COVID-19 Antibodies Post Infection: An Analysis of the benefits and the Effect of Antibodies during the COVID-19 pandemic

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ABSTRACT

The current COVID-19 pandemic has left the world scrambling for a solution to tremendous suffering. Many tactics are being employed in order to study the deadly virus and discover treatment options. Determining if a patient has coronavirus antibodies is being used to detect if the patient previously had the virus. In addition to detecting previous infection the antibodies have a multitude of beneficial purposes. Patients who have antibodies are claiming they can't get Covid-19 again and are volunteering for plasma donations as a therapeutic treatment. A study was done in a local orthodox community in order to test which patients have the antibodies and if there are any symptoms and/or previous health conditions that correlate with a positive result. The study concluded that the community was far from reaching herd immunity and that there was a commonality found in positive patients. Currently, generating antibodies are being used in the Covid-19 vaccine to achieve herd immunity without having most of the population infected with the virus, saving millions of lives, and ending the pandemic. This paper discusses the background of the Covid-19 virus, Covid-19 antibodies, and its practical applications during the pandemic.

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I. OVERVIEW OF VIRUSES AND ANTIBODIES

A. Overview of viruses and the human immune system

Viruses are small, obligate intracellular parasites, that depend on host cells to carry out metabolic and biosynthetic machinery, having significant effects on their host. Every day the average human is exposed to the hidden world of microorganisms around us and breathes in about 100,000,000 viruses (Morrow, 2020). Once inhaled, the small virus, ranging from 20 to 400 nanometers in diameter, can become active by hijacking the host cell's machinery (Drexler, 1970).

Our body has brilliant ways to combat the attack of viruses on our host cells. The first line of defense is from non-specific macrophages, dendritic cells, and neutrophils. These cells can engulf and destroy viruses which will either prevent the virus from causing symptoms or slow its progress. The second line of attack is called cellular immunity and is carried out by T cells and B lymphocytes. T cells detect viruses from specialized proteins on their surface that enable them to recognize virally infected cells (Laing). The T cells then signal the B cells to make plasma cells that make antibodies, immunoglobulin proteins. An important aspect of our immune system is that it never forgets a virus that it has encountered. If a person has had more than one cold in his lifetime it means that it must have come from a different strain of a virus (Funk, 2020).

Our body makes $3x10^7$ antibodies that are each a different shape, allowing many different viruses to be neutralized. They are our key antiviral effectors that both eliminate infected cells and neutralize viruses, preventing future cell infection. This is our body's major line of defense against reinfection and therefore it is key for our plasma producing antibodies to survive and maintain in our blood (Moreno-Altamirano, 2019).

B. Discovery of antibodies

The discovery of antibodies began in the 1890s by Emil Behring and Shibasaburo Kitasato in Robert Koch's Hygiene Institute in Berlin. On December 4th, 1890 they published an article showing that serum from an animal actively fighting diphtheria toxin can be used to treat a fatal dose in another infected animal. With dreams of discovering this in humans, a pharmaceutical company, Farberwerke Hoechst, immunized sheep against diphtheria. Paul Ehrlich moved to Koch's Institute in 1889 and decided to work on the large-scale production of an antiserum to diphtheria toxin. He used rabbits and guinea pigs and proposed his side-chain theory of toxicity which would come to be the discovery of antibodies. He explained that toxins mediated their effects on cells from protein side chains which triggered cells to produce antibodies when injected into an animal (Llewelyn, 1992).

Following this discovery, the lab began using plasma donations to cure patients of the measles outbreak in 1944. Agammaglobulinemia patients, patients with a low number of antibodies in the blood, used immunoglobulin injections to prevent infection. Normal immunoglobulin was prepared from 1,000 random donations of human plasma that would typically contain antibodies to hepatitis A, measles, mumps, and other viruses. Specific immunoglobulin on the other hand, comes from patients who have recovered from a certain disease (Llewelyn, 1992).

C. Mechanism of antibodies

Antibody production is part of the body's primary immune response. The first step in the production of antibodies comes after the encounter with a foreign substance in the body. This encounter stimulates B cells to differentiate into clonal plasma cells which will secret antibodies. Each cell can release thousands of antibody molecules into the body's circulation. This produces

2,000 antibody molecules per second. Antibodies will prevent a toxic protein or virus from binding to their target by binding to the antigen and therefore blocking the ability of the cells binding sites ("Boundless Biology."). Antibodies then coat an infected cell with IgG which is recognized by killer lymphocytes. The lymphocytes recognize the cells because of receptors for the Fc region of IgG on their surface. Phagocytes can also target an antigen through the Fc receptors. This combination induces the bursting/lysis of the target cell. Antibodies have the ability to work together in a process called agglutination. This causes the viruses to stick together and therefore make the immune cells able to target them more easily (Laing).

The active components of antibodies are proteins called immunoglobulins. IgG is the prototype antibody; it is a glycoprotein with a weight of 150,000 Daltons. The molecule consists of four polypeptides; two identical heavy chain-light chain heterodimers bonded by a disulfide bridge to form a Y-shaped structure. Each heavy chain comprises one variable and three constant immunoglobulin domains, whereas light chains consist of a single variable and a single constant Ig domain. Each domain comprises about 110 amino acids. The important parts of the antibody are the binding site and the Fc region which initiates the host defense mechanisms. The hinge region is a stretch of amino acids in the central area of the heavy chains that links the two chains by disulfide bonds (Adlersberg, 1976). This flexible region allows the linking of two identical antigens by the same antibody. The multiple binding sites allows for a rapid destruction of viruses. The antigen-binding site is formed by the two globular variable domains, one derived from the heavy chain (VH) and the other from the light chain (VL). The folds of each of the V domains form three short loops of amino acids-the hypervariable loops or complementarity determining regions (CDRs). This variable region is precisely where the antigen is recognized by

the antibody. Due to its variability in amino acid composition and length of the loops, antibodies use incredible specificity (Boundless Biology).

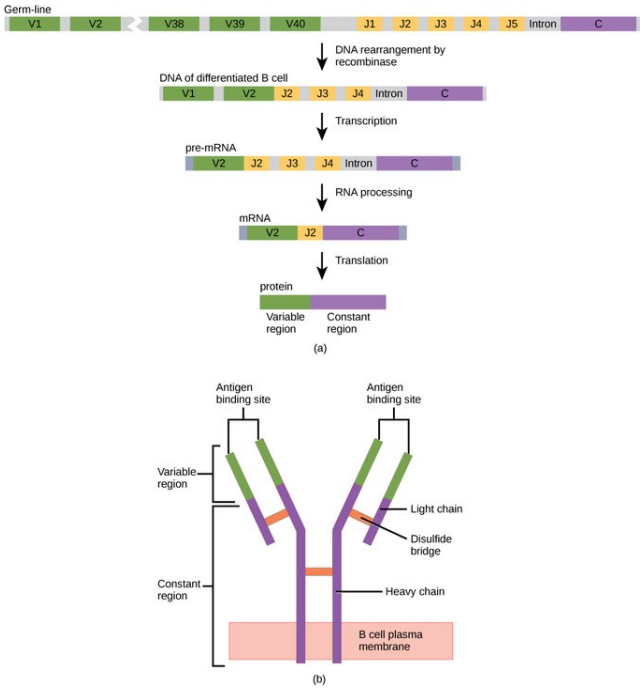

Figure 1. Structure of an antibody (Boundless Biology)

Antibodies are most effective when viruses are present in large fluid spaces like a serum or surfaces like the respiratory tract. Antibodies can neutralize a virus by 1) recognizing viral antigens on virus-infected cells which can lead to antibody-dependent cytotoxic cells destroying the virus or complement-mediated lysis. 2) blocking virus-host cell interactions. (Klimpel, 1996).

When a virus infects our body there is the initial lag phase until the level of antibodies rises quickly, gets to a plateau, and then once the virus is destroyed, stabilizes at a low level. The first antibody to appear is IgM, next is IgG. A memory response is saved by producing memory cells and keeping them in the body's circulation and tissues for years. Therefore, if there is a new attack there is a much shorter lag phase that is dominated by IgG production. (Llewelyn, 1992).

II. COVID-19

A. Overview of the current pandemic

The Covid-19 pandemic began in Wuhan China and was identified in patients suffering from a respiratory disease. There have been 141,057,106 cases reported worldwide and 3,015,043 deaths reported as of April 2021 *("Coronavirus cases",* 2021). The virus has spread rapidly and has mutated into many different strands from the initial virus. By march of 2020 due to the quick global spread, the virus outbreak was declared a pandemic (Klein, 2020).

