

## Cytopenia in Influenza and possible treatment strategies (Drug and Vaccine)

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### ABSTRACT

Viruses consistently present a major health danger and require a proper, balanced reaction from our immune system. Among viruses, human influenza viruses often cause morbidity and mortality, especially in populations at high risk. These viruses cause apoptosis in peripheral blood monocytes and tissue culture cells. Hemophagocytosis-induced pancytopenia has also been frequently correlated with the newly emerging influenza virus infection in latest years. Leukopenia, particularly in influenza B virus, has been discovered to be a common finding in influenza infection. If the virus and the resulting antiviral reaction continue, the inflammatory feedback on the hematopoietic system becomes chronic. Here, we have reviewed effect of Influenza on hematological factors specially cytopenia.

**Keywords:** Influenza virus, hematological factors, cytopenia

### INTRODUCTION

Viruses are Small binding intracellular parasites requiring replication of host cellular machines. That said, there is a huge range of viruses, even medically appropriate ones. Viruses that can infect people in the range of 20 to 260 nm are estimated to be at least 30 distinct kinds and can trigger pathologies, ranging from meningitis, enterocolitis,

respiratory manifestations, encephalitis, sexually transmitted diseases, and hepatitis [1-7]. Viruses are structurally made up of a protein capsid that protects their genomic material and in some instances promotes entry into the host cell. Some viruses with the lipid bilayer enveloped viruses that also contain membrane glycoproteins can communicate with entry receptors on the surface of the host cells can also be encircled [8,9]. The virus genome may consist of DNA

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or RNA. RNA genomes can be coded, similar to a mRNA molecule (positive-strand RNA) or have a supplementary RNA molecule (negative-strand) to be copied into a positive strand that can then be translated into a cellular machine [10-15].

Viruses consistently present a major health danger and require a proper, balanced reaction from our immune system. Indeed, both the virus itself and the subsequent immune response can have a tremendous effect on the hematopoietic cycle. This can be useful as it helps increase the body cell response to fix the viral infection. However, if the virus and the resulting antiviral reaction continue, the inflammatory feedback on the hematopoietic system becomes chronic [16-20].

### *About Human influenza viruses*

Viral infections are entered from epithelial or mucosal barriers that cause local invasion. Viral RNA in infected cells is acknowledged during influenza virus infection by pathogen recognition receptors (PRRs), which its result is the secretion of pro-inflammatory cytokines, type I interferons, chemokines, and eicosanoids [20-22]. CD8 + T, plasmacytoid and NK cells are also all involved in cytotoxicity and viral infection control [11-14]. Human influenza viruses often cause morbidity and mortality,

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especially in populations at high risk [21,22]. The categories of main influenza (H1N1) is shown in Table 1.

They are single-stranded RNA (ssRNA) and Orthomyxoviridae family members. This family reflects enveloped viruses whose genome consists of segmented single-strand negative-sense RNA sections [24]. This family has four genera: A, B, C and Thogoto viruses, of which only genera A and B are clinically applicable to individuals. The nucleoprotein loosely encapsidates the eight genome sections of influenza A and B viruses [25]. Influenza virus is comparatively susceptible to harmful environmental effects as an enveloped virus. However, it can survive up to several hours depending on environmental conditions (humidity and temperature) and significantly longer in water at low temperatures (< 20 °C). Influenza viruses are susceptible to lipid and detergent. Depending on the type of virus, they are also susceptible to heat and low pH [26,27]. When assessing human infections, the hematological factors are regularly evaluated. Surprisingly, in tiny animal models they are rarely determined. Influenza A Virus (IAV) infection represents a prevalent acute infection in both human and veterinary medicine with a high disease burden. The mouse represents a well-

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established model of IAV susceptibility in an adaptive host [25-28].

**The effects of Influenza virus on blood cells**

Influenza virus has been proved to cause apoptosis in peripheral blood monocytes and tissue culture cells [27]. The immunopathological mechanisms and the role played by leukocyte virus infection in relation to disease pathology in general and leukocyte death in particular have not been clarified [21,22]. Early lymphopenia has

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been reported in infected patients and it has been shown that human inoculation with virus causes a reduction in T- and B-cell numbers during disease [23].

Hematological abnormalities such as pancytopenia or isolated leucopenia are also known to be associated with influenza infection that is shown in Table 2.

**Table 1.** Categorization of influenza H1N1

Types of category	Testing	Reference
A	No for H1N1	[23]
B1	No for H1N1	
B2	No for H1N1	
C	Test for H1N1 is essential with starting treatment	

**Table 2.** The most types of cytopenia in influenza infection

Type of cytopenia	Reference
Lymphocytopenia	[29-32]
Thrombocytopenia	[33,34]
Eosinopenia	[35]
Leukopenia	[36]

Hemophagocytosis-induced pancytopenia has also been frequently correlated with the newly emerging avian influenza virus infection in latest years. Leukopenia, particularly in influenza B virus, has not been discovered to be a rare finding in influenza infection [37]. Leukopenia is self-limited in most circumstances and usually resolves spontaneously soon after the subsidence of fever [38]. It has been suggested that transient influenza A-induced leukopenia in peripheral blood lymphocytes is caused by Fas-FasL-mediated apoptosis [39].

Lymphocytopenia was a feature of serious influenza and also a significant risk of nosocomial infection in hospitalized patients with serious influenza, long neglected [29,40].

During influenza A infections, leucopenia is known to happen commonly, but thrombocytopenia, pancytopenia, and anemia are uncommon. There are few reports that the fresh virus A (H1N1) could lead to cytopenias. In a Chinese research of 426

instances, lymphopenia was discovered in adolescents at a rate of 68 % while in kids it was discovered almost 92 % [41].

