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Research Article

IS COVID VACCINE IMMUNITY SUCCESS STORY GIVES "A LOT OF HAPPY TEARS"?

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ABSTRACT

Acquiring vaccinated could rescue your life. COVID-19 vaccines furnish powerful protection against grave illness, hospitalization and death. The SARS-CoV-2 pandemic is now better controlled in background with entry to fast and reliable testing and highly effective vaccination
Eradication of coronavirus disease 2019 (COVID-19) appears practically impossible, as already spread globally to several million people. There is an urgent need to improve, appreciate and comprehend the knowledge of the immunology of this disease by developing vaccines and medicines for the prevention and treatment of patient. Viruses are obligate intracellular parasites require their host to replicate them and propagate. Respiratory viruses cause serious emerging infectious diseases. Not only the disastrous original influenza viruses, SARS, MERS, or COVID-19, but seasonal influenza viruses regularly lead to serious morbidity and mortality. Many viruses infect humans and most are regulated by the immune system with controlled injury to host tissues. Some viruses, however, do cause damage to the host. These viral antigens can be either approved by the B cells or presented by MHC complexes to the T cells, resulting in antibody production, elevated cytokine production, and cytolytic activity in the acute phase of infection. Contaminated humans can, after convalescence, produce aggressive defensive responses by generating a memory T-cell pool against SARS-CoV and MERS-CoV. Memory T cells were not constant in the long term and, upon reactivation, became local harm due to cross-reactivity.

INTRODUCTION

Innate immunity, is the first line of defense against pathogens, representing a critical systemic response to prevent infection (1) Active immunity is acquired through the exposure to a pathogen, which triggers the production of antibodies by the immune system (2) The acute respiratory syndrome is a disease caused by the SARS-CoV-2 virus (COVID-19), where symptoms include difficulty breathing, high fever, and cough (3)

Covid-19 ,belonging to the genera Betacoronavirus and the family Coronaviridae in Gorse *et al*., 2020 [4] origin of this virus, SARS-CoV-2 probably arises from a natural selection in the animal host or a selection in humans (5) This virus is preferred in cells of the respiratory tract, epithelial hair cells of the airways and type 2 alveolar pneumocytes in SARS-CoV infections [6] Infections caused by a coronavirus, in general, will be mediated by T lymphocytes, which will become active the moment the pathogen presented by antigen-presenting cells (dendritic cells or macrophages) is recognized [7].

In the moment of activation, there will be the production of inflammatory mediators (IFN–I, TNF-β, IL-1, IL-6, CCL2) and probably the production of perforin and granzyme B, processes that usually occur in others airways infections [8]

In more severe cases, high pathogenesis is observed caused by an intense inflammatory process that isn't controlled by the cytokine storm (release of inflammatory mediators: IFN-α, IL-1β, IL-6, TNF-α, CCL2, CCL5, among others), responsible for the development of lung injuries, which culminates in respiratory failure, organ failure and death (9,10)

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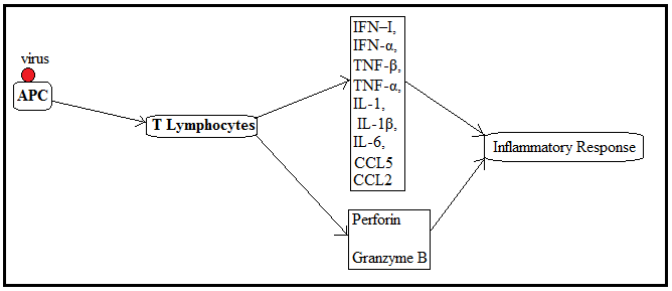
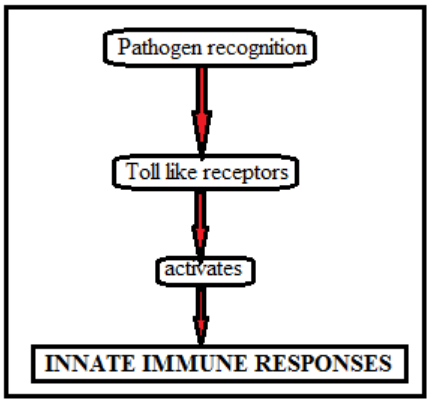
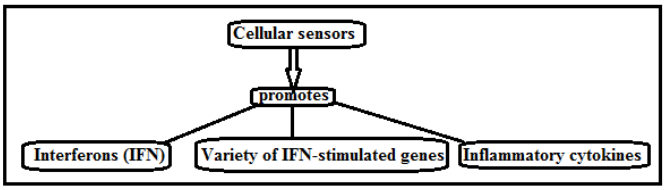


