REVIEW OF LITERATURE
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LOCAL CHEMOTHERAPEUTICS

Improvement in infusion therapy in burn has lead to a reduction in mortality due to shock, but the local management of burn wound still remains a very challenging problem in terms of morbidity and mortality.

Looking back at the ancient times various substances often exotic have been used. Thus 430 BC saw the use of tincture and extract of tea leaves by Chinese and Japanese, butter with rod orchro or bark of fig tree by Sushutra, boiled cow dung by Pappyrus (1500 BC), a mixture of gum, goat's hair and milk of a lady who has given birth to a son used by Egyptian (5th and 6th century), mixture of honey and bran for local application was used by Celsus of ancient Rome, various emollients preparations were used by Paulus of Aeigna (625 - 690 AD) and a mixture of white lead, oil of roses and wax had been used by Rhazes (580 - 920 AD).

Later during the 16th century and afterwards, upto 19th century Ambrose pone (1517-1590) suggested the use of ointment for the treatment of burn wounds.
Cleev's (1951) used five different complex preparations on different parts of the body area involved in burn. David Cleghron (1792) used vinegar and chalk poultices locally. Edward Kentish (1797) advocated pressure bandages to relieve pain and to stop blister formations. Marjolin (1797) described certain scars after burn known to be cancer and Marjolin's ulcer. Sir James Earle (1799) suggested the use of ice cold water and reported that it acts as a good analgesic and prevents oedema formation.

William Clowe's (1544-1604) stands out in history as the first surgeon, since the middle ages to use the physical signs of burns; where the skin was burnt off, and parts were made raw and painful, to guide his local treatment. Hidamis (1607) in his book 'Decombustion' insisted that the classification of burn should be a guide for treatment, classifying burns into three degrees by external appearance; redness and blistering; withering of skin without charring, and eschar formation and charring. He warned against cooling burnt skin which hardens the tissues. In very deep burns, he made incisions to let the moisture escape, as otherwise gangrene and infection would supervene. So he was also the first to perform escharotomy. Wiseman (1676) observed that an organ which is burnt superficially is far more painful than deep. He too classified burns into four degrees like L. Heister (1682-1785) who also included time factor as a further
diagnostic aid. In 1814 Boyer classified burns into three degrees (1) Erythema, (2) Blister leading to superficial ulcer, and (3) Charring of skin and eschar formation. Dupytren's (1832), a famous French surgeon classified burn into five degrees according to the depth of involved tissues.

1. Erythema or superficial ecchymosis which blanches on pressure.

2. Cutaneous inflammation with loss of epidermis and the development of vesicles filled with serum.

3. The destruction of a portion of the papillary body.

4. The disorganisation of whole dermis upto the subcutaneous cellular tissue, and

5. The formation of eschar.

He also described the four periods during natural course of burn injury (1) Period of irritation, (2) Period of inflammation, (3) Period of suppuration, and (4) Period of exhaustion. In addition, he also noted about the gastro-intestinal tract haemorrhage in burn cases. Later Curling (1842) recognised gastric and duodenal ulcer as a cause of this gastro-intestinal haemorrhage. He also suggested the use of saline bath for local wound management.
As far the local management is concerned, Passowant (1856) suggested the use of saline baths, Hobra (1861) treated burn cases in warm water bath, believing that Dupytren's last degree of burn were of academic interest only and he returned to the three degree classification which defined the 3 stages as, erythema with swelling, with pain, blistering with bacterial haemorrhage and eschar devoid of sensation. (Hobra (1866).

The dry method of dressing was the principal method between 1863 - 1868. Syme (1834) in his principles of surgery stated that this form of therapy had almost superseded the filthy and useless application of carson oil and linimentom aquae calcis.

The 19th and 20th centuries introduced two new principles in the local treatment of burns (1) skin grafting (Pollock, 1971) and (2) open treatment (Coopland, A., 1887), Stocher, 1894 and Raid, 1898) in addition to newer local applicants. However, Bonisson had used open treatment about 400 years back and hence this was not an entirely new approach. Lusgarten (1871) suggested and Wiltms (1901) carried out excision of burn tissue for the first time but he never grafted the excised area. Jauzehoric (1968) revived the idea of excision of burnt tissue and immediate skin grafting, thus adding a footnote to a contemporary principle of early tangential excision and early grafting.
Lister (1868-1885) used 2.5 percent carbolic acid topically, but it was soon discarded because of its toxicity, causing local gangrene and after absorption through the burnt area causing systemic toxicity i.e. muscle twitchings, weakness, excitement, nausea, vomiting, delerium and hypotension.

