ISSN 2582 – 6050

Available Online at www.ijpscr.info
International Journal of Pharmaceutical Sciences and Clinical Research 2022; 2(2):50-57

RESEARCH ARTICLE

A Concise Review on C-Reactive Protein and their Test

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Received: 15-03-2022; Revised: 01-04-2022; Accepted: 30-04-2022

ABSTRACT

Interactions in conjunction with the inherent optical properties of quantum dots (QDs) resulted in lower background single increased sensitivity and ability to detect C-reactive protein (CRP) down to 0.79 mg/L with only microliters serum sample in addition the developed assay in simple past and can quantitatively detect CRP with a detection limit up to 200 mg/L clinical test result of our QD-based immune filtration assay, which are well correlated with the traditional latex enhance immune agglutination aggregation. The gene coding for CRP is located on chromosome 1q23.2 which fall within a linkage region thought a harbor a systemic lupus erythematous (SLE) susceptibility gene. Recently, two single nucleotide polymorphisms (SNPs) in the CRP gene (+838, +2043) have been shown to be associated with CRP level and/SLE risk in in a British family based cohort and also to investigate the impact of three additional CRP tag SNPs bracket (−861, −390, +90) on serum protein electrophoresis risk and serum CRP levels. The blood of patients with allergic diseases has been tested for the presence of CRP. No relationship was found between allergic symptoms and the presence of this substance in the blood except in the cases of urticaria of hundred patients with infective customer 14 head CRP values off 2 plus or higher only two of these did not have diagnosis other than their asthma. Initially carrier CRP was usually present roughly in proportion to the extensiveness of the lesions, but there were two notable exceptions to this.

Keywords: Chris-Atkins-Munch-Peterson test, Coombs test, C-reactive protein test, C-reactive protein, Inflammation, Pyrrolidonyl arylamidase test, Rapid plasma reagin test, Vascular diseases

INTRODUCTION

C-reactive protein (CRP) is an acute-phase protein found in the blood, the levels of which rise in response to inflammation: CRP is synthesized by the liver in response to factors released by macrophages and fat cells (adipocytes).

CRP levels are not elevated in systemic lupus erythematous (SLE) unless serositis or synovitis is present. Elevations of CRP in the absence of clinically significant inflammation can occur in renal failure. CRP level is an independent risk factor for atherosclerotic disease.

Patients with high CRP concentrations are more likely to develop stroke, myocardial infarction, and severe peripheral vascular disease.

One study found that testing for CRP levels is a better indicator of cardiovascular disease (CVD) than the low-density lipoprotein (LDL) test. However, it is important to know that a CRP test is not a test for heart disease. It is a test for inflammation in the body.

Test is also used for people suffering from autoimmune diseases such as lupus and rheumatoid arthritis. They also cause inflammation. A doctor might test Someone with either condition to see

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if anti-inflammatory medication is working, though the CRP test cannot determine, where the inflammation is taking place.

A variation of the CRP test, the high-sensitivity CRP (hs-CRP), is used to check for CVD.

It is a simple blood test. A sample is drawn from a vein, most likely in your arm. No special preparation is needed (like fasting) and the test is not painful beyond a sting on the arm from, where needle is inserted. The test may be affected by medications you take, so ask your doctor if you need to cut back beforehand. The blood sample is tested at a laboratory.

Result can be illustrated as below:

- hs-CRP level of lower than 1.0 mg/L – Low risk of CVD (heart disease)
- hs-CRP level of 1.0 mg/L and 3.0 mg/L – Moderate risk of CVD
- hs-CRP level of more than 3.0 mg/L – High risk of CVD.

A high level could also be a sign of cancer, infection, inflammatory bowel disease, lupus, rheumatoid arthritis, tuberculosis, or another disease. It could also be high, because you are in the second half of your pregnancy or you are using birth control pills. The hs-CRP test is most useful for people who have a 10–20% chance of having a heart attack within the next 10 years. The test is not helpful for people with a higher or lower risk.

Because your CRP level can vary, the test should be done two times (2 weeks apart) to determine your risk of heart disease. It is also important to remember that you could have a high reading without necessarily having heart disease. Hence, it is important to check your LDL levels as well to get a full picture of your CVD risk.

Fortunately, the same statin medications that lower LDL have also been shown to lower CRP levels. In addition to any medicine, you should make some lifestyle changes (cut down on fatty foods, stop smoking, and start exercising) at the same time.

