The Research of Medical Science Review
ISSN: 3007-1208 & 3007-1216 Volume 3, Issue 12, 2025

HEMATOLOGICAL DISORDERS AND IMPAIRED WOUND HEALING: MECHANISMS, CLINICAL CHALLENGES, AND MANAGEMENT STRATEGIES

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DOI: https://doi.org/10.5281/zenodo.20457539

Keywords
Wound healing, Hematological disorders, Hypoxia, Angiogenesis, Platelets, Hemostasis.

Article History
Received: 24 October 2025
Accepted: 08 December 2025
Published: 22 December 2025

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Abstract

Wound healing is a complex, highly programmed biological cascade that includes four overlapping stages: hemostasis, inflammation, proliferation, and remodeling. It is based on the structural and functional integrity of blood components that include erythrocytes, leukocytes, platelets, and plasma proteins as the key elements that supply the important molecular machinery of tissue repair. This review will address how these molecular and cellular pathways are interrupted in the case of particular hematological conditions like anemias, coagulopathies, and the leukemic process, and highlight the therapeutic issues of these high-risk groups. Localized hypoxia observed in red blood cell disorders such as sickle cell disease and anemia prevents the production of collagen and angiogenesis. Infection becomes chronic, with a long-term period of inflammation, which is caused by dysfunctions of the immune system, including leukemia. Moreover, platelet and clotting diseases, such as thrombocytopenia and hemophilia, impair primary hemostasis and decrease the supply of essential growth factors, including PDGF and TGF-beta; thus, preventing the substitution of the healing phase with the proliferative one. In addition to cellular deficiencies, they frequently amplify oxidative stress and cytokine signaling dysregulation, which provides a highly hostile microenvironment and destroys the extracellular matrix. This multi-systemic interference implies the need to monitor blood viscosity and microcirculation specifically and provide high-quality clinical care that is based on the treatment of hematological pathology and the application of modern therapeutic techniques like platelet-rich plasma (PRP), recombinant growth factors, and stem cell therapy. Such disruptions can be important to understand to achieve better patient outcomes and prevent life-threatening complications.

INTRODUCTION

Wound healing is a multifaceted, dynamic, and natural biological process in which the body recovers damaged tissue, usually skin, and restores its structure and barrier properties. It is a highly programmed cascade that comprises four phases that are distinct but overlapping: hemostasis, inflammation, proliferation, and remodeling. Tissue repairing is mainly carried out by blood components, which provide the required cellular and molecular machinery

needed for each step. To instantly stop bleeding, platelets form clots, and to maintain a structural scaffold, plasma provides various proteins, including fibrinogen. At the same time, white blood cells protect against infection, balance inflammatory signaling, and red blood cells maintain the supply of oxygen and nutrients that meet the high metabolic needs of cellular regeneration (Arboix et al., 2016).

Hematological disorders represent a large spectrum of disorders that deal with the production, functioning, or quality of these essential blood cells and plasma proteins. Either inherited, like sickle cell disease or hemophilia, or obtained through nutritional deficiencies, chronic illness, or exposure to the environment, these conditions severely impair the repair system of the body. Disorders of red blood cells, mostly anemias, cause inadequate oxygen supply, which causes a hypoxic wound environment that halts collagen production and angiogenesis. The disorder of white blood cells, such as leukemia and cytopenias suppress the immune system, making it not strong enough to clear up the debris. This makes one more susceptible to chronic infection. In addition, platelet and clotting disorders disrupt primary hemostasis, resulting in prolonged bleeding, excessive hematoma generation, and inability to transition to the proliferative healing stage (Arboix et al., 2016; Echeverry & Dalton, 2018). The physiological effects of these blood disorders are not limited to the nutrient deficiency. Some hemolytic diseases result in excessive iron deposition in the tissues, which causes chronic inflammation and oxidative damage, making the wound difficult to close, especially in leg ulcers. Also, malignant conditions such as leukemia may impair microcirculation, which means that the body cannot create the new capillaries necessary to nourish regenerating tissue (Hoffman et al., 2006).

Although the role of blood components in wound healing has been documented, there is a substantial research void regarding the impact of hematological disorders on chronic wound healing. There is a frequent divide in the current literature between wound care and hematology, and no synthesized information exists on how general dysfunction of the blood governs localized cellular failure. This review will examine how particular hematological conditions, such as anemias, coagulopathies, and leukemic processes, disrupt the molecular and cellular processes of wound healing and emphasize the potential therapeutic issues in the high-risk population.

Physiology of Wound Healing

Wound healing is a complicated biological process through which the integrity of the tissue is restored once injured. It happens in four overlapping stages, as shown in Figure 01. These phases are coordinated and regulated, cellular and molecular activities that are mediated by extracellular signaling pathways. The platelets, neutrophils, macrophages, and fibroblasts are some of the most important cells that are involved in this process because they are essential in forming clots, immune defense, tissue regeneration, and the production of the extracellular matrix (Singh et al., 2017). Depending on the degree of tissue injury, wound healing can be either by primary or secondary intention. The healing process can be affected by several factors that may include malnutrition, hypoxia, immunosuppression, chronic diseases, and surgical trauma. Thus, the study of the physiological processes of wound healing is necessary to minimize complications and enhance patient outcomes for clinicians and researchers. Clinicians and other researchers should understand these physiological processes to reduce complications and maximize patient outcomes (Young & McNaught, 2011).

Hemostasis allows the cascade of enzymatic activations resulting in the platelet-fibrin polymer clot. This clot closes the damaged area, stops the additional bleeding as the tissue regeneration process proceeds. As the wound begins to heal, the plug gradually begins to remodel, and it breaks down during normal tissue restoration (Strodtbeck, 2001).

The second phase of wound healing is inflammation that takes place amid the initial 24 hours following injury and may take as long as 2

weeks in healthy wounds and much longer in non-healing chronic wound (Singh et al., 2017).

The granules of enzymes, histamine, and other active amines released by mast cells are the cause of the typical signs of redness, swelling, inflammation, and pain surrounding the wound. The most important cells during the inflammatory stage are the neutrophils, monocytes, and macrophages. They remove infection and debris in the wound and release soluble mediators, including proinflammatory cytokines and growth factors, that prepare the wound for the second stage of healing. Cytokines involved in the regulation of wound healing inflammation (Ellis et al., 2018).

This stage comprises cell proliferation, angiogenesis, and deposition of new extracellular matrix. and the development of granulation tissue - processes which are mediated by the release of cytokines and growth factors secreted by the cells within the wound site and by the activity of the local microenvironment, including pH and oxygen tension. Notably, the involvement of macrophages and polarization of phenotypes at this proliferative phase or at the injury response could have profound downstream remodeling consequences (Gonzalez et al., 2016).

The fibroblasts attach growth factors and also release more growth factors and extracellular matrix molecules. Growth factors stimulate both autocrine and paracrine signals to fibroblasts and invading capillaries. At the same time, those epithelial cells begin to proliferate in their inner parts, which are moving inwards along the edges of the wounds to cover the injury, supported by collagen. The collagen comes out in the form of strands parallel to the stress lines of the wound (Hosgood, 2006).

In this phase, there is inward proliferation of endothelial cells around the edges of the wound to enclose the wound, reinforced by collagen. Instead of having a basket weave look of the collagen, like in an unwounded dermis, the collagen looks like strands in the wound that are parallel to the stress lines of the wound (Singh et al., 2017). Such dissimilar construction is what causes the difference in the appearance between intact dermis and scar tissue. The regulation of collagen synthesis by the fibroblasts is due to the growth factors at the wound site, and there exists a fine balance between the rate of collagen synthesis and degradation (Reinke & Sorg, 2012).

The last phase of wound healing may require a period of up to 2 years and will lead to the formation of normal epithelium and scar tissue maturation. This stage is accompanied by a synthesis and degradation equilibrium as the collagen and the other proteins deposited in the wound get better organized. They will eventually re-acquire some sort of structure found in unwounded tissue. Nonetheless, injuries invariably do not heal equally well in terms of tissue (Čoma et al., 2021).

