STM JOURNALS

Journal of Artificial Intelligence Research & Advances
ISSN: 2395-6720
Volume 7, Issue 3
www.stmjournals.com

Artificial Intelligence in Transfusion Medicine and in Our Mission to "BEAT COVID"

Jerard Seghatchian*
International Consultancy in Innovative Manufacturing and Quality, Safety of Blood derived Bioproducts, London, England, UK

Abstract

The key objectives of this study are: (1) Demystifying the buzzword of Artificial Intelligence (AI) and comparing neuronal networking similarity of machines with some mammals; (2) Exploring, from outside sources, the breath of some computerized procedural data generated in laboratory and clinical areas of medicine, by robotic tools in the cutting age of transfusion medicine; (3) Expressing views on the variabilities of covid-associated long lasting microcirculatory disseminated pathogenic autoimmune complications, some leading to development of vasculitis and organ failure in some but can be slowly reversed when patients recover; (4) Focusing on our mission to "beat-covid", with a proposal for clinical trials, taking into account ways to optimally improve the clinical efficacy of inducing passive immunity through the use of a standardized levels of coronavirus neutralizing antibodies hyperconcentrate recovered timely by a validated affinity column adsorption procedure from coronavirus infected convalescent plasma, obtained by aphaeresis for plasma exchange therapy (PET); (5) Overcoming the potential toxicities of the use of uncontrolled convalescent plasma, until a validated vaccine that covers all variants of coronavirus that appear in the scene and even then to be used as a re-boosting strategy, as the circulatory levels of the coronavirus NAB appears to be short, about 3 months. Some recommended DDR protocols are proposed to achieve the beat-covid objectives, by inducing immunity, in line with personalized precision transfusion where AI and Machine Learning expectedly have major impacts in big data and pattern analyses, for the selection of antiviral drug and other forms of prevention and treatment therapies.

Keywords: *Artificial intelligence, artificial neural network, machine learning theragnostics, coronavirus infection, passive immunotherapy*

Author for Correspondence E-mail: jseghatchian@btopenworld.com

INTRODUCTION

A series of novel tools has been recently developed, falling under the broad term "Artificial Intelligence (AI) and (ML)", with the goal to leverage the computing power of modern day machines. AI-based algorithms that are capable of the most diverse tasks in transfusion practice, from supervising complex robots for high-throughput screening of blood samples, through the collection and automated serological testing procedures, processing/storage, to ultimate delivery into needed patient as vein-to-vein. Today, therefore automation computerization and machine learning would enabling us to extrapolating meaningful patterns out of the breadth of data generated in many current fields of laboratory diagnostic, development and clinical research (DDR), in the most coordinated automated (robotic) diagnostic devices, processes and procedures in the ways we could not possibly have just a few decades ago and to better understand even natural patterns of biological system in adult and pediatrics, through advancement of available modern 'Omics' analysis and other robotic tools [1–3].

Covid-19, or simply coronavirus, is amongst a series of unexplained newer pneumonia virus, similar to the severe acute respiratory syndromes (SARS), that binds to angiotensin converting enzyme-2 (ACE2) receptors on the endothelial cell membrane surfaces of lungs,

heart, kidney, intestines, skin etc. for the entry into cellular machinery. The infected patients show enormous abnormalities in hemostasis and prothrombotic disturbance and age-related immune reactions, cytokine storms and other biological response modifiers that are known to contribute to the development of multiple organ dysfunction; often leading to death, despite numerous classical clinical interventions [4–6].

Clinical efficacy of Coronavirus Convalescent plasma (CCP) therapy on preventing and patient treatment is one of the promising treatment strategies that are currently perused with rigors, in the absence of availability of a reliable safe and highly effective vaccine as the first choice. The clinical efficacy and safety of convalesce plasma therapy, as a passive immunotherapy, for some infection such as Ebola is well established and now become amongst WHO recommendations but it remains unclear if such an approach is effective in coronavirus patient as some controversial view are expressed in ever grooving reports that are still growing fast, but are mainly based on the observational small numbers of cases.

Clearly a matched control study and meta-analysis is critically required to estimate the potential clinical efficacy and safety of coronavirus convalescing plasma therapy (CCPT), where artificial intelligence and machine learning in big data and patterns analyses have proven to be extremely useful [1–3]. Current large-scale analyses using Omics [1, 2] and Benford laws suggest that CCPT may have some clinically relevant impact in reducing significantly the rate of mortality in the CCPT group compared with the standard group [2], but clearly more like with like trials and larger sample sizes are needed to confirm not only mortality rates but also the toxic events associated in CCPT therapies, as the efficacy must go hand on hand with safety as the two pillars of advanced personalized precision transfusion practices. In this context it should be reconsidered that viral infection depending upon its severity and affinity binding with its entry receptors sites on cells such as "ACE-2" might create enormous damages such as autoantibodies generation in some cases, complement activation, cytokine storms, in early severe cases with potential being overcome either physiologically or otherwise by innovative methodology being reversible and of course irreversible coagulopathy often leading to microcirculatory blocking and inflammatory thrombotic events leading to organ failure and for sure the concept of death is coming (DIC) like mortality [4].