The Covid virus is part of a large group of viruses that cause gastrointestinal illnesses in animals and respiratory illness in humans. The virus belongs to the subfamily Coronvirinae from the order Nidovirales. The classes that affect humans are Alphacoronaviruses and Betacoronaviruses. The virus is zoonotic meaning it is developed in animals and then is transmitted to humans from direct contact. All Covid epidemics have originated in bats. The virus was transmitted through intermediary animal hosts, in this case specifically seafood sold in a Wuhan market. When the virus is viewed under the microscope, its large peplomers give the appearance of a crown and therefore the name corona was developed. The virus was not known to be deadly until the Sars-Covid outbreak of 2003 and the MERS-Covid outbreak of 2012 (Mackenzie, 2020).

B. Details and mechanism of virus

The virus is a single-stranded positive sense RNA molecule. It is one of the largest known RNA viruses with a genome size between 27-32kbp. The virus has 6 open reading frames as seen in figure 2. The first reading frame encodes for polyprotein1 a, and the next four encode

structural proteins: one of which is the famous envelope glycoprotein spike which recognizes host cell receptors. The other three encode membrane proteins that shape the virions, envelope proteins that assemble and release the virions, and the nucleocapsid protein that package the RNA genome after the genome enters the targeted cell (Alanagreh, 2020).

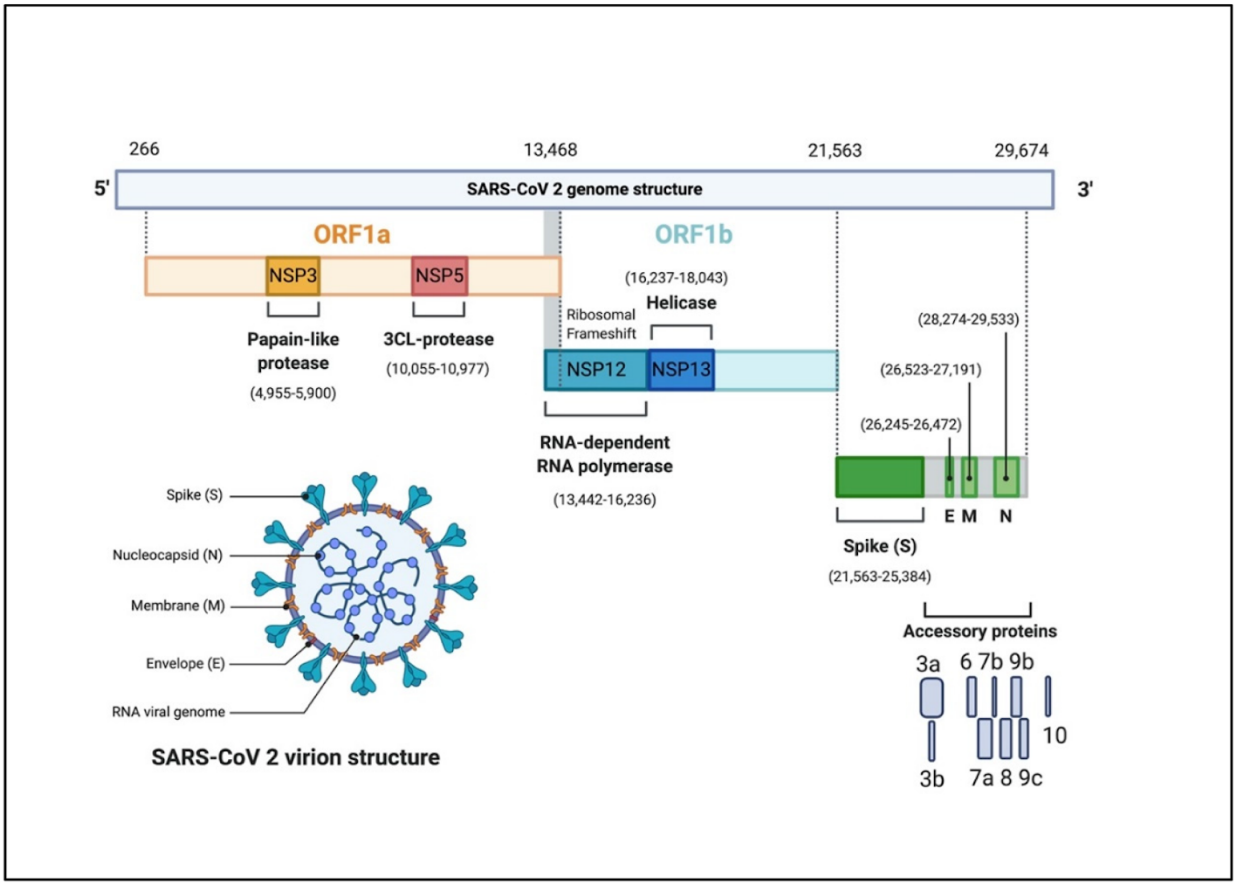

Figure 2. Diagram of SARS-CoV virion structure (Covid-19 Scientific Updates).

The virus mostly infects ciliated bronchial epithelial cells and type 2 pneumocytes. It binds to the cells surface receptors, angiotensin-converting enzyme 2 and S glycoprotein. The S glycoprotein will bind to ACE2 which cleaves the S protein into S1 and S2. The S1 unit facilitates the binding of the virus to the target cells. S2 causes the fusing of the cell membranes allowing the virus to enter through endocytosis (Alanagreh, 2020).

Once the virus is within the cell the viral RNA is unwrapped in the cytoplasm. The ORF1ab and ORF1a are translated into polyproteins pp1a and pp1ab which get cleaved by RTC. The RNA is then replicated into full length RNA genomes. Once the structural proteins are made the nucleocapsids are formed in the cytoplasm and then budded off into the ER and then the Golgi for the virions to be released from the cell (Alanagreh, 2020).

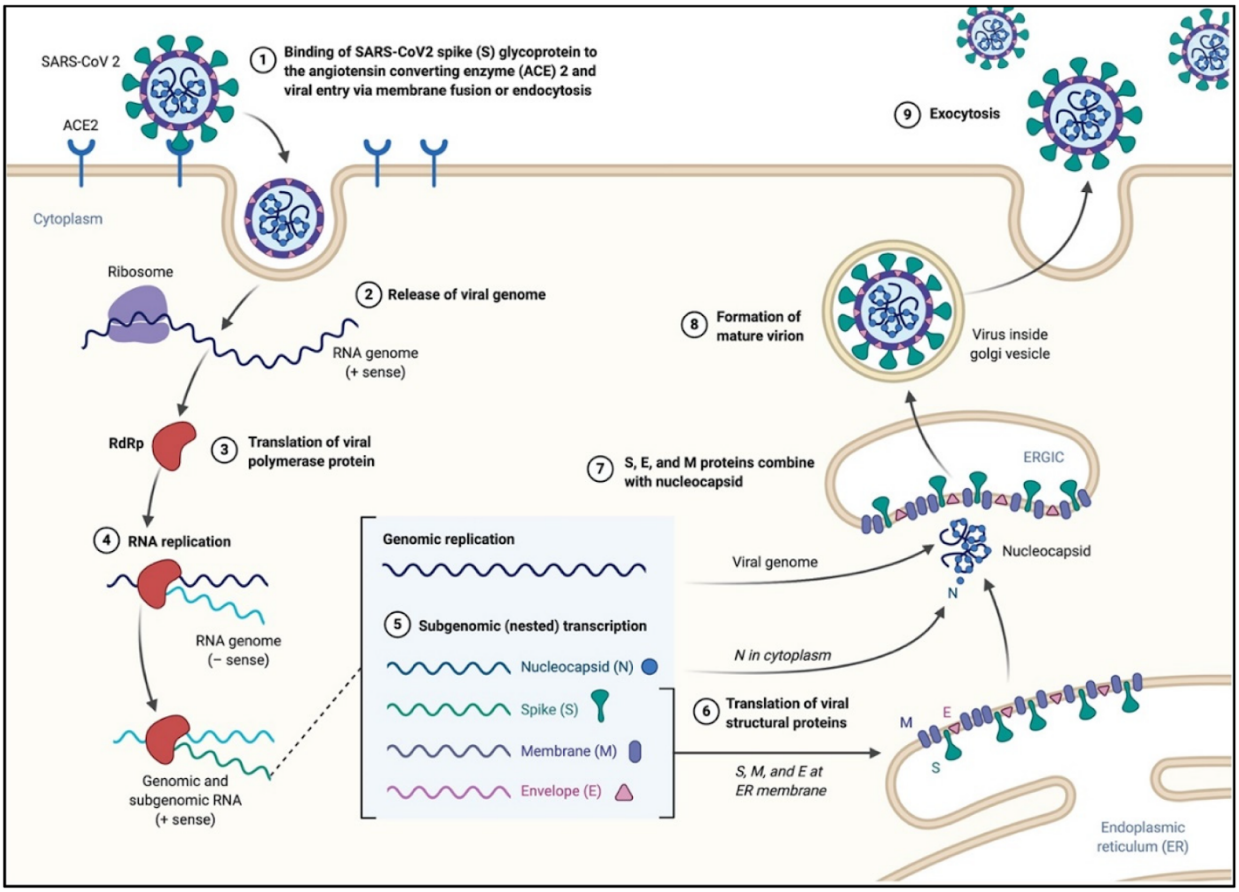

Figure 3. Representation of the life cycle of the SARS-CoV 2 virus (Covid-19 Scientific Updates).