Role of Blood Components in Wound Healing

The basic components of the healing process are blood components, and each type of cell has a particular role in the restoration of tissues. Platelets arrive first, and they combine with each other to create a fibrin clot to prevent bleeding, but in the process, they release growth factors to indicate the beginning of repair (Golebiewska & Poole, 2015). The defense system of a body is provided by white blood cells (neutrophils and macrophages), which eliminate the debris and avoid infection as well as release cytokines, which control the transition between the healing stages (Olczyk et al., 2014). The red cells form the transport system of utmost importance and transport the oxygen and the nutrients that are needed to sustain the metabolism of cells and the formation of new tissue. Lastly, plasma proteins such as fibrinogen and albumin are the structural scaffold and medium of transport that are essential as the biochemical signals required to aid in the regeneration process are delivered to the wound site (Monroe & Hoffman, 2012).

One of the most basic functions of red blood cells (RBCs) is to carry oxygen to the injured tissues, which is the aerobic energy needed in all processes of repairing a cell. In the wound microclimate, the RBCs are constantly exposed to reactive oxygen species (ROS), discharged by activated neutrophils and macrophages.

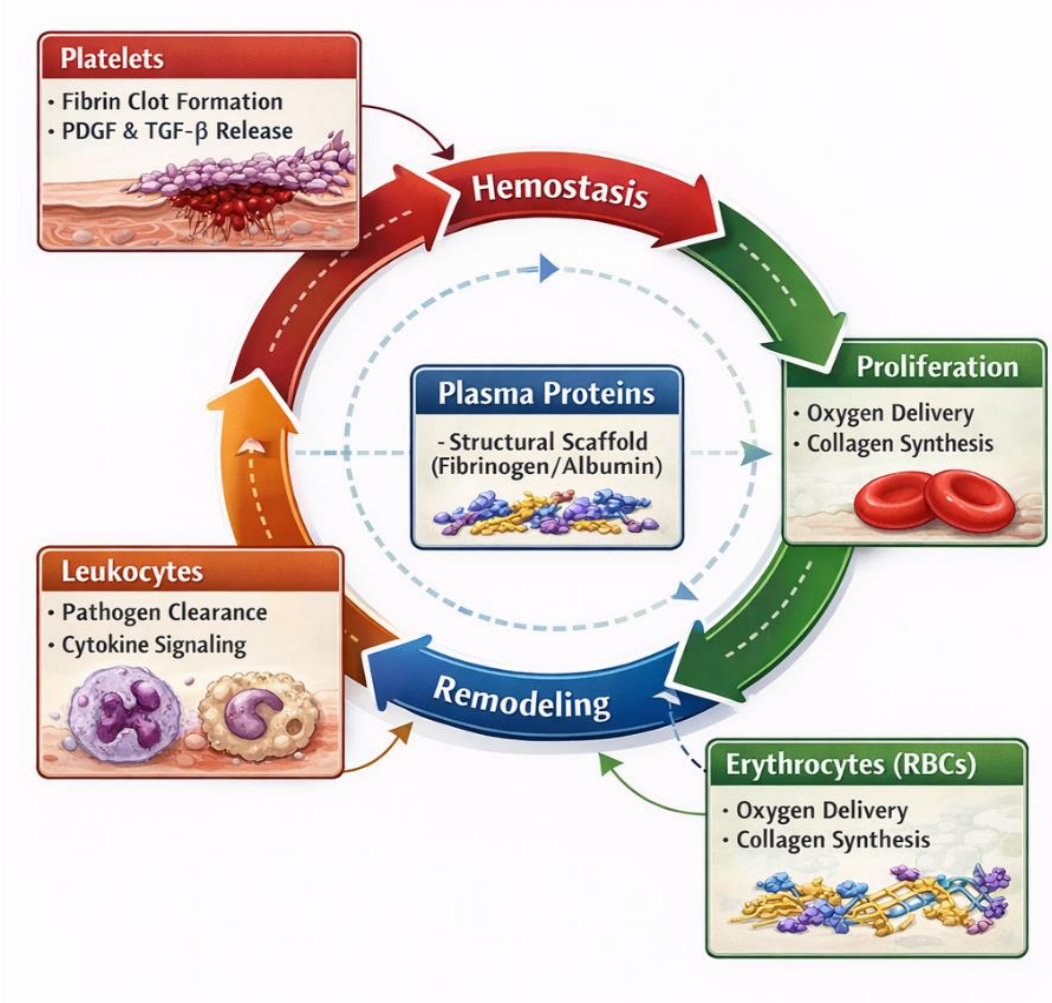

Figure 01. Phases of Wound Healing

In order to counteract the effects of oxidative stress and preserve their functionality, RBCs have a complex antioxidant system. These are enzymatic antioxidants like: superoxide dismutase, catalase (Gonzales et al., 1984), glutathione peroxidase, and peroxiredoxin-2 (PRDX-2), and non-enzymatic low molecular weight antioxidants like glutathione (Nakanishi et al., 2023). Though most of the ROS released into the plasma is neutralized prior to their ability to be absorbed by the cells, high uptake is observed in the microcirculation where RBCs are brought into proximity or into direct contact with the neutrophils, macrophages, and endothelial cells. This protective system greatly determines wound healing; any disturbance to the functioning of the RBC results in local hypoxia that greatly halts the collagen production and regeneration of the tissue (Reinke & Sorg, 2012).

The primary mediators of the inflammatory stage and the key to protection of the wound-site infection are white blood cells (WBCs). The function of these cells is to remove cellular debris, disarm pathogens, and produce the signaling molecules that regulate the shift between inflammation and tissue repair. In the initial phases of healing, neutrophils infiltrate the wound to offer the initial defense mechanism by phagocytosis and the production of antimicrobial enzymes. After that, macrophages become the conductors of the healing process; on the one hand, they proceed with the elimination of pathogens, and on the other, they release the

necessary number of cytokines and growth factors that initiate the proliferative stage of fibroblasts and endothelial cells. Moreover, platelets attract white blood cells to the harmed area by launching cell-cell interactions and reacting to platelet-emitted cues, which route the white blood cells through rolling, arrest, and transmigration out of the microcirculation into the injured tissue. Such a tightly regulated immune response is essential, and any impairment or failure of the activity of white blood cells, as is frequently observed in hematological malignancies or cytopenias, halts the healing process and leaves the wound extremely vulnerable to long-term infection (Humphry & Armstrong, 2022).

Platelets become major triggers of the healing cascade. When any cell or tissue is injured, platelets stick together to seal ruptured vessels and, at the same time, discharge a condensed cocktail of bioactive signaling molecules out of their granules. These factors comprise platelet-derived growth factor (PDGF), transforming growth factor -b (TGF -b), and insulin-like growth factor 1 (IGF -1), which are vital in stimulating cell growth and differentiation (Schär et al., 2015). Due to this regenerative ability, platelet derivatives have become essential therapeutic instruments in clinical and surgical practice, including oral and maxillofacial surgery, orthopedics, and dermatology (Nakanishi et al., 2023).The utility of platelets in the healing of tissues is not due to the activity of a specific growth factor alone, but to the complex interaction of factors that are present in platelet release. The given regenerative process is further enhanced by a complex cross-talk between platelet-secreted factors and the target cells of the wound, including fibroblasts and endothelial cells (Frelinger III et al., 2018). These different types of cells communicate with each other by direct cell-cell contact and soluble mediators exchange to facilitate the latter stages of healing. Although platelets are evidently the first responders, which precondition repair, the molecular control of these relations is an area of active investigation, where the successful regeneration process cannot take place without the impeccable balance of the hematological environment (Eppley et al., 2004).

Converting the platelet plug to a fibroin clot requires several coagulation factors, as they provide scaffolds for platelet plug stabilization. The activation of this process is stimulated by a dynamic interplay of platelets and the coagulation cascade in which individual platelets serve as specialized surfaces that execute pro-coagulant activity. The exposure of phosphatidylserine (PS) on the platelet membrane occurs because of the binding of key platelet receptors to particular ligands. This PS-exposing surface serves as a very potent catalyst, and procoagulant factors are bound to it, resulting in a tremendous increase in thrombin production at the injury site.

