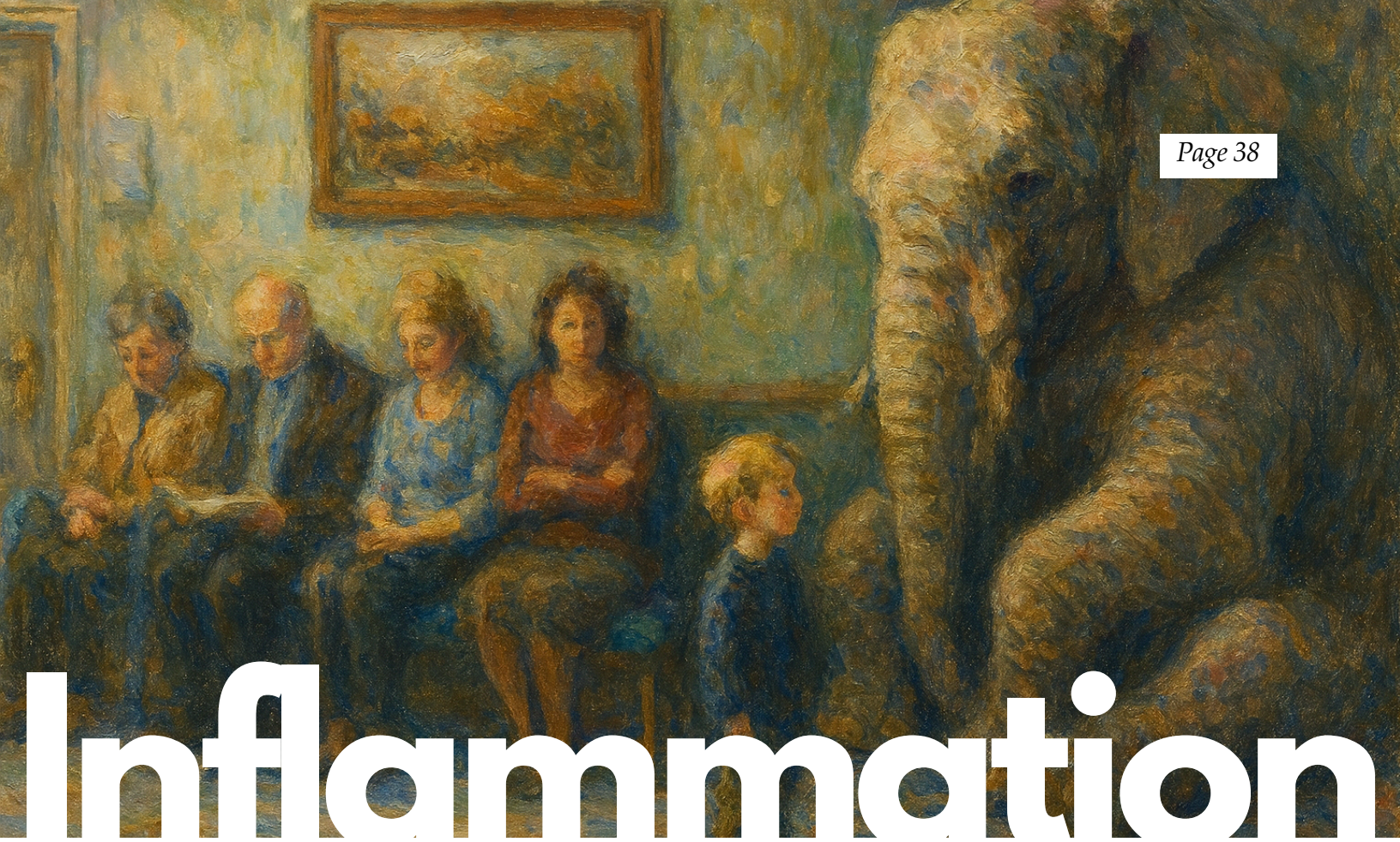


Inflammation

the co-conspirator in cardiovascular risk

by Cliff Dominy PhD

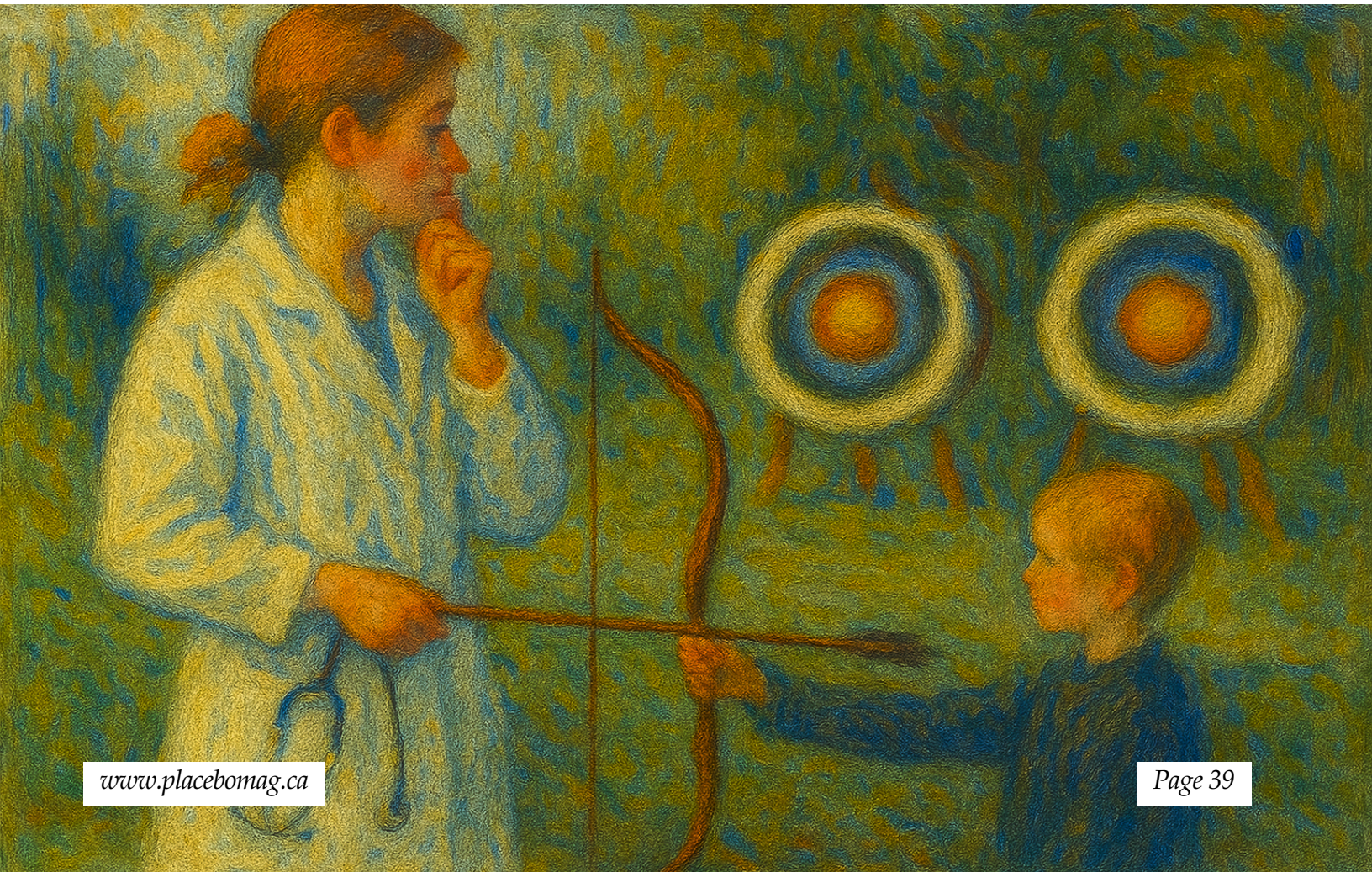
"The time for taking action has now arrived"

The American College of Cardiology has released a scientific statement identifying inflammation as a necessary factor in the development of cardiovascular disease (CVD). It joins the prime suspect, the apoB-containing lipid particles, as an actionable drug target in both primary and secondary populations. The college has called for the widespread adoption of high-sensitivity CRP screening to identify individuals with chronic inflammation, but normal cholesterol, who remain vulnerable to the disease.

