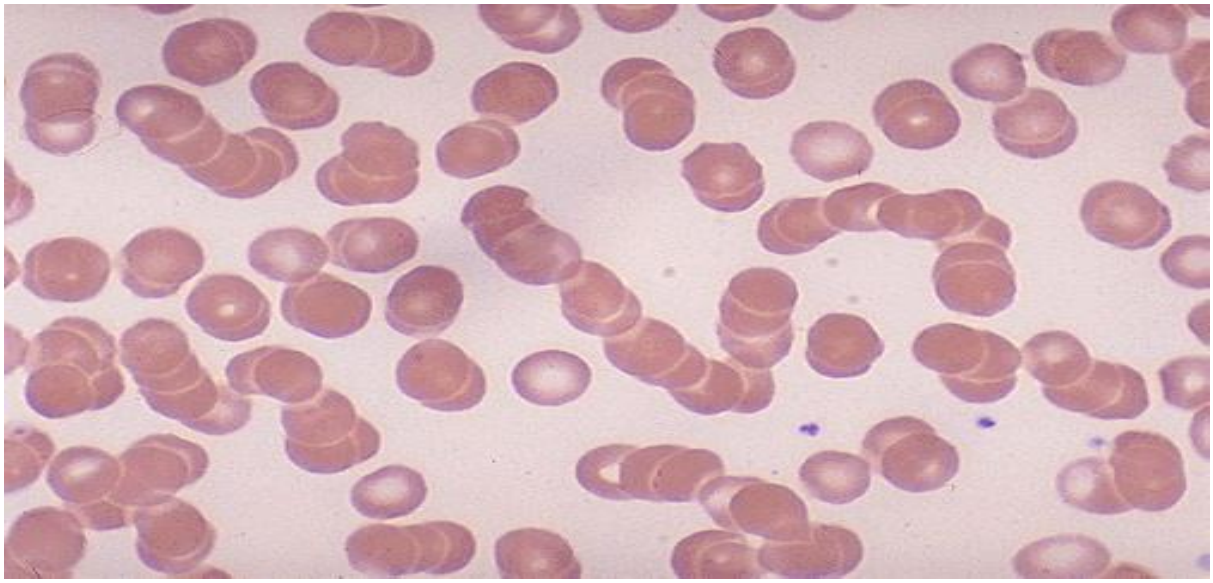
Animal fats & plant oil oxidation in pathophysiology of atherosclerosis: heart attack, stroke & peripheral vascular disease

After a fatty meal, a person experiences postprandial lipemia, where fats from the meal are converted into blood fats like triglycerides and lipoproteins, which can be detected in blood tests within hours. The presence of these triglyceride-rich chylomicrons can make the blood appear cloudy or "lipemic." While it is normal for blood fats to rise after a fatty meal, excessive levels can be a sign of cardiovascular risk. Testing for postprandial lipemia can provide more information about your long-term health. High levels of blood fats, also known as hyperlipidemia, can cause red blood cells to stick together in chains that appear under a microscope. This phenomenon is known as rouleaux.



As illustrated above: Rouleaux are stacks of red blood cells that resemble stacked coins and are caused by the presence of certain proteins and fats in the plasma that disrupt the normal repulsive forces between red blood cells.

Rouleaux indicates the stacking of red blood cells, which can signify underlying conditions such as inflammatory diseases, infections, or certain cancers like multiple myeloma. Rouleaux can be associated with increased blood fats, and this is linked to defective efferocytosis, a process that becomes impaired in chronic inflammatory conditions like atherosclerosis and obesity. Defective efferocytosis leads to the accumulation of apoptotic cells and lipids, which promotes inflammation

and plaque formation in arteries. an increased blood fat level, or dyslipidemia, can inhibit pancreatic beta cells, a process known as lipotoxicity. Chronic exposure to high levels of free fatty acids (FFAs) can impair beta cell function, leading to reduced insulin production and eventual cell death. This process contributes to the development of type 2 diabetes.

A chylomicron is a large lipoprotein particle, rich in triglycerides, that transports dietary fats, cholesterol, and fat-soluble vitamins from the intestines to the rest of the body via the bloodstream. These particles are produced in the intestinal cells after a meal and are essential for processing dietary lipids. They are a type of very-low-density lipoprotein (VLDL) and are responsible for the milky appearance of blood after a high-fat meal.

Free radicals oxidise LDL cholesterol. Many meats are already naturally high in LDL, whereas plants contain no LDL. When plant oils, especially those rich in polyunsaturated fatty acids like linoleic acid, are oxidised, they form harmful products, such as aldehydes. So, cholesterol reading will not indicate the presence of oxidised plant oils present in the body, which could be contributing to heart disease.