In a platelet-fibrin thrombus, the association is mutually supportive and self-affirming. Though the activated platelets cause a balance between the response of coagulants by release of numerous pro- and anticoagulant activities, the resultant thrombin gives a feedback mechanism that further activates more platelets. The result of this interaction is a localized heterogeneity in the clot, which is a dense vascular-oriented fibrin network. This fibrin network continues to be extended and then used to recruit more platelets and stabilize them so that the structural integrity of the hemostatic seal remains intact. It is this synergy between cellular platelets and soluble coagulation factors that finally causes the wound to switch between active bleeding and stasis, which prepares the wound before it enters the next phase of repair, which is the inflammatory and proliferative stages (Hethershaw et al., 2014).

Hematological Disorders Affecting Wound Healing

The hematological disorders are significant in the evaluation of wound healing efficiency since the erythrocytes, leukocytes, platelets, and coagulation factors in the blood are involved to control various stages of tissue repair. The healing of a wound is divided into four overlapping stages, which are hemostasis, inflammation, proliferation, and remodeling. These phases can be disrupted by any

abnormality in blood cells or clotting mechanisms, resulting in delays in the healing process, chronic wounds, or excessive bleeding. Anemia, thrombocytopenia, leukemia, hemophilia, and bone marrow failure disorders are known to have a significant negative effect on wound repair through the inhibition of oxygen, immune response, and clot formation, as shown in Fig 02 (Rodriguez-Merchan, 2012).

A weaker immunity and lower oxygen availability to the tissues make patients with hematological disorders more vulnerable to infections. Infection also retards the healing of wounds by increasing inflammation and destruction of regenerating tissues. In extreme cases, there is development of chronic wounds, especially in patients with leukemia, aplastic anemia, or other disorders of the bone marrow. Such zones as chronic wounds are typified by a continuity of inflammation, bacterial colonization, and tissue remodeling (Szpaderska et al., 2003).

Wound healing can also be affected by the therapies applied in the treatment of hematological diseases. The bone marrow may be suppressed by chemotherapy, radiotherapy, and immunosuppressive drugs, which result in anemia, leukopenia, and thrombocytopenia. These complications are also associated with treatment, which further deteriorates the healing process of the wounds by lowering immune capacities, platelet activity, and oxygenation of tissues. Thus, patients with hematological conditions should be carefully managed during surgery or wound management to avoid delayed healing and complications (Mohamed Rohani & Fisal, 2025).

Anemia is a hematological disease where there is a low level of red blood cells (RBCs) or the amount of hemoglobin in the blood. This is because hemoglobin is the one that delivers oxygen to the body tissues; consequently, anemia results in inadequate delivery of oxygen to the wound site. Various cellular activities that require oxygen to facilitate wound healing are fibroblast proliferation, collagen synthesis, angiogenesis, and epithelialization. When the oxygen level is low, then these mechanisms work slowly and hence the tissue regeneration is delayed, and the healing process takes long (Guo & DiPietro, 2010). Along with the inhibition of oxygen supply, anemia may impair the inflammatory period of wound healing. Neutrophils and macrophages need a sufficient amount of oxygen to form reactive oxygen species, which assist in destroying bacteria at the wound site. This antimicrobial defense mechanism is impaired in anemic patients because of the low oxygen levels, which predispose a patient to infection and further postpone wound healing. Hypoxia of tissues also makes the enzymes that help in collagen synthesis less active, and this makes the structural integrity of new tissue weak (Hunt & Hopf, 1997).

Moreover, anemia has a potential impact on hemostasis, changing the red blood cell/platelet contact. Decreased RBC mass may lessen platelet margination to the vascular endothelium that may hamper platelet adhesion and aggregation in the early phases of wound healing. This means that the patients who have intense anemia, in most cases, have sluggish clot formation and do not have their wounds closed quickly. Thus, treatment of anemia by measuring it with nutritional supplements or medically is relevant to enhance the delivery of oxygen in the blood and permit wound healing (Velnar et al., 2009).

Sickle cell disease is a genetic hematologic condition which is resulted by mutation of the β-globin gene, which causes the synthesis of a defective hemoglobin. The red blood cells undergo rigidity and attain the shape of a sickle in low oxygen conditions. These malignant cells are less pliant, and they are more likely to block small blood vessels, leading to the development of microvascular blockage and the decreased blood supply to the tissues. This compromised circulation contributes to the ischemia of the tissues and reduced oxygen transportation that will considerably slow down the wound healing process (Minniti et al., 2010).

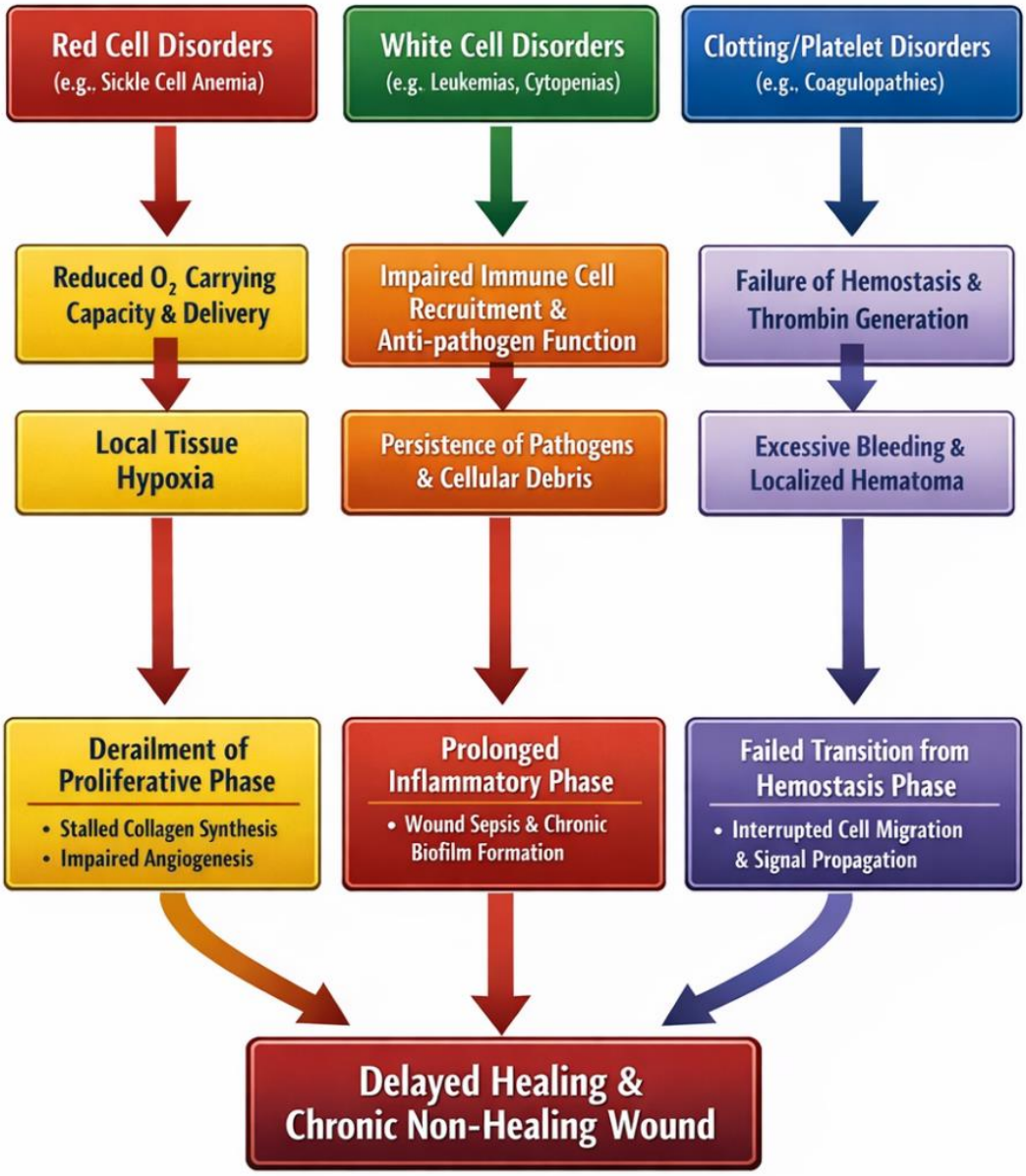

Figure 02. Hematological Disorders affecting Wound Healing

Chronic leg ulcers are one of the main complications that are observed with sickle cell disease. They are normally located around the ankle area and are brought about through recurring instances of Vaso-occlusion, chronic inflammation, and low oxygenation of tissues. Obstruction of the small blood vessels due to blockage results in the inability to supply sufficient nutrients and oxygen to the tissues involved, which retard the cell proliferation, collagen formation, and angiogenesis- critical wound repair processes. Moreover, hemolysis during sickle cell disease exposes free hemoglobin into the blood, which diminishes the nitric oxide concentrations and leads to dysfunction of the vascular system and poor recovery (Kato et al., 2018).