C. COVID-19 antibody response

The Covid-19 antibody response is aimed at neutralizing the trimeric spike glycoprotein S, the protein responsible for allowing the virus to fuse with the host membrane, as shown in Figure

4. (Wang, 2020). Antibodies target the receptor-binding domain, S1 domain, by having an identical fit to the spike protein as it has to the ACE-2 receptor that the virus normally binds to. The virus surface is then covered with antibodies blocking all of its normal binding sites. The virus is now unable to enter into host cells. Additionally, a virus covered by antibodies is sticky and therefore attracts other antibody coated viruses. This large cluster formed will call the attention of immune cells much more efficiently than the individual virus. This simple action of the antibody leaves the virus disabled and unable to enter a host cell (Fiedler).

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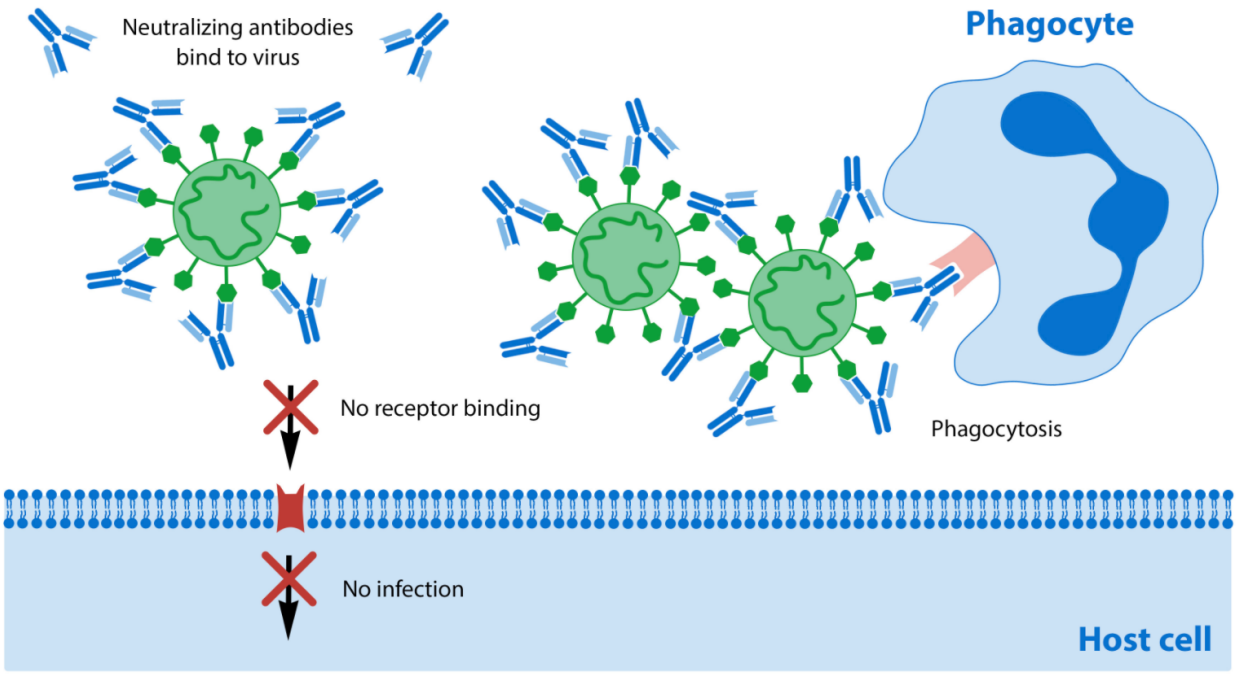

Figure 4. Representation of a Covid-19 antibody blocking the binding sites on the SARS-CoV-2 virus, forming clusters that are significantly more noticeable by the phagocyte (Fiedle, 2020)

D. Antibodies to COVID-19

A study analyzed the IgG and Fabs from 10 COVID-19 positive individuals. Antibodies were detected using the sandwich ELISA mechanism. Figure 5 shows, through a log distribution

graph, that antibodies were detected on the fourth day of the patient's symptoms and in other cases after 7 days. The antibody concentration then increased on the 12th day of symptoms (Fei Xiang, 2020).

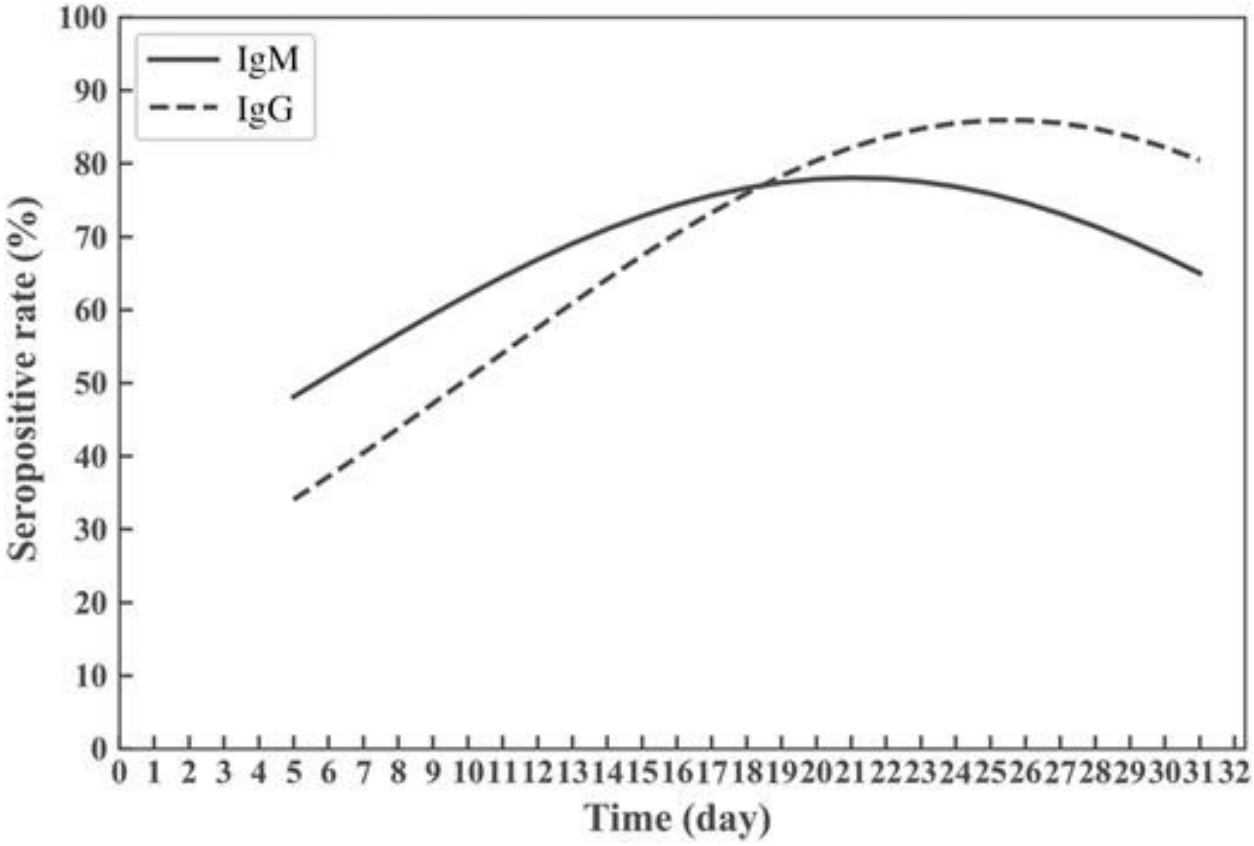

Figure 5. Distribution graph of the time vs. rate of the detection of 2 types of Covid-19 antibodies (Fei Xiang, 2020).

A study led by Ai-Long Haung in Chongqing Medical University, tested 285 patients that were hospitalized in China for Covid-19. All the patients developed antibodies within two to three weeks of their first symptoms. All the patients produced specifically IgM antibodies, the initial antibody that the body makes. Only a short while later the patients produced IgG antibodies which gives long term immunity ("Study Finds Nearly Everyone Who Recovers From COVID-19 Makes Coronavirus Antibodies", 2020).

