



## C-Reactive Protein: Clinical Relevance and Interpretation From Medical Laboratory and Health Informatics Perspectives

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### Abstract

**Background:** C-reactive protein (CRP) is a highly conserved acute-phase biomarker synthesized by hepatocytes in response to inflammatory stimuli, primarily mediated by IL-6. It exists in pentameric (pCRP) and monomeric (mCRP) isoforms, each with distinct immunological functions. CRP plays an essential role in innate immunity through ligand binding, complement activation, and phagocytic enhancement.

**Aim:** To provide a comprehensive review of the clinical relevance, diagnostic applications, and factors affecting CRP measurement from medical laboratory and health informatics perspectives.

**Methods:** This narrative review synthesizes experimental, clinical, and epidemiological findings regarding CRP structure, regulation, clinical utility, diagnostic techniques, and interfering variables. It also incorporates FDA-cleared assay technologies and point-of-care innovations.

**Results:** CRP demonstrates rapid kinetic response, rising within hours of inflammation and declining promptly upon resolution. Its elevations correlate with infectious, autoimmune, traumatic, and neoplastic conditions. High-sensitivity CRP (hsCRP) enables cardiovascular risk stratification by detecting low-grade inflammation. Elevated CRP levels also predict venous thromboembolism risk, cancer propensity, heart failure progression, and frailty in aging populations. Numerous factors—including medications, lifestyle, genetics, and comorbidities—modulate CRP concentrations and complicate interpretation.

**Conclusion:** CRP remains a vital biomarker for diagnosing and monitoring inflammation across diverse clinical scenarios. Its usefulness depends on proper contextual interpretation, integration with clinical findings, and awareness of interfering variables. Advances in diagnostic technology have improved CRP measurement accuracy, accessibility, and clinical value.

**Keywords:** C-reactive protein, inflammation, hsCRP, biomarker, diagnostics, cardiovascular risk, laboratory medicine.

### Introduction

C-reactive protein (CRP) represents a pivotal biomolecule in the detection, modulation, and understanding of inflammatory processes within the human body. Initially discovered in 1930 by Tillet and Francis, CRP was identified through its binding affinity for the C carbohydrate antigen present in the capsular polysaccharides of *Streptococcus pneumoniae* during acute inflammatory states. This characteristic interaction provided the basis for its nomenclature and established its role as a critical acute-phase protein. Structurally, CRP is a pentameric protein synthesized predominantly by hepatocytes in response to pro-inflammatory cytokine signaling. The protein has an approximate molecular weight of 115 kDa and exhibits a distinctive "jelly-like lectin fold," which is critical for its ligand-binding capabilities and subsequent immune functions [1]. The structural organization of CRP underlies its biological function and defines its dual role in inflammatory processes. CRP exists primarily in two isoforms: the pentameric form (pCRP) and the monomeric form (mCRP). The

pentameric isoform is the circulating form found under normal physiological conditions, characterized by its anti-inflammatory properties. In contrast, the monomeric isoform emerges predominantly at sites of tissue injury or inflammation, displaying pro-inflammatory activity. The transition from pCRP to mCRP occurs through the dissociation of the pentamer into individual subunits, a process that is triggered by cellular and extracellular stressors, tissue damage, or inflammatory signals. This structural dissociation is significant as mCRP contributes to pathophysiological processes, including platelet activation, leukocyte recruitment, and endothelial cell dysfunction, all of which are central to the development of various disease states, particularly cardiovascular disorders [2][3]. The existence of these isoforms underscores CRP's capacity to act as both a regulator and amplifier of inflammation, depending on the physiological context and the presence of pathological stimuli.

CRP synthesis is tightly regulated by cytokines, particularly interleukin-6 (IL-6), which induces hepatic transcription of the CRP gene during

infection or tissue injury. This acute-phase protein serves as a rapid-response marker for inflammatory stimuli, with plasma concentrations capable of increasing dramatically within hours of insult. Beyond its role as a biomarker, CRP actively participates in the recognition and clearance of apoptotic cells, necrotic debris, and pathogenic microorganisms. CRP achieves this through its binding affinity to molecular structures such as phosphocholine, phospholipids, histones, chromatin, and fibronectin. Upon ligand binding, CRP activates the classical complement pathway and engages Fc receptors on phagocytic cells, thereby facilitating the efficient removal of potentially harmful cellular and microbial components. This dual functionality—serving as both a sensor of cellular stress and an effector molecule—illustrates CRP's central position within innate immune defense mechanisms. Experimental and clinical evidence has elucidated additional roles of CRP in specific organ systems. Animal studies investigating alveolitis have demonstrated that CRP exerts protective effects within lung tissue, attenuating neutrophil-mediated alveolar injury and limiting protein leakage into pulmonary spaces. These findings indicate that CRP not only serves as an inflammatory mediator but also possesses organ-specific cytoprotective properties, reducing collateral tissue damage during acute immune responses. Conversely, pathological activation of CRP may exacerbate disease processes in certain contexts. For example, in autoimmune conditions such as systemic lupus erythematosus (SLE), CRP may bind to autoantibodies that expose phosphocholine residues, leading to complement activation and subsequent tissue damage. This mechanism illustrates the dual nature of CRP, wherein it can contribute to both protective immune clearance and detrimental inflammatory amplification depending on the immunological environment [4][5][6].

