CHAPTER 12

The Development of Wound Management Products

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Objectives

The reader will be challenged to:

- Distinguish between passive, interactive, and bioactive products
- Analyze the characteristics of an ideal wound dressing
- Review the development of products for wound management.

Introduction

Throughout history, many diverse materials of animal, vegetable, and mineral origin have been used to treat wounds. They range from the hot oils and waxes reported in the Ebers papyrus[1] to the animal membranes and feces of the Middle Ages to the picked oakum of the 19th century. Some of these products have survived; both absorbent cotton and Gamgee tissue were as familiar to the surgeon of 1880 as they are to the physician of today. The first monographs related to wound dressing materials appeared in early London and Edinburgh hospital dispensatories followed later by the British Pharmaceutical Codices and the British Pharmacopoeia.[2] Information relating to the development of wound management products is reflected in similar publications in the United States Pharmacopoeia and in other national standards.

Until 1960, advances in the design and efficacy of wound management products had been spasmodic and limited to the adaptation of available materials that were being used for other purposes. The older products (eg, absorbent cotton, lint, and gauze) were primarily of the plug-and-conceal variety and could be considered *passive* products that took no part in the healing process. Little attention was paid to the functional performance of a product, and minimal consideration was given to the healing environments required for different wound types.

A new generation of products was potentiated by the advances in knowledge of the humoral and cellular factors associated with the healing process and the realization that a

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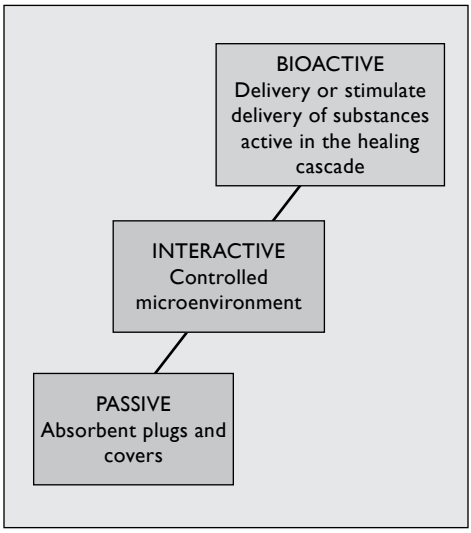

Figure 1. Classification of wound management product activity.

controlled microenvironment at the wound surface was needed if wound healing was to progress at the optimal level. These environmental control dressings are classified as *interactive* dressings; current developments are directed at bioactive products (Figure 1), which will directly or indirectly stimulate some part of the healing cascade (Figure 2) and optimize the wound microenvironment to allow the free movement of cells, cytokines, and growth factors involved in the healing process.

This chapter surveys the progressive development of wound management products and offers performance profiles for different product groups with their possible clinical usage. The ever-increasing new product appearance in the medical market, many of which are "me-too" duplicates of other products, precludes the use of brand names and allows a broader perspective of the advances in real-term formulations.

Linteum and Oakum

Linteum was the first woven fabric to be recognized as a surgical material. In 1816, William Cade King, Governor of St. Bartholomew's Hospital, London, presented a sample of patent lint to the House Committee to consider its adoption within the hospital.[3] It consisted of a cloth that had its nap raised on one side by scraping with a knife to produce a soft pile. With the advent of the Crimean War came power-driven machines, which stimulated William Bradbury Robinson of Chesterfield, England to produce a lint machine that could produce an amount of woven material equal to 6 people working on hand machines. The lint was also bleached and purified. It was often formed into dossils (cylindrical pieces), pledgets (oval shaped), and boulsters or tents (conical compresses).

In 1819, Abraham Rees summarized the uses as follows:[4]

1. To stop blood in fresh wounds by filling with dry lint—in large hemorrhages, dip lint into alcohol or oil of turpentine
2. To agglutinate and heal wounds when spread with ointments
3. To dry wounds and ulcers, thus forwarding the formulation of a cicatrix
4. To keep the tops of wounds at proper distance so that they do not hastily unite before the bottom is well digested and healed
5. To prevent the access of air.

He added, "that when used to dress deep wounds a thread should be tied to each portion before insertion to assist in its removal." This product was used with minimal modification for more than 100 years.

A similar development on fibrous materials was to be initiated by another war stimulus (Table 1). Dr. Lewis A. Sayre of New York wrote enthusiastically about the use of oakum in the American Civil War.[1] This was a fibrous mass produced by shredding tarred or untarred rope, the former sometimes being referred to as marine lint (a name also retained for tow impregnated with fresh Stockholm tar). An edition of *The Lancet*[5] in 1870 reported that it "absorbs discharges, destroys bad odors, and supersedes the use of lint, ointments, and linseed meal or bread poultices." Picking oakum was often considered good occupational therapy for prisoners, with obvious difficulties in producing good and reproducible quality. In 1871, Southall Son and Dymond, manufacturing chemists of Birmingham, England, reduced selected quality rope to oakum. Joseph Samson Gamgee[6] referred to this material in his clinical lectures at Queen's Hospital, Birmingham, in 1876. He told of his extensive use of oakum as an absorbent dressing either by itself