Another study was done with hospitalized patients testing positive for Covid-19. The study used a magnetic chemiluminescent enzyme immunoassay in order to detect antibodies in the patients. 100% of the patients had IgG antibodies 17-19 days after their symptoms appeared and 94% of patients developed IgM antibodies, 20-22 days after symptoms.

Although antibody tests do not detect a virus currently in a patient, and therefore can not be used as a diagnostic test, it is conclusive that the development of antibodies signifies the history of an immune response to a virus. This detection can give physicians insight into how to treat the deadly virus (Long, 2020).

III. PERSONAL RESEARCH

A. Background

Amid the pandemic beginning in April 2020, I began volunteering at a local adult medical clinic. The office is a general care adult medical practice that services the local orthodox Jewish community but has branched out to service many other patients. After a painful month of high COVID-19 infection rate during March many people in the community were walking around saying, “I had symptoms therefore, I must’ve had the virus” (discussion with community member). The physicians in the office wondered who exactly in the community has developed antibodies? Was it only people who tested positive for the virus? What about people who had previous health conditions, did they have a higher chance of being positive? Are there specific symptoms that are a definitive to assume one had Covid-19? What about family members with no symptoms who were living in the same household of a positive patient? The clinic began booking appointments for 150 patients a day with the goal of rapidly testing all their patients for Covid-19 antibodies.

B. Methods

Using an excel spreadsheet, as shown in Figure 6, I began assisting in their research by analyzing 1000 patients who were tested for COVID-19 antibodies. I grouped everyone into one of three categories indicating their probability for being positive. Low chance: no symptoms, no direct exposure to anyone with definitive Covid-19 test results. Medium chance: exposure to someone with a definitive positive, physical contact exposure (medical workers), any symptoms including fever, muscle ache, gastro-intestinal symptoms, chills, cough, shortness of breath etc. High chance: spouse positive for COVID-19 test, spouse with positive antibody test, received a Covid-19 nasal swab test, anosmia, emergency room visit because of symptoms, needed a chest scan, or had fever for more than 5 days. I took into account symptoms only occurring from February 2020 and afterwards.

In addition to sorting patients by their chance of testing positive for antibodies I included: age, gender, ethnicity, town, state weight, BMI, diabetes, asthma, cancer history, stroke history, obesity, high blood pressure, smoking history, fever, if patient had taken a COVID-19 PCR test, results of Covid-19 test, exposure to Covid-19, malaise, anosmia, cough, shortness of breath, headache, and having the chills.

C. Results

1	Age	Gender	Race	Town	State	Weight (#)	BMI	Diabetes	Asthma	cancer	CAD	obesity	HBP	Former smoker	Current smoker	medium or low)	Fever	Covid nasal test	exposure	malaise	Anosmia	antibody results	Cough	SOB	Headache	Chills
61	41	male	white	Bronx	NJ	191	28.9	no	no	no	no	no	no	no	no	low	no	no	yes	no	no	Positive	no	no		
62	29	male	white	Englewood	NJ			no	no	no	no	no	no	no	no	**medium**	no	no	yes	no	no	Negative	no	no	no	no
63	45	female	white	teaneck	NJ	140	26.5	no	no	no	no	no	no	no	no	**low**	no	no	no	no	no	Negative	no	no	no	no
64	43	male	white	Teaneck	NJ	138	21	no	no	family history	no	no	no	no	no	**high**	no	no	no	no	yes	Negative	yes	no	yes	no
65	38	female	white	Englewood	NJ			no	no	no	no	no	no	no	no	**low**	no	no	no	no	no	Negative	no	no	no	no
66	69	female	white	West Milford	NJ	191	32.8	no	no	family history	no	no	no	no	no	**high**	no	no	no	no	no	Negative	yes	yes	yes	no
67	71	male	white	West Milford	NJ	197	29.1	yes	no	yes	no	no	yes	no	no	**medium**	yes	no	yes	no	no	Negative	yes	no	no	no
68	77	Female	White	Fair Lawn	NJ	135	25.5	no	yes	family history	no	no	yes	yes	no	**low**	no	no	no	no	no	Negative	no	no	no	no
69	55	male	white	Teaneck	NJ	194	29.5	no	no	family history	no	no	yes	no	no	**medium**	no	no	no	yes	no	Negative	yes	no	no	yes
70	21	male	white	Teaneck	NJ	152		no	no	no	no	no	no	Juule	Juule	**low**	no	no	yes	no	no	Negative	no	no	no	no
71	49	male	white	Englewood	NJ	191	26.6	no	no	family history	no	no	no	no	no	**low**	no	no	possible	no	no	Negative	no	no	no	no
72	40	female	white	Livingston	NJ	129	22.1	no	no	family history	family history	no	no	no	no	**medium**	no	no	possible	no	no	Negative	no	no	yes	no
73	57	male	white	Teaneck	NJ	160	21.1	no	no	family history	no	no	no	no	no	**low**	no	no	possible	no	no	Negative	no	no	no	no
74	50	female	white	Teaneck	NJ	118	21.6	no	no	no	no	no	no	no	no	**medium**	no	no	no	yes	no	Negative	no	no	no	no
75	23	male	white	Teaneck	NJ	138	20.4	no	no	no	no	no	no	no	no	**low**	no	no	yes	no	no	Negative	no	no	no	no
76	20	male	white	Teaneck	NJ	142	20.5	no	no	no	no	no	no	no	no	**high**	yes	no	yes	yes	yes	Negative	no	yes	no	no
77	17	male	white	Teaneck	NJ			no	no	no	no	no	no	no	no	**low**	no	no	yes	no	no	Negative	no	no	no	no
78	37	female	white	Teaneck	NJ	125	20.2	family history	no	no	no	no	no	no	no	**low**	no	no	no	no	no	Negative	no	no	no	no
79	46	female	white	Englewood	NJ	129	22.1	no	no	no	family history	no	no	no	no	**medium**	no	no	possible	yes	no	Positive	no	no	no	no
80	33	female	white	Teaneck	NJ	115	17.5	no	no	no	no	no	no	no	no	**low**	no	no	possible	no	no	Negative	no	no	no	no
81	49	male	white	Englewood	NJ	166	26.8	no	no	no	no	no	yes	no	no	**medium**	no	negative	no	yes	no	Positive	yes	no	yes	no
82	34	male	white	Teaneck	NJ	213	28.9	no	no	no	no	yes	no	no	no	**low**	no	no	yes	no	no	Negative	no	no	no	no
83	41	male	white	Closter	NJ	151		no	no	family history	no	no	no	no	no	**low**	no	no	no	no	no	Negative	no	no	no	no
84	27	Female	white	New York	NY	125		no	no	no	no	no	no	no	no	**high**	yes	no	possible	no	yes	Positive	yes	no	no	no
85	75	female	white	Fort Lee	NJ	104	19.1	no	no	family history	no	no	no	no	no	**medium**	yes	no	no	no	no	Negative	yes	no	no	no
86	36	male	white	New York	NY	215	30	no	no	no	pulminary em	yes	yes	yes	yes	**medium**	no	no	no	no	no	Negative	yes	no	no	no
87	59	male	white	Englewood	NJ	201		Prediabetes	no	family history	no	no	yes	infrequent	infrequent	**medium**	no	no	possible	no	no	Positive	yes	no	no	no
88	31	male	white	Englewood	NJ	241	33.6	no	no	no	no	yes	no	no	no	**low**	no	no	yes	no	no	Negative	no	no	no	no
89	30	female	white	Englewood	NJ	139	23.9	no	no	no	no	no	no	no	no	**medium**	no	no	yes	no	no	Negative	no	no	no	no
90	34	male	white	Springfeild	NJ	158	25.9	no	yes	no	no	no	no	no	no	**medium**	no	no	no	no	no	Negative	yes-allergies	yes	no	no
91	59	female	white	Englewood	NJ			family history	no	no	no	yes	no	no	no	**low**	no	no	yes	no	no	Negative	no	no	no	no
92	65	male	white	Englewood	NJ	193		no	no	no	no	no	yes	no	no	**low**	no	no	no	no	no	Negative	no	no	no	no
93	55	male	white	Bergenfield	NJ	204	26.9	no	no	no	no	no	yes	no	no	**low**	no	no	yes	no	no	Negative	no	no	no	no
94	42	female	white	Bergenfield	NJ	148		no	no	no	no	no	family history	no	no	**high**	yes	no	no	yes	yes		no	no	no	no
95	47	female	white	Bergenfield	NJ			no	no	no	no	no	no	no	no	**medium**	no	no	yes	no	no	Negative	yes	no	no	no
96	46	male	white	Bergenfield	NJ	181	26.7	no	yes	family history	no	no	no	no	no	**low**	no	no	possible	no	no	Negative	no	no	no	no
97	71	female	white	Fort Lee	NJ	128		prediabetes	no	no	no	no	no	no	no	**low**	no	no	yes	no	no	negative	no	no	no	no
98	74	male	white	Fort Lee	NJ	22		no	no	no	no	no	no	no	no	**low**	no	no	yes	no	no	negative	no	no	no	no
99	33	male	white	Englewood	NJ	153		no	no	family history	no	no	no	no	no	**medium**	no	no	no	no	no	negative	yes	no	no	yes
100	26	male	white	Bergenfield	NJ	196	28.9	no	yes	no	no	no	no	no	no	**low**	no	no	no	no	no	Positive	no	no	no	no
101	24	male	white	Bergenfield	NJ	268	40.7	no	no	no	no	yes	no	no	no	**low**	no	no	no	no	no	Negative	no	no	no	no
102	22	male	white	Bergenfield	NJ	191		no	no	no	no	no	no	no	no	**low**	no	no	no	no	no	Negative	no	no	no	no
103	68	female	white	Wayne	NJ	117	19.5	no	no	no	no	no	yes	no	no	**low**	no	no	no	no	no	negative	no	no	no	no
104	69	female	white	Teaneck	NJ	103	20.8	no	no	no	family history	no	no	no	no	**low**	no	no	no	no	no	negative	no	no	no	no
105	29	female	white	Englewood	NJ	131		no	no	no	no	no	no	no	no	**medium**	no	no	no	yes	no	negative	no	no	yes	no
106	32	female	white	Passaic	NJ	215		no	no	no	no	no	no	no	no	**medium**	no	no	yes	no	possible	negative	no	no	no	no
107	33	male	white	Englewood	NJ			no	no	no	no	no	no	no	no	**medium**	yes	no	no	yes	no	negative	yes	no	no	no
108	34	male	white	Edgewater	NJ	187	26.8	family history	no	family history	no	no	no	no	no	**low**	no	no	no	no	no	negative	no	no	no	no
109	45	male	white	bergenfield	NJ	180	25.1	no	no	no	family history	no	no	no	no	**medium**	no	no	no	no	no	negative	yes	no	no	no
110	44	female	white	Franklin Lake	NJ	144	24.7	no	no	no	no	no	yes	no	no	**low**	no	no	no	no	no		no	no	no	no
111	49	male	white	Franklin Lake	NJ			no	no	no	no	no	no	no	no	**medium**	yes	no	possible	no	no	negative	yes	no	no	no
112	82	female	white	Teaneck	NJ	112	21.2	prediabetes	no	family history	no	no	yes	yes	no	**medium**	no	no	possible	no	no	negative	yes	no	no	no
113	37	male	white	bergenfield	NJ	156	25.2	no	yes	family history	no	no	family history	no	no	**medium**	no	no	possible	no	no	negative	yes	yes	no	no
114	41	female	white	Teaneck	NJ	128	21.6	no	no	no	no	family history	family history	no	no	**low**	no	no	no	no	no	negative	no	no	no	no
115	51	male	white	Teaneck	NJ	176		no	no	no	no	no	yes	no	no	**low**	no	no	no	no	no	negative	no	no	no	no
116	41	male	white	Teaneck	NJ	176	26	no	no	family history	no	no	no	yes	no	**low**	no	no	no	no	no	negative	no	no	no	no