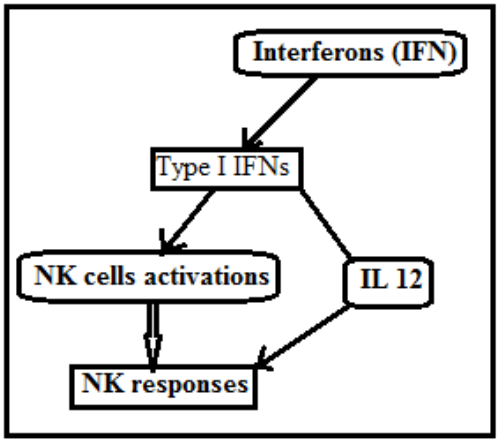
The innate immune defenses are initiated via pathogen recognition receptors of the Toll-like receptor (TLR) family or a family of DExD/H box RNA helicases (11)



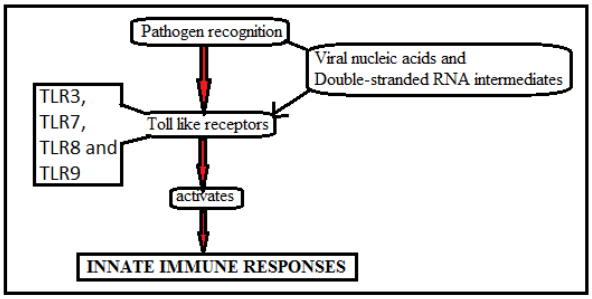
Cellular sensors promote the expression of type I (α/β) interferons (IFN) and a variety of IFN-stimulated genes and inflammatory cytokines (12)



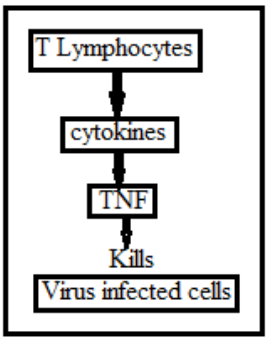
Type I IFNs also activate natural killer (NK) cells and induce other cytokines such as interleukin (IL)-12 that promote NK responses.(13)



Virus infections usually activate the endosomal TLRs (TLR3, TLR7, TLR8 and TLR9) that recognize viral nucleic acids and double-stranded RNA intermediates (14)



cells, for example, can directly destroy virus-infected cells or release cytokines, such as tumor necrosis factor (TNF), that damage cells. With some non-cytopathic virus infections, such as HCV and HBV, destruction of infected cells by CD8+ effector T cells is the main cause of damage to the liver (15)



Most often, the cell subsets involved are T helper 1 (TH1) cells, but TH17 cells may contribute to inflammatory responses during HIV, HCV and influenza virus infections (16)

TH2 cells are rarely associated with inflammatory responses during viral infections, but a TH2 cell response can occur during severe lung responses to RSV infection (17)

Alternatively, antibody-mediated inflammatory reactions involve toxicity following engagement of IgG with Fc receptors on inflammatory cells, which causes inflammatory mediator release(18)

Viruses such as RSV express antigens that may induce an IgE response and type I hypersensitivity might partially account for lung lesions in some children infected with RSV(19)

Many cell types can produce IL-10, including subsets of activated DCs, macrophages (when infected with some viruses), activated regulatory T (TReg) cells, B cells and some subsets of NK cells following stimulation with TLR ligands(20)

Chronological record of significant events

Immunity against smallpox.----------Edward Jenner

Coined the term vaccine----------Louis Pasteur.

Importance of cells in immunity------.Metchnikoff-

Humoral theory----------Emil Von Behring

Alexin as complement---------- Bordet.

