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|  | **WILLIAM E. CASWELL** | The Response to Covid-19(An Interim Report) ***Seven different approaches to developing a vaccine against covid-19 are being undertaken among 80 or more agencies, worldwide. The work that shows promise for our future, follows certain established paths. Its developments create reasons to believe that an answer will appear soon.***  Rarely does CCCC issue a newsletter in mid-month, but these are unusual times. We feel that reasons for optimism in the battle against covid-19 should be shared. This Interim Report, which is longer than usual because of its technical nature, explains the progress currently being reported by *The Economist* magazine. Because that article seems to assume knowledge of biology by the reader, we have re-written the story by adding further explanations.   1. **Overview**   Now into five months of world-wide recognition[[1]](#footnote-1) of the covid-19 threat (identified on January 10, 2020), more than 86 companies worldwide are seeking a vaccine, including a biotech firm in Ottawa and one in Vancouver. A successful vaccine would not only protect those persons injected from getting sick, such a vaccine, being able to reduce the number of susceptible people, would further prevent the virus from spreading.  Be aware of three affected groups: First, most people’s immune systems are quite capable of fighting the bacteria. Second, another group succumbs to the virus, but survives; now their systems are better prepared to deal with the virus next time around (the same role that many vaccines would play). The third group succumbs to the virus completely (dies). All three groups spread the virus to others. Veterinarians have been using vaccines to protect farm animals against coronaviruses (a broad classification of covid-19) for years, so the viruses are not new, but the variations are.   1. **Who**   Among the international vaccine developers in the race are:  Abcellera (Canada)  Sanofi Pasteur (France)  Johnson & Johnson (US)  University of Oxford (UK)  Can-Sino Biologics (China)  Serum Institute of India (India)  University of Queensland (Australia)  German Centre for Infection Research (Germany)   1. **Why**   Vaccines are the least profitable of a pharmaceutical firm’s endeavors. Often, by the time the vaccine has been developed the pandemic has passed away on its own (which was the case with Zika,  the 2009 flu pandemic, and the 2010 H1N1 influenza pandemic) leaving the pharmaceutical companies  *1 “So many possibilities, so little time”. Economist magazine, 18 April 2020*  holding the bag which has amounted to hundreds of millions of dollars. Making vaccines is more complicated than making pills. Whole viruses have to be grown up in some standard way and be purified not to cause further harm. Those using the protein approach have to filter them so that only the desired antigen gets into the patient’s body. Dozens of checks are done each step of the way.  The ‘why’ is a collective understanding of the importance of a solution to the world society. For example, Johnson & Johnson (US), as well as Sanofi (France) have made the commitment to sell the covid-19 vaccines on a not-for-profit basis.   1. **When**   Overall a ‘fast’ timeframe of about 10 months is anticipated – October 2020). The Ebola virus solution (initiated by Canadian researchers) took 10 months, the fastest vaccine development in recent history. Vaccine solutions must past through three test phases:  Phase I – Trials with healthy volunteers, carefully controlled and protected, called safety trials. *Can-Sino Biologics*’ (China) solution has passed phase I and is already approved for pursuing phase II trials.  Phase II – Trials designed to find out if the vaccine can provoke an immune response capable of fighting off the virus.  Phase III – Trials with vaccines proven to provoke the right immune response, by applying them to large groups of people – and discovering deficiencies, if any.  A preferred trial approach by some specialists is the “challenge” trial that was used successfully for the Zika virus fight. In order to speed up the results, instead of vaccinating many volunteers (with and without the viral infection) and seeing how many still got sick, the “challenge” trials take healthy volunteers and inject them with the actual virus and then inject the vaccine. This runs into the problem of ethics, although participants are guaranteed good care and the option to pull out at any time. The “challenge” approach speeds up trial times by many weeks.   1. **What**   Words that will be part of this conversation, are:  ***SARS-COV-2*** is the specific covid-19 virus. It is closely related to SARS-COV virus, the cause of the SARS outbreak in 2003. (Its solution was an inactivated vaccine – as described in section 6e, below.)  ***Virus*** is a tiny, parasitic bacteria that is unable to reproduce by itself. It hi-jacks the reproduction system of the host (human) cell to reproduce in great quantities.  ***Antigens*** are cells that provide signals within the body that tell the immune system that an invader is at hand. It arises because the infected human cell has the ability to send out a distress signal. Our systems ensure that those cell proteins will be displayed (as antigens) on the surface of the invader waving them like little flags to draw the attention of the immune system. “Come and get me”, they cry out. Thus, the antigen activity must be at the heart of every vaccine. (Humans have a second related alarm system: Some healthy human cells engulf virus particles without becoming infected and, through a process, create antigens.) It takes about two weeks after infection for the body to build its antigens.  ***Antibodies*** are produced by the human’s internal immune system to specifically destroy an identified virus or infection. They are proteins that stick to the antigen and not only prevent further infection, but also flag the virus for destruction. Since antibodies are proteins, they can be mass produced by current pharmaceutical processes. Such an approach was used against Ebola. Injecting antibodies into everyone may confer immunity on the uninfected.  ***Cells****,* of which it is estimated that we humans have about 25 trillion. Each cell contains about one million molecules, most of them protein. The cell can be viewed as a chemical factory making thousands of needed chemicals in the protein format. There are more than 200 kinds of cells.  Obviously, blood cells are structured very differently from optical cells or liver cells. To summarize, each cell has proteins, DNA, RNA and genes – all of them, described below.  ***DNA*** has the main purpose to store the body’s genetic information – and to give instructions of what to do next. The first two letters of DNA stand for ‘**D**eoxyribo**N**ucleic’ followed by a third, ‘**A**cid'. DNA is held in a steady shape by ladder-like rungs, called bases, connecting between two helixes. (Chemical compounds are broken into categories of either base or acid.) That is, the DNA has structure because of these base pairs – and the structure is unique for each person. The very long, complicated DNA string extends for 3 billion pairs of repeating sections (nucleotides – described below).  ***RNA*** has the job of transcribing the DNA instruction into an understandable form and sending the instructions to the ‘things’ that make the body work the way it does. For the most part, those working ‘things’ are proteins. It is RNA that plays the messenger role between the DNA and the proteins. Besides its differing function from DNA, RNA departs from DNA in that it is a single helix, rather than a double helix and has one nitrogenous base (of 4) that differs from DNA (see nucleotide).  ***Proteins*** are the workers. While the DNA calls the shots in the human story, DNA does none of the work. It tells its cell what to do, informing the cell’s chemical factories which protein molecules to fabricate. That message moves along the RNA chains. Then the protein does the job needed such as moving a muscle or heating up our bodies when it is cold outside. The proteins in the liver cell have different instructions from DNA than do the proteins in the optical cells. Each human cell carries about 1 million protein molecules.  ***Nucleotide*** is a compound, which makes up the DNA. It is formed of molecules consisting of (a) a base (or more formally, a nucleobase), (b) carbon sugar ribose (or more formally, a carbohydrate) and (c) a phosphate group. Nucleotides are molecules that make up the basic building blocks (repeating chain sections) of DNA and RNA. Thus, the nucleotides form the nucleic acids DNA and RNA, both of which are essential biomolecules within all life-forms on Earth. Nucleotides are composed of four sub-unit molecules to form a nitrogenous base. The four nitrogenous base units present in DNA are guanine (G), adenine (A), cytosine (C) and thymine (T) and in RNA, guanine, adenine, cytosine, and uracil. While computers have a binary code to identify its instructions, the DNA has 4 codes to identify all of its instructions, namely G, A, C & T. The contradiction of DNA and RNA called acids while composed of billions of base pairs is answered by the fact that acidic phosphates are dominant within the DNA and RNA molecules.  ***Genes*** are instructions within the DNA, made up of 23,000 different pieces grouped into various combinations of genes (called chromosomes) that are chock full of specific information telling your body what to do, and when to do it – such as when to turn your hair gray or to not have any hair left at all. Genes instruct us to have blue eyes, long legs, amber skin, to be a boy or a girl, and so on.    ***Genome*** is a full description of a cell’s DNA, that is the specific arrangement of the billions of the helix’s base pairs for the human, a dog, a sunflower, or a virus. Each cell in a person contains the same unique DNA message.   1. **How**   At least seven methods, all claimed to be equally valid at this point in time, are being used to develop a vaccine against covid-19. Methods ‘a’, ‘b’ & ‘c’ below, however, are more pursued by developers because they offer an ability to manufacture quickly in large quantities. This trait, that the other solutions lack, offers a clear advantage to bring about world-wide distribution.   1. This method puts genes of the covid-19 virus into the genome of a harmless virus and injects that virus into the human, thus presenting the human immune system with the antigen. Ebola, and some veterinary vaccines (**recombinant vector**) form this type. 2. Another vaccine approach is to add the covid-19 gene to a harmless virus’s outer coat in the lab. The targets are the spike proteins that appear on the virus’s outer layer, a method used currently for hepatitis B vaccine. The result is lots of copies of the free-floating spike proteins without any complex attachments (**protein subunit** vaccine) – hence greater ease of replication. 