An important period called the saline wet dressing antiseptic era extended between 1885 to 1910. Wet dressing with sodium bicarbonate were first applied - followed by solution of picric acid or boric acid advocated by Oppenheimer (1906). A. Maclellan (1903) and E.J. Elliot (1906) described picric acid poisoning following its use on dressings applied to burns. Picric acid induces tachycardia, nausea, vomiting, diarrhoea, moderate fever, disoria, renal insufficiency, discoloured urine, stupor, coma and collapse. The systemic absorption of boric acid is known to be followed by rashes with desquamation of skin, restlessness, confusion and weakness, hypothermia, hypotension, tachycardia and renal injury.

From 1910 to 1926 wax containing 250 mg% of beta naphthol was applied at a temperature of 50°C to 60°C. Beta naphthol causes extreme hepato-renal damage with convulsive seizures and even death. Dewittson (1894-1933) advocated the use of tannic acid application on burn surfaces in 1925 at Henry ford hospital he claimed that this agent decreases the fluid loss, relieves the pain
and produces a clean scar. Later on, Maclure of the same hospital in 1944 described it as a hepato-toxic agent and attributed many deaths of its toxicity. Aldridge (1933) advised the use of gention violet as an escharolytic agent on burn surfaces.

At the turn of the 19th century, the emphasis was to avoid infection and with the advent of the 20th century, a better understanding of the pathophysiology of burns elucidated causes and indicated methods of better systemic treatment of burns, and counteracting shock. Reiss (1890) and Tommaroli (1897) introduced the systemic treatment of shock by intravenous saline transfusion in severely burnt patients. This treatment of shock in the 4th decade of this century has now become a standardised procedure especially after the remarkable work of Davidson (1926), Underhill (1930) and Bdalock (1931).

This was the turning point and since the mid 20th century there has been an increased understanding of the metabolic, nutritional, immunological and wound healing processes improving the overall management of burn patients. But the local treatment still leaves a lot to be learned.

In 1942, Allen and Koch used petroleum gauze piece locally with strict immobilization, this type of occlusive dressing were used in army hospitals during world war II.
Wallace of Edinburgh (1949) in England and Pulaki, Artz and Bloker (1950) in U.S.A. reintroduced the exposure method of burn wound, later on other surgeons accepted the same method with a view that development of a crust provides physiological covering to burn wound, thus reducing the harmful effects of raw area.

Work of Leidberg, Reiss and Artz (1953) indicated septicaemiae as a primary cause of death in burns as a result of uncontrolled local growth and staphylococi as the main organism. With the availability of antibacterial agents against gram positive organisms, pseudomonas emerged as the major organism responsible for sepsis and death. This lead other workers to find out newer antibacterial agents effective against gram negative organisms and other microbials which can penetrate burn surface and thus minimize the growth of such microbials. Since then various antimicrobials were tried and some are still in use, e.g. 0.5% silver nitrate (Moyer, 1960), Mefanid or sulphamylon (Moncrief, 1974), Silver sulphadiazine (Fox, Jr. and others, 1969), Cerium nitrate (Williams, W. Monafo, Som N. Tandon, 1975), Cerium nitrate and silver sulphadiazine (Fox, C.L. Jr. and others, 1975), but these agents are effective mainly in controlling the microbial population, not erradicating bacteria from the wound. It is stated that from an average of $10^7$ micro-organisms per gram of tissues, reduction to $10^4$ per gram
of tissue occurs as a result of these agents (Artz, C.P. et al, 1979). Besides this limited local activity, these agents also have some advantages and disadvantages.

0.5% silver nitrate dressing benefits the burn patients, but this causes metal toxicity, depletion of body salt and necrobiosis. It was soon replaced by silver sulphadiazine because it has dangerous side-effects. Silver sulphadiazine has the following advantages, (1) it readily penetrates eschar, (2) Eschar does not adhere to dressing, (3) this drug inhibits nearly all pathogenic bacteria and fungi and exerts prominent action against pseudomonas (Rosenkraz, 1972), but at the same time it also has some disadvantages - (1) It is absorbed through the raw surface causing crystalluria, (2) Bacterial resistance to these drugs which is plasmid mediated, (3) Adverse reactions including burning, rashes and itching, (4) It is also a very costly drug, and (5) Difficulty in daily application on burn surfaces.