Figure 6. Screenshot of excel sorted data. This figure only includes patient 61-116 but is a representation of 1,000.

The data shown in Figure 6. showed that out of 1,000 patients, 170 which is 17.1%, were positive for COVID-19 antibodies. The average age of these 170 patients is 44.3 and the average BMI was 26.2. 107 of the 170 patients that were positive were part of the high-risk category. 36 of the positive patients have high blood pressure and 17 were obese. When analyzing the symptoms, it is noted that 73.5% of patients with a fever were positive, 68.3% of patients with malaise were positive, 100% of patients with anosmia were positive, 63.3% with a cough, 75.8% who had shortness of breath, 60.9% with a headache, 78.8% of patients who had the chills, and 71% of patients with G.I. symptoms.

antibody results	Count	%	Avg. Age	BMI
Negative	825	82.9%	43.9	26.2
Positive	170	17.1%	44.3	26.2
Total	**995**	**100%**		

predicted risk			Positive
medium	406	41%	46
low	430	43%	16
high	**158**	**16%**	107
Blank	6	1%	
	1000		**169**

	Positive			yes	yes	yes	yes	yes	yes
predicted risk (high medium or low)	**antibody results**	**Avg. Age**	**BMI**	**Diabetes**	**Asthma**	**cancer**	**CAD**	**obesity**	**HBP**
medium	46	42.9	25.6	0	0	0	0	5	9
low	16	46.4	27.8	0	1	1	0	1	3
high	107	44.7	26.1	4	1	3	1	11	24
Total	**169**			**4**	**2**	**4**	**1**	**17**	**36**
"High" that tested positive									

Ages			Negative	Positive	Positive rate	Positive BMI
35	**288**	29%	235	51	18%	24.15
45	**336**	34%	287	46	14%	26.47
55	**170**	17%	136	34	20%	27.81
65	**95**	10%	77	18	19%	25.87
	111	11%	90	21	19%	26.98
	1000		**825**	**170**		

Figure 7. Data analysis

Risk Profile	Positive % Rate	Negative % Rate
high	67.3%	32.7%
low	3.1%	96.9%
medium	11.6%	88.4%

Figure 8. Percentage of positive patients in each predicted risk category

State	Count
NY	178
NJ	816
OH	1
CA	1
NJ	2
CT	2
	1,000

Figure 9. Analysis of patients tested based on state

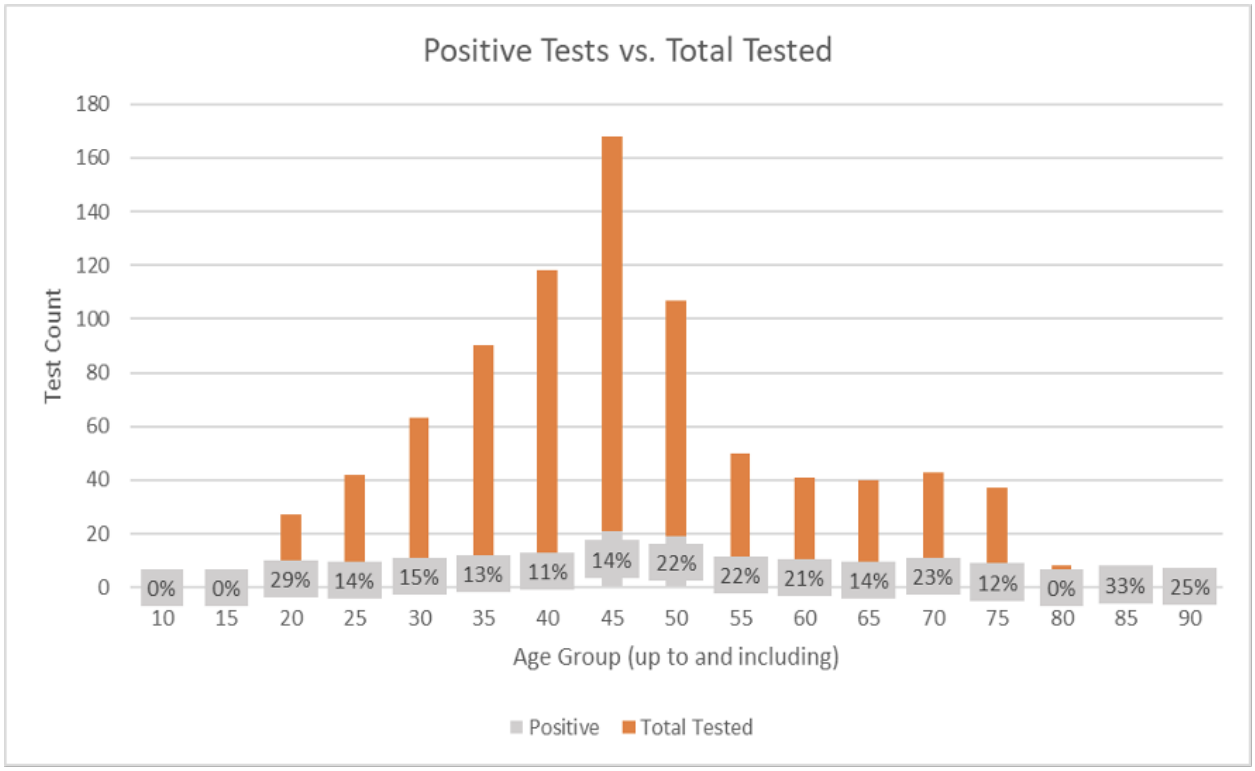

Figure 10. Analysis of positive patients vs. the total patients tested

Age Group	Positive Test Rate
<35	12.6%
>=35	16.3%

Age Group	Negative	Positive	% of Total Tests	% of Total Positive Tests
10	2	0	0.3%	0.0%
11-15	6	0	1.0%	0.0%
16-20	15	6	2.4%	5.1%
21-25	32	5	5.2%	4.3%
26-30	47	8	7.6%	6.8%
31-35	70	10	11.3%	8.5%
36-40	94	12	15.1%	10.3%
41-45	126	21	20.3%	17.9%
46-50	69	19	11.1%	16.2%
51-55	32	9	5.2%	7.7%
56-60	27	7	4.3%	6.0%
6165	30	5	4.8%	4.3%
66-70	27	8	4.3%	6.8%
71-75	29	4	4.7%	3.4%
76-80	8	0	1.3%	0.0%
81-85	4	2	0.6%	1.7%
86-90	3	1	0.5%	0.9%