In fact the early removal of cytokine and inflammatory elements with some high throughput membrane, with adsorption function, are emerging as novel blood purification technologies in critically ill patient [4, 6–8]. Similarly, some online technologies including drug therapy and plasma exchange therapy are used to restore hemostasis and laboratory haematological abnormalities. Mobile modern fully computerized plasmapheresis procedures, with on line adsorption affinity column procedure, are found to be extremely useful for the timely collection of coronavirus neutralizing antibodies from patients who recovered from coronavirus infection, so called coronavirus convalescent plasma (CCP), who benefit from plasma donation by the reduction of infection-induced prethrombotic status and recipients who may need some high affinity neutralizing antibodies against coronavirus as preventative or therapeutic strategies [5].

This concise manuscript aims to highlight as a small step forward in the application of such measures against the coronavirus disease pandemic. This would be a small step forward, while we are waiting to produce an effective, validated vaccine and witnessing increasing demands for testing and self-isolation which are the two most effective current strategies. This targeted strategy consists of using fully recovered COVID 19 Heroes, that is, brave volunteers, as the source of antibodies in plasma collected by plasmapheresis or affinity column-derived antibodies, both would be sterilised and pathogen inactivated for substitution therapy for use in those populations in need of antibody. This includes the use of PET in critically ill patients as a

supportive measure, with the added value, in those at potential risk of infection as no vaccine is yet available and even if such a vaccine is available it can be used as a method of rebousiting the circulatory levels of the neutralising antibodies (NAB) against coronavirus infection.

The plasmapheresis procedure is especially targeted to male donors, who are able to undergo multiple double, or even triple plasmapheresis procedures. As some of these donors have already been in an infection induced-hypercoagulable state and prone to thrombosis and DVT; this strategy will be partially aimed at improving their health with the use of citrate based anticoagulants and removal of high molecular weight viscous components which contribute to the untoward clinical effects of DVT. Moreover the repeated targeted plasmapheresis or plasma exchange of selected individuals would undoubtedly lower their state of hypercoagulability and normalize their hypercoagulability. The recipients of such a derived FFP-product would benefit from the 2–3 doses of viral inactivated antibodies, which could neutralize the viral antigens even at very low concentration if present in the early stage. So, this practice would be a double-edged sword with benefits for both donors and recipients alike.

In this report some of the future developments of this strategy, together with how to overcome optimally the untoward effects, including the transfusion of harmful autoantibodies to recipients by using uncontrolled and untreated convalescent plasma from a single individual, compared with the selected pool, are highlighted.

Needless to highlight that in Covid era, all things are delicately are interconnected. Some are inspired by philosophical interrogation, while others offered as humorous social commentary and some others of scientific educational value, but all might excite readers' and publishers' mind and stimulate the intellects.

Here with AI in right place for allowing to speak the current trends in covid including newer vaccine with 90% immune efficacy and safety that one might argue that is good news in prevention but not addressing passing the disease to others, and much remained to wait for UK-MHRA views before be launched not mentioning its –70° storage and then kept in fridge to be used within 5 days otherwise wasted!!! Also some infrastructural changes have to be delivered in mass scale vaccination. Moreover some of the issues such as development of autoantibodies in view of potentially high affinity binding of the spike proteins to ACE-2 receptors for cell entry, infection induced complement activation, cytokine storms, and abnormality in heamostatic and other aspects of coagulability etc. that need to be addressed timely amongst other issues as highlighted below:

Back to Basic on the Influence of Applied Computerized AI Tools in Transfusion

On reflection, based on newer outside sources, the impacts of AI on the advancement of stem cell therapy and many other fields including transfusion/transplantation is longstanding as McCarthy, one of the leading designers, has invented this term in 1955. He defined it as the science and engineering of making intelligent machines with central goals of reasoning, knowledge, planning, learning, perception, communication, and even the ability to move and manipulate objects. In fact, the multidisplinary nature of AI spans across numerous sciences and professions, including computer science, psychology, linguistics, philosophy, neurosciences and applied transfusion medicine/transplantation sciences [3].

Conceptually, AI-based approaches could not only be used for machines that dissect and isolate the immune particularities of individual patient's disease in a matter of minutes (personalized medicine), but also to create the treatment that is customized to patient's genetic specificity and immune system capability. In addition, AI could be used also for optimization of clinical trials of innovative stem cell and gene therapies in patients by precise planning of treatments, predicting clinical outcomes, simplifying recruitment and retention of patients, learning from inputted data and applying to new data, thus lowering

their complexity and costs that are of the matters of current concerns to all in health care systems [2, 3].

Similarly AI-based algorithms and machine learning can be leveraged to quickly process the wealth of data generated by latest generation omics approaches, such as metabolomics, indicating that technical advances in the field of mass spectrometry-based omics approaches have been highly instrumental to expanding our understanding of the impact of blood storage lesion(s). Especially with respect to red blood cell units, a life-saving blood-derived therapeutic with a relatively limited shelf life (35–42 days depending on the National guidelines) and with plenty of other innovative achievements through computerization and automation from the donor, through validated testing, processing and storage, ultimately to the recipient [2].