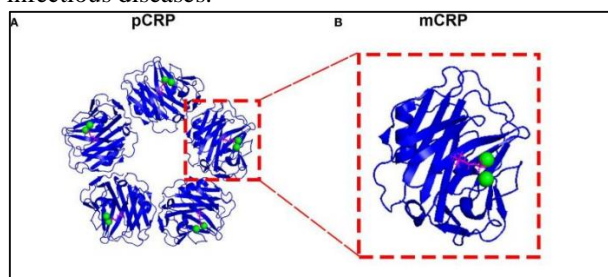
The kinetics of CRP differentiate it from other inflammatory markers, such as erythrocyte sedimentation rate (ESR). Unlike ESR, which indirectly reflects inflammatory activity and is influenced by multiple plasma components, CRP concentrations respond rapidly to inflammatory stimuli, often rising within 6 to 8 hours and peaking at approximately 48 hours. Upon resolution of the inciting insult, CRP levels decline quickly, reflecting its dynamic regulation in acute-phase responses. Persistently elevated CRP levels may indicate ongoing chronic inflammation, as seen in persistent infections or autoimmune disorders such as rheumatoid arthritis. Furthermore, CRP levels are highly sensitive to both infectious and non-infectious stimuli, making it a versatile biomarker for a wide spectrum of clinical conditions. CRP elevation can be markedly pronounced in acute infectious states, trauma, and tissue necrosis, reflecting the recognition of pathogen-associated molecular patterns (PAMPs) and alarmin-

mediated inflammatory responses. The magnitude of CRP elevation often correlates with the severity of the underlying condition, making it a valuable prognostic indicator in clinical practice. In contrast, more modest increases in CRP may result from subclinical or low-grade inflammatory stimuli, such as sleep deprivation, periodontal disease, obesity-related inflammation, or metabolic syndrome. These lower-level elevations underscore the sensitivity of CRP to a broad array of physiological and environmental stressors, extending its utility beyond acute infectious or inflammatory conditions [7].

Lifestyle factors and behavioral patterns further modulate CRP levels. Epidemiological studies have consistently demonstrated that increased sedentary behavior is associated with elevated CRP concentrations, whereas engagement in regular physical activity—both light and moderate-to-vigorous intensity—correlates with lower CRP levels. This relationship suggests that CRP reflects not only acute inflammatory processes but also chronic physiological stressors related to lifestyle and metabolic health. These findings highlight the integrative nature of CRP as a biomarker, capturing both disease-related inflammation and lifestyle-influenced subclinical inflammatory states [8]. CRP's functional versatility extends to its role in immune surveillance and host defense. By binding to apoptotic and necrotic cellular components, CRP aids in maintaining tissue homeostasis and preventing inappropriate immune activation. Its involvement in complement activation and phagocytosis ensures rapid clearance of potentially harmful cellular debris, reducing the likelihood of secondary inflammation or tissue injury. At the same time, dysregulated CRP activity may contribute to pathogenic processes, particularly in autoimmune and cardiovascular diseases, where its pro-inflammatory actions exacerbate endothelial dysfunction, promote leukocyte adhesion, and facilitate thrombus formation. These complex interactions highlight the need for careful interpretation of CRP levels in clinical practice, integrating both laboratory findings and the patient's overall inflammatory context [7][8][9].

In summary, CRP is a highly conserved, multifunctional acute-phase protein that plays a central role in inflammation, immune defense, and tissue homeostasis. Its structural isoforms, pentameric and monomeric, provide distinct biological functions, with pCRP serving predominantly anti-inflammatory roles and mCRP exhibiting pro-inflammatory effects. The protein's regulation by cytokines, particularly IL-6, and its ability to activate complement and mediate phagocytosis underscore its essential contribution to innate immunity. Clinically, CRP serves as a rapid and sensitive biomarker for acute and chronic inflammation, with levels reflecting both disease severity and lifestyle factors. Its dual roles in

protection and pathogenesis exemplify the complexity of immune regulation, emphasizing the importance of understanding CRP's molecular mechanisms, functional diversity, and clinical relevance in both research and patient care contexts. By elucidating the intricate interplay between CRP's structure, function, and regulatory pathways, clinicians and researchers can leverage this biomarker for diagnostic, prognostic, and therapeutic purposes, ultimately enhancing patient outcomes across a range of inflammatory and infectious diseases.



