Paparella: Volume I: Basic Sciences and Related Principles

Section 7: General Surgical Principles:

Chapter 32: Wound Healing

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Wound repair and tissue regeneration are processes fundamental to life. Without successful wound repair, surgery of any type could not be done. A century ago, surgeons had no choice but to accept open, infected wounds. Since Lister's application of antisepsis, knowledge of the mechanisms and methods of wound repair have grown to the point where the healing wound is the expected norm rather than the extraordinary outcome. The surgeon, regardless of his specialty, who has a fundamental knowledge of the healing process and the various factors that affect it, is able to influence tissue repair to the ultimate benefit of the patient.

Until recently, the physician could only provide a suitable macroenvironment to support wound repair. Recent advances in knowledge about human growth factors now make it possible to affect and probably to control the process, rate, and eventually the character of the healing wound.

The Nature of the Healing Wound

The regulation of repair can be divided into three distinct phases: biochemical activation, cellular activation, and cellular response. Biochemical activation involves the translation of mechanical injury into biochemical signals that can be understood by the body. The trigger that starts the cascades in action is Hageman's factor. When injury causes disruption of the microcirculation, plasma comes in contact with tissue proteins and the basement membrane. This contact causes activation of Hageman's factor and circulating platelets. Activated Hageman's factor, in turn, activates four cascades that amplify the initial response and, consequently, result in cellular activation. The clotting cascade is activated, producing fibrin, to aid in hemostasis, and thrombin, which produces maximal release of platelet alpha granules. The complement cascade produces many biologically active molecules, with C5a being the most important in wound repair. C5a is a potent chemoattractant for neutrophils and monocytes. The kinin cascade results in the production of bradykinin, which causes microvascular vasodilation at the wound periphery, and the activation of plasminogen produces plasmin, which degrades fibrin. Fibrin degradation products, which result from the enzymatic breakdown of fibrin, are themselves biologically active molecules that can cause monocyte migration and vasodilation.

The biochemical amplification stage results in the influx of cells into the newly created wound. The initial cellular response to wounding involves neutrophils, monocytes, and platelets. Neutrophils are the cells that are responsible for debridement in the wound response. They have no known regulatory activity but provide the main host defense activity in the wound. Platelets accumulate at the wound site in response to the initial injury. In response to thrombin, platelets release their alpha granules, which contain locally acting growth factors. These growth factors signal the local mesenchymal and epidermal cells to move, to divide,

and to increase their synthesis of collagen and glycosaminoglycans. This initial release of growth factors by platelets is thought to be the initiator of the actual reparative response. Following the arrival of neutrophils into the newly created wound are monocytes, which then become wound macrophages. These cells perform many functions in the wound. They assist the neutrophils in host defense and produce many of the same growth factors that are initially released by the platelets. They are though to be the source of locally acting growth factors throughout repair until the wound is healed.

There are five locally acting platelet-derived factors that are presently thought to contribute to wound repair. These are platelet-derived growth factor (PDGF), platelet-derived angiogenesis factor (PDAF), platelet-derived epidermal growth factor (PDEGF), transforming growth factor beta (TGF-B), and platelet factor 4 (PF-4). PDGF is a mitogen and chemoattractant for fibroblasts and smooth muscle cells. At very low concentrations (0.5 to 1.0 nanog/mL), it causes fibroblast migration, and at slightly higher concentrations, (2 to 5 nanog/mL), it causes fibroblast mitosis. Macrophages also produce a growth factor with identical activity. PDAF is nonmitogenic chemoattractant for capillary endothelial cells, which is recovered from thrombin-released platelets. Its identity is not presently known. It produces a dose-dependent capillary endothelial cell migration and inflammation-free angiogenesis in the rabbit corneal assay. Macrophages also produce a similar factor. PDEGF causes migration and mitosis of epidermal cells with very similar biologic activity to salivary gland EGF. TGF-B is released from platelet alpha granules and has many known functions. It is a very potent chemoattractant for monocytes, it inhibits endothelial cell mitosis, and at certain concentrations, inhibits fibroblast mitosis. However, it stimulates collagen and glycosaminoglycan synthesis by fibroblasts. Finally, PF-4 is a chemoattractant for neutrophils and may be partially responsible for the initial influx of neutrophils into the wound space.

