

## COVID-19: Antibody Tests and Neutralising Antibodies

Lars Peter Nielsen, Professor in Virology and Consultant in Clinical Microbiology

*Prior to determining which of the plethora of tests to choose from regarding the determination of the presence of antibodies against SARS-CoV-2 and the worldwide pandemic, the following points should be at the forefront of your decision-making process:*

### **A quick test or a laboratory-based test**

Quick tests can be read after 10-20 minutes and only require a drop of blood from a finger prick. The Biosynex test can be read after 10 minutes. Laboratory based-tests require much more time to obtain results and require conventional blood testing. Laboratory-based tests can provide a graded result while quick tests only provide a positive or negative response.

Laboratory-based tests require skilled personnel and specialised equipment in order to attain results while the quick test only requires a health care professional (doctor/nurse/pharmacist) to carry out the test

### **Sensitivity and specificity**

A test's *sensitivity* is of course a very important parameter when determining which test to use. Many of the available quick tests demonstrate a very low sensitivity, which is of course unacceptable in as much as they may not pick up antibodies which may result in a degree of immunity and furthermore, lead to unnecessary isolation.

If a test is not particularly *specific* results may indicate that there are antibodies in individuals which are not relevant. This is particularly unfortunate in that individuals may then consider themselves to have a degree of immunity even though they are as vulnerable to infection as anyone else. Therefore, *sensitivity* and *specificity* values should be as close to 100% as possible.

It is important to note that laboratory-based tests can pick up very low levels of antibodies which may be difficult to interpret clinically. Does a low concentration of antibodies offer any degree of immunity? This is not known at the present time.

Test versus test studies in which one is a very sensitive laboratory-based test and the other a quick test often demonstrate a lower *sensitivity* in the quick test. This does not render the quick test as being of no value as long as it can identify the individuals that have a degree of protection against future infection. In reality, it renders them very useful.

### **Which reagents are included in the test?**

Antibody tests for the Corona pandemic can be undertaken in many ways and it is important to be sure exactly what you wish to use your chosen test for before determining which test you should choose.

Most tests target only a portion of the pandemic virus. This is done in order to ensure a high degree of *specificity*. Tests that utilise the knowledge of how the virus enters our cells are the most appropriate to predict whether the antibodies that are being measured do in fact offer protection against infection for SARS-CoV-2.

Tests that utilise other parts of the virus are possibly more *sensitive*, but do NOT provide information as to whether an individual is protected or not. These tests can be used to carry out epidemiological studies (how many people have been infected), but they are not particularly useful for the diagnosis of individuals.

Biosynex's test uses a small area of the virus which binds to the structures in the cells that can be infected. Antibodies that act against these parts will theoretically provide protection against infection of the cells and therefore offer protection – see under neutralising antibodies.

### **Which antibodies are identified in the test?**

Antibodies are categorised in different classes depending upon their structure. The different antibodies have different functions in the body and it is important to be able to distinguish between the different types.

When infected by a virus, the immune system will respond by producing antibodies which are named IgM. These antibodies do not bind particularly well to the virus, however, when they do, other parts of the immune system become activated. As the immune response matures IgM antibodies are gradually replaced by IgG antibodies which are far more specific and it is typically these antibodies that provide protection to infection with the same virus.

The detection of IgM antibodies is therefore a sign of the start of a reaction against a viral infection while the detection of IgG indicates that an individual has formed potent antibodies against a specific virus.

Many tests do not differentiate between the two different types of antibodies which renders it impossible to determine whether an individual is still vulnerable to infection. These tests cannot be recommended for usage in individual patients. In general terms, it is preferable to use a test that is able to identify both IgG and IgM antibodies and provides the results distinctly.

### **Do the antibodies prevent infection with the same virus?**

An important reason for antibody testing is to determine whether an individual is protected against infection in the coming months to years. In order to determine this definitively a laboratory-based blood test must be undertaken and found to be positive as regards the antibodies.

Only by mixing the individual's blood serum with the virus and adding cell cultures which allow the virus to multiply are we able to determine whether the antibodies found in the blood serum can prevent additional infection of the cells.

If this is indeed the case, we are dealing with **neutralising antibodies** (= protective antibodies) which are among the best signs that the detected antibodies will offer protection against infection of the virus which results in SARS-CoV-2. This allows us to determine whether individuals have immunity against the virus in question. The examination of neutralising antibodies can only be carried out in specialist laboratories in which the infectious virus can be handled. As you would imagine, examinations of this type are both costly and time consuming.

In studies carried out at the Pasteur Institute (Institut Pasteur, France) it has been determined that the IgG antibodies detected with the Biosynex COVID-19 BSS POC test are indeed neutralising antibodies and that patients with a positive Biosynex antibody test therefore have a degree of protection.

In other words: If the Biosynex test has detected IgG antibodies and a minimum of 14 days have passed since the initial signs of COVID-19 symptoms have begun one can expect to be protected against reinfection for a minimum of several months.