3.1: Pathology

The previous section examined the importance of clotting factors in maintaining the necessary integrity of the circulatory system and fluidity of blood. However, there can be instances where there are disequilibria of other components such has macronutrients. There are three main macromolecules which include proteins, carbohydrates, and lipids. This section is largely focussed on altered blood lipid concentrations.

Lipids have multiple essential functions in the body:

- **Compartmentalization**: Every cell in the human body is separated from the external environment by a phospholipid bilayer structure. Additionally, lipids are also used in sub-cellular compartmentalization.
- **Energy storage**: Lipids contain the highest energy per gram (compared to other macronutrients) and are used as efficient energy storage molecules. Generally, the more reduced a carbon atom is in a biological molecule, the more energy is stored.
- **Cellular signalling**: Different biochemical pathways rely on the presence or absence of specific lipids, such as the inflammatory response or hormones signalling.
- **Dietary absorption**: The body uses different lipids (often stored as bile) to aid the digestion and absorption of hydrophobic or fatty substances.

Although lipids are critical for normal physiological functioning, excess cholesterol or fatty acids in the blood can lead to a condition referred to as **hyperlipidemia**.

Types of Biological Lipids

It is recommended to consume ~20-35% of the total daily caloric intake from dietary lipids. There are three main types of lipids that are also shown in Figure 3.1:

- Triglycerides: These lipids have an invariant glycerol backbone (3-carbon chain with 3-hydroxyl groups) where each hydroxyl group is esterified to a fatty acid. The type of fatty acid that is bound to the glycerol can vary. These molecules are highly non-polar and comprise ~95% of dietary lipid uptake (fats and oils).
- Phospholipids: These are similar to triglycerides in that they have a glycerol backbone. However, phospholipids only have two fatty acid groups and the third group is a phosphate head group. The phosphate headgroup drastically alters the properties of the lipid, in that there is now a highly hydrophilic moiety on one end of the molecule and two lipophilic tails on the other. Phospholipids comprise ~2% of the dietary lipids.
- Sterols: These are compounds based on a cyclopentaphenathrene ring (3 six membered rings and 1 five membered ring) and comprise approximately 3% of dietary lipids. In mammals, the most commonly known sterol lipid is cholesterol and all steroid-based hormones and bile acids are synthesized from cholesterol.