These growth factors can produce all the known biologic activity that is required to produce granulation tissue and reepithelialization. Their activity has been demonstrated in cellular assay systems and various animal models of wound healing and repair.

Cellular Components of the Wound

Polymorphonuclear Leukocytes and Lymphocytes

The process of normal granulation tissue formation and epithelialization can proceed uninhibited in the face of major reductions in the populations of neutrophils and lymphocytes. However, the wound cannot successfully resist infection without these two cell types, and an infected wound does not heal. The lymphocytes act in conjunction with macrophages to mount an immune response against bacteria and foreign substances.

In the wound, neutrophils phagocytize and kill bacteria. Their bacterial killing relies on several biochemical mechanisms. One of the most important mechanisms is the formation of active reduction products of oxygen. The active substances formed from molecular oxygen are bacteriocidal. Low oxygen tensions found in the wound space in healthy patients can hamper the neutrophil's killing activity. Changing the oxygen tension in the wound is possible by ensuring adequate perfusion and oxygenation. This factor has a profound effect on the size of infectious necrosis in animal experimental models.

Platelets and Macrophages

Platelets and macrophages, as discussed earlier, are critically important to wound repair. Platelets appear in the wound immediately after wounding. Their dual role in coagulation and release of growth factors is well documented in cellular, animal, and human studies.

Macrophages are also critical to successful repair. They enter the wound from the second day after wounding and are present until the reparative process is complete. Macrophages release growth factors similar to those released from platelets. In contrast to the platelet, which stores the growth factors in its alpha granules, the macrophages produces the growth factors in response to local biochemical and environmental stimuli. This regulation of growth factor release is emerging as a possible repair control mechanism.

The macrophage produces angiogenesis factors which generate capillary growth. Animal and cellular experiments show that the macrophage is sensitive to its local oxygen microenvironment. When placed in an oxygen environment similar to that found in the healing wound space, the unstimulated macrophage produces angiogenesis factor. When the oxygen tension is raised to levels found in connective tissue, the production of angiogenesis factor ceases. In addition, the macrophage produces angiogenesis factor in response to other immunologic and biochemical messages. Bacterial endotoxin is one such mediator that can stimulate the macrophage to produce angiogenesis factors. Other mediators such as interferon, TGF-B, and interleukin 2 are currently under investigation. As we understand the control mechanisms that regulate the production of growth factors, we eventually will understand the mechanisms that regulate granulation tissue formation and epithelialization.

Capillary Endothelial Cells

Neovascularization occurs in response to angiogenesis factors from platelets and macrophages. The process of angiogenesis consists of the sprouting of endothelial cells from existing venules and capillaries near the wound edge. The capillaries initially respond to chemoattractants, which cause them to migrate toward the source of the angiogenesis factor. Then, back from the leading endothelial cell, mitosis occurs in a process that elongates the new capillary bud. This mitosis is also under the control of growth factors. Fibroblast growth factor, produced by endothelial cells themselves, is probably responsible for the division of endothelial cells, and the angiogenesis factors from platelets and macrophages have been shown to be potent chemoattractants for capillary endothelium without having any mitogenic effect.

New capillary endothelium produces enzymes that degrade the fibrin and collagen in the wound space. Basement membranes are incomplete initially in the new capillary buds, and this factor may account for the fragility of these new vessels.