**Fig. 1:** C-Reactive Protein Isoforms and Their Phosphocholine Complexes. Zhou HH, Tang YL, Xu TH, Cheng B. C-reactive protein: structure, function, regulation, and role in clinical diseases. *Front Immunol.* 2024;15:1425168. doi: 10.3389/fimmu.2024.1425168

### Specimen Collection

Accurate measurement of C-reactive protein (CRP) relies on the collection of high-quality blood specimens, typically obtained from peripheral venous access. The procedure is usually performed by a trained phlebotomist following standardized aseptic techniques to minimize patient discomfort and prevent complications. Initially, a tourniquet is placed snugly around the patient's upper arm to promote venous distention. The patient may be instructed to pump the fist several times to enhance venous prominence, facilitating identification of an appropriate vein. The phlebotomist palpates the antecubital fossa or other accessible venous sites, selecting a vein that is sufficiently prominent and straight to allow smooth insertion of the needle. After identifying the site, the skin is cleansed using an alcohol pad and allowed to air-dry completely to reduce the risk of infection and ensure aseptic conditions. Once the venipuncture site is prepared, a sterile needle is introduced into the vein, and blood is drawn into an evacuated collection vial. The tourniquet is then released to restore normal venous circulation, and the needle is carefully withdrawn. Immediate manual pressure is applied to the puncture site to achieve hemostasis, which typically occurs within one minute. A sterile bandage or gauze is applied to protect the site and prevent subsequent bleeding or hematoma formation. Minor complications from venipuncture, including localized oozing, bruising, or tenderness, are common and generally self-limiting. Infection at the venipuncture site is rare when proper aseptic technique is employed.

Although CRP can be detected in other body fluids, such as synovial fluid, these are not routinely utilized for clinical assessment, as peripheral venous blood remains the standard specimen for accurate measurement [9].

Prior to specimen collection, a review of the patient's medication history is essential, as several pharmacologic agents may influence CRP levels. For instance, anti-inflammatory medications, statins, or corticosteroids can modulate circulating CRP concentrations and affect test interpretation. Fasting is not required for CRP assessment, and no additional dietary or lifestyle preparations are necessary, which simplifies patient compliance and enhances test accessibility. Quantification of CRP is most commonly performed using immunoassays or laser nephelometry, which provide rapid, cost-effective, and accurate results. Immunoassays rely on antibody-antigen interactions to detect and measure CRP concentrations, while laser nephelometry evaluates light scatter from CRP-antibody complexes in suspension. For the detection of low-grade inflammation or cardiovascular risk assessment, high-sensitivity CRP (hsCRP) assays are preferred, offering precise measurements at concentrations between 0.3 and 1.0 mg/L. The designation "high-sensitivity" refers exclusively to analytical capability rather than distinct clinical interpretation. These assays enable clinicians to detect subtle variations in baseline CRP levels, which may indicate early or chronic low-grade inflammatory processes [9][10].

Recent technological advancements have expanded the availability of point-of-care CRP testing, enabling rapid and reliable assessment of serum CRP levels at or near the bedside. The ProCiseDx CRP Assay, FDA-cleared in 2022, delivers quantitative results from serum samples in under five minutes using a compact fluorescence-based platform, enhancing clinical efficiency in urgent care and outpatient settings. Similarly, the Siemens Revised CRP (RCRP) Flex Reagent Cartridge Assay, cleared in 2023, offers a high-sensitivity analytical range from 5.0 to 250.0 mg/L, suitable for cardiovascular risk stratification and other clinical applications. These platforms reduce turnaround time and allow prompt clinical decision-making, particularly in scenarios requiring rapid risk assessment or monitoring of inflammatory status. Innovative approaches continue to expand CRP testing capabilities, including low-cost, rapid diagnostics suitable for resource-limited environments. For example, paper-based microfluidic immunoassays integrated with smartphone readouts, such as the CRP-Chip, offer portable and accessible alternatives for point-of-care evaluation. Such technologies are particularly valuable in remote or under-resourced settings, providing timely assessment of CRP without the need for centralized laboratory infrastructure [9]. In conclusion, the collection and analysis of CRP specimens require adherence to precise phlebotomy protocols and consideration of

patient-specific factors that may influence test results. Modern immunoassay and high-sensitivity technologies, combined with point-of-care innovations, have enhanced the accuracy, speed, and accessibility of CRP measurement. These advancements allow clinicians to obtain reliable inflammatory biomarkers efficiently, supporting informed diagnostic, therapeutic, and prognostic decisions across a range of clinical settings [9].