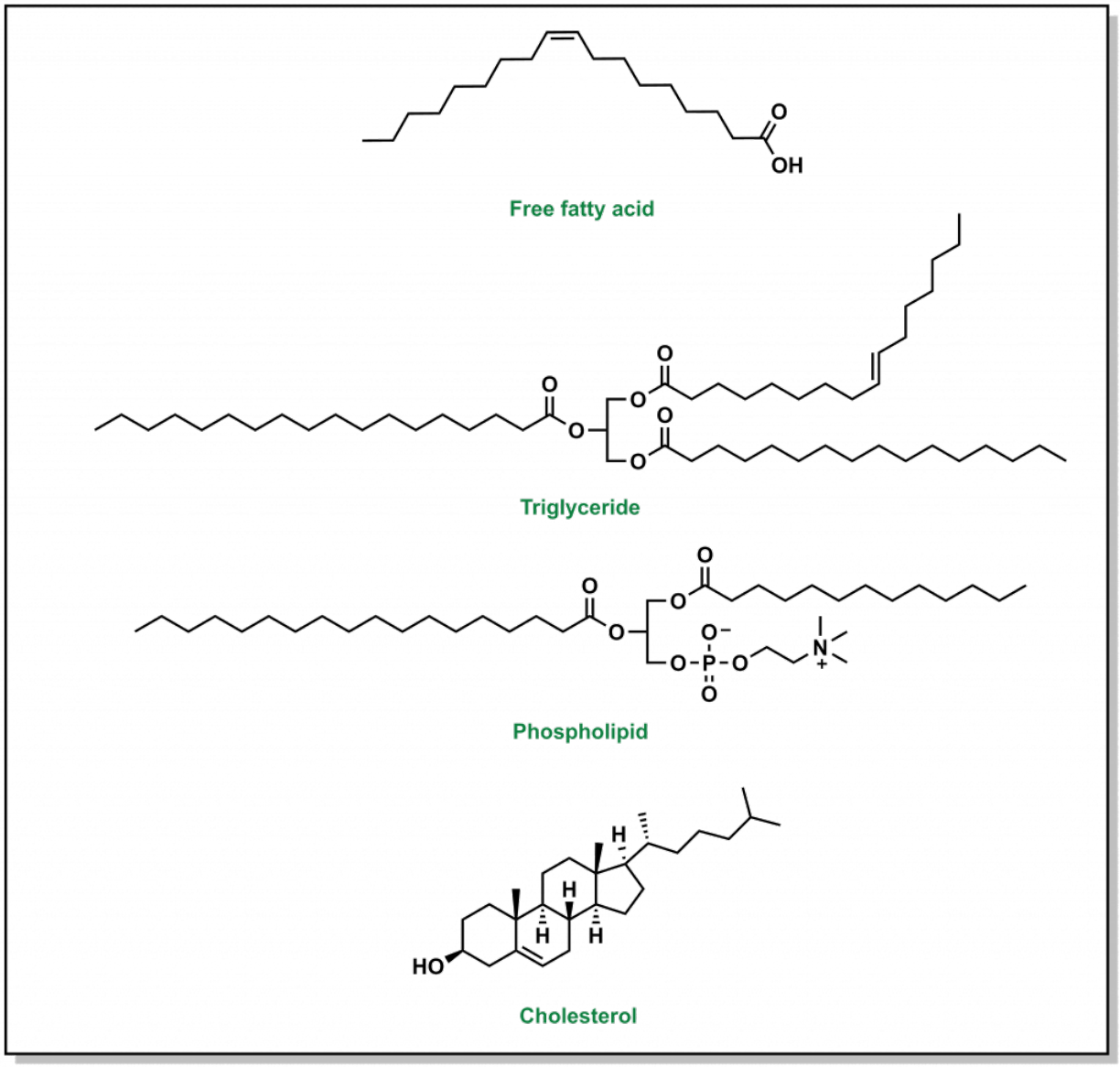

Figure 3.1 Representative structures of a generic fatty acid and the three main types of lipid macromolecules.

Lipids are very different from the other macromolecules in that they are largely hydrophobic and do not associate with water. Considering that the human body is ~70% water and that lipids are essential for every single cell in the body, transporting them across the body in the aqueous environment of blood is challenging because of the hydrophobicity. Therefore, lipids are transported in a complex particle comprised of both proteins and lipids, which are referred to as **lipoproteins**. The structure of a lipoprotein is shown in Figure 3.2. Lipoproteins have an outer shell of phospholipids intercalated with different proteins (referred to as apolipoprotein), and the inside is occupied with triglycerides and cholesterol. These lipoproteins travel through the blood stream and facilitate the transport of lipids.