Currently, enormous medical databases (big data) have been generated, helping us to better characterize the impacts of many factors on the quality of stored blood bioproducts; and even to characterize the impact of fresh versus stored blood in autologous healthy and heterologous chronically or massively transfused recipients, such as thalassemia or trauma patients. Harnessing a wealth of much useful quality assured recorded data, helping in therapeutic decision making to the benefit of all concerned. As for the applications of other computerized tools, concurrently several unsupervised or partially supervised automated methods such as omics and modern follow cytometers have been applied to big data and patterns analyses in the field of transfusion medicine to extrapolate meaningful clues for mechanistic or laboratory and clinical studies and there are some urgent calls for some powerful machines to help in summarizing and interpret the outcomes. Furthermore, immunotherapy with its recent giant leap into the fields of oncology is yet another field for applied AI, with the need to test a large number of chemical modifications of therapeutic agents, towards the individual variability of cancer cells, where the second generation genetic sequencing has already filled tons of computer memory networks.

Similarities between Some Mammalians Neuronal Networks and the AI Networking

Theoretically, based on personal insights on the topic of neuronal comparability there are some similarities between artificial neuronal network of AI tools and the behaviour and intelligence of an octopus, the smart cookie, possessing some half a billion neuronal networks to control the eight-legged cephalopods, often settled on the calm ocean floor, cognitively exhibiting behaviour that borders on higher mammalian: they use tools, learn through trial and error and even appear to do a double-take on catching sight of their own reflection in a mirror. At the same time, remaining cognitively very different from other animals and with one huge orange eye gazing out contemptuously perusing our shortcomings and questioning what is the problem with human species? Perhaps in respect to our failure to our new critical mission statement "Beat-Covid Timely", and added points that we are even more polluting the 'Earth' seas, with coronavirus and are still going for our romantic and aromatic appetite for grilled squids and others joys of life even during crises despite the second self isolation rule and due to the potential dreadful localized lock down and second waves with increasing number of loss of lives.

Others, like myself, consider that there might be some similarity in the behaviour and intelligence of some sentient birds such as peacocks, "the hobby of life time behavioral studies, the symbol of vanity'', a bird that with due astonishment repeatedly performing the same flamboyant dances, well-coordinated with the neural activities, by shimming sound of their own plumages, admiring self achievements, stating "if you have it flaunt it" and with the monopoly of wisdom on social behaviour intervention competence, wanting to be always in front of events rather than behind and not wanting to know about the restriction cycles of panic and neglect. Even spreading some most colorful spores, in line with their most colorful feathers, as a kind remainder to observers, to keep apart in 2 m distance with mask on to protect their lungs, as there might be disguise all around them, a new dance the "coronavirus dance'' from a minuscule bundle of RNA, covered with spikes crowns. Rather invisible to naked eyes, aiming to entering the

lung tissues and destroying the lives of plenty of predisposed and matured individuals, though my tiny colorful spores, (possibly say peacocks), while sharing the same mode of entrance on the same sites in the lungs, but at least are not virus types. Nevertheless stay safe, stay apart, be conscious of the imposed measures of self isolation and the recent rule of 6 in the UK and follow the rules of surveillance society to avoid more coming restrictive disabling rules during this health and economical crises.

Some others comparing AI with the behaviour of our most loved friends, highly noble well trained sentient dogs, also using tools to learn through trial and error, often resting semi-consciously or positioning themselves for some tender loving care (TLC). However, always ready for due strolls or to catch skillfully the indicated targets on demand. In the UK, they even have been trained to identify and catch individuals carrying coronavirus through acquired experience and gained skills to identify infection induced peculiar aromas. Another step forward to "mission critical beat covid timely" in airports in order to reduce the viral load spread internationally through travelling. Someone said applied AI allows you to "reach for the sky and stars" far above "the cloud" that for many of us is hard to envisage. Even reportedly there appears to be some sign of lives in other planets beyond our comprehension.

As a cautionary note, nevertheless, while the use of these newer AI tools have been the subjects of tremendous optimism but might occasionally suffer from some drawbacks over the excessive reliance. This brings me to quote the Douglas Adams' novel (The Hitchhiker's Guide to the Galaxy), that our ancestors made a big mistake in coming down from the trees in the first place, or that even the trees had been a bad move, and nobody should have ever left the blue oceans, similar to the octopus, etc.