Thermal injury results in striking anatomic, metabolic and physiological disturbances which prejudice survival of burn patients. The main cause of morbidity and mortality in these patients is toxicaemia due to absorption of toxins from injured surface of burn invaded by micro-organism. So the new concept of burn cure is restoration of impaired barrier by using various covering materials as skin substitutes.
BIOLOGICAL DRESSINGS

Autogenous skin grafting is the best dressing material amongst all suggested till this time, but it has its own limitations in the form of limited supply, unfitness of the already shocked patient for surgical procedure involved in skin grafting and refusal of patient or his attendant on religious, sentimental or economic grounds. To overcome this problem, various temporary biological and synthetic covering materials for short periods till the healing of wound has taken place or permanent in place of lost skin has been suggested by different workers.

Various materials used for skin substitutes are listed below.

1. Biological -

   a) Human allograft (Homograft)
      - living donor
      - cadaver donor fresh
      - cadaver donor frozen
      - Amniotic membrane.

   b) Xenograft (Hetrograft)
      - Living donor fresh
      - frozen, radiated or dried.

   c) Tissue derivatives
      - Collagen sheet fabrics or sponges,
      - Bioplast fibrin.
2. **Synthetics** -

   - Solid silicon, polymer membrane, other plastics,
     Microporous material.

3. **Composite materials** -

   - Surface membrane (Silicone, microporous trydron).

   Adherent substrate -

   - Collagen, cotton gauze, synthetic polymer sponge,
     vetour, flecking or fabric.

**Homograft**:

Paulock (1871), Cirdner (1881) and Shede (1881) were pioneers in this field. Cirdner (1881) treated a lightening burn with the skin from a suicide victim, Shede (1881) used skin from amputation specimen as well as from a cadaver in limit of 24 hours. Ivunova (1890) stressed the use of foetal skin as a homograft on burn surface because of its more energetic vitality.

In the middle of the present century, Dogo (1952) of Italy, noted the usefulness of cadaver skin obtained in a viable state, it was useful where it was possible to preserve the tissue till the time of application. He measured skin viability by determining the tissue oxygen taken up in the Warburg apparatus, the skin was preserved at 3°C in physiological solution. The oxygen consumption of cadaver skin was noted to be unaffected up to 16 hours after death.
Brown (1952) used allografts as emergency dressings for burn. He stated that skin may be removed even a day after death, if the cadaver has been placed in cold storage. Eade (1958) and Morris (1966) observed that the homograft have organisational and debridemental effects on healing.

Miller (1967) had reported that healed epidermis shows alteration in the architecture, and the dermis contains oedematous connective tissue in 2nd degree burn, where homograft was not used, when homograft was used, the healed epidermis shows normal architecture with reorganizable basal layer and normal collagen bodies in the dermis. James O'Neil Jr. (1967) used temporary homograft coverage over open wounds including 2nd and third burns, such coverage was a distinct benefit following eschar separation in burn injury. Sharma et al (1978) reported the same results. Allograft skin besides being a satisfactory biological dressing, have their own limitations. Cadavers suitable for skin donation are limited in number. Bexter (1970) has estimated six physician hours and hospital cost of $225, per patient treated by the use of cadaver homograft.

Amniotic Membrane -

The quest for a cheap, painless and easily available biological dressing having most of the
properties of the ideal skin substitute led the people to use amniotic membrane.

The amnion is the inner foetal membrane, its inner surface is in contact with the amniotic fluid and foetus, its outer surface is separated from decidua of uterus by chorion. It has the following parts -

1. Placental amnion - lines the inner aspect of placenta.
2. Reflected amnion - lines rest of the amnion.
3. Dependent amnion - overlies the internal os of cervix.

Histologically it has five layers - (1) epithelium, (2) basement membrane, (3) composite layer, (4) fibroblastic layer, (5) sponge layer. The thickness of the membrane is variable due to variable amount of mucin and fluid in spongy layer. Normally the thickness is 1/50 to 1/2 mm which can be increased to as much as 2 - 5 mm.