In addition to this, sickle cell disease patients are usually characterized by enduring inflammatory processes and predisposed to infection, both of which complicate the wound healing process even further. Repeated tissue damage, oxidative stress, and compromised immune response are also known to be associated with the chronic characteristics of leg ulcers in such patients. This has led to protracted, chronic wounds in patients with sickle cell disease, which have been hard to cure and necessitate the provision of holistic management with a focus on the management of the infection, enhanced blood flow, and supportive wound care measures (Guo & DiPietro, 2010).

Leukemia is a set of hematological malignancies, which can be defined as the uncontrolled growth of abnormal white blood cells in the peripheral blood and the bone marrow. These rogue blood cells disrupt the normal cellular production and functioning of the other blood cells, such as red blood cells, platelets, and normal immune cells. Consequently, leukemia has a serious impact on the wound healing process because it impairs immune responses, limits oxygen supply, and causes a higher risk of infection (Guo & DiPietro, 2010).

Immune system failure is one of the most significant impacts of leukemia on wound healing. In leukemia, there is sometimes an increase in the number of white blood cells, but they are usually immature and defective in their functions. As a result, they are unable to combat pathogens or get rid of rubbish in the wound area properly. Such a low immune response contributes to a high risk of bacterial infection and extends the inflammatory period of wound healing. The continued inflammation may be harmful to the tissues around and slow the process to the proliferative stage, essential in tissue regeneration (Velnar et al., 2009).

Another effect of leukemia is that it suppresses bone marrow and hence limits the production of normal red blood cells and platelets. Low concentration of red blood cells results in anemia and low oxygen supply to the wound, which decelerates the activity of the fibroblasts and collagen synthesis. Meanwhile, thrombocytopenia may weaken the ability of platelets to form clots and delay the process of bleeding in the early wound healing process (Velnar et al., 2009).

Moreover, chemotherapy and radiotherapy are some of the treatments that are used in the management of leukemia, and they may further impair the immune system and bone marrow functioning. These treatments lower the count of viable immune system cells and interfere with their capacity to regenerate tissues, thus exposing wounds to infection and healing at a slower pace. Hence, wounds take a long time to heal in leukemia patients, and they need close medical care when having surgery or recovering from an injury (Guo & DiPietro, 2010).

Thrombocytopenia is a hematological condition, which is the shortage of platelets in the blood. Platelets are essential in the hemostasis stage of wound healing because they develop the first platelet plug and activate the events that result in the formation of fibrin clots. This clot is also known to prevent bleeding but also serves as a temporary matrix to aid migration of the inflammatory cells and fibroblasts into the wound site. In case of the decrease in the number of platelets, there is a dysfunction in forming a stable clot, which results in longer bleeding and the retardation of the beginning of the wound healing process (Guo & DiPietro, 2010). Platelets also secrete various growth factors that are necessary in repairing the tissues, in addition to the role they play in forming clots. These growth factors cause the fibroblast proliferation, collagen synthesis, and angiogenesis when wound healing is in the proliferative phase. The lower count of platelets in thrombocytopenic patients causes a lower release of these growth factors and retards tissue regeneration and wound healing in the body (Velnar et al., 2009).

Moreover, insufficient platelet activity may extend the inflammatory stage and predispose to such complications as excessive bleeding and infection. Since platelets are also involved in immune response control at the wound bed, a deficiency of them can reduce the body's capability of the body to curb microbial infiltrations. Consequently, patients with thrombocytopenia could take longer to heal, and

they might need medical care to restore normal platelet counts and aid in proper wound healing (Szpaderska et al., 2005).Hemophilia is a hereditary bleeding disorder that is hereditary and is represented by the lack of selective clotting factors, the most prevalent being factor IX in Hemophilia B or factor VIII in Hemophilia A. These clotting factors are very important in the coagulation cascade, which stabilizes the platelet plug, and it becomes a fibrin clot in the hemostasis stage of wound healing. The lack or decreased activity of these factors in hemophilia patients causes the failure to form clots, which is followed by an increase in bleeding time after trauma or surgery. This may cause a delay in hemostasis, which may seriously disrupt the initial phases of wound healing (Encinas-Ullan et al., 2023).

Since the formation of clots is required to form a temporary matrix that cells can migrate on, disrupted coagulation during hemophilia reduces the inflammatory cell, fibroblasts, and endothelial cell response to the wound site. This leads to a slowing down in the development of the hemostatic stage to the inflammatory and proliferative stages of wound healing. Ongoing bleeding can also interfere with the development of granulation tissue that is required for the development and closure of a wound (Guo & DiPietro, 2010). Moreover, the frequent bleeding in hemophilic patients may lead to damage to tissues, inflammation, and predisposition to infection, which adversely influence the process of healing. Severe cases of wounds reopening because of an unstable clot formation may lead to chronic or recurrent bleeding. Proper control of hemophilia by providing the replacement therapy with clotting factors and adequate wound management is hence necessary to ensure normal healing of the wound and the avoidance of complications (Mannucci & Tuddenham, 2001).

Polycythemia is a blood condition that develops as a result of having an excess of red blood cells (RBCs) in the blood, therefore increasing the level of hematocrit and making the blood highly viscous. This disease can be divided into primary polycythemia, which is a condition due to abnormal growth of bone marrow, or secondary polycythemia, which is a reaction to chronic hypoxia or other pathological conditions. The presence of an excess amount of red blood cells causes the blood to become thicker, thereby slowing down the circulation and decreasing efficient circulation in the small capillaries (Guo & DiPietro, 2010).

Wound healing may be adversely influenced by impaired microcirculation, which is due to the elevated viscosity of blood. Correct circulation of blood is required to supply oxygen, nutrients, immune cells, and growth factors to the injured tissue. Slow blood circulation in polycythemia decreases the perfusion of tissues and supply of oxygen to the wound area, which may slow down the cell proliferation, collagen production, and angiogenesis. Ineffective circulation could also expose the patient to the risk of tissue ischemia and thrombosis, which worsens the healing process (Spivak, 2002). Lower oxygen and nutrient levels may increase the inflammatory process and delay the process of developing new blood vessels and granulation tissue. This results in the patient with polycythemia having late wound healing and increasing the likelihood of complications like thrombosis or tissue necrosis. The appropriate regulation of the level of hematocrit and careful observation of the circulation are thus necessary to promote the normal wound healing recovery in patients having this disorder (Velnar et al., 2009).

Molecular and Cellular Mechanisms in Wound Healing

Molecular signals and cellular activities interact in a complex manner to regulate wound healing and coordinate tissue repair. At physiological conditions, the healing process is characterized by overlapping stages that involve inflammatory cells, growth factors, cytokines, and extracellular matrix factors. These molecular and cellular pathways can be interrupted by a hematological disorder, resulting in delayed or poor wound healing. On the cellular level, a number of cell types are actively engaged in wound repair, and they include platelets, neutrophils, macrophages, fibroblasts, endothelial cells, and keratinocytes. Platelets trigger the healing process by clotting

down and releasing growth factors, including platelet-derived growth factor, transforming growth factor- 2, and vascular endothelial growth factor. These secretions draw in immune cells and trigger the growth and formation of fibroblasts and angiogenesis. During hematological diseases like thrombocytopenia or when the platelets are dysfunctional, the secretion of such growth factors is impaired, and thus, the process of tissue repair is slowed down, and the wound heals are at a slower pace (Guo & DiPietro, 2010). The neutrophils and macrophages are necessary during the inflammatory stage to eliminate bacteria, dead cells, and debris in the wound bed. These immune cells also produce cytokines and chemokines that control the functions of other cells that are involved in healing. These immune cells are either defective and fewer in number in diseases like leukemia or neutropenia, making the body susceptible to infection and extending the period of inflammation. Continuous inflammation may destroy the tissues around and cause the wound to stop at the proliferative stage (Eming et al., 2014).

