Lipids Made Easy:

Lessons From Lipid Clinic

Introduction

- While working as a chemical pathology registrar I undertook 4 year of lipid clinics.
- Understanding lipid disorders doesn't need to be daunting.

Objectives

- 1. To understand some fundamental concepts, such as what lipids are and the lipid pathway.
- 2. To know which questions to ask and what investigations to arrange when reviewing someone with hypercholesterolaemia in general practice.
- 3. To discuss some memorable cases, which may help you, if faced with similar scenarios in the future.

Basic, but fundamental concepts to understand lipids

- What are lipids and what are lipoproteins?
- What is the exogenous and endogenous lipid pathway?

Basic, but fundamental concepts for understanding lipids

- Now made easy (hopefully)

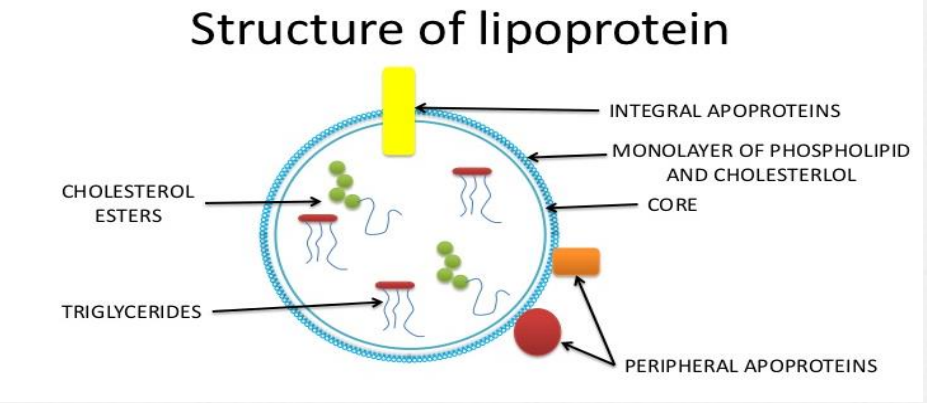
What are lipids and what are lipoproteins?

- Lipid definition: soluble in organic solvents and insoluble in water (includes bile acids, phospholipids, fat soluble vitamins and lipoproteins).
- We need some lipids e.g. for lipid membranes of cells, making fat soluble etc, but too much can accumulate in vessels and causes atheroma/CVD.
- HDL, LDL, VLDL (liver made triglycerides) and chylomicrons (diet triglycerides) are the four main lipoproteins in our bodies.

Lipoproteins Job Description: transport fats around the body in plasma

- Plasma is a hydrophilic environment. Cholesterol and triglycerides are hydrophobic.

- Lipoproteins contain in their core (and thus allow the travel of) hydrophobic cholesterol/triglycerides in plasma.



Lipoproteins (HDL, LDL, TG, CM)