Standard blood cholesterol tests don't measure oxidised oils or their harmful byproducts, such as aldehydes, which contribute to heart disease. A standard LDL cholesterol test measures the *amount* of LDL cholesterol, not the *quality* of the LDL or the presence of these harmful oxidised byproducts. Therefore, dietary choices emphasising whole foods and a balanced intake of healthy fats with antioxidants are crucial for heart health beyond standard cholesterol management.

Cold-pressed virgin olive oil is considered the very best oil for cooking, of superior quality because it retains not only all of its sensitive aromatic properties, but also the antioxidants and nutrients that are often diminished by the high-speed machinery and elevated temperatures used in modern oil extraction methods. However, people would not realise just how sensitive it is to oxidation and present standards do not reflect scientific findings by the Australian Rural Industries Research & development corporation in its documented research paper on the 'effect of Storage Containers on Olive Oil Quality', which researches olive oils changes with time, temperature and exposure to oxygen and light. These findings expose poor storage and transport conditions that have never been addressed since reported in 2009. Current industry practices mean that the olive oil you buy may already have oxidised while sitting on the shelves before it was purchased. Considerations would be the time from press to bottling not being more than 4 hours maximum, the container never being clear or plastic, with the better option being tin, and when held in the very best tin container, never more than 4 months. On top of this is the storage in the home and exposure to allow oxidation and cooking methods, and temperatures.

Polyunsaturated oils can become dangerous due to processing methods like high-temperature cooking or industrial refining, which cause chemical changes like oxidation. Seed oils involve high heat and harsh chemicals. This can transform some polyunsaturated fats into harmful trans fats, and some processes may use synthetic antioxidants like BHA or BHT, which are known carcinogens. Seed oils are extracted with hexane. Hexane is toxic, particularly through chronic exposure, which can cause neurotoxicity leading to nerve damage, muscle weakness, and even paralysis. When polyunsaturated oils are heated to high temperatures, especially for frying, they are susceptible to oxidation. This process can generate a range of cytotoxic and genotoxic lipid oxidation products (LOPs).

These extraction processes can create harmful compounds such as lipid oxidation products (LOPs), trans fats, and other toxic aldehydes that are linked to

Increased health risks:

- **Increased risk of chronic diseases:** Ingesting these harmful compounds can contribute to the development and progression of non-communicable diseases (NCDs).
- **Atherosclerosis & Cardiovascular disease:** Aldehydic LOPs are linked to atherosclerosis and cardiovascular disease.
- **Cancer:** Some aldehydic LOPs have been found to have mutagenic and carcinogenic effects.
- **Inflammation:** Aldehydic LOPs can exert potent pro-inflammatory effects.
- **Neurotoxicity:** Some of these compounds may have neurotoxic properties.

What happens inside the body?

Macrophages internalise the modified LDL particles via scavenger receptors. If the cell becomes overwhelmed, the lipid-laden macrophages themselves form the fatty streak/deposit (plaque precursor). This disease process can start for some in their teens. When the lipid-laden foam cells (derived from macrophages or smooth muscle cells) can no longer manage the excess cholesterol, they undergo various forms of programmed cell death (apoptosis). The accumulation of these dead, lipid-rich cells, which are not efficiently cleared by other immune cells (a process called efferocytosis), leads to the formation and expansion of a large, unstable **necrotic core** within the plaque.