The third wound healing stage consists of fibroblast activation, collagen deposition, and also angiogenesis. The fibroblasts produce extracellular matrix materials, including collagen and fibronectin, that offer structural support to the formation of new tissues. Meanwhile, the new blood vessels are created by the endothelial cells for efficient delivery of oxygen and nutrients to the injured tissue. Impaired angiogenesis and collagen production can be caused by hematological defects that lead to reduced oxygen delivery, e.g., anemia or vascular occlusion in sickle cell disease, which slows down tissue regeneration (Velnar et al., 2009). Signaling pathways stimulated by cytokines, growth factors, and reactive oxygen species at the molecular level control wound healing progression. Disturbance of these signaling with hematological disorders may result in the imbalance of tissue damage and repair, which eventually results in chronic wounds or slow healing (Singer & Clark, 1999). Hematological disorders have overall negative effects on wound healing because they interfere with several physiological processes. Red blood cells, platelets, and white blood cells have vital functions to play in the delivery of oxygen, the formation of clots, defense against immunity, and tissue building. In anemia, the decrease in the level of hemoglobin causes the hypoxia of tissues, deceleration of fibroblast proliferation, collagen development, and angiogenesis. The sickle cell disease results in microvascular blockage, which further restricts the supply of oxygen and nutrition, a factor that leads to chronic ulcers. Platelet disease, e.g., thrombocytopenia or hemophilia, compromises hemostasis and the discharge of growth factors like PDGF and TGF-b causing hindrance in the formation of clots and the onset of tissue repair. (Velnar et al., 2009).

Immunodeficiency due to leukemia and any other disorder that suppresses immune cells makes the microbial defense weak, the inflammatory process more prolonged, and the risk of infection is high. Disorders of blood viscosity, including polycythemia, cause disruption of microcirculation and disturbance of nutrients and oxygen delivery to the wound site. All these abnormalities disrupt all stages of wound healing and lead to delayed wound healing, chronic wounds, and increased risk of complications. In wound management, effective wound management should involve management of both the underlying hematological disorder and the environment of the local wound (Guo & DiPietro, 2010).

A condition of low oxygen supply in tissues is referred to as Hypoxia. Oxygen plays an essential role in wound healing as it facilitates several cellular and molecular events, which include fibroblast growth, collagen formation, angiogenesis, and defense against microbes. The low oxygen levels may be caused by systemic factors, including anemia or cardiovascular disease, or local ones, including inadequate microcirculation, infection, or tissue edema (Eming et al., 2014). Hypoxia is an example of a signaling stimulus observed in the early wound healing, which triggers hypoxia-inducible factors (HIFs), which are mainly HIF-1alpha. HIF-1 manages the expression of genes that relate to angiogenesis, energy metabolism, and

erythropoiesis, enabling the cells to adjust to low oxygenation scenarios. Controlled hypoxia can thus facilitate the process of angiogenesis, and the introduction of endothelial progenitor cells into the wound to assist in the formation of new vessels (Eming et al., 2014). Nevertheless, hypoxia may be harmful in the long-term or extreme. Prolonged low oxygen damages fibroblast activity and collagenation, impairs the immune system, and slows epithelialization. Reactive oxygen species (ROS) are also augmented under the conditions of hypoxia and may contribute to the disease burden in case of the failure to control them. In chronic wounds, including diabetic foot ulcers or ischemic ulcers, chronic hypoxia is one of the factors that lead to delayed healing, susceptibility to infections, and chronic inflammation (Schreml et al., 2010). Tissue hypoxia is usually worsened by hematological diseases. As an example, anemia decreases oxygen-carrying capacity, and sickle cell disease causes microvascular blockage, limiting the delivery of oxygen to tissues. Through elevated blood viscosity, polycythemia affects the circulation of blood, too, causing local hypoxia. The treatment approaches to hypoxia include the use of supplemental oxygen therapy, the hyperbaric oxygen approach, and the use of interventions to enhance the local perfusion (Velnar et al., 2009). Altogether, hypoxia is a two-sided sword in wound repair: short-term, hypoxic conditions induce an adaptive reaction and angiogenesis, but chronic or severe hypoxia suppresses cells and slows down the healing process. The balance between hypoxia-stimulating signaling and oxygen-sensitive cellular activities is important in order to maximize optimal wound management, especially in individuals with a hematological or vascular condition (Sen, 2009).

The development of new blood vessels out of the preexisting vessels is known as angiogenesis, which is a major part of the proliferative stage of wound healing. It promotes adequate delivery of oxygen and nutrients to regenerative tissues as well as an avenue for immune cells to the wound site. The growth factors that play the main role in the regulation of this process include vascular endothelial growth factor (VEGF), fibroblast growth factor (FGF), and platelet-derived growth factor (PDGF), and the local oxygen tension and extracellular interactions (Eming et al., 2014). Delayed or chronic wound healing has a significant role in impaired angiogenesis. It may be due to systemic, local tissue hypoxia, or as a result of hematologic disorders. As an illustration, in the case of anemia, the lack of oxygen-carrying capacity decreases the stimulus to the proliferation of endothelial cells and the growth of capillaries. Microvascular occlusion in sickle cell disease limits perfusion, and angiogenesis cannot occur normally. Thrombocytopenia and platelet dysfunction lower the supply of VEGF and other pro-angiogenic factors, and diabetes and chronic inflammation impair the endothelial cells, and remodeling of the matrix inhibits the formation of new vessels further (Guo & DiPietro, 2010). On the molecular level, the disturbed angiogenesis is linked to the disorganization of such signaling paths as HIF-1alpha, VEGF, and nitric oxide (NO). In physiological hypoxia, HIF-1alpha stabilizes and triggers the expression of VEGF to stimulate angiogenesis. Nonetheless, during protracted hypoxia or in patients with hematological disorders, HIF signaling may be impaired or defective, leading to poor growth of the vessels. This results in chronic tissue hypoxia, sluggish formation of granulation tissue, and retarded epithelialization. Chronic wounds are usually poorly vascularized, and capillaries are weak; because of this, the delivery of oxygen and nutrients is impaired, which leads to poor healing (Sen, 2009). Angiogenesis-restorative approaches to therapy are topical or systemic growth factor therapy, hyperbaric oxygen therapy, and cell-based therapies, e.g., endothelial progenitor cell transplantation. Correction of underlying hematological abnormalities, enhancement of local oxygenation, and the enhancement of VEGF signaling can greatly enhance angiogenesis and hasten wound repair (Falanga, 2005).

The initial but important process of wound healing is the inflammatory stage, where the immune cells, neutrophils, macrophages, and lymphocytes invade the wound and eliminate rubble, pathogens, and the tissue that has been

damaged. This stage, too, predetermines a microenvironment, high in cytokines, chemokines, and growth factors, which mediate further tissue repair. A balanced response in inflammation is mandatory: lack of inflammation may slow the pathogen clearance, but hyperinflammation or prolonged inflammation may result in tissue damage and hampering of healing (Guo & DiPietro, 2010).

This balance is usually interrupted by hematological disorders. In leukemia, the uncontrolled growth of erroneous white blood cells undermines the neutrophil and macrophage functions, which pollutes the immune system and extends the inflammatory process. Correspondingly, neutropenia causes a decrease in the number of immune cells and predisposes a person to infection and a delay in the onset of the proliferative stage. Conversely, chronic inflammatory-related disorders, including sickle cell disease, may trigger repeated tissue ischemia-reperfusion injury, leading to the sustained inflammatory signaling that destroys endothelial cells and extracellular matrix constituents (Eming et al., 2014). The molecular pathologic changes that define inflammatory imbalance include the dys-regulated production of cytokines. This disproportion extends the state of inflammatory response, exacerbates oxidative stress, and inhibits angiogenesis and granulation tissue formation, which slows down wound healing (Velnar et al., 2009). The management of the inflammatory imbalance includes the management of the underlying hematological disorder, management of the infections, and, in some situations, the therapies that regulate the activity of the cytokines. As an example, it is possible to supervise the activity of immune cells, and anti-inflammatory treatment in particular directions can be used to return the inflammatory environment to normal (Sen, 2009).

