving bone marrow suppression, hypersplenism (secondary to portal hypertension), and subsequent splenic sequestration.

Note: the standard set of LBTs differs between areas. The BSG recommends assessing bilirubin, albumin, ALT, ALP, and GGT when first investigating potential liver disease, with an FBC *'if not already performed within the previous 12 months'*.[1]

Abbreviations
AAC=Accelerated Access Collaborative; **AIH**=autoimmune hepatitis; **ALD**=alcohol-related liver disease; **ALP**=alkaline phosphatase; **ALT**=alanine aminotransferase; **AMA**=antimitochondrial antibody; **ANA**=antinuclear antibody; **AST**=aspartate aminotransferase; **AUDIT**=Alcohol Use Disorders Identification Test; **BALLETS**=Birmingham and Lambeth Liver Evaluation Testing Strategies; **BMI**=body mass index; **BSG**=British Society of Gastroenterology; **CKD**=chronic kidney disease; **CMV**=cytomegalovirus; **COPD**=chronic obstructive pulmonary disease; **CVD**=cardiovascular disease; **DMARD**=disease-modifying antirheumatic drug; **EASD**=European Association for the Study of Diabetes; **EASL**=European Association for the Study of the Liver; **EASO**=European Association for the Study of Obesity; **EBV**=Epstein–Barr virus; **FBC**=full blood count; **FIB-4**=Fibrosis-4; **GGT**=gamma-glutamyl transferase; **GI**=gastrointestinal; **HAV**=hepatitis A virus; **HbA_{1c}**=glycated haemoglobin; **HBV**=hepatitis B virus; **HCV**=hepatitis C virus; **HEV**=hepatitis E virus; **HF**=heart failure; **IBD**=inflammatory bowel disease; **INR**=international normalised ratio; **LBT**=liver blood test; **LDH**=lactate dehydrogenase; **LFT**=liver function test; **LKM**=liver kidney microsomal; **MASH**=metabolic dysfunction-associated steatohepatitis; **MASLD**=metabolic dysfunction-associated steatotic liver disease; **MI**=myocardial infarction; **NG**=NICE Guideline; **NSAID**=nonsteroidal anti-inflammatory drug; **OTC**=over-the-counter; **PBC**=primary biliary cholangitis; **PSC**=primary sclerosing cholangitis; **PMH**=past medical history; **PT**=prothrombin time; **PTH**=parathyroid hormone; **RA**=rheumatoid arthritis; **RBC**=red blood cell; **RCGP**=Royal College of General Practitioners; **SMA**=smooth muscle antibody; **T2DM**=type 2 diabetes mellitus; **UGT**=uridine diphosphate glucuronosyltransferase; **ULN**=upper limit of normal; **USS**=ultrasound scan; **U&E**=urea and electrolytes; **WBC**=white blood cell.

2. Contextual Interpretation of Results[1,4,5,10]

- LBTs are regularly checked for unexplained or nonspecific symptoms, almost as a measure of wellbeing
  - o in this context, >20% will have abnormal LBTs, and most of these individuals will not have significant liver disease[10]
- Moreover, the degree of LBT abnormality does not always correlate with disease severity
  - o LBTs may be normal even in advanced liver disease, and are often abnormal in the absence of significant underlying liver disease
- Therefore, interpreting LBTs in isolation is not helpful when diagnosing or ruling out liver disease, and additional history-taking, examination, and/or investigation is usually required (see *4. History, Examination, and Screening* and *5. Further Investigations and Repeat Testing*)
- Review previous LBTs (if available) and assess trends, e.g. mild fluctuation or progressive increase.

3. Indications to Check LBTs[1,4,9,11–17]

- Indiscriminate testing of LBTs in response to nonspecific symptoms that are **not** suggestive of liver disease is likely to lead to unnecessary patient concern, further testing, and investigation
- Opportunistic testing of LBTs is not recommended for asymptomatic people without risk factors for liver disease.

