PreventID® CRP 1/3

Manual (FOR PROFESSIONAL USE)

REF KST02612TP
KST02612GP

Intended Use

PreventID® CRP 1/3 is a semi quantitative test used to detect high sensitive CRP (hsCRP) in whole blood for the prediction of first and recurrent cardiovascular events. The sensitivity of the test is 1 mg/L CRP.

Introduction

C-reactive protein (CRP) is a nonspecific acute-phase protein formed by hepatocytes and it is considered to be an indicator of acute injury, bacterial infection and inflammation. In addition, several studies have shown that CRP additionally serves as an indicator of myocardial infarction or other future cardiovascular disease (CVD) as well as a parameter for monitoring [1, 2].

While in acute inflammation of other genesis, the CRP level increases in a very short time (about 6 hours), but can also fall off again as quickly, slightly elevated CRP levels are permanently increased and – in the absence of obvious inflammation – can be used for the CVD prediction [1].

Inflammatory reactions in the vessel wall play a role in the initiation, growth and destabilisation of atherosclerotic plaques (destabilisation means tearing of a plaque and thus the risk of vascular occlusion). Atherosclerotic plaques in the vessel walls are associated with a slightly elevated CRP level (range> 1 mg/L to <10 mg/L). Therefore, CRP is a predictor of cardiovascular disease for primary prevention in clinically healthy people [4].

"High sensitive CRP" means that CRP is measured in the range close to normal levels, i. e in a range between 0.5 and 10 mg/L. **PreventID® CRP 1/3** allows to determine whether CRP is less than 1 mg/L, between 1 and 3 mg/L or above 3 mg/L. If the determined CRP concentration is above 3 mg/L, a re-determination should be carried out after 2 to 3 weeks. When the value is repeatedly increased and other causes (acute infection or other chronic inflammatory diseases) can be excluded, then the determined CRP concentration can be used for the risk stratification [3].

Test Principle

PreventID® CRP 1/3 3 is a sandwich immunoassay. The test contains a nitrocellulose membrane strip with an immobilised mouse anti-CRP antibody in the test line region (T), an immobilised goat anti-rabbit antibody in the reference line region (R) as 3mg/L CRP semi-quantitative reference marker, another immobilised goat-anti-mouse antibody in the control line region (C) and a mouse anti-CRP antibody as well as a rabbit antibody which are coupled with colloidal gold on the conjugate pad.
During the assay the analyte (i. e. CRP antigen) in the blood reacts with the colloidal gold coupled CRP antibody on the conjugate pad thus forming an antibody – antigen – colloidal gold complex while the liquid is moving along the membrane all complexes and conjugates are transported along the membrane. When the complexes reach the respective immobilised mouse anti-CRP antibody on the membrane, they are trapped and will form a sandwich complex consisting of: immobilised antibody – antigen (analyte) – antibody – colloidal gold. Only when the applied blood sample contains a certain concentration of CRP, the formation of this sandwich complex will result in a visible purple T-line. The liquid colloidal gold conjugates also migrate to the reference line and a fixed visible intensity of R (3 mg/L marker) is developed. The liquid colloidal gold conjugates continue to move to the control area (C) band on the membrane. There, this conjugate will form a complex with the immobilised anti mouse antibody resulting in the formation of a purple coloured control (C) line. This indicates that the test has been performed correctly. The test line (T) intensity is used to semi-quantitatively determine CRP concentration in the blood sample.

Materials

Materials Provided

- Test devices with sample droppers, individually packed TEST
- Bottles with buffer solution BUF
- Manual

Materials Required but not Provided: Alcohol pad, sterile lancet, timer or stop watch

Storage and Stability

Store the test between 4 °C and 30 °C; do not freeze. The test device is sensitive to humidity as well as to heat. Perform the test immediately after removing the test device from the pouch. Do not use it beyond the expiry date.