Three major patterns of angiogenesis emerge and help to explain the three forms of healing. Primary repair occurs when the two wound edges are coapted in close proximity. The capillary buds can connect with each other across the wound space. This process occurs primarily in bone repair when precisely cut bones are approximated, but it rarely occurs clinically. Secondary repair occurs when soft tissue wounds are approximated by sutures or

when the wound is left open. Granulation tissue is produced to fill the wound space, which is then covered by epithelium. The third type of angiogenesis is the joining of the old vasculature of the wound. This process can be easily viewed clinically as one watches the skin graft change from the cadaveric white color to the pink of a well-vascularized skin graft.

Fibroblasts

This large protein-synthesizing cell forms the backbone of the reparative process. The strength of the wound is dependent on the formation and remodelling of new collagen. These collagen molecules are monomers of a long, thin triple helix that polymerize after secretion into the extracellular space and form strong insoluble fibers that bridge the wound and support growing vessels.

Fibroblasts appear to originate from primitive precursor cells in the tissue surrounding the wound. This hardy cells functions best in a somewhat stressful environment, i.e. a slightly acidic reducing environment with a high concentration of lactate. Some fibroblasts are similar to smooth muscle cells, have myofibrils, and are called myofibroblasts. Functionally, they may be important in wound contraction.

The fibroblast is metabolically active. It synthesizes collagen, mucopolysaccharides, and elastin and has enzymes directed toward glycolytic metabolism and the Krebs' cycle as well. These metabolic processes require B vitamins, ascorbate, oxygen, amino acids, and trace metals such as zinc, iron, and copper.

Components of Repair

The important components of healing are (1) epithelialization, (2) connective tissue regeneration and repair (granulation tissue formation), and (3) wound contraction. All tissue repair includes one or more of these processes. Connective tissue repair includes not only collagen and mucopolysaccharide (currently named proteoglycans) synthesis but also vascular and lymphatic regeneration. Regeneration or hyperplasia of the existing cells of an organ may also occur to compensate for the loss of cellular function in the damaged area. Repair of damage to the liver and the kidney is the prime example of these processes in humans.

Collagen Synthesis and Lysis

Collagen is the principal structural component of repair. It is a triple helix of three long amino acid chains that contain approximately 1,000 amino acids each. There is a length-to-width ratio of about 200:1. This protein contains hydroxyproline and hydroxylysine, which are found in few other proteins. A few unique steps in its synthesis are noteworthy. Hydroxyproline and hydroxylysine can be formed only after proline and lysine have been incorporated into the peptide chain. This hydroxylation is accomplished by specific enzymes, together with molecular or dissolved oxygen and alpha-ketoglutarate, ferrous iron, and ascorbic acid as required cofactors. Lactate has been shown to stimulate the appearance of prolyl hydroxylase. Without the hydroxylation of proline, collagen cannot leave the cell. By the time that the collagen molecule, now called pro-collagen, has been transported to the extracellular space, it has assumed a superhelical formation and is then ready to polymerize and form fibrils.

The molecules polymerize through ionic and covalent crosslinks. Intramolecular and intermolecular binding are enhanced by crosslinks between lysine groups after oxidation of the epsilon-amino group to an aldehyde by lysyl oxidase. These bonds give collagen its leathery strength. Crosslinking can be inhibited by beta-amino-proprionitrile administration, which causes weak connective tissues and poor healing. This is the cause of a disease called lathyrism, which occurs in animals fed sweet peas (the natural source of beta-amino-proprionitrile).

New collagen formation begins as early as the second day after wounding, and the peak rate of synthesis in primarily closed wounds occurs between days 5 and 7. Active new collagen formation lasts from 6 months to 1 year. Why, then, do not all scars become enlarged, bulky, or hypertrophic? The fact that they do not is due to a dynamic struggle within the wound in which collagen lysis is occurring at the same time as collagen synthesis, and a balance must be struck between the two processes. The principal enzyme participating in collagen lysis is collagenase, which is produced by inflammatory cells and epidermal cells. Synthesis of collagen is complex and requires large amounts of nutrition, energy, and oxygen. Lysis is less energy dependent, seemingly requires no oxygen, and usually continues although synthesis may be blocked. Obviously, numerous factors can sway the balance in favor of lysis and poor repair.