Main Indications for Checking LBTs

- **Nonspecific symptoms suggestive of liver disease**, e.g. fatigue, nausea, or loss of appetite
- **Evidence of chronic liver disease**, e.g. symptoms or signs of portal hypertension, cirrhosis, or liver failure (including ascites, peripheral oedema, hepatosplenomegaly, and spider naevi)
- **Conditions associated with an increased risk of developing liver disease**—including coexisting autoimmune disease, e.g. RA and coeliac disease (increased risk of AIH), and IBD (around 10% risk of comorbid PSC)
- **Monitoring of potentially hepatotoxic drugs** (see *9. Pharmacological Causes*)—various drugs are associated with liver disease and may require LBT monitoring. Notably:
  - o **statin monitoring—statins can cause a transient rise in liver aminotransferases but do not cause liver disease;** they are likely to be beneficial in MASLD (note: **CVD is a more common cause of death than liver disease in MASLD**—see the Primary Care Hack on MASLD/MASH) and are associated with reduced primary liver cancer
    - – current monitoring of LBTs for statins is unnecessary and costly
    - – a single baseline ALT is all that is required—if this is <3x ULN, commence the statin and repeat ALT only if clinically indicated (note: NICE[18] and NHS AAC[19] guidelines do recommend further measurements of ALT/AST as part of early statin monitoring)
  - o **DMARD monitoring:**
    - – discussion with the specialist team and withholding of therapy may be warranted if ALT and/or AST >100 U/l, or an unexplained reduction in albumin <30 g/l
- **Family history of liver diseases**, e.g. haemochromatosis or Wilson's disease (both autosomal recessive disorders); this may warrant more specific, relevant tests
- **Suspected alcohol misuse and dependence**—to identify physical health complications, e.g. liver inflammation and injury (elevated ALT/AST) and portal hypertension (platelet reduction), and to assess liver synthetic function (PT/INR); see *10. Alcohol-related Liver Disease*
- **Suspected acute or chronic viral hepatitis** (e.g. HBV, HCV, HAV, CMV, EBV)—standard LBTs in addition to hepatitis serology
- **Suspected primary or secondary liver malignancy on examination**, in addition to an urgent, direct-access USS
- As part of **screening for MASLD** in the presence of its cardiometabolic risk factors and/or features of the metabolic syndrome, and/or when hepatic steatosis is found incidentally on USS (see the Primary Care Hack on MASLD/MASH).

4. History, Examination, and Screening[1,3,4,14,18,19]

- Review current clinical status, PMH and comorbidities, family history, travel history, sexual history, occupation, tattoos, prescribed and/or OTC medications, herbal remedies, illicit drug use, and alcohol intake
- Ask about specific signs and symptoms (e.g. jaundice, arthralgia, weight loss, abdominal pain, pruritis, skin hyperpigmentation), as well as tick bites and muscle injury
- Consider assessing BMI and waist-to-height ratio[18], and examining for jaundice, anaemia, ascites, hepatosplenomegaly, and other signs of chronic liver disease (e.g. spider naevi, palmar erythema, gynaecomastia, asterixis)
- Screen for MASLD and features of the metabolic syndrome (see the Primary Care Hack on MASLD/MASH).

5. Further Investigations and Repeat Testing[1,4,9,20,21]

- **Continually repeating LBTs to see whether they normalise is usually an inefficient strategy in primary care**, and is generally only appropriate if transient causes are suspected in the clinical context (e.g. simple viral illness or suspected drug-induced cause)
  - o the BALLETS study (2013)[21] found that 84% of abnormal LBTs in primary care remained abnormal on retesting 1 month later, and 75% were still abnormal after 2 years
- Early additional investigation should be considered, informed by LBT results (see Figure 1)
- **Consider an early targeted liver screen, irrespective of level or duration of abnormal LBTs**. Tests to consider are listed to the right.

Tests to consider in a targeted liver screen include:

- HbA_{1c}
- lipid profile
- USS
- coeliac screen
- iron studies
- autoimmune profile (anti-SMA, AMA, anti-LKM antibodies, ANA)
- immunoglobulins
- HBV/HCV serology
- HIV
- TFTs
- alpha-1 antitrypsin
- FIB-4, if MASLD is suspected
- serum or urine copper/caeruloplasmin (if family history of Wilson's disease, and/or aged <45 years)
- if acute hepatitis is suspected, also consider HAV, HEV, CMV, and EBV serology.