Precautions

1. For *in vitro* diagnostic use only.
2. Do not eat or smoke while handling specimen. Wear protective gloves and wash hands thoroughly after performing the test.
3. Avoid splashing or aerosol formation while handling specimen and performing the test.
4. All samples and materials used should be treated as potentially infectious and disposed in a biohazard container. Clean all contaminated objects and surfaces carefully.
5. The same lancet should only be used for one person and should not be shared with another person, because the used lancet is biohazard.
6. Do not use test if the pouch is torn or if the membrane of the test device is visibly damaged. Note the expiry date.
7. Read the instruction carefully before performing the test.
8. Do not mix reagents from different lots.
9. If you have any questions please contact Preventis GmbH.

Test Procedure

1. Remove the test device and the sample dropper from the pouch and place it on a flat, dry surface.
2. Clean the second or third finger by rubbing it with an alcohol pad.
3. **Prick fingertip** with a sterile lancet.
4. Massage near the site to obtain blood flow. Place the tip of the sample dropper into the blood sample and make sure the sample dropper is slightly lower than the blood sample so that the blood will automatically flow into the sample dropper. **Fill the sample dropper with blood sample** until it reaches the black line *(Fig. 1)*. If insufficient blood sample, massage near the site again to obtain more blood flow and fill the sample dropper until the black line.
5. Then place the tip of the sample dropper vertically into the sample application window of the test device. Place two fingers over the vent hole of the sample dropper (blocking air flow) and squeeze the top of the sample dropper to **expel the blood sample (about 40 µL) into the sample application window** *(Fig. 2)*.

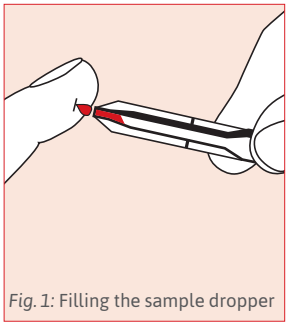

Fig. 1: Filling the sample dropper

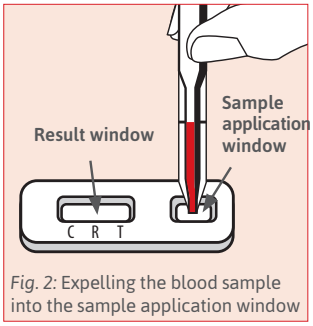

Fig. 2: Expelling the blood sample into the sample application window

Note: If the vent hole is not completely blocked (not pictured in *Fig. 2!*), blood sample will not be completely expelled from the sample dropper.

6. Open the bottle with buffer solution and hold it upside down. Make sure holding the bottle vertically (drops may contain air-bubbles if not holding the buffer bottle vertically), **slowly add 3–4 hanging drops of buffer solution** into the sample application window.
   Note: Add the next drop after the precious drop is absorbed into the sample application window.
7. As the test begins to work, you will see purple colour dyes move across the result window in the center of the test device.
8. **Interpret test results at 5 minutes.** Do not interpret test results after 7 minutes.

Caution: The above interpretation time is based on reading the test results at room temperature of 15 °C to 30 °C.

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Test Interpretation

1. A colour line will appear at the left section of the result window to show that the test is working properly. This band is the **control line (C).**
2. The middle section of the result window indicates the **reference line** (**R**).
3. The right section of the result window indicates the **test line** (**T**).

CRP concentration less than 1 mg/L: Control line and reference line are visible. The test line is not visible, indicating that CRP level is less than 1 mg/L *(Fig. 3a)*.

➨ CRP concentration less than 1.0 mg/L = low relative risk for CVD

CRP concentration of 1 mg/L to less than 3 mg/L: Control line, reference line and test line are visible. The intensity of the test line (T) is weaker than the intensity of the reference line (R) indicating that CRP level is 1 mg/L to less than 3 mg/L *(Fig. 3b)*.

➨ CRP concentration between 1.0 mg/L and 3.0 mg/L = average relative risk for CVD

CRP concentration of 3 mg/L: Control line, reference line and test line are visible. The intensity of the test line (T) is similar to the reference line (R) indicating that CRP level is 3 mg/L *(Fig. 3c)*.

➨ CRP concentration of 3.0 mg/L = average relative risk for CVD

CRP concentration higher than 3 mg/L: Control line, reference line and test line are visible. The intensity of the test line (T) is darker than the reference line (R) indicating that CRP level is higher than 3 mg/L *(Fig. 3d)*.