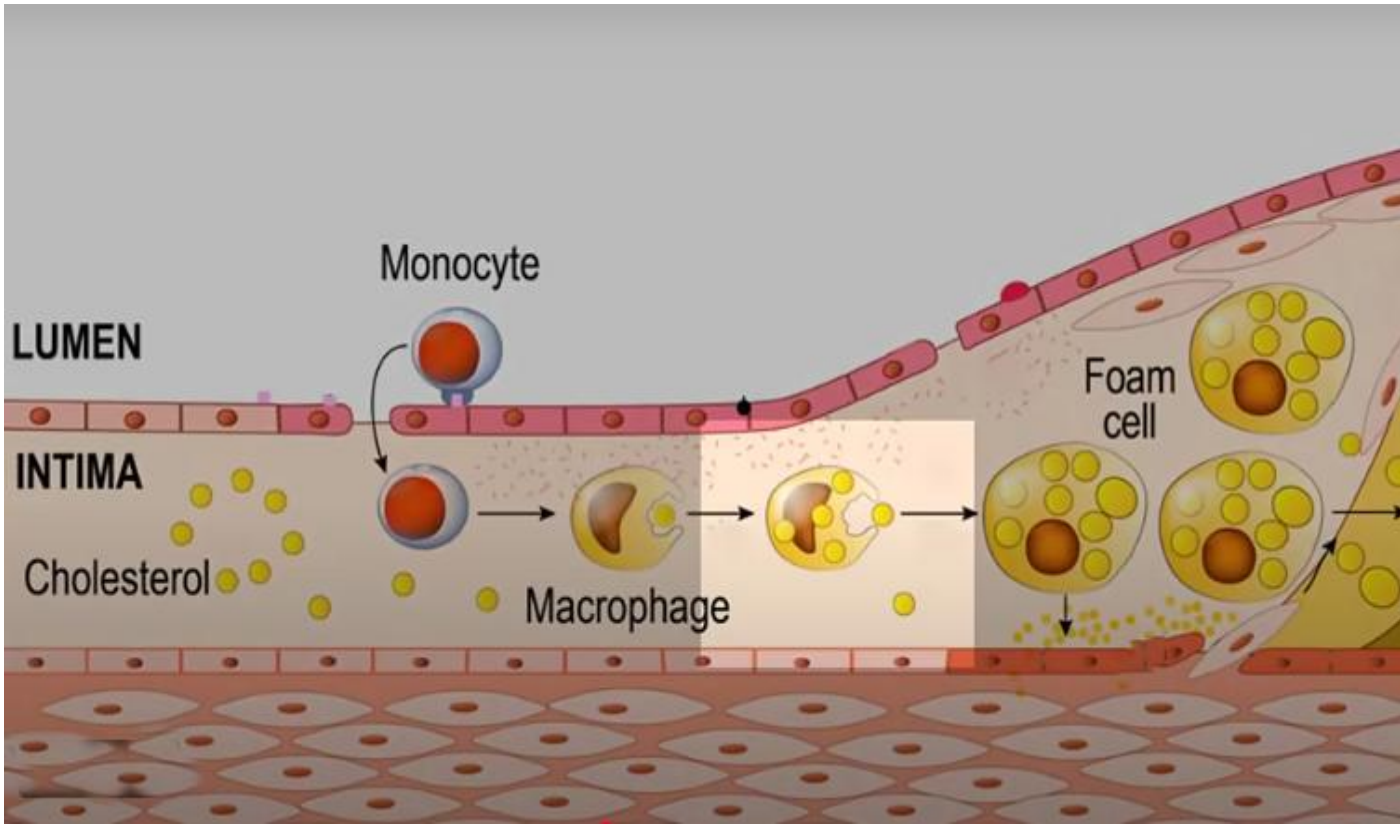
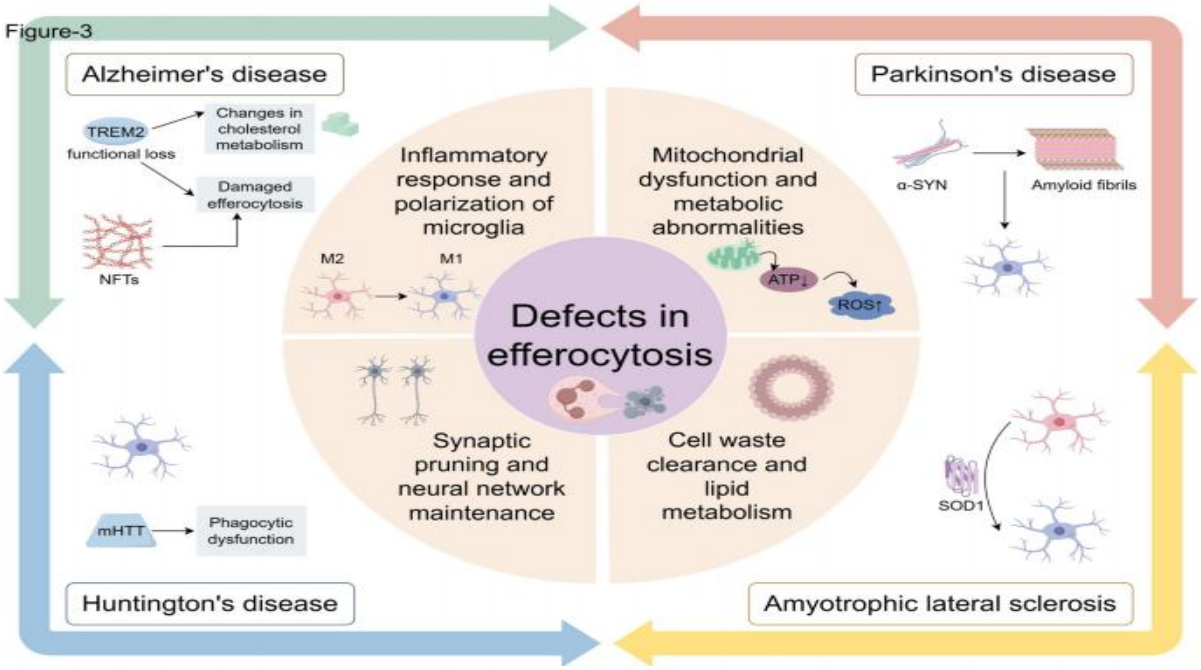


Illustration: Overview of the Development of Atherosclerosis.

