Guest Editorial

Negative Evidence: COVID-19 Vaccines and Disorders of Hemostasis

Jane M. Orient, M.D.

Introduction

The general public has repeatedly been told that COVID-19 vaccines are "safe and effective."[1,2] The mantra of their exceptional safety is repeated despite the tacit evidence to the contrary. This series of editorials attempts the difficult task of scrutinizing that optimistic official narrative.[3-5] This fact-finding mission seeks ***negative evidence*** related to the side effects of COVID-19 vaccines. Negative evidence is defined as the unexpected lack of data that logically should be present under specific circumstances.[3] Existence of negative evidence suggests that essential information has been intentionally omitted to cover up a nefarious activity. Any thorough investigation should include a process that tests for negative evidence.

This installment explores the significance of negative evidence related to the potential link between the COVID-19 vaccines and serious disorders of hemostasis. Additionally, it discusses research paradigms that can be applied to elucidate the nature of such an adverse effect.

COVID-19 Vaccines and Hemostasis Disorders—an Ignored Crisis?

According to official sources, the primary safety concerns about COVID-19 vaccines are limited to very few, very mild, and very rare side effects.[1,2] Among such allegedly negligible drawbacks, hemostasis disorders are listed along with Guillain-Barré syndrome for the adenoviral vector vaccines.[1] In contrast, mRNA vaccines are said to be virtually risk free, with the exception of "enormously" rare cases of mild and self-limiting myocarditis.[1,2]

Despite those reassurances, a myriad of various adverse events following COVID-19 vaccinations including hemostatic disorders has been reported by patients, their families, and third parties such as independent pathologists and even morticians.[3-6] Those reports appeared mainly on social media and in the "alternative press." However, they were also reflected in the Pharmacovigilance databases such as VAERS.[7]

In general, mainstream media outlets have been dismissive of such statements, calling them "unconfirmed hoaxes."[8] However, even the official press could no longer ignore existence of the serious hemostasis problems that emerged after the administration of the adenovector vaccines when those events were reported by prestigious medical journals.[9-11] Yet, the significance of those inconvenient thrombotic events started to be minimized very quickly. The thrombotic events were explained away as rare irregularities exclusive to the adenovector vaccines and not associated with the mRNA vaccines.[2, 12]

Mainstream media repeated reassurances of a similar nature to calm the worried public. However, the masses continued to worry since the comforting official statements did not reflect objective reality. Postings describing symptoms of thrombosis occurring after COVID-19 vaccines were continuing to dominate social media (SM). All attempts by officialdom to disrupt that endless stream were unsuccessful. At a certain point, mainstream medicine unleashed a massive Twitter campaign aimed specifically at *"highlighting the low potential of developing a blood clot from vaccines."*[13] It was all to no avail. The steady wave of SM posts about thrombotic complications of vaccines continues unabated today.

The remarkable persistence of those very disturbing personal SM reports, which contrasted with the cheerful official narrative about vaccines, was truly thought-provoking. It prompted this examination of the purported links between all types of COVID-19 vaccines and serious hemostasis problems.

Terminology of Hemostasis Disorders

Despite its clinical importance, hemostasis is not well understood by physicians who are not hematologists. Therefore, we will explain its essential concepts first. Terminology related to abnormal hemostasis has not been standardized and can be confusing.[14-16] This is a list of the most common terms related to disorders of hemostasis:

- ***Hypocoagulability*** *(bleeding diathesis)*: impaired clot formation[17]
- ***Hypercoagulability*** *(thrombophilia, thrombosis, prothrombotic state)*: excessive clot formation[18]
- ***Macrovascular thrombosis***[19]
- ***Microvascular thrombosis***[20]
- ***Hypo/hypercoagulability*** (*DIC: disseminated intravascular coagulation*)[21]
- ***Thrombo-inflammation*** (*PIC: pulmonary intravascular coagulopathy*)[22,23]
- ***Vaccine-induced immune thrombotic thrombocytopenia*** (VITT)[10,24]

Some authors use the term coagulopathy very broadly to define any type of abnormal hemostasis resulting in either *hypo- or hypercoagulation*.[25] Others apply the same term in a narrower sense to describe only *hypocoagulation*.[17] Due to such ambiguity, it is advisable to either avoid the use of this term or define it clearly before use.

Hypocoagulability results in impaired clot formation leading to a bleeding diathesis. It is classified into:

- *Disorders of primary hemostasis* (when caused by a platelet abnormality),
- *Disorders of secondary hemostasis* (when caused by defects in the extrinsic and/or intrinsic pathway of the coagulation cascade), and
- *Hyperfibrinolysis* (when there is increased clot degradation).[16]

Although clinical features may overlap, typically mucocutaneous bleeding (e.g., epistaxis, petechiae, gastrointestinal bleeding) is associated with disorders of primary hemostasis, while bleeding into potential spaces (e.g., hemarthrosis, intramuscular bleeding) is characteristic of disorders of secondary hemostasis.

Hypercoagulability **(thrombosis)** is categorized by the type of blood vessel affected and its anatomical location: [26,27]

- *Arterial thrombosis* (atherothrombosis) usually follows the erosion of an atherosclerotic plaque leading to formation of platelet-mediated thrombi. Those clots can cause serious ischemic injuries in vital organs. In fact, cardiac ischemia and ischemic cerebrovascular events (strokes) are the most severe clinical manifestations of this process. Ischemia of vital organs can progress slowly (e.g., claudication or stable angina). It can also have an acute onset as seen in cases of cardiovascular infarction or thrombo-embolization (e.g., atrial fibrillation, mechanical valve prostheses).[27]
- *Venous thromboembolism* (VTE) is the third common vascular disease after myocardial infarction and stroke. It is exemplified by the two well-known and intertwined clinical diagnoses: *deep venous thrombosis* (*DVT*) and *pulmonary embolism* (*PE*). The pathomechanism underlying VTE is not well understood, despite recent progress in molecular hematology. Yet, it appears that combination of stasis and hypercoagulability, with some contribution of endothelial damage, is a factor responsible for VTE. Chronic inflammation, hyperlipidemia, and autoimmunity seem to contribute to VTE, but to a lesser degree than in atherothrombosis.[27]

Macrovascular thrombosis is thrombosis of large vessels. In the past, macrothrombosis was considered to be the most important form of thrombosis due to its well-known clinical significance and huge economic impact of the morbidity it caused.[19] However, with the advancements in the fields of molecular pathomorphology and pathophysiology, attention has shifted to microthrombosis.[28]

Microvascular thrombosis refers to thrombosis occurring within the microcirculation, i.e., in terminal arterioles, metarterioles, capillaries, and venules. While those microvessels are small in diameter, the microcirculation actually represents the largest proportion of the surface area of the vasculature. The importance of microthrombosis was initially underappreciated. However, with time it has been discovered that it plays a crucial role in a number of significant clinical diseases such as thrombotic thrombocytopenic purpura, sepsis, disseminated intravascular coagulation, antiphospholipid syndrome, and most recently in COVID-19 disease and in COVID-19 vaccine side effects.[29-31] Microvascular thrombosis is probably an evolutionary adaptive response, which can become maladaptive under certain circumstances. Its role was likely to prevent pathogens present in the tissues from reaching the systemic circulation via the capillaries.[32] That defensive mechanism works well most of the time, but occasionally it can become destructive.

Disseminated intravascular coagulation (*DIC*), also called consumption coagulopathy and defibrination syndrome, is a systemic ***hypo/hypercoagulability*** state with the potential for causing both thrombosis and hemorrhage. It can present as an acute, life-threatening emergency or a chronic, subclinical process, depending on the degree and tempo of the process and the contribution of morbidities from the underlying cause.[21]

Thrombo-inflammation (*PIC: pulmonary intravascular coagulopathy*) is a peculiar form of inflammation-mediated microhypercoagulability, which occurs in lungs of patients with COVID-19 pneumonia. That process is distinct from classic DIC.[22,23,33,34] The PIC concept has been propounded by McGonagle et al., who described it as a type of the macrophage activation syndrome (MAS) associated with diffuse pulmonary immunothrombosis occurring during severe COVID-19 disease.[23] Despite similarities to MAS, PIC has many unusual features setting it apart from the classic MAS. PIC can unmask the subclinical cardiovascular disease that can be present in older individuals. Such unmasking can result in severe cardiovascular compromise. This mechanism explains the increased cardiovascular mortality observed in older patients with severe COVID-19.

