Human amniotic membrane: a versatile wound dressing

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Human amniotic membrane proved to be a versatile and useful temporary biologic dressing in studies involving 120 patients. Wounds, both traumatic and nontraumatic in origin, responded to a protocol that allowed coverage of tissues as diverse as exposed bowel, pleura, pericardium, blood vessels, tendon, nerve and bone. Wounds unresponsive to usual therapeutic measures responded to membrane application. Ease of availability, negligible cost and facilitated wound healing make this temporary biologic dressing generally superior to either cadaver skin allograft or pigskin xenograft. Human amniotic membrane dressings are therefore a useful adjunct in the care of the complicated wound.

Dans des études impliquant 120 patients la membrane amniotique humaine s'est avérée un pansement biologique temporaire utile et versatile. Les blessures, traumatiques ou non, ont répondu à un protocole qui prévoyait le recouvrement de tissus aussi divers qu'un intestin, une plèvre, un péricarde, des vaisseaux sanguins, un tendon, un nerf ou un os mis à nu. Des blessures ne réagissant pas aux mesures thérapeutiques habituelles ont répondu à une application de membrane. Sa grande disponibilité, son coût négligeable et son effet bénéfique sur la cicatrisation des blessures rendent ce pansement biologique temporaire généralement supérieur aux allogreffes de peau d'origine cadavérique ou aux xénogreffes de peau de porc. Les pansements de membrane amniotique humaine constituent donc une mesure d'appoint utile dans le traitement des blessures compliquées.

The main goal in management of an open wound is to obtain a clean and closed wound in the shortest time. Deleterious effects of an open wound are many and are related mainly to the size and site of the wound. Fluid, heat and nutrient loss, continuing contamination and sepsis, and associated pain and decreased mobility may seriously hamper patient recovery, and early coverage of a major burn wound may be lifesaving. The search for an ideal wound cover as a substitute for the patient's skin began more than a century ago and continues today. In the late 1800s Girdner,[1] Reverdin[2] and Lee[3] used cadaver and animal skin to cover burn wounds. Davis[4] in 1910 reported attempts to graft pieces of amniotic sac onto granulating wound, and 3 years later Sabella[5] described the treatment of a burned patient with portions of amniotic membrane.

These early attempts at substitution for the patient's skin were designed to provide permanent coverage and failed because of immunologic rejection. Years later Dogo[6] initiated the use of split-thickness cadaver skin allografts as temporary biologic dressings for large burn wounds, a procedure popularized by Brown and associates.[7] Removal of such dressings and replacement with another skin allograft or an autograft prior to rejection was an important factor in the increasing rate of survival from major burns. The rejection reaction is unpredictable and occurs unevenly. Edema and cellular reaction produce unhealthy granulation tissue susceptible to bacterial invasion, and the concomitant systemic response may be severe and cause further debilitation in the burn patient.

Difficulties in obtaining adequate supplies of cadaver skin led to a search for substitute tissues. In 1957 Rogers, Converse and Silvetti[8] proposed concerted investigation into the use of bovine embryo skin as a temporary dressing for large skin wounds. Bromberg, Song and Mohn[9] later reported the results of their laboratory and clinical investigations with pigskin xenografts, which, because of their commercial availability, have become popular in many centres.

The use of human amniotic membrane as a temporary biologic dressing has been evaluated recently, both experimentally and clinically, by Robson and Krizek.[10] In a series of 50 rat burns infected with 10^8 Pseudomonas aeruginosa organisms, this dressing was shown to be 1000 times more effective than split-thickness human skin grafts in decreasing bacterial contamination. In another experimental model human amniotic membrane was found to be as effective as split-thickness isograft skin but superior to split-thickness allograft and xenograft skin in decreasing bacterial contamination of full-thickness skin defects created on the backs of rats.[11] The usefulness of human amniotic membrane in the management of open wounds was further substantiated by Robson and associates[12,13] in a study of 150 patients, and by Colocho and colleagues[14] in their use of the amnion layer alone as a physiologic wound dressing in 107 patients with partial-thickness burns and split-thickness graft donor sites.

We undertook the study described below to evaluate the usefulness and versatility of human amniotic membrane as a temporary biologic dressing in a wide variety of common and challenging clinical situations, and to determine an optimal protocol for its use.