THE CURRENT STATUS OF CORONAVIRUS INFECTIVITY PATTERNS AND IMMUNOTHERAPY PROGRESSION

The outbreak of coronavirus has been an enormous global public health threat and economic crisis, causing worldwide concerns. Due to the high pathogenicity and infectivity, samples containing live coronavirus should be handled with due care under bioassay level 3 (BSL-3) condition. The neutralization assay is a standard evaluation procedure for coronavirus related vaccine and antibodies potency evaluation, as the core ingredient of diagnosis for neutralization serology for vaccinotheary or creating the passive immunity. It is therefore crucially important that all parameters of such an assay to be validated, ensuring optimal performance of materials used, such as their stability, sensitivity and specificity as the essential requirements for any antigen or antibodies testing, but also a rapid turnaround time. The later is of particular relevance to coronavirus as a planned large scale age-related monitoring, followed by contact tracing, which are proposed by WHO internationally to tame this infection, where artificial intelligence, in big data and procedural analyses are undoubtedly of great help.

Unfortunately, since the emerging of COVID-19 on the scene, little progress are made internationally to tame this virus and in the UK we are still debating about possible fire or circuit break to overcome the ever growing rate of the second waves of infection. Meanwhile many investigators inclusively have reviewed the mechanisms of coronavirus infection and the current status of the use of convalescent plasma for inducing passive immunotherapy by plasma exchange therapy (PET) to the benefit of donors and recipients alike [4–6].

Currently there is a national scheme in the UK and many other countries, to collect CCP by plasmapheresis, for its potential use in the absence of a validated vaccine. In this context we proposed some newer protocols, as a step forward, to encourage the application of a more standardized and harmonized preventive measures, using the well established affinity column for preparation of hyperconcentrate neutralizing antibodies from pooled convalescent plasma (P-NAB) for immune therapy and comparing various existing protocols, on merits, to turn some unresolved

challenges in coronavirus infection therapy to opportunities. Moreover, it is also critical that in parallel to deal with some toxicological aspects by removing the impact of toxic agents such as infection-induced, complements activation and cytokines storms and also overcoming the induced abnormalities often leading to thrombotic events despite anticoagulant therapy and acute organs' injury [4–8].

The Age-Related Variabilities in the Autoimmune Responses of the Binding of Coronavirus' Spike Protein RBD to ACE2 on Cells

The recent outbreak of the COVID-19, lead to some intriguing disease dynamics, in some age-related affected patients, with some being mainly asymptomatic or mild, while some subset others; affected patients experienced a more long-lasting severe complications including dyspnea, acute respiratory syndrome, thrombosis in microcirculatory thrombosis, endothelial damage with thrombo inflammation, lethal DIC and multi-organ failure. Intriguingly these complications increased dramatically in over 65 years of age, with some comorbidity factors (i.e. respiratory, cardiovascular diseases, obesity, hypertension, diabetes, etc.) and subsequent to an exacerbated immune and inflammatory response [9]. Apparently, these rebound events were clinically observed for weeks, or even months, after the onset of symptoms, in some people, when neutralizing antibodies were already present and the viral load was relatively low and when the highest IgG, IgA or IgM antibody levels were already present in the critically ill patients, and reportedly even vasculitis was observed in some children who develop a Kawasaki-like disease, all suggesting that it could be the result of immune response to covid infection, which becomes alloimmune with generation of autoantibodies to some self-proteins, involved in the virus cellular entry complex, acting as physiological antibody's defense systems [4, 10–13].

In fact it is well documented that viral binding to ACE2 is essential for both entry to cells and infection progression and the high affinity binding of SARS-CoV-2 to ACE2, through its spike protein RBD, might lead to induction of the immune response to the self-components involved in the cellular entry through ACE2 and causing a rebound effect as the consequences of physiological autoimmune alloimmunization response to infection [4, 14]. These are also consistent with an autoimmune/alloimmune disease evolution, which can be fatal in some cases but slowly reverse when patients recover.

Such as autoantibodies to ACE2 could presumably be generated directly when ACE2 complexes with viral proteins, or by the exposure of infection induced -ACE2 cryptic epitopes or denatured structures and then target an autoimmune response, while the binding of SARS-CoV to ACE2 for cell entry was previously identified in ARDS. However, the binding of SARS-CoV-2 to ACE2 might have a much higher affinity, in some cases depending upon the degree of virility, this infective agent and this could favor the immune system extended reactivity to the whole pathogenic complex, involving viral and self-components [15–17]. The higher affinity of this highly viral virus is of essence for supporting our earlier autoimmune proposal [4] in line with the concept that strong interaction highly viral infective virus could lead to the alteration or the ternary structure of ACE2, favoring the exposition of cryptic or hindered epitopes, and contribute to autoantibody generation. Moreover, some acute clinical events, such as the strong inflammatory and complements activations and cytokine storms, the chemo attraction of monocytes and macrophages to multiple pathological sites might be involved [18, 19]. Hence the removal of biological modifiers in the early phases of infections is highly warranted and some studies in these directions have already begun.

The Current Status of Progression on Some Unresolved Issues

Recently in line affinity column adsorption and blood purifications system, pathogen reduction technologies are planned in view of the presence of some residual infectious agents including viable covid antigen, as the essential part of the convalescent plasma therapy. These efforts are aimed to improve the clinical safety of pooled neutralizing antibodies (P-NAB) hyperconcentrate that could be resuspended in

appropriately selected available plasma pool containing the balanced levels of all plasmatic active principals, ensuring its optimal effectiveness. This should include optimal levels of albumin, as often coronavirus patients showed considerable deficiency in albumin, apart from other haemostatic abnormalities, to be in line with the best practice and with the concept of personalized precision transfusion.