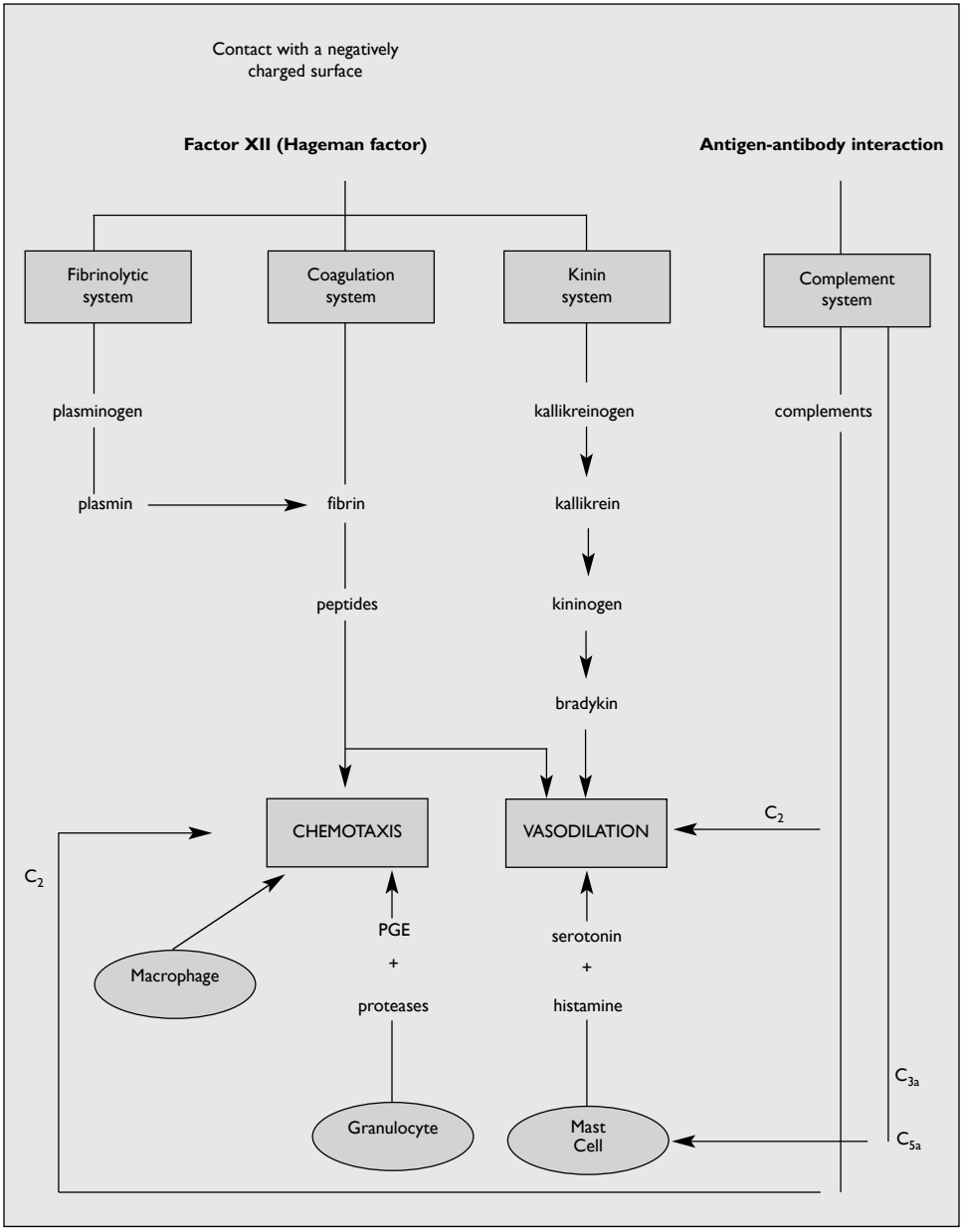

Figure 2. Healing cascade, cellular and humoral factors.

or over a thin layer of fine cotton or stitched into gauze bags to make absorbent pads.

Gamgee also noted that in 1870, M. Alphonso Guerin of Paris had reported a method of dressing amputation stumps using cotton wool. This was raw cotton that, although nonabsorbent, had been washed and carded. Gamgee, wishing to emulate Guerin, obtained the best quality cotton available, a material prepared as packing for jewelers' goods, and rejected all lesser grades as

Table 1. Nineteenth century products
Lewis A Sayre • oakum fiber
Joseph Samson Gamgee • oakum on cotton pads
M. Alphonso Guerin • washed and carded cotton
Joseph Samson Gamgee • jewelers cotton and tiffany
Robinson's & Son, Chesterfield • gauze and cotton tissue

Table 2. Surgical Materials, British Pharmaceutical Codex, 1923	
Cotton wools	15
Gauzes	13
Tows	4
Gauze and cotton tissue	2
Bandages	9
Protectives (Jaconet etc.)	4
Emplastrums	32
Lints	8

unsuitable. His interest encouraged the production of better grades in which the fibers were treated to remove traces of grease and thus were not only rendered absorbent but had a markedly reduced level of bacterial contamination. In 1880, Gamgee wrote a paper describing experiments in which he had used the cotton pads covered with tiffany, a fine bleached gauze used by nurserymen to stretch under the roofs of their conservatories to protect their plants from invading birds. Working in collaboration with Robinson and his son of Chesterfield, England, Gamgee showed that the gauze could be made more absorbent by bleaching, thus formulating the Gamgee tissue, which was the forerunner for today's gauze and cotton tissue. It was the first-named pad to be designed using a woven fabric and a fibrous mass with the criterion of function as the basis of the design.

The 1923 British Pharmaceutical Codex,[7] then the only accepted source of quality standards for pharmaceutical products, gave monographs for gauze and cotton tissue: 8 lints, 13 gauzes, and 15 cotton wools (Table 2). The 1988 British Pharmacopoeia[2] still contained 12 gauze products and 3 fibrous absorbents but excluded lint and Gamgee tissue (Table 3). Gauze, the survivor of those early fabrics, although currently contraindicated as a wound contact dressing, is used widely in surgery. The 2007 British Pharmacopoeia, however, contains monographs for absorbent cotton and absorbent viscose wadding only, and the current European Pharmacopoeia[8] has a monograph for absorbent cotton only. This diminution of formal standards for the materials used to formulate wound management products can only mean that the patient has fewer safeguards against exaggerated claims made by product manufacturers.

Table 3. Surgical Materials British Pharmacopoeia 1988	
Gauze products	9
Ribbon gauze	3
Dressing pads	5
Fibrous absorbents	3
Surgical felts	3
Bandages	20
Surgical tapes	7
Impregnated gauze	3
Stockinette	8
Adhesive dressings	4
Film dressings	1
Foam dressings	3

Absorbents[9]

The overall function of clinical absorbents is self-explanatory, and they have demonstrated minimal development in the past decades. Absorbents are required to absorb and retain a wide range of fluids from the blood and serous exudate of damaged tissue to the variable gut content met during surgical intervention.[6,7] They are found in a number of forms: fibrous (staple), fabric, and fiber plus fabric.

Fibrous absorbents. These absorbents are made from cotton staple or from the fibers of vis-

cose or cellulose; viscose and cotton and viscose or cotton and acrylic fibers may be combined.

Absorbent cotton is available in different qualities varying with the length and diameter of the cotton staple. It is available in the form of rolls and balls and is used for cleansing and swabbing wounds, preoperative skin preparation, and the application of topical medicaments to the skin.

The absorption, performance, and physical character of absorbent viscose vary markedly with the manufacturing process. Viscose is available in the bright or dull form, the latter containing a particulate material, such as titanium dioxide, within the fiber. The fibers are, in general, a continuous staple with a crenate transsectional profile, but smooth and laminated forms are available, which show different degrees of absorptive capacity and wet tensile strength.

Some fibrous absorbents were developed containing a proportion of acrylamide or other synthetic polymeric fiber. These frequently enhance the absorptive performance and give body to the fleece, thus improving fluid retention and avoiding fluid squeeze out, which is caused by fleece collapse after wetting.

Cellulose wadding is produced from delignified wood pulp and manufactured in a multiple laminate material form. It is used in large pieces to absorb large volumes of fluid in incontinence, but is not used in contact with a wound unless enclosed in an outer fabric sleeve to prevent fiber loss to the wound.

Fabric absorbents. Absorbent lint is a closeweave cotton cloth with a raised nap on one side, which offers a large surface area for evaporation when placed with the nap upward on an exuding wound. It is generally unacceptable for modern wound management.

Absorbent gauze is the most widely used absorbent and consists of a cotton cloth of plain weave that is bleached and made reasonably free from weaving defects, cotton leaf, and shell. It may be slightly off white if sterilized. It absorbs water readily, but its performance may be reduced by prolonged storage or exposure to heat.

Surgical usage of absorbent gauze. Gauze products are primarily absorbents when used preoperatively, perioperatively, and postoperatively. Perioperatively, they may protect tissue and organs by occluding areas not involved in the procedure, which may establish tissue viability.[8] To contribute to hemostasis, the gauze fabric may contain a proportion of viscose incorporated with the cotton either in the warp and the weft or exclusively in the weft. A maximum level of 45% of viscose is widely accepted.

Gauze products fall into 2 broad categories—the swab or sponge type (produced by folding and stitching the cloth) and the plain cloth. The swab type includes swabs, strips, pads, and pledgets. The plain type includes packs and ribbon. They are available with and without a radio opaque (X-ray detectable) element, and some are colored with a suitable nontoxic dye for recognition and use by the anesthetist.

Nonwoven fabrics include a wide range of products manufactured from synthetic and semisynthetic fibers. Nonwoven viscose fabric swabs are available in folded pieces of various dimensions. They are occasionally used in error as a single wound dressing. They have a lower total absorptive capacity than gauze, but absorb more quickly because of the random orientation of the viscose fibers. They can replace the more sophisticated cotton swab for general purpose swabbing and cleansing procedures. As fabrics, they constitute the outer layer on a number of wound dressing pads: sometimes suitably coated with a polymer to reduce adherence at dressing change.

A cellulose sponge is a cavity foam cellulose-based sponge available in sheets and thin bands. It is for absorption at small sites in surgery.