#### **Indications**

C-reactive protein (CRP) measurement is widely utilized in clinical practice as a biomarker to detect and monitor inflammatory processes. The test is primarily indicated when acute or chronic inflammation is suspected, providing clinicians with critical information to guide diagnosis, management, and prognosis. Conditions in which CRP assessment is particularly relevant include autoimmune diseases such as systemic lupus erythematosus (SLE) and rheumatoid arthritis, where inflammatory activity can fluctuate and early detection is essential to prevent organ damage and monitor therapeutic response. In these contexts, CRP serves as a sensitive indicator of ongoing systemic inflammation, complementing other laboratory and clinical parameters to provide a comprehensive assessment of disease activity. CRP levels may also rise in response to a wide spectrum of infections, including bacterial, viral, and fungal etiologies, thereby aiding in the detection and differentiation of infectious from non-infectious causes of systemic inflammation. Beyond autoimmune and infectious conditions, CRP measurement is valuable in evaluating tissue injury, trauma, and postoperative inflammatory responses. For example, in surgical patients, rising CRP levels may indicate early postoperative complications, such as wound infection, abscess formation, or anastomotic leak. Monitoring trends in CRP concentrations allows clinicians to distinguish between normal postoperative inflammatory responses and pathologic processes that require intervention. The rapid kinetics of CRP, with levels increasing within hours of an inflammatory stimulus and declining promptly upon resolution, make it a practical tool for dynamic monitoring of patient status [10][11][12].

High-sensitivity CRP (hsCRP) assays have emerged as a tool for evaluating low-grade, subclinical inflammation in individuals who may otherwise appear healthy. These assays detect CRP concentrations at much lower levels than conventional tests, typically in the range of 0.3 to 1.0 mg/L, allowing the identification of subtle inflammatory activity that may correlate with long-term health risks. One area of considerable interest is the potential utility of hsCRP in cardiovascular risk assessment. Epidemiological studies have demonstrated a correlation between elevated hsCRP levels and the development of cardiovascular disease, suggesting

that subclinical inflammation contributes to atherogenesis and vascular injury. However, the clinical application of hsCRP for cardiac screening remains controversial due to its limited specificity; elevated CRP can result from numerous non-cardiac conditions, including infections, trauma, and other inflammatory states, which complicates interpretation. As a result, ongoing research seeks to define the precise role of hsCRP in cardiovascular risk stratification and to determine whether it can meaningfully inform clinical decision-making in preventive cardiology [10][11][12].

The United States Food and Drug Administration (FDA) has cleared several CRP assay formats for clinical use. Conventional CRP assays are routinely employed to evaluate patients with suspected infection, inflammatory disorders, or tissue injury. These assays provide rapid and accurate quantification of CRP, facilitating diagnosis and monitoring of therapeutic interventions. High-sensitivity assays are specifically indicated for individuals without overt disease to assess baseline inflammatory status, which may contribute to early risk identification and preventive strategies. In addition, specialized cardiac CRP (cCRP) assays have been developed to identify and stratify patients at risk for cardiovascular events. cCRP testing is particularly relevant for individuals with other risk factors for cardiovascular disease, providing an adjunctive biomarker to complement established risk assessment tools such as lipid profiles, blood pressure measurements, and lifestyle assessments. Overall, the indications for CRP testing encompass a broad spectrum of clinical scenarios, ranging from acute and chronic inflammatory conditions to infection, tissue injury, and potential cardiovascular risk evaluation. Its rapid response to inflammatory stimuli, accessibility through standardized assays, and versatility in different patient populations make CRP an indispensable component of modern clinical diagnostics. Clinicians must interpret CRP results in the context of the patient's overall clinical picture, including history, physical findings, and other laboratory markers, to ensure accurate and actionable decision-making. By providing timely insights into inflammatory processes, CRP measurement enhances patient care, guiding therapeutic interventions, monitoring disease progression, and supporting preventive strategies in both acute and chronic clinical contexts [10][11][12].

#### **Potential Diagnosis**

C-reactive protein (CRP) has emerged as a clinically significant biomarker for the prediction, stratification, and monitoring of various disease states. Its elevation provides insight into systemic inflammatory activity, which is increasingly recognized as a critical factor in the pathophysiology of cardiovascular, oncologic, and thromboembolic disorders. In patients with a history of venous

