MANAGEMENT OF ACUTE HAND INJURIES

A BIOLOGICAL APPROACH

MANAGEMENT OF ACUTE HAND INJURIES

A BIOLOGICAL APPROACH

PAUL M. WEEKS, M.D.

Professor of Surgery (Plastic and Reconstructive Surgery), Washington University School of Medicine; Plastic Surgeon-in-Chief, Barnes Hospital; Director, Milliken Hand Rehabilitation Center, Irene Walter Johnson Institute of Rehabilitation, St. Louis, Missouri

R. CHRISTIE WRAY, M.D.

Assistant Professor of Surgery (Plastic and Reconstructive Surgery), Washington University School of Medicine; Plastic Surgeon-in-Chief, St. Louis County Hospital, St. Louis, Missouri

With 339 illustrations

SAINT LOUIS

THE C. V. MOSBY COMPANY

1973

Printed in the United States of America

Distributed in Great Britain by Henry Kimpton, London

Library of Congress Cataloging in Publication Data

Weeks, Paul M
Management of acute hand injuries.

1. Hand-wounds and injuries. I. Wray, Robert Christie, joint author. II. Title. [DNLM: 1. Hand injuries—Therapy. WE830 W396m 1973]
RD559.W4 617'.1 73-8641
ISBN 0-8016-5370-3

PREFACE

The initial phase of the development of hand surgery as a specialty was characterized by rapid and exciting advances through technical skills. Understandably, these advances have reached a plateau. It is difficult to advance beyond this plateau because of the biological processes of tissue repair and regeneration that come into play after the technical feats of the surgeon have been completed. In terms of ultimate function, these biological processes can produce either a favorable environment that permits complete functional recovery or an unfavorable environment that compromises functional recovery. At the present time, the surgeon has three basic approaches to aid him in the production of a favorable biological environment for tissue repair and regeneration: biochemical control of repair and regeneration, surgical techniques that provide an optimal wound milieu, and postoperative management designed to favorably alter tissue repair and regeneration. The first and last of these approaches present the new frontiers in hand surgery—the second has reached a plateau.

The goal of this book is to provide the surgeon with a basic approach to the management of acute hand injuries founded on the biology of tissue repair and regeneration. Thus the book is divided into three sections. The first section provides the surgeon with the basic background of these biological processes, that is, skin, cartilage, and tendon repair, and bone and nerve regeneration. The second section correlates the selection of the method of initial management of the acutely injured hand with the ultimate biological activity of the injured tissue. The third section emphasizes the means of evaluating the contribution of these biological processes to the ultimate functional result—be it favorable or unfavorable. Certainly such a charge is unobtainable at our present level of knowledge of the biological processes. Yet this book represents an attempt to direct attention to these processes, with the realization that a single advancement in the understanding of even one of them can markedly influence the favorable control of repair or regeneration and consequently the ultimate functional result in a variety of conditions.

With pleasure we acknowledge the enthusiasm, interest, and assistance of those who have contributed to the organization and ultimate realization of this book. In particular, we acknowledge Mrs. Mary Carey, who converted scribbled notes into coherent chapters; Mrs. Mary Jo Bakowski, who researched each topic; and Mr. Alan Neider, who converted our thoughts into clear and concise illustrations.

Of particular note has been the generosity of Mr. Thomas Moore, which led to the establishment of the Milliken Hand Rehabilitation Center. This center has provided the opportunity for development, investigation, and evaluation of methods that aid in the production of a favorable biological environment—as presented in the final section of this book.

Paul M. Weeks
R. Christie Wray

CONTENTS

SECTION ONE

THE BIOLOGICAL BASIS FOR MANAGEMENT

SECTION ONE THE BIOLOGICAL BASIS FOR MANAGEMENT

1 Wound healing and tissue coverage

The incurrence of a wound initiates acceleration of normal physiological processes toward the restoration of tissue integrity. As a result of this acceleration, a new phenomenon is introduced—contraction—which aids in wound closure but which by its very nature is most detrimental functionally. The only major difference in the healing of perfectly coapted wounds and open wounds is the time required for healing to be completed and the degree of tissue contraction associated with open wounds. We will limit our discussion to the healing of an open wound since it manifests the physiological principles more clearly. All surgery is based on the premise of obtaining adequate healing of the operative wound; thus a thorough understanding of this fundamental biological process is mandatory.

CELLULAR PHENOMENON

A wound may be inflicted by blunt trauma, laceration, or avulsion, or may result from tissue coagulation by thermal, electrical, or chemical agents.