Figure 11. Patients tested organized by age

Gender	Positive % Rate	% of Total Tests	% of Total Positive Tests
Female	**12.9%**	**44.2%**	**35.9%**
Male	**18.2%**	**55.8%**	**64.1%**

Figure 12. Analysis of positive patients according to gender

D. Discussion

The medical condition that was found with the most correlation to testing positive for COVID-19 antibodies is hypertension, high blood pressure. 36 of the 170 positive patients were reported to have high blood pressure. The same discovery was found in studies from China and the U.S. where high blood pressure was in fact the most common pre-existing condition found in those hospitalized with Covid-19. In Italy specifically, one study found that 30-50% of patients hospitalized were found to have high blood pressure (Nazario, 2020). Out of the patients that had died from COVID-19 in the hospital, 76% had high blood pressure. The overall risk of death for patients with high blood pressure is doubled compared to the usual mortality risk (Nazario, 2020). Dr. Steven Rough, a cardiologist in Sharp Chula Vista Medical Center said: "What was found is that COVID infects the cells that help regulate blood pressure, suggesting a possible link between hypertension and severe COVID infection. More studies are needed to determine if there is, in fact, a cause and effect" (*"High Blood Pressure's Connection to COVID-19*"). With this risk found in patients with hypertension the CDC specifically warns these patients to remain indoors and be as cautious as possible ("Certain Medical Conditions and Risk for Severe COVID-19 Illness").

Another interesting finding from this study was that 17 of the 170 positive patients were obese. Additionally, the other positive patients had an average of a 26.2 BMI which is in the overweight category. Obesity is in fact included on the CDC's list for patients that are considered high risk which agrees with the connection found in the clinics study *("Certain Medical Conditions and Risk for Severe COVID-19 Illness").* Obesity causes an inflamed immune system which alters leucocyte counts and affects cell-mediated immune response (Heredia, 2012). This inflammatory response causes an increase in the CD4 T cell subsets Th2 and T regulatory cells

which inhibits our immune cell's ability to reduce the infection. One paper discusses the correlation and claims that "susceptibility to acute respiratory distress syndrome (ARDS), the primary cause of COVID-19 mortality, is significantly greater among individuals with obesity". This paper sorted through 1,733 studies on the correlation between BMI and COVID-19 and found that not only did being obese increase the chances of contracting the virus but increased the chances of becoming severely ill from it as well. "Pooled analysis showed individuals with obesity were more at risk for COVID-19 positive, >46.0% higher; for hospitalization, 113% higher; for ICU admission, 74% higher; and for mortality, 48% increase in deaths" (Popkin, 2020). This confirms the findings found in the study I was a part of, that obesity is in fact corelated with Covid-19 and its severity.

Interestingly, with the start of the pandemic majority of countries in the world have an obesity rate of at least 20% which is at its historical highest and has yet to go down. There is a concern that as we simultaneously declare that obesity is putting patients at high risk, obesity is only getting worse through the sedentary conditions of the pandemic. "These adjustments have caused food system problems, including changes in food consumption and physical activity patterns, and remote telework environments that may exacerbate current trends in the prevalence of individuals with obesity" (Popkin, 2020). Although the CDC has advised many to stay home schools are doing gym class over zoom and adults are advised to do any home exercise that they can.

Another strong correlation found in the study is between anosmia and patients positive for Covid-19 antibodies. 100% of patients that reported a loss of smell tested positive for antibodies. This long-lasting symptom can be caused by the COVID-19 virus particle causing an inflammatory response inside a patient's nose which affects its sustentacular cells. These cells

support sensory neurons in the nose and therefore cause the loss of the olfactory, or smell, neurons abilities (Vanderbilt University Medical Center, 2020). The receptors in human tissue for the COVID-19 virus are found mostly in the "human nasal cavity and in the supporting cells of the olfactory tissue". In most cases the nerves can regenerate so that a patient can regain their sense of smell but in some cases, they are unable to. In a study done in Teheran, Iran, researchers tested 100 patients, that were positive for COVID-19, by sniffing different odors and being asked to identify them. The study concluded that 96% of patients had some sort of olfactory dysfunction and 18% had a total loss of smell (Moein, 2020)

The exact length of this uncomfortable symptom is currently unknown to scientists. A study done in Guy's and St Thomas' Hospital in London by Claire Hopkins followed around 202 patients for a full month and discovered that 49% of them reported a total recovery of their senses. 41% of the patients reported an improvement, leaving 10% of patients to feel no change at all (Reiter, 2020). For many other patients not only did they not regain their sense of smell, but they developed smelling a repulsive odor to many neutral smelling things. While interviewing patients taking the antibody test during my study one women stated: "At first, I couldn't smell anything, and I thought that was terrible until 2 months later I began smelling foul odors wherever I went. The smell of chicken made me extremely nauseous and now, 11 months later I still can't go near it" (interview with anonymous patient). Claire Hopkins explained this sensation to be coming from the sensory neurons rewiring in order to properly recover. She adds that patients whose smell never returns but remains neutral may be due to the virus killing their olfactory sensory neurons as opposed to just damaging them (Marshall, 2020). Scientists are nervous that this leads patients to be more vulnerable to events like a fire or food poisoning

because of their inability to smell. A study done in 2014 showed that anosmia patients are actually twice as likely to be in a hazardous event (Marshall, 2020).

Something noteworthy found in the study is the fact that many patients in the high-risk category, did not test positive for antibodies. 32.7% of high prediction patients who either got a Covid nasal swab, went to the hospital because of symptoms, or lived with and remained in contact with a positive spouse surprisingly did not contract the virus. This automatically raises the question, why did those patients not test positive? Is it possible for someone to be completely immune and just never contract the virus? After all there are many family members of a positive patient who claimed that they must have antibodies but were proven wrong from their antibody results.

E. Conclusion

In response to the results found in this study along with results across the board on Covid-19 patients, the CDC has recommended that the elderly along with people with obesity and hypertension should remain at home as much as possible during this pandemic. Additionally, it is this population that is in the first groups that are eligible to receive the Covid-19 vaccine.

IV. ANTIBODY APPLICATIONS

A. Antibody immunity

After analyzing the results of Covid-19 antibody tests the natural follow up question is: what is the practical difference for patients who test positive for antibodies? Do the antibodies offer any protection against the virus? Does it make a patient completely immune? Do they last forever? Understanding the immunity status will help give the world a better picture of how we will recover from this deadly virus. Many governments are claiming that Covid-19 antibodies

cause a patient to be completely immune from the Covid-19 virus. Governments have come up with things like “immunity passport” and “risk-free certifications” that allow people to travel and resume life as if they are totally protected from reinfection (“‘Immunity Passports’ in the Context of COVID-19.”).

The Israeli government gives immunity status to anyone who tested positive for antibodies. They claim that a person with antibodies can be around a positive Covid-19 patient and not only not contract the virus themselves, but they are unable to pass it onto others as shown in Figure 13. Israel has strict quarantine laws after traveling but exempts anyone that can show a positive antibody test. In a certain school in Jerusalem positive antibody patients were told to sleep in the same bedroom with positive Covid-19 patients and told they can come and go freely without causing any harm. They were told by the Ministry of Health that there is no problem to sleep in the room with a positive patient and then travel to the supermarket because they cannot pass the virus to anyone.