#### ***Treatment of cytopenia caused by Influenza virus***

Some treatments that may be used include:

Drugs that stimulate the bone marrow are very good. For chemotherapy-induced neutropenia and some other causes, the growth factors Leukine, Neulasta, or Neupogen may be applied to induce the creation of white blood cells [42-45]. For chemotherapy-induced anemia, there are also some medications that may be used [45] (Table 3). Also, blood transfusions, immunosuppressive drugs if influenza is due to an autoimmune condition and finally, bone marrow transplant or stem cell transplant in influenza related to cancer [45,46].

Table 3. Drugs list for the types of cytopenia

Type of cytopenia	Treatment	Reference
Lymphocytopenia	Epoetin alpha	[42, 43]
Thrombocytopenia	Prednisone, Dexamethasone, Promacta	[45, 47]
Eosinopenia	Darbepoetin alfa, Epoetin alpha	[45-47]
Leukopenia	Darbepoetin alfa	[45-47]
Chemotherapy-induced anemia	Epoetin alpha	[45]
Chemotherapy-induced neutropenia	Leukine, Neulasta, Neupogen	[42-45]

## DISCUSSION

Leucopenia, anemia and thrombocytopenia observed during influenza A (H1N1) infection are reported to have improved with the resolution of symptoms of viral infection and not to cause permanent cytopenia and serious complications [36].

A study investigated the prevalence of cytopenia, which in children positive for influenza A (H1N1) infection is a hematological complication. In the three primary cell groups, platelets, leucocytes and erythrocytes, cytopenia was determined with declines. Decreases were also analyzed in leucocyte and leucocyte

subgroups (lymphocytes, granulocytes) [43]. A platelet count below  $150,000/\text{mm}^3$  has been assessed in all age groups as thrombocytopenia. A leucocyte count below  $6,000/\text{mm}^3$  in kids under 2 years of age and a leucocyte count below  $4,000/\text{mm}^3$  in kids between 2-17 years of age was regarded leucopenia. A lymphocyte count below  $1,800/\text{mm}^3$  in kids under 2 years of age and a lymphocyte count below  $1,000/\text{mm}^3$  in kids between 2-17 years of age was regarded lymphopenia; Neutrophil counts below  $1,100/\text{mm}^3$  in kids under 2 years of age and neutrophil counts below  $1,500/\text{mm}^3$  in kids between 2-17 years of age were regarded to be neutropenia. Hemoglobin values below 10.5 g/dL in children 2 years of age, below

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11.5 g/dL in children 2-9 years of age, below 12.5 g/dL in boys 10-17 years of age and below 12.9 g/dL in girls 10-17 years of age were recognized as anemia[44]. Hematocrites below 32 percent, 33 percent, 35 percent and 36 percent, respectively, were regarded anemia after the iron deficiency and vitamin B12 deficiency anemias were excluded. A cytopeniagiemsa stain was performed for each patient (classical method) and peripheral blood smears. A hematology specialist then evaluated the results. Leukopenia in patients with atypical lymphocytes (Larger cytoplasm of rare eosinophilic granules and normal lymphocytes 1.5-2 times larger than expected) was observed. The report on peripheral smear indicated that lymphocytes were being served. Furthermore, the blood count results of leukopenia were consistent with peripheral smear outcomes of leukopenia. Atypical blastic species-specific cells have not been observed [45].

Influenza infection increases the incidence of acute MI [45,46] within 7 days of detection of type A or type B viruses, whereas after day 7 there is no increased incidence. There is no understanding of the exact mechanism by which influenza contributes to acute coronary syndrome and

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cardiovascular disease. In humans, platelets are central to the thrombosis process and uncontrolled platelet activation is the main factor in unstable coronary syndromes and acute MI. In addition to their role in thrombosis, platelets in various types of infections contribute significantly to the immune response. Platelets involve and form heterotypic aggregates with neutrophils during the initial stages of infection [46]. In Gram-positive bacterial infections, heterotypic aggregates between platelets and neutrophils are observed, with Gram-negative bacterial components and single-stranded virus infections such as encephalomyocarditis virus. Platelets have a critical adaptive immune function by forming platelet-bacterial complexes that slow bacterial clearance and increase immunity to antibacterial agents. Influenza virus is acknowledged as a virus receptor by cell-surface sialic acid. Influenza creates efficient infection in the epithelial cells of the lungs, which can lead to different levels of disease severity. In humans, Toll-like receptor 7 (TLR7) is one pattern recognition receptor which mediates the original reaction to ssRNA viral nucleic acids [47]. Once activated, TLR7 causes a cascade of signaling events leading to main interferon secretion and immune system activation. Platelets express TLR7 at any

specified moment, although not all platelets in a single express TLR7. Whether platelets contribute to the general activation of neutrophils through other TLRs (TLR7 which becomes activated by viral ligand) is unknown during influenza infection or if the connection between platelets and neutrophils during infection becomes pathologically imbalanced [48,49].

Although there have been many reports of influenza A H1N1 illness, including prevention, pathogenic mechanism, new drug research, virus identification and growth of vaccines, very few scientists have concentrated on the hematological markers of this worldwide pandemic disease. Therefore, it is essential to establish convenient hematologic diagnostic criteria as a reference [50,51].

### CONCLUSION

Initial diagnosis, treatment, and control of influenza are of excessive worth for the future. In this study, we reviewed effect of Influenza on cytopenia. We know that if the virus and the resulting antiviral reaction continue, the inflammatory feedback on the hematopoietic system becomes chronic. Therefore, it is essential to establish convenient hematologic diagnostic criteria as a reference.

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