3. Rather than adding an independent gene, ***(nucleic-acid*** vaccines) are those that introduce the gene for the antigen as a piece of the virus’s DNA or RNA molecule (where the virus’s gene is stored). The production of nucleic-acid vaccines is completely independent of viruses or cells, making unwanted contamination most unlikely, thus ensuring that this vaccine is safe for high-scale production. 4. Presents the immune system with a strain of the virus that has been hobbled in a way not to cause sickness (**live-attenuated** vaccine); used with measles & mumps. 5. Or the lab can present the immune system with a virus that had been completely inactivated (**inactivated** vaccine). Salk polio, and seasonal flu vaccines are examples. 6. Presents the immune system with the antigen, itself harvested from the blood of those already infected. The original approach for hepatitis B. During the flu pandemic of 1918-19, doctors clotted the blood of victims and centrifuged it to separate out the antibodies   that the blood contained (convalescent plasma – **CP** vaccine). The CP  approach worked for SARS and H1N1 influenza. The Mayo clinic (U.S.) will conduct randomized control trials of CP for covid-19 solutions within a few weeks.   1. This last method is based on presenting the immune system with BCG vaccine used for tuberculosis which has had an effect well beyond TB itself. This approach will explore other unrelated vaccines (***parallel remedies***) in a similar, somewhat random, fashion.   The approximate number of firms addressing these directions are:  Protein subunit (b) 27  RNA/DNA nucleic acid (c) 20  Recombinant vector (a) 10  Parallel remedies (g) 4  Inactivated (e) 3  CP (f) 1  Other (d +) 22  Some experts, including Bill Gates who has funded tens of billions of dollars towards vaccines, believe that governments should take the risk to build several different types of production facilities now (at $150 million each) for the leading candidate covid-19 vaccines, even though no one knows which one(s) will be eventually selected. This entails making a necessary waste in order to develop a lead on getting the vaccine out to the people as quickly as possible. For this reason, Johnson & Johnson (U.S.) has committed $1 billion to expanding its manufacturing capability. The G20 nations have asked WHO (World Health Organization) to outline a plan for the equitable distribution of the vaccine and other goods to fight covid-19. Since the disease’s sourcing and manufacturing response is likely to come from the G20 nations, a viable distribution method may be in the works.   1. **Reviewing the Obstacles**   **Showing how well the vaccine works** must become part of the trials.  **Find any rare problems the vaccine may encounter** must also become part of the mix.  **Manufacturing the vaccine in large enough quantities to serve the whole world.** That would be 7 billion doses. Today, the world makes 5 billion doses/year of vaccines of which the largest part is the seasonal flu vaccine.  **Restricting it to ‘our country first’** selfishness may be combatted by the efforts of the G20 nations and WHO as noted in the last paragraph of #6 above.  **How much capacity can be developed beforehand** (without knowing which answer will come first)? This is noted in section 6, last paragraph.  **No RNA or DNA vaccine has ever been licenced** for use in humans. “We have a car design, but we don’t know if it can move.” So brave new steps need to be taken.  **Rate of dosage has to be established.**  Some vaccines have to be injected twice (Prolia, antibody for bone repair for example, and shingles vaccine Zostavax and recombinant vaccine, Shingrix). How can we ensure this will not be the case for the covid-19 response?  **Adjuvants** effectiveness have to be mastered (chemical factors that can make a big difference to the effectiveness of the vaccine, but for reasons that are not well understood). BCG vaccine used against tuberculosis seems to have a stimulating effect that goes well beyond TB. Therefore, it presents an option to explore for SARS-COV-2 virus serum (see 6g).  **Antibody dependent enhancement** wherein antibodies, for reasons that are not understood, can make a viral infection more damaging instead of improving the situation, as in the case of dengue fever vaccine, and seen also with the SARS vaccine itself.  **Scaled up vaccine production** for SARS-Cov-2 will put pressure on the ability to produce other disease vaccines. Even today, there are worldwide shortages for yellow fever and measles vaccines.   1. **Conclusion**   An effort unlike any other in the world history is in the works to defeat covid-19. Wish us all a  speedy recovery.  Bill |  |
| *Bill Caswell* is an experienced coach of CEOs and executives around the globe.He is the author of 27 books, written, by a CEO for CEOs. \_\_\_\_\_\_\_\_\_\_\_\_ *CCCC Events* COVID-19 willing May 2020*Launch of online courses*-Personalities (PAVF)-Getting it Done (OAK)-Painless Meetings-Best Kept Mgt Secrets (English & Spanish) Deferred*Planning*Benson CentreCornwall ON, Canada21-27 June 2020*Practical MBA* The Business InnOttawa ON, Canada For more information,  write us at: bill@*caswellccc.com*  More than 180 CCCC Newsletters are available at [www.caswellccc.com](http://www.caswellccc.com). |

1. [↑](#footnote-ref-1)