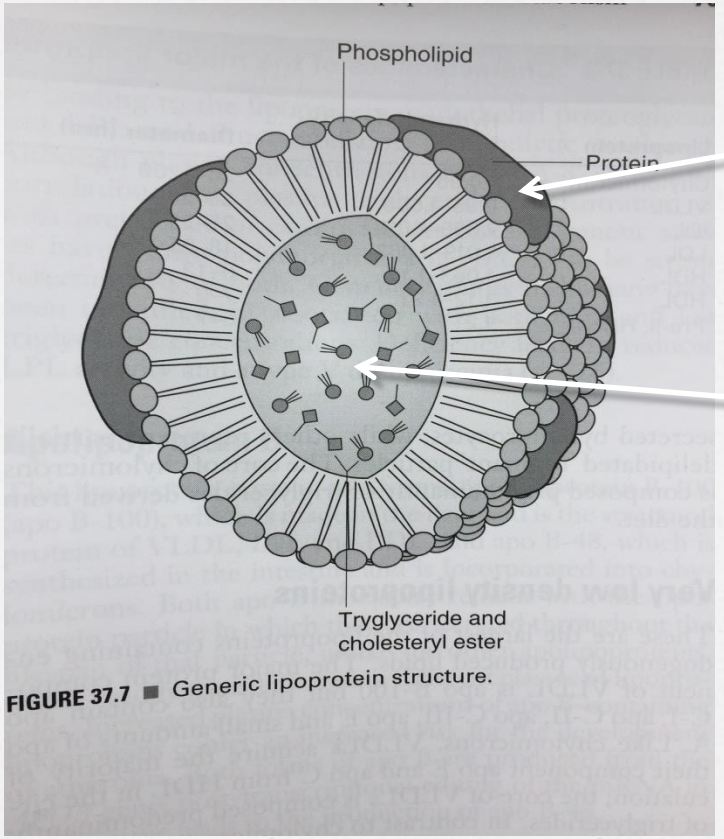


FIGURE 37.7 ■ Generic lipoprotein structure.