Within this balance of synthesis and lysis, which leads to the integrated replacement of the collagenase structure of the wound, the wound acquires a normal blood supply and gains strength. Mechanical stresses of normal activity influence the collagenous structure. The tensile strength of a primarily closed skin wound reaches about 20 per cent of normal at 7 days and about 50 per cent of normal in 3 to 4 weeks. The remodeling process is not perfect, and neither the tensile strength nor the elasticity of the scar tissue ever fully regains its normal status. A sign that the healing process is continuing properly is the formation of a 1-cm wide induration (healing ridge) after 7 to 9 days. When the surgeon can feel this ridge throughout the length of the wound, it can be concluded that dehiscence is highly unlikely.

Proteoglycans (Mucopolysaccharides)

The ground substance is composed of glysoaminoglycans, which are synthesized by the fibroblasts. These combine with proteins to form proteoglycans, which appear to play a role in attaining the proper environment for collagen polymerization and may aid collagen fiber formation.

Epithelialization

Epithelial cells at the edge of a wound proliferate and migrate. In primary healing, mitoses appear in the basal layer of the squamous epithelium a few days after the wounding, and the epithelial cells advance across the wound surface and into a favorable plane between dead and living tissue at the edge of the wound. The new epithelium is usually thinner and less pigmented than normal. In an open wound that is kept moist, well oxygenated, and viable on its surface by dressing with Teflon film or microporous tape, epithelialization is rapid, with cells migrating over the surface of the wound. A wound that has been allowed to dry epithelializes by cells burrowing under the eschar and slowly separating the mobile from the immobile scar tissue. This is a slow process that consumes more energy than does surface

migration. For example, epithelialization is more rapid under an intact blister than it is after the blister has been debrided and the base of the blister allowed to dry.

Wound Contraction

Contraction is a rather mysterious process by which open wounds on certain portions of the body spontaneously shrink and close. By migration of the surrounding skin into and across the defect, the wound actually shrinks. Contraction differs from contracture, which is loss of joint motion from shrinking scar tissue. Contraction involves the entire thickness of a wound and, in humans, becomes an especially prominent part of the healing of wounds in the back of the neck and in the trunk and face, where skin is loose. Wounds of the extremities contract less well and depend more on connective tissue formation and epithelialization for eventual healing. The contractile force has been measured and is compatible with forces exerted by smooth muscle cells. This force is independent of collagen formation and other measurable biochemical components of the wound. It apparently depends on the contractile force of the "myofibroblast", a fibroblast that contains myofibrils indistinguishable from those of smooth muscle. These cells contract under the same chemical signals as smooth muscle cells. The wise clinician often relies on contraction to close wounds in favorable areas so that large defects may heal with small scars. If skin grafts are prematurely placed on a rapidly contracting wound, contraction may be inhibited, and a large skin graft scar may result, although previously the wound was destined to become covered by normal skin if left to heal naturally. The literature is confusing about this point. Experience with patients strongly suggests that skin grafts inhibit but do not abolish contraction.

Healing of Special Tissues

The pattern of connective tissue healing is similar in all areas of the body, differing only in rate and extent. More specialized tissues heal in different ways.

Nerves

The distal portions of wounded peripheral nerves degenerate, whereas neural sheaths reanastomose. The axon then regenerates through the healed sheaths, advancing as much as several centimeters per week. This explains the delayed but often remarkable reappearance of function in the end-organ. Unfortunately, the individual nerve sheath is unable to seek out and rejoin its original distal end. Instead, it heals to the nearest distal axon sheath. Therefore, regenerating motor fibers, for example, may find themselves filling sensory neural sheaths, growing uselessly into sensory end-organs. The best regeneration, therefore, is found in the "purer" peripheral nerves.