Oxidative stress arises when the production of reactive oxygen species (ROS) and the antioxidant defense mechanisms of the body are in imbalance. Activated neutrophils and macrophages are the major producers of ROS in wound healing during the inflammation stage. RMOS are signaling molecules at physiological levels that stimulate angiogenesis, fibroblast growth, and pathogen defense. Nonetheless, over-accumulation of ROS may cause cellular membrane, proteins, and DNA damage, thereby worsening tissue repair and extending the inflammatory period (Guo & DiPietro, 2010). Underlying hematological pathologies usually worsen oxidative stress in wounds. Indicatively, sickle cell disease is a repeated process of ischemia and reperfusion caused by the microvascular blockage resulting in high ROS production and leading to tissue chronic damage. Equally, anemia lowers the amount of oxygen supply, which ironically enhances the production of ROS because of the hypoxia-induced dysfunction of mitochondria. The antioxidant defenses may be weakened by leukemia and other diseases of the immune cells, which further enhances the oxidative damage at the wound site (Eming et al., 2014). Too much oxidative stress disrupts the major healing pathways, such as collagen deposition, endothelial cell activity, and migration of the keratinocytes. The continued ROS presence might be able to destroy extracellular matrix proteins and suppress angiogenesis, reducing the rate of granulation tissue and epithelialization. Pro-inflammatory cytokine synthesis is also enhanced by chronic oxidative stress and maintains an inflammatory microenvironment that is harmful and prevents wound healing (Encinas-Ullan et al., 2023). Antioxidant therapies (vitamin C, vitamin E, and N-acetylcysteine), topical pretreatment with ROS-scavenging agents, and increasing tissue perfusion through improving oxygen balance are all therapeutic interventions to counter oxidative stress. Redox balance, tissue damage reduction, and successful wound healing can be achieved by correcting the underlying hematological disorder and taking antioxidant interventions (Sen, 2009).

Growth factors are key signaling molecules that control the cellular processes involved in successful wound healing, such as cell proliferation, migration, angiogenesis, and extracellular matrix production. Vascular endothelial growth factor (VEGF), platelet-derived growth factor (PDGF), transforming

growth factor-beta (TGF-B), epidermal growth factor (EGF), and fibroblast growth factors (FGFs) are key growth factors that are involved in the process of tissue repair. Such molecules coordinate platelet, immune cell, fibroblast, endothelial cell, and keratinocyte interactions to respond to stimuli by progressing through the hemostasis, inflammatory, proliferative, and remodeling phases in a timely manner (Guo & DiPietro, 2010). Hematology disorders may considerably lower the level of growth factors and their action. The quantity of functional platelets is reduced in thrombocytopenia and platelet dysfunction, leading to reduced release of PDGF, TGF-B and VEGF at the wound site. On a similar note, in leukemia and other disorders that weaken the immune cells, the attraction of cytokine-producing cells is hampered, lowering the concentration of growth factors locally. Ischemia and vascular diseases also reduce tissue oxygenation, inhibiting upregulation of VEGF caused by hypoxia and disabling angiogenesis (Drews, 2003). The lowered activity of growth factors has several undesirable impacts on wound healing. The fibroblast growth is reduced, collagen deposition and extracellular matrix formation are blocked, and angiogenesis is retarded. Keratinocyte migration and epithelialization are also suppressed, further delaying wound healing and enhancing the chances of chronic wound formation. The relative impact of decreased growth factors, combined with hypoxia, oxidative stress, and inflammatory imbalance, provides an adverse wound environment, which slows tissue regeneration (Guo & DiPietro, 2010).

Clinical Implications

The hematological disorders are crucial in the clinical course of wound healing as the healing of damaged tissues depends on the sufficient supply of oxygen, the effective activity of immune cells, and appropriate coagulation. A change in the components of blood, including erythrocytes, leukocytes, and platelets, can interfere with a sequence of hemostasis, inflammation, proliferation, and remodeling, which leads to various clinical problems, like non-healing wounds, delayed healing, increased vulnerability to infections, and the development of non-healing ulcers. A significant clinical outcome is the development of chronic wounds, which do not follow the stages of the healing process and do not disappear in the short term (Wilkinson & Hardman, 2020). Prolonged inflammation, retarded cell proliferation, and disturbed extracellular matrix remodeling are the main features of chronic wounds. Recent research shows that systemic conditions of blood circulation and immune competence are an important cause of delayed tissue healing and chronic wound formation, which are a major burden on the healthcare systems in any country globally (Meznerics et al., 2022). Delayed wound healing is also another clinical implication. Fibroblast growth, collagen production, and angiogenesis all require adequate oxygenation and delivery of nutrients. These processes can be disrupted by hematological abnormalities, which decrease the oxygen-carrying capacity, or inappropriate platelet activity, which prolongs the inflammatory phase and retards tissue regeneration. These are impairments that normally take time to heal and also predispose to complications in the process of healing (Urao et al., 2022). Hematological dysfunction also exposes the patient to wound infection because of poor immune responses. Loss of leukocyte activity and inflammatory signaling can limit the body's ability to get rid of the pathogens invading it. Consequently, microorganisms are able to inhabit the surface of the wound, which results in the development of biofilms that further suppress the healing of the tissue and also lead to chronic infection. Those pathological processes can eventually result in non-healing ulcers, especially in those with generalized diseases or impaired hematologic conditions (Millán-Reyes et al., 2025). Non-healing ulcers are those that have sustained inflammation, microbial colonization, and impaired tissue remodeling, and this may necessitate advanced treatment modalities like growth factor therapies, platelet-based therapies, or special wound healing plans to promote healing (Uccioli et al., 2015). On the whole, hematological disorders have a profound effect

on wound healing, thus facilitating the development of chronic inflammation, infection, and tissue regeneration impairment, where early clinical treatment methods and specific therapeutic interventions warrant special attention (Zhou et al., 2025).

Therapeutic Approaches

Therapeutic management of wounds in patients with hematological disorders must include therapeutic interventions that can be used to restore normal hemostasis, enhance immune response, and tissue regeneration. Since blood abnormalities may disrupt oxygen delivery, coagulation, and cell repair, a number of modern and supportive treatment options are employed to enhance wound healing and prevent challenging problems, including chronic ulcers and infections, as shown in Figure 03. Blood transfusion refers to a significant treatment procedure for patients with critical hematologic defects like anemia or bleeding disorders. Red blood cell transfusion enhances oxygen carrying capacity and tissue perfusion necessary in the metabolism of cells, collagen synthesis, and angiogenesis during wound healing. Sufficient delivery of oxygen enhances the growth rate of fibroblasts and helps to form new blood vessels, which helps in repairing tissues and shortening the healing process (Abdelhakim & Ogawa, 2025).

Platelet-rich plasma is a regenerative treatment based on autologous blood, which includes a high concentration of platelets and bioactive growth factors. PRP also secretes a variety of cytokines and growth factors that promote cell growth, angiogenesis, and extracellular matrix. Clinical trials have proved that PRP is highly effective in the closure of wounds and shortening of the healing period with chronic ulcers and other hard-to-heal wounds (Pineda-Cortel et al., 2023).

Growth factor therapy is provided by placing recombinant growth factors topically or injected into the body where tissue repair is required in order to stimulate the biological functions of tissue repair. Keratinocyte migration, fibroblast activation, and collagen production are stimulated by molecules, e.g., epidermal growth factor, basic fibroblast growth factor, and PDGF. These treatments are useful in re-establishing the damaged healing condition that is typically found in chronic wounds and have been reported to promote re-epithelialization and tissue repair (Ahmed et al., 2025).

Stem cell therapies, especially the mesenchymal stem cells is a potential option in the treatment of non-healing and chronic wounds. MSCs facilitate the process of tissue healing by the paracrine signaling pathway, stimulating angiogenesis, and regulating inflammatory processes. Recent clinical reports indicated that stem cell therapy has a major effect on wound healing rates, vascularization, and decreases the healing duration of chronic wounds and ulcers (Sun et al., 2025).

