



COVID-19 and SARS Coronavirus 2: Antibodies for the Immediate Rescue and Recovery Phase

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The world is in the grip of a devastating SARS-CoV-2 pandemic causing a major health havoc and economic hardship/slowdown. In most affected countries mitigation of transmission by quarantining and social distancing is beginning to reduce hospitalization rates. However, current estimates are that the pandemic will continue for many months. What can be done immediately to control the damage and manage a transition to normalcy?

One approach is to reduce disease severity. A near-term possibility is to treat high risk patients with repurposed existing drugs (1). Another is to use antivirals such as remdesivir, a nucleotide analog, which has been previously shown to have efficacy against MERS disease in a monkey model (2, 3) and now under clinical investigation in China, USA and elsewhere. Recent preliminary results showed some efficacy and more in-depth studies are still underway (3). New compounds will undoubtedly emerge from the laboratory. Antibodies offer promising treatment options. Convalescent SARS antibodies administered early in acute illness were shown to reduce disease severity (4). Efforts are well-underway to manufacture therapeutic gamma globulin from COVID-19 convalescent sera, or alternatively to derive neutralizing monoclonal antibodies (5, 6).

A second approach is to protect high risk persons such as the elderly and persons with pre-existing conditions that include high blood pressure, diabetes, and obesity. Antibodies can be used to protect the vulnerable from infection. After WW II commercial gamma globulin was widely available affording short term protection against measles, paralytic poliomyelitis, hepatitis A, and hepatitis B (7–11). In the 1950s, a large scale blinded efficacy trial found that gamma globulin given to 100,000 children successfully blunted poliomyelitis attack rates (9). To prevent SARS-CoV-2 infections, gamma globulin antibody preparations or monoclonal antibodies can be given to those at high risk of fatal outcome. This requires use of another tool—epidemiology. Careful studies in populations suffering high infection rates should be able to identify risk factors for severe and fatal disease. Protective gamma globulin, once on the market, can be made available to self-identified high-risk persons through family health care providers. Persons in at high risk commercial occupations, health care workers and care givers should be protected. Commercial tests for detecting SARS-CoV-2 IgG antibodies are now on the market. Antibody testing can identify those who are immune and those who at risk and eligible for immunoprotection.

Progress is being made in developing neutralizing monoclonal human antibodies while at the same time the population of COVID-19 convalescents is growing rapidly. These antibodies should be put to work to help manage the pandemic. This will require that immune products be shown to prevent SARS-CoV-2 infections in human volunteers (12). SARS-CoV-2 has been adapted to grow in Vero cells (13). While there is risk, COVID-19 in young adults is seldom a severe disease. There is a long history of using a human challenge model to establish candidate therapeutic and preventive products for microbial pathogens (14–16). Such an approach should help shorten

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the typical long time it takes for vaccine/therapeutic testing. Once a protective level of antibody in humans can be correlated with an *in vitro* value it should be possible to screen candidate products more swiftly. The degree of protection may not confer complete sterilizing immunity but should impede viral spread to pulmonary stage and progression to severe disease. To avoid possible antibody-dependent enhancement (ADE) of COVID-19 infections, the Fc terminus of IgG antibodies should be removed or inactivated. However, this should be studied further to determine whether the risk of ADE outweighs the potential benefits afforded by antibody-dependent cellular cytotoxicity (ADCC) or antibody-dependent cellular phagocytosis (ADCP) (17, 18). Strategic exploitation of antibody-based approaches can help us return to normalcy. Indeed, as an example, using

widespread serological testing, Germany is issuing “immunity certificates” to those who can safely re-enter the normal work force.

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