CHAPTER 1

What Causes Cardiovascular Disease?

To best understand how and when stents can be used to treat blockages in the heart arteries, we first need to explore what causes these blockages in the first place. As a cardiologist, my primary goal is to prevent heart disease from developing. I often tell my patients, "The best thing I can do for you is to help you manage your risk factors so that you won't need a stent in the first instance." Focusing on prevention and reducing risk can lower the chances of needing interventions like stents or bypass surgery.

Cardiovascular disease (CVD) is one of the leading causes of death globally, driven by risk factors like high blood pressure, smoking, obesity, and a sedentary lifestyle. CVD encompasses a range of conditions that affect the heart and blood vessels, such as coronary artery disease (CAD), heart failure, and stroke. The table below highlights the various conditions that fall under CVD, illustrating its multifaceted nature and how it can impact individuals at different stages of life. Understanding these conditions is crucial in recognizing risk factors, prevention strategies, and treatment options for maintaining long-term heart health.

Table 1.1 summarizes the main categories of cardiovascular disease, including coronary artery disease, heart failure, arrhythmias, and other vascular disorders.

Coronary Artery Disease

CAD is primarily caused by atherosclerosis, a condition where plaque builds up inside the arteries. Plaque, a fatty substance of fat, calcium, and other materials, gradually accumulates on the arterial walls. When these arteries

TABLE 1.1 Common Conditions That Make Up Cardiovascular Disease

Condition	Description
Coronary artery disease (CAD)	A condition where the arteries that supply blood to the heart muscle become narrowed or blocked due to plaques made of waxy/fatty material.
Hypertension (high blood pressure)	A condition where the force of the blood against the artery walls is consistently raised, increasing the risk of heart disease, stroke, and other cardiovascular complications.
Heart failure	A condition where the heart is unable to pump blood efficiently or relax appropriately, leading to fluid accumulation, fatigue, and shortness of breath.
Arrhythmias	Irregular heartbeats that can lead to problems such as palpitations, dizziness, or fainting. A common example is atrial fibrillation or AFib.
Peripheral artery disease (PAD)	A condition where the arteries that supply blood to the legs and feet become narrowed due to plaque, causing pain and poor circulation.
Stroke	Occurs when blood flow to a part of the brain is interrupted, causing brain cells to become damaged and can lead to neurological compromise.
Congenital heart defects	Structural heart problems present from birth that can affect normal blood flow around the circulatory system.
Aortic aneurysm	An abnormal bulge/dilatation in the wall of the aorta, which can lead to life-threatening rupture if untreated.
Cardiomyopathy	A disease of the heart muscle that makes it harder for the heart to pump blood to the rest of the body.
Valvular heart disease	Conditions where one or more of the heart valves don't function correctly, usually because they are narrowed (stenosed) or leaky. Common conditions include aortic stenosis or mitral regurgitation.

narrow, they cannot deliver enough oxygen-rich blood to the heart, resulting in chest pain (angina), shortness of breath, or even a heart attack.

Atherosclerosis: The Root of the Problem

Atherosclerosis is the process by which plaque builds up in the arteries over time. Think of your arteries as flexible tubes that carry blood, like water pipes in a house. Over time, just as pipes can develop mineral buildup that slows water flow, arteries can accumulate fatty deposits that restrict blood flow as seen in Figure 1.1.

FIGURE 1.1 Atherosclerotic plaque formation in an artery. The image illustrates the gradual buildup of fatty deposits, cholesterol, and cellular debris within the arterial wall, leading to plaque formation. As the plaque enlarges, it narrows the artery, restricting blood flow and increasing the risk of cardiovascular events such as heart attacks and strokes. *crevis/Adobe Stock Photos*

This process begins when the smooth inner lining of the arteries (called the endothelium) becomes damaged or irritated. Figure 1.2 shows how plaque builds up as lipids and immune cells accumulate in the artery wall, triggering ongoing inflammation. Over time, this can cause the plaque to grow and become unstable. Our goal is to contain this process, reduce inflammatory cell activity, and where possible, promote plaque stabilisation or regression.