Cellular immunity ----------Robert Koch-

Anaphylaxis----------Richet

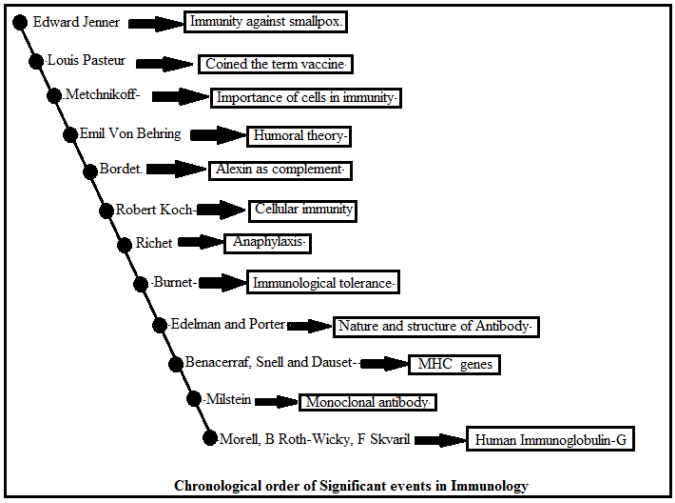
Immunological tolerance----------Burnet-

Nature and structure of Antibody---------Edelman and Porter-

MHC genes----------Benacerraf, Snell and Dauset--

Monoclonal antibody----------Milstein

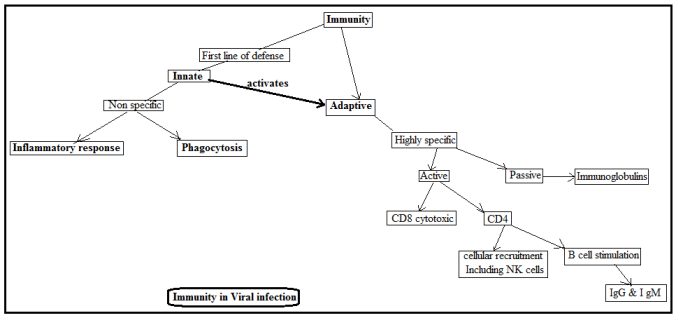
Human Immunoglobulin-G ----------Morell, B Roth-Wicky, F Skvaril –



Chronological order of Significant events in Immunology

The discovery of antitoxin by Behring and Kitasato became the first major success of modern therapeutic immunology (21) The earliest use of immunization is unknown, but, about 1000 AD, the Chinese began practicing a form of immunization by drying and inhaling powders derived from the crusts of smallpox lesions. Around the 15th century in India, the Ottoman Empire, and east Africa, the practice of inoculation (poking the skin with powdered material derived from smallpox crusts) was quite common (22)

Humans evolved with a unique immune system consisting of innate and adaptive immunity. Both innate and adaptive immunity comprised different types of cells, immune players, and associated with different functions.



Innate immunity

The innate component of the immunity system involves the recognition of certain foreign (non-self) molecules to generate one of two types of innate immune responses: inflammatory responses and phagocytosis (23)

It is defined as the first line of defense against pathogens, representing a critical systemic response to prevent infection and maintain homeostasis, contributing to the activation of an adaptive immune response (24)

Adaptive immunity

The resistance that an individual acquires during life is known as acquired immunity or adaptive immunity.

Adaptive or acquired immunity is the active component of the host immune response, mediated by antigen specific lymphocytes. Unlike the innate immunity, the acquired immunity is highly specific to a particular pathogen, including the development of immunological memory (25)

Like the innate system, the acquired system includes both humoral immunity components and cell-mediated immunity components.

Adaptive immunity can be acquired either 'naturally' (by infection) or ‘artificially’. Adaptive immunity can also be classified as 'active' or 'passive'. Active immunity is acquired through the exposure to a pathogen, which triggers the production of antibodies by the immune system (26)

Passive immunity is acquired through the transfer of antibodies or activated T-cells derived from an immune host either artificially or through the placenta; it is short-lived, requiring booster doses for continued immunity.

The adaptive response: T cells

Adaptive immunity plays a major role in the clearance of SARS-CoV-2 from the body and consists of cell mediated immunity and humoral immunity.

T cells (cellular response

Types of T cells: CD8+ cytotoxic T cells kill the cells in which the virus is multiplying and help to slow down or stop the infection. CD4+ helper T cells bring in other cells of the immune system and stimulate B-Cells to produce antibodies specific to that virus.