Another unresolved challenging problem requiring special attention is the development of autoantibodies against ACE-2 as some infected patients are expected to develop an anti-spike autoantibody to ACE-2 and these anti-spike will "look like" ACE2. This therefore might at least open some relevant unresolved age-related questions: (a) firstly how ageing influences the function of immune cells and exacerbate coronavirus disease? This concept is also relevant to vaccine response amongst older population, who are already frail and experiencing increased inflammation due to frailty and allowing more bacteria to enter to gut, lungs, kidney and skin as the physiological barriers as well as accumulating more senescent cells induced inflammation. Accordingly blocking induced inflammation and the cytokine storms, with Dexamethasone, in the early stages of infection, as it is now becoming routine practice would be understandably highly relevant and promising approach; (b) Secondly, the concept of alloantibody to ACE-2, leads to another question about some long-term infected patients who might have negative antibody tests because they have robust anti-anti-COVID-19 antibodies responses, which might questionably mop up most anti-COVID-19 antibodies; ironically, might anti-COVID-19 antibodies responses render people more susceptible to infection?

THE CURRENT STATUS OF THE BEAT COVID STRATEGIES AND NEWER DEVELOPMENT IN PRODUCTION OF SAFER CORONAVIRUS CONVALESCENT PLASMA DERIVATIVES

From the preventative and therapeutics standpoints, in the absence of a validated vaccine against most of the known variants of coronavirus and despite some partial success with some antiviral and other drug to delay the mortality rate; that having their own side effect as previously described [6], and the limitations of using convalescent plasma as it stands, that is highly difficult to justify (without some newer strategies to be put in place to create a much safer and harmonized passive immunity against coronavirus infection), to be in line with the best practice and precision transfusion, some newer interventional studies for creating safer mode of therapy are highly welcoming and meanwhile all suggested procedures for the interventional programs must remain of the table for the continual quality and safety improvements.

Convalescent Plasma Banks Programs

Currently, many blood establishments internationally, including the UK NHS blood service establishments and most other countries, have supported the introduction of convalescent plasma programs and incorporating many modern mobile and highly automated, fully computerized plasmapheresis technologies to create large banks of convalescent plasma. This source plasma is usually obtained from either plasma donors, consisting of ex patients and front line willing individuals or new asymptotic donors, with due vigilance as required, when introducing new practices. Furthermore, some quality assurance programs have also to be in place to maintain confidence in working practices as the cornerstones around which these changes are managed and for regularly updating the guidelines on the evidence-based approach. Moreover, behind the scenes many clinical, academic, hospital and manufacturing laboratories investigators have both innovated and maintained essential services under the most challenging circumstances. Moreover, plenty of volunteers are registering in the UK to participate the phase III oxford vaccine trials as a new initiative where the use of AI would be clearly on agenda for both procedural and large data and patterns analyses.

Newer Diagnostic Development and Research (DDR) Strategies

From the laboratory stand point, with newer advancement in modern flow cytometry technologies, some researchers are using this

technology to characterize which types of T cells are robotically targeting the immune response and at the same time exploring the status of T-cell exhaustion as a major challenge in the development of timely immunotherapy in the Beat Covid challenges.

Moreover the use of our earlier proposed pooled CCP or pooled cadaveric serum to obtain mixed nature of physiologically produced antibodies against coronavirus are progressing well but still in planning stages as the backup that will be also overcoming some toxilogical substances such as cytokines, activated complements, depleted fibrinolytic parameters and induced coagulopathy in the early interventional measure. These could be carried out either with the in line use immunoadsorption high affinity membranous matrix and blood purification system in critical ill with unstable circulatory inflammatory status near bed side, or using newer specific column during extracorporeal circulation with the newer biocompatible porous polymers adsorbent micro beads that reduces effectively the levels of various inflammatory factors, in particular in patients with septic shocks [7, 8].

To ensure that these processes are achieved in the most effective standardized way under the c GMP regulatory adherence, we must be encouraging the input of some associated manufacturing to get involved, focusing on the use of Cadaveric Serum availability, working tendom to produce pooled hyperconcentrate NAB and keeping the final products in frozen or freeze dry or spray dry format, the later being the preferred option, to be readily available for use.