Neuropatties are small squares or strips of nonwoven absorbent viscose with thread stitched through the nonwoven fabric and left long. They are used as spot absorbents, particularly in neurosurgery. They are frequently moistened in saline before application. The threads are left outside the surgical area. On completion of surgery, the recovery of each pattie is facilitated by lifting each thread. Products vary in size and shape, and there is also a device for attaching the ends of all the threads, thus producing a mini count rack.

Fiber plus fabric absorbents. Gauze and cellulose wadding consists of a thick layer of cellulose wadding enclosed in a tubular-form gauze. The properties of the 2 separate materials have already been described. Combined, gauze and cellulose wadding tissue are used as an absorbent and protective pad. Together, they should only

be used as a wound dressing with a nonadherent layer placed between the pad and the wound. This combination has a high absorbency and, because of its thickness, the additional property of insulation, which results in raising the temperature at the skin surface. This increase in temperature has been shown to accelerate the wound-healing rate. On a highly exuding surface, there is a tendency for the cellulose wadding element to collapse when wet and become a semisolid wet mass, which may cause difficulty in practice. In such fluid-loss situations, gauze and cotton tissue are preferred.

Gamgee tissue is a thick layer of absorbent cotton enclosed in a tubular form gauze. It has the same uses as gauze and cellulose wadding tissue but has the advantage of a higher absorbent capacity and less wet collapse. It is also softer in use and thus conforms more easily to the wound surface. It should be used in place of gauze and cellulose wadding tissue on highly exuding surfaces, such as burns, but, as previously stated, it should not be used in direct contact with the wound surface but rather placed upon a nonadherent dressing.

Ideal Wound Dressing

In the 1960s, the recognition that gauze was a passive product that plugged and concealed but did little to encourage wound healing resulted in the creation of a minimal set of criteria for an ideal wound dressing. Such a dressing would allow a wound to heal at the optimum rate concomitant with the physiological state of the patient. Gauze and similar materials did not meet these requirements and their uses have diminished relative to the development of new products, which meet some, but not all, of the stated criteria.

The performance parameters of an ideal wound dressing[9] specified in 1979 were the result of observations in clinical situations of failures of the then contemporary dressings to optimize wound healing. The dressing criteria are as follows:

- To remove excess exudate and toxic components
- To maintain a high humidity at wound/dressing interface
- To allow gaseous exchange
- To provide thermal insulation
- To afford protection from secondary infection
- To be free from particulate or toxic contaminants
- To allow removal without trauma at dressing change.

Acceptable handling characteristics were also specified to include variability of size, resistance to tear and disintegration when wet or dry, conformability, sterilizability, and disposability.

These parameters were the initial stimuli for the development of functionally designed *interactive* products using the advances in the technology of materials. They have since been expanded to incorporate our increased knowledge of the humoral and cellular factors associated with the healing process. They mark the progression toward the production of an ideal wound dressing. ***However, it should be emphasized that no single dressing will produce the optimum microenvironment for all wounds or for all of the healing stages of one wound. The spectrum of performance requires that following wound diagnosis, treatment progresses by prescribing the most suitable dressing.***

The first progression toward interactive products was the development of wound dressing pads with high-absorptive capacity, slow strike through, and a low-adherence wound contact surface. These were initially available in simple-sleeved pads containing cotton, viscose, or cellulose fibers with an outer sleeve of gauze or nonwoven fabric. They were reformulated as laminate pads with multiple layer cores, having outer sleeves of cotton, which were viscose or nonwoven fabric that may have been treated with a polymer (polypropylene) to reduce adherence. The multilayer core is designed to increase absorptive capacity and to prolong usage by delaying strike through to the outer surface. This delay is facilitated by using a fluid-retardant layer within the upper and outer sleeve, which encourages lateral rather than vertical movement of fluid within the pad. ***Strike through is undesirable because it provides a band of wet dressing that may allow transmission of airborne organisms to a clean wound, or bacteria from an infected wound to the outer dressing surface, thus acting as a possible vector in infection transmission.***

Pads with wound-contact surfaces designed to be of low adherence were produced for low exudate and drying wounds where high adherence

can be expected and high absorptive capacity becomes irrelevant. They vary from aluminum-coated fabrics to perforated polymeric films or heat-bonded polyethylene films. The wound contact film is attached to an absorbent fibrous mat and an outer woven or nonwoven fabric. In some products, the polymeric film forms a continuous sleeve on both dressing surfaces. These low-adherence, low-absorptive capacity dressings are sometimes centered on adhesive backing to produce an island dressing, which may be used as a postoperative adhesive dressing or in the more familiar form of a first-aid island or strip dressing for superficial injuries.

Low-adherence primary dressing manufacturers found difficulties in producing wound-dressing pads that would meet all the ideal parameters—in particular, that of low adherence. They produced low-adherence wound contact products that consisted of partially open-cell structured nylon or viscose fabric, which may be finished with a silicone coating. The open-cell structure allows fluid transmission to a secondary, superimposed absorbent dressing, which can be changed when necessary without disturbing the primary, low-adherent contact layer.

The 2-layer system heralded the concept of a primary and secondary wound management regime where the primary dressing would meet the requirements of permeability, nonadherence, and bacterial impermeability and the secondary dressing would meet the need for absorption, protection, and insulation. This concept resulted in a number of products being specified as primary dressings and their associated secondary pads as low- or high-exudate absorption performers.

Impregnated Dressings

Close-weave gauze and open-weave tulles are used as carriers of medicated and unmedicated ointments to the wound surface and were developed initially to lower adherence and, subsequently, release systems for antibacterials and antibiotics.

Paraffin gauze (tulle dressing). Paraffin gauze was developed during World War I. It is bleached cotton or combined cotton and viscose cloth impregnated with yellow or white soft paraffin. It is available as sterile, individually wrapped, single pieces. The paraffin is present to prevent the dressing from adhering to a wound. The gauze, which may be leno in nature, is coated so all the threads of the fabric are impregnated, but the spaces between the threads are free of paraffin. The material is used primarily in the treatment of wounds, such as burns and scalds, where the protective function of the stratum corneum is lost and water vapor can escape. Paraffin-gauze dressing functions by reducing the fluid loss while the water barrier layer is reforming. The 2 properties of the paraffin gauze that are most useful are those of nonadherence and semi-occlusiveness.

In addition to burns and scalds, the dressing is used as a wound contact layer in lacerations, abrasions, and ulcers as a packing material to promote granulation. Postoperatively, it is used as a vaginal or perineal dressing and for sinus packing. A recent development has been the substitution of cotton gauze with cellulose acetate and a paraffin emulsion impregnation.

Examples of available impregnations that are recommended for the reduction of infection are povidone iodine 10%, chlorhexidine 0.5% w/w, and cod liver oil with honey. Diffusion of the antibacterial agent into or onto an infected and exuding wound has been shown to be minimal. The possibility of development of resistant strains of infective organisms together with an increased incidence of sensitivity reactions has reduced the usage of these products and has led to the development of antibacterial products containing silver ions. One such material uses a vapor-permeable film as a base with a coating of a controlled-release polymer that dissolves in either water or water vapor to release silver ions to the wound. The sustained release is said to continue over a period of 5–7 days. A similar product contains activated carbon, which may be used as a deodorizing dressing. Silicone dressings have been used clinically as an alternative to paraffin gauze for the fixation of pediatric skin grafts where it was found that changing the outer absorbent dressing was painless as was the removal of the silicone dressing itself so that no analgesia or anesthesia was required. Generally, silicone dressings have a porous, semitransparent wound contact layer consisting of a flexible, polyamide net coated with silicone. The dressing is nonabsorbent, but the pores within its matrix allow the passage of exudate from the wound to a secondary dressing.

Its use is limited to minor skin grafts because the dressing requires a margin of healthy skin for application of at least 2 cm surrounding the wound. Reports have indicated that use of silicone dressings leads to improvements in the appearance (eg, scar size, erythema, elasticity) and symptoms (eg, pruritis, burning pain) after application to hypertrophic scars and keloids.[10] Silicone dressings are thought to effect this by promoting hydration of the scar and applying pressure, thereby flattening scar tissue, increasing wound elasticity, and reducing discoloration.