Intestines

Intestinal healing has not been well studied. The rate of healing varies from one portion of the intestine to the other. Clinical experience has shown that wounds in the colon and in the esophagus are the most precarious of all. Usually the intestinal anastomosis regains strength rapidly; by 1 week to 10 days, it is even stronger than normal intestine. The colon and esophagus contain little collagen. Since the normal reaction to injury includes collagen lysis, there is a critical period, usually from the fourth to ninth day after operation, when

anastomoses are likely to leak. The balance between collagen synthesis and lysis is shown. Any event that delays synthesis or that exaggerates lysis is likely to increase the risk of rupture. Meticulous and gentle surgical technique can ensure better healing by reducing tissue injury. Furthermore, trauma, even when it is distant from the wound, tends to excite a collagenolytic reaction in the nearby intestine. Because of this loss of tissue, perforation is as likely to occur near an anastomosis as in the anastomosis itself. The presence of local infection, which often occurs near esophageal or colon anastomoses, increase the likelihood of perforation.

Bone

The healing of bone depends upon the synthesis of collagen. However, bone healing includes a unique process, i.e. the condensation of hydroxyapatite crystals on specific points in the collagen fiber. A long period of time is required for full calcification and attainment of final strength. The time lapse, however, is in the same range as that experimentally noted for the full development of fibrous tissue strength in soft tissue wounds. The clinical importance of calcification is so vital that the impression is gained that bone healing is protracted. Many textbooks give detailed descriptions of bone healing, and it is not discussed in further detail here.

Skin Grafts

The skin graft is a rather special tissue. The circulation to the graft is totally interrupted. A remarkable inosculation of the small vessels of the host to those of the graft occur during the critical three or four days that follow placement of the graft. When enough vessels have joined, circulation to the skin graft is reestablished, and the graft survives. Clinically, the graft is cadaveric for 1 or 2 days. It then becomes purple as red cells find their way into graft vessels. As these cells find egress and their time spent in the graft diminishes, the graft becomes pink. After reestablishment of the circulation, the immune mechanisms can now attack a homograft. In the accelerated form, this process usually occurs between 4 and 10 days, indicating that circulation is relatively completed at that time. The collagen of an autograft eventually is remodeled, and a competent circulation is permanently attained.

Suture Materials

The properties of the ideal suture material are difficult to determine. Wire is one of the most inert suture materials and maintains its tensile strength for a long time. However, wire sutures are painful and sometimes are difficult to tie. Plastic sutures often come untied, and some plastic fibers are so inert that they are not fixed in tissue. Silk is an animal protein and is nearly inert in human tissue. It loses its strength; i.e. it is "absorbable" over a long period of time, making it unsatisfactory for suturing arterial prostheses or cardiac valves. Silk sutures, because of their irregularity and multifiber construction, are a have for bacteria. On occasion, silk sutures form a nidus for small abscesses, which migrate to the surface and are discharged. Many plastic fibers (especially in larger sizes) will follow the same path, despite common belief to the contrary.

Catgut, which is made from the submucosa of sheep intestine, eventually resorbs, but the resorption time is variable. Catgut provokes a considerable inflammatory reaction. Some

of what we call "catgut" is now actually manufactured from reconstituted bovine collagen. These "collagen sutures" appear to cause less inflammation and are somewhat more constant in their absorption times.

Sutures of polyglycolin or polygalactin have reasonable strength and handling characteristics. They are hydrolyzed by extracellular enzymes, and their half-life in tissue is more predictable than catgut. Polyglycolic sutures lose half their strength by about 2.5 weeks. This is a little early for major wounds created in extensive operations, and such sutures should be chosen with some caution and with proper regard for the task of the healing process.

The more reactive a suture is, the more likely it is to be the site of inflammation and infection.

Skin closure is best accomplished by microporous tape. The use of this method has been associated with lower infection rates and no greater dehiscence rates.