Several factors can contribute to this damage, and we will dedicate a chapter on this vital topic itself, but in short, these factors include:

- **High blood pressure:** The constant force of blood against artery walls can cause small injuries over time.
- **Smoking:** Harmful chemicals in tobacco damage the arteries, making it easier for plaque to develop.
- **High cholesterol:** Too much low-density lipoprotein (LDL) cholesterol, amongst other factors, can enter the artery walls and contribute to plaque formation. I never like the notion of "good" and "bad" cholesterol as all cholesterol plays an important role in our body, and we will expand on this a little later to give you a deeper understanding.
- **High blood sugar (diabetes):** Elevated sugar levels can weaken the artery walls and make them more vulnerable to plaque buildup.
- **Genetics (family history):** If you have a close relative, such as a parent or sibling, who developed heart disease at an early age, your own risk is higher. While we can't change our genes, knowing that heart disease runs in the family is an essential signal that we need to be extra mindful of the risk factors we can control. This means paying close attention to maintaining a healthy lifestyle, managing blood pressure and cholesterol, and staying active to reduce overall risk.

All these risk factors play a significant role in cardiovascular health, though some, like genetics, are not modifiable. However, having a strong family history of heart disease does not mean your risk is beyond your control.

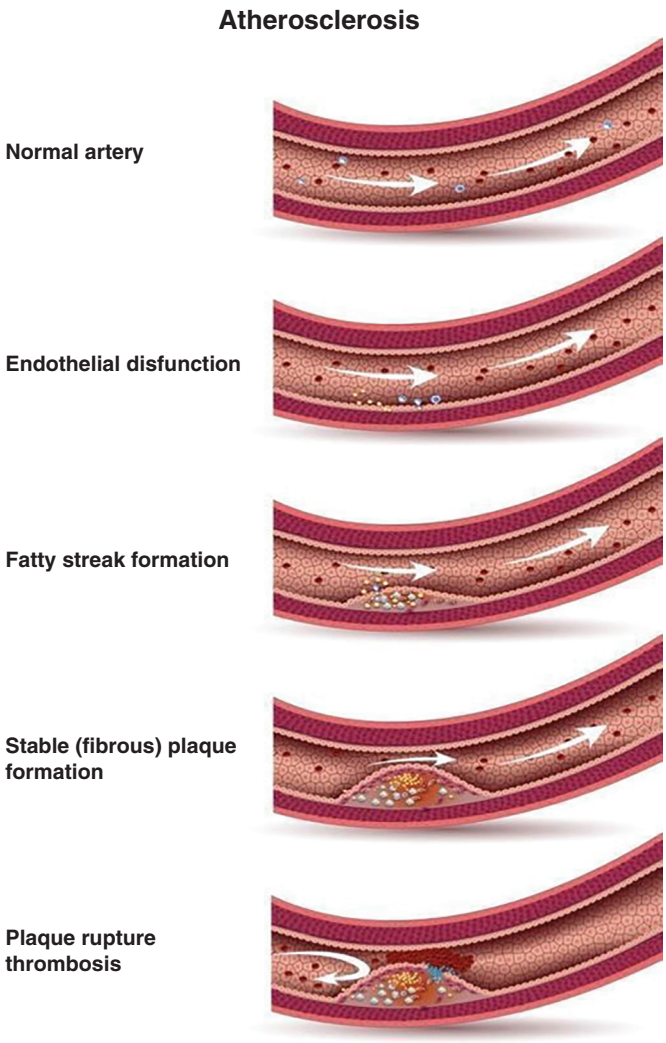
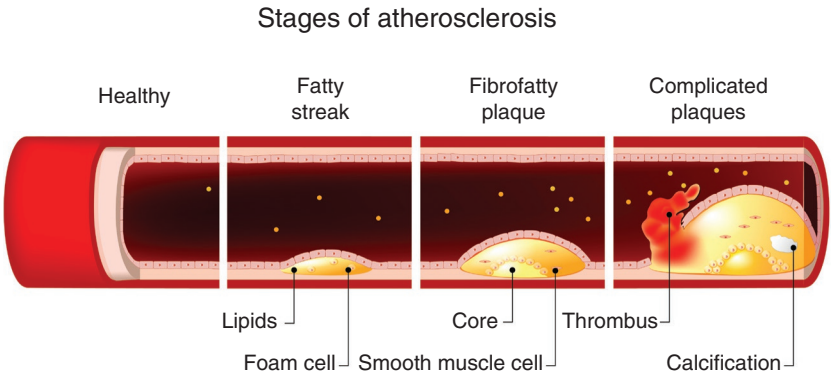