Other impregnations now available include gauze pads saturated with zinc sulfate, zinc oxide, or hypertonic saline, coated with a partially hydrated hydrogel or hydrogel acemannan derived from *aloe vera*.

Deodorizing Dressings

These dressings were developed as functionally specific primary dressings. Infected wounds frequently produce obnoxious odors that are embarrassing to the patient and may have a detrimental effect upon the wound-management procedure. Fungating carcinomas and venous ulcers are but 2 of the conditions that would be advantaged by the use of a deodorizing dressing.

Deodorizing dressings have been formulated from the high gaseous sorptive material, activated carbon, incorporated into a woven fabric or a fibrous mat backed by a nylon sleeve, a vapor-permeable film, or a polyurethane foam. In each formulation, the objective is to reduce odor. Therefore, the dressings must be large enough to cover the entire malodorous area. One product encourages direct contact of the carbon layer with wound exudate. This dressing adsorbs polarized bacteria onto the surface of the charcoal cloth used in the formulation. The silver present in the dressing exerts a bactericidal effect, which gradually diminishes as wound exudate saturates the material. It follows that once the activated carbon has absorbed serum plus bacteria it will cease to act specifically as a deodorizer.

Polymeric Dressings

Despite the advances in fiber technology and better understanding of the physiological parameters associated with wound healing, the fabric dressing development process has failed to provide the optimum microenvironment for wound healing, in particular, by the controlled absorption of wound exudate to allow a moist environment without tissue maceration due to excess moisture. The incorporation of new technology fibers, such as acrylics and viscose variants, and the production of nonwoven fabrics in swab and pad formulations were the precursors to the use of synthetic and semisynthetic polymers with prespecified performance parameters that would produce the required microenvironment for differing wound types at various stages of healing. The first of these interactive polymeric products appeared in the 1960s, and ongoing development has resulted in polymeric films, polymeric foams, particulate and fibrous polymers, hydrogels, xerogels, and hydrocolloids. The polymers range from polyurethane to naturally occurring polysaccharides and collagens.

Polymeric films.[11] Studies of superficial wounds emphasized the importance of avoiding dehydration and maceration of a wound surface while maintaining a moist wound interface and a gaseous exchange system similar to healthy skin.[11–13] These requirements potentiated the development of a material that would, in part, mimic the performance of skin. The resultant products were transparent, synthetic, adhesive films generically described as vapor-permeable adhesive membranes or synonymously as vapor-permeable films. They consist of transparent polyurethane or other synthetic film of low reflectance, evenly coated on one side with a synthetic adhesive mass.

The films are adhesive and cohesive, producing intimate adhesion to a dry skin surface and nonadhesion to a wet surface. They have highly elastomeric and extensible properties that contribute to both their conformability and their resistance to shear and tear. The products are sterile and particle free.

The films also possess permeability functions that are essential to their efficacy as wound management materials. It should be noted that the removal of the stratum corneum results in a water vapor loss from tissues between 3,000 g/m^2 and 5,000 g/m^2 over 24 hours. This loss will result in progressive dehydration, which could be of great significance, particularly in a full-thickness burn. The loss through a positioned vapor-permeable membrane is reduced to 2,500 g/m^2 over 24

hours or less, depending upon the structure of the membrane. This reduction allows excess fluid to be lost by water-vapor transmission through the membrane, but prevents dehydration and maintains a moist wound interface. Where the volume of exudate produced is significantly greater than the volume removed as vapor, the water impermeability will result in serous effusion accumulating below the film. Obtrusive exudate can be aspirated using aseptic technique, or preferably, the entire dressing can be changed or upgraded to one with greater vapor permeability. Impermeability to water prevents wetting from external sources.

The importance of a moist interface to wound healing is now well recognized. It allows the rapid migration of keratinocytes across the wound surface, precludes trauma due to adherence at dressing change, and contributes to gaseous diffusion in the damaged tissue. Oxygen and carbon dioxide transfer are accomplished by intramolecular diffusion through the membrane and by solution in the wound-surface moisture. The oxygen permeability of the films is variously described as 4,000 to 10,000 cm^3 m^2 24 hours at ambient atmospheric pressure. The pO_2 and pH levels of the wound surface are directly related to gaseous permeability and contribute to cellular activity. The wound is protected against secondary infection by the bacterial impermeability of the film to organisms, such as *Pseudomonas aeruginosa*, *Staphylococcus aureus*, and *Escherichia coli*.

The physical performance is applicable to the management of superficial tangential wounds, such as dermabrasions, split-skin graft donor sites, and burns. In a dermabrasion, hemostasis must first be obtained and the margin of the wound dried before the film is applied. Correctly positioned film may be left *in situ* until epithelization is complete. In its application for the treatment of burns, careful disinfection must precede the positioning of the film. It is only recommended for superficial and clinically clean burns and contraindicated for deep burns where it retards the separation of necrotic tissue.

Pressure ulcers can be covered with a vapor-permeable film with the added advantage of film resistance to shear and low frictional surface properties, which protect the dermal layers from additional physical abrasion while producing the minimal barrier to normal skin function. This performance allows the film to be used as a prophylactic in areas that are traumatized by pressure but not ulcerated.

Film dressings can also be used for the retention of cannulae and tubes in operating rooms and patient care units. Specific products have now been produced with a variable water-vapor permeability to reduce the build up of moisture beneath the film and the resultant infective hazard.

Technological development has resulted in several new intelligent vapor-permeable films that allow high permeability in high-exudate conditions, but respond to low exudate by a reduction in the moisture vapor transmission rate, thus maintaining the moist environment conducive to the optimization of the microenvironment. Recently, film dressings impregnated with an antibacterial (silver) for the management of infected wounds or a deodorizer (charcoal) for malodorous wounds have been developed.

Polymeric Foams

Foam dressings were developed alongside film dressings and have certain properties in common, but differences in their structure and composition have important implications for their performance in the clinical situation. The dressings are available as sheet dressings and foams formed *in situ*.

The sheet dressings are mainly polyurethane foams where the absorbency and water-vapor permeability are varied either by a physical modification to the foam or by combining the foam with an additional sheet component. They have many of the attributes of an ideal dressing with the added advantage of the ability to be tailored for particular applications, such as that of a tracheostomy dressing, without particle loss to the wound or loss of conformable characteristics.

Partially expanded, modified polyurethane foam was developed by Lock.[12] It comprised a lower layer of open cells and an upper hydrophilic surface with closed impermeable layers, which reduced the loss of water vapor and prevented strike through of absorbed fluid. This primary dressing expands when it becomes wet and conforms to the contours of the wound producing an environmental chamber with entrapped solutes and cell debris. It is claimed this function en-

hances the inflammatory response of the wound and subsequently stimulates the production of granulation tissue and revascularization. These polyurethane foam dressings are recommended specifically for the management of stasis ulcers with a superimposed absorbent pad and graduated pressure applied either by stretch bandages or elasticized stockings.

A foam dressing with the prime function of absorbency has been designed for the management of burns. It consists of a highly absorbent hydrophilic polyurethane foam, backed with a moisture permeable polyurethane membrane and bonded to an apertured polyurethane net on the wound contact face. It is capable of absorbing and retaining large volumes of fluid even under pressure. The backing, while permeable to water vapor, is impermeable to water thus avoiding strike through. As the exudate level decreases, the membrane retains moisture and prevents the drying of the wound. The apertured polyurethane net interface reduces adherence to the wound surface. While recommended for burns, these dressings have been used successfully on other exuding lesions.