Initially, vasodilatation in the traumatized area, thrombosis of damaged vessels, and contraction of muscular vessels are observed. In the area immediately surrounding the wound, protein and fluid are exuded from the intact but injured vessels. An outpouring of vascular fluids rich in fibrin occurs (Fig. 1-1). Albumin, which is of smaller molecular size than globulin, readily passes between the vascular endothelial cell junctions and into the extracellular spaces. The resulting fluid shift renders the damaged area edematous and produces a relative vascular insufficiency in the wound as evidenced by a very low tissue Po_2 (5 to 10 mm Hg) for the first 10 days after the wound occurs (Fig. 1-2). Polymorphonuclear cells and mononuclear cells of vascular origin migrate into the wound. Macrophages that appear in the wound matrix originate from the bone marrow.

Within 48 to 72 hours after the wound is incurred, the quantity of lymphocytes and mononuclear cells has peaked and begins declining. The neutrophilic leukocytes, which exhibit minimal direct phagocytic activity, undergo cell lysis and degranulation to prepare the extracellular matrix for removal by the macrophages. Monocytes, whose role is primarily one of phagocytosis, actively ingest both neutrophilic granules and fibrin. During the first 3 to 4 days, devitalized tissues and fibrin are phagocytized to prepare the wound for the ingrowth of new capillaries. Obviously the burn wound that exhibits extensive tissue destruction requires an extended period of autogenous wound débridement before granulation tissue can begin forming. Surgical removal (débridement) of as much devitalized tissue as feasible at the time of initial wounding will aid in shortening this period of phagocytosis.

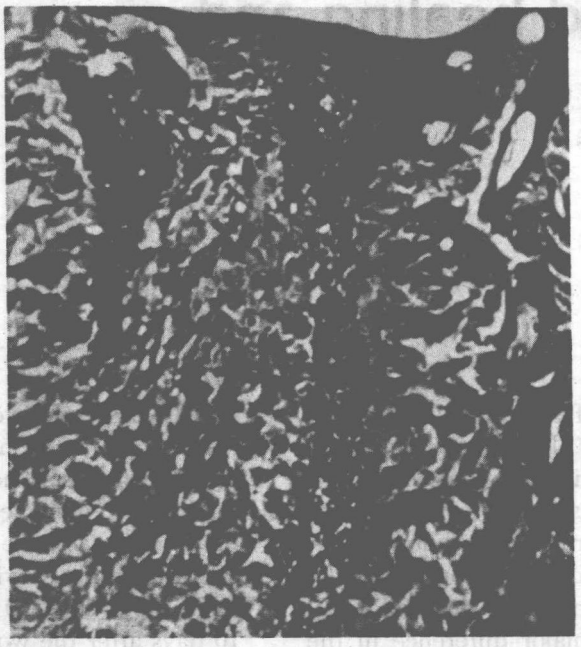


Fig. 1-1. The incised wound at 48 hours exhibits cellular debris between the dermal edges and complete repair of the surface epithelium.

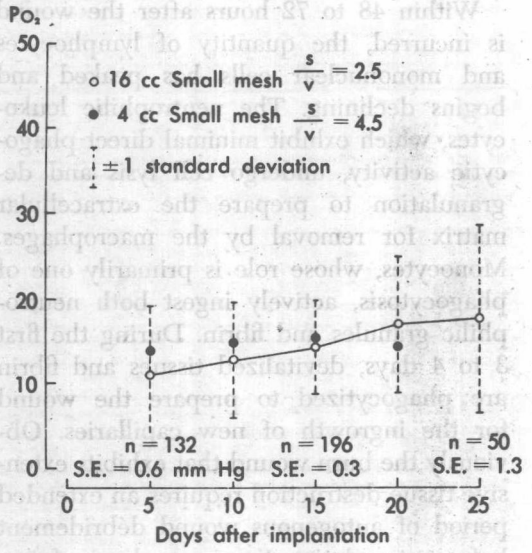


Fig. 1-2. Oxygen tension of wound fluid at 15 to 25 days aspirated from the implanted wire mesh cylinders. (Reprinted with permission from Hunt, T. K., and others: Respiratory gas tension and pH in healing wounds, Am. J. Surg. 114: 302, 1967.)

