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Why Rapid test? Hotzone solutions group considerations

#### **HUMAN DEFENSE MECHANISM**

The environment contains a wide variety of potentially harmful organisms (pathogens), such as bacteria, viruses, fungi, protozoa and multicellular parasites, which will cause disease if they enter the body and are allowed to multiply. The body protects itself through various defense mechanisms to physically prevent pathogens from entering the body or to kill them if they do.

The immune system is an extremely important defense mechanism that can identify an invading organism and destroy it. Immunization prevents disease by enabling the body to more rapidly respond to attack and enhancing the immune response to a particular organism.

Each pathogen has unique distinguishing components, known as antigens, which enable the immune system to differentiate between 'self' (the body) and 'non-self' (the foreign material). The first time the immune system sees a new antigen, it needs to prepare to destroy it. During this time, the pathogen can multiply and cause disease. However, if the same antigen is seen again, the immune system is poised to confine and destroy the organism rapidly. This is known as adaptive immunity.

Vaccines utilize this adaptive immunity and memory to expose the body to the antigen without causing disease, so that when then live pathogen infects the body, the response is rapid and the pathogen is prevented from causing disease. Depending on the type of infectious organism, the response required to remove it varies. For example, viruses hide within the body's own cells in different tissues, such as the throat, the liver and the nervous system, and bacteria can multiply rapidly within infected tissues.

#### *The immune response*

An immune response is triggered when the immune system is alerted that something foreign has entered the body. Triggers include the release of chemicals by damaged cells and inflammation, and changes in blood supply to an area of damage which attract white blood cells.

White blood cells destroy the infection or convey chemical messages to other parts of the immune system. As blood and tissue fluids circulate around the body, various components of the immune system are continually surveying for potential sources of attack or abnormal cells.

#### *Antigens and antibodies*

Antigens are usually either proteins or polysaccharides (long chains of sugar molecules that make up the cell wall of certain bacteria). An antigen is a molecule that stimulates an immune response and to which antibodies bind – in fact, the name is derived from "antibody generators." Any given organism contains several different antigens. Viruses can contain as few as three antigens to more than 100 as for herpes and pox viruses; whereas protozoa, fungi and bacteria are larger, more complex organisms and contain hundreds to thousands of antigens.

An immune response initially involves the production of antibodies that can bind to a particular antigen and the activation of antigen-specific white blood cells.

Antibodies (immunoglobulins; Ig) are protein molecules that bind specifically to a particular part of an antigen, so called antigenic site or epitope. They are found in the blood and tissue fluids, including mucus secretions, saliva and breast milk. There are five classes of antibody – IgG, IgA, IgM, IgD and



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IgE, which have a range of functions. They can act as 'flags' to direct the immune system to foreign material for destruction and form part of the innate / humoral immune response. Normally, low levels of antibodies circulate in the body tissue fluids. However, when an immune response is activated greater quantities are produced to specifically target the foreign material.

Vaccination increases the levels of circulating antibodies against a certain antigen. Antibodies are produced by a type of white blood cell (lymphocyte) called B cells. Each B cell can only produce antibodies against one specific epitope. When activated, a B cell will multiply to produce more clones able secrete that particular antibody. The class of antibody produced is determined by other cells in the immune system, this is known as cell-mediated immunity.

#### *Primary response*

Upon exposure to a pathogen, the body will attempt to isolate and destroy it. Chemicals released by inflammation increase blood flow and attract white blood cells to the area of infection. Specialist cells, known as phagocytes, engulf the target and dismantle it. These phagocytes then travel to the nearest lymph nodes where they 'present' the antigens to other cells of the immune system to induce a larger, more specific response. This response leads to the production of antigen-specific antibodies.

Circulating antibodies then find the organism and bind to its surface antigens. In this way it is labelled as the target. This specific response is also called the adaptive or cell-mediated immune response, since the immune system adapts to suit the type of invader.

When the body is first exposed to an antigen, several days pass before this adaptive response becomes active. Upon first exposure to a pathogen, immune activity increases, then levels off and falls. Since the first, or primary, immune response is slow it cannot prevent disease, although it may help in recovery.