thromboembolism (VTE), elevated CRP levels may serve as a predictive marker for recurrent thrombotic events. This association is particularly relevant in populations with comorbid conditions such as cancer, obesity, or COVID-19, where systemic inflammation contributes to a hypercoagulable state, endothelial dysfunction, and increased thrombotic risk. Measurement of CRP in these individuals can assist clinicians in identifying patients at heightened risk, thereby guiding prophylactic interventions and individualized monitoring strategies [13]. Beyond thromboembolic risk, CRP serves as a valuable indicator in the evaluation of cardiovascular disease. High-sensitivity CRP (hsCRP) measurements, particularly when analyzed in combination with other biomarkers, provide nuanced insights into the prevalence and progression of heart failure in the population. For instance, the log-transformed hsCRP-to-high-density lipoprotein cholesterol ratio (Ln HCHR) and the log-transformed hsCRP-to-lymphocyte count ratio (Ln HCLR) have demonstrated positive associations with heart failure prevalence in the United States. These ratios integrate inflammatory burden with lipid and immune parameters, offering a composite risk profile that reflects both systemic inflammation and cardiometabolic stress [14]. Elevated CRP levels themselves are considered independent risk factors for cardiac mortality. Epidemiological studies have consistently shown that higher CRP plasma concentrations are directly proportional to the risk of cardiovascular events, including myocardial infarction, stroke, and progressive heart failure. This relationship underscores the importance of CRP as a prognostic tool in cardiovascular medicine, complementing traditional risk factors such as dyslipidemia, hypertension, and diabetes [13][14].

In oncology, CRP elevation has been observed to correlate with increased cancer risk, particularly for gastric, colorectal, and lung malignancies. Chronic low-grade inflammation is a recognized contributor to tumorigenesis, and elevated CRP levels may reflect an underlying inflammatory milieu that promotes cellular proliferation, angiogenesis, and immune evasion. As such, CRP has been proposed as a potential biomarker for cancer risk stratification, aiding clinicians in identifying individuals who may benefit from targeted screening or surveillance programs [15]. Among patients already diagnosed with cardiovascular disease, CRP remains a critical prognostic marker. Elevated CRP levels are independently associated with increased risk for both heart failure with reduced ejection fraction (HFrEF) and heart failure with preserved ejection fraction (HFpEF). In these contexts, CRP not only reflects systemic inflammation but may also indicate ongoing myocardial stress, endothelial dysfunction, and heightened susceptibility to adverse cardiac remodeling [16]. Beyond specific disease states, CRP is increasingly recognized as a marker of frailty,

particularly in older adults. Frailty represents a multisystem condition characterized by reduced physiologic reserve, impaired resilience to stressors, and increased vulnerability to adverse outcomes. Low-grade chronic inflammation, as reflected by elevated hsCRP levels, has been closely linked to the development and progression of frailty. This association underscores the utility of CRP as a biomarker not only for disease prediction but also for identifying individuals at risk for functional decline and adverse health outcomes [17].

In summary, CRP has multifaceted clinical relevance as a biomarker. Its elevation can aid in predicting VTE risk, stratifying cardiovascular and oncologic risk, and identifying individuals at risk for frailty progression. The integration of CRP measurements with other clinical and laboratory parameters enhances its diagnostic and prognostic utility, providing a comprehensive tool for individualized patient assessment and management. Its rapid response to inflammatory stimuli, combined with the accessibility of both conventional and high-sensitivity assays, positions CRP as a cornerstone biomarker in contemporary clinical practice.

#### **Normal and Critical Findings**

C-reactive protein (CRP) serves as a sensitive biomarker for systemic inflammation, and its quantification provides valuable clinical insights into both acute and chronic pathophysiologic processes. Laboratory reference ranges for CRP are not fully standardized, and reporting formats vary across institutions. Results are commonly expressed in milligrams per deciliter (mg/dL) or milligrams per liter (mg/L), with high-sensitivity CRP (hsCRP) typically reported in mg/L to allow for detection of subtle elevations associated with low-grade inflammation. Accurate interpretation of these laboratory values requires contextualization within the patient's clinical presentation, comorbid conditions, and additional laboratory findings, as CRP elevations are nonspecific and can reflect a wide range of inflammatory stimuli [18][19]. CRP concentrations below 0.3 mg/dL are generally considered normal in healthy adults. Such values reflect the absence of active systemic inflammation and are typically observed in asymptomatic individuals without recent infections, tissue injury, or autoimmune activity. However, even within this "normal" range, slight variations may occur due to minor physiologic fluctuations or transient inflammatory responses to mild stressors. Values between 0.3 and 1.0 mg/dL are often interpreted as minor elevations and may occur in contexts that induce low-grade inflammation without overt clinical disease. Conditions associated with this range include obesity, pregnancy, metabolic disorders such as diabetes, and lifestyle factors such as sedentary behavior and cigarette smoking. Minor elevations may also be influenced by oral health conditions like gingivitis or periodontitis, acute viral illnesses such as the common cold, and genetic polymorphisms that

affect CRP synthesis or clearance. Recognition of these subtle changes can inform early intervention strategies, particularly in patients at risk for cardiometabolic disorders or systemic inflammation [18].