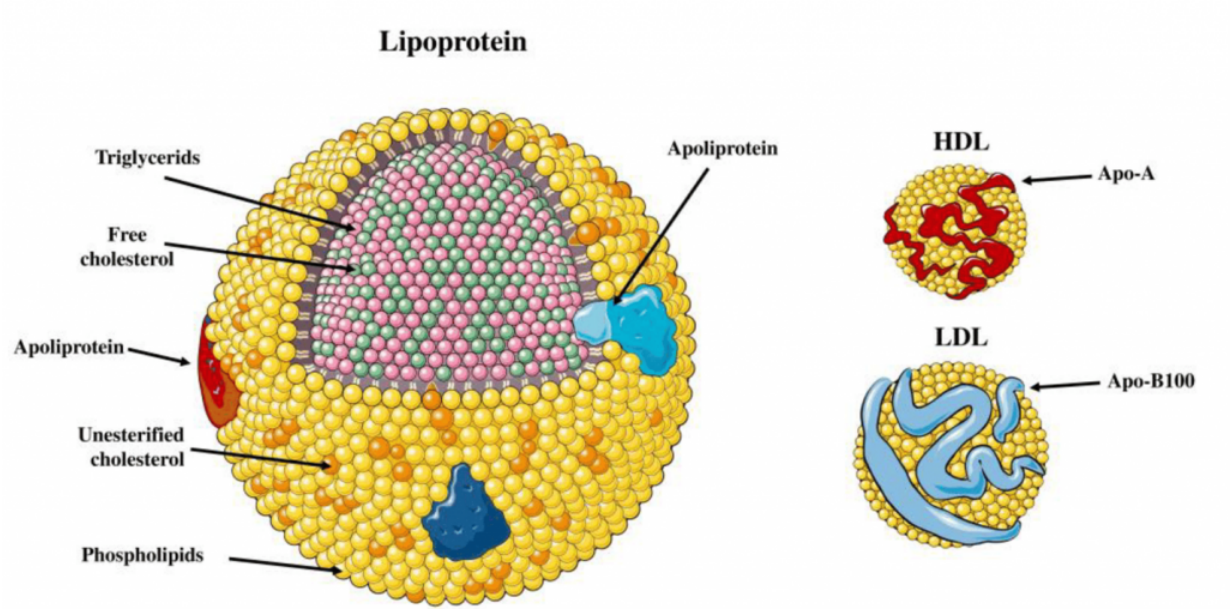

Figure 3.2 Representative structure of a lipoprotein. Image Source: (Fig 2) by Stamatios Lampsas, Maria Xenou, Evangelos Oikonomou, Panteleimon Pantelidis, Antonios Lysandrou, Savvas Sarantos, Athina Goliopoulou, Konstantinos Kalogera, Vasiliki Tsigkou, Athanasios Kalpis, Stavroula A. Paschou, Panagiotis Theofilis, Manolis Vavuranakis, Dimitris Tousoulis, Gerasimos Siasos is used under a CC-BY 4.0 license.

Lipoproteins have different names based on their composition and density. (Figure 3.3) Lipids that are high in protein content are referred to as high density lipoproteins (**HDLs**) and if they have intermediate, low, or very low densities of lipoproteins they care called **IDL**, **LDL**, and **VLDL**, respectively. HDLs are also relatively small in diameter (5-10 nm) compared to LDL and VLDL which are 20 – 50 nm. There are also larger classes of lipoproteins called **chylomicrons** which are important for digestion and absorption of fats. Colloquially, the HDLs are often thought of as “heathy cholesterol” and the LDLs and VLDLs are referred to as the “unhealthy fats”. From a general sense, larger particles have higher lipid content and lower stability.