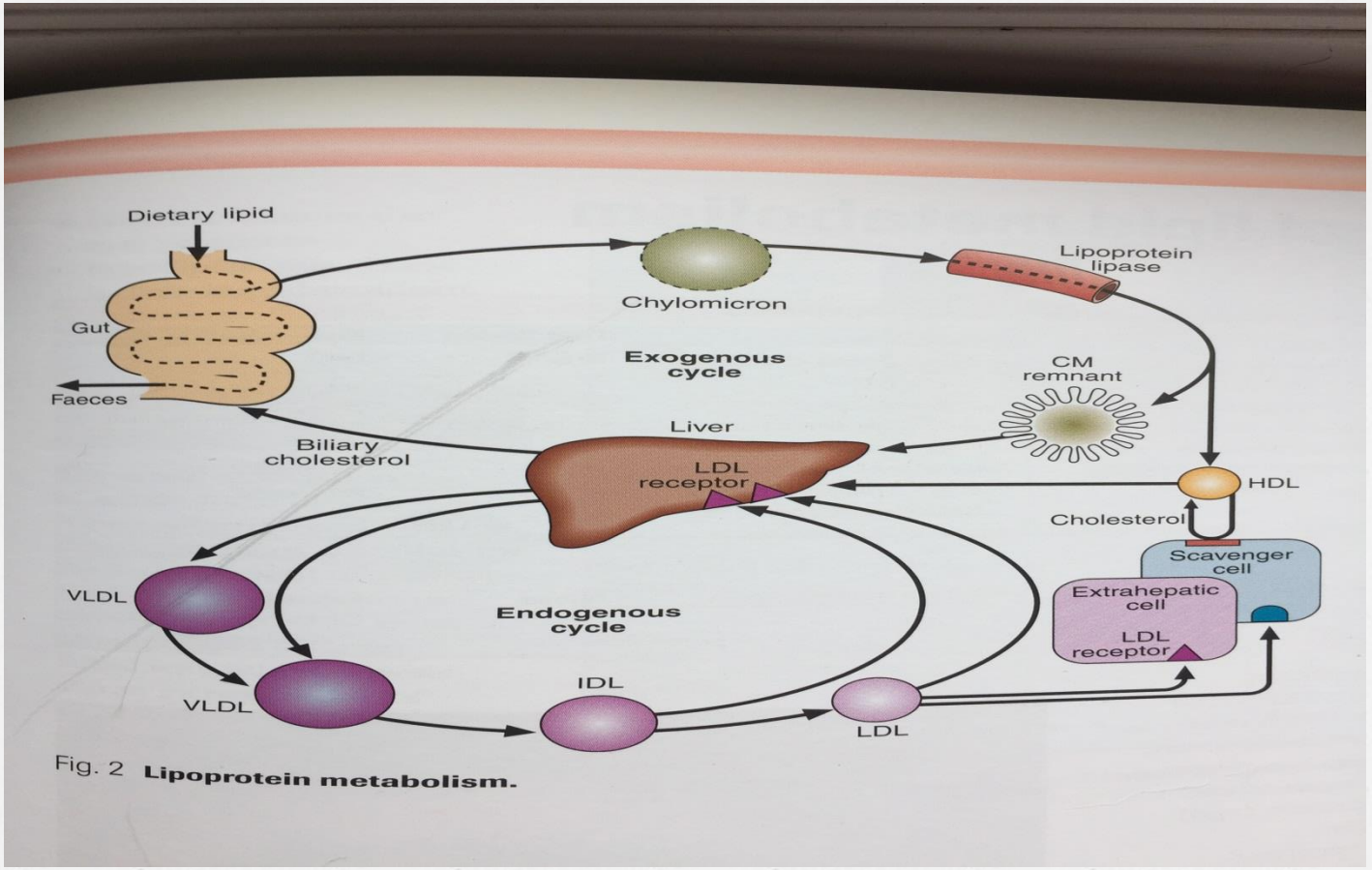
Type of protein (apoliop) here

and

Content/Ratio of TG/Cholesterol here

Decides if the lipoprotein is HDL, LDL, triglyceride or a chylomicron molecule.

The Lipid Pathway: Made Easy!



Summary: CM, HDL, LDL, TG

- Chylomicrons: made in gut after meal, not present in fasting plasma. Main carrier to exogenous (diet) triglycerides.
- VLDL: made in liver. Main carrier of endogenous (liver made) triglycerides.
- LDL: made from VLDL. Main carrier of cholesterol.
- HDL: smallest lipoprotein. Protective function. Takes cholesterol to liver for excretion.

A commonly faced lipid scenario in General Practice

Miss Jones

- 27 year old female.
- Comes to a 10 minute appointment very upset. Uncle is in CCU.
- He had a heart attack. One of the nurses mentioned high cholesterol.
- She’s been googling and is very worried she’s now going to have a heart attack and wants her cholesterol checked.

Miss Jones

- Would you measure her cholesterol?
- What questions would you ask her during the consultation?

Miss Jones

- Her total cholesterol is 8mmol/L.
- What test should you have done first and/or should do you do now?

Miss Jones

- Full (fasting if possible) lipid profile.
- TC 8mmol/L.
- HDL 1 mmol/L.
- LDL 6.1 mmol/L.
- TG 2 mmol/L.

- What are you worried about? Differential Diagnosis.
- What questions would you ask her now?
- What other tests should you do before referring to lipid clinic?

Familial Hypercholesterolaemia (FH)

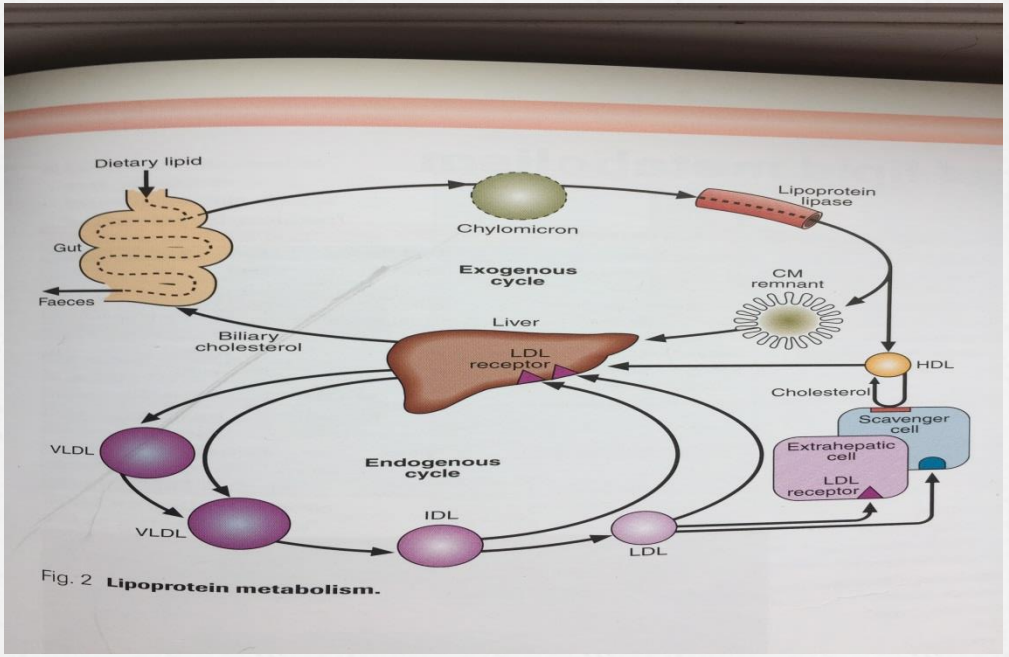
- Familial Hypercholesterolaemia (FH) should be considered.
- Adults with a total cholesterol >7.5 mmol/L or LDL-C >4.9 mmol/L, (especially if there is a personal or family history of premature CVD <60 years old).
- Children <16 if total cholesterol >6.7 mmol/L or LDL-C >4.0 mmol/L.
- If FH is considered please refer patients to the lipid clinic