T cell immune responses seen a year after infection

Strong and longstanding T cell responses were seen even when people were not reinfected or vaccinated Like in most countries where the Omicron variant had become dominant and caused a high spike in daily cases, the third wave in India propelled by Omicron caused a large number of reinfections in unvaccinated people and breakthrough infections even among the fully vaccinated. However, across the world, the Omicron variant was found to cause only mild disease in fully vaccinated people and in those with previous infection. This was real-world proof that previous infection and/or full vaccination with two doses provide protection against progression of disease to a severe form.

"T cells are very important in fighting viruses," says Dr. Kari Nadeau at Stanford University.

Scientists developing some of the coronavirus vaccines have noticed that their experimental products spark a strong T-cell response. That includes the vaccine from the University of Oxford, which is in an advanced stage of testing.

Protective effect

Laboratory studies undertaken in all countries have only studied the neutralization ability of sera of people who have recovered from COVID-19 and people who have been fully vaccinated. This could only shed light on the ability of past infection and/or vaccination to prevent infection by highly transmissive variants with immune escape. But no studies have been done to evaluate the protective effect of memory T cell immune responses against severe disease 12 months after primary infection. A new study from Wuhan addresses this gap. The results were published in the journal *The Lancet Microbe*.(27)

Independent of severity

The researchers found that neutralizing antibodies were detectable even 12 months after infection in "most individuals", and it remained stable 6-12 months after initial infection in people younger than 60 years. The researchers found that "multifunctional T cell responses were detected for all SARS-CoV-2 viral proteins tested".

And most importantly, the magnitude of T cell responses did not show any difference immaterial of how severe the disease was. While the ability of antibodies to neutralise was nearly absent against the Beta variant, it was reduced in the case of the Delta variant.

In contrast, the T cell immune responses were detectable in all the 141 individuals tested 12 months after infection and even when they had lost the neutralising antibody response. And the T cell responses were responding against the Beta variant in most of the 141 individuals.

Neutralizing antibodies

"SARS-CoV-2-specific neutralizing antibody and T cell responses were retained 12 months after initial infection. Neutralizing antibodies to the D614G, Beta, and Delta were reduced compared with those for the original strain, and were diminished in general. Memory T cell responses to the original strain were not disrupted by new variants," they write

Robustness of T cells

The study reveals the durability and robustness of the T cell responses against variants, including Delta, even after one year of infection. Most importantly, the robust and longstanding T cell responses were seen in people who have not been reinfected or vaccinated. This would mean even in the absence of vaccination, a person who has been infected by the virus even one year ago would have robust immune responses, which would offer protection against disease progressing to a severe form requiring hospitalization. But the neutralizing antibodies were found to diminish at the end of 12 months. It might be recalled that except the Oxford vaccine (AstraZeneca), none of the trials evaluated the ability of the vaccines to prevent infection. The endpoint of all vaccine efficacy studies was to evaluate if vaccinated people developed symptomatic disease or not.

The adaptive response: B cells

B Cells (Antibody response)

- produce antibodies that are specific to that virus.
- IgM antibodies are produced first and disappear after a few weeks.
- IgG antibodies are produced at the same time or 2-3 days later, and titres (levels) usually remain for months or years.
- .Memory cells respond rapidly if they come in contact with the same virus again, killing the virus and accelerating an antibody response

Natural killer (NK) cells

These are innate lymphocytes that play a critical role in the immune response to viral infection.(28)

Since the advent of the COVID-19 pandemic, studies examining the immune response in COVID-19 have noted that NK cells are less abundant in the peripheral blood of severe COVID-19 patients than in healthy donors (29)

A concurrent increase in NK cell frequency in the lungs of critically ill patients suggests that peripheral depletion of NK cells may be due to trafficking to the site of infection (30)

It is found that SARS-CoV-2 nonstructural protein 1 (Nsp1) mediates down regulation of NKG2D-L and that Nsp1 alone is sufficient to confer resistance to NK cell killing. (31)

Additionally, immune profiling has uncovered significant, severity-associated phenotypic and transcriptional changes in the peripheral NK cells that remain in the blood of COVID-19 patients. In severe COVID-19, peripheral blood NK cells become activated and exhausted (32)

Researchers find 2 paths to 'super immunity' against Covid-19, no correlation with age

There are two paths towards "super immunity" against coronavirus disease (Covid-19) and both provide roughly equal levels of enhanced immune protection, according to a new study.They found that the additional antigen exposure from Covid-19 substantially boosts immunity regardless of whether it occurs before or after vaccination.