The first person to report the attempt of grafting pieces of lining of amniotic sac on granulating wound was John Staiger Davis, a medical student in 1910 at John Hoffkins University. Sabella (1913) used amniotic membrane on raw surface caused by burn and ulceration. He observed reduced pain, rapid epithelialization and absence of infection after application of amniotic membrane. Kubanyi (1941-48) reported the use of amniotic membrane in burns, traumatic loss of skin and to prevent intra-abdominal adhesions. Pinkerton (1942) reported the use
of amnioplastin to prevent adhesion between flexor tendon and their sheets. Hensen (1950) used amniotic membrane in the management of non-healing ulcer of skin and compared granulation tissue to that of other methods as plaster of paris. Jullian A. Sterling (1956) successfully used the amniotic membrane over old infected flame burns.

Pigeon (1960) observed the following effects in burn patients dressed with amniotic membrane.

A. Immediate effects:

1. Pain relieved at once after application and no further analgesics were needed.
2. Antibiotics were used only after development of complications.
3. The dressing were generally found dry.
4. Healing of wound was rapid and complete.

B. Delayed effects:

1. No discolouration was observed.
2. Minimal scar tissue.
3. No contracture were observed.
4. He also stated that amniotic membrane undergoes changes similar to that of cornified cells.
Trelford and associates (1975) reported the use of amnion alone in full thickness fresh surgical wounds leading to decrease in pain, fluid loss and secondary infection and hence decrease in hospital stay.

Bose, B. (1979) recently reported the use of amniotic membrane over burn wounds specially in developing countries like India.

Xenograft -

The use of heterologous tissue as a temporary dressings for full thickness skin defects was largely a result of the difficulty of obtaining adequate amounts of homografts. Brown (1954) and Jevis (1976) have shown that adherence of allograft and xenograft is similar. Heterografts provides a readily available, easily stored and sterilized dressing in contrast to homografts.

Canine skin had been used by Snitzer et al (1960) in treatment of tissue injury. Bromberg, B.E. et al (1965) and Elliot and Hoehn (1973) have used pig skin. Variable results have been reported ranging from early re-epithelisation to conversion of full thickness skin loss, with porcine xenograft coverage of donor sites and partial thickness burns. Salisbury (1973) has reported that incorporation of xenograft tissues on healing donor sites occurs in 35 percent of cases. There appears to be no significant difference in the effectiveness of fresh
compared with fresh frozen or frozen, irradiated procin skin.

The most striking advantages with procine xenograft is that of immediate and lasting pain relief. Xenograft has most of the properties of ideal skin substitute. A viable xenograft is antigenic but dead is not. The major problem is the propensity to digestion by wound collagenase and subsequent infection.

**Collagen Sheets** - Collagen is a fibrous protein present in many animal tissues, like skin, muscles and bone. Its structure and immunologic chemistry are well characterized and antigenicity can be altered. It possesses a haemostatic effect and when implanted in living animals in pure form, no antigenic reaction is seen. Collagen sheets are derived from serous, subserous layer of freshly slaughtered cattle intestine, and these are available in 4" x 6" size packed in cylindrical glass tubes containing ethylene oxide which act as sterilizing agent.

Sinha (1972), Shankar (1973) and Gupta et al (1976) used collagen sheets as primary cover material in the management of burns. Gupta and Chaturvedi (1974) used it to cover donor area. Thuksal and Gupta (1976) have used collagen material in repair of hernia and to cover surgical defects. Ehlan (1978) used collagen sheets as biological dressing in 35 patients and reported it in
prevention of infection and rate of healing. Jain et al (1976) reported similar findings.

The beneficial effect of collagen sheets include: (1) prevention of air born infection, (2) minimizing fluid loss, and (3) promoting formation of health and pink granulation tissue. But it is an expensive material and is not available at every centre.

**Synthetic materials** - The problems associated with biological materials provided an impetus to search for synthetic materials, with ideal properties, or for skin prosthesis. Many of these materials adhere by entrapment of coagulum in the interesitces of the material.