Moderate elevations, defined as CRP levels between 1.0 and 10.0 mg/dL, typically indicate a more pronounced inflammatory response. These levels are commonly observed in patients with autoimmune conditions such as rheumatoid arthritis, systemic lupus erythematosus, and other connective tissue diseases. Inflammatory responses secondary to malignancies, myocardial infarction, pancreatitis, or bronchitis also contribute to CRP concentrations within this range. Monitoring these values over time provides clinicians with an objective measure of disease activity and response to treatment, allowing for adjustments to pharmacologic interventions, immunomodulatory therapies, or lifestyle modifications. Persistently elevated CRP within this range often signifies ongoing inflammation that may warrant further diagnostic evaluation to identify underlying etiologies [18]. Marked elevations, defined as CRP levels exceeding 10.0 mg/dL, are typically associated with acute bacterial infections, systemic vasculitis, major viral infections, or significant trauma. These values reflect a robust acute-phase response, with rapid hepatic synthesis of CRP in response to pro-inflammatory cytokines such as interleukin-6. Clinically, this degree of elevation often prompts urgent evaluation and management, including microbiological testing, empiric antimicrobial therapy, and supportive care to mitigate complications arising from systemic inflammation. Extremely elevated CRP levels, exceeding 50.0 mg/dL, are almost exclusively observed in severe bacterial infections, including sepsis, pyelonephritis, and pneumonia, and indicate the need for intensive monitoring and aggressive therapeutic interventions [18][19].

When applied in cardiovascular risk assessment, high-sensitivity CRP (hsCRP) provides additional stratification for individuals without clinically evident disease. HsCRP levels below 1 mg/L correspond to low cardiovascular risk, indicating minimal subclinical inflammation and a favorable prognosis. Values between 1 and 3 mg/L suggest moderate risk, reflecting a measurable but not yet pathologic inflammatory burden that may contribute to endothelial dysfunction, atherogenesis, and future cardiovascular events. HsCRP levels above 3 mg/L identify high-risk individuals, representing a state of persistent low-grade inflammation that correlates with increased likelihood of myocardial infarction, stroke, or progressive atherosclerotic disease. In this context, hsCRP can complement traditional risk assessment tools such as lipid profiles, blood pressure measurements, and lifestyle evaluations, offering a more nuanced understanding of systemic

inflammatory status [18][19]. Interpretation of CRP values requires integration with clinical assessment, patient history, and other laboratory parameters. Serial measurements can provide insight into the trajectory of inflammatory responses, allowing clinicians to monitor disease progression, evaluate therapeutic efficacy, and detect early complications. In addition, the distinction between conventional CRP and hsCRP testing informs the specificity of interpretation, with hsCRP particularly useful for low-grade inflammation and cardiovascular risk assessment, while conventional CRP is better suited for identifying overt inflammatory or infectious processes. Accurate understanding of these laboratory thresholds enables targeted clinical interventions, timely adjustments to treatment regimens, and improved patient outcomes through proactive management of both acute and chronic inflammatory conditions.

#### **Interfering Factors**

C-reactive protein (CRP) is a widely used biomarker for inflammation, yet its levels are subject to modulation by multiple pharmacological, physiological, and genetic factors. Awareness of these interfering variables is essential for accurate interpretation, particularly when CRP measurements guide clinical decisions in infection, autoimmune disease, or cardiovascular risk assessment. One of the most commonly recognized pharmacological influences involves nonsteroidal anti-inflammatory drugs (NSAIDs). These agents exert anti-inflammatory effects by inhibiting cyclooxygenase-mediated prostaglandin synthesis, which indirectly diminishes CRP production by attenuating systemic cytokine signaling, particularly interleukin-6. Similarly, statins, which are primarily used for lipid-lowering purposes, have pleiotropic anti-inflammatory effects that reduce CRP levels independently of lipid reduction. This effect has been documented in both short-term and long-term therapy, and it complicates interpretation of CRP values in patients using these medications for cardiovascular risk management. Magnesium supplementation has also been reported to reduce CRP levels, potentially through mechanisms involving modulation of oxidative stress and systemic inflammation, further underscoring the influence of nutritional interventions on inflammatory biomarkers [20].