Familial Hypercholesterolaemia (FH)

- Autosomal dominant
- Prevalence 1/500 quoted, BHF says more common.
- Significantly high TC and LDL (from birth - big clue! Previous normal lipid profile while not on medication/without other cause of lower result. FH very unlikely)
- Without treatment **significant** risk of premature CHD.
- Children treated from 8-10 years old. Then have same CHD risk as general population.

Understanding the lipid pathway is useful!

4 types of FH; classic FH due to mutation LDL receptor genes



Another common lipid scenario in General Practice

Mrs Davies

- 50 year old lady comes in for a routine check up.
- She has put on a stone in weight and has been feeling tired lately.
- Her lipid profile results are back the next day

  -TC 8mmol/L

  -HDL 1 mmol/L

  -LDL 6.1 mmol/L

  -TG 2 mmol/L

Mrs Davies

-TC 8mmol/L
-HDL 1 mmol/L
-LDL 6.1 mmol/L
-TG 2 mmol/L

What do you do?

- Could she have FH?
- What questions do you ask her?
- What other results would be really useful to help you decide what to do?

Mrs Davies

- HbA1c 38 mmol/L.
- Renal function - eGFR >90ml/min/1.73m².
- Liver function normal.

- TSH 20 mIU/L (reference range 0.27-4.2)
  fT4 4nmol/L (reference range 12-22)

- Do you start a statin?

Mrs Davies

- If significant hypothyroidism is identified
  - -and patient does not have established CVD,
  - -and there is no concern of a genetic dyslipidaemia,
  - -exclude other secondary causes of dyslipidaemia (alcohol, DM, liver, renal disease, advise on diet).

Do not start lipid lowering medication but first repeat the lipid profile once patient is euthyroid. If dyslipidaemia persists when patient is euthyroid, re-consider lipid lowering treatment

Repeat lipid profile

	Repeat Result	Initial Result
Total Cholesterol	4.5	8
HDL cholesterol	1	1
LDL Cholesterol	2.6	6.1
Triglycerides	2	2

Lipid Assessment in Primary care –Primary Prevention

- **Before considering lipid lowering therapy do the following:**

- A full lipid profile should be requested (cholesterol, HDL, Non-HDL and triglycerides). The patient does not need to be fasted; however a fasting sample is advantageous in suspected hypertriglyceridaemia.

- Secondary causes of hyperlipidaemia should also be investigated and treated (e.g. hypothyroidism, renal impairment, liver disease, DM, alcohol excess, obesity and medications).

Lipid assessment in primary care: Primary Prevention

- **Before considering lipid lowering therapy do the following:**

- Measure TSH, HbA1c and baseline liver and renal function.
- Consider measuring CK.
- Council the patient on smoking cessation, alcohol consumption and weight loss (if appropriate).
- When deciding if lipid lowering therapy should be offered their cardiovascular risk should be estimated using an appropriate cardiovascular disease (CVD) risk calculator (e.g. QRISK®3).

QRISK3 Score

Caution

- Statins should be avoided in patients with liver transaminases (ALT & AST) of >3 times upper limit of normal.
- or creatine kinase (CK) of persistently >5 times upper limit of normal.