FIGURE 1.2 Plaque formation in the artery of the heart. Plaque is a complex material consisting of lipids, calcium, and other substances that can accumulate in the lining of the arteries, causing a narrowing of the artery lumen and reduced blood flow to the heart muscle. The formation of plaque is a multistep process involving lipid accumulation, inflammation, and the recruitment of immune cells to the arterial wall. These events can lead to the development of atherosclerosis, a chronic inflammatory condition that is a major risk factor for heart disease.

A great deal can still be done to lower your overall risk through lifestyle changes, medication when necessary, and proactive management of other risk factors. Taking the right steps can significantly reduce the likelihood of future cardiovascular events and improve long-term heart health.



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Plaque Progression

When the endothelium is damaged, cholesterol and other substances seep into the artery walls. The body's immune system, sensing a problem, sends white blood cells called macrophages to clean up the cholesterol. However, instead of solving the issue, these cells can become overwhelmed and become foam cells (immune cells like macrophages that have absorbed too much cholesterol, making them swollen and "foamy"), forming fatty streaks, the earliest stage of plaque buildup.

Over time, these fatty streaks grow, harden, and become larger plaques. Some plaques remain stable, meaning they don't pose an immediate threat. But others can become inflamed and rupture. When a plaque breaks open, the body forms a blood clot at the site. If the clot becomes large enough, it can completely block the artery, cutting off blood supply to the heart and triggering a heart attack.

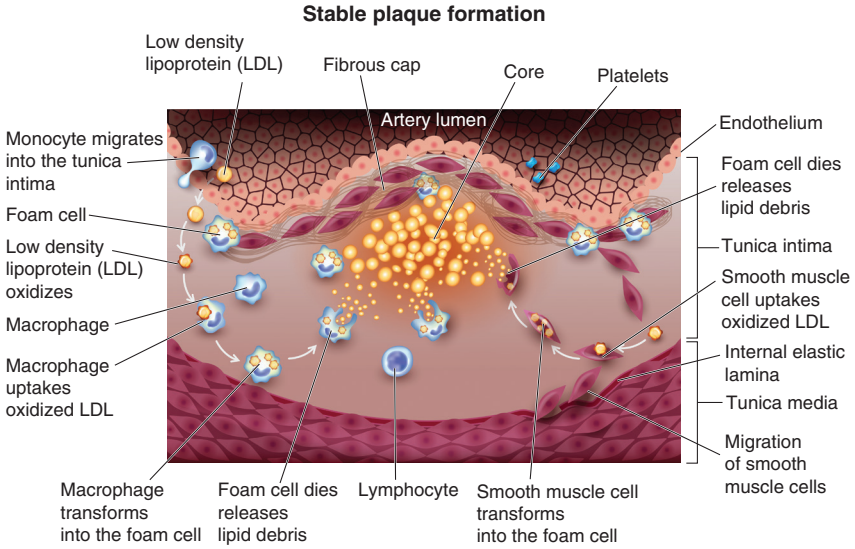
Why It Matters

The narrowing and blockages caused by atherosclerosis do not just affect the heart; they can also reduce blood flow to the brain (increasing the risk of stroke) or to other parts of the body (leading to conditions like peripheral artery disease). That's why managing risk factors like keeping blood pressure and cholesterol in check, eating a heart-healthy diet, and staying physically active is essential to preventing and slowing plaque progression throughout our body.

The Role of Inflammation in CAD

An often-overlooked aspect of plaque buildup is inflammation. While many people think of CAD as simply a "plumbing problem" caused by clogged arteries, the reality is more complex. Inflammation is key in how plaques form, grow, and sometimes become unstable.