New tissue formation is initiated by the budding of capillaries, that is, granulation tissue formation. Capillary buds are formed continuously behind the advancing syncytium of fibroblasts that have made their appearance in the wound by the third day. Wound fibroblasts are probably derived from resident fibrocytes, that is, fibrocytes normally present in the tissue prior to injury. These cells exhibit motion only when proliferating or actively secreting collagen and mucopolysaccharides. The fibroblasts migrate on a fibrin network oriented in the open wound by contraction of the blood clot, thus centrally aligning the fibrin network attached to the wound margins and base. Migrating fibroblasts act as a leading edge for the capillary buds and deposit collagen and mucopolysaccharide to provide a framework on which the immature capillaries can build. Cell migration is gained by the action of the ruffled undulating membrane of the fibroblast. When this

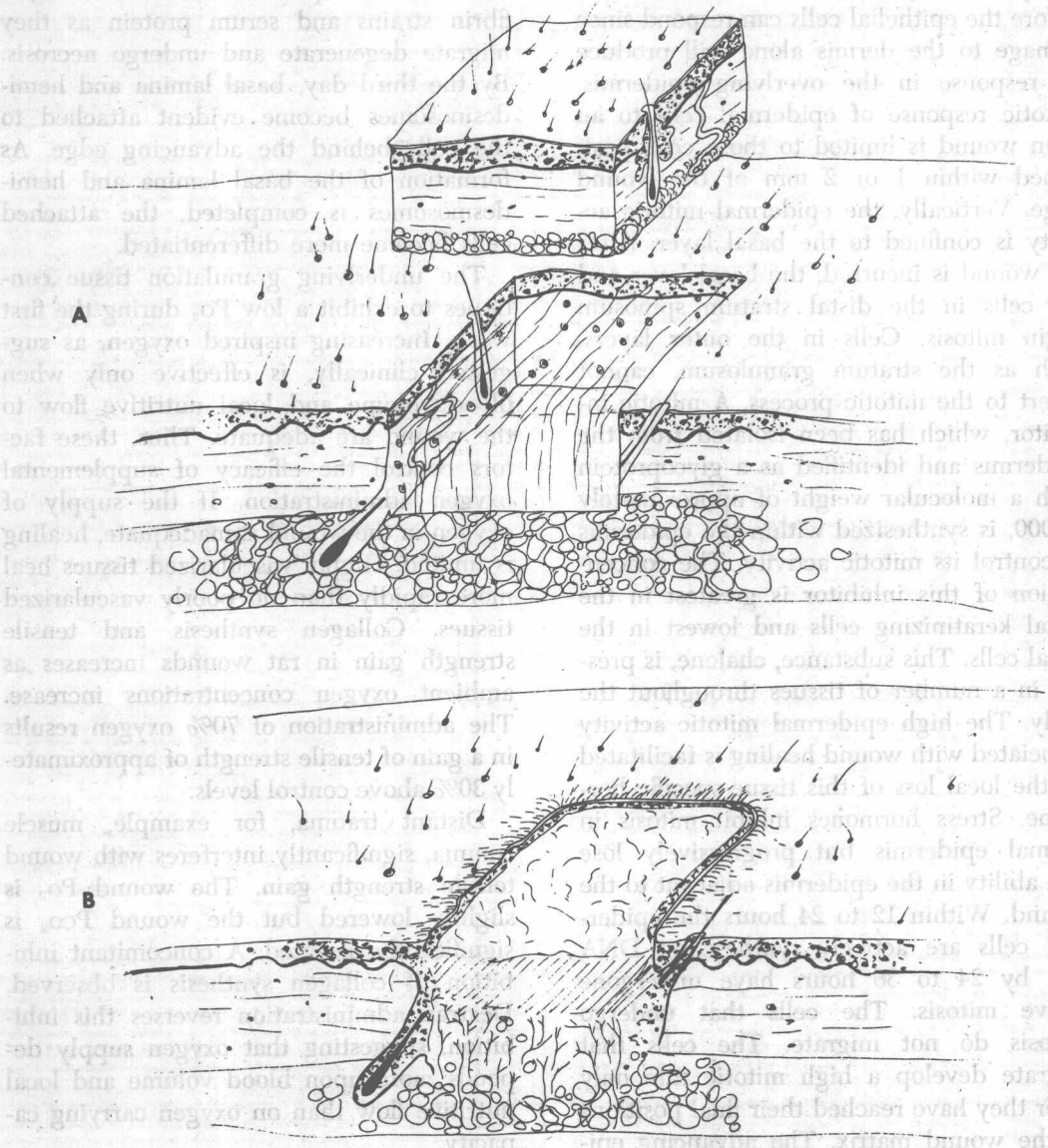


Fig. 1-3. A, The full-thickness block of tissue has been removed. Note the hair follicles and sweat glands have been transected at various levels below the epithelial surface. B, Epithelialization occurs by migration of the epithelium from the edges of the wound and from the transected skin appendages at the various levels indicated.

membrane contacts a second fibroblast, migration in that particular direction is inhibited (contact inhibition) and redirected to areas clear of fibroblasts. Thus, all cell migration is subsequently directed toward the center of the fibrin coagulum of the wound (Fig. 1-3).