Many schools and institutions are not allowing their students to attend large social gatherings unless the students have proof of a positive antibody test. In an interview with Dr. Fauci, he stated: “The White House coronavirus task force was discussing the idea of “certificates of immunity,” which could be issued to people who had previously been infected” (Mandavilli, 2020). Before reopening the Dean of University of New England planned to assign dormitory roommates to students based on antibody test results. “Ideally, a student without antibodies would be paired with one who has them to prevent roommates from infecting each other” (Wolfe, 2020). He even mentioned the thought that they can require that all students returning to campus must have COVID-19 antibodies. “I think you could certainly require students to have the antibody test” (Wolfe, 2020). One Yeshiva in Far Rockaway made a rule

that students can only attend large affairs if they can show documentation of a positive antibody result, otherwise students have to quarantine for 14 days before returning to campus. Additionally, on many dating websites people are writing “Covid antibody positive” on their status to give others reassurance that they can be physical safely, because they can not have or pass the virus to others (Konstantinovsky, 2020).

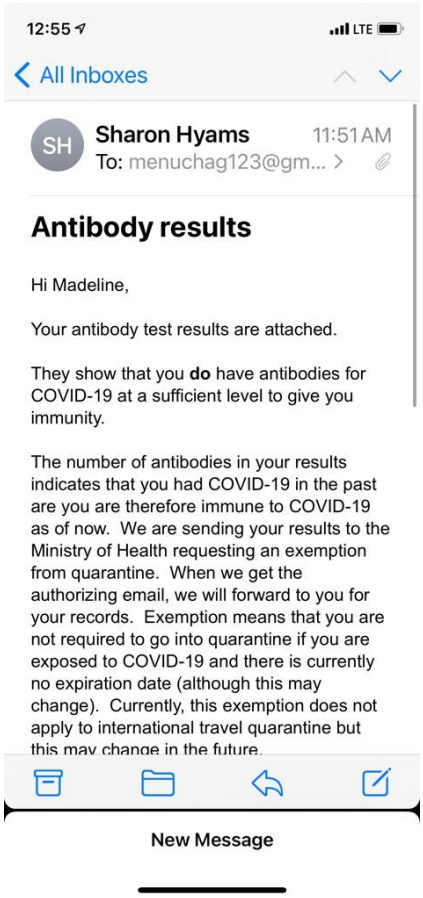

Figure 13. Email received from Israel’s’ Ministry of Health proclaiming immunity to an antibody positive test result

B. Plasma donation

As COVID-19 was spreading rapidly among patients and scientists still had no solution for how to treat the disease, they turned to convalescent plasma donation as a main option. Patients who have recovered from a virus generate neutralizing antibodies that remain in their plasma. A

recovered patient can then donate their plasma to a newly ill patient in order to donate their immune IgG and reduce the viral load in an infected patient. *("Study: COVID-19 Antibodies in Donated Blood Plasma Decline Within First Few Months After Symptom Onset").* This treatment began in the 1880's when humans hoped to take antibodies from animals. It was then used to treat diseases like scarlet fever, influenza, chickenpox, and the Ebola virus outbreak and has recently evolved to be used in cancer therapy (Marano, 2016). In 2003, during the SARS coronavirus infection a study was done which found a reduction in mortality by 23% for patients that received plasma therapy (Tiberghien, 2020). A study was done with Covid-19 patients where viral levels were calculated before and after a patient received a plasma donation. The results found that "SARS-CoV-2 virus load after convalescent plasma transfusion significantly dropped from 55 × 105 to 3.9 × 104 to 180 copies per milliliter" (Tanne, 2020). In a more detailed study convalescent plasma was used to treat 5 critically ill patients with COVID-19 hospitalized in Shenzhen, China. The results were: "Following plasma transfusion, body temperature normalized within 3 days in 4 of 5 patients, the SOFA score decreased, and PAO2/FIO2 increased within 12 days. Viral loads also decreased and became negative within 12 days after the transfusion, and SARS-CoV-2–specific ELISA and neutralizing antibody titers increased following the transfusion. ARDS resolved in 4 patients at 12 days after transfusion, and 3 patients were weaned from mechanical ventilation within 2 weeks of treatment. Of the 5 patients, 3 have been discharged from the hospital, and 2 are in stable condition at 37 days after transfusion" (Shen, 2020). After reviewing additional studies and seeing improvement in patients, physicians believed that this can be a possible treatment to help COVID patients. "Although a vaccine for COVID-19 is currently not available, the combination of the immune

IgG antibodies with antiviral drugs can offer short-term and medium-term solutions against COVID-19" (Jawhara, 2020).

Hospitals and organizations began sending out mass emails to recruit patients to donate their plasma. The requirements were that the patients must be 18 years of age, weigh more than 110lb, and have previously had COVID-19. Donations were recommended between 14 and 28 days after recovering from the virus. Special equipment was used that would extract the plasma and antibodies from a donor's blood and then circulate the blood back into the donor (Tiberghien, 2020). The CDC is using phrases as shown in Figure 14. like "Recovered from COVID? Save lives" in order to attract donors. Hospitals were setting up testing centers for recovered patients to go to in order to collect donations in a safe and organized manner ("Social Media Toolkit: Donate Blood Plasma and Help Save Lives"). In an interview with one recovered Covid-19 patient he stated: "After being in the hospital for 14 days fighting the deadly virus, I know how it feels. I have donated my plasma 23 times and will continue as long as they let me. If we have an opportunity to save lives at no cost there is no reason everyone eligible isn't running to help" (Anonymous donor, 2020). This old method of treatment has proven to be extremely useful during the Covid-19 pandemic.

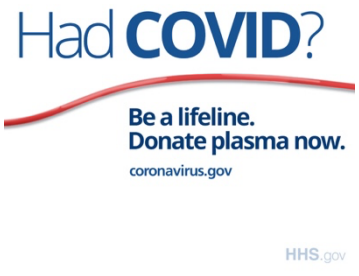

Figure 14. CDC advertisement urging people to donate plasma (“Social Media Toolkit”, 2021).

C. Herd Immunity

“'Herd immunity', also known as 'population immunity', is the indirect protection from an infectious disease that happens when a population is immune either through vaccination or immunity developed through previous infection” (“Coronavirus Disease: Herd Immunity, Lockdowns and COVID-19”). Ideally herd immunity is achieved through a population being vaccinated and not by patients having all contracted the virus. Once a significant amount of the population is immune, the virus is unable to travel and spread to the select few that are not. Each virus has a different threshold of immune patients that are required to achieve this status of herd immunity. The measles threshold was found to be at 95% while the polio threshold is only 80% (“Coronavirus Disease: Herd Immunity, Lockdowns and COVID-19”).

When conducting the antibody tests in the clinic many community members made drastic statements like this: “the whole community was sick, we must have developed herd immunity”. After analyzing the results of the 1,000 antibody tests it was clear that these statements were false. Only 17.1% of patients tested positive for antibodies, a number far from even a majority. Many communities just like this one, are claiming herd and are therefore now living life as normal and disregarding CDC instructions to stop the spread of the pandemic. The ultra-orthodox community in Brooklyn NY has taken this approach and resumed life as normal: schools are open, wedding halls at full capacity, synagogues, shopping centers, and all indoor dining is back to normal. It is estimated that around 70% of the community is immune in some sort of way. “That’s the feeling, that they’ve had it, everybody they know has had it, and the people they know who haven’t had it have some kind of immunity that we just don’t understand

yet" (Hanau, 2020). This community is so insulated that they have successfully slowed down the spread of the virus amongst themselves by reaching such a drastically high percentage of patients that are immune. Whether their disregard to rules is acceptable or not, through pain and suffering the community has reached a level of immunity that the world is hoping for.

Dr Faucci has stated that between 70%-90% of our population will need to be vaccinated or have been previously infected to achieve herd immunity to the coronavirus (McNeil, 2020). As of February 2021, there are 103,557,049 people in the world with Covid-19 and around 10% of the world vaccinated to the virus (Worldmeters, 2021). The world hopes that with the rapid spread of the COVID-19 vaccine we will achieve herd immunity without having people suffer through contracting the virus.

D. How long do antibodies last?

Although antibodies offer immunity benefit to whoever has them, there is the burning question of how long do they last for? Is a person immune for their lifetime or does their body stop generating the antibodies? An anonymous patient in my study tested positive for antibodies in May 2020 but when retested in June, tested negative. Another anonymous patient tested positive on that same day in May 2020 and as of February 5^{th,} 2021 is still testing positive for antibodies.