"It makes no difference whether you get infected and then vaccinated, or if you get vaccinated and then a breakthrough infection," said FikaduTafess, co-author of the study. "In either case, you will get a really, really robust immune response — amazingly high."(33)

Hybrid immunity' gives best Covid protection

After two years of a pandemic that has seen nearly 500 million people infected and billions vaccinated, the studies highlighted the importance of getting jabbed for those who have natural immunity after recovering from the disease (34)

How much immunity does a previous COVID-19 infection offer?

COVID prevalence was similar across provinces, gender and age, but differed across racial groups (35)

How long does immunity against COVID-19 last after vaccination?

Reports of health agencies in parts of the world considering a booster dose against fading immunity, particularly among the elderly, even after two doses of vaccine, has raised the uncomfortable question in India, which is struggling to vaccinate its vast population.

Though breakthrough infections – people testing positive for COVID-19 even after vaccination – have been reported in Karnataka, Dr. MudassirAzeez Khan, Head of Community Medicine at Mysore Medical College and Research Institute (MMC & RI), in a presentation at a recent meeting of the newly constituted Mysore District Technical Experts Committee on COVID-19, argued against the need for a booster dose.

"A breakthrough infection itself will act like a booster dose. A human body produces better antibody response against COVID-19 through natural infection than a third dose of vaccination," he said.

Why do scientists and experts say that it is not a viable option to tackle the SARS-CoV-2 virus outbreak?

Right from the time it became obvious that the SARS-CoV-2 virus outbreak was not confined to China, but scaling other shores too, the theory of herd immunity has been floating around. Initially, herd immunity, an important tool in epidemic control, was proposed as a means to overcome the pandemic. Only a certain proportion of the population needs to be infected in order to stop large outbreaks, either through naturally-acquired disease, or through vaccination. Since a vaccine is not available for COVID-19 yet, some people advocated that the infection be allowed to spread in the community until herd immunity is achieved.

Why this being is stoutly opposed?

In the World Health Organization's (WHO) 'Science in 5' video series, the organization's chief scientist, SoumyaSwaminathan, explains herd immunity with the help of a common childhood infectious disease — measles — for which there is a very effective vaccine. "To achieve herd immunity in the population, for measles, you need about 95% of the people to have immunity or antibodies," she explains. "Even if you have 5% of children [who are] not vaccinated, these others actually have enough protection in the population to prevent the measles virus from actually going from one person to the next. So, it is really like having a barrier of people who are protected, who break that chain of transmission."

For the SARS-CoV-2, Dr. Swami Nathan thinks that at least 60-70% of the population should have immunity to really break the chain of transmission. "If you allow this to happen naturally, it will take a long time, of course, but more importantly, it is going to do a lot of collateral damage," adds Dr. Swaminathan.

Covid-19 immunity could last for months: New research clarifies previous findings

The duration of immunity to Covid-19 has been a subject of research through the pandemic, and studies so far have provided various results. In July last year, a study suggested that immunity might be lost in months

A new study suggests that the body's immune response to the novel coronavirus can last for at least eight months after the onset of symptoms from the initial infection.

The duration of immunity to Covid-19 has been a subject of research through the pandemic, and studies so far have provided various results. In July last year, a study suggested that immunity might be lost in months. As The Indian Express reported back then, researchers from King's College London drew this conclusion from a drop they observed in the antibody levels in recovered Covid-19 patients over time — from a "potent level" in 60% of study participants during the peak of infection to only 16.7% retaining that level of potency 65 days later. While that study suggested that recovered Covid-19 patients are likely to remain susceptible to re-infection, the new study suggests that nearly all Covid-19 survivors have the immune cells necessary to fight re-infection.

Lack of immunity makes China vulnerable to second wave of virus infection

China still faces an enormous challenge of a potential second wave of COVID-19 infections, with a lack of immunity among a major threat, a top medical advisor of the country has warned. Doctor Zhong Nanshan, senior medical advisor of the Chinese government on Saturday was quoted in an exclusive CNN report as saying: "The majority of ... Chinese at the moment are still susceptible to the Covid-19 infection, because (of) a lack of immunity."