Wound healing needs adequate nutritional support, especially in patients with hematological systemic or hematological disorders. Proteins, vitamins, zinc, and iron are some of the nutrients that are important in the formation of collagen, the immune system, and cell proliferation. (Jafarzadeh et al., 2024). All in all, all these therapeutic options, including blood transfusion and regenerative medicine, nutritional support, etc., are designed to restore the overall hematological imbalance and increase the biological processes involved in the effective wound repair.

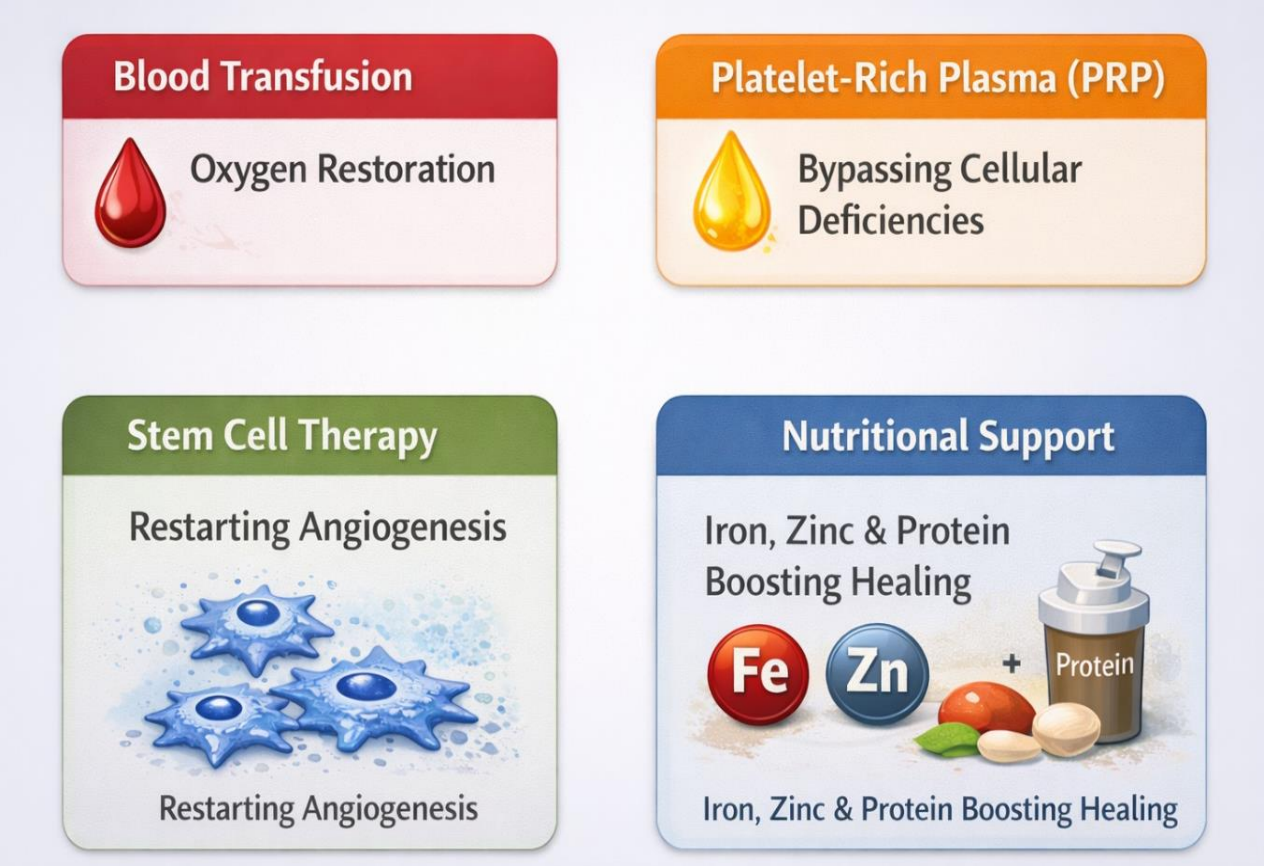

Figure 03. Modern Therapeutic Approaches in Wound Healing of Hematological Patients

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Conclusion

To sum up, hematological diseases have a significant adverse effect on the wound healing process because they disrupt the oxygen supply, the development of stable clots, and the immune system. The future therapeutic approaches will be personalized regenerative medicine, such as Targeted growth factor therapies like recombinant growth factors, utilized to preserve a low growth factor environment in the patient to inhibit complications and optimize wound healing, Advanced cell-based interventions like the platelet-derived mesenchymal stem cells (MSCs) applied to stimulate angiogenesis and control the inflammatory state of the tissue in chronic ulcers. The given review sheds light on the fact that deviation of any component of the blood, particularly the oxygen-carrying capacity of erythrocytes, the protective activity of white blood cells, or the regenerative communication of platelets, can halt the healing process and result in the inability to heal the wound. This leads to an increased risk of infections, excessive development of hematoma, and a delay in the process of tissue regeneration, which is more common clinically. Effective management should hence involve a combination of the management of the systemic blood condition along with local wound care expertise. The gap in the literature in relation to the integrated clinical treatment of chronic wounds in individuals with multifaceted hematological backgrounds should therefore be filled. The gap in the existing literature regarding hematology and wound care will inevitably require bridging to create a set of multidisciplinary procedures that reduce complications and provide optimal patient recovery.

REFERENCE

Abdelhakim, M., & Ogawa, R. (2025). Emerging Therapies in Chronic Wound Healing: Advances in Stem Cell Therapy, Growth Factor Modulation, Mechanical Strategies and Adjuvant Interventions. *Dermatology and Therapy*, *15*(12), 3533-3545.

Ahmed, A.-B., Thatcher, S., Khorsandi, J., Ahmed, Z., Lee, M., Jaouhari, A., Bond, B., & Merchant, A. (2025). Platelet-Rich Plasma (PRP) and Recombinant Growth Factor Therapies in Cutaneous Wound Healing: Mechanisms, Clinical Applications, and Future Directions. *Journal of clinical medicine*, *14*(23), 8583.

Arboix, A., Jiménez, C., Massons, J., Parra, O., & Besses, C. (2016). Hematological disorders: a commonly unrecognized cause of acute stroke. *Expert review of Hematology*, *9*(9), 891-901.

Čoma, M., Fröhlichová, L., Urban, L., Zajíček, R., Urban, T., Szabo, P., Novák, Š., Fetissov, V., Dvořánková, B., & Smetana Jr, K. (2021). Molecular changes underlying hypertrophic scarring following burns involve specific deregulations at all wound healing stages (inflammation, proliferation and maturation). *International Journal of Molecular Sciences*, *22*(2), 897.

Drews, R. E. (2003). Critical issues in hematology: anemia, thrombocytopenia, coagulopathy, and blood product transfusions in critically ill patients. *Clinics in chest medicine*, *24*(4), 607-622.

Echeverry, G., & Dalton, A. (2018). Hematologic disorders. *Anesthesiology Clinics*, *36*(4), 553-565.

Ellis, S., Lin, E. J., & Tartar, D. (2018). Immunology of wound healing. *Current dermatology reports*, *7*(4), 350-358.

Eming, S. A., Martin, P., & Tomic-Canic, M. (2014). Wound repair and regeneration: mechanisms, signaling, and translation. *Science translational medicine*, *6*(265), 265sr266-265sr266.

Encinas-Ullan, C. A., De la Corte-Rodriguez, H., Gomez-Cardero, P., & Rodriguez-Merchan, E. C. (2023). Orthopedic surgical procedures in people with hemophilia. *Blood Coagulation & Fibrinolysis*, *34*, S5-S8.

Eppley, B. L., Woodell, J. E., & Higgins, J. (2004). Platelet quantification and growth factor analysis from platelet-rich plasma: implications for wound healing. *Plastic and reconstructive surgery*, *114*(6), 1502-1508.

Falanga, V. (2005). Wound healing and its impairment in the diabetic foot. *The Lancet*, *366*(9498), 1736-1743.

Frelinger III, A. L., Gerrits, A. J., Neculaes, V. B., Gremmel, T., Torres, A. S., Caiafa, A., Carmichael, S. L., & Michelson, A. D. (2018). Tunable activation of therapeutic platelet-rich plasma by pulse electric field: Differential effects on clot formation, growth factor release, and platelet morphology. *PLoS One*, *13*(9), e0203557.