Types of test

- CRP test
- Rapid plasma reagin (RPR) test for the diagnosis of syphilis.
- Coombs test.
- Urease test.
- Oxidase test
- Bile solubility test.
- Pyrrolidonyl arylamidase (PYR) test.
- Catalase test.
- Germ tube test.
- Optochin susceptibility test.
- Methyl red (MR) test.
- Nitrate reaction test.
- Hydrogen sulfide test.
- Ames test.
- Potassium hydroxide test.
- Kiglersin agar test.
- Chris-Atkins-Munch-Peterson (CAMP) test.
- Citrate utilization test.

Types of CRP

1) Conventional CRP.
2) High sensitivity CRP
3) Cardiac CRP.
4) Coombs test

Red cells coated with complement or immunoglobulin G (IgG) antibodies do not agglutinate directly when centrifuged. These cells are said to be sensitized with IgG or complement. In order to occur an additional antibody, which reacts with the Fc portion of the IgG antibody, or with the C3b or C3d component, it must be added to the system. This will form a "bridge" between the antibodies or complement coating the red cells, causing agglutination.

Types of Coombs test

Direct Coombs test (direct antiglobulin test – DAT) Direct the direct Coombs test is used to detect antibodies (IgG or C3) that are stuck to the surface of red blood cells. Many diseases and drugs can cause this. These antibodies sometimes destroy red blood cells and cause anemia.

This is the test that is done on the newborn's blood sample, usually in the setting of a newborn with jaundice. The two most commonly recognized forms of antibody-mediated hemolysis in newborns are Rh incompatibility and ABO incompatibility.

Procedure of direct Coombs test:

- Prepare a 5% suspension in isotonic saline of the red blood cells to be tested.
- With clean pipette add one drop of the prepared cell suspension to a small tube.
- Wash three times with normal saline to remove all the traces of serum.
- Decant completely after the last washing.
- Add two drops of Anti-human serum.
- Mix well and centrifuge for 1 min at 1500 RPM.
- Resuspend the cells by gentle agitation and examine macroscopically and microscopically for agglutination.
- Indirect Coombs test (indirect antiglobulin test) [Figure 1].
- The indirect Coombs test looks for free-flowing antibodies against certain red blood cells. It is most often done to determine if you may have a reaction to a blood transfusion.

Negative result

No clumping of cells. This means that you have no antibodies to red blood cells.

Positive result

Clumping (agglutination) of the blood cells during a direct Coombs test means that you have antibodies on the red blood cells and that you may have a condition that causes the destruction of red blood cells by your immune system (hemolysis). This may be due to:

- Hemolytic anemia,
- Chronic lymphocytic leukemia or similar disorder,
- Erythroblastosis fetalis (hemolytic disease of the newborn),
- Infectious mononucleosis,
- Mycoplasmal infection,
- Syphilis,
- Systemic lupus erythematosus and,
- Transfusion reaction, such as one due to improperly matched units of blood.

Urease test

Urea is the product of decarboxylation of amino acids. Hydrolysis of urea produces ammonia and carbon dioxide (CO_2). The formation of ammonia alkalinizes the medium and the pH shift is detected by the color change of phenol red from light orange at pH = 6.8 to magenta (pink) at pH = 8.1. Rapid urease-positive organisms turn the entire medium pink within 24 h.

Uses of urease test

This test is used to differentiate organisms based on their ability to hydrolyze urea with the enzyme urease [Figure 2].

CRP test

C-reactive protein (CRP), also known as Pentraxin 1, is a non-glycosylated protein in the Pentraxin family that also includes Pentraxin 2/SAP and Pentraxin 3/TSG-14. CRP is an acute phase reactant, a protein made by the liver and released into the blood within a few hours after tissue injury, the start of an infection, or other cause of inflammation.
A high level of CRP in the blood is a sign that there may be an inflammatory process occurring in the body. Inflammation itself is not typically a problem,