Silicon polymer membranes have been the most widely utilized because of their permeability to water (Travis, M.J. et al, 1978). Kornbeg et al (1977) have used this silicon membrane banded to cotton gauze for temporary skin substitution, but it lacks elasticity and creates non-uniform pattern of adherence. Other materials - Polyurethane, Polyvinyl chloride polymers, nylon mesh, decron velours, amino acid film and Polyhydroxyethyl-Methacrylate, have been introduced, all of which have ideal properties of water permeability, elasticity and variable degree of adherence to the wound (James et al, 1973; Lamkey et al, 1977; Townsend, 1977), but the infection is a major liability when used with latter wounds.
(Zachary et al, 1982), another drawback to dressing applied as a foam particularly Polyurethane appears to be the incorporation of the agent with the cells of the healing wound and subsequent foreign body giant cell reaction (Salisbury, R.E., et al, 1979). In an apparent departure from derived properties of wound covering, a gas permeable dressing employing a hydrocolloid polymer complex has been demonstrated in a well designed clinical trial to significantly promote partial thickness wound and patient comfort (Madden, M.R., et al, 1984). This study suggests that synthetic wound dressing may justify their greater expense and seem as a model for evaluation of all similar dressings. Another major advance in burn wound closure has been the development of skin substitute which potentially can be incorporated directly into the healing of wound. Three major elements of artificial skin are epidermal surface (Tsoa, M.L. et al, 1982 and O'Connor, N.E. et al, 1984), underlying matrix (Bell, E. et al, 1981 and Yannus, I.V. et al, 1982) and human epidermal cells in culture with loss of HLA - DR antigen expression (Eisinger et al, 1979), but these artificial skin substitutes are still in phase of trial and available in limited centres in developed countries.

Disadvantages of biological dressings - Inspite of being the best dressing material for burn wounds,
biological dressings have certain disadvantages in the
form of
1. Sub-graft suppuration,
2. High cost,
3. Lyophilized allograft skin shows less adherence to the
wound and is of sufficient thickness, undergoes dermal,
epidermal separation after application to the wound
with subsequent dessication of exposed dermis.
4. Potential transmission of disease like hepatitis in
case of cutaneous allograft.

NEWER TOPICAL AGENTS

The problem of burn wound sepsis is now becoming
increasingly important, because the systemic delivery of
antibiotics at burn wound site is suboptimal. There has
been an introduction of many treatment modalities directed
at this problem, e.g. Topical antimicrobial oint. (Fox,
C.L. Jr., Rapport, B.W. and Stanford, W., 1969), early
surgery i.e. escharotomy or skin grafting (Burke, J.F.,
Bondoc, C.C. and Quinby, W.C., 1974) or amniotic membrane
application (Bose, B., 1979).

Topical agents should play an important role in
the management of burn injury. Since the availability
of various topical agents, the topical burn therapy has
contributed substantially to the reduction in sepsis
to fight against infection. A number of techniques with topical agents have been evolved in mid 1960s, that have substantially decreased the incidence of burn wound sepsis, but each has its own advantages and disadvantages.

Amongst the many topical agents used are - silver nitrate, where the silver ions are immediately precipitated and are responsible for the discolouration of the local area. This agent also leads to Na\(^+\), K\(^+\) and Cl\(^-\) deficits and alkalosis (Mayer, 1960). Silver sulphadizine (S.S.D.) which exerts a prominent antibacterial action against pseudomonas but poorly penetrates eschar (Rosenkraz, 1972). Sulphamylon, which is freely soluble and readily diffusible through the eschar (Leidburg, Moncrief and Mason, 1960), but since sulfamylon is a potent inhibitor of carbonic anhydrase, it may induce acid base rearrangements leading to acidosis.

Recently topical application of PVP, a complex of iodine with polyvinyl, pyrrolidone (M.de.Knoch, 1985) has been used, which destroys both gram positive and gram negative bacterial cells.

The excellent antibacterial properties of PVP make it particularly suitable as a topical agent on burn wound. However, like so many other topical agents, ointments, it lacks the ability to actively penetrate
burnt tissue, and this distracts it considerably from its usefulness in treatment of burns.

Povidone iodine can easily be applied locally or alongside aserbine (Knock, D.M., 1985). P.V.P. is effective against a wide range of gram positive and gram negative bacteria as well as some fungi, but it causes pain on application and excessive drying of eschar (Schwartz, Shires and Spancer, 1988). Prolonged treatment with povidone iodine does not have any effect over thyroid glands (Balogh, D., Baner, M. and Richabone, G., 1984).

Neomycin powder (Wellcome & Burrough's) which can also be used locally has the following ingredients, i.e. Neomycin sulphate, Zinc bactricin and polymycin B.

