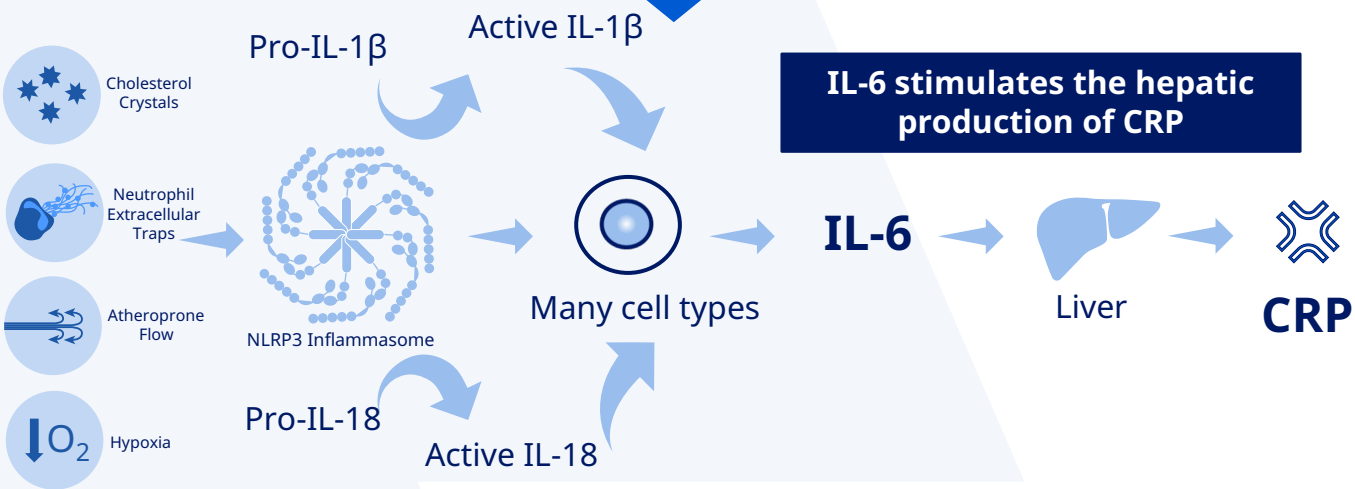
hsCRP as a biomarker in ASCVD

What is systemic inflammation?

Systemic inflammation refers to a sustained activation of the immune system, including release of proinflammatory cytokines such as IL-6

This activation has been suggested to play a key pathophysiological role in several CVDs such as ASCVD (IHD/stroke/PAD), AMI and HF[1,2]

What is the link between IL-6 and CRP?[3,4]



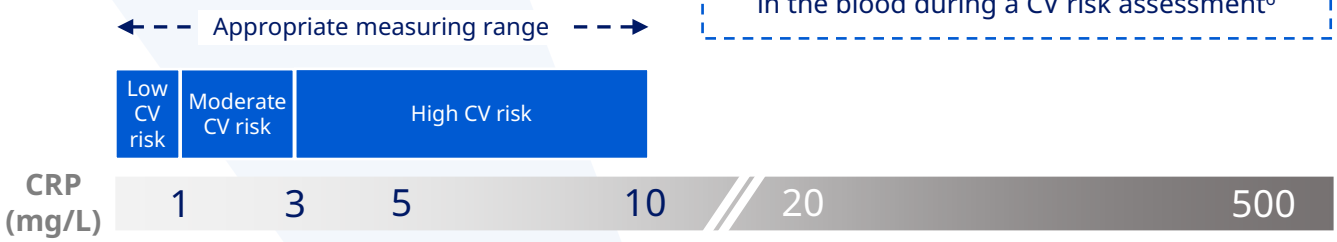
IL-6 stimulates the hepatic production of CRP

CRP is an acute phase protein* produced by the liver in response to circulating cytokines such as IL-6, IL-1 and TNF during tissue injury, inflammation or infection[3,5]

What do CRP and hsCRP levels indicate?

hsCRP assay

Can measure trace amounts of CRP **(1–10 mg/L)** in the blood during a CV risk assessment[6]



Conventional CRP measurement **(>10 mg/L)** is used to find or monitor conditions that cause inflammation (e.g., sepsis, IBD, rheumatoid arthritis)[6–9]

Acute phase reaction due to infections or non-infectious inflammatory conditions

Conventional CRP assay

*Refers to class of proteins whose plasma concentration increase or decrease in response to inflammation

AMI, acute myocardial infarction; ASCVD, atherosclerotic cardiovascular disease; CRP, C-reactive protein; CV, cardiovascular; CVD, cardiovascular disease; HF, heart failure; hsCRP, high-sensitivity C-reactive protein; IHD, ischaemic heart disease; ; IBD, inflammatory bowel disease; IL-6, interleukin-6; MI, myocardial infarction; NLRP3, NOD [nucleotide oligomerization domain], LRR [leucine-rich repeat] and PYD [pyrin domain]-containing protein 3; PAD, peripheral artery disease; TNF, tumour necrosis factor

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What is the evidence supporting hsCRP as a predictor of CV risk?

Residual inflammatory risk (RIR) is defined as **hsCRP levels ≥2 mg/L**, which has been observed in up to 66% of patients with ASCVD in RWE studies[10–14]

- In a combined analysis of the PROMINENT, REDUCE-IT and STRENGTH trials in **statin-treated patients**, RIR was associated with an **increased risk of CV events**, regardless of LDL-C levels[15]
- Similar results were observed in **statin-intolerant patients** from the CLEAR-Outcomes trial[16]

In a CANTOS* sub-study in patients who had a **prior MI and received statin therapy**, achieving **on treatment hsCRP levels <2 mg/L** with the anti-inflammatory IL-1β inhibitor canakinumab was associated with **improved CV outcomes[17]**

What are the guideline recommendations for hsCRP?

ACC/ AHA[18,19]	• Measurement of hsCRP is not stipulated in primary prevention • However, if measured, **knowledge of risk-enhancing factors (e.g., hsCRP ≥2.0 mg/L)** can be **particularly useful** in intermediate-risk patients (ASCVD risk of 7.5% to ≤20%) to **determine whether statin treatment is appropriate**)
ESC[20]	• The routine **collection of urinary or circulating biomarkers** is **not recommended** in primary prevention • New studies confirm that **CRP has limited additional value for risk prediction** • **Cardiac biomarkers are promising** but further work is needed
SMART Risk Score[21–23]	• The **ESC-endorsed SMART risk score** includes **hsCRP** as a **risk predictor for recurrent CV events** (MI, stroke or CV death) in patients with a history of CV Click here to access

What factors should be considered when interpreting hsCRP in the clinic?

hsCRP is generally a reliable predictor of CV risk, but should be interpreted in the context of the patient

Women have slightly higher hsCRP levels than men, in study populations with and without ASCVD[24–26]

Black/African American patients as well as **Hispanic** and **South Asian** patients have **slightly higher hsCRP** levels than white patients[24,27,28]

*Patients had a history of MI and hsCRP levels ≥2 mg/L at baseline

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ACC, American College of Cardiology; ASCVD, atherosclerotic cardiovascular disease; AHA, American Heart Association; CKD, chronic kidney disease; CRP, C-reactiveA protein;CV, cardiovascular; CVD, cardiovascular disease; ESC, European Society of Cardiology; hsCRP, high-sensitivity C-reactive protein; LDL, low-density lipoprotein; LDL-C, low-density lipoprotein cholesterol; MI, myocardial infarction; RIR, residual inflammatory risk; RWE, real-world evidence

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