Newer Safer Alternatives to CCP and the Potential Use of Localized Delivery Covid-NAB Hyperconcentrate

In parallel we should pursue with more rigors the newer insight into the design of some cost-effective methodologies for harvesting, expansion, manipulation and purification of the cultured cells and into the extracellular vesicles involvement, *in vitro* production of reproducible human cells, stem cell extracellular vesicles for substitution therapy and of the antibody delivery on some local sites, as applied for many developing functional materials in transfusion/transplantation and tissue engineering and in some others current novelty related to DDR of cellular and plasmatic derivative of blood components and their artificial alternatives that still are amongst novelties in transfusion medicine [20–23]. However, despite all these newer initiatives our palates for excellence fall into insignificance when considering the tragic events of numbers of deaths and our heart goes out to all suffering families and connections and to our health care front line staff as they have to meet the demand during this crises directly head on. With the above objectives in minds more diagnostic development and research in the Beat-Covid domains are still needed, where AI and machine learning will be of great values in big data and patterns and procedural analyses and numerous planned studies; and the journey in this direction has already begun. Noteworthy to mention that the fresher insights from longitudinal plasma proteomics with viral response signature of multiple cytokines and other bioactive materials reveals enormous plasma proteins difference between infected patients and controls as well as appearance of some 200 protein discriminants between severe and mild groups as a significant diagnostic achievements. Newer flow cytometry tools are other tools that help in better characterization of changes that occur [2, 20–23].

Newer Development in Vaccine as a Breakthrough Milestone

One of the currently perused treatment strategies, that are being explored by many investigators internationally, is the development of a safe and high affinity vaccine against coronavirus infection that apart from inducing high affinity neutralizing antibodies to also help the killer T destroying cells to get rid of symptoms. Nevertheless while the developing high affinity antibodies to provide immune efficacy is a must, the strategy to stop transmission of infection and its related toxic effects such as the development of autoantibodies to spike constituent of virus bind to its receptor (ACE-2) for cell entry and other toxic elements such

as complement activation, cytokine storm, coagulopathy and microcirculatory inflammatory thrombosis etc. are also important to be overcome; hence there are many other questions to be addressed.

Interestingly according to press release today, "The Interim Pfizer/BioNTech Covid Vaccine'', as one of such a mRNA based candidate effective vaccine, found to be more than 90% effective in preventing Covid, in the study participants without evidence of prior infection, and that can be considered as a milestone breakthrough for the front line staffs to be used twice a week. This report is based on the first interim efficacy analyses of a trial that provided 90% protection at 7 days after the second dose protection of about 28 days after the initiation of the vaccination but more in-depth data might be required for license application and UK-MRAH application and might prove to be an overstated result until the trial is completely finished as there are plenty of unresolved questions to be addressed, i.e., being a double dose vaccine trials, and must be kept in very low temperature and usable up to 5 days kept in fridge, and if not used, is a waste, hence would create some delivery problem and changes in the current infrastructure for usage, that nowadays could be overcome, as understandably a phase-1 clinical trial to test VXA-COV-1, an oral Covid-19 vaccine candidate has been initiated with the first dose.

Also it is not very clear that vaccine will as effective in over 65 age groups, and for what duration; though the preliminary study covered the age 12, young and over 55 etc. Moreover we are expecting soon the results of Oxford and other phase-3 trials for other targeted groups. Therefore much more remains to be done in this journey as the focus is not only generating neutralizing high affinity binding antibodies to protect, in particular, those most in need first, such as home care and frontline staffs, but most importantly to stop the entry to cells but also stopping the disease transmission too as well as having considerable impacts on various toxicity as mentioned above.

CONCLUSION

Coronavirus disease has spread globally affecting more than 41 million people worldwide and causing millions of deaths. Although the majority cases of the infected groups are mild and asymptomatic, but given the staggering number of global infections, substantial populations of susceptible patients with medical comorbidities develop critical respiratory illness. In particular, patients with haematological malignancies and other risk factors are more prone to severe disease and increased mortality. Because of the limitations of various preventative or therapeutic agents, the development of new treatment strategies is imperative to improve patient outcomes and attenuate the infection outbreaks.

One of the treatment strategies that are being explored by many investigators internationally is convalescent plasma, a therapy that has been used historically with some success to treat other viral outbreaks such as EBOLA with success, as proposed originally by this author. The basic concept of such a plasma therapy is based on the transfusion of previously collected blood plasma from a recovered COVID-19 population of patients to newly symptomatic individuals. Preliminary data indicates that this therapeutic approach is relatively safe and can reduce viral load and improve clinical conditions, but convalescent plasma collection practices and transfusion must be robust and supported by well designed observational studies, randomized and case-controlled clinical trials.

In line with our core critical mission statement of the beat-covid, we do propose the use a harmonized rather than standardized bioproduct to explore some innovation in engineering to develop a standardized therapeutic solution against coronavirus infection and the use of AI and robotic tools for procedural and big data analyses in the advancement diagnostic and R&D programs in blood transfusion medicine.

Currently we are in a planning stage focusing on the most urgent need for clinical trials on a standardized and validated pool of coronavirus neutralizing, in cryosupernatant as safest plasma derived bioproducts for prevention and treatment on coronavirus infection. Also taking into considerations the potential toxicity

of CCP in general that has largely been ignored so far and using the well -established and most effective and available mode of inducing a passive immunotherapy, particularly in the absence of availability of vaccine and the limitation of the antimicrobial drug therapies [6]. Such a preparation will be of great demand for rebousiting the neutralizing antibody levels as its circulatory half life is relatively short, about 3 months in most cases.