New COVID Antibody Test Screening for Immunity

Working toward that goal, researchers in Hong Kong have developed a device that allows someone to directly see their antibody levels following vaccination. The device, detailed in a new paper published Friday in the journal *Science Advances*, is on par with conventional coronavirus antibody testing platforms. It could be used as a better way to conduct mass screening for COVID immunity, to monitor someone's immune status after the jab, or to even tailor vaccine dosing to an individual's immune needs.(36)

Under-5-Minute Immunoblot Assays by Vortex Fluidic Device Acceleration

The VFD-accelerated immunoblot assay (VAIA) improves conventional processing time from a hours-long process to <5 minutes. Here, VAIA is performed with three major immunoassay formats with purified proteins and diluted bio fluids.(37)

Corona virus crisis

So many people are counting on a vaccine to help end the coronavirus pandemic that any hint of bad news gets a lot of attention. That's proving to be the case for a series of studies examining how long antibodies persist in people who have been infected with the coronavirus. Antibodies help ward off infections. In some diseases, they can prevent re-infection, though scientists can't say for sure if that's true for the coronavirus. And it's also not clear how long antibodies linger. Three recent studies – from China, Britain and now the United States – have called into question how long people carry antibodies after infection. But the reality may be less dire than recent headlines suggest. Scientists have noticed that people with milder symptoms — or no symptoms at all — tend to have a weaker immune response to the coronavirus. And Yang's letter, published online in *The New England Journal of Medicine,* focused on people with mild illness.(38)

Protection against SARS-CoV-2 after Covid-19 Vaccination

The duration and effectiveness of immunity from infection with and vaccination against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) are relevant to pandemic policy interventions, including the timing of vaccine boosters. The duration of this protection over longer periods remains uncertain and warrants ongoing study.(39,40)

Covid Vaccines

Recent studies have shown that vaccination confers more durable protection against severe outcomes of hospitalization and death than against symptomatic and asymptomatic infection (41,42)**.**

- 'GERMAN–US' vaccine: Pfizer-BioNTech; BNT162b2; New messenger RNA (mRNA) -
- 'US'vaccine: Moderna; mRNA-1273 for spike protein; New messenger RNA (mRNA)

- 'British' vaccine: Oxford-AstraZeneca; ChAdOx1 nCoV19 / Covershield; inactivated virus – Adenovirus from Chimpanzee;
- D 'Russian' vaccine: Gamaleya Institute; Sputnik V; Two human adenoviruses vector

'Indian' vaccine

Bharat Biotech, Hyderabad / ICMR's National Institute of Virology, Pune; Covaxin; Traditional whole cell inactivated virus, The WHO Emergency Use Listing process determines whether a product can be recommended for use based on all the available data on safety and efficacy and on its suitability in low- and middle-income countries. Vaccines are assessed to ensure they meet acceptable standards of quality, safety and efficacy using clinical trial data, manufacturing and quality control processes. The assessment weighs the threat posed by the emergency as well as the benefit that would accrue from the use of the product against any potential risks

As of 12 January 2022, the following vaccines have obtained EUL (Emergency Use Listing Procedure)

- The Pfizer/BioNTechComirnaty vaccine, 31 December 2020.
- The SII/COVISHIELD and AstraZeneca/AZD1222 vaccines, 16 February 2021.
- The Janssen/Ad26.COV 2.S vaccine developed by Johnson & Johnson, 12 March 2021.
- The Moderna COVID-19 vaccine (mRNA 1273), 30 April 2021.
- The Sinopharm COVID-19 vaccine, 7 May 2021.
- The Sinovac-CoronaVac vaccine, 1 June 2021.
- The Bharat Biotech BBV152 COVAXIN vaccine, 3 November 2021.
- The Covovax (NVX-CoV2373) vaccine, 17 December 2021.
- The Nuvaxovid (NVX-CoV2373) vaccine, 20 December 2021

Special Precautions

Vaccine should be administered with caution in persons with a history of any bleeding or coagulation disorder such as

A. Clotting factor deficiency
B. Coagulopathy
C. Platelet disorder

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