Vaccine-induced immune thrombotic thrombocytopenia (*VITT*) is said to be an extremely rare hemostatic disorder that can occur after vaccination with COVID-19 adenovector vaccines.[1,10,24] The adenovector appears to stimulate autoantibodies to platelet factor 4 (PF4), which activate platelets and causes thrombosis in the absence of heparin. That process is very similar to spontaneous or autoimmune heparin-induced thrombocytopenia (HIT). Patients affected by VITT typically present with thrombosis, especially with cerebral vein thrombosis (CVT). Isolated thrombocytopenia (without thrombosis) has been reported as well.

PIC and VITT are the two hemostasis disorders which are specifically associated with COVID-19 infection and vaccination. However, all forms of the nonspecific abnormal hemostasis described above can certainly occur in patients with COVID-19.[35-36] All of them can cause substantial morbidity and mortality. Moreover, the SARS-CoV-2 spike protein has been clearly implicated in the etiology of those hemostatic disorders.[37,38]

The mechanism of action of COVID vaccines relies on the introduction of the SARS-CoV-2 spike protein into the healthy body to produce protective immunity.[39] It is therefore unsurprising that the concerns about the accidental induction of abnormal hemostasis by all types of COVID-19 vaccines have been raised by laypeople and scientists alike.[40,41] What is surprising is that those legitimate concerns have been arrogantly dismissed by members of medical officialdom.[42] The anointed experts have reached the "consensus" that any risk of vaccine-associated hemostasis disorders is absolutely acceptable.[24] It is because, according to them, thrombosis is estimated to occur at least 100-fold more often in patients with severe COVID-19 who were not vaccinated than in patients with COVID-19 who were. Furthermore, they posit that total morbidity and mortality associated with COVID-19 remain significantly higher in nonvaccinated patients than in those vaccinated. Those claims are sufficient in their opinion to disregard any risks of vaccines. Surprisingly to them, the public does not concur. And apparently no amount of "fact-checking" can persuade members of public who are skeptical of vaccines to change their minds.[43]

Basics of Normal and Abnormal Hemostasis

To fully understand the devastating impact of the hemostatic adverse effect of vaccines, one must be conversant in the basic aspects of physiology and pathophysiology of hemostasis. Those are difficult matters for everybody. Even physicians who are not trained as hematologists may struggle with comprehension of the intricate mechanisms involved in hemostasis. The following are the most rudimentary basics of this process. To understand it better, interested readers are encouraged to peruse the references cited here.[14,15,44-46]

Normal hemostasis (Figure 1) is the process of blood clot formation at the site of vessel injury aimed at preventing blood loss. Hemostasis occurs when a blood vessel wall is disrupted. It is a complex phenomenon, which is fast, localized, and well regulated. Abnormal bleeding or thrombosis occurs when any element of this cycle is missing or impaired.

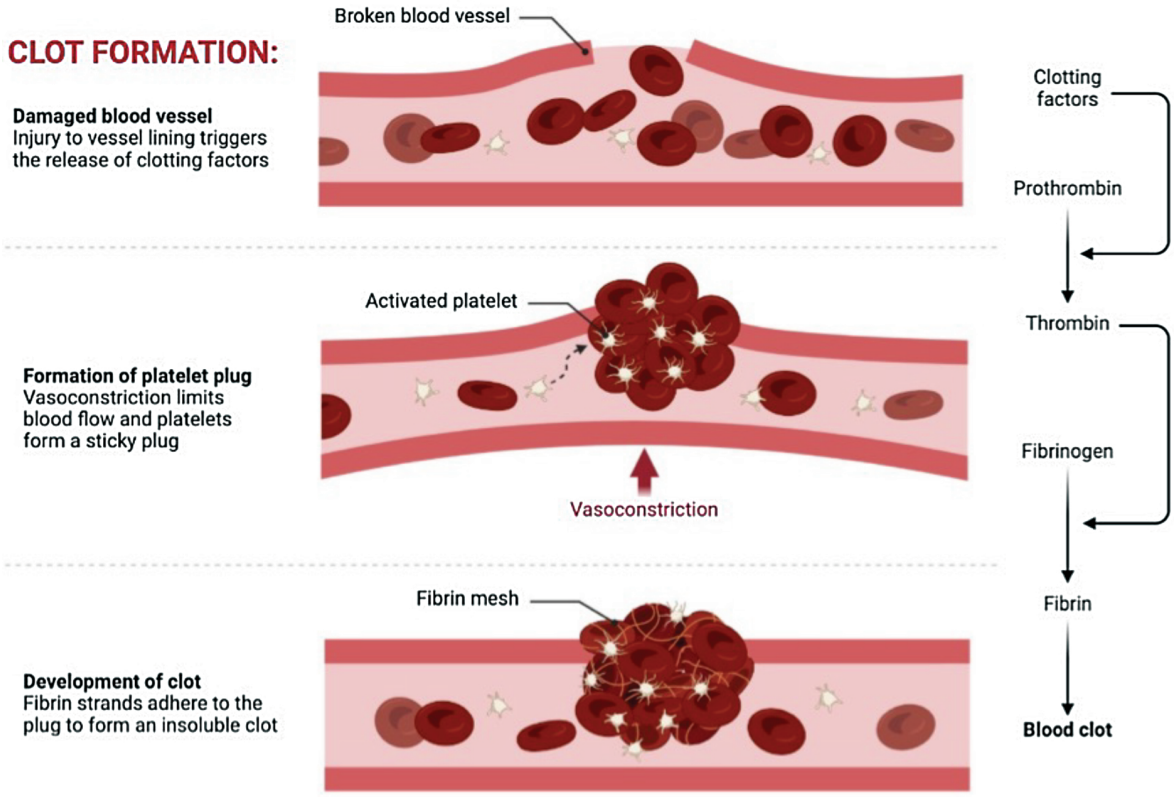

Figure 1. Normal Hemostasis: Focus on Clot Formation

The process of hemostasis involves interlinked sequences of coagulation and fibrinolysis. A clot is initially formed immediately to stop bleeding. This is followed later by clot lysis and tissue remodeling. Consequently, the abnormal bleeding can be caused either by defective clot production or by its increased lysis. The opposite abnormality, thrombosis, occurs when there is an enhanced clot production or decreased lysis of the clot. The following phases are part of normal hemostasis:

- ***Vasoconstriction:*** A vascular spasm occurs as the first response of the vessel to injury. The smooth muscles causing the spasm are controlled by vascular endothelium, which releases intravascular signals to initiate contractions.
- ***Platelet plugging:*** Platelets are activated (Figure 2) at the site of vascular injury. This leads to formation of a platelet plug, which serves as both a mechanical barrier and a molecular facilitator of initial hemostatic response. That response includes the exposure of procoagulant phospholipids on the platelet surface and the assembly of components of the clotting cascade.

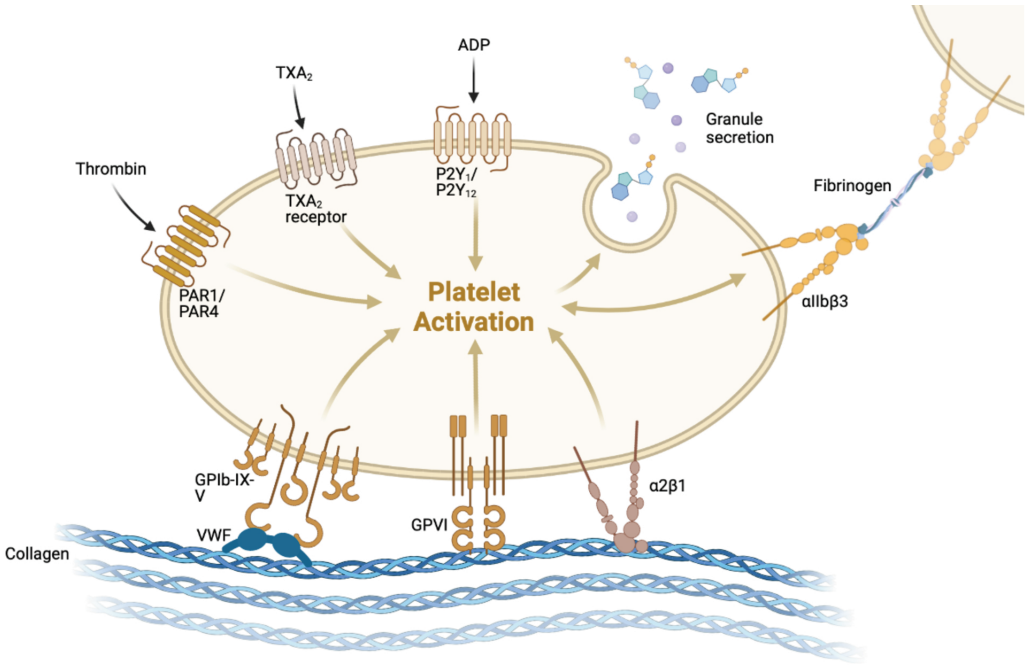

Figure 2. Platelet Activation. Under conditions of pressure shear, von Willebrand factor **(VWF)** forms a bridge between exposed **Collagen** and the platelet glycoprotein **GPIb-IX-V** receptor complex on the platelet membrane (*left bottom side of the figure*). Exposed collagen also binds directly to platelet **GPVI** receptors (*middle bottom part of the figure*). Activated during this process, platelets change shape and release the contents of their granules (*right upper side of the figure*). Those granules contain **ADP, TXA_2** and **thrombin**, which interreact with the shown receptors **P2Y, TXA_2, PAR1/ PAR4** (*Upper part of the Figure*). In addition, activation is triggered by binding of **fibrinogen** to integrin **αIIbβ3** and **collagen** to integrin **α2β1** as shown.