Prosthetic Materials

New prosthetic are constantly being tested. Among the metals, cobalt-chromium (Vitallium) alloys and titanium alloys have been the most successful. Solid implants of these metals, such as new joint components, have worked well. Metal mesh prostheses, used to restore form or to repair hernias, allow good healing, but the mesh eventually fractures from fatigue and disintegrates. Plastic fibers are longer lasting, and polypropylene mesh has replaced metal mesh for hernia repairs. Teflon and nylon are almost inert. Teflon, however, has an unwettable surface and, in finer mesh, prevents the growth of connective tissue for the interstices. Solid prostheses of nylon, silicon, or Teflon have the same property and consequently may migrate. Dacron has a more wettable surface and allows penetration and fixation by connective tissue.

Migration has been one of the most serious problems with plastic inserts. When migration is limited by the proximity of bone or when a formed prosthesis can actually be fixed into place by nonabsorbable suture at a fixed point, success has been more uniform. Even the best of plastic is still a foreign body, and infection and contracture around plastic prostheses remain a major problem. Therefore, autologous tissue, when its use is technically feasible, is preferred for grafting into an infected or potentially infected area.

Factors Affecting Healing

Healing has a high priority in the body economy, and mild to moderate nutritional deficiencies do not affect it. However, major nutritional depletion retards healing.

Vitamin A has proved important to repair. Collagen synthesis and epithelialization suffer in its absence. Vitamin A deficiency is probably the most common vitamin deficiency in our culture. Requirement for burned patients may rise as high as 25,000 units per day.

The best known nutritional deficiency affecting healing is scurvy. As noted previously, ascorbic acid is necessary for the hydroxylation of proline and release of collagen from the fibroblast. A dose of 1 or 2 gm of ascorbic acid per day for 1 week is sufficient to restore

most levels of this deficiency.

Protein depletion (as opposed to temporary starvation) also retards healing if weight loss exceeds approximately 20 per cent of original body weight. Classic experiments by Localio and co-workers (1948) show that administration of methionine alone causes healing, which is retarded by protein depletion, to return almost to normal. Wound dehiscence and infection tend to occur more often in patients who have lost significant amounts of weight and who have low serum albumin concentrations.

Vitamin D depletion interferes with bone healing but not with soft tissue repair. Probably, most of the B complex vitamins are important to repair, but the literature on the effects of clinical deficiency is not complete. The injured patient's needs for the B complex vitamins may not be much greater than normal.

Zinc deficiency also is related to retarded wound healing. An indolent wound with a yellow-gray exudate suggests zinc deficiency. The administration of zinc sulfate, 220 mg, three times daily for a few weeks (a pharmacologic dose), appears to be safe and effective in returning wound healing to normal. The mechanisms of the effect of zinc is not known.

Diabetes retards healing; however, the actual mechanism is not clear. Diabetic vascular disease leads to oxygen deficiency, which can retard healing. Poor circulation may also lower the temperature of the wound and impede healing. Carbohydrate metabolism is prominent in healing tissue and probably fulfills its energy requirements. If carbohydrate metabolism is interfered with, possibly because of poor insulin supply, healing would be expected to slow.

Tests of healing in poikilothermic animals have shown that the rate of healing is dependent on temperature. For this reason and possibly because of poor oxygen supply, cutaneous wounds on the extremities, which are cool, heal less rapidly than those on the trunk, which is warm.

Wounds in ischemic tissue heal poorly or not at all. Obviously, many factors are associated with ischemia. Recent research suggests that oxygen supply probably governs the rate of healing under normal conditions. As noted before, molecular oxygen is necessary for the hydroxylation of lysine and proline on which many subsequent processes in collagen formation depend. If wounds are closed under tension or if shock or hypotension occurs, healing may not proceed normally.