6. Common Patterns of Abnormal LBTs[1,3–5,20]

- The pattern of abnormal LBTs is often more informative than individual LBT changes, especially if there is no obvious underlying cause
- The magnitude of LBT abnormality does not necessarily correlate with clinical significance, but as a general guide LBTs <2–3x ULN are considered borderline/mild
- Look for the predominant pattern of enzyme alteration (see table, right).

Pattern	ALT/AST	ALP/GGT	Bilirubin	Notes
Hepatocellular	↑	↔	↑ or ↔	• Causes include MASLD, ALD, viral hepatitis, AIH, and drug-induced liver injury (e.g. paracetamol overdose) • Consider targeted further investigation and USS (see Figure 1).
Cholestatic/ obstructive	↔	↑	↑ or ↔	• Causes include PBC, PSC, biliary obstruction (e.g. from gallstones, strictures, malignancy), drug-induced liver injury, and hepatic congestion (e.g. secondary to HF) • Consider USS and targeted further investigation (see Figure 1).
Mixed hepatocellular/ cholestatic	↑	↑	↑ or ↔	• Often seen in the context of medication use (see *9. Pharmacological Causes*).
Isolated raised bilirubin	↔	↔	↑	• Often suggestive of Gilbert's syndrome, but haemolysis should also be excluded (see *8. Isolated Raised Bilirubin*).
Failure of liver synthetic function	• Jaundice, low albumin, and prolonged PT/INR • See Figure 1.			

↑ = Raised ↓ = Lowered ↔ = Unchanged

7. Interpreting Raised ALP[1,3,4,22]

- **If ALP is raised, check GGT:**
  - o if GGT is normal, think 'bone' origin and consider investigations such as calcium, phosphate, magnesium, PTH, U&E, and vitamin D levels (see the Primary Care Hack on abnormal calcium levels)
    - – if there is no obvious cause, consider bony metastases
  - o if GGT is high, think 'liver' origin and consider a targeted liver screen and USS (see Figure 1)
- **ALP isoenzyme electrophoresis** can also be requested to determine the source of a raised ALP, if unclear
- Consider checking **AMA** and **ANA** if raised ALP of liver origin persists, to exclude PBC
  - o PBC is much more common in women and in those aged >50 years, and often presents with intense, widespread itch.

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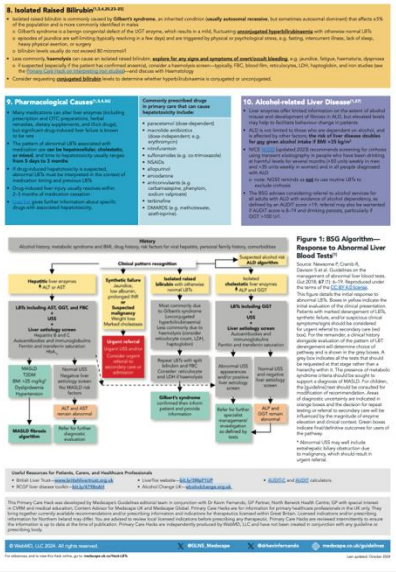

bitly

Identification and Management of People with MASLD and MASH in Primary Care

Medscape UK X Guidelines
Primary Care Hacks

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What Is MASLD?[1–7]

- There has been recent international consensus to rename nonalcoholic fatty liver disease (NAFLD) to improve awareness and patient identification and reduce stigma;[1] using this terminology, the EASL, the EASD, and the EASO produced an updated guideline in 2024[2]
- NAFLD is now termed **metabolic dysfunction-associated steatotic liver disease (MASLD)**[1]
  - MASLD encompasses individuals who have **hepatic steatosis and at least one cardiometabolic risk factor**[3]
- **Metabolic dysfunction-associated steatohepatitis (MASH)** replaces nonalcoholic steatohepatitis (NASH).[3] MASH is defined by inflammation of hepatocytes and carries a risk of progression to fibrosis, cirrhosis, and HCC[3,4]
- **MetALD** describes individuals with MASLD who consume more than recommended amounts of alcohol per week (defined as 3.75–7.50 units/day [30–60 g/day] in men and 2.50–6.25 units/day [20–50 g/day] in women)[2]
  - for all adults in the UK, the recommended alcohol intake is ≤14 units/week (i.e. 112 g/week, or 2.0 units/day [16 g/day]), best spread evenly over ≥3 days[5]
- **MASLD is primarily a metabolic disease heavily influenced by lifestyle factors, and is the liver's manifestation of the MetS alongside hypertension, insulin resistance and dysglycaemia, dyslipidaemia, and obesity/increased** waist circumference.[6,7]