Our body's immune system responds to injury or harmful substances by triggering inflammation, a natural defense mechanism. However, when inflammation is persistent due to factors like high cholesterol, high blood pressure, diabetes, smoking, or even chronic stress, it can worsen plaque buildup.



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Inflammatory cells gather at the site of artery damage and try to "clean up" harmful substances, but in the process, they can also contribute to plaque formation. More concerningly, inflammation can weaken the structure of plaques, making them unstable. When a plaque becomes fragile and ruptures, it can suddenly expose its contents to the bloodstream, rapidly forming a blood clot. This clot can block blood flow entirely, triggering a heart attack or stroke.

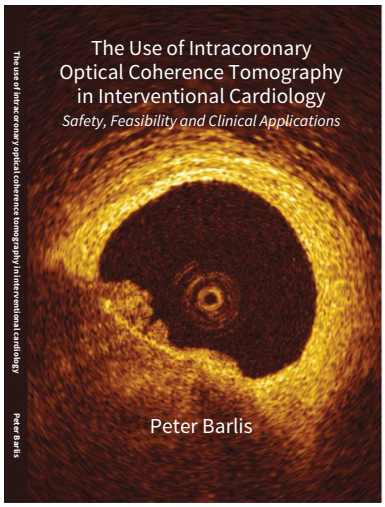
Inflammation and My Research

My research has focused on understanding how these inflammatory cells contribute to heart attacks. I have been able to detect pockets of inflammatory cells, including macrophages, using optical coherence tomography (OCT), a

cutting-edge imaging technique that uses laser light to scan inside coronary arteries. These immune cells cluster in a structure known as the fibrous cap, a thin protective layer that sits over plaques.

The thinner the fibrous cap, the more vulnerable the plaque is to rupture. This means that even if a plaque isn't completely blocking an artery yet, it could become dangerous at any moment if it ruptures and triggers a clot. We can identify these high-risk plaques through OCT imaging before they cause a heart attack, allowing for earlier and more targeted treatments.

A figure I used for the cover of my PhD thesis illustrates this process in detail, and I frequently bring it out to show patients during their consultation. Unlike the simplified diagrams often seen in medical illustrations, real-life plaques inside arteries can look quite different. Advanced imaging techniques like OCT allow us to move beyond traditional methods and better understand arterial health more precisely.



How Imaging Guides Treatment

Cardiologists can make more informed treatment decisions using imaging technologies such as OCT. Not every plaque requires a stent or surgery; many can be managed with medications that reduce inflammation and stabilize plaque. However, placing a stent may be necessary to reinforce the artery and restore blood flow in highly unstable cases.

Since introducing OCT to Australia in 2009, I have seen firsthand how this technology has transformed how we detect and treat CAD. Many laboratories worldwide now use these advanced imaging tools, and continued research is helping us refine treatments to improve patient outcomes.

The increasing understanding of inflammation's role in heart disease has also led to new treatment strategies. Some medications, in addition to traditional cholesterol-lowering drugs, now target inflammation directly. These advances provide hope that in the future, we will not only be able to treat blockages more effectively but also prevent dangerous plaques from forming in the first place.

Conclusion

Cardiovascular disease is not the result of a single cause but rather a complex interplay of factors, ranging from high blood pressure and elevated cholesterol to inflammation, genetics, and lifestyle habits. At the core of many heart conditions lies atherosclerosis, a gradual process of plaque buildup that narrows and weakens arteries throughout the body. Far from being a simple "plumbing" issue, we now understand that inflammation plays a critical role in plaque development and instability, significantly increasing the risk of heart attacks and strokes.

Advanced imaging techniques like OCT are helping us detect vulnerable plaques earlier and with greater precision, allowing for more targeted interventions, often before a major event occurs. Just as importantly, this growing knowledge reinforces the importance of prevention: managing risk factors, making informed lifestyle choices, and taking action early.

By understanding what causes cardiovascular disease, we become better equipped to prevent it, detect it earlier, and treat it more effectively. The ultimate goal remains not only to treat heart disease when it occurs but to prevent it from developing in the first place. That's where real progress and true heart health begin.