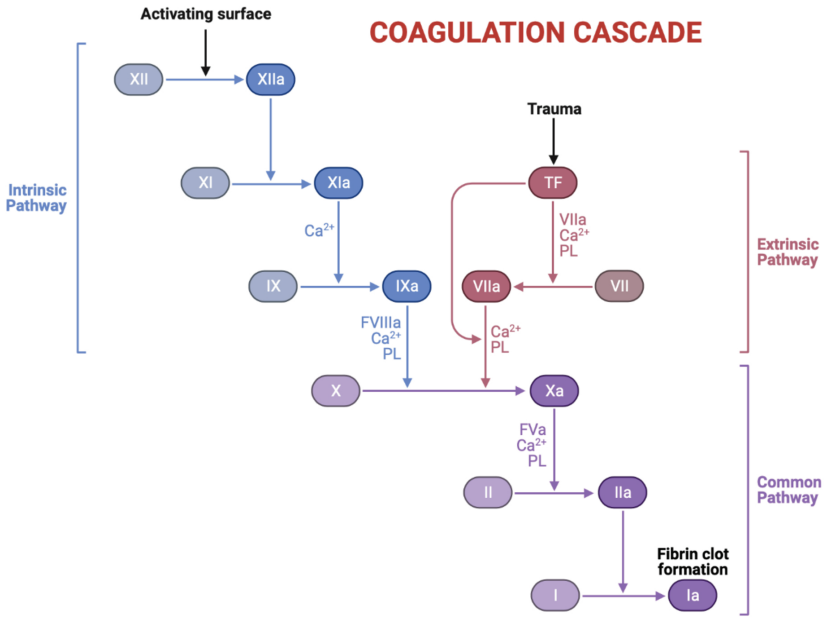

Figure 3. Coagulation Cascade

- ***Fibrin deposition:*** The clotting cascade is initiated (Figure 3). The cascade involves sequential activation of proenzymes or zymogens (inactive precursor proteins) into active enzymes. This process has been called "a cascade" since it is characterized by stepwise response amplification. In general, the term "cascade" describes a bit-by-bit process whereby something (e.g., information) is successively passed on, typically with increasing speed. Primary physiologic events initiating clotting involve the exposure of tissue factor at the wound site, its interaction with factor VIIa and the subsequent generation of activated factor X. The components of the intrinsic pathway (i.e., factors VIII, IX, XI) are responsible for amplification of this process.
- ***Termination:*** This phase involves antithrombin, tissue factor pathway inhibitor, and the protein C pathway. This step is critical in mediating the proper extent of clot formation.
- ***Fibrinolysis:*** To restore the patency of the vessel that was narrowed by the plug, plasminogen and tissue plasminogen activator (tPA) bind to fibrin, and tPA converts plasminogen to active, proteolytic plasmin, which cleaves fibrin, fibrinogen, and a variety of plasma proteins and clotting factors. The plasminogen/plasminogen-activator system is another complex sequence, which parallels the coagulation cascade.
- ***Constant immune system involvement:*** This is technically not a step but a continuous process, which has been added recently as a part of the hemostasis process to acknowledge the role of immune system in its control. *This is very significant considering the fact that vaccines act via modification of the immune system*.

Abnormal hemostasis resulting in thrombosis is explained by the elegant theory known as Virchow's triad.[47,48] According to this concept, thrombosis occurs due to combination of vascular endothelial injury, stasis (slowed blood flow), and hypercoagulability caused by alterations in constituents of the blood.

Recent research showed that the dramatic microthrombosis and macrothrombosis seen in severe COVID-19 infection is still fully explained by the Virchow's triad model.[49] Most importantly, a critical component of the triad, the endothelial injury, has been showed to be caused by the spike protein through activation of the alternative complement pathway.[50] *Therefore, once again the COVID-19 vaccines are at least theoretically capable of producing severe thrombotic states.* In such a context, the unwillingness of officialdom to acknowledge those obvious facts is striking but unfortunately not unexpected, as discussed below.

Tyranny of the Politicized Narratives Imperils the Search for Truth

Previous editorials have discussed the politicization of science and medicine as well as the emergence of agenda-driven narratives that replaced the unbiased reporting of objective facts.[4,5] Science and medicine must remain impartial for the greater common good.[51,52] Politicization of those fields perverts the role of the top medical and scientific experts. Instead of serving as objective qualified arbiters in the scientific disputes involving contentious matters, corrupted experts aid and abet their political leaders in the execution of unsavory, hidden-agenda-driven schemes: a phenomenon that has been recently dubbed "Orwellian Science."[53]

However, for a time being—although it is not certain how long this will last—we are not yet living in the perfect Orwellian world. There is still the internet, which preserves the free flow of information, even though officialdom's censorship is encroaching rapidly into the market of ideas under the pretense of fighting "misinformation." Moreover, the majority of the people, even those without scientific training, have enough analytical skills to detect the obvious politically motivated deception.

Public trust in the previously highly respected scientific institutions and affiliated experts has been eroding in recent decades.[54] The unreasonable policies promulgated by those experts during the COVID-19 pandemic have delivered the final blow to their already crumbling trustworthiness and prestige.[55,56] This twilight of the scientific gods created a vacuum that has to be filled by new authority figures.[57] Disillusioned with the old scientific establishment, the public started to yearn for a new type of medical expert who would respect the concept of personal freedom.[58] This created an unprecedented demand for views on scientific and medical topics that would challenge the official narrative. This demand was fulfilled surprisingly fast. The large domain of scientific and medical dissidence blossomed virtually overnight from the small seed of the hibernating medical freedom movement.[57] This miracle growth occurred despite officialdom's aggressive censorship and persecution of medical dissidents. After being banned from the legacy platforms such as YouTube or Twitter, medical dissenters migrated to alternative digital outlets and were able to maintain their relevance.

These developments are encouraging; however, it would be naïve to assume that anyone who identifies as a scientific dissident and questions the official narratives is an honest, impartial, and well-qualified person. There are unfortunately many bad actors in the midst of the legitimate scientific dissidents. Some such unsavory characters push their own politically motivated narratives. The noisy battle of competing political narratives further muddies the water and imperils the

quest for objective truth. And knowing the truth is essential for successful clinical care.

The harsh realities of the polarized scientific landscape must be well understood by patients and clinicians who are eager to know the objective facts related to the adverse effects of the COVID-19 vaccines, including their negative impact on hemostasis.

Power Asymmetry

The politicized narrative is not the only obstacle preventing the objective examination of crucial medical problems. One of the toughest is the huge asymmetry between the capacities and powers of scientists who serve officialdom compared to the dissident researchers.[6, p70] Lack of essential resources, including access to modern research equipment, technical staff, and advice from officially funded consultants, precludes the dissident researchers from performing the complex research projects that officialdom scientists can easily conduct. The role of the scientific dissidents is limited to critique of the studies performed by officialdom researchers and to the scientific education of the public. Those are naturally very valuable tasks. However, those activities cannot provide direct answers to crucial questions such as the nature of the impact of the COVID-19 vaccines on hemostasis.

In addition to their limited capacity to perform meaningful scientific inquiry, the dissident scientists and physicians are very vulnerable to the repressions that are being unleashed on them by the political powers. Under the guise of combating "misinformation," officialdom has implemented a vast array of aggressive strategies aimed at silencing scientific and medical dissenters.[59-63]

Officialdom is keenly aware of the threat posed by successful questioning of the official narratives by the dissident researchers. Therefore, nonconforming scientists and physicians are targeted by malicious lawsuits, which can impose huge monetary penalties. They are subjected to administrative actions by their licensing and certifying boards, which can result in revocation of their specialty certifications and medical licenses, depriving them of the ability to work in their profession.