Golebiewska, E. M., & Poole, A. W. (2015). Platelet secretion: From haemostasis to wound healing and beyond. *Blood reviews*, *29*(3), 153-162.

Gonzalez, A. C. d. O., Costa, T. F., Andrade, Z. d. A., & Medrado, A. R. A. P. (2016). Wound healing-A literature review. *Anais brasileiros de dermatologia*, *91*, 614-620.

Guo, S. a., & DiPietro, L. A. (2010). Factors affecting wound healing. *Journal of dental research*, *89*(3), 219-229.

Hethershaw, E. L., La Corte, A. C., Duval, C., Ali, M., Grant, P. J., Ariëns, R. A., & Philippou, H. (2014). The effect of blood coagulation factor XIII on fibrin clot structure and fibrinolysis. *Journal of Thrombosis and Haemostasis*, *12*(2), 197-205.

Hoffman, M., Harger, A., Lenkowski, A., Hedner, U., Roberts, H. R., & Monroe, D. M. (2006). Cutaneous wound healing is impaired in hemophilia B. *Blood*, *108*(9), 3053-3060.

Hosgood, G. (2006). Stages of wound healing and their clinical relevance. *Veterinary Clinics: Small Animal Practice*, *36*(4), 667-685.

Humphry, E., & Armstrong, C. E. (2022). Physiology of red and white blood cells. *Anaesthesia & Intensive Care Medicine*, *23*(2), 118-122.

Hunt, T. K., & Hopf, H. W. (1997). Wound healing and wound infection: what surgeons and anesthesiologists can do. *Surgical Clinics of North America*, *77*(3), 587-606.

Jafarzadeh, A., PourMohammad, A., & Goodarzi, A. (2024). A systematic review of the efficacy, safety and satisfaction of regenerative medicine treatments, including platelet-rich plasma, stromal vascular fraction and stem cell-conditioned medium for hypertrophic scars and keloids. *International wound journal*, *21*(4), e14557.

Kato, G. J., Piel, F. B., Reid, C. D., Gaston, M. H., Ohene-Frempong, K., Krishnamurti, L., Smith, W. R., Panepinto, J. A., Weatherall, D. J., & Costa, F. F. (2018). Sickle cell disease. *Nature reviews Disease primers*, *4*(1), 18010.

Mannucci, P. M., & Tuddenham, E. G. (2001). The hemophilias—from royal genes to gene therapy. *New England Journal of Medicine*, *344*(23), 1773-1779.

Meznerics, F. A., Fehervari, P., Dembrovszky, F., Kovacs, K. D., Kemeny, L. V., Csupor, D., Hegyi, P., & Bánvölgyi, A. (2022). Platelet-rich plasma in chronic wound management: a systematic review and meta-analysis of randomized clinical trials. *Journal of clinical medicine*, *11*(24), 7532.

Millán-Reyes, M. J., Afanador-Restrepo, D. F., Carcelén-Fraile, M. d. C., Aibar-Almazán, A., Sánchez-Alcalá, M., Cano-Sánchez, J., Mesas-Aróstegui, M. A., & Castellote-Caballero, Y. (2025). Reducing infections and improving healing in complex wounds: a systematic review and meta-analysis. *Journal of clinical medicine*, *14*(9), 3237.

Minniti, C. P., Eckman, J., Sebastiani, P., Steinberg, M. H., & Ballas, S. K. (2010). Leg ulcers in sickle cell disease. *American journal of hematology*, *85*(10), 831.

Mohamed Rohani, M., & Fisal, A. A. (2025). The dental management of patients with common hematological disorders and bleeding tendency. *Special Care in Dentistry*, *45*(4), e70090.

Monroe, D. M., & Hoffman, M. (2012). The clotting system–a major player in wound healing. *Haemophilia*, *18*, 11-16.

Nakanishi, Y., Matsushita, T., Nagai, K., Araki, D., Hoshino, Y., & Kuroda, R. (2023). Fibrin clot and Leukocyte-rich platelet-rich fibrin show similar release kinetics and amount of growth factors: A pilot study. *Journal of Orthopaedic Surgery and Research*, *18*(1), 238.

Olczyk, P., Mencner, Ł., & Komosinska-Vassev, K. (2014). The role of the extracellular matrix components in cutaneous wound healing. *BioMed research international*, *2014*(1), 747584.

Pineda-Cortel, M. R., Suarez, C., Cabrera, J.-T., Daya, M., Bernardo-Bueno, M. M., Vergara, R. C., & Villavieja, A. (2023). Biotherapeutic applications of platelet-rich plasma in regenerative medicine. *Tissue Engineering and Regenerative Medicine*, *20*(6), 811-828.

Reinke, J., & Sorg, H. (2012). Wound repair and regeneration. *European surgical research*, *49*(1), 35-43.

Rodriguez-Merchan, E. (2012). Surgical wound healing in bleeding disorders. *Haemophilia*, *18*(4), 487-490.

Schär, M. O., Diaz-Romero, J., Kohl, S., Zumstein, M. A., & Nesic, D. (2015). Platelet-rich concentrates differentially release growth factors and induce cell migration in vitro. *Clinical Orthopaedics and Related Research®*, *473*(5), 1635-1643.

Schreml, S., Szeimies, R., Prantl, L., Karrer, S., Landthaler, M., & Babilas, P. (2010). Oxygen in acute and chronic wound healing. *British Journal of Dermatology*, *163*(2), 257-268.

Sen, C. K. (2009). Wound healing essentials: let there be oxygen. *Wound repair and regeneration*, *17*(1), 1-18.

Singer, A. J., & Clark, R. A. (1999). Cutaneous wound healing. *New England Journal of Medicine*, *341*(10), 738-746.

Singh, S., Young, A., & McNaught, C.-E. (2017). The physiology of wound healing. *Surgery (Oxford)*, *35*(9), 473-477.

Spivak, J. L. (2002). Polycythemia vera: myths, mechanisms, and management. *Blood, The Journal of the American Society of Hematology*, *100*(13), 4272-4290.

Strodtbeck, F. (2001). Physiology of wound healing. *Newborn and infant nursing reviews*, *1*(1), 43-52.

Sun, Y., Zhu, M., & Qiu, L. (2025). Efficacy of mesenchymal stem cells and platelet-rich plasma therapies on wound healing: A Systematic Review and meta-analysis. *Regenerative therapy*, *30*, 75-91.

Szpaderska, A., Walsh, C., Steinberg, M., & DiPietro, L. (2005). Distinct patterns of angiogenesis in oral and skin wounds. *Journal of dental research*, *84*(4), 309-314.

Szpaderska, A. M., Egozi, E. I., Gamelli, R. L., & DiPietro, L. A. (2003). The effect of thrombocytopenia on dermal wound healing. *Journal of Investigative Dermatology*, *120*(6), 1130-1137.

Uccioli, L., Izzo, V., Meloni, M., Vainieri, E., Ruotolo, V., & Giurato, L. (2015). Non-healing foot ulcers in diabetic patients: general and local interfering conditions and management options with advanced wound dressings. *Journal of wound care*, *24*(Sup4b), 35-42.

Urao, N., Liu, J., Takahashi, K., & Ganesh, G. (2022). Hematopoietic stem cells in wound healing response. *Advances in Wound Care*, *11*(11), 598-621.

Velnar, T., Bailey, T., & Smrkolj, V. (2009). The wound healing process: an overview of the cellular and molecular mechanisms. *Journal of international medical research*, *37*(5), 1528-1542.

Wilkinson, H. N., & Hardman, M. J. (2020). Wound healing: cellular mechanisms and pathological outcomes. *Open biology*, *10*(9).

Young, A., & McNaught, C.-E. (2011). The physiology of wound healing. *Surgery (Oxford)*, *29*(10), 475-479.

Zhou, H., Kong, B., Cheng, Y., Meng, S., Dong, H., Qi, C., Kong, T., Zhao, Y., & Liu, Z. (2025). Ultrafast Self-Gelling, Adhesive, Anti-Bacterial Coacervate-Based Powders for Enhanced Hemostasis and Wound Healing. *Small*, *21*(3), 2409164.

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