Neomycin was isolated from streptomycetes fraidal in 1949 and is effective against gram negative species that are highly sensitive, E. coli, enterobacter and proteus vulgaris. Gram negative micro-organism which can be inhibited by neomycin include Staphylococcus aureus, streptococcus faecalis and mycobacterium tuberculosis. The hypersensitivity reaction is primary skin rashes in 6-8% of patients. The most important toxic effect of neomycin is nephrotoxicity (Kurian et al, 1960; Lert and Sherlock, 1960 and Berk and Caulinan, 1970).
Polymyxin B discovered in 1947 is a bactericidal, polypeptides derived from spore forming rods, found in soil by various strains of bacillus polymyxa. The antibacterial effect of polymyxin is unique in that, it is directed at bacterial cell membrane and induces major defects in permeability of bacterial cell (Gale et al, 1972; Corcoran and Huhan, 1931). The sensitivity to polymyxin B is apparently related to the phospholipid content of the cell wall membrane complex (Brown and Wood, 1972). The antibacterial activity of polymyxin B is restricted to gram negative bacteria including Pseudomonas aeruginosa, E. coli, Klebsiella, Salmonella, Partousella, Bredetella and Shigella (Kucers and Benett, 1975). Because of extremely nephrotoxicity (Rayan, K.J. et al, 1969; Price, D.J.E. et al, 1970; Koch-Weser, et al, 1970; Renold et al, 1975, and Flick and Cluff, 1976) associated with parenteral use of this drug is now rarely used except orally for prophylaxis, otic and ophthalmic and topical gram negative infection (Enno, et al, 1978; Gurwith et al, 1979). Polymyxin B applied to intact or denuded skin or mucus membrane produces no systemic reaction because of almost complete lack of absorption of the antibiotic from these sites. Hypersensitivity is uncommon.

Bacitracin is an antibiotic produced by the tracy I strain of bacillus subtilis. The history, property and uses of bacitracin have been reviewed by
Meleney and Johnson (1949). This peptide antibiotic inhibits cell wall synthesis (Strominger, 1973). It is bactericidal in vitro against a variety of gram positive cocci and bacilli, Neisseria, H. influenza and T. pallidum, Actinomycoses, Furobacterium, Enterobacteriaces, Pseudomonas, Candida Torule and Nocardia are resistant (Merk, A., Samdo and Gerald, L., Mondell, in Goodman & Gillman, IV Ed.). Because of its high rate of nephrototoxic reactions that followed its systemic use, it is now limited to topical application. It is often combined with polymyxin B and neomycin to provide broad spectrum coverage. Little systemic absorption occurs from topical application and allergic reactions are rare (Goodman and Gillman, 1975; Kucers and Benett, 1975).

The combination of drug treatment utilizing PVP + Neosporin powder may act as complementary to each other (Sinha et al, 1988).

Clinical and investigatory tools of assessment of burn wound sepsis among others are surface culture and sensitivity report, regarding the type of infectious organism and quantitative estimation of these organisms indicating the degree of infection.

Burn wound biopsy provides three parameters for assessment of infection.
1. The first quantitative bacteriology.

2. The second is qualitative bacteriology.

3. The third parameter of burn wound biopsy is 'histologic', where perilymphatic, perivascular and intraluminal accumulation of bacteria prove without doubt invasive burn wound infection (Krupp, S., Baechler, M. and Bille, J., 1985).

In the qualitative bacteriology, immediate gram staining shows the presence of bacteria and the identification of bacteria from wound biopsies provides precise identification. The organisms which have been recovered from culture of wound swabs and wound biopsies are as follows:

A. Gram negative bacilli - Enterobacter spp., Klebsiella spp., E. coli, Pseudomonas, Aeruginosa etc.

B. Gram positive bacilli - Enterococci, Staph-epidermis, Staph. aureus, Streptococcus.

C. Other opportunistic infections. Fungal e.g. Candida spp., yeast and viral infection.

It should be kept in mind that the microbial etiology of burn wounds of the patients could at any burn unit leads changing with time and attentions in the flora occur as a series of mini-epidemics with a succession of predominant organism.
In view of the organism found locally, a topical anti-microbial with a total spectrum coverage and minimal side effects and at the same time easy to apply with minimal strain on nursing personnel is desirable. PVP with Neosporin may fill this gap which has been unfulfilled to date. The nearest to this appears to be amniotic membrane but it too has some disadvantages especially sub-graft suppuration.

This study would examine the efficacy of PVP and neosporin powder in the above light especially in comparison to amniotic membrane application.

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