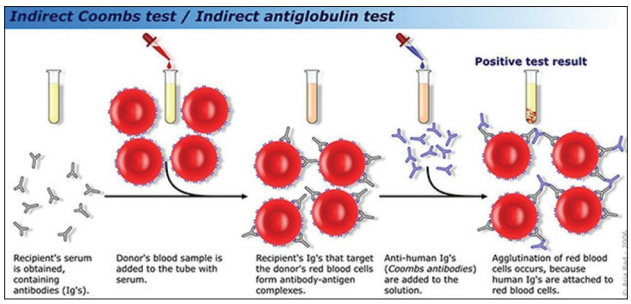


Figure 1: Indirect Coombs test

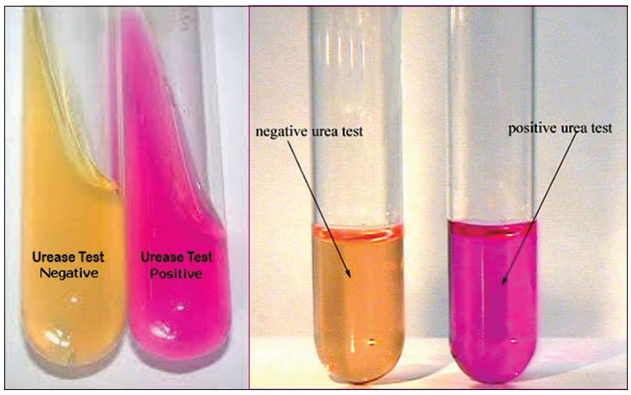


Figure 2: Urease test

but it can indicate a host of other health concerns, including infection, arthritis, kidney failure, and pancreatitis. High CRP levels may put patients at increased risk for coronary artery disease (CAD), which can cause a heart attack.

A CRP test is a blood test designed to measure the amount of CRP in the blood [Figure 3].

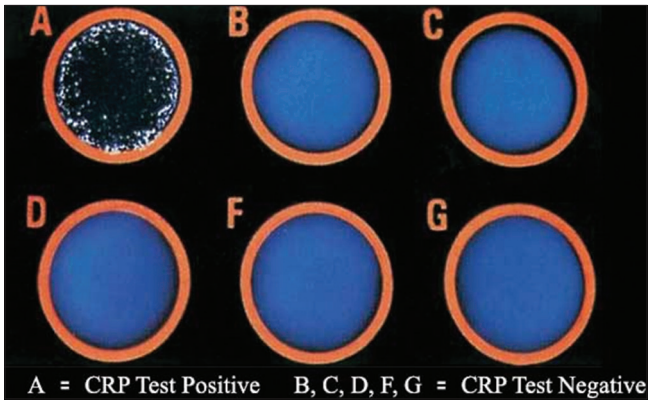


Figure 3: C-reactive protein test

PYR test

PYR test is used for the detection of pyrrolidonyl arylamidase(alsocalledpyrrolidonylaminopeptidase) activity in *Streptococcus pyogenes* (Group A strep), *Enterococcus* spp., some coagulase-negative staphylococci, and some Enterobacteriaceae. It is also known as PYR (L-pyrrolidonyl-β-naphthylamide) which serves as a substrate for the detection of pyrrolidonyl peptidase [Figure 4].

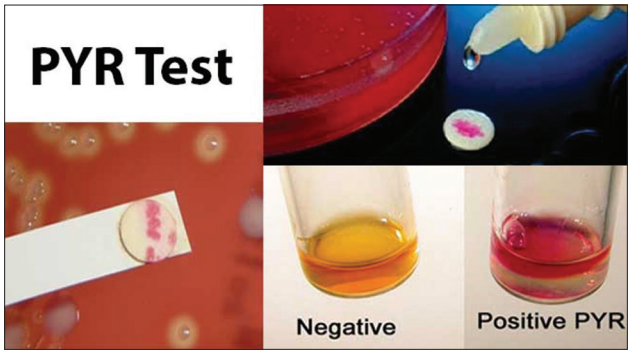


Figure 4: Pyrrolidonyl arylamidase test

CAMP test

CAMP test is used to distinguish the species *Streptococcus agalactiae* from other species of beta-hemolytic Streptococcus. *S. agalactiae*, a member of the Lancefield Group B streptococci, is one of the causative agents of mastitis in cows. CAMP is an acronym for the authors of this test (Christie, Atkinson, Munch, and Peterson) which was identified in 1944 [Figure 5].