In respect to beat-covid attempts while debates on centralized contact tracing, as often as monthly, with a better degree of efficacy, in order not demoralize people, and to bring infection rate right down are still continuing whatever terms used (i.e. as the fire break or circuit break) appears to be not effective to bring the rate infection down promptly and some behaviour changes in some populations must be in place; nevertheless more investigative studies are essential even for some rebousiting strategies if any of the forward going vaccine trials become fruitful to be implemented as a potential breakthrough by the end of this year. Watch the space.

Therefore, looking forward some additional works in the following ideas are planned but require a proper team working strategies at international levels in the spirit of oneness to the benefit of all. This also means collaborating with some related manufacturers ensuring these efforts are carried out in the most effective standardized way under the cGMP regulatory adherence and, focusing on the availability of some Cadaveric Serum protocol working in tendom to produce pooled hyperconcentrate NAB and keeping the final products in frozen or freeze dry or spray dry format, to be readily available for use as the best option.

Clearly, comparative clinical trials, using as an alternative strategy by re-suspending the so called the P-NAB hyperconcentrate in a mini pool of viral inactivated cryosupernatant that are currently available in some blood establishments [4–6] or even in commercial SD plasma before transfusion to fulfill all the requirement in using the balance levels of both haemostatic and proteins contain of plasma substitution therapy. The use of these types of bioproducts can provide not only a higher safety standard with balanced doses of P-NAB with a longer-lasting immune response being sourced from human-derived plasma, a type of bioproduct in excess to levels of circulating antibodies to coronavirus antigens but also would be entitled with the important role of dumping the toxicological aspects caused by infection, and supplying the required levels of albumin that are depleted upon infection in covid patient.

Moreover in parallel we should peruse with more rigors the newer insight into the design of some cost-effective methodologies for harvesting, expansion, manipulation and purification of the cultured cells and into the extracellular vesicles involvement *in vitro* production of reproducible human cells, stem cell extracellular vesicles for substitution therapy and of the antibody or drug delivery on some local sites, as applied for many developing functional materials in transfusion/transplantation that still are amongst novelties in transfusion medicine [20–22].

Looking into future perspectives, on reflection the scope of AI and machine learning in combination with natural human intelligences remains limitless and infinite. However, how long before we could see the real impact of AI and related tools remains the most pertinent question? Can these combined tools effectively and accurately predict properties of newer diagnostic, development and research strategies? Not forgetting the speed and accuracy to be fit for purposes. Clearly complementing human intelligence with artificial intelligence and metabolomics in big data analysis in transfusion medicine could have enormous impacts on continual progress in many areas of transfusion medicine and transplantation sciences.

I can only hope that in line with our main objectives, this commentary will be of some educational values by bringing in some fresher thoughts in the applications of newer technological tools, such as AI and

Metabolomics and Machine Learning and on in line affinity column and blood purification systems in plasma exchange therapy when facing some highly important physiological/hematological/immunological abnormalities created by coronavirus infection that are becoming amongst the most intriguing unresolved challenging crisis, to all at international levels, in transfusion medicine related fields.

ACKNOWLEDGEMENT

I would like to take this opportunity to thank the editor of this journal for their editorial support and the opportunity to share my personal views on some useful applications of AI in the procedural and large data analysis research/development of coronavirus related transfusion medicine that provide some newer information on limitless power of AI in bridging and linking computerization to transfusion science and transfusion medicine.