- Avoid high dose statins in mild renal impairment. When eGFR <30 ml/min/1.73m^2, do not start a statin but seek advice from the renal team.

Lipid assessment in primary care: Secondary Prevention

- For secondary prevention (i.e. in those with evidence of CVD) lipid modification therapy should be offered without delay.

- Secondary causes of hyperlipidaemia should also be investigated and treated (e.g. hypothyroidism, renal impairment, liver disease, alcohol excess, obesity and medications).

Help!
Who to call

- Non-urgent advise: ESR advise and guidance service, endocrine/lipid disorder (response within two working days).
- Urgent: duty biochemist ext 5238
- Dr Kok-Swee Gan and Dr Balasubramani

A final interesting case presenting to General Practice then the lipid clinic

Background

- 36 year old man referred to the lipid clinic by his GP.
- Has a low HDL cholesterol of 0. 2 mmol/L (normal 1-2mmol/L).

Background

- PMH: Asthma, personality disorder.
- DH: Carbamazepine OD, inhalers and tramadol as required.
- FH: No premature cardiovascular disease (Parents developed angina in their late 60’s).
- SH: Delivery driver. Attends the gym most days. Ex smoker.
- Poor diet: No fruit/vegetables

Examination findings

- Heart sounds normal, no carotid bruits. Pedal pulses easily palpable. No peripheral stigmata of high cholesterol
- 0/E muscular physique.

Examination findings

- There’s a subtle clue in the history.
- Any thoughts?

Background

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- Poor diet: no fruit/vegetables
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Anabolic steroid use history

- 18 year history of regular cycles of anabolic steroids (injections and tablets).

- Preparations contained testosterone derivatives; metandienone, testosterone enanthate, testosterone propionate, testosterone cypionate and oxymetholone.

Anabolic steroids

- Anabolic steroid use is a known independent risk factors for cardiovascular disease
- A low HDL cholesterol is a known independent risk factors for cardiovascular disease
- There isn’t much, but some literature on the associations between anabolic steroids AND low HDL cholesterol.

Lipid profile

Total cholesterol	**5.8 mmol/L**
HDL cholesterol	0.2 mmol/L
LDL cholesterol	4.8 mmol/L
Triglycerides	1.7 mmol/L