Emerging pharmacological interventions have expanded the spectrum of CRP-modulating agents. Biologic therapies, particularly interleukin-6 receptor antagonists such as tocilizumab, demonstrate robust CRP-lowering effects in autoimmune conditions including rheumatoid arthritis. Tocilizumab inhibits IL-6-mediated hepatic CRP synthesis, effectively reducing systemic inflammation and improving clinical outcomes. Similarly, glucagon-like peptide-1 receptor agonists, widely used in the management of type 2 diabetes mellitus, have

demonstrated anti-inflammatory properties that manifest as reductions in CRP levels. These agents may influence CRP through modulation of insulin sensitivity, adipose tissue inflammation, and endothelial function. The pharmacologic modulation of CRP by these agents emphasizes the necessity of considering medication history and therapeutic interventions when interpreting CRP concentrations in clinical practice [21]. Lifestyle and behavioral factors also substantially influence CRP levels. Sustained physical activity is associated with reductions in both conventional and high-sensitivity CRP (hsCRP), likely reflecting decreased adipose tissue-derived inflammatory cytokines and improved endothelial function. Sleep quality similarly impacts CRP, with sleep deprivation or disrupted circadian rhythms promoting low-grade systemic inflammation. Stress-reduction strategies, including mindfulness and cognitive behavioral therapy, have been linked to modest declines in CRP, potentially through attenuation of hypothalamic-pituitary-adrenal axis activation. Dietary patterns exert an additional influence; adherence to anti-inflammatory diets rich in fruits, vegetables, whole grains, and omega-3 fatty acids correlates with lower CRP levels. These lifestyle factors underscore the importance of integrating behavioral assessments into CRP interpretation, particularly in chronic disease management or cardiovascular risk stratification [22].

Genetic variation further contributes to inter-individual differences in CRP levels. Single-nucleotide polymorphisms (SNPs) within the promoter region of the CRP gene influence baseline CRP synthesis and circulating concentrations. These polymorphisms can modify hepatic responsiveness to pro-inflammatory cytokines, leading to persistent inter-individual variability even in the absence of overt disease. Understanding these genetic influences is critical when interpreting CRP levels in both research and clinical settings, as they may explain otherwise unexplained deviations from expected normative ranges [23]. Demographic and physiological variables also act as confounders. CRP levels are generally higher in women compared to men and tend to increase with advancing age, reflecting age-related changes in immune function and low-grade chronic inflammation. Chronic conditions such as obesity, diabetes, metabolic syndrome, smoking, and insomnia are associated with persistent low-level inflammation and can contribute to mild CRP elevation. These conditions necessitate careful contextualization of CRP results to distinguish pathologic from physiologic or lifestyle-related elevations [23].

Mental health disorders, particularly depression and anxiety, have been examined for potential associations with CRP. While some studies report higher CRP concentrations in individuals with depressive or anxious symptoms, these associations often weaken after adjustment for confounding variables including medical comorbidities,

demographic factors, and lifestyle influences. This suggests that elevated CRP in these populations may be indirectly related to systemic inflammation through secondary factors such as obesity, inactivity, or metabolic dysregulation rather than representing a direct causal pathway [24]. In summary, the interpretation of CRP levels is influenced by a complex interplay of pharmacological, lifestyle, genetic, physiological, and psychosocial factors. NSAIDs, statins, and emerging biologics can suppress CRP concentrations, while chronic conditions, age, sex, and behavioral factors may elevate baseline levels. Genetic polymorphisms further contribute to variability, and mental health conditions may indirectly modulate CRP through associated comorbidities. Accurate clinical interpretation requires careful consideration of these interfering factors, integrated with patient history, medication use, lifestyle assessment, and laboratory methodology, to ensure that CRP measurements reliably reflect the underlying inflammatory state and guide evidence-based clinical decision-making [24].

### **Complications**

The interpretation of C-reactive protein (CRP) levels is inherently complex due to the diverse array of conditions that can induce its elevation. Marginal increases in CRP may reflect low-grade or subclinical inflammation, lifestyle factors, or minor physiological variations, making them difficult to interpret in isolation. Reliance on a single CRP measurement without considering the broader clinical context can lead to misdiagnosis or inappropriate clinical decisions. This is particularly relevant when CRP values fall within the intermediate range of 1 mg/dL to 10 mg/dL, where distinguishing between acute infection, chronic inflammatory disorders, or transient inflammatory responses becomes challenging. Persistent CRP elevation is frequently observed in chronic autoimmune conditions such as rheumatoid arthritis and systemic lupus erythematosus (SLE). In these cases, ongoing inflammatory activity maintains elevated CRP levels, limiting the utility of CRP as a standalone predictive marker for cardiovascular disease or other secondary complications. Moreover, individuals with chronic systemic inflammation may demonstrate fluctuating CRP values in response to minor stressors, infections, or treatment interventions, further complicating clinical interpretation [24][25].