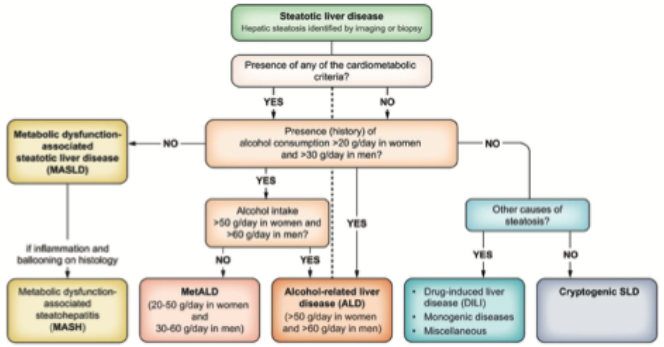
Cardiometabolic Risk Factors[2,8,9]

- BMI ≥25 kg/m² (23 kg/m² if high-risk ethnic minority) or waist circumference ≥94 cm (37.0 inches) for men (≥90 cm [35.4 inches] in men of South Asian or Chinese ethnicity, or ≥85 cm [33.5 inches] in men of Japanese ethnicity) or ≥80 cm (31.5 inches) for women of all ethnicities
- HbA_{1c} 39–47 mmol/mol, fasting plasma glucose of 5.6–6.9 mmol/l (100–125 mg/dl), or 2-hour plasma glucose during OGTT of 7.8–11 mmol/l (140–199 mg/dl), or established T2D
- BP ≥130/85 mmHg or antihypertensive drug treatment
- Plasma triglycerides ≥1.70 mmol/l or lipid-lowering treatment
- Plasma HDL-cholesterol ≤1.0 mmol/l in men, ≤1.30 mmol/l in women, or lipid-lowering treatment.

Secondary Causes of Hepatic Steatosis[2,8,10]

- Drug-induced liver injury, e.g. amiodarone, methotrexate, tamoxifen, and corticosteroids
- Endocrine disorders, such as hypothyroidism, PCOS, panhypopituitarism, or growth hormone deficiency
- Nutrient deficiency or malnutrition, such as from acute weight loss due to bariatric surgery or fasting, total parenteral nutrition, or small intestinal bacterial overgrowth
- Chronic hepatitis C virus infection.

Flowchart for SLD and Its Subcategories[2]



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Note: 50 g of alcohol equates to 6.25 units, and 60 g equates to 7.5 units.

How Common and Serious Is MASLD?[2,11–13]

- MASLD is now the most common liver disorder in Western countries, and has been estimated to affect up to 30% of adults in the UK[11,12]
  - MASH has been estimated to affect up to 5% of the UK population[11]
- MASLD (specifically progressive MASH) is the fastest growing indication for liver transplantation in Western countries[13]
- MASLD is also associated with an increased prevalence and incidence of CVD[2]
  - CVD is a more common cause of death than liver disease in MASLD[2]
- MASLD is highly prevalent in people living with T2D.[2]

Screening for MASLD in Primary Care[2,14]

- The appearance of steatosis on abdominal USS is operator-dependent and a normal USS does not rule out MASLD[14]
- Consider case-finding strategies for MASLD with liver fibrosis in those who have abnormal liver enzymes, cardiometabolic risk factors, and/or incidental radiological signs of hepatic steatosis[2]
- The EASL, the EASD, and the EASO recommend looking for MASLD with liver fibrosis in individuals with one or more of the following:[2]
  - T2D
  - abdominal obesity and ≥1 additional metabolic risk factor
  - abnormal liver blood test results.

Useful Resources

- The British Liver Trust:
  - *Coffee consumption and the liver—the potential health benefits*
  - *MASLD, NAFLD, and fatty liver disease*
- The EASL:
  - *Non-alcoholic fatty liver disease (NAFLD): how you can reduce the risk for your liver and for other health issues?*

Hugh

Age	72
History	Non-specific malaise for around 3 weeks with mild headache and pain in his left knee
PMH	Generalised moderate OA affecting back and both knees
Systemic enquiry	Nil of note
Examination	Unremarkable
Bloods	FBC/LFT/U&E normal ESR 35 CRP <1

What do you do next?

