Burns Research Institute
Foundation for research and education in wound healing and burn care

BURNS RESEARCH INSTITUTE
RED CROSS HOSPITAL
VONDELLAAN 13
1942 LE BEVERWIJK
THE NETHERLANDS
TEL: (+) 31 251 265564
FAX: (+) 31 251 265562

PRELIMINARY MACROSCOPIC AND MICROSCOPIC PRE-CLINICAL RESULTS

Comparison of
Hydrogels
with and without
glycerine:

Elasto-Gel

VERSUS

Visigel

STUDY NO: 9438295626019
JUNE 1996

This preliminary report contains the results of a comparative animal study evaluating hydrogel wound dressing materials with and without glycerine.

BRI STUDY NUMBER: 9438295626019

AUTHORS:

M.J. Hoekstra — Burns Research Institute, Red Cross Hospital, Vondellaan 13, 1942 LE Beverwijk, the Netherlands

Tel: (+) 31 251 265564
Fax: (+) 31 251 265562

R.P. Dutrieux — Leiden Wound pathology Institute
Johan Huizingalaan 403,1066 TX Amsterdam

Tel: (+) 31 20 6691992
Fax: (+) 31 20 6691992

J.S. du Pont — Burns Research Institute, Red Cross Hospital, Vondellaan 13, 1942 LE Beverwijk, the Netherlands

Tel: (+) 31 251 265556
Fax: (+) 31 251 265562

COPY NO: 01

SUBMITTED TO: Ed Stout | Southwest Technologies

OBJECTIVE:

Purpose and Rationale:

The purpose of this study is the evaluation of a standard hydrogel wound dressing material Visigel® (Utermöhlen, the Netherlands) (=NDM® Wound Dressing ClearSite®, USA) and a hydrogel with 65% glycerine as water soluble humectant Elasto-Gel™ (Southwest Technologies, USA).

The earliest synthesis of one of the first unrecognised precursors to a hydrogel of potential biomedical importance, poly-2-hydroxy ethylmethacrylate or polyHEMA, came from Du Pont in 1936.
But it was Wichterle and his co-workers in Prague, Czechoslovakia, during the 1950's who developed polyHEMA as a general purpose surgical material. Wichterle and Lim were the first to propose hydrogels for those medical uses where the hydrophilicity of polymers may play an important role.

Much research work has been carried out on hydrogels as temporary skin substitutes or as burn wound dressing materials. The tissue-like structure of most hydrogels has contributed to their biocompatability by minimising mechanical irritation to surrounding tissue. Particularly the elastic modulus has to be similar to those of the surrounding tissue. Resistance to degradation by enzymatic systems or other mechanisms, absence of diffusion of impurities, permeability to water soluble substances and preservation of mechanical properties are fundamental requirements.

Hydrogels are three-dimensional networks of hydrophilic polymers.
These interact with aqueous solutions by swelling to a certain equilibrium and retain a significant proportion of water within their structure.
They are insoluble in water and non-degradable.

Several types of the polyethylene oxide polymer hydrogel have found clinical application and are the basis of commercial products.
Vigilon® and Spenco 2nd Skin™ are well known hydrogel wound covering materials produced by radiation cross-linking of high molecular weight insoluble polyethylene oxide copolymer which can swell to a high degree with water. Geliperm® is an insoluble cross-linked polyacrylamide agarose polymer containing 95% water as the dispersion phase.

Hydrogels can give reduction of pain by protecting exposed neurons from dehydration on base of a favourable permeability profile within acceptable