Meanwhile, marked changes have occurred in the epithelial cells at the wound margins during the first 24 hours of the

injury. The epidermis must be damaged before the epithelial cells can respond since damage to the dermis alone will produce no response in the overlying epidermis. Mitotic response of epidermal cells to an open wound is limited to those cells positioned within 1 or 2 mm of the wound edge. Vertically, the epidermal mitotic activity is confined to the basal layer. After the wound is incurred, the basal layer and the cells in the distal stratum spinosum begin mitosis. Cells in the outer layers, such as the stratum granulosum, cannot revert to the mitotic process. A mitotic inhibitor, which has been isolated from the epidermis and identified as a glycoprotein with a molecular weight of approximately 30,000, is synthesized within the epidermis to control its mitotic activity. The concentration of this inhibitor is greatest in the distal keratinizing cells and lowest in the basal cells. This substance, chalone, is present in a number of tissues throughout the body. The high epidermal mitotic activity associated with wound healing is facilitated by the local loss of this tissue-specific hormone. Stress hormones inhibit mitosis in normal epidermis but progressively lose this ability in the epidermis adjacent to the wound. Within 12 to 24 hours the epidermal cells are actively synthesizing DNA and by 24 to 36 hours have undergone active mitosis. The cells that undergo mitosis do not migrate. The cells that migrate develop a high mitotic rate only after they have reached their final positions in the wound matrix. The advancing epidermal cells move as a sheet onto the wound matrix, ever maintaining their attachments with adjacent epidermal cells. Since a basal lamina has not developed at this time, the cells are migrating directly upon the wound matrix. As the cells migrate, they become flattened and appear less differentiated, as evidenced by a quantitative increase in the number of free ribosomes and a decrease in rough endoplasmic reticulum and number of tonofilaments. Some of the epidermal cells that ingest fibrin strains and serum protein as they migrate degenerate and undergo necrosis. By the third day, basal lamina and hemidesmosomes become evident attached to the cells behind the advancing edge. As formation of the basal lamina and hemidesmosomes is completed, the attached cells become more differentiated.

The underlying granulation tissue continues to exhibit a low Po_2 during the first week. Increasing inspired oxygen, as suggested clinically, is effective only when blood volume and local nutritive flow to the wound are adequate. Thus, these factors control the efficacy of supplemental oxygen administration. If the supply of oxygen in the wound is inadequate, healing is limited. Highly vascularized tissues heal more rapidly than do poorly vascularized tissues. Collagen synthesis and tensile strength gain in rat wounds increases as ambient oxygen concentrations increase. The administration of 70% oxygen results in a gain of tensile strength of approximately 30% above control levels.

Distant trauma, for example, muscle trauma, significantly interferes with wound tensile strength gain. The wound Po_2 is slightly lowered but the wound Pco_2 is significantly elevated. A concomitant inhibition of collagen synthesis is observed. Dextran administration reverses this inhibition, suggesting that oxygen supply depends more upon blood volume and local nutritive flow than on oxygen carrying capacity.

Activator substances may play a role in initiating and regulating the progression of the inflammatory process from the exudative to the reparative (proliferative) phase. Current data indicate the existence of a connective tissue activating substance which is water- and saline-soluble polypeptide and has a molecular weight between 4,000 and 10,000. This substance possesses one or more labile sulfhydryl groups per molecule that are essential to its biological ac-

tivity. The substance is widely distributed; the absolute amount in a tissue is related to cell density. When this activator is exposed to synovial fibroblasts, the fibroblasts promptly exhibit a hypermetabolic state characterized by a 3- to 40-fold increase in hyaluronic acid formation, glucose uptake, lactate formation, and hydrogen ion liberation. Concomitantly, the formation of soluble and fibrous collagen is depressed. Within 7 to 9 days, the rate of hyaluronic acid synthesis levels off and decelerates, allowing the cells to shift to a state that favors the production of collagen. Thereafter, collagen synthesis is the dominant activity of these cells. The need for a signal is readily apparent, and it is suggested that the connective-tissue activator is at least in part responsible.