Efferocytosis, or the process of **"cellular burial,"** prevents inflammation and promotes tissue repair. The combination of excessive cell death and the body's inability to clear the dead cells drives the development of the dangerous necrotic core. Dead cells and their debris contribute to the necrotic core, promoting further inflammation as the cell contents spill into the surrounding area. The process is similar to autoimmune disease, and which the **macrophage becomes a foam cell and attacks the body's arterial wall.** As oxidative stress continues with the wrong fuel being sent into the system, the body is unable to repair and clear the damaged arteries.



Shared mechanisms and disease-specific pathways of neurodegenerative diseases caused by defective efferocytosis. Efferocytosis: the art of cellular clearance and novel perspectives in disease therapy, Gege Li, Jiashuai Xu, Xiaohan Tian, Jingyi Xiao, Junqi Long, Yining Chen, Wenzhi Shen & Shuangtao Zhao

Foam cells secrete pro-inflammatory cytokines (such as TNF-α, IL-1β) and chemokines that continuously recruit more inflammatory cells (like monocytes and leukocytes) to the plaque site. This persistent inflammation exacerbates the disease progression and the overall damage to the arterial wall. This disease progression is from the continued influx of dangerous LDLs in which the body is unable to cope with the influx of dangerous oils and fats. Foam cells release inflammatory cytokines and chemokines, which recruit more inflammatory cells to the site, causing a persistent inflammatory cycle that damages arterial walls and promotes disease progression. The chronic inflammatory environment in the plaque driven by factors like TNF-α and oxidized low-density lipoprotein impairs the function of phagocytes. This creates a vicious cycle: failed efferocytosis leads to more inflammation, which further impairs the clearance process. The Endothelial cells form a single-cell layer lining all blood vessels, capillaries, and lymphatic vessels, a line of protection, which comes under attack from the foam cell. The process begins with an excess of LDL, or "bad cholesterol," in the blood. Macrophages in the artery wall take up and internalize modified LDL, a process that is part of a normal immune response, but becomes problematic when lipid levels are too high. Foam cells weaken the endothelium and impair its function primarily by releasing **pro-inflammatory cytokines**, generating **oxidative stress**, and inducing programmed cell death, which damages the endothelial barrier and increases its permeability.

Foam cells contribute to plaque instability by both a direct and indirect thinning of the fibrous cap, increasing the risk of rupture. Indirectly, foam cells release inflammatory mediators, including matrix metalloproteinases (MMPs), that break down the collagen and extracellular matrix (ECM) in the cap. Directly, foam cells and other inflammatory cells can undergo apoptosis (programmed cell death), leading to a loss of vascular smooth muscle cells (VSMCs) that are crucial for maintaining the cap's structure. While the body moves to protect the damaged artery wall with smooth muscle forming scar tissue, the foam cell again allows this area to come under attack, which can result in a stroke or heart attack. The verse rings true indeed: the life of the flesh is in the blood. Perfect health requires perfect circulation.

Summary

Macrophages internalise modified LDL particles through scavenger receptors, leading to foam cell formation that can start in adolescence. When foam cells are overwhelmed with cholesterol, they undergo apoptosis (programmed cell death). Inside the artery wall, monocytes differentiate into macrophages. Macrophages attempt to clear the oxidised LDL, but they ingest so much that they become overloaded and transform into foam cells. Inefficient clearance of these dead cells by other immune cells (efferocytosis) leads to a necrotic core, making plaques unstable. These foam cells accumulate, creating fatty streaks, and release inflammatory signals that attract more immune cells. Over time, smooth muscle cells also migrate to the area to form a fibrous cap over the buildup, creating a hardened, advanced plaque that can narrow arteries.

- **Choose heart-healthy foods**: Focus on a diet rich in fruits, vegetables, and other plant-based foods, and limit processed foods, red meat, and other high-cholesterol sources.
- **Properly prepared olives at every meal.** Oil in the olive as eaten in the fruit is preferable to extracted animal fats or processed oil. "**Olives may be so prepared as to be eaten with good results at every meal**". The "advantages sought by the use of butter may be obtained by the eating of properly prepared olives".
- **Cook at lower temperatures**: High cooking temperatures can promote cholesterol oxidation.
- **Vegan/Plant-based diets** are important in treating & preventing chronic disease.

The Role of Oxidative Stress in Atherosclerosis, Matthew Batty, Martin R. Bennett, Emma Yu 2022

Efferocytosis: the art of cellular clearance and novel perspectives in disease therapy, Gege Li, Jiashuai Xu, Xiaohan Tian, Jingyi Xiao, Junqi Long, Yining Chen, Wenzhi Shen & Shuangtao Zhao 2025

A plant-based diet and coronary artery disease: a mandate for effective therapy, Caldwell B Esselstyn 2019