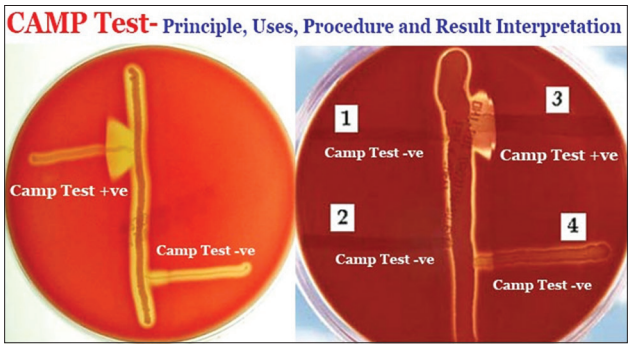


Figure 5: Chris-Atkins-Munch-Peterson test

Analytical profile index (API) 20E test

API identification products are test kits for identification of Gram-positive and Gram-negative bacteria and yeast.

API strips give accurate identifications based on extensive databases and are standardized, easy-to-use test systems [Figure 6].

Kligler's Iron Agar (KIA) test

The Kligler's Iron Agar test employs a medium for the identification of Enterobacteriaceae, based on double sugar fermentation and hydrogen sulfide production. In 1918, Kligler described a medium for detection of H_2S and differentiation of Salmonella spp. Bailey and Lacey further modified the medium by substituting phenol red indicator for Andrade indicator. This medium became known as KIA. It is recommended for determination of H_2S production by enteric Gram-negative bacilli and for detection of H_2S produced by some strains of Pseudomonas [Figure 7].

The MR test

Detects the production of sufficient acid during the fermentation of glucose and the maintenance of conditions such that the pH of an old culture is sustained below a value of about 4.5, as shown by a change in the color of the MR indicator which