Recently, in California the bill AB2098 has been signed into law because of lobbying by the "misinformation busters"[62,64] (Figure 4). That unprecedented bill puts unconstitutional restrictions on free speech of physicians by penalizing them for dissemination of information about COVID-19 that officialdom deems false. And all of this is just the tip of the iceberg of repressions and harassments that the dissenting physicians or scientists can face daily while having no means of recourse.

Researching While in Ideological Fog and Under Political Fire

Under these circumstances, dissident physician-scientists who have very limited research means are forced to study the perplexing hemostatic effects of COVID-19 vaccines with the following less than ideal methods:

- Formulating theory-driven hypotheses about COVID-19 vaccine and hemostasis by translating lessons from COVID infections or from direct vaccine-related hypotheses;
- Scrutiny of the official studies focused on COVID-19 vaccine and hemostasis;
- Examining the significance of the negative evidence related to COVID-19 vaccine and hemostasis;

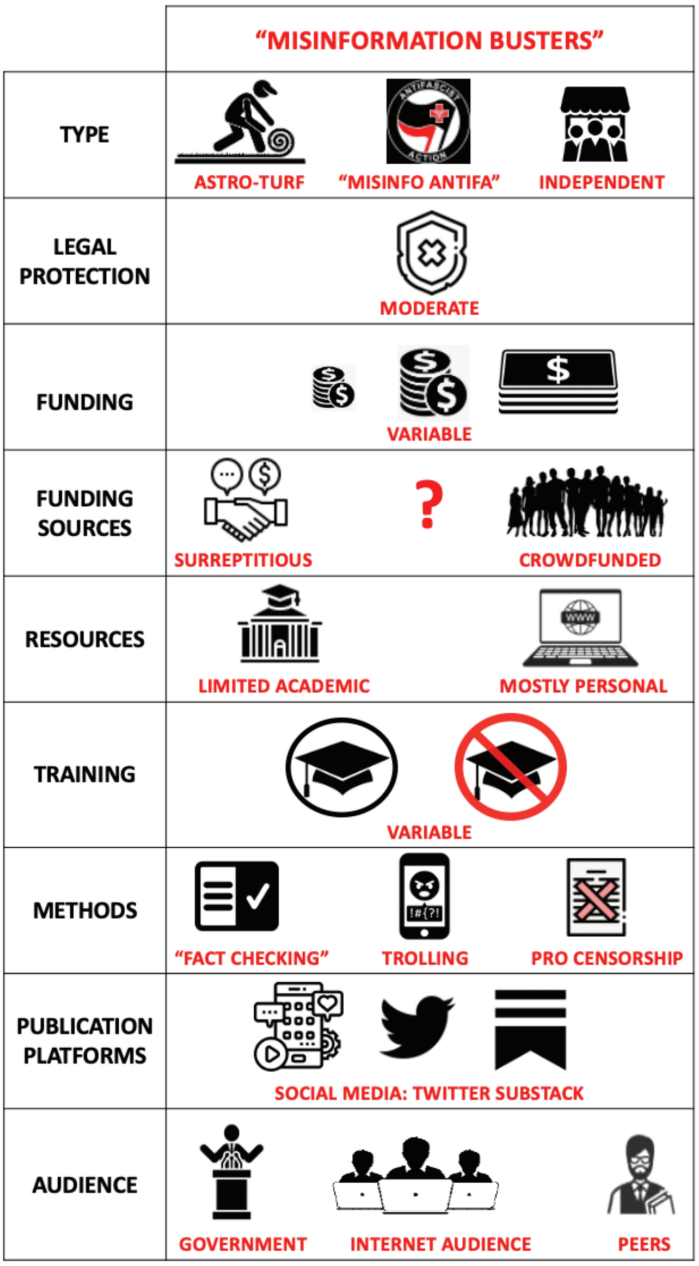

Figure 4. Characteristics of "Misinformation Busters"

- Exploring the vaccine manufacturers' documentation filed with regulatory agencies;
- Analysis of the pharmacovigilance data; and
- Investigation of anecdotal data from mainstream and alternative publication media.

All the simplistic paradigms listed here are conjectural. They cannot replace formal, carefully designed research studies. Yet, they may be sufficiently useful to perform basic risk/benefit analysis of the use of the COVID-19 vaccines in the context of their very likely negative impact on hemostasis. Having the results of a risk/benefit analysis that is as objective as possible under the circumstances can assist patients in making an informed decision about the use or avoidance of the novel COVID-19 vaccines.

Theory-Driven Hypotheses

Theory-driven conclusions and hypotheses are considered to be low-tier evidence in the hierarchy of evidence-based

medicine.[65] Theory-driven *conclusions* can indeed yield variable results due to their purely conjectural nature. However, theory-driven *hypotheses* have been proven to be useful in formulation of the initial hypotheses that may be subsequently tested by a variety of experimental studies. Understandably, this method is one of the most frequently used approaches by the dissident scientists, due to its practicality. The following are the most common theory-driven hypotheses related to impact of COVID-19 vaccines on hemostasis.

Translation of Lessons from COVID Infections

SARS-CoV-2 spike protein as common denominator: The SARS-CoV-2 spike protein has been implicated in the etiology of hemostatic disorders occurring during severe COVID-19 infection.[37,38,66] Endothelial injury, which is a part of Virchow's triad, has been showed to be caused by the spike protein through activation of the alternative complement pathway.[50] The mechanism of actions of COVID vaccines relies upon the introduction of the SARS-CoV-2 spike protein into the healthy body to produce protective immunity. Therefore, the COVID-19 vaccines are at least theoretically capable of producing severe thrombotic states.[40,41]

Overarching Role of Microthrombosis: Microthrombosis has been frequently proposed as the main pathology and main cause of death in COVID-19.[67] However, many researchers argued that COVID-19-related micro- and macrothrombosis is triggered by the whole virus, not the spike protein.[67] Hence, it was implied that since vaccine produces only the spike protein, it will be safe since spike protein is just an innocent chemical compound without the virus and it cannot cause the thrombotic cascade on its own. However, this dogma has been challenged, first indirectly by McFadyen et al. and subsequently by other researchers, who demonstrated that spike protein can in fact cause microthrombosis.[37,50,68,69] Therefore, microthrombosis remains a viable overarching hypothesis that can connect pathologies present in COVID-19 infection, adverse reaction to vaccines, and long COVID-19.

Direct Vaccine-related Hypotheses

Platelet factor 4 (PF4) activation by adenovirus vector: This is a widely accepted hypothesis explaining the etiology of vaccine-induced immune thrombotic thrombocytopenia (VITT). According to this model, the adenoviral vaccines appear to stimulate autoantibodies to platelet factor 4 (PF4), which activates platelets and causes thrombosis in the absence of heparin, similar to spontaneous or autoimmune heparin-induced thrombocytopenia (HIT).[10,24]

mRNA vaccine-related immune thrombocytopenia: Senef et al. have discussed the possibility that in addition to adenoviruses vectors, the mRNA vaccines can induce abnormal hemostasis via the mechanism similar to the one described in VITT.[70] Those authors cited a series of case studies describing such a clinical presentation in patients who received mRNA vaccines.

Metaflammation hypothesis: The possibility that a process known as metaflammation can play a role in the etiology of COVID-19 vaccine-induced abnormal hemostasis is a brand new speculative hypothesis. Beyond the cursory review here, readers are encouraged to consult the literature related to general concept of metaflammation and its role in COVID-19 infection.[71-74] Currently, there is no extensive literature dealing with this specific vaccine-abnormal hemostasis theory, but research continues. Metaflammation is a portmanteau of metabolism and inflammation. It is still a rather poorly understood state. It occurs in conditions associated with metabolic dysfunction, such as obesity and insulin resistance. It can be induced also by early stages of viral infection and by certain medication, hence, possibly also by vaccines. While it is sometimes referred to as a low-grade inflammatory state, it differs significantly from classic acute inflammation. It is much harder to detect metaflammation as compared to classic inflammation. Hence its presence may be overlooked. However, despite its stealthy nature, metaflammation can still cause thrombosis, perhaps through a mechanism similar to immunothrombosis.[75] The combination of low detectability and thrombogenic capabilities makes the metaflammation hypothesis into an attractive theory, which could explain some enigmatic cases of clot formation after COVID-19 vaccination. However, until proven by empiric studies this concept remains purely speculative.