Once antigen-specific T and B cells (lymphocytes) are activated, their numbers expand and following an infection some *memory* cells remain resulting in memory for the specific antigens. This memory can take a few months to fully develop.

#### *Secondary response*

During subsequent exposures to the same pathogen, the immune system is able to respond rapidly and activity reaches higher levels.

The secondary immune responses can usually prevent disease, because the pathogen is detected, attacked and destroyed before symptoms appear. In general, adults respond more rapidly to infection than children. They are able to prevent disease or reduce the severity of the disease by mounting a rapid and strong immune response to antigens they have previously experienced. In contrast, children have not experienced as many antigens and are more likely to get sick.

Memory of the infection is reinforced and long-lived antibodies remain in circulation. Some infections, such as chickenpox, induce a life-long memory of infection. Other infections, such as influenza, vary from season to season to such an extent that even an adult is unable to adapt.

#### *Vaccination*

Vaccination utilizes this secondary response by exposing the body to the antigens of a particular pathogen and activates the immune system without causing disease. Clinically, measured IgG antibody levels are generally considered to be indicative of an individual's immune status to particular pathogens. A common example of this practice are titers drawn to demonstrate serologic immunity to measles, mumps, and rubella (MMR), hepatitis B virus, and varicella (chickenpox), among others.



Are rapid tests reliable and useful?

**1 Expert comment on different types of testing for COVID-19 (Mar 30, 2020)**

<https://www.sciencemediacentre.org/expert-comment-on-different-types-of-testing-for-covid-19/>

The overall answer is "yes".

**So, why healthcare authorities are reluctant to use them?**

Traditionally, the healthcare academia has certain acceptance criteria when comes to lab testing and treatment schemes. Lab testing should be done in large numbers of samples collected by a variety of methods (blood; urine; tissues; bronchoalveolar lavage; sputum; nonlaryngeal swabs; breathing) along with comparison of different methodologies in order to define both specificity and sensitivity (both = accuracy) of a lab test for a specific pathogen or medical condition. The gold standard for a drug for a given disease is the double-blind placebo-controlled method that is indicative if a drug is superior to placebo while eliminating the bias of human subjectivity. This the normal approach in everyday fight for better diagnosis and treatment of diseases. The main disadvantage of both approaches is that they require time – could be months or even years. Time is the sole enemy during a pandemic since time costs lives in a fast-changing human environment. On going pandemic brought into surface a neglected third approach that is the use of already existing laboratory approached and drugs (e.g. hydroxychloroquine; colchicine; BCG vaccine) that might be helpful for the management of current Covid-19 disease. The role of both IgM and IgG in the immune response to external pathogens is well established for a variety of diseases along with the verification of effective immunization. This means that past experience can be applicable today. It seems that sticking to the past is a problem. A second problem might be the fact that many companies around the globe took pandemic as a mean for making profit by manufacturing rapid tests of very low quality – same happened with large shipments of masks made in China; same happened with low quality condoms in the era of HIV/AIDS; same happened during the Athens2004 Olympic Games when more than 50 companies emerged offering CBRN equipment (it was the first Summer Olympiad after 9/11 and anthrax letters) and then disappear just after the games without providing aftersales support. In that respect, those responsible for Public Health might be reluctant to support rapid tests for national screening purposes. But the solution is simple: test the rapid test with real Covid samples (unfortunately there are thousand of patients available in our hospitals worldwide) and perform a background check of the manufacturer. Do they have similar tests? Do they cover a variety of diseases? How long have they been in the market? Do they implement related ISO Standards? Do they have the necessary approvals and certifications – although bureaucracy might be a burden in the midst of a pandemic? A "serious" company will never offer a low quality (accuracy) product that might jeopardize its future position in the healthcare/diagnostics market. Since pandemic and its consequences are here to stay at least by the end of 2020, there is still time to make what is necessary in order to take advantage of the benefits rapid tests are offering in a variety of fields from diagnosis to screening and immunity verification in the day after. ■ JG

**Note:** There was no mention to under the table and behind closed doors games and negotiations, since these are common practices even during pandemics. There is no objection to the fact that money should move around but this can be done together with the selection of reputable products that will save lives and assist communities regaining their compromised normality.

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