Studies comparing the effect of this connective-tissue activator on synovial fibroblasts and dermal fibroblasts revealed that the latter are less sensitive to the connective tissue activator and apparently have metabolic requirements best met by the extracts of dermal cells. These studies reinforce the concept of the differences in fibroblasts of diverse origins.

FIBROUS TISSUE AND GLYCOSAMINOGLYCAN SYNTHESIS

The primary metabolic function of migrating fibroblasts is synthesis of collagen. What evokes synthesis of this protein? Messenger RNA extracted from *E coli* initiates, in cell-free systems, protein synthesis with formyl (CHO) methionine, alanine, or serine in the lead position. In the production of these proteins, the cells remove the formyl group from methionine or split off the entire formyl methionine unit after synthesis of the protein chain has been initiated. Further studies reveal that messenger RNA uses a special codon, AUG GUG, at the beginning of a strand to order the initiation of protein synthesis with formylated methionine in the lead position. Thus, only the formylatable variety of methionine transfer RNA can initiate synthesis, suggesting that this variety of transfer RNA has a special configuration that fits into a particular site on the ribosome.

Substantiation of this point is provided by the addition of puromycin to the medium. Puromycin has a structure similar to that of the end of a transfer RNA molecule that attaches to an amino acid through its NH_2 group and subsequently forms a peptide bond with the adjacent amino acid. However, because puromycin lacks the free carboxyl (COOH) group of an amino acid and cannot form a second peptide bond, chain elongation is prevented and the aberrant polypeptide chain is immediately expelled from the cell. Thus, the formyl group may be utilized to initiate formation of the first peptide bond that activates nascent polypeptide production.

The initial step in collagen synthesis is the formation of a polypeptide chain whose amino acid sequence is formed in response to messenger RNA (Fig. 1-4). In such a polypeptide chain of 1,000 amino acid residues, approximately 330 are glycine, 130 proline, 100 hydroxyproline, 110 alanine, and the remaining residues distributed among fourteen other amino acids. The amino acids may be arranged on the polypeptide chain in a variety of configurations, but the sequences glycine-proline-hydroxyproline and glycine-proline-alanine are the most frequent. Hydroxyproline and hydroxylysine are obtained by hydroxylation of proline and lysine after the amino acids are incorporated into the polypeptide chain but before the chain can be extruded from the cell. Proline hydroxylation is accomplished in the presence of molecular oxygen, iron (Fe^{++}), alpha ketoglutarate, ascorbate, and proline hydroxylase. A similar environment is necessary for lysine hydroxylation except that the enzyme responsible is a different hydroxylase. Hydroxylase preferentially hydroxylates prolines in the position im-