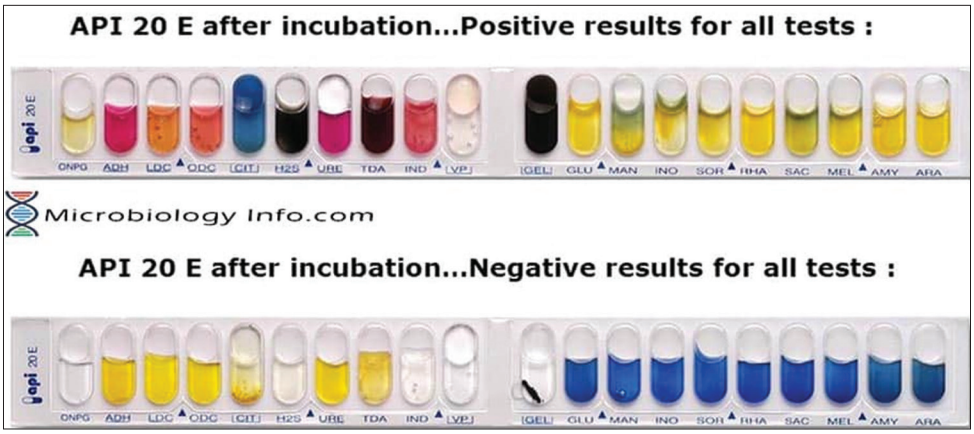


Figure 6: Analytical profile index test

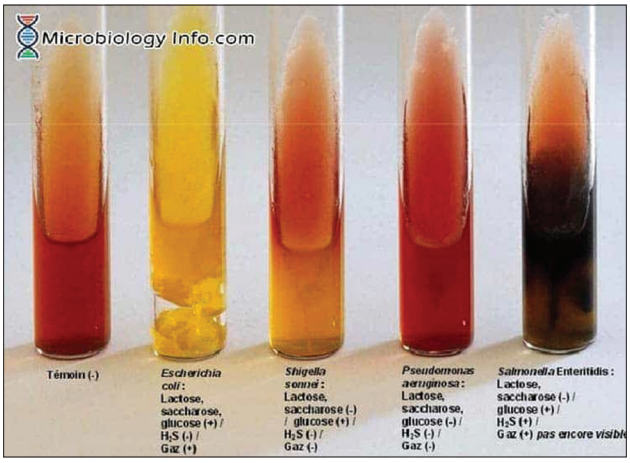


Figure 7: Agar test

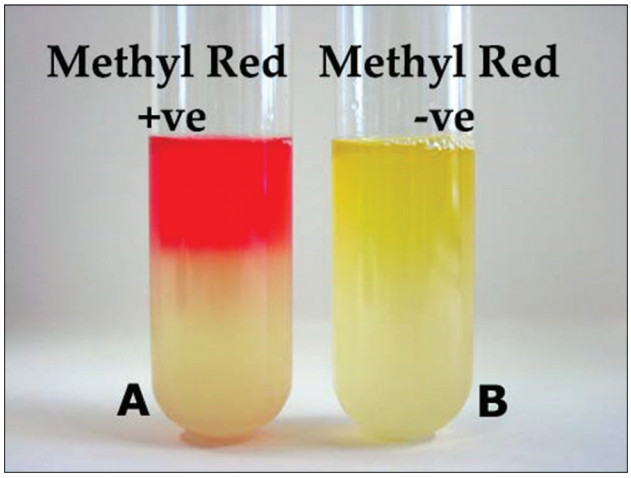


Figure 8: Methyl red test

is added at the end of the period of incubation. The MR test detects the production of sufficient acid during the fermentation of glucose and the maintenance of conditions such that the pH of an old culture is sustained below a value of about 4.5, as shown by a change in the color of the MR indicator which is added at the end of the period of incubation [Figure 8].

Optochin susceptibility test

A positive presumptive identification of *S. pneumoniae* is made when a well-defined zone of inhibition results around the impregnated disk. Other alpha-hemolytic streptococci do not display this clear zone of inhibition when in the presence of optochin. The chemical tests showing the fragility of the bacterial cell membrane and causes S. pneumoniae to lyse due to changes in surface tension [Figure 9].

Function of CRP

- The measurement of CRP is widely used to monitor various inflammatory States. CRP binds to damaged tissue to nuclear antigen and to certain pathogenic organism in a calcium-dependent manner. The function of CRP is failed to be related to its role in the innate immune system.
- CRP binds to determinants on microorganisms and damaged cells
- CRP activates the classical complement pathway.
- CRP is actively transported to the nucleus of cells.
- CRP is protective against the development of autoimmunity in mice.
- CRP protects mice from pneumococcal syndrome.
- CRP protects mice from pneumococcal

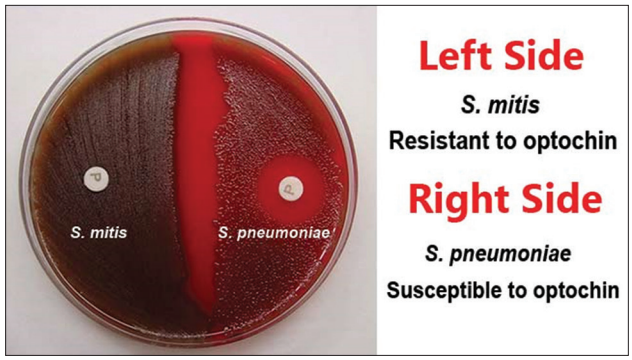


Figure 9: Optochin susceptibility test

syndrome.

- CRP uses Fc receptors to opsonize bacterial and particulate antigens.
- Interaction of CRP with Fc receptors leads to the production of inflammatory cytokines.
- Other names: CRP, serum used.
- A CRP test may be used to find or monitor conditions that cause inflammation. These include:
- Use
- Bacterial infections, such as sepsis, a severe, and sometimes life-threatening condition
- A fungal infection
- Inflammatory bowel disease, a disorder that causes swelling and bleeding in the intestines
- An autoimmune disorder such as lupus or rheumatoid arthritis
- An infection of the bone called osteomyelitis.

Need of CRP test

You may need this test if you have symptoms of a serious bacterial infection.

Symptoms include:

1) Fever
2) Chills
3) Rapid breathing
4) Rapid heart rate
5) Nausea and vomiting.

If you have already been diagnosed with an infection or have a chronic disease, this test may be used to monitor your treatment. CRP levels rise and fall depending on how much inflammation you have. If your CRP levels go down, it is a sign that your treatment for inflammation is working.

During a CRP test

A health-care professional will take a blood sample from a vein in your arm, using a small needle. After the needle is inserted, a small amount of blood will be collected into a test tube or vial. Youmay feel a little sting when the needle goes in or out. This process usually takes <5 min.

Need to prepare for the test

You do not need any special preparations for a CRP test.

Risks to the test

There is very little risk to having a blood test. You may have slight pain or bruising at the spot, where the needle was put in, but most symptoms go away quickly.

Know about a CRP test

A CRP test is sometimes confused with a hs-CRP test. Although they both measure CRP, they are used to diagnose different conditions. An hs-CRP test measures much lower levels of CRP. It is used to check for risk of heart disease.