1. Look up "Raised ESR" on GPnotebook before realising you've used up your 3 open access pages
2. Check a myeloma screen
3. Trial of steroids for possible PMR
4. Refer urgently to rheumatology for possible GCA
5. Arrange abdominal USS to exclude renal carcinoma
6. Wait & see if he develops any symptoms

Use of CRP & ESR in Primary Care

- BJGP 2019 & BMJ 2012 
- Commonly requested in primary care for diagnosis & monitoring of inflammatory conditions, infections, autoimmune conditions and cancers
  - Linear increase in requests over last 15 years
- Often both ESR & CRP checked
  - False-positives common leading to increased appointments, tests & referrals
  - Discordant results also common

- Which is better ESR or CRP?
  - Little evidence comparing…
- **Guiding principle as always is treat the patient not the number**

- **ESR**
  - Rule of thumb for ULN
    - Women – (age+10) divided by 2
    - Men – age divided by 2
  - NB affected by gender, age, pregnancy, temperature, drugs, smoking, plasma protein concentrations & RBCs
  - Rises over 24-48 hours and decreases slowly taking weeks to normalise
  - **ESR >100mm/hr >97% PPV for significant illness**
    - Rule out malignancy esp. myeloma or renal & GCA
  - Evidence suggests ESR better for suspected myeloma (BMJ 2018) but protein electrophoresis or urinary BJP preferable if strong clinical suspicion
  - RA – refer if clinical suspicion of RA even with normal inflammatory markers (NICE NG100 2018)

- **CRP**
  - Rises more rapidly in response to infection (within 12 hours); $t_{1/2}$ 12-24 hours and 3-7 days to normalise
  - Not affected by above factors
  - Can be useful to check CRP if elevated ferritin

- **BJGP 2019**

BJGP

  - Large observational studies comparing diagnostic accuracies of CRP & ESR and also whether checking both improves accuracy
  - Little difference in accuracy of CRP & ESR
    - CRP had slightly superior diagnostic accuracy for infections
    - CRP equivalent for autoimmune conditions & cancers
    - **CRP should generally be 1st-line test**
  - **Testing multiple inflammatory markers simultaneously did not increase ability to rule out disease**
    - Associated with more abnormal & discordant results and increased costs
    - NPV of a single test similar to that of multiple tests
  - Overall, inflammatory markers have low accuracy for disease outcomes with the exception of PMR
    - Inflammatory markers have poor sensitivity and should not be used as a rule-out test
  - "***For every 1000 inflammatory marker tests performed, anticipate 236 false positive results generating an additional 710 GP appointments, 229 phlebotomy appointments and 24 referrals in the next 6 months***"

- **Key take-home messages:**
  - Normal inflammatory markers useful in ruling out only a few specific conditions – PMR, GCA, myeloma & infection of hip revisions
  - Raised inflammatory markers very common and do increase probability of a condition being present but further evidence required
  - Inflammatory markers are too non-specific to be a useful tool for diagnosing serious underlying disease
  - If raised inflammatory markers incidentally found and no clues from history or examination for cause, wait & see if symptoms develop
  - If levels markedly raised (ESR>100mm/h) likelihood of disease much higher and focused history, examination & investigations required to establish a diagnosis

Hugh

Age	72
History	Non-specific malaise for around 3 weeks with mild headache and pain in his left knee
PMH	Generalised moderate OA affecting back and both knees
Systemic enquiry	Nil of note
Examination	Unremarkable
Bloods	FBC/LFT/U&E normal ESR 35 CRP <1

I phoned Hugh to discuss his results.

His headache had settled but he was still feeling non-specifically unwell. Nothing new on history.

Hugh gradually improved over the subsequent 2 weeks without treatment or further investigation.