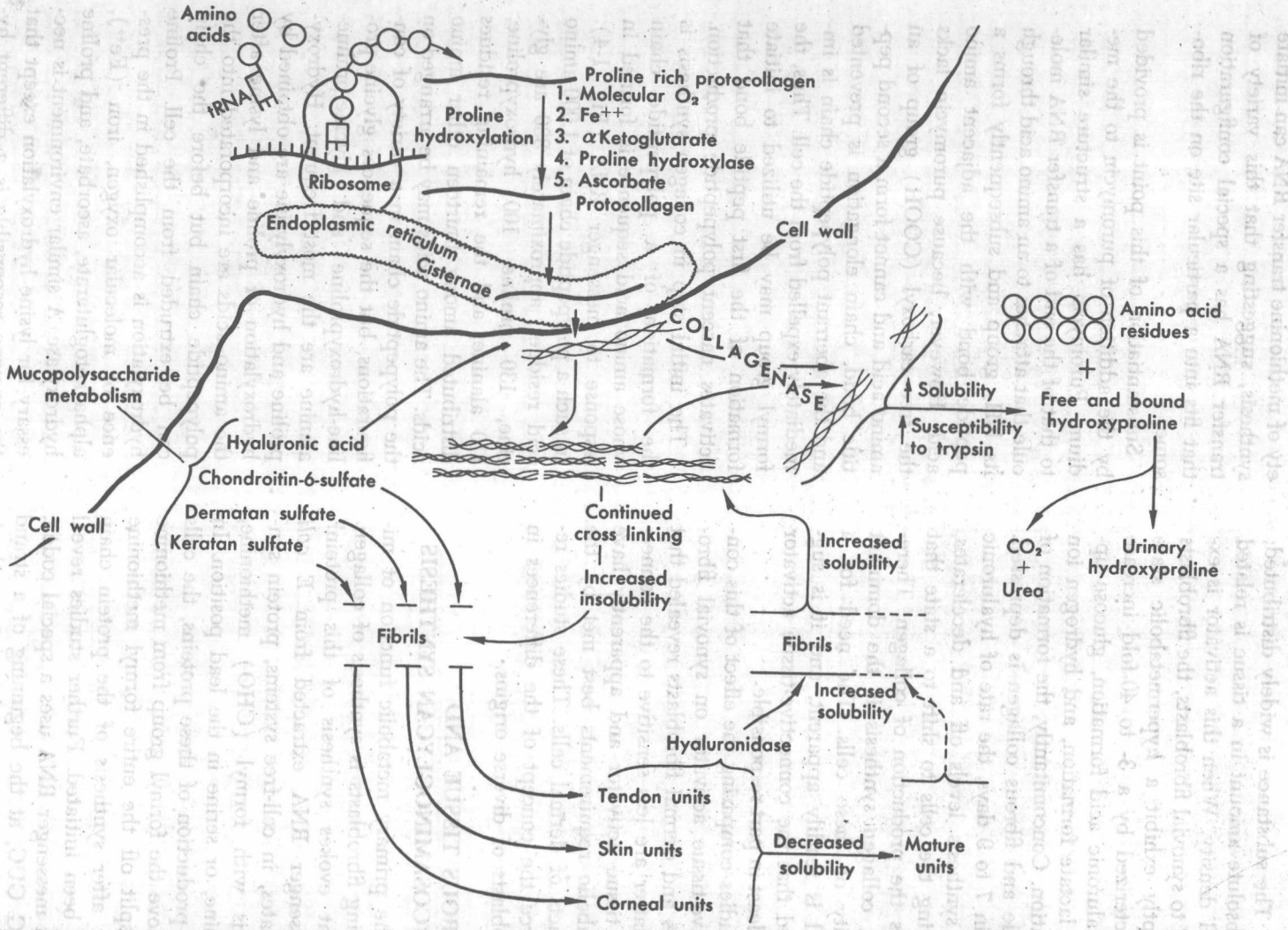
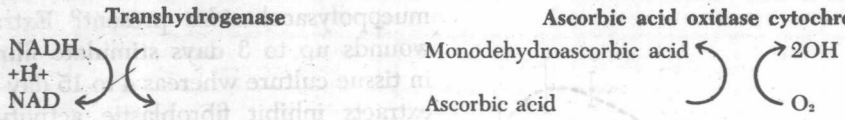


Fig. 1-4. A schematic representation of the synthesis and degradation of collagen. Note the ultimate structural organization of collagen and the glycosaminoglycan involved.



mediately preceding glycine and protocollagen proline.

Inhibition of collagen formation at this level could result from anaerobic conditions, or the presence of chelating agents which would bind the Fe^{++} cofactor, or a dietary deficiency of vitamin C. Of these three, vitamin C deficiency has historically been of greater interest to investigators. Studies suggest that the role of ascorbic acid is in microsomal electron transport leading to proline hydroxylation, as schematized above.

A deficiency of L-ascorbic acid markedly impairs the cells' ability to synthesize collagen in response to wounding. Yet, under these same conditions some collagen is formed. Evidence suggests that an ascorbic acid–dependent and an ascorbic acid–independent system are available within the cell for collagen production. Ascorbic acid is required in the maintenance of rapidly formed labile wound collagen but not in the maintenance of structural collagen. Thus, the scorbutic individual exhibits marked impairment of wound tensile strength gain.

Normal collagen synthesis requires the production of polypeptide chains that are released from the ribosomes along the endoplasmic reticulum and deposited extracellularly at points where the cisternae of the endoplasmic reticulum and the external cell membrane are in close apposition. The extruded polypeptide chains aggregate on the surface of the cell to form the basic collagen unit—tropocollagen.

Three polypeptide chains, approximately 1,000 amino acid residues in length, wrap around each other to form a superhelix. These three chains are bound together by hydrogen bonds between the oxygen atoms that are located where amino acids are joined by peptide linkages in an adjacent chain. Subsequent structural organization is based on the development of intramolecular and intermolecular crosslinks. Such linkages result in the tensile strength gain of the nascent collagen fibers. As the number of intermolecular crosslinks increases, the collagen fibrils become increasingly insoluble, as evidenced by the fibrils' resistance to solubility in increasing concentrations of saline. An optimal number of linkages exists for maximum collagen fiber stability.