Scrutiny of the Official Studies Focused on COVID-19 Vaccine and Hemostasis

Unable to perform their own original studies, dissident researchers are frequently focused on scrutinizing the research papers published by officialdom scientists. They assess the quality of the research methods and validity and sincerity of their conclusions. Such criticism is invaluable since it allows them to expose the agenda-driven biases and dishonesty of the mainstream scientists. Mathew Crawford has recently observed that since the onset of the COVID-19 pandemic there is an increase in published studies in which the politically correct authors' conclusion does not match the results of their own data analyses.[53] He suggests that those authors use this incongruent approach to avoid being censored and retaliated against by those academic activists who concentrate only on reading the conclusion section of the studies. An alternative explanation of this phenomenon is that some of those authors are so ideologically biased that they actually draw conclusions that are inconsistent with reality but fit well into their preferred political narrative.

A comprehensive search of the literature for the papers dealing with the potential hemostatic complication of COVID-19 vaccines has confirmed the above pattern of explicit cognitive dissonance by the vast majority of authors.[12,24,40-42,76-79] The most shocking example of a strong political bias is in the "consensus paper" whose authors concluded, in defiance of common sense and logic, that the risks of vaccine-associated hemostasis disorders is absolutely acceptable.[24] However, in virtually all papers on this subject there was a similar, albeit less explicit, hiatus between the inconvenient data and their ideologically palatable interpretation. Almost all authors included standard statements that "vaccines are safe and effective" and that the data they present should not be interpreted as a contradiction of this dogma.

Examination of the Negative Evidence Related to COVID-19 Vaccine and Hemostasis

It is remarkable that the potential link between COVID-19 vaccines and abnormal hemostasis has been ignored by officialdom. This indifference continues despite its immense pathophysiological and clinical significance, augmented by the serious concerns of the public, who keep reporting incidents of abnormal hemostasis after receiving COVID-19 vaccines.

The sole exception to this rule is VITT. However, even in those rare instances the official actions were aimed at pacifying the public concerns rather than at thorough investigation of the dangerous side effects of the vaccines.[24] This regrettable disinterest in exploring a possible association between COVID-19 vaccines and abnormal hemostasis is reflected both by the inferior quality and even more striking scarce quantity of scientific publications focused on these very concerning matters.

Figure 5 demonstrates clearly that we are dealing here with the classic negative-evidence scenario. That figure presents the graphic results generated by the National Library of Medicine TimeLine Tool. This program was used for the side-by-side comparisons of the number of publications in the year 2022 (until Oct 20) related to "COVID vaccine and thrombosis" versus "COVID-19 and thrombosis." The vaccine-related publications represent a small fraction (9 percent) of the publications dedicated to studies of abnormal hemostasis in COVID-19 in 2022. This is truly ironic, since we were told by officialdom that in that year, the number of cases of severe COVID-19 decreased, allegedly thanks to the robust vaccination campaign enforced by the mandates. At the same time, we know from tacit observation that the incidence of vaccine-related thromboses has increased. Obviously, officialdom is much more interested in studying the decreasing phenomenon than in paying attention to the problem that is on the rise.

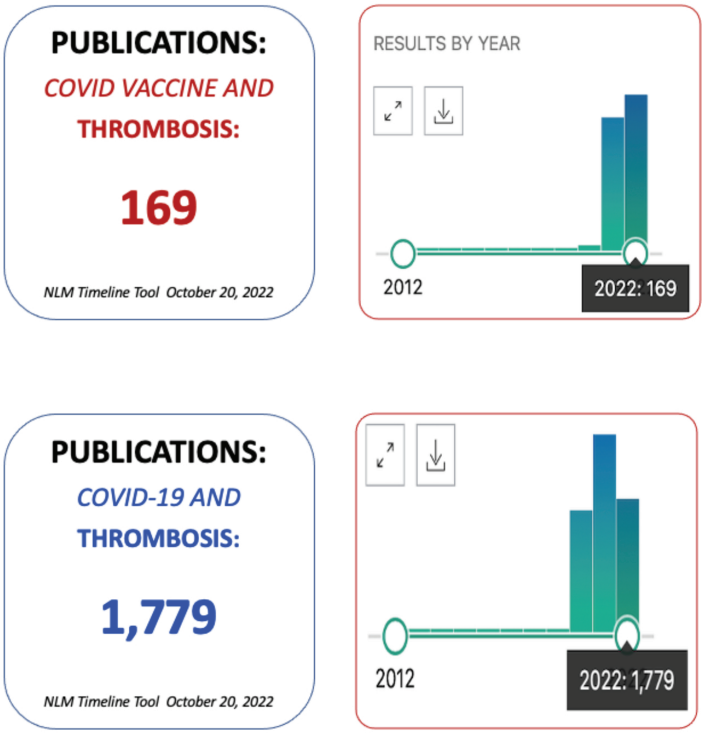

Figure 5. Number of Publications Related to "COVID Vaccine and Thrombosis" compared to "COVID-19 and Thrombosis." Source: National Library of Medicine Timeline Tool, run on Oct 20, 2022.

Review of the Vaccine Manufacturers' Documentation Filed with Regulatory Agencies

Vaccine manufactures have the obligation under the law to file detailed documentation with the regulatory agencies, which is supposed to contain the results of animal and human safety studies.[5] Theoretically, such documentation may serve as a source of valuable data related to vaccine side effects. However, those data are truly valuable only if the manufacturer has presented them with honestly and openness.

Regulatory agencies including the Food and Drug Administration (FDA) and the Centers for Disease Control and Prevention (CDC) have established very strict requirements and protocols for the development, testing, and approval of vaccines. Those standards are available online.[80-81] Moreover, the FDA maintains the summary page of its approved COVID-19 vaccines, which contains links to the pertinent documentation.[82] The FDA briefing documents containing the summaries of the safety studies for the Pfizer and Moderna COVID-19 vaccines are available on that agency's website.[83-84]

Concerning the incidence of DVT as a side effect of the Pfizer vaccine, the data contained in their briefing materials are very reassuring. There was no statistical difference between subjects receiving the vaccine and the control group up to one month after vaccination.[83]

The question however remains: could those data be trusted?

Pharmacovigilance Databases

Large pharmacovigilance database such as the Vaccine Adverse Event Reporting System (VAERS) are very useful to independent researchers. The data collected by such databases are typically available without restriction to any member of the public. Therefore, dissident scientists can easily analyze them for presence of a safety signal.[85] In the past such databases, including VAERS, were considered to be reliable and useful, also by officialdom scientists, as is evidenced by past publications.[86-88]

However, after the COVID-19 pandemic and introduction of the controversial vaccines, officialdom has suddenly changed its mind regarding the reliability of those pharmacovigilance systems. This sudden change of heart is exemplified by the publications in which mainstream scientists started to accuse "antivaccine activists" of scaring the public by the misuse of databases like VAERS.[89] Suddenly, the medical mainstream has deemed those databases to be very unreliable and flooded with unverified misleading reports. Apparently, officialdom was displeased by independent studies claiming that the VAERS data contain multiple reports of thrombosis in patients receiving COVID-19 vaccines.[7]

Consistency was never a hallmark of officialdom. The very same mainstream scientists who were very critical of VAERS have turned into VAERS enthusiasts when the data from it show results consistent with their favored narrative. This is illustrated by the VAERS-based study performed by Welsh et al.[12] in which the danger of vaccines-related thrombotic event was found to be negligible. Yet, this renewed appreciation of VAERS-like databases was soon followed by rekindled skepticism after European researchers reported that analysis of data contained in the global database VigiBase showed that all types of COVID vaccines are clearly associated with thrombosis.[77,79]

Review of the Anecdotal Data

The value of anecdotes is underappreciated by modern algorithm-based scientific paradigms. This is unfortunate since it is well known that information derived from anecdotes, when used properly, has led to several important scientific discoveries.[90] The key to proper use of data derived from

anecdotes is to understand their context and limitations. Like any type of data, anecdotal evidence can be misused.