➨ CRP concentration higher than 3 mg/L = high relative risk for CVD

Invalid: If after performing the test, no reference line and control line are visible within the result window, the result is considered invalid. Some causes of invalid results are not following the directions correctly, such as insufficient amount of sample or buffer added or the test may have deteriorated beyond the expiry date *(Fig. 3e)*.

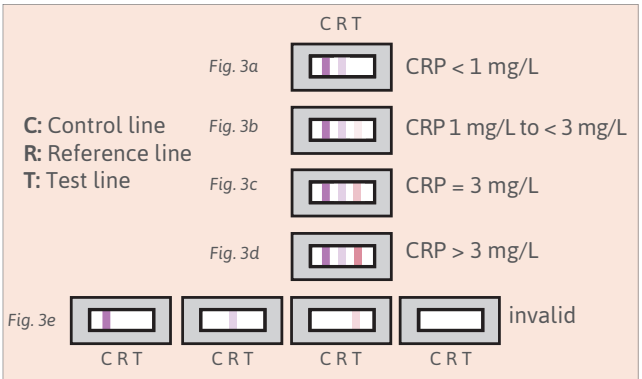

Fig. 3: **PreventID® CRP 1/3** Test interpretation

Note: Generally, the higher the CRP level in the specimen, the stronger the colour of the test line (T) will be. Very higher CRP level specimens can cause reduced colour intensity of the test line (T) (so called "*Hook Effect*").

Note: A positive result will not change once it has been established at 5 minutes. However, in order to prevent any incorrect results, the test result should not be interpreted after 7 minutes. Interpreting test results after 7 minutes, the sensitivity of the test will be higher than 1 mg/L.

Some specimens with a high rheumatoid factor concentration may in the presence of bacterial infections or in patients with acute or chronic inflammatory diseases yield a non-specific positive result. The **PreventID® CRP 1/3** test for risk stratification of CVD should therefore be carried out only in apparently healthy people.

Test Characteristics

The AHA (American Heart Association) and CDC (Center for Disease Control) states that concentrations of less than 1.0 mg/L defined as low risk, 1.0–3.0 mg/L as average risk and concentrations higher than 3.0 mg/L defined as high risk referring for hs-CRP and cardiovascular disease.

Sensitivity and Specificity

The IMMAGE 800 of Beckman Coulter is used as gold standard for hs-CRP concentration for the purpose of this study.

The relative sensitivity of the **PreventID® CRP 1/3** was – depending on the lot – at least 97 % for the concentration <1 mg/L, 94 % for the hs-CRP concentration between 1 and 3 mg/L and for the concentration >3 mg/L 97 % or higher.

Specificity testing with various microorganisms showed no interference with the **PreventID® CRP 1/3** test: all positive samples remain positive, all negative samples remain negative in their ranges.

Potentially interfering chemical substances such as pain medication, lipids, hemoglobin, bilirubin and glucose were supplemented to clinically defined negative normal blood. These samples were tested using the **PreventID® CRP 1/3** test and showed no interference.

In conclusion: the data demonstrate the **PreventID® CRP 1/3** test is substantially equivalent to IMMAGE-800 for the purpose of determining Cardiac Risk.

Test Limitations

Test results are only reliable if you follow the instructions for use carefully. Although the **PreventID® CRP 1/3** is very accurate in detecting CRP, a low incidence of false results can occur. Other clinically available tests are required if questionable results are obtained.

As with all diagnostic tests, a definitive clinical diagnosis should not be based on the results of a single test, but should only be made by the physician after all clinical and laboratory findings have been evaluated.

References:

1. Ridker et al. (2002) N Engl J Med 347 : 1557-1565
2. Ridker et al. (2000) N Engl J Med 342 : 836-843
3. Rifai N, Ridker PM (2001) Clin Chem 47: 403-411
4. Shah PK (2000) Circulation 101: 1758-59

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Status: 2018-11-21

US: all products: Research Use Only. Not for use in diagnostic procedures.

Temperature limitation	Manufacturer
IVD *In vitro* diagnostic device	LOT Lot number
REF Catalogue number	Expiry date
To be used with	Do not reuse
Read user instructions	Contains sufficient for <n> tests
Keep away from sunlight	

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