During this early period the fibroblasts are also synthesizing glycosaminoglycans (mucopolysaccharides). The importance of these substances must not be overlooked. Seven distinct mucopolysaccharides have been described. All except keratan sulfate are composed of repeating units of hexosamine (galactosamine or glucosamine) and uronic acid. Keratan sulfate is composed of a repeating unit containing galactose and 6-sulfoglucosamine. Hyaluronic acid is composed of repeating units of glucosamine and glucuronic acids which form a polymer associated with a small amount of protein. The other mucopolysaccharides occur in tissues in the form of protein-polysaccharide complexes.

In granulating wounds, the isolation and identification of each mucopolysaccharide has shown the presence of hyaluronic acid, chondroitin-4-sulfate and dermatan sulfate. Chondroitin-4-sulfate and dermatan sulfate increase progressively from the fifth to seventeenth day (Fig. 1-5). No chondroitin-6-sulfate is present. Following an initial fall from the fifth to the tenth day, the hyaluronic acid fraction remains relatively constant. What is the significance of the

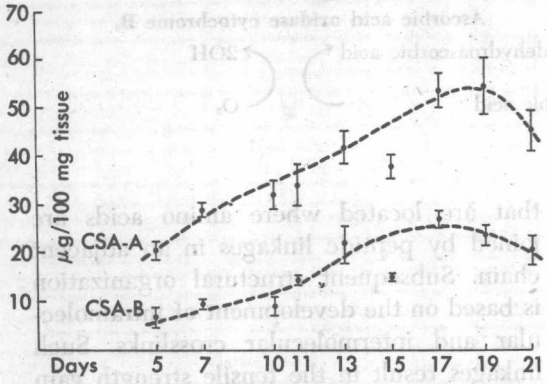


Fig. 1-5. Chondroitin-4-Sulfate (CSA-A) and dermatan-sulfate (CSA-B) content of skin wound granulation tissue. Results expressed as mean ± 1 S.D. (Reproduced from Bentley, J. P.: Rate of chondroitin sulfate formation in wound healing, Ann. Surg. 165:186, 1967.)

mucopolysaccharides present? Extracts of wounds up to 3 days stimulate fibroblasts in tissue culture whereas 4 to 15 day wound extracts inhibit fibroblastic activity. Furthermore, mucopolysaccharide determines, in vitro, the diameter of collagen fibril formation. When dermatan sulfate is added to a collagen solution, larger fibers can be observed aggregating than when chondroitin-4-sulfate is added. In vivo the fine collagen fibrils of the cornea are associated with keratan sulfate, while the heavier fibers of skin are complexed with a high content of dermatan sulfate, and the thick fibers in tendons are associated with chondroitin sulfate. Thus, the mucopolysaccha-