REFERENCES

1. Seghatchian J. Editorial: An Introductory Commentary on the Use of Artificial Intelligence, Machine Learning and TQM, as Novel Computational Tools in Big Data Patterns or Procedural Analysis, in Transfusion Medicine. *Transfus Apher Sci.* 2020; 59(6): 102985p.
2. D'Alessandro A. Benford's Law and Metabolomics: A Tale of Numbers and Blood. *Transfus Apher Sci*. 2020; 59(6): 103019p. [in press].
3. Sniecinski I, Seghatchian J. Artificial Intelligence: A Joint Narrative on Potential Use in Pediatric Stem and Immune Cell Therapies and Regenerative Medicine. *Transfus Apher Sci*. May 2018; 57(3): 422–424p.
4. Amiral J, Vissac AM, Seghatchian J. Covid-19, Induced Activation of Hemostasis, and Immune Reactions: Can an Auto-Immune Reaction Contribute to the Delayed Severe Complications Observed in Some Patients? *Transfus Apher Sci.* 2020; 59(3): 102804p.
5. Seghatchian J, Lanza F. Convalescent Plasma, an Apheresis Research Project Targeting and Motivating the Fully Recovered COVID 19 Patients: A Rousing Message of Clinical Benefit to Both Donors and Recipients Alike. *Transfus Apher Sci.* 2020; 59(3): 102794p.
6. Putter JS, Seghatchian J. An Update on COVID-19 Infection Control Measures, Plasma-Based Therapeutics, Corticosteroid Pharmacotherapy and Vaccine Research. *Transfus Apher Sci*. 2020; 59(5): 102934p. https://doi.org/10.1016/j.transci.2020.102934
7. D'Alessandro A, Tiffany T, Dzieciatkowaska, M, Hill RC, Richado F, *et al*. Serum Proteomics in COVID-19 Patients: Altered Coagulation and Complement Status as a Function of IL-6 Level. *J Proteome Res.* 2020; 19(11): 4417–4427p.
8. Gang Chen, Yangzhong Zhou, Jie Ma, Peng Xia, Yan Qin, Xuemei Li. Is There a Role for Blood Purification Therapies Targeting Cytokine Storm Syndrome in Critically Severe COVID-19 Patients? *Renal Failure*. 2020; 42(1): 483–488p. DOI: 10.1080/0886022X.2020.1764369
9. Yang J, Zheng Y, Gou X, Pu K, Chen Z, Guo Q, *et al*. Prevalence of Comorbidities and Its Effects in Patients Infected with SARS-CoV-2: A Systematic Review and Meta-Analysis. *Int J Infect Dis*. 2020; 94: 91–5p.
10. Varga Z, Flammer AJ, Steiger P, Haberecker M, Andermatt R, Zinkernagel AS, *et al.* Endothelial Cell Infection and Endotheliitis in COVID-19. *Lancet*. 2020; 395(10234): 1417–8p.
11. Picchianti Diamanti A, Rosado MM, Pioli C, Sesti G, Laganà B. Cytokine Release Syndrome in COVID-19 Patients, a New Scenario for an Old Concern: The Fragile Balance between Infections and Autoimmunity. *Int J Mol Sci*. 2020; 21(9): 3330p.
12. To KK, Tsang OT, Leung WS, Tam AR, Wu TC, Lung DC, *et al*. Temporal Profiles of Viral Load in Posterior Oropharyngeal Saliva Samples and Serum Antibody Responses during Infection by SARS-CoV-2: An Observational Cohort Study. *Lancet Infect Dis*. 2020; 20(5): 565–74p.
13. Connors JM, Levy JH. Thromboinflammation and the

Hypercoagulability of COVID-19. *J Thromb Haemost.* 2020; 18(7): 1559–1p.
14. Lan J, Ge J, Yu J, Shan S, Zhou H, Fan S, *et al*. Structure of the SARS-CoV-2 Spike Receptor-Binding Domain Bound to the ACE2 Receptor. *Nature*. 2020; 581(7807): 215–20p.
15. Glowacka I, Bertram S, Herzog P, Pfefferle S, Steffen I, Muench MO, *et al*. Differential Downregulation of ACE2 by the Spike Proteins of Severe Acute Respiratory Syndrome Coronavirus and Human Coronavirus NL63. *J Virol*. 2010; 84(2): 1198–205p.
16. Tai W, He L, Zhang X, Pu J, Voronin D, Jiang S, *et al.* Characterization of the Receptor-Binding Domain (RBD) of 2019 Novel Coronavirus: Implication for Development of RBD Protein as a Viral Attachment Inhibitor and Vaccine. *Cell Mol Immunol.* 2020; 17(6): 613–20p.
17. Yilla M, Harcourt BH, Hickman CJ, McGrew M, Tamin A, Goldsmith CS, *et al.* SARS-Coronavirus Replication in Human Peripheral Monocytes/Macrophages. *Virus Res.* 2005; 107(1): 93–101p.
18. Chauhan AJ, Willen L, Brown TP. COVID-19: A Collision of Complement, Coagulation and Inflammatory Pathways. *J Thromb Haemost.* 2020; 18(9): 2110–2117p. Doi 10.111/jth 14981
19. Antonelou MH, Seghatchian J. Update on Extracellular Vesicles Inside Red Blood Cell Storage Units: Adjust the Sails Closer to the New Wind. *Transfus Apher Sci.* 2016; 55(1): 92–104p. https://doi.org/10.1016/j.transci.2016.07.016.[10DOI:10.1016/j.transci.2018.05.004
20. Seghatchian J. The Secrets of Human Stem Cell-derived Transfusable RBC for Targeted Large-Scale Production and Clinical Applications: A Fresh Look Into What We Need Most and Lessons to be Learned. *Transfus Apher Sci*. 2020; 59(4): 102862p. DOI: 10.1016/j.transci.2020.102862
21. Seghatchian J, Amiral J. Spotlights on the Current Perspectives on Applications of Human Blood Cell Culture and Organoids: Introductory Remarks. *Transfus Apher Sci*. 2020; 59(4): 102861p. DOI: 10.1016/j.transci.2020.102861
22. Lanza F, Seghatchian J. An Overview of Current Position on Stem Cell Therapy in Transfusion Science and Medicine: From Fictional Promises to Factual and Perspective from Red Cell Substitution to Stem Cell Therapy. *Transfus Apher Sci*. 2020; 59(5): 102940p. doi: 10.1016/j.transci.2020.102940

Cite this Article
Jerard Seghatchian. Artificial Intelligence in Transfusion Medicine and in Our Mission to "BEAT COVID". *Journal of Artificial Intelligence Research & Advances.* 2020; 7(3): 10–21p.