CRP functions as a nonspecific marker of inflammation, and its concentrations are influenced by demographic and physiological variables, including age, sex, obesity, and coexisting comorbidities such as diabetes and metabolic syndrome. In older adults, baseline CRP levels tend to be higher, reflecting low-grade systemic inflammation associated with aging. Similarly, sex-specific differences and chronic medical conditions contribute to variability in CRP, underscoring the importance of contextualizing laboratory results within each patient's unique health

profile. To improve diagnostic accuracy and reduce potential complications arising from misinterpretation, CRP measurements should be integrated with other laboratory parameters, clinical assessments, and imaging studies when indicated. This comprehensive approach allows clinicians to differentiate between acute infection, chronic inflammatory states, and low-grade physiological elevations, ensuring appropriate clinical management and mitigating the risk of misdiagnosis or unnecessary interventions. Proper contextualization of CRP values is essential for guiding treatment decisions, monitoring disease progression, and evaluating the effectiveness of therapeutic interventions [24].

#### **Patient Safety and Education**

Patient education regarding C-reactive protein (CRP) testing is a critical component of safe and effective clinical care. Patients should understand that CRP is a nonspecific marker of inflammation and that elevated levels indicate the presence of inflammatory processes rather than a definitive diagnosis. Clear communication about the purpose of the test helps patients comprehend its role in assessing infection, autoimmune conditions, cardiovascular risk, or other inflammatory disorders. By understanding why the test is performed, patients are better prepared to engage in their care and to interpret the significance of the results alongside their healthcare provider's guidance. It is also important for patients to recognize the factors that can influence CRP levels. Certain medications, including nonsteroidal anti-inflammatory drugs, statins, and biologics, can lower CRP levels, whereas conditions such as obesity, smoking, metabolic syndrome, and chronic inflammatory diseases may increase baseline values. Lifestyle habits, such as diet, exercise, stress, and sleep quality, can similarly affect results. Awareness of these variables empowers patients to provide accurate medical and behavioral histories, enabling clinicians to interpret CRP results in the proper context. Patient education contributes directly to safety by reducing the risk of misinterpretation and unnecessary interventions. When patients understand potential confounders and the limitations of CRP as a nonspecific biomarker, they are less likely to draw incorrect conclusions or experience undue anxiety about marginal elevations. Additionally, patients can participate actively in their management by adhering to recommended interventions, lifestyle modifications, or follow-up testing. Education fosters informed decision-making, encourages adherence to treatment plans, and strengthens collaboration between patients and healthcare providers, ultimately improving diagnostic accuracy and the quality of care delivered [25].

#### **Clinical Significance**

C-reactive protein (CRP) serves as a valuable biomarker in clinical practice, reflecting the presence

and intensity of systemic inflammation. Significantly elevated CRP levels, typically above 50 mg/dL, are strongly associated with acute bacterial infections, with studies suggesting that roughly 90% of such cases exhibit this degree of elevation. This makes CRP a useful tool for distinguishing bacterial infections from viral or noninfectious causes of inflammation, particularly when combined with clinical assessment and other laboratory parameters. Beyond bacterial infections, CRP has been investigated as a prognostic marker across a variety of infectious diseases. In viral infections such as hepatitis C, elevated CRP levels have been associated with disease progression and severity, reflecting the underlying inflammatory response. Similarly, in tropical and vector-borne infections like dengue and malaria, CRP has demonstrated potential as an indicator of disease burden, severity, and complications, although its nonspecific nature requires careful interpretation in the context of other clinical findings [25][26][27]. These studies highlight the utility of CRP not only in identifying infection but also in guiding risk stratification and monitoring therapeutic response in patients with acute or chronic infectious conditions. However, mild or moderate elevations in CRP may have limited clinical significance. Values in the lower ranges may result from minor inflammation, chronic low-grade conditions, or lifestyle factors such as obesity, smoking, or sedentary behavior. Without clinical correlation, these modest increases can be misleading and may not indicate an acute pathological process. Therefore, interpretation of CRP must consider patient history, comorbidities, and presenting symptoms to ensure appropriate clinical decision-making. Integrating CRP levels into the broader clinical context enhances its reliability as a diagnostic and prognostic marker while minimizing the risk of overdiagnosis or unnecessary intervention [25][26][27].

#### **Conclusion:**

C-reactive protein is a central biomarker reflecting the presence and severity of systemic inflammation. Its rapid kinetics, structural versatility, and involvement in both protective and pathological immune responses make it clinically indispensable. Significantly elevated CRP levels are strongly associated with acute bacterial infections and can assist in distinguishing them from viral or noninfectious etiologies. CRP also provides prognostic insights in viral illnesses, tropical infections, cardiovascular disease, and oncologic conditions, although its nonspecific nature requires careful interpretation within the broader clinical context. Mild or moderate elevations may reflect lifestyle factors or chronic low-grade inflammation, emphasizing the need for comprehensive patient assessment. Integrating CRP with additional laboratory markers, imaging, and clinical evaluation

enhances diagnostic precision and prevents misinterpretation. As technological advances improve measurement sensitivity and accessibility, CRP will continue to support informed decision-making across acute care, chronic disease management, and preventive medicine.

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