Current Literature

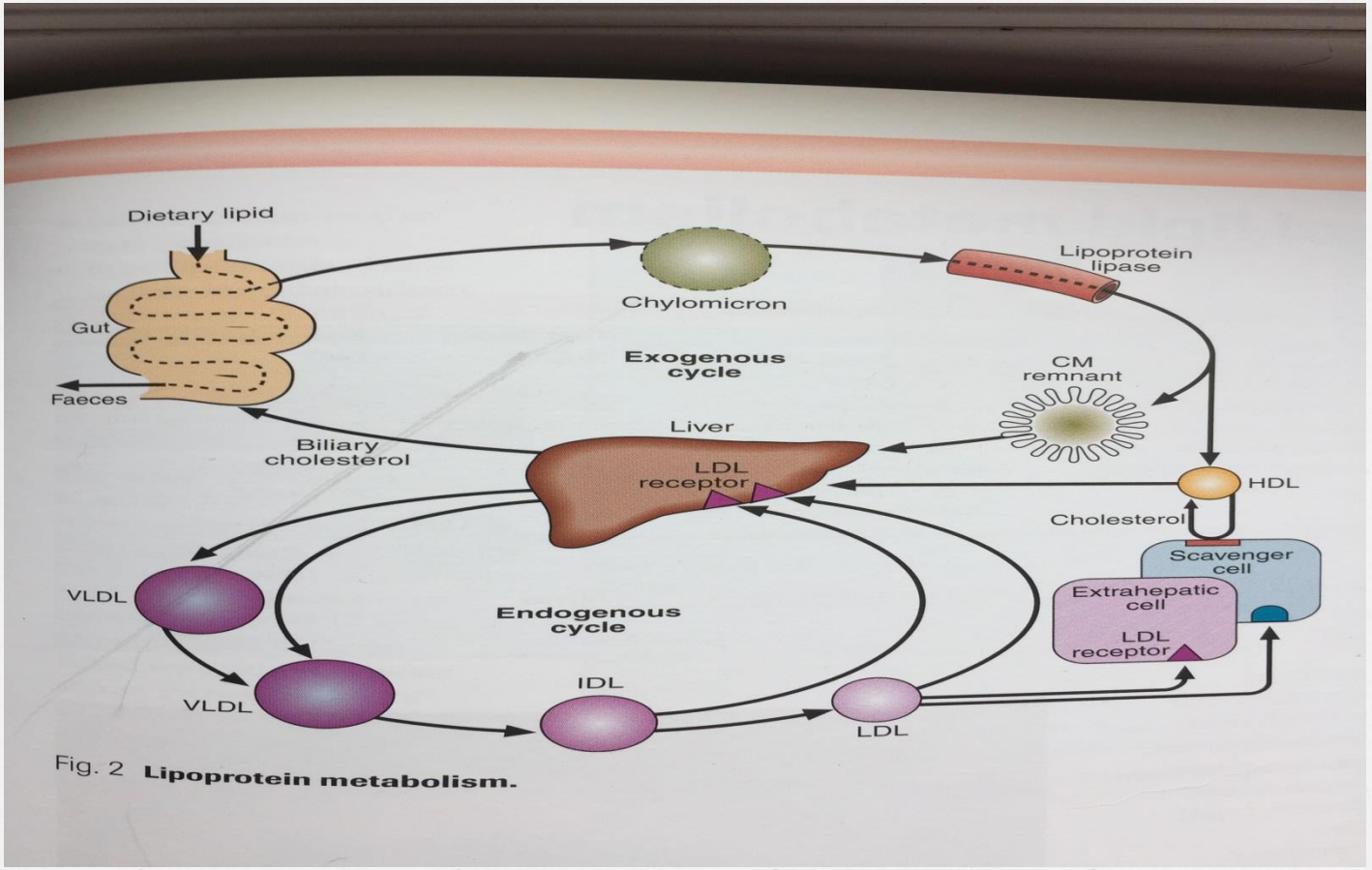
- Narayanan, D et al. 2012. A reversible rise in the total cholesterol to HDL ratio in a body builder.

- Case report; demonstrating low HDL cholesterol of similar levels to our patient in a man taking anabolic steroids, with reversion to normal two months after stopping use

Mechanism

- Still unclear.
- Angell, P et al Anabolic Steroids and Cardiovascular Risk.
- One review paper cited one study which suggested as there was an increase in hepatic triglyceride lipase (HL) with anabolic steroid use in their study that HL may have a catabolic effect on HDL (*the good lipoprotein shuttling LDL to liver to be excreted).*

The Lipid Pathway: Made Easy!



Discussion

- We strongly suspect that the patient's low HDL cholesterol is secondary to anabolic steroid abuse.
- He was advised to stop taking anabolic steroids immediately, and agreed to do so.
- His lipid profile was reassessed three months later.

Repeat lipid profile

	Repeat Result	Initial Result
Total Cholesterol	4.8	5.8
HDL cholesterol	1.0	0.2
LDL Cholesterol	3.3	4.8
Triglycerides	1.1	1.7

Objectives

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- 2. To know which questions to ask and what investigations to arrange when reviewing someone with hypercholesterolaemia in general practice.
- 3. To discuss some memorable cases, which may help you, if faced with similar scenarios in the future.

Please remember

- A full lipid profile is needed (fasting is best).
- Think of genetic and secondary causes of dyslipidaemia (DM, alcohol, renal, liver function, alcohol, diet).
- Always check thyroid function (hypothyroidism can cause significant hypercholesterolaemia).
- Check liver and renal function prior to considering starting statins (?+CK).
- Don’t ignore the young fit patient with a family history of IHD and hypercholesterolaemia it could be FH.
- If in doubt call duty biochemistry for urgent queries or endocrine/lipidologist referral.

Questions?