A study was done with 188 COVID-19 patients testing their immune response including antibodies, memory B cells, helper T cells, and killer T cells. "Antibodies against SARS-CoV-2 spike and receptor binding domain (RBD) declined moderately over 8 months, comparable to several other reports. Memory B cells against SARS-CoV-2 spike actually increased between 1 month and 8 months after infection. Memory $CD8^+$ T cells and memory $CD4^+$ T cells declined with an initial half-life of 3 to 5 months. This is the largest antigen-specific study to date of the

four major types of immune memory for any viral infection". According to this study, as shown in Figure 15., immunity is generated from COVID-19 patients for at least 6 months after infection in 95% of pateints. Although the study does note that a basic serological antibody test does not indicate immunity because it is only testing for antibodies and not the other immune responses (Jennifer, 2021). Another study done by the New England Journal of Medicine examined 1,107 patients who had recovered from COVID-19 and tested positive for the antibodies. These patients were tracked, and it was found that after a 4-month period their antibody count had not declined (Schimelpfening, 2021). A study in England was done with patients who previously were infected by COVID-19 and it was found that 99% of patients still had antibodies to SARS-CoV-2 for three months after infection. The study continued until six months after infection and found that 88% of patients were still testing positive ("How Long Do Covid Antibodies Last?", 2021).

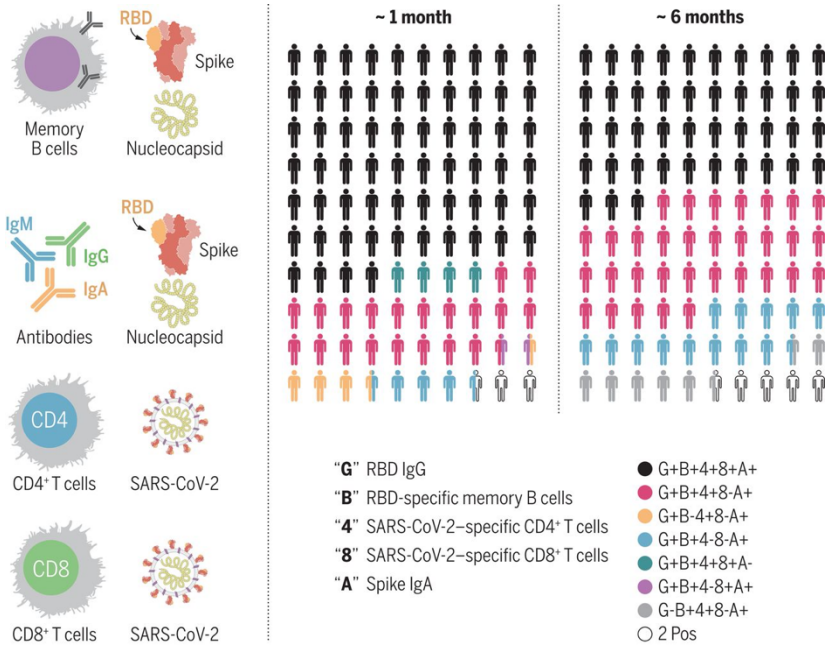

Figure 15. Image depicting the patients that have tested positive vs. negative for IgG, memory B cells, T cells, and spike IgA (Jennifer, 2021).

E. Antibody Count

Although my study did not include the actual number of antibodies found in patients, many studies do in fact include this information. Some patients are seeing results with extremely high numbers and some very low. A study in Fudan University in Shanghai measured antibody levels in COVID-19 patients released from the local hospital. The study found that "Antibody levels were significantly higher in the older (60 to 85 years) and middle-aged subjects (40 to 59 years) than in younger patients (15 to 39 years). The 10 patients with undetectable antibodies were younger (median age, 34 years), and 8 of them were women… significantly higher antibody levels were found in men (47%) than in women (53%)" (Mary Van Beusekom, 2020). In a recent study done with monozygotic patients before and after receiving the flu vaccine, it was found that immune response is less affected by genetics then it is environmental factors such as diet, life habits, and previous infection/exposure. Non-heritable influences were found to be 77% responsible for immune responses (Brodin, 2015). This can explain why close family members had such different reactions from the same Covid-19 virus infection.

With Covid-19 specifically, it was found that antibodies will target a different part of the virus in mild cases and in severe cases. Antibodies that recognize the spike protein stop the virus's ability to bind to the ACE2 region of the cell and therefore prevent its entry into the cell. Antibodies that recognize other viral components do not stop the viral spread (Conger, 2020). "The study found that people with severe Covid-19 have a lower proportion of antibodies targeting the spike protein used by the virus to enter human cells than of antibodies targeting proteins of the virus's inner shell" (Conger, 2020). 254 patients were part of the study ranging

from asymptomatic to severe infection; 25 patients were treated from home and 25 died from the virus. The study found that "those people with mild illness tended to have a higher proportion of anti-spike antibodies, and those who died from the disease had more antibodies that recognized other parts of the virus, indicating the virus had entered the patient's cells and was rapidly spreading" (Conger, 2020). The varying immune responses explain the phenomenon that patients have varying antibody counts. A patient who had a mild reaction to the virus and whose body generated antibodies immediately to the spike protein never had the virus enter their cells and therefore did not need a strong inflammatory response. These patients are likely to have a low number of antibodies because their body was able to eliminate the virus quickly (Conger, 2020). "People with asymptomatic and mild illness had lower levels of antibodies overall than did those with sever disease. After recovery the levels of IgM and IgA decreased steadily to low or undetectable levels in most patients over a period of about one to four months" (Conger, 2020). This low antibody count will lead to the number decreasing sooner and quicker than a patient who needed a stronger response to the virus. Patients with a much more severe reaction including death do not have antibodies against the spike protein because the virus was able to enter their cells, it wasn't neutralized at the surface. Therefore these patients developed antibodies towards inner layers of the virus that were used to fight the virus once it had successfully entered the host cell.

F. COVID-19 Vaccine

Since the begging of the pandemic biotech companies across the world have been racing and using all their resources to develop a COVID-19 vaccine. As of now there are two vaccines

that are approved for emergency use by the FDA in the united states: Pfizer-Biotech and Moderna. (*"Information about the Pfizer-BioNTech COVID-19 Vaccine").*

Rather than inserting an inactivated or weakened virus into a patient's body, both of these companies use a lipid nanoparticle-formulated mRNA vaccine. The mRNA encoding the perfusion spike glycoprotein of SARS-CoV-2 is injected into our muscle and is used by the cell to make this specific Covid-19 spike protein. Once the protein is made the mRNA is degraded by the cell. The cell then uses our body's natural immune system to generate immunity. The cell displays the spike protein on its surface where our body's immune system can recognize it as foreign and begin to develop antibodies against it (*"Understanding MRNA COVID-19 Vaccines")*.

The vaccine is able to replicate the primary response of our immune system, causing the body to react as if the virus is actually there, which will prepare the body for real infection. The plasma cells will generate antibodies and the memory B cells will remain dormant for years storing the memory of the virus. The antibodies produced from the vaccine are stronger and longer lasting then those produce naturally from the virus. The vaccine contains a much higher concentration of the spike protein then actually found in the virus (*"Why a vaccine can provide better immunity than an actual infector?", 2020).*

All the vaccines that are currently in development are programming the human body to make antibodies specifically against the spike protein. However, as discussed earlier, people who contract the virus can produce antibodies for any of the other viruses' proteins like its' nucleocapsid, spike protein, and membrane envelope. Most antibody tests that are currently on the market are used to detect the antibody specific to the nucleocapsid protein. This does in fact prove that a person has had the virus, even though it is not testing for the spike protein

antibodies. Because of this discrepancy people who have gotten the vaccine are testing negative on COVID-19 antibody tests because they do not have the nucleocapsid antibodies rather only the spike protein antibodies. This does not mean the person is less immune to the virus, without the spike protein the virus can not even enter the cell, it merely means that the vaccine does not generate antibodies to anything other than the spike protein.

So far, the vaccines are working with the different COVID mutations that are currently known. If the virus mutates its infamous spike protein, then the antibodies that the vaccine makes will become ineffective. Therefore, the world is in such a race to eliminate the virus and get the entire population vaccinated before the virus has an opportunity to mutate.

V. Conclusion

Antibodies are proven to be the human bodies main mechanism in fighting off infection. In the case of the COVID-19 pandemic scientists are using antibodies in every way they can. Whether generating herd immunity, plasma donation, or creating them artificially from the vaccine they have been the most promising solution to ending the pandemic. Although the number of months that antibodies may last for ranges between 4, 5, 6, 7, 8 depending on the study done, the human body produces memory B cells that last much longer. Antibody data seems promising and exciting with the new vaccines creating antibodies in millions of patients. Although many feel the end of the pandemic is near, there are still many questions left unanswered. Why in fact do some people lose their antibodies and not others? Are there factors related to the infection that will affect immunity? Although antibodies may be gone memory B cells remaining dormant with the memory of the virus, can this provide enough immunity? Why do some people have a higher antibody count then others? How long will antibodies that are generated from the vaccine last? It is hard to answer these questions without a significant amount of more time and more studies conducted.

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