Low-absorptive capacity primary foam dressings have been produced from a carboxylated styrene butadiene rubber latex foam. The foam is bonded to a nonwoven fabric coated with a polyethylene film, which has been vacuum ruptured. The basic foam is naturally hydrophobic, and a surface-active agent is incorporated to facilitate the uptake of wound exudate. The polyethylene film layer is particularly effective in preventing adherence, and the dressing is recommended for minor wounds and abrasions where exudate levels are low and adherence is a prominent hazard at dressing change.

Foam Cavity Wound Dressings

One major problem in wound management is the treatment of large cavity wounds produced either perioperatively (eg, pilonidal sinus) or by trauma (eg, pressure ulceration). ***It is necessary to occlude the cavity by packing to absorb excess exudate, prevent fistula formation, and stimulate the production of granulation tissue, neovascularization, and collagen deposition.***

The traditional procedure is to pack the cavity with ribbon gauze (see cellulosic absorbents) variously impregnated. The subsequent removal of such a dressing is difficult, and the pain and stress associated with the dressing change may require low-level anesthesia and the use of a special procedures or operating room.

A foam that could be formed *in situ* was developed by Dow Corning[13] and found to be clinically superior to ribbon gauze. Its status in cytotoxic terms was open to question, and it was taken off the market, but a similar product has now been developed and is used with comparable clinical success. This material consists of a 2-component foam, mixed prior to use and poured directly into the wound where the dressing expands to 4 times its original volume. It then sets to a soft spongy foam that accurately conforms to the contours of the wound cavity. The resulting stent may be removed twice daily, soaked in a mild antiseptic, rinsed in saline, and replaced. A new dressing is formed when required, usually after 7 to 10 days, to match the reduction in size of the cavity. It does not adhere to tissue, and the slight pressure produced on the cavity surfaces contributes to the production of granulation tissue. It is indicated for the management of pilonidal sinus, hydradenitis suppurativa, perianal and perineal wounds, and dehisced abdominal wounds.

Other cavity wound dressing developments have been based upon the tailoring of prepacked absorption foam fragments into nonwoven outer layers of various dimensions. These foam pillows are positioned directly in the wound and, unlike the *in situ* foams, have high absorbency and can be removed and replaced with ease at predetermined intervals.

A polyurethane/polyacrylic polymer sheet described as a hydroactive dressing is also available. It has an island configuration with a unique adhesive portion. It is nonadhesive to the wound surface and, due to its high absorptive capacity when positioned on a wound, such as a pressure or venous ulcer, expands and conforms to the wound cavity. It has the ability to re-adhere once lifted, enabling manipulation of the product for fit or assessment of the wound without dressing change. The polymer wicks fluid into the upper layers of the dressing where it escapes through the backing.

Along with the vapor-permeable films, the foams continue to evolve toward a more precise control of the wound microenvironment.

Hydrogels[14]

Hydrogels, or water polymer gels, are 3-dimensional networks of hydrophilic polymers prepared from materials, such as gelatin, polysaccharides, cross-linked polyacrylamide polymers, polyelectrolyte complexes, and polymers or copolymers derived from methacrylate esters. They interact with aqueous solutions by swelling to an equilibrium value and retain a significant proportion of water within their structure. They are insoluble in water and are available as dry or hydrated sheets or a hydrated gel in an individual delivery system. The tissue-like structure of most hydrogels will contribute to their biocompatibility by minimizing mechanical irritation to surrounding cells and tissues. Sheet hydrogels currently used as wound dressings possess most of the properties of an ideal dressing. Their high moisture content maintains a desirable moist interface with the surface of the wound, which facilitates cell migration and prevents dressing adherence. The gels are able to absorb fluid into the polymer matrix and swell in a 3-dimensional manner, and they maintain a sheet form without intruding into the wound cavity. Water can be transmitted through the saturated gel while the unsaturated gel has a water-vapor permeability comparable to that of vapor-permeable membranes.

The first wound management hydrogel product developed was a cross-linked polymer of polyacrylamide and agarose. The mesh size allowed the absorption and desorption of both high molecular-weight proteins and low molecular-weight solutes. While this performance parameter is essential in its function as an environmental dressing, it could also be utilized to transport compounds to the wound and thus act as the release component in a sustained-release system. Some success has been evident in using topical antibacterials in this way, but it would seem that there may be a greater potential still to be exploited. The ability to sustain release can be seen from the results of the growth curves of L929 and epithelial cells growing *in vitro* beneath a nutrient-saturated hydrogel.[15] Growth is maintained at a higher level than that observed with the control where the cells are surrounded by media. The cells become a confluent layer adhering to the lower surface of the gel. This property can be utilized to transfer epithelial seed cultures to large partial-thickness wound areas and thus supplement the current practice of skin grafting. If the epithelial layer is derived from the patient's own tissue, this may avoid problems associated with graft rejection.

Diffusion rates from the hydrogel can also be controlled by the degree of cross linkage. For example, initial cross linking of aqueous solutions of sodium alginate and calcium chloride followed by external cross linking of the produced suspension using poly-L-lysine or poly-ethylene-imine will result in a predetermination of the mesh size and thus control the release rate of sorbed compounds, such as polypeptides or growth factors.

Other hydrogel properties could also be utilized as release mechanisms. Gel synapsis at the Theta, Ø, critical temperature of temperature-sensitive hydrogels results in expansion or collapse of the hydrophilic networks. This process could be used to design a release system for wound management where a drug could be incorporated into the hydrogel structures at one temperature and the active component released abruptly as the critical temperature approaches 32°C when phase separation occurs. pH-sensitive hydrogels may be polybasic or polyacidic and will preferentially release compounds in a pH-changed environment. This property is being developed for periodontal medication using glassy hydrophobic hydrogels, which become highly hydrated from pH2 to pH6. The pH changes in infected wounds might well be used to initiate the release of topical antibacterials until the pH reverts to normal and the sustained-release system ceases to operate. All of these properties have been the subject of investigation with the objective of developing new products.

It has been observed that the use of a hydrogel frequently results in a marked reduction in pain response in patients. It is suggested that the high humidity protects the exposed neurons from dehydration and also produces acceptable changes in pH. A secondary effect, which may contribute to this response, is the property of the gels to immediately cool the wound surface and maintain a lower temperature for up to 6 hours. In a wound, this lowering of temperature results in a reduction of the inflammatory response.

Hydrogel sheets or gels of similar composition have been developed to allow continuity of

formulation and function in, for example, cavity wounds. The wound volume is filled with the amorphous hydrogel, and the hydrogel sheet is superimposed over the wound. Hydrogels are nonadherent, so a secondary dressing, such as a vapor-permeable film, will be required.

Hydrogels have been developed to produce a moisture "donor" effect for necrotic wounds that require debriding. They are at present available only in the amorphous hydrogel form. Some manufacturers have produced gauze pads presaturated and impregnated with a hydrogel. Recent developments have been directed at producing hydrogel sheets bonded onto a vapor-permeable film to control water-vapor transmission and to prevent the possible hazard of wet hydrogels becoming dry sheets, which would be incompatible with a healing surface.

The recommendation for use of these products includes the management of donor sites and superficial operation sites and also the treatment of chronically damaged epithelium. In chronic ulcers, they are used to promote autolytic debridement and to encourage granulation and the formation of a cellular matrix.

Particulate and Fibrous Polymers[16]

The group of xerogel dressings includes synthetic, semisynthetic, and naturally occurring products embracing a range of polysaccharide materials, such as alginates and dextranomers. They are in an ongoing state of development with new and "me-too" products appearing at frequent intervals.

The xerogel dressings may be regarded as a subgroup of products within the larger group of polysaccharide dressings. The latter contains the well known cellulosic dressing products, such as gauze and absorbent cotton (these have been dealt with earlier in this chapter under Absorbents). However, the products that consist of dextranomer beads, dehydrated hydrogels of the agar/acrylamide group, calcium alginate fibers, and dehydrated granulated Graft T starch polymers are identified specifically as xerogels,[16] the material remaining after the removal of most or all of the water from a hydrogel (or the disperse phase from any type of simple gel).

Particulate dextranomer. Dextranomer is prepared from dextran, a naturally derived polymer of glucose produced by cultures of a microorganism, *Leuconostoc mesenteroides*. The gel is formed when the dextran molecules comprising the disperse phase of the hydrogel are crosslinked by a chemical process utilizing epichlorhydrin and sodium hydroxide.

The dextranomer is supplied in beads of 100 μm to 300 μm diameter containing poloxamer 187, polyethylene glycol 300 (PEG 300), and some water. A paste formulation is also available, which is the dextranomer in polyethylene glycol 600 (PEG 600). The beads are offered as discrete particles or enclosed in a low-adherence pouch for insertion into a cavity wound. One company (Pharmacia AB, Sweden) offers a polymeric net that can be placed into a cavity wound before the addition of either granules or paste, facilitating removal of the product. A vapor-permeable film is superimposed on the dextranomer dressing in a low exuding wound to control evaporation and retard drying of the dressing. The dextranomer acts as a selective sorbent, as the hydrophilic beads will absorb the aqueous component of wound exudate and dissolved materials ranging from inorganic salts to low molecular-weight proteins. Dextranomer has a pore size that produces an exclusion limit of 1,000 to 8,000 Daltons, precluding the sorption of viruses and bacteria. Microorganisms are removed from the wound by a capillary action between the beads, a function that is absent from the paste formulation. This function, however, demonstrates a marked increase in absorbing capacity for malodorous elements and pain-producing compounds released during the inflammatory response.

It may be used as a debriding agent on sloughy and exuding wounds where the objective is to produce a clean tissue bed for the production of a granulating tissue. It is not a product that should be used beyond this phase of the wound-healing process, as its continued application will impair epithelization. Dextranomer is not biodegradable and both granules and paste must be carefully removed with saline to avoid particulate residues and the subsequent development of granulomas.

Fibrous polymers. Alginate fibers are derived from alginic acid, which is a polyuronic acid composed of residues of D-mannuronic acid and L-guluronic acid. Alginic acid is obtained chiefly

from algae belonging to the Phaeophyceae, a species of *Laminaria*.

The isomeric acids are present in varying proportions dependent upon the seaweed source. Calcium alginate is capable of gel formation. The guluronic acid forms an association with calcium, providing the stimulus to produce the continuous disperse phase of a hydrogel. Ca^{2+} ion and a phospholipid surface promote the activation of prothrombin in the clotting cascade. ***Calcium alginate products are used as the source of these ions to arrest bleeding, both in superficial injuries and as an absorbable hemostat in surgery. The rate of biodegradation is related to the sodium/calcium balance in the preparation.***

The alginates are produced in fiber form and have been developed as a fleece or layered needled fabric. When applied to a bleeding surface, the availability of the Ca^{2+} ions and the fibrous matrix contribute to coagulation, and serum absorption produces a gel-like mass. The dressings may be removed either with sterile 3% sodium citrate solution followed by washing with sterile water or with sterile normal saline.

The wet integrity of the dressing, which facilitates removal from the wound, may be improved by incorporating fibers of greater strength, such as viscose (rayon) staple fiber, or fibers that interact with the alginate fibers when wet, such as chitosan staple fibers.

Alginate gauze and staple products are applied using normal sterile dressing procedures. The frequency of change will be a matter for clinical assessment of the injury and depend on the type of wound and the degree of exudation.

The primary hemostatic usage of calcium alginate is in the packing of sinuses, fistulae, and bleeding tooth sockets. The use of calcium alginate as a hemostatic agent dates back to the 1950s. Its subsequent development as a xerogel, which is converted to a hydrogel in the presence of wound exudate, came in the late 1970s. It was at this stage that the significance of the Ca^{2+} and Na^{+} ion ratios became apparent in physical differences between the gel strength of products containing high or low Na^{+} ion levels. This discovery has led to a range of Ca/Na alginate dressings in the form of fibrous and fabric preparations, which have different absorptive capacities and gelling properties. The alginates also have been cross formulated with a collagen type 1 and chitosan to increase the possible bioactivity.

Recent studies have indicated an auto oxidation property of alginates, which stimulates the production of hydrogen peroxide. In addition to containing Ca^{2+} ions, alginates have been identified as contributing to the initial inflammatory response required to kick start the healing cascade by causing lysis of mast cells with the subsequent release of histamine and 5HT.

Alginate dressings have been used successfully as hemostats for lacerations and abrasions and are effective in the management of hypergranulation (proud flesh), interdigital maceration, and heloma molle. They are used in hospitals and communities to accelerate healing in intractable skin and pressure ulcers and in the successful management of diabetic ulcers, venous ulcers, and burns.

Alginates have also proven to be useful autolytic debriding agents. When applied to these injury types, the alginate must be covered by a secondary dressing of foam or film.

Hydrocolloids[17]

Hydrocolloid dressings have developed from the adhesive flanges used for long-term protection of skin surrounding a stoma. The barrier produced prevented the excretions from eroding or denuding the skin, and the flange acted as a base for the adhesive attachment of ostomy collection devices. The development of the hydrocolloid as a wound management product has resulted in new formulations and a range of technologically superior products available in adhesive sheet, granular, and paste forms.

The early hydrocolloid dressings consisted of composite agents based on naturally occurring hydrophilic polymers. In general, they have a pressure-sensitive adhesive layer composed of a so-called hydrocolloid, dispersed with the aid of a tackifier in an elastomer and, secondly, a film coating composed of a variable vapor-permeable but water-impermeable, flexible, elastomeric material. One of the first hydrocolloid dressings described had a pressure-sensitive adhesive hydrocolloid layer, which consisted of a mixture of gelatine and sodium carboxymethylcellulose, 40%–50% by weight, dispersed in polyisobutylene with an antioxidant and a tackifier (mineral oil and terpene resin). This mixture was

then laminated with a semi-open–cell, flexible polyurethane foam previously laminated with a closed-cell, flexible polyurethane film. A currently available hydrocolloid dressing is a flexible mass with an adherent inner face and an outer vapor-permeable polyurethane foam. The modified formulation is as follows: sodium carboxymethylcellulose 20%; polysiobutylene 40%; gelatine 20%; pectin 20%. This product is also available as a paste of similar formulation allowing a continuous fill for cavity wounds.

Other hydrocolloid dressings with formulations consisting of sodium carboxymethylcellulose combined with karaya gum or sodium carboxymethylcellulose alone are also available.

The adhesive formulation of hydrocolloids gives an initial adhesion higher than some surgical adhesive tapes. After application, the absorption of transepidermal water vapor modifies the adhesive flow to maintain a high-tack performance throughout the period of use. *In situ*, the dressings provide a gaseous and moisture-proof environmental chamber strongly adhered to the area surrounding the wound and offering protection against contamination from incontinence or other sources. In the wound contact area, the exudate is absorbed to form a gel that swells in a linear fashion with a higher moisture retention at the contact surface. This higher moisture retention results in an expansion of the gel into the wound cavity with the continued support and increasing pressure from the remainder of the elastomeric dressing. The larger the volume of exudate, the greater the expansion into the cavity, up to the limitation imposed by the availability of the gel. ***The advantage of this system is that it applies a firm pressure to the floor of a deep ulcer, a basic surgical maxim for the production of healthy granulating tissue. It is this function that contributes to its recommended usage for venous ulcers.***

The formed colloidal gel will also produce a sorption gradient for soluble components within the serous exudate and thereby allowing the removal of toxic compounds arising from bacterial or cellular destruction. The moist gel is soft and conforms to the wound contours. When the dressing is removed, the gel remains in the wound and can be washed away with normal saline. No damage to the wound results from this procedure. During use, the dressing in contact with the wound liquifies to produce a pus-like liquid with a somewhat strong odor. The hydrocolloids are suitable for de-sloughing and for light-to-medium exuding wounds but are contraindicated if an anaerobic infection is present. They have been used successfully in the treatment of chronic leg ulcers, pressure ulcers, and skin barriers in the management of stomas.

As with hydrogels, hydrocolloids are available in both powder and paste form where the powders and pastes have similar formulations to that of the hydrocolloid mass in the sheet dressing. This versatility will allow larger cavity wounds to be treated with a continuous hydrocolloid system.

A recent development for deep exuding pressure ulcer management is a hydrocolloid dressing with a formulation including sodium alginate in a spiral form rolled into a round disc, which can be positioned in the cavity and covered with a hydrocolloid sheet dressing. A further advance has been the development of thin hydrocolloid sheets with improved conformability and a degree of transparency that allows the wound to be observed without removal of the dressing. This latter product is comparable in performance with a vapor-permeable film. ***It should be noted that although the hydrocolloids are primarily considered to be interactive dressings, incorporating silver into their formulation, as has been done by several manufacturers, must contribute a bioactive function to the material.***

Superabsorbents

Superabsorbent hydrocolloid dressings are highly absorbent and entrap exudate so that it cannot be squeezed out once absorbed. One product incorporates the highly absorbent material into an island pad covered by a nonwoven absorbent and surrounded by an extra thin hydrocolloid as the adhesive portion. The covering acts as a transfer layer while its surface stays dry.[18]

Hydrofibers

Hydrofibers are fibers of carboxymethylcellulose formed into flat, nonwoven pads for application to large, open wounds. They appear as a textile fiber and are presented in the form of a fleece held together by a needle-bonding process. Hydrofibers are also available as a "ribbon" for packing cavities. The dressing absorbs and inter-

acts with wound exudate to form a soft, hydrophilic, gas-permeable gel that traps bacteria and conforms to the contours of the wound while providing a microenvironment that is believed to facilitate healing. The resultant gel is similar to a sheet hydrogel, but it does not dry out or wick laterally, which ensures that there is no maceration of the skin surrounding the wound. The high absorbent capacity reduces the frequency of dressing changes.

Hydrofiber dressings are easy to remove without causing pain or trauma and leave minimal residue on the surface of the wound. They may be applied to exuding lesions, including leg ulcers, pressure areas, donor sites, and most other granulating wounds, but for deeper cavity wounds and sinuses, the ribbon packing is generally preferred.[18]

Bioactive Products

When developing interactive products, the environment sought was obtained, but some chronic injuries still refused to respond adequately. Since most wounds, when not infected, heal spontaneously in endocrinologically and nutritionally normal mammals, it had always been considered axiomatic that the rate of healing represents a biologic maximum and therefore could not be accelerated beyond the available capacity of the tissues. However, the experimental use of processed cartilage and cartilage extracts showed the potential to stimulate through topical application the normal or enhanced activity of the acellular and cellular mechanisms involved in tissue repair. Such products may be considered to produce a localized systemic intervention and can be defined as bioactive.

A brief reexamination of the healing cascade (Figure 2) is sufficient to identify those parts of the cycle that could be influenced by such materials either by correcting some deficiency in the biochemical pathway or by stimulating the involved cellular elements to increase their activity and accelerate their biofunction.

The initial inflammatory response is predominantly acellular by comparison with the regeneration and repair processes. It is in these 2 latter processes that the designated bioactive compounds need to perform as the biologic primers for cell proliferation and tissue reconstruction.

Naturally occurring polysaccharides, such as hyaluronic acid and chondroitin sulphate, are glycosaminoglycans (GAGs), which have been shown to be involved in diverse structural and organization functions in tissues. They and other GAGs, such as heparin and dermatan sulphate, show a partial specification for cell surface interactions, cell/cell interactions, cell substrate interactions, or cell proliferation. They have an important bioactive influence on the microenvironment and, therefore, on tissue regeneration. Noncollagenic proteins, such as fibronectin (C1g) laminin and chondronectin, are still to be fully characterized, but their *in vitro* effects on cell division are well documented. Fibronectin demonstrates chemokinesis on fibroblasts (general stimulation of movement) and, in the presence of a concentration gradient, chemotaxis (directional movement stimulated by a gradient of diffusable substance) and hapotaxis (directional movement stimulated by a gradient of substrate adhesiveness). These proactive materials are now becoming available after being challenged for their levels of quality, safety, and efficacy.

Polymeric materials, such as pectins, alginates, and chitosan, which act as pro-oxidants are important. In other words, in the presence of traces of transition metal catalysts, such as iron and copper ions, they interact with dissolved molecular oxygen to form superoxide, which dismutases spontaneously to form hydrogen peroxide.[15] This reactive oxygen species initiates oxidative processes and has been shown at concentrations of 10^{-6} M to 10^{-9} M to stimulate both the proliferation of fibroblasts and the macrophage respiratory burst. The Superoxide Assisted Fenton Reaction is as follows:

$$Fe^{3}+ + O_2 \downarrow Fe^{2}+ + O_2$$

$$Fe^{2} + H_2O_2 \downarrow Fe^{3} + \bullet OH^{-} + -OH$$

The use of hydrogen peroxide has been discouraged in wound management. Its toxicity in fibroblast cultures and its tissue destruction properties in vivo have been reported at higher concentrations than those quoted here. At these low concentrations, there is a 20% increase in murine fibroblast proliferation over a period of 3–6 days. Work involving the use of low passage number human fibroblasts has also shown substantially

higher increases.[19]

The generation of superoxide also contributes to leukotaxin formation, which could reinitiate the inflammatory response in recalcitrant wounds. The resultant influx of monocytes/macrophages would contribute further superoxide and hydrogen peroxide to the wound environment. Following NADPH oxidase activity, the higher concentrations of hydrogen peroxide would initially inhibit the proliferation of fibroblasts, but as its concentration falls, the rate of cell division is enhanced leading to collagen synthesis.

Further investigations completed and in progress have identified similar antioxidant activity in other hydrogel and hydrocolloid products.[19]

It would appear that the application of antioxidant wound contact materials to soft tissue lesions in patients whose intrinsic antioxidant defenses are compromised by age, dietary deficiency, or physiological deficiency, such as diabetes, would contribute to an improved antioxidant status in the wound locality and thus establish and maintain the reducing environment necessary for energy production and hence cell division.[20] This process, plus the maintenance of moist wound healing, could contribute to the rate of healing and repair of the soft tissue injury by normalizing the complete bioenvironment.

Growth Factors

The year 1986 was a landmark in wound healing. This was the year that Cohen and Levi-Montaleini shared a Nobel prize for their work on epidermal and nerve growth factors. This research stimulated many other workers to investigate the potential of other growth factors.

Growth factors and cytokines are polypeptides transiently produced by cells that exert their hormone-like function on other cells via specific cell-surface receptors and thereby increase the mitotic index of proliferating cells. They have been broadly classified as paracrine when they act upon neighboring cells and autocrine when they act upon producing cells. Their activities overlap, and the effect of most of them depends on the group and pattern of regulatory molecules to which the cell is exposed.[21] Growth factors are so named because of their stimulatory effect on cell proliferation. They display both stimulatory and inhibitory activities even with the same cells depending on the state of activation and differentiation of the cells and the presence of other stimulating factors. Several growth factors have been identified in wounds, but their precise functions are still a matter of debate.

Three types of growth factor are recognized based upon the apparent cellular response: proliferative, migratory, or producing an alteration in the phenotypic state.

The proliferative response can be stimulated by the following:

1) The cell moves from the resting state, inducing DNA replication and proving the competence of the cell; the cell is then sensitive to the progressive factor that leads to cell replication
2) Chemoattractants stimulate migration or movement of cells
3) The transforming growth factors produce a phenotypic alteration. There are 5 families of peptide growth factors that are thought to be involved in wound healing: epidermal growth factor (EGF), transforming growth factor-ß (TGF-ß), platelet-derived growth factor (PDGF), insulin-like growth factor (IGF), and fibroblast growth factor (FGF).

Macrophages are the cells pivotal in bringing about the first stages of healing after which they then control and direct it before finally stopping it when the repair is complete. The cells modulate the immune response by induction of lipoxygenase products through stimulation of the arachidonic acid cascade.[22] In addition to aiding debridement at the wound site, they are involved in the secretion and synthesis of the collagenases neutrophil elastase and matrix metalloproteinase 8 (MMP 8) preparatory to laying down new extracellular matrix (connective tissue). They are a source of the growth factors PDGF and TGF-ß and regulate fibroblast migration and proliferation by production of the cytokine interleukin-1ß (IL-1ß).[23,24]

The possible bioactivity of platelet-derived angiogenesis factor (PDAF), of platelet-derived growth factor (PDGF), and their interrelationship with the healing cascade is summarized in Figure 3.

A commentary in *The Lancet*[25] emphasized the clinical potential of the cytokine TGF-ß, which exhibits autocrine, paracrine, and endocrine ef-

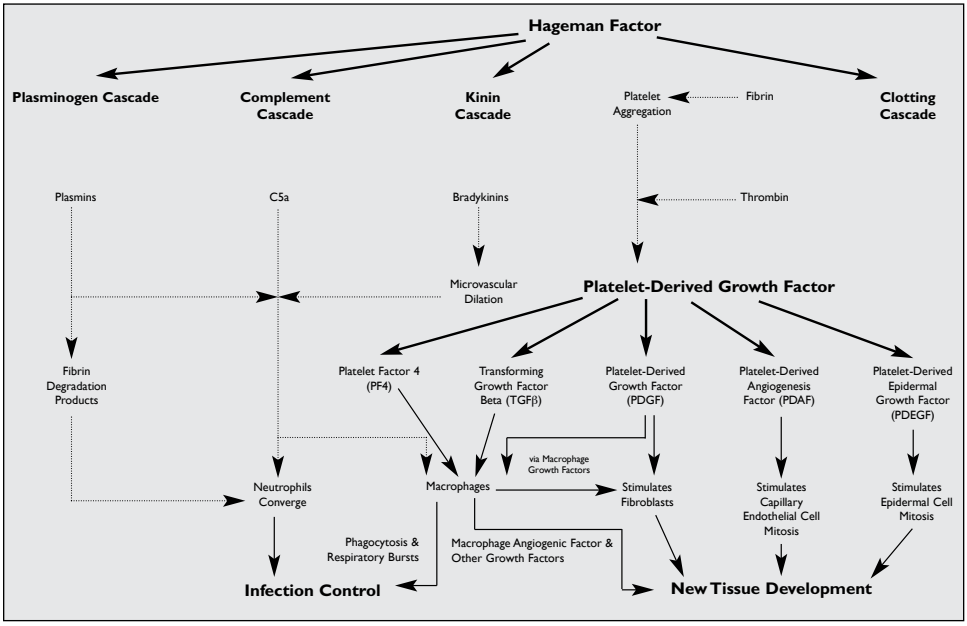

Figure 3. Platelet-derived growth factors and their interrelationship with the healing cascade.

fects. TGF-ß acts through the heteromultimers of receptors on the cell surface. Clinical interest has been focused on this growth factor's role in extracellular matrix deposition and leukocyte infiltration, which are important factors in wound healing. The chemotactic effect of TGF-ß on fibroblasts stimulates the deposition of collagen and other components of the extracellular matrix. Dermal wounds in rats are reported to heal with reduced scarring, and a clinical trial on venous ulcers showed a marked promotion of healing.[25]

The ongoing development of these products and their introduction as pharmacological agents in wound management are dependent upon a number of factors, not the least of which is the level at which the increase in cell replication is considered to be therapeutically significant and is further complicated by the difficulty of determining the rate in connective tissue.

The quantitative and qualitative effects must be the subject of new laboratory and clinical assessment procedures. The use of reproducible models, such as skin graft donor sites or implanted wound tissue sampling devices and bioassay techniques using cell cultures, will contribute to our characterization and ultimate usage of these factors.

The clinical expectation of application is wide, and the number of organizations involved internationally in research development and production is in the hundreds. There would therefore appear to be sufficient interest and available resource to ensure an in-depth evaluation of these bioactive materials that by enhancement or inhibition of inflammation, fibroplasia, epithelization, angiogenesis, connective tissue repair, and contraction may act as the normalizer in nonhealing wounds or the accelerator in normal wounds.

Future Development

Inevitably, new products will continue to become available for wound care in hospitals and the community. There will be extensions to the range of collagen products as well as that of membranes and skin substitutes as research techniques become more sophisticated. Conversely, some products, such as antiseptics and antibacterial materials in their present form, will disappear from the wound-care armamentarium. There is, and will continue to be, an increased interest in the use of biosurgical agents, such as leeches and maggots.

For the foreseeable future, *interactive* materials

will continue to be the first choice for wound management, as they are undoubtedly effective, and their price is competitive when compared to some of the previously described materials and whose use is recommended for wounds requiring specialized treatment. However, there is a real need for more evidence-based information about the comparative efficacies of these interactive materials for wound care to aid the selection of the most appropriate wound-management product to be used on any wound.

Evidence-based practice in wound care has not kept pace with the number of products marketed, and there is a great paucity of reliable information about the effectiveness of individual products or of their comparative effectiveness with products of a similar formulation. At present, it is impossible to select the best hydrocolloid, alginate, or hydrogel or to know that one dressing in a group is superior to another for application to a particular wound type. This has serious implications for both prescribers and patients.

Many of our preconceived ideas of tissue repair will have to be reexamined in the light of the new information these products will reveal. In addition, clinicians need to re-educate themselves with regard to not only the use of bioactive products but also the application of the innovative interactive materials in the management of their patients' wounds. It is a disturbing fact that despite the availability of these technologically and clinically advanced products, many wounds are still dressed with a gauze fabric—an original passive out-of-sight, out-of-mind dressing. The famous remark of the French surgeon, Ambroise Paré (1510–1590) "…que je pensay et Dieu la guarist," meaning, "I dressed (the wound) and God healed it" could well be the current fatalistic philosophy of many healthcare providers and produce a delay in the adoption of new products and procedures.

Ongoing developments, particularly at the cellular level, will hopefully result in successful and speedy healing of most, if not all, wounds with the resultant alleviation of pain and distress in both man and animals, as the management of soft-tissue injuries in animal species is becoming increasingly important, and many research activities are currently being progressed in this area.

Take-Home Messages for Practice

- The reader should understand the differences in formulation and function of passive, interactive, and bioactive materials.
- The reader should be able to compile a practice-based care plan, diagnose the healing stage at each dressing change, and select appropriate materials to ensure that healing progresses satisfactorily to effectively manage the wounds for each patient.

Self-Assessment Questions

1. Which of the following dressings would be suitable to treat a full-thickness burn with moderate exudate?
   A. Absorbent lint
   B. Hydrocolloid
   C. Water vapor permeable film (or polymeric film)
   D. Foam

2. Glycosaminoglycans belong to which class of wound management products?
   A. Passive
   B. Interactive
   C. Bioactive

3. Which of these growth factors stimulate epidermal cell mitosis?
   A. TGF-ß
   B. PDGF
   C. PDAF
   D. PDEGF

Answers: 1-C, 2-C, 3-D

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