His bloods were not repeated

“

‘The art of medicine consists in amusing the patient while nature cures the disease’

Voltaire 1694-1778

Hamish

Age	21
History	Ongoing lethargy since glandular fever a few months ago
PMH	Nil
Bloods	Hb normal WCC 3.2 (4-11) with neutropenia 1.2 (2.0-7.5)

Low white cell counts: neutropenias

- Usually seen transiently following a viral infection
  - Usually within 1-2 days and may persist for weeks
- If no recent infection, consider:
  - **Ethnicity**
    - Black Africans & some Middle Eastern & Jewish ethnic groups can have normal neutrophil counts down to 1.0 or lower
  - **Nutritional**
    - B12 & folate deficiency, alcohol dependency, anorexia
  - **Sepsis**
  - **Iatrogenic**
    - Chemotherapy, colchicine, carbimazole, PTU, clozapine, sulfasalazine, antibiotics (including penicillins), SUs, ACE inhibitors, bendroflumethiazide, ranitidine & NSAIDs
  - **Autoimmune** e.g. SLE, RA
  - **Bone marrow pathology** e.g. leukaemia, myelodysplasia, aplastic anaemia
  - **Splenomegaly**

Neutropenias - management

CLASSIFICATION	NEUTROPHIL COUNT ($x10^9/L$)
Mild	1.0-2.0
Moderate	0.5-1.0
Severe	<0.5

- **Medication review**
  - Drug-induced neutropenias should recover within a few days – recheck FBC 1 week & advise patient to seek urgent medical attention if become unwell or pyrexial

- **Risk of infection rises as neutrophil count falls**
  - **Significant risk if <0.5** but if <1.0 then the patient should be warned about the risk of infection
  - If severe & prolonged may be offered protective isolation in hospital

CLASSIFICATION	NEUTROPHIL COUNT ($x10^9/L$)
Mild	1.0-2.0
Moderate	0.5-1.0
Severe	<0.5

- **If moderate or severe neutropenia:**
  - If unwell or fever arrange urgent referral
  - If well and apyrexial
    - Advise to seek urgent medical attention if becomes unwell or febrile
    - Repeat FBC 48 hours, if neutropenia persists d/w specialist
  - **In persistent moderate neutropenia with no obvious cause**
    - Examine for lymphadenopathy & splenomegaly
    - Consider checking blood film, ANA, anti-CCP, haematinics & ferritin, serum protein electrophoresis, HIV status, hepatitis serology

- **If mild neutropenia**
  - Repeat FBC 1-2 weeks. If persists >6 weeks investigate further as above
  - Only refer haematology if neutrophils persistently <1.0 or if other FBC abnormalities develop
  - If stable after a few months and no other abnormalities, check annually for 2 years after which no further follow-up required if patient is well

Low white cell counts: lymphopenias

- Lymphocyte count usually 1.5-4.0x10^9
- **Common especially in the elderly – no further investigation required if >0.5 in absence of any symptoms**
- Wide differential diagnoses!
  - Acute illness & chronic infection including HIV or TB
  - Autoimmune disease or connective tissue disorder
  - Corticosteroid or other immunosuppressive therapy
  - Renal or cardiac failure and pancreatitis
  - Malignancy – both haematological and non-haematological and treatments both chemotherapy or radiotherapy
  - Cryptogenic

- **Base any further investigation or referral on clinical history or examination rather than the lymphopenia itself!**
  - Consider FBC, blood film, haematinics, Ig, anti-CCP. ANA, HIV if <1.0 or <0.5 in over 70s
  - Can monitor isolated lymphopenia >1.0 in otherwise well patient <70y with normal examination & investigations. Repeat FBC 6-monthly for 1 year. If normal no further tests

Thrombocytopenia

- Low platelet count defined as <150
  - Usually asymptomatic until platelets <50, spontaneous bleeding more common <20-30
    - Often bruising, petechiae & mucosal bleeding but more serious bleeding can occur
  - Avoid NSAIDs or anticoagulants if platelets <50-70

- Differential diagnoses:
  - **Spurious** (platelet aggregates or clumps)
  - **Infection especially viral including HIV**
    - Consider HIV testing in anyone with unexplained low WCC or platelet count >4 weeks
  - **Alcohol excess or liver disease**
  - **Hypersplenism**
  - **ITP**
    - Can be spontaneous or triggered by other autoimmune conditions, lymphoproliferative disorders, medication (classically quinine), infection & vaccination
  - **DIC** – acute or chronic
  - **Iatrogenic** e.g., heparin-induced thrombocytopenia
  - **Bone marrow failure** e.g., haematological malignancy or metastatic solid tumour

Thank-you for listening. Any questions?

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 Kevin Fernando