CONCLUSION

Much has been learned about the biological properties of CRP through *in vitro* and *in vivo* studies. These studies suggest that CRP plays an essential role in the recognition of self and foreign molecules. This interaction leads to an activation of the adaptive immune system early in the course of an inflammatory or infectious process. Through interaction with the complement system and Fc receptors on phagocytic cells, CRP plays a direct role in the clearance of these molecules. However, recent findings of the ability of CRP to interact with Fc receptors and the generation of transgenic models should lead to new insight into this ancient and versatile member of the innate immune system. CRP levels predict future cardiovascular events in patients with chronic stable angina independently

of CAD severity. CRP concentrations are also higher in patients with acute coronary syndromes and correlate with number of complex vulnerable plaques in these patients. These findings indicate that serum CRP levels are a marker of CAD activity and may be a bio-chemical marker of the diffuse inflammatory process that leads to multifocal plaque instability.

CRP levels are associated with blood pressure, pulse pressure, and hypertension, but adjustment for life course confounding and a Mendelian randomization approach suggests that the elevated CRP levels do not lead to elevated blood pressure.

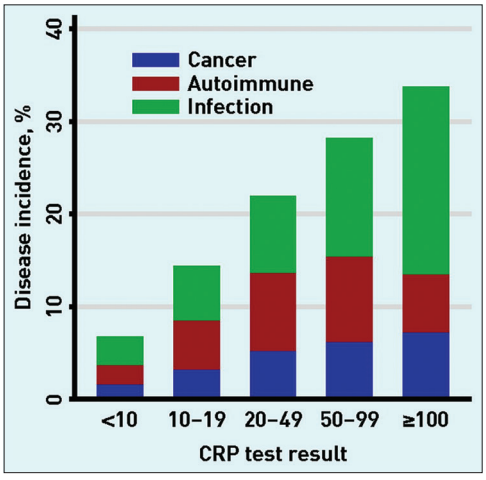
In a large study, we demonstrate that CRP levels but not a genetic variant associated with CRP levels were related to hypertension. Furthermore, the CRP association with hypertension was essentially abolished by statistical adjustment for confounding factors. We conclude that elevated CRP levels do not lead to elevated blood pressure.

CRP is a marker of systemic inflammation and has been postulated to increase the risk of the development of hypertension.[1] Although a large number of studies show that higher levels of circulating CRP are related to higher blood pressure,[1-10] these associations may be non-causal. Factors that increase CRP levels (such as obesity, smoking, adverse socioeconomic circumstances, and various disease states) may themselves influence blood pressure levels. The conventional approach to this issue is to statistically adjust for such confounding factors, but this approach may be misleading given measurement error in the assessment of confounders or the presence of unmeasured confounders, both of which lead to inadequate statistical control and residual confounding.[11] Further, because most studies of this association have been cross-sectional,[2-7] reverse causality cannot be excluded from the study. We demonstrated recently that in a situation in which observational epidemiological studies and randomized controlled data have given discrepant findings (that of vitamin C and CVD risk) taking into account a wide range of confounding factors acting over the life course leads to observational study results being close to those of randomized trials.[12,13] In addition, a potentially powerful approach to avoiding residual confounding and reverse causation is through Mendelian randomization.[14,15] In this approach, genotypes that influence the variable of interest are directly related to the outcome. The genotypes will not be associated with confounding factors, such as obesity, smoking, and social circumstances, nor will they be related to disease processes that themselves influence CRP levels.[15] Thus, the association between genotype and outcome can give an unconfounded test of whether CRP levels causally influence outcomes. Therefore, we have applied this method, using the (dbSNP_1800947) 1059G/C polymorphism within the exon 2 of the CRP gene, which is associated with CRP concentrations,[16] to investigate whether CRP levels influence blood pressure in the British Women's Heart and Health Study.

Below CRP test for chronic disorder as mentioned below:

S. No.	Chronic disorders	Test indication
1.	Rheumatoid arthritis	CRP test
2.	Inflammation	CRP test
3.	Cardiovascular disease	CRP test
4.	Anemia	Coombs test
5.	Jaundice	Coombs test
6.	Coronary artery disease	CRP test
7.	Pneumoniae	Optochin susceptibility test
8.	Syphilis	Coomb's test
9.	Heart attack	CRP test

CRP: C-reactive protein



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