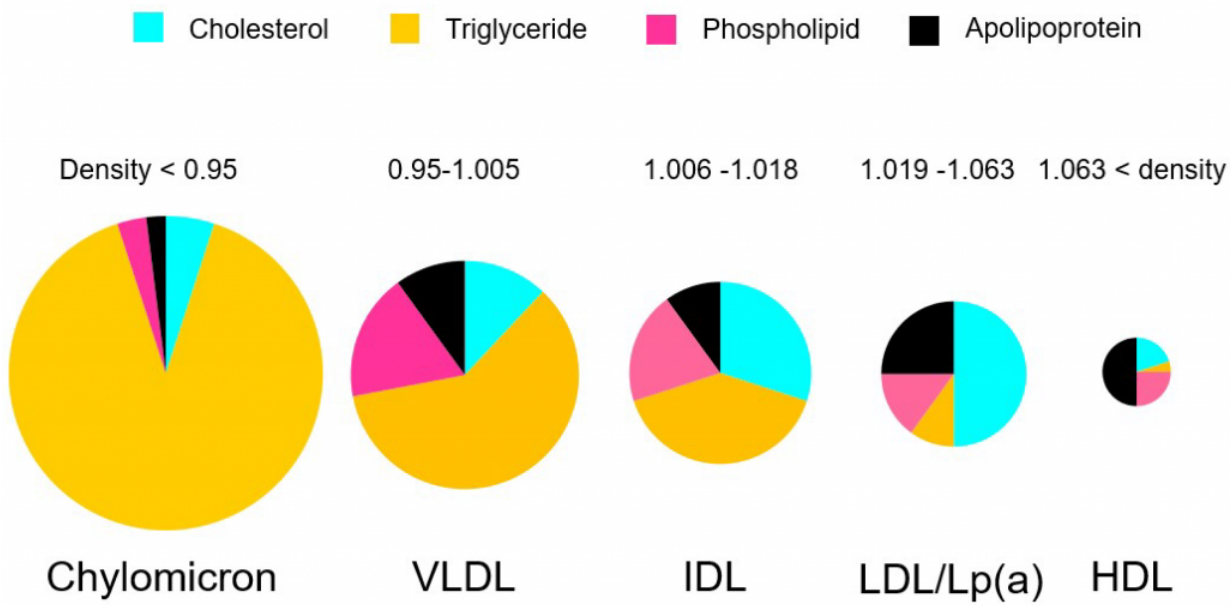

Figure 3.3 Approximate proportion of lipids and proteins in different types of lipoproteins. Image Source: (Fig 1) by Hayato Tada, Atsushi Nohara and Masa-aki Kawashiri is used under a CC-BY 4.0 license.

Hyperlipidemia occurs when there is an excess of lipids leading to a high concentration of LDL and VLDL. These fats can precipitate out of the blood stream and start to nucleate on the arterial walls and form a blockage of blood flow. (Figure 3.4) These blockages are referred to as plaques and reduce the arterial lumen, leading to a reduction in blood vessel elasticity, and create a nucleation site for additional thrombi. The primary goal of treating hyperlipidemia is to reduce concentrations of LDL and VLDL.

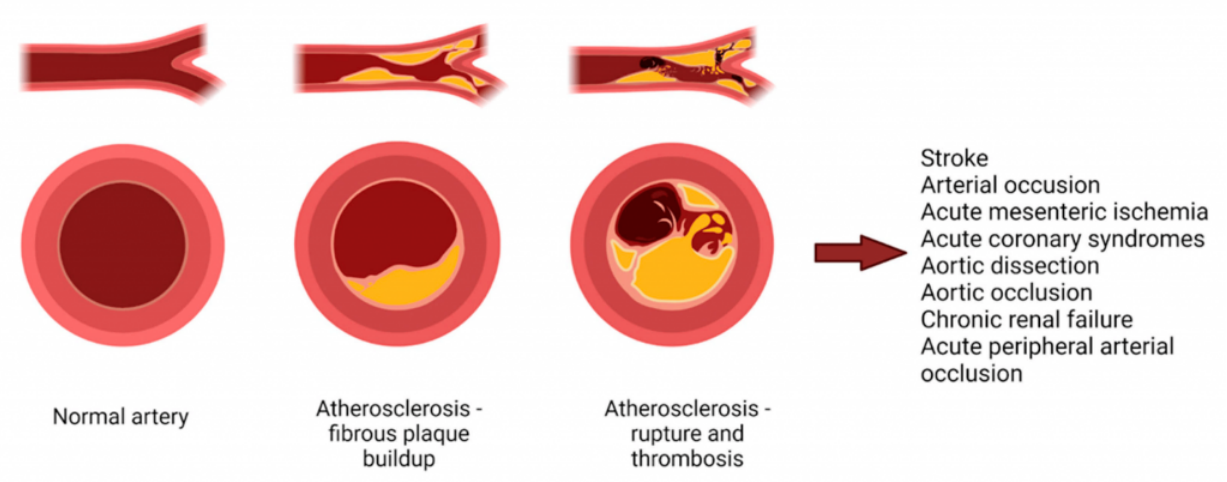

Figure 3.4 Effects of hyperlipidemia on the arterial lumen. Image Source: (Fig 1) by Dragos Cretoiu, Ruxandra Florentina Ionescu, Robert Mihai Enache, Sanda Maria Cretoiu and Silviu Cristian Voinea is used under a CC-BY 4.0 license.