Adrenocortical steroids are well known for their depressive effects on healing. Patients who are taking anti-inflammatory steroids at the time of operation run a great risk of wound infection. Recent information shows that administration of vitamin A can counteract the effects of anti-inflammatory steroids on wound healing. The effect is seen with both systemic and topical administration of vitamin A. However, the systemic use of vitamin A in patients who are receiving cortisone for control of inflammatory disease must be undertaken with caution. Since vitamin A can counteract the effects of cortisone on the wound, it also can presumably counteract the anti-inflammatory effects of cortisone.

Use of hyperbaric oxygen has been vigorously advanced as an aid to repair. Though the importance of oxygen to repair is well established and though we know that modest

prolonged increases of arterial pO_2 often accelerates repair and increases resistance to infection, the case for intermittent hyperbaric oxygen is less clear. It seems to be highly effective in the treatment of chronic refractory osteomyelitis and in the treatment of osteoradionecrosis. Recent work suggests that it may aid burn repair. However, the role of hyperbaric oxygen in the treatment of wounds and injuries is not yet fully established.

Infection and Resistance

The wound presents an ideal site for bacterial growth because the carbon dioxide tension is high, the oxygen tension is low, and the environment is moist and dark. Yet, wounds obviously have some resistance to infection, since virtually all wounds are contaminated while they are open, yet relatively few become infected. Numerous studies have shown that there are three prerequisites for wound infection: (1) a receptive host, (2) contamination by microorganisms, and (3) a culture medium in the wound. In the prevention of infection, the patient's resistance and the state of the wound must be considered as much as the degree of bacterial contamination. "Trauma to the wound is as important a cause of postoperative infection as is the introduction of bacteria".

The more organisms that contaminate the wound, the more likely is the occurrence of an infection. However, many other factors are involved in determining the probability of infection. For example, clostridial infections occur if dead tissue is present in the wound. Antibiotics reach the wound and obviously influence the type of bacteria that may cause infection. Adrenocortical steroids and diabetes diminish the patient's resistance to infection. Sutures also increase susceptibility. Studies on nonsuture closure of skin show that the number of infections was decreased when skin sutures were avoided.

The administration of preventive antibiotics can be effective in averting infection. The probability of effectiveness depends on matching the susceptibility of the potential infecting organism with the appropriate antibiotic. There is little use, and some potential harm, in giving antibiotics to well patients with surgically clean wounds. The probability of efficacy rises as the expected rate of infection rises above 4 to 5 per cent.

Recent studies on white blood cell function show that killing some species of bacteria depends on an adequate oxygen supply to the human granulocyte. Although tests on human wounds have not been done, this finding adds credence to the dictum that gentle surgery and good blood perfusion of the injured area are essential to resistance to infection.

Care of the Wound

Postoperative local care of the closed wound involves cleanliness and protection from trauma. Sutured wounds can be infected by the external application of bacteria, particularly during the first 3 to 4 days. Taped wounds resist surface contamination within hours. Most wounds can be exposed to the atmosphere safely at any time after operation. However, if a wound is likely to be contaminated or traumatized, it should be protected by some sort of dressing for at least the first 4 days. Protection from contamination may require repeated cleansing as well as numerous changings of the dressing.

Contaminated wounds with a high probability of becoming infected can be left open for 4 or 5 days and then closed. This method, called delayed primary closure, is highly effective in preventing infection. Under military conditions, its use has been almost mandatory. To be successful with this technique, however, the surgeon must recognize the shaggy fibrin exudate on the open wound, which suggests that infection is established and wound closure contraindicated.

Care of the wound starts in the preoperative period and ends only months later. One must be clean, gentle, and skillful in surgical technique and attentive to postoperative protection of the wound. The wound is susceptible to major systemic physiologic disorders such as hypovolemia, anoxia, shock, hypotension, starvation, and drug administration. "Although wound healing is in many ways a local phenomenon, the ideal care of the wound is essentially the ideal care of the patient".