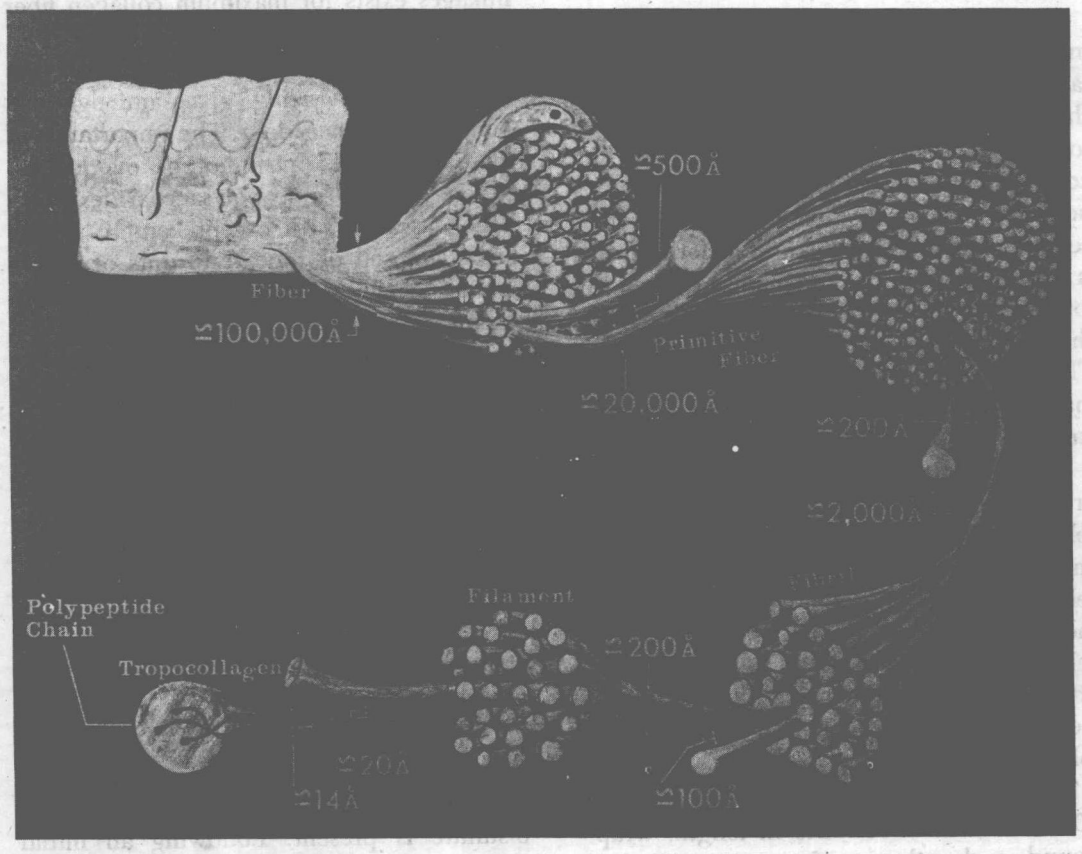


Fig. 1-6. Organization of the components of the collagen fiber. (From Bryant, W. M., Greenwell, J. E., and Weeks, P. M.: Alterations in collagen organization during dilatation of the cervix uteri, Surg. Gynec. Obstet. 126:27, 1968.)

rides aid in orientation of the collagen subunits during aggregation to form fibrils and contribute to determining ultimate fiber size and functional capacity. This difference in function is particularly striking when one compares the cornea, exhibiting impeccable clarity, with the Achilles tendon.

FIBROUS TISSUE ORGANIZATION

The levels of collagen organization are represented in Fig. 1-6. At the molecular level, polypeptide chains form the triple helix characteristic of tropocollagen. End-to-end attachment of the tropocollagen units produces a filament that is 140 to 200 angstroms in diameter and of unlimited length. These filaments are longitudinally organized into fibrils measuring aproximately 2,000 A in diameter. The primitive fibers formed are 100,000 A in diameter and visible with the light microscope.

Of particular importance are the dimensions of the spaces between the longitudinally oriented components. The following approximate spacings between components have been suggested: polypeptide chains, 10 to 16 A; filaments, 100 A; fibrils, 200 A; primitive fibers, 500 A; and fibers, 1,000 A. Study of the effects of tanning agents on collagen offers further support of the existence of large gaps between collagen components. The introduction of crosslinks—5 A in length—during tanning fails to bridge the gaps between the larger components.

The state of organization of collagen at any component level is dependent upon the balance of cohesive and dispersive forces between components (Fig. 1-7). An imbalance of these forces will be reflected by a change in the tissue's compliance. Progressive increase in cohesive forces accounts for the progressive insolubility of nascent collagen in solutions exhibiting increased dispersive forces. If the solution's dispersive forces exceed the cohesiveness of the collagen, the collagen becomes soluble. The forces contributing to cohesiveness include hydrostatic forces, electrovalent bonds, covalent bonds, and the mucopolysaccharide milieu. The hydrostatic forces exerted by the solution are relatively insignificant. Electrovalent bonding permits variation in distance between polypeptide chains from 10 to 16 A without disruption of the bond. However, a covalent bond such as hydrogen spans only 2.8 A. In view of the spatial organization of collagen components, it is evident that the cohesive forces contributed by electrovalent and covalent bonds are operative only at the polypeptide chain and tropocollagen levels. The distances between filaments, fibrils, primitive fibers, and fibers preclude such bonding. This, coupled with evidence from earlier discussion, suggests a limit to which collagen molecules can interact with each other to form fibrils, thereby limiting the diameter of the fibrils. To form the larger fibers, fibrils interact with a spacer. The precise contributions of the glycoproteins and mucopolysaccharides to the organization of collagen are unknown. The interaction of these two groups of substances with collagen has been inferred from the experimental data available. Further aggregation to form bundles would require electrostatic interaction between larger fibers and the glycosaminoglycans or glycoproteins. Apparently an optimal quantitative and qualitative relationship exists. When the fiber systems are overloaded with the spacer, a decrease in fiber tensile strength occurs.

The dispersive forces include mechanical deforming force, osmotic swelling, and the mucopolysaccharide milieu. In a system of isolated fibers, extrinsic stress will be applied as a shearing force between longitudinally oriented collagen fibers. Initially, however, when extrinsic force is applied to a segment of skin, the resiliency of the fiber weave accounts for the lengthening. All subsequent stress acts as a shearing