There is a plethora of anecdotal evidence around us pertaining to the correlation between COVID-19 vaccines and hemostasis disorders, of variable relevance. There are reports about hemostasis problems occurring after COVID-19 vaccines from people whom we know well and trust. There are also numerous posts of that nature on social media. Such tacit data are less reliable, but their frequency and persistence indicate that they likely reflect a real phenomenon. Finally, there are recurrent stories in the alternative news outlets about unusually large blood clots that have been found by morticians during embalming.[91-93] Those sensational accounts are very popular with the public and are reposted virally throughout the internet. Their veracity and significance are difficult to ascertain from the objective vantage point. However, those articles are also very popular with officialdom's "fact-checkers," who debunk them with dedication and zeal.[94]

The evidentiary value of each anecdote varies. However, the following is easy to conclude about the pattern of their appearance. There is clear preponderance and pervasiveness of anecdotal data suggesting that COVID-19 vaccines are associated with distinct hemostatic abnormalities. This signal is sufficiently strong to provide impetus for further studies of those phenomena and also for warning the public about those perils of COVID-19 vaccinations.

Conclusions

This fact-finding process has revealed that serious disorders of hemostasis, including macro- and microthrombosis, could be induced by the mRNA vaccines. Therefore, contrary to the official narrative, such adverse events are not limited to adenovector vaccines. Moreover, there are well-recognized theoretical mechanisms that explain why those types of dangerous side effects can be caused by mRNA vaccines. Additionally, there is compelling negative evidence that mainstream medicine is actively covering up knowledge about those adverse reactions and their mechanisms, to the grave detriment of patients, who are being injured and who are denied the information necessary to give proper informed consent.

We live in very troubled times, an era of the rampant politicization of medicine and science, when political narratives are replacing objective truth. The organizations that were established to protect the American public are being used to oppress and deceive us.

We can find consolation in the knowledge that there is a group of dedicated dissident researchers, laboring relentlessly in the thick ideological fog and under enemy fire.

We must continue to advocate for our patients, against all the odds, inspired by the words of Winston Churchill: *"We shall not fail or falter; we shall not weaken or tire. Neither the sudden shock of battle, nor the long-drawn trials of vigilance and exertion will wear us down.* ***Give us the tools, and we will finish the job.***"

Jane M. Orient, M.D., is a practicing general internist and serves as executive director of AAPS and managing editor of the Journal. Contact: jane@aapsonline.org.

REFERENCES

1. Centers for Disease Control and Prevention. Safety of COVID-19 Vaccines; updated Oct 31, 2022. Available at: https://www.cdc.gov/coronavirus/2019-ncov/vaccines/safety/safety-of-vaccines.html. Accessed Nov 4, 2022.
2. Edwards KM, Orenstein W. COVID-19: Vaccines. UpToDate; Oct 17, 2022. Available at: https://www.uptodate.com/contents/covid-19-vaccines. Accessed Oct 22, 2022.
3. Orient JM. Negative evidence: antibody dependent enhancement. *J Am Phys Surg* 2022;27(1):2-6. Available at: https://www.jpands.org/vol27no1/orient.pdf. Accessed Apr 16, 2022.
4. Orient JM. Negative evidence: postmortem examinations of post-COVID-19 vaccine fatalities. *J Am Phys Surg* 2022;27(2):35-41. Available at: https://www.jpands.org/vol27no2/orient.pdf. Accessed Jul 15, 2022.
5. Orient JM. Negative evidence: COVID-19 vaccines and fertility. *J Am Phys Surg* 2022;27(3):69-77. Available at: https://www.jpands.org/vol27no3/orient.pdf. Accessed Oct 22, 2022.
6. Moore A. More embalmers report bizarre blood clots amid COVID vax campaign. *Clark County Today*; Sep 7, 2022. Available at: https://www.clarkcountytoday.com/news/more-embalmers-report-bizarre-blood-clots-amid-covid-vax-campaign/. Accessed Oct 23, 2022.
7. Redshaw M. April 16th VAERS data show reports of blood clotting. Children's Health Defense California Chapter; Apr 27, 2021. Available at: https://ca.childrenshealthdefense.org/home-page/april-16th-vaers-data-show-reports-of-blood-clotting/. Accessed Oct 23, 2022.
8. Funke D. Fact check: 1 million COVID-19 vaccine adverse events are unverified. *USA Today*, Jan 6, 2022. Available at: https://www.usatoday.com/story/news/factcheck/2022/01/05/fact-check-1-million-covid-19-vaccine-adverse-events-unverified/9103381002/. Accessed Oct 23, 2022.
9. PBS. Why would a COVID vaccine cause rare blood clots? Researchers have found clues. *PBS NewsHour*; Apr 14, 2021. Available at: https://www.pbs.org/newshour/health/why-would-a-covid-vaccine-cause-rare-blood-clots-researchers-have-found-clues. Accessed Oct 23, 2022.
10. Greinacher A, Thiele T, Warkentin TE, et al. Thrombotic thrombocytopenia after ChAdOx1 nCov-19 vaccination. *N Engl J Med* 2021;384(22):2092-2101. doi:10.1056/NEJMOA2104840.
11. Schultz NH, Sørvoll IH, Michelsen AE, et al. Thrombosis and thrombocytopenia after ChAdOx1 nCoV-19 vaccination. *N Engl J Med* 2021;384(22):2124-2130. doi:10.1056/NEJMOA2104882.
12. Welsh KJ, Baumblatt J, Chege W, Goud R, Nair N. Thrombocytopenia including immune thrombocytopenia after receipt of mRNA COVID-19 vaccines reported to the Vaccine Adverse Event Reporting System (VAERS). *Vaccine* 2021;39(25):3329. doi:10.1016/J.VACCINE.2021.04.054.
13. Ahmed W, Vidal-Alaball J, Vilaseca JM. A social network analysis of Twitter data related to blood clots and vaccines. *Int J Environ Res Public Health* 2022;19(8). doi:10.3390/IJERPH19084584.
14. Bergentz SE. Disorders of hemostasis and thrombosis. In: Pyeritz RE, ed. *Emery and Rimoin' s Principles and Practice of Medical Genetics and Genomics*. Vol 32. 7th ed. Academic Press; 2023:173-211. doi:10.1016/B978-0-12-812534-2.00003-5.
15. Kaushansky K, Levi M. *Williams Hematology: Hemostasis and Thrombosis*. 1st ed. McGraw Hill; 2017.
16. Ma A. Approach to the adult with a suspected bleeding disorder. UpToDate; September 2022. Available at: https://www.uptodate.com/contents/approach-to-the-adult-with-a-suspected-bleeding-disorder. Accessed Oct 22, 2022.
17. Hunt BJ. Bleeding and coagulopathies in critical care. *N Engl J Med* 2014;370:847-859. doi:10.1056/NEJMRA1208626/SUPPL_FILE/NEJMRA1208626_DISCLOSURES.PDF.
18. Heit JA. Thrombophilia: common questions on laboratory assessment and management. *Hematology Am Soc Hematol Educ Program* 2007:127-135. doi:10.1182/ASHEDUCATION-2007.1.127.
19. Rumbaut RE, Thiagarajan P. Arterial, venous, and microvascular hemostasis/thrombosis. In: Rumbault R, ed. *Platelet-Vessel Wall Interactions in Hemostasis and Thrombosis*. Morgan & Claypool Life Sciences; 2010. Available at: https://www.ncbi.nlm.nih.gov/books/NBK53453/. Accessed Oct 25, 2022.
20. Bray MA, Sartain SE, Gollamudi J, Rumbaut RE. Microvascular thrombosis: experimental and clinical implications. *Transl Res* 2020;225:105. doi:10.1016/J.TRSL.2020.05.006.
21. Levi M. Pathogenesis and diagnosis of disseminated intravascular coagulation. *Int J Lab Hematol* 2018;40 Suppl 1:15-20. doi:10.1111/IJLH.12830.
22. Connors JM, Levy JH. Thromboinflammation and the hypercoagulability of COVID-19. *J Thromb Haemost* 2020;18(7):1559-1561. doi:10.1111/JTH.14849.
23. McGonagle D, O'Donnell JS, Sharif K, Emery P, Bridgewood C. Immune mechanisms of pulmonary intravascular coagulopathy in COVID-19 pneumonia. *Lancet Rheumatol* 2020;2(7):e437. doi:10.1016/S2665-9913(20)30121-1.
24. Elalamy I, Gerotziafas G, Alamowitch S, et al. SARS-CoV-2 Vaccine and thrombosis: an expert consensus on vaccine-induced immune thrombotic thrombocytopenia. *Thromb Haemost* 2021;121(8):982. doi:10.1055/A-1499-0119.