Methods

Patients

Included in the study were 120 patients in need of temporary biologic dressings. Their wounds were mainly full-thickness defects of diverse origin and certain partial-thickness defects. Accurate clinical and photographic records were kept.

Material

Fresh amniotic membranes were obtained at the time of delivery from women who were seronegative for syphilis and had no history of premature rupture of the membranes or endometritis. Meconium-stained or foul-smelling membranes were discarded. With aseptic technique, membranes were removed from the placenta, not separated into amnion and chorion, and washed four times with sterile normal saline, once with 0.025% sodium hypochlorite solution, then four times with normal

saline. With each wash the membranes were agitated thoroughly to dislodge any adherent clot. Thereafter they were refrigerated in individual sterile containers at 4°C. Cultures done at repeated intervals were uniformly sterile. No material was used after 6 weeks of storage.

Protocol for use of membranes

The area to be covered is cleansed with saline, and any exudate or medications are removed. All eschar and devitalized tissue must be removed. Human amniotic membranes are placed so as to adhere closely to the underlying wound surface without air pockets or wrinkles. They should cover the entire wound surface and, because of their great pliability and adherence, can be tucked into recesses and overhanging areas.

In full-thickness defects the chorion (dull aspect) is placed on the wound and the amnion (shiny surface) faces upwards. Membranes are changed every 48 hours unless there is heavy contamination or infection; then they are changed more frequently. In severely infected areas membranes should not be used while there is a great amount of free pus. Instead, such areas should initially be cleaned frequently with moist dressings (for 24 to 48 hours) and the membranes applied subsequently. "Take" is evident when the membrane becomes firmly adherent to the tissue bed without underlying accumulation of debris or pus. Thick membranes are gently peeled off the wound surface, while thinner ones are removed by rubbing the wound surface with dry gauze. Membrane removal leaves underlying healthy granulation tissue. Once consistent take has occurred the wound is ready for permanent autogenous skin grafting or closure. Whenever possible, more superficial dressings are not used since the dry superficial layer of amniotic membrane forms a firm and pliable wound cover, facilitating observation. Collections of serum or purulent material beneath the membrane may be evacuated by unroofing the small blebs or changing the membrane. In mobile patients a firm dressing is applied to prevent dislodgement.

In partial-thickness wounds the membrane should be applied with the amnion against the wound surface. The membrane is allowed to remain in place undisturbed while epithelialization progresses beneath it. Spontaneous separation of the membrane occurs when epithelialization is complete.

Clinical experience

The clinical use of human amniotic membrane as a temporary biologic dressing is limited only by the surgeon's imagination and the availability of the membrane. Experience derived from the management of 120 patients with wounds of diverse origin has enabled us to categorize wounds into various clinical types (Table I).

Ulcers

Human amniotic membrane was used in the management of 30 skin ulcers of diverse origin, mainly of the leg; the underlying problems included venous stasis, arterial disease and diabetes. Decubitus ulcers and ulcers resulting from soft-tissue infection were similarly treated. Most of the chronic ulcers had failed to respond to routine wound care.

In small ulcers human amniotic membrane kept the wounds bacteriologically clean, thus allowing spontaneous closure to occur (Fig. 1). In large ulcers the membranes were used to prepare the wound for subsequent definitive closure. Most of these patients were treated as outpatients.

Elective surgical wounds

Certain surgical wounds may be left open for various reasons after elective procedures. Human amniotic membrane can then be used to cover the wound, preventing contamination, in preparation for definitive closure. Thirty wounds were thus treated. Included were wounds from radical vulvectomy, radical mastectomy and open amputation. Following radical excision of pilonidal sinuses human amniotic membrane was similarly used to provide a pain-free, clean wound without the use of sitz baths; this resulted in rapid mobilization of the patient and reduced the time required for healing and convalescence.

Infected wounds

In 21 infected wounds human amniotic membranes were used to decrease wound bacterial counts, usually after incision and drainage of an incisional abscess. Once the counts were 10^5 bacteria or fewer per gram of tissue, as evidenced by take of the membrane, delayed wound closure was performed. Rapid reduction of bacterial counts permitted successful secondary wound closure. This treatment was particularly useful in the following two cases:

Case 1: Following abdominoperineal resection of the rectum and colon, dehiscence of the abdominal wound with exposure of small bowel loops occurred in a severely debilitated patient. Human amniotic membrane was applied to the small bowel and the open wound and was changed frequently. This resulted in coverage of the entire wound surface and small bowel with healthy granulation tissue and facilitated successful subsequent autograft closure.