Inflammation has had a strong association with the development of atherosclerotic plaque, but it has been unclear if it is necessary or sufficient to develop the disease. An abundance of evidence now suggests that an excess of apoB-containing lipoprotein particles in a proinflammatory environment is the primary driver of plaque buildup in the coronary arteries. In addition, the speed at which plaque accumulates may be exacerbated by other factors such as age, high blood pressure, insulin status, and smoking.

While lipid-lowering therapy has successfully reduced death from major-adverse cardiac events (MACE), significant residual risk remains. Blocking the inflammatory component of CVD may require a more nuanced therapeutic approach, however. The immune system plays a vital role in defending the body against infection and tumour development- healthy physiological responses that should not be suppressed. The statement acknowledges the need to develop drugs that selectively inhibit the CVD-associated inflammatory pathways. These include the NLRP6 inflammasome and JAK-STAT response, which are involved in activating pro-inflammatory cytokines. This makes the regulators of these responses, interleukin-1β and interleukin-6 respectively, viable drug targets.

The evidence supporting the ACC decision can be summarised as follows.



Clinical trials

1. ***Statins***

- The JUPITER trial (2008) reported rosuvastatin reduced cardiovascular events by 44% (relative risk) in a population without cardiovascular disease, normocholesterolemia (LDL-C < 130 mg/dL), and chronic inflammation (hsCRP > 2mg/L).

2. ***Interleukin 1β***

- The CANTOS Trial (2017) tested the efficacy of canakinumab, an anti IL-1B monoclonal antibody, in reducing MACE in a secondary population post-myocardial infarction. It reported a 15% relative reduction in clinical outcomes without affecting LDL-cholesterol levels.

3. ***Colchicine***

Two trials have tested low-dose colchicine, a broad anti-inflammatory, in reducing MACE.

- The COLCOT trial (2019), reported a 23% reduced risk of ischemic events in a post-myocardial infarction population.
- The LoDoCo2 trial (2020) had a 31% lower risk of MACE in a population with stable coronary disease.

4. ***Lifestyle***

- The GISSI-HF trial (2008) reported a modest 9% reduction in all-cause mortality in a population with heart failure taking omega-3 fat supplements.
- The PREDIMED trial (2018) showed a similar reduction in MACE in a population following the Mediterranean diet (both olive oil and nut arms).

What's available?

- In 2023, the FDA approved Lodoco® (colchicine) as an anti-inflammatory drug for the treatment of cardiovascular disease.

- Canakinumab has received approval for various inflammatory and auto-inflammatory conditions, but not for treating CVD.

- Rosuvastatin is a common lipid-lowering therapy that has an anti-inflammatory component.

"Clinicians will not treat what they do not measure"

Call to action

Despite the development of a wide range of lipid-lowering therapies, CVD risk remains a clear and present danger for many. It is estimated that in a "healthy" population (LDL-C <70 mg/dL), individuals with chronic inflammation (hsCRP > 2 mg/L) have nearly double the mortality risk from heart disease as people without the condition.

The authors of the ACC Statement summed things up perfectly when they wrote, "We have thus entered an era when the evidence linking inflammation with ASCVD is no longer exploratory but is compelling and clinically actionable. The time for taking action has now arrived."

Reference

Mensah, G, Arnold, N, Prabhu, S. et al. Inflammation and Cardiovascular Disease: 2025 ACC Scientific Statement: A Report of the American College of Cardiology. JACC. null2025, 0 (0) .