25. Vanderwerf JD, Kumar MA. Management of neurologic complications of coagulopathies. In: *Handbook of Clinical Neurology*. Vol 141. Elsevier; 2017:743-764. doi:10.1016/B978-0-444-63599-0.00040-5.
26. Battinelli EM, Freedman JE, Loscalzo J. Thrombosis. In: *Vascular Medicine: A Companion to Braunwald's Heart Disease*. 2nd ed. W.B. Saunders; 2013:133-137. doi:10.1016/B978-1-4377-2930-6.00010-0.
27. Previtali E, Bucciarelli P, Passamonti SM, Martinelli I. Risk factors for venous and arterial thrombosis. *Blood Transfus* 2011;9(2):120. doi:10.2450/2010.0066-10.
28. Kwaan HC. Microvascular thrombosis: a serious and deadly pathologic process in multiple diseases. *Semin Thromb Hemost* 2011;37(8):961-977. doi:10.1055/S-0031-1297375.
29. Rzymski P, Perek B, Flisiak R. Thrombotic thrombocytopenia after COVID-19 vaccination: In search of the underlying mechanism. *Vaccines (Basel)* 2021;9(6). doi:10.3390/VACCINES9060559.
30. Douxfils J, Favresse J, Dogné JM, et al. Hypotheses behind the very rare cases of thrombosis with thrombocytopenia syndrome after SARS-CoV-2 vaccination. *Thromb Res* 2021;203:163-171. doi:10.1016/J.THROMRES.2021.05.010.
31. Islam A, Bashir MS, Joyce K, et al. An update on COVID-19 vaccine induced thrombotic thrombocytopenia syndrome and some management recommendations. *Molecules* 2021;26(16). doi:10.3390/MOLECULES26165004.
32. Dixon B. The role of microvascular thrombosis in sepsis. *Anaesth Intensive Care* 2004;32(5):619-629. doi:10.1177/0310057X0403200502.
33. Wagner DD, Heger LA. Thromboinflammation: from atherosclerosis to COVID-19. *Arterioscler Thromb Vasc Biol* 2022;42(9):1103-1112. doi:10.1161/ATVBAHA.122.317162.
34. Wang Z, Gao X, Miao H, Ma X, Ding R. Understanding COVID-19-associated coagulopathy: from PIC to SIC or DIC. *J Intens Med* 2021;1(1):35-41. doi:10.1016/J.JOINTM.2021.03.002.
35. Gómez-Mesa JE, Galindo-Coral S, Montes MC, Muñoz Martin AJ. Thrombosis and coagulopathy in COVID-19. *Curr Probl Cardiol* 2021;46(3). doi:10.1016/J.CPCARDIOL.2020.100742.
36. Cucker A, Peyvaldi F. COVID-19: Hypercoagulability. UpToDate; Sep 27, 2022. Available at: https://www.uptodate.com/contents/covid-19-hypercoagulability#H954993573. Accessed Oct 23, 2022.
37. Zheng Y, Zhao J, Li J, et al. SARS-CoV-2 spike protein causes blood coagulation and thrombosis by competitive binding to heparan sulfate. *Int J Biol Macromol* 2021;193:1124. doi:10.1016/J.IJBIOMAC.2021.10.112.
38. De Michele M, d'Amati G, Leopizzi M, et al. Evidence of SARS-CoV-2 spike protein on retrieved thrombi from COVID-19 patients. *J Hematol Oncol* 2022;15(1):1-5. doi:10.1186/S13045-022-01329-W/TABLES/1.
39. Mascellino MT, di Timoteo F, de Angelis M, Oliva A. Overview of the main anti-SARS-CoV-2 vaccines: mechanism of action, efficacy and safety. *Infect Drug Resist* 2021;14:3459. doi:10.2147/IDR.S315727.
40. Yamada S, Asakura H. Coagulopathy and fibrinolytic pathophysiology in COVID-19 and SARS-CoV-2 vaccination. *Int J Mol Sci* 2022;23(6). doi:10.3390/IJMS23063338.
41. Iba T, Levy JH. Thrombosis and thrombocytopenia in COVID-19 and after COVID-19 vaccination. *Trends Cardiovasc Med* 2022;32(5):249-256. doi:10.1016/J.TCM.2022.02.008.
42. Elsheikh S, Lip GYH. Editorial commentary: COVID-19 and COVID-19 vaccination: observations on thrombosis and thrombocytopenia. *Trends Cardiovasc Med* 2022;32(5):257. doi:10.1016/J.TCM.2022.03.002.
43. Spencer S. COVID-19 vaccine opponents misrepresent CDC webcast on causes of blood clots. FactCheck.org; Sep 29, 2022. Available at: https://www.factcheck.org/2022/09/scicheck-covid-19-vaccine-opponents-misrepresent-cdc-webcast-on-causes-of-blood-clots/. Accessed Oct 23, 2022.
44. Versteeg HH, Heemskerk JWM, Levi M, Reitsma PH. New fundamentals in hemostasis. *Physiol Rev* 2013;93(1):327-358. doi:10.1152/PHYSREV.00016.2011/ASSET/IMAGES/LARGE/Z9J0011326480007.JPEG.
45. Bonar RA, Lippi G, Favaloro EJ. Overview of hemostasis and thrombosis and contribution of laboratory testing to diagnosis and management of hemostasis and thrombosis disorders. *Methods Mol Biol* 2017;1646:3-27. doi:10.1007/978-1-4939-7196-1_1.
46. Marder V, Aird W, Bennett J, Shulman S, Gilbert W. *Hemostasis and Thrombosis: Basic Principles and Clinical Practice*. 6th ed. Wolters Kluwer, Lippincott Williams & Wilkins; 2012.
47. Bagot CN, Arya R. Virchow and his triad: a question of attribution. *Br J Haematol* 2008;143(2):180-190. doi:10.1111/J.1365-2141.2008.07323.X.
48. Dickson BC. Virchow's triad. *Br J Haematol*. 2009;145(3):433. doi:10.1111/j.1365-2141.2009.07617.x.
49. Mehta JL, Calcaterra G, Bassareo PP. COVID-19, thromboembolic risk, and Virchow's triad: lesson from the past. *Clin Cardiol* 2020;43(12):1362-1367. doi:10.1002/clc.23460.
50. Yu J, Yuan X, Chen H, et al. Direct activation of the alternative complement pathway by SARS-CoV-2 spike proteins is blocked by factor D inhibition. *Blood* 2020;136(18):2080-2089. doi:10.1182/BLOOD.2020008248.
51. Schmid-Petri H, Bienzeisler N, Beseler A. Effects of politicization on the practice of science. *Prog Mol Biol Transl Sci* 2022;188(1):45-63. doi:10.1016/BS.PMBTS.2021.11.005.
52. Mazzuca C, Santarelli M. Making it abstract, making it contestable: politicization at the intersection of political and cognitive science. *Rev Philos Psychol*; Published online May 21, 2022. doi:10.1007/S13164-022-00640-2.
53. Crawford M. The science virus, part I: Orwellian science. *Rounding the Earth*; Jan 7, 2022. Available at : https://roundingtheearth.substack.com/p/the-science-virus-part-i-orwellian. Accessed Oct 23, 2022.
54. Hotez PJ. Mounting antiscience aggression in the United States. *PLoS Biol* 2021;19(7). doi:10.1371/JOURNAL.PBIO.3001369.
55. Lasco G. Medical populism and the COVID-19 pandemic. *Global Public Health* 2020;15(10):1417-1429. doi:10.1080/17441692.2020.1807581.
56. Hotez PJ. Anti-science kills: From Soviet embrace of pseudoscience to accelerated attacks on US biomedicine. *PLoS Biol* 2021;19(1). doi:10.1371/JOURNAL.PBIO.3001068.
57. Hotez PJ. America's deadly flirtation with antiscience and the medical freedom movement. *J Clin Invest* 2021;131(7). doi:10.1172/JCI149072.
58. Ezell JM. The medicalization of freedom: how anti-science movements use the language of personal liberty and how we can address it. *Nature Medicine* 2022;28(2):219-219. doi:10.1038/s41591-021-01640-y.
59. Office of the Surgeon General. *Confronting Health Misinformation*. US Department of Health and Human Services; 2021. Available at: https://www.ncbi.nlm.nih.gov/books/NBK572169/. Accessed Oct 23, 2022.
60. Roozenbeek J, van der Linden S. How to combat health misinformation: a psychological approach. *Am J Health Promotion*. 2022;36(3):569-575. Available at: doi:10.1177/08901171211070958/ASSET/IMAGES/LARGE/10.1177_08901171211070958-FIG3.JPEG. Accessed Nov 7, 2022.
61. Johnson SS. The urgent need for coordinated and comprehensive efforts to combat misinformation. *Am J Health Promotion*. 2022;36(3):559-561. doi:10.1177/08901171211070957A.
62. De Beaumont Foundation. New Report. *Disinformation Doctors: Licensed to Mislead*. de Beaumont; Dec 15, 2021. Available at: https://debeaumont.org/news/2021/disinformation-doctors-report/. Accessed Oct 23, 2022.
63. Resneck J. Turning the tide against medical disinformation will take all of us. American Medical Association. AMA Leadership Website; Oct 5, 2022. Available at: https://www.ama-assn.org/about/leadership/turning-tide-against-medical-disinformation-will-take-all-us. Accessed Oct 23, 2022.
64. Neitzel A. AB2098 signed into law . *MisinformationKills's Newsletter*; Sep 30, 2022. Available at: https://misinformationkills.substack.com/p/ab2098-signed-into-law. Accessed Oct 24, 2022.
65. Burns PB, Rohrich RJ, Chung KC. The levels of evidence and their role in evidence-based medicine. *Plast Reconstr Surg* 2011;128(1):305. doi:10.1097/PRS.0B013E318219C171.
66. Walls AC, Park YJ, Tortorici MA, et al. Structure, function, and antigenicity of the SARS-CoV-2 spike glycoprotein. *Cell* 2020;181(2):281-292.e6. doi:10.1016/J.CELL.2020.02.058.
67. Chen W, Pan JY. Anatomical and pathological observation and analysis of SARS and COVID-19: Microthrombosis Is the main cause of death. *Biol Proced Online* 2021;23(1):1-12. doi:10.1186/S12575-021-00142-Y/METRICS.
68. McFadyen JD, Stevens H, Peter K. The emerging threat of (micro) thrombosis in COVID-19 and its therapeutic implications. *Circ Res* 2020;127(4):571-587. doi:10.1161/CIRCRESAHA.120.317447.
69. NeutralResearcher. Micro-thrombosis in COVID-19. NeutralViewPoint Substack; Oct 27, 2022. Available at: https://neutralresearcher.substack.com/p/micro-thrombosis-in-covid-19. Accessed Oct 26, 2022.
70. Seneff S, Nigh G, Kyriakopoulos AM, McCullough PA. Innate immune suppression by SARS-CoV-2 mRNA vaccinations: the role of G-quadruplexes, exosomes, and microRNAs. *Food Chem Toxicol* 2022;164:113008. doi:10.1016/J.FCT.2022.113008.
71. Itoh H, Ueda M, Suzuki M, Kohmura-Kobayashi Y. Developmental origins of metaflammation: a bridge to the future between the DOHaD theory and evolutionary biology. *Front Endocrinol (Lausanne)*. 2022;13. doi:10.3389/FENDO.2022.839436.
72. Hotamisligil GS. Inflammation, metaflammation and immunometabolic disorders. *Nature* 2017;542(7640):177-185. doi:10.1038/nature21363.

73. Muskiet FAJ, Carrera-Bastos P, Pruimboom L, Lucia A, Furman D. Obesity and leptin resistance in the regulation of the type I interferon early response and the increased risk for severe COVID-19. *Nutrients* 2022;14(7). doi:10.3390/NU14071388.
74. Belchior-Bezerra M, Lima RS, Medeiros NI, Gomes JAS. COVID-19, obesity, and immune response 2 years after the pandemic: a timeline of scientific advances. *Obes Rev* 2022;23(10). doi:10.1111/OBR.13496.
75. Grover SP, Mackman N. Neutrophils, NETs, and immunothrombosis. *Blood* 2018;132(13):1360-1361. doi:10.1182/BLOOD-2018-08-868067.
76. Brazete C, Aguiar A, Furtado I, Duarte R. Thrombotic events and COVID-19 vaccines. *Int J Tuberc Lung Dis* 2021;25(9):701. doi:10.5588/IJTLD.21.0298.
77. Smadja DM, Yue QY, Chocron R, Sanchez O, Lillo-Le Louet A. Vaccination against COVID-19: insight from arterial and venous thrombosis occurrence using data from VigiBase. *Eur Resp J* 2021;58(1). doi:10.1183/13993003.00956-2021.
78. Kaur RJ, Dutta S, Bhardwaj P, et al. Adverse events reported from COVID-19 vaccine trials: a systematic review. *Indian J Clin Biochem* 2021;36(4):427-439. doi:10.1007/S12291-021-00968-Z.
79. Konstantinides SV. Thrombotic complications of vaccination against SARS-CoV-2: What pharmacovigilance reports tell us—and what they don't. *Eur Respir J* 2021;58(1). doi:10.1183/13993003.01111-2021.
80. FDA. Vaccine Development—101; 2020. Available at: https://www.fda.gov/vaccines-blood-biologics/development-approval-process-cber/vaccine-development-101. Accessed Jul 17, 2022.
81. CDC. Vaccine Testing and Approval Process; 2014. Available at: https://www.cdc.gov/vaccines/basics/test-approve.html. Accessed Jul 17, 2022.
82. FDA. FDA Approved COVID-19 Vaccines. FDA Summary WebPage; Jul 13, 2022. Available at: https://www.fda.gov/emergency-preparedness-and-response/coronavirus-disease-2019-covid-19/covid-19-vaccines. Accessed Jul 17, 2022.
83. Pfizer. Pfizer-BioNTech COVID-19 Vaccine (BNT162, PF-07302048) Vaccines and Related Biological Products Advisory Committee Briefing Document; 2020. Available at: https://www.fda.gov/media/144246/download. Accessed Jul 17, 2022.
84. Moderna. Moderna COVID-19 Vaccines. Vaccines and Related Biological Products Advisory Committee December 17, 2020, Meeting Briefing Document—FDA; 2020. Available at: https://www.fda.gov/media/144434/download. Accessed Jul 17, 2022.
85. Meyboom RHB, Egberts ACG, Edwards IR, et al. Principles of signal detection in pharmacovigilance. *Drug Saf* 1997;16(6):355-365. doi:10.2165/00002018-199716060-00002.
86. Institute of Medicine (US) Board on Health Promotion and Disease Prevention. Improving Detection of and Response to Adverse Events. Vaccine Safety Forum. National Academies Press; 1997. Available at: https://www.ncbi.nlm.nih.gov/books/NBK232983/?report=classic. Accessed Jul 16, 2022.
87. Shimabukuro TT, Nguyen M, Martin D, DeStefano F. Safety monitoring in the Vaccine Adverse Event Reporting System (VAERS). *Vaccine* 2015;33(36):4398-4405. doi:10.1016/J.VACCINE.2015.07.035.
88. Varricchio F, Iskander J, Destefano F, et al. Understanding vaccine safety information from the Vaccine Adverse Event Reporting System. *Pediatr Infect Dis J* 2004;23(4):287-294. doi:10.1097/00006454-200404000-00002.
89. Wadman M. Antivaccine activists use a government database on side effects to scare the public. *Science*; May 26, 2021. doi: 10.1126/science.abj6981.
90. Simons A. 10 Accidental discoveries that changed the world. *Reader's Digest*, Feb 3, 2022. Available at: https://www.rd.com/list/10-accidental-discoveries-put-to-good-use/. Accessed Jul 18, 2022.
91. Trigoso E. Embalmers have been finding numerous long, fibrous clots that lack post-mortem characteristic. *Epoch Times*, Sep 2, 2022. Available at: https://www.theepochtimes.com/embalmers-have-been-finding-numerous-long-fibrous-clots-that-lack-post-mortem-characteristics_4696015.html. Accessed Oct 24, 2022.
92. Dong Y, Corson A. Fibrous clots, foreign matter in blood after COVID jabs: Is there a way to detox? *Epoch Times*, Sep 18, 2022. Available at: https://www.theepochtimes.com/health/fibrous-clots-foreign-matter-in-blood-after-covid-jabs-is-there-a-way-to-detox_4738079.html. Accessed Oct 24, 2022.
93. Skorbach D. Mystery clots appear in 50–70 percent of deceased: funeral director. *Epoch Times*, Sep 6, 2022. Available at: https://www.theepochtimes.com/mystery-clots-appear-in-50-70-percent-of-deceased-since-2020-says-funeral-director_4712358.html. Accessed Oct 24, 2022.
94. Carball I. Mike Adams' flawed analysis of a clot sent by embalmer Richard Hirschman doesn't demonstrate any link between blood clots and COVID-19 vaccines. Health Feedback; Sep 12, 2022. Available at: https://healthfeedback.org/claimreview/mike-adams-flawed-analysis-clot-embalmer-richard-hirschman-doesnt-demonstrate-link-between-blood-clots-and-covid-19-vaccines-epoch-times/. Accessed Oct 24, 2022.