Case 2: Human amniotic membrane was applied directly to parietal pleura in a 58-year-old debilitated man in whom dehiscence of the thoracotomy wound occurred after esophagectomy for esophageal carcinoma. In 14 days the entire wound and pleura were covered with healthy granulation tissue, allowing successful closure.

Contaminated surgical wounds

In the management of 12 patients with contaminated surgical wounds human amniotic membrane was used to decrease wound bacterial counts to levels that allow delayed definitive wound closure. In particular, the membranes proved extremely useful in the management of heavily contaminated appendectomy wounds. Following closure of the peritoneum and deep fascia the superficial wound layers were left open and human amniotic membrane was applied. The membrane was changed every 24 to 48 hours until take was evident. Delayed primary wound closure was then performed on the ward with Steri-Strips (medical products division, Minnesota Mining & Mfg. Company,

Table I—Clinical types of wounds managed with dressings of human amniotic membrane	
Type of wounds	No. of patients
Ulcers	30
Elective surgical wounds	30
Infected wounds	21
Contaminated surgical wounds	12
Nonhealing or poorly healing wounds	10
Burns	10
Traumatic soft-tissue wounds	7

FIG. 1A—Chronic venous stasis ulcer.

FIG. 2A—Pyoderma gangrenosum of perineoscrotal area; deep, burrowing ulcers with necrotic base and undermined edges with black, "lifeless" appearance; anal stump evident.

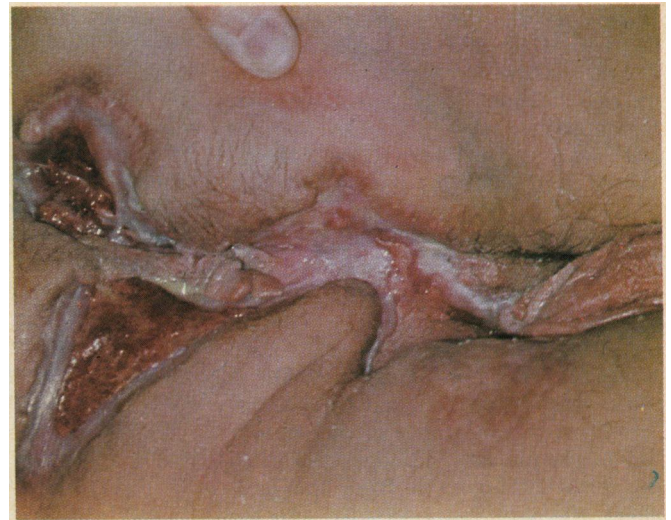FIG. 1B—Human amniotic membrane applied to ulcer.

FIG. 2B—After 6 weeks of application of human amniotic membrane, undermined edges filled in, new epithelium at periphery, and significant healing and wound contraction.

FIG. 1C—Ulcer completely healed in 3 weeks.

FIG. 3—Major full-thickness burn wound after separation of eschar; large membranes used to advantage.

3M Center, St. Paul, Minn.) and was uniformly successful.

Nonhealing or poorly healing wounds

In 10 patients with nonhealing or poorly healing wounds of diverse origin human amniotic membrane was applied to stimulate healing and granulation tissue formation. Most of these wounds had failed to respond to routine wound care and systemic support. The change in wound appearance following application of the membranes was often striking, as in the following cases:

Case 3: A 45-year-old man underwent total proctocolectomy for Crohn's disease. Pyoderma gangrenosum of the perineum developed thereafter, with sloughing and ulceration of almost the entire perineoscrotal area, which was completely resistant to all forms of treatment for 18 months. Frequent dressings and sitz baths necessitated narcotic analgesia. The wound prior to the application of human amniotic membrane is shown in Fig. 2A. Steroids and azathioprine were being administered for control of the Crohn's disease.

Pain was relieved when application of human amniotic membrane was begun. Every 48 hours the membrane was removed in a sitz bath and another applied. No débridement or other form of wound care was used. Within 3 weeks there was a remarkable transformation in appearance of the wound: the deeply undermined edges had filled in, epithelial ingrowth from the periphery was progressing rapidly, and the ulcer base was replaced with healthy, bright-red granulation tissue. By 6 weeks more than two thirds of the ulceration had healed and wound contraction and epithelialization were striking (Fig. 2B). Fatal cerebral hemorrhage interrupted this progression of events, but the near-total healing evidenced prior to death was striking.

Case 4: In a 58-year-old man a chylous fistula developed after pharyngolaryngectomy and radical neck dissection for recurrent hypopharyngeal radiation therapy. A large area of tissue adjacent to the tracheostoma broke down, with deep undermining of the wound edges, exposing the common carotid artery. After 4 weeks of application of routine dressings (sodium hypochlorite 1:20) minimal healing was evident. Human amniotic membrane was applied directly to the exposed carotid artery and remaining wound surface and tucked under the deeply undermined wound edges. Over the next 4 weeks healthy granulation tissue filled the wound, obliterating the undermined

edges and providing almost complete coverage of the exposed carotid artery. This allowed successful closure of the defect with a deltopectoral flap.

In two cases human amniotic membrane was applied directly to bone:

Case 5: Following aortocoronary bypass grafting, postoperative sternal dehiscence occurred in a 61-year-old man. The wound was resutured, but 2 days later dehiscence recurred, the wire sutures tearing through friable bone edges. Human amniotic membrane was applied to this deep wound, directly covering the pericardium and the two lateral edges of the sternum. Frequent dressing changes were initially needed, but after 3 weeks healthy granulation tissue covered the pericardium and sternal surfaces, and delayed wound closure was performed.

Case 6: In a 50-year-old man a distal tibial fracture remained ununited despite two attempts at open reduction and bone grafting, and osteomyelitis developed at the fracture site. Following curettage and saucerization of the area human amniotic membrane was applied directly to the bony cavity and adjacent exposed tendon. Healthy granulation tissue began to cover areas of exposed bone. The many remaining islands of pearly, avascular bone were removed on the ward and human amniotic membrane was reapplied to healthy, bleeding bone. Four weeks later, prior to coverage with a cross-leg flap, the entire bony cavity and exposed tendon were covered with healthy, bright-red granulation tissue. Because the exact extent of devitalized bone was accurately determined, management was facilitated.

Burns

Ten patients with full-thickness or deep partial-thickness burns were treated with human amniotic membrane. In full-thickness burns, once the eschar had been removed the membrane was applied to provide coverage and to promote the growth of healthy granulation issue prior to autografting (Fig. 3). Areas of the wound not ready for grafting (as shown by failure of the membrane to take) were prepared with frequent membrane changes until take was evident. Granulation tissue in the areas ready for grafting was kept healthy until the entire wound was ready for grafting. Débridement of the burn surface by frequent changes of membrane decreased the number of grafting procedures necessary to close the wound. With massive burns and lim-

ited autograft supply the membrane covered the wound while donor sites healed. Membrane dressings reduced pain significantly, permitting early mobilization, especially with burns of the hand.

Certain deep partial-thickness burns covered with human amniotic membrane after separation of the eschar showed accelerated healing of the remaining dermal elements. Coalescing epithelial islands were seen beneath the membrane, which separated spontaneously when epithelialization of the underlying wound was complete. Healthy, pliable, normal skin, without hypertrophic scar, was produced. Human amniotic membrane was not used in the initial treatment of partial-thickness burns since thermal injury often results in a wound with patchy areas of partial- and full-thickness loss.

Traumatic soft-tissue wounds

In seven patients who had suffered severe soft-tissue and bony trauma human amniotic membrane was used as the immediate cover for contaminated wounds to protect exposed bone, nerves, tendons and vessels, and to maintain tissue viability until definitive closure was possible. In wounds in which the tissue viability was questionable the membranes were used to delineate areas of dead tissue and thus permit accurate débridement.

Discussion

Human amniotic membrane has been used successfully as a temporary biologic dressing in diverse clinical situations. Histologically the membranes consist of two loosely connected tissues, amnion and chorion. The amnion, or inner layer, is derived from the epiblast and is continuous with the embryonic ectoderm.[15] The inner surface is composed of cuboidal or flattened epithelial cells; the outer surface is covered with mesenchymal connective tissue. The chorion has a mesenchymal component in contact with the amnion, and an external ectoderm composed of transitional epithelium. Pigeon[16] has stated that since amniotic membrane is formed by fetal ectoderm it is really an extension of the infant's skin. Lister[17] found ultrastructural and functional similarities between fetal skin and amnion and chorion. Hence human amniotic membrane can be considered analogous to fetal skin allo-

graft. This may account for certain of its beneficial effects when used as a wound dressing.

In treating this series of patients we made no attempt to separate the membrane into its two layers since the thicker two-layered membrane provided a more satisfactory temporary wound cover; no disintegration occurred within 48 hours when adherence of the membrane was maintained. Douglas[18] demonstrated initial neovascularization of chorion applied to experimental wounds, and Robson and Krizek[13] showed decreased bacterial growth when a temporary biologic dressing took initially on a granulating site. Therefore we applied the chorion to the wound surface of all full-thickness wounds. Colocho and colleagues[14] showed conclusively that no vascularization occurs when the amnion is applied to the wound. Therefore in partial-thickness defects, for which vascularization is not desirable, we placed the amnion against the wound surface. This provided wound coverage, and the membrane dessicated spontaneously when epithelialization was complete.

All biologic dressings currently used (cadaver skin allograft, pigskin xenograft and human amniotic membrane) serve specific functions:

● Reduction of bacterial contamination and prevention of further contamination.

● Reduction of fluid, protein, heat and energy loss.

● Reduction of pain.

● Promotion of healing.

● Protection of underlying structures.

● Increase in mobility.

● Prediction of tissue viability when such is initially questionable.

● Preparation of full-thickness defects and recipient sites for autografting or delayed closure.

● Psychologic improvement in the patient.

Cadaver skin allograft and pigskin xenograft have certain disadvantages compared with human amniotic membrane. Cadaver skin is difficult to obtain; legal problems and the exclusion of cadavers with a history of malignant disease, hepatitis or syphilis are further difficulties. Personnel must be available at all times to procure the skin in a sterile manner, usually in the operating room. Baxter[19] estimated that the cost of har-

vesting the skin of one cadaver was $225 and that it required, on the average, 6 hours of physicians' time. Pigskin is commercially available but costs approximately $280/m². Wood and Hale[20] have estimated the cost of pigskin dressings in an adult with burns of 44% of his body surface to be $219/d. Both allograft and xenograft skin dressings are limited in size and shape. Human amniotic membrane is readily available and freely obtainable, and may be large.

One of the main benefits of wound coverage with a biologic dressing is prevention of contamination and reduction of infection. Eade[21] showed that in burns, granulation tissue is always heavily contaminated with organisms; coverage with fresh viable or preserved nonviable autograft or allograft permitted granulation tissue to destroy contained organisms rapidly. Morris, Bondoc and Burke[22] believed that this antibacterial effect lay in the intimate closure of the open wound provided by the biologic dressing, which prevented further bacterial contamination and allowed the host's defence mechanisms to deal with the infection effectively. Larson[23] found that the decrease in the count of bacteria paralleled the rapid increase in the count of leukocytes beneath the graft. This was confirmed by Saymen and colleagues,[24] who showed that in uncovered infected rat wounds leukocytes tended to migrate from the muscle surface to the base, and that this migration reversed after the application of allograft skin. They suggested that this alteration in cell migration might modify leukocyte function and result in greater bactericidal activity. The reduction in bacterial contamination and reversal of leukocyte migration did not occur in the absence of wound coverage. Burleson and Eiseman[25] found that the antibacterial effect of biologic dressings was related to the adherence to the underlying wound bed. "Skin that stuck sterilized." They demonstrated with pigskin that this adherence was related to a fibrin–elastin biologic bond.

Experimentally human amniotic membrane has proven equal to autograft skin and superior to allograft and xenograft skin in decreasing bacterial counts in open granulating wounds.[10,11] Clinically the ability of human amniotic membrane to de-

crease bacterial counts was equal to that of allograft skin and superior to that of xenograft skin, probably because of the greater pliability and adherence of human amniotic membrane with intimate wound closure and obliteration of dead space.[13] In addition, the mechanical débridement that accompanies frequent membrane changes allows host resistance factors in the granulating bed to function at peak efficiency. The initial take of membrane to the granulating bed probably contributes to this salutary effect since the lack of effectiveness of xenograft skin in decreasing bacterial counts has been related to its inability to take initially on a granulating wound surface.[19] The recent reduction in the neomycin content of commercial pigskin has further decreased this dressing's effectiveness.[26,27]

Other mechanisms have been postulated for the antibacterial properties of human amniotic membrane. Lysozyme, a bactericidal protein, is present in high concentration in human amniotic membrane, and progesterone, which is bacteriostatic for certain gram-positive organisms, is also present.[28] Allantoin is present as well (C.W. Brigden, personal communication, 1977). Indeed, the beneficial effect of maggots on contaminated wounds has been considered to be due to their excretion of allantoin.

Skin graft survival and successful closure of a contaminated wound by suture or skin graft have been shown to correlate accurately with a wound concentration of 10^5 or fewer bacteria per gram of tissue, except for β-hemolytic streptococci, whose concentration must be lower for successful grafting or wound closure.[19,29] Allograft take has been found to correlate accurately with a wound concentration of 10^5 bacteria per gram of tissue, and this forms the basis of the allograft test. In this way the previous subjective evaluation of wound readiness for grafting or delayed closure has been replaced by objective allograft testing of the wound surface. Take of human amniotic membrane to the wound surface invariably predicts successful autograft take or wound closure. This has particular application in the management of contaminated, infected and burn wounds and chronic skin ulcers. Delineation of areas of dead tissue to limit the extent of débride-

ment is especially important in hand and face injuries, wringer injuries and wounds caused by gunshot or other high-velocity projectiles, in which excessive débridement can severely restrict function and result in cosmetic deficiency.[30]

Promotion of healing following wound coverage with a biologic dressing has been reported by many authors.[31-34] In rabbits, wound healing was accelerated after the application of human amniotic membrane: the repair process started earlier, the migration of fibroblasts and the development of collagen were hastened during the first 6 to 8 days of healing, and epithelialization occurred sooner.[35] In addition, allograft skin seems to have an organizational effect on the healing wound:[22] second-degree burns not covered by allograft showed edema and inflammation in the dermis, with disorganization of normal maturation and loss of cell polarity, whereas in wounds covered by allograft the epidermis showed normal structure with a recognizable basal layer and a normal-appearing collagen layer in the dermis.[36] Hypertrophic scarring and keloid formation seem to be prevented in this way.

We did not use human amniotic membrane for split-thickness skin graft donor sites, which heal rapidly with routinely used dressings and rarely pose a problem clinically.

Conclusions

Human amniotic membrane was used successfully as a temporary biologic dressing for various wounds in 120 patients. The membrane is easily obtained, at little or no cost. It provides excellent wound coverage and has distinct advantages compared with other biologic dressings.

References

1. GIRDNER JH: Skin grafting with grafts taken from the dead subject. Med Rec 20: 119, 1881
2. REVERDIN JL: Greffe épidermique. Bull Soc Imp Chir Paris 10: 511, 1869
3. LEE EW: Zoografting in a burn case. Boston Med Surg J 103: 260, 1880
4. DAVIS JS: Skin transplantation. With a review of 550 cases at the Johns Hopkins Hospital. Johns Hopkins Hosp Rep 15: 307, 1910
5. SABELLA N: Use of fetal membranes in skin grafting. Med Rec NY 83: 478, 1913

6. DOGO G: Survival and utilization of cadaver skin: preliminary note. Plast Reconstr Surg 10: 10, 1952
7. BROWN JB, FRYER MP, RANDALL P, et al: Postmortem homografts as "biological dressings" for extensive burns and denuded areas; immediate and preserved homografts as life-saving procedures. Ann Surg 138: 618, 1953
8. ROGERS BO, CONVERSE JM, SILVETTI AN: Preliminary clinical studies on bovine embryo skin grafts. Transplant Bull 4: 24, 1957
9. BROMBERG BE, SONG IC, MOHN MP: The use of pig skin as a temporary biological dressing. Plast Reconstr Surg 36: 80, 1965
10. ROBSON MC, KRIZEK TJ: The effect of human amniotic membranes on the bacterial population of infected rat burns. Ann Surg 177: 144, 1973
11. ROBSON MC, SAMBURG JL, KRIZEK TJ: Quantitative comparison of biological dressings. J Surg Res 14: 431, 1973
12. ROBSON MC, KRIZEK TJ, KOSS N, et al: Amniotic membranes as a temporary wound dressing. Surg Gynecol Obstet 136: 904, 1973
13. ROBSON MC, KRIZEK TJ: Clinical experiences with amniotic membranes as a temporary biologic dressing. Conn Med 38: 449, 1974
14. COLOCHO G, GRAHAM WP III, GREENE AE, et al: Human amniotic membrane as a physiologic wound dressing. Arch Surg 109: 370, 1974
15. BAILEY FR, MILLER AM: Textbook of Embryology, 2nd ed, Wood, New York, 1911
16. PIGEON J: Treatment of second-degree burns with amniotic membranes. Can Med Assoc J 83: 844, 1960
17. LISTER UM: Ultrastructure of the human amnion, chorion and fetal skin. J Obstet Gynaecol Br Commonw 75: 327, 1968
18. DOUGLAS B: Homografts of fetal membranes as a covering for large wounds — especially those from burns; experimental and clinical study (preliminary report). J Tenn Med Assoc 45: 230, 1952
19. BAXTER CR: Homografts and heterografts as a biological dressing in the treatment of thermal injury. Presented at the first annual congress of the Society of German Plastic Surgeons, Munich, Sept 28, 1970
20. WOOD M, HALE HW JR: The use of pigskin in the treatment of thermal burns. Am J Surg 124: 720, 1972
21. EADE GG: The relationship between granulation tissue, bacteria, and skin grafts in burned patients. Plast Reconstr Surg 22: 42, 1958
22. MORRIS PJ, BONDOC C, BURKE JF: The use of frequently changed skin allografts to promote healing in the non healing infected ulcer. Surgery 60: 13, 1966
23. LARSON D: in discussion, ibid
24. SAYMEN DG, NATHAN P, HOLDER IA, et al: Control of surface wound in-

fection: skin versus synthetic grafts. Appl Environ Microbiol 25: 921, 1973
25. BURLESON R, EISEMAN B: Mechanisms of antibacterial effect of biologic dressings. Ann Surg 177: 181, 1973
26. HABAL MB: On the cutaneous porcine heterograft (E). Plast Reconstr Surg 57: 367, 1976
27. A short note on the physiologic response to the cutaneous xenograft as a biologic dressing (C). J Trauma 14: 94, 1974
28. GALASK RP, SYNDER IS: Antimicrobial factors in amniotic fluid. Am J Obstet Gynecol 106: 59, 1970
29. ROBSON MC, HEGGERS JP: Surgical infection. II. The β-hemolytic streptococcus. J Surg Res 9: 289, 1969
30. BURKE JF, BONDOC CC: A method of secondary closure of heavily contaminated wounds providing "physiologic primary closure". J Trauma 8: 228, 1968
31. ROBSON MC, HEGGERS JP: Bacterial quantification of open wounds. Milit Med 134: 19, 1969
32. GILLMAN T, PENN J, BRONKS E, et al: Reactions of healing wounds and granulation tissue in man to auto-thiersch, autodermal, and homodermal grafts; with analysis of implications of phenomena encountered for understanding of behaviour of grafted tissue and genesis of scars, keloids, skin carcinomata, and other cutaneous lesions. Br J Plast Surg 6: 153, 1953
33. ZAROFF LI, MILLS W JR, DUCKETT JW JR, et al: Multiple uses of viable cutaneous homografts in the burned patient. Surgery 59: 368, 1966
34. O'NEILL JA JR, GROSFELD JL, BOLES ET JR: The extended use of skin homografts. Arch Surg 99: 263, 1969
35. BAPAT CV, KOTHARY PM: Preliminary report on acceleration of wound healing by amnion membrane graft. Indian J Med Res 62: 1342, 1974
36. MILLER TA, SWITZER WE, FOLEY FD, et al: Early homografting of second degree burns. Plast Reconstr Surg 40: 117, 1967

BOOKS

PROBLEM SOLVING IN IMMUNOHEMATOLOGY. Case Reports For Pathologists And Medical Technologists. Arthur Simmons. 204 pp. Illust. Year Book Medical Publishers, Inc., Chicago, 1977. $15.35, spiral bound. ISBN 0-8151-7654-6

PROTEINS OF ANIMAL CELL PLASMA MEMBRANES. Vol. 1, 1977. D.F.H. Wallach. 154 pp. Eden Press Inc., Montreal, 1977. $18. ISBN 0-88831-011-0

RECENT ADVANCES IN CLINICAL BIOCHEMISTRY. No. 1. Edited by D.G.M.M. Alberti. 298 pp. Illust. Churchill Livingstone, Edinburgh; Longman Canada Limited, Don Mills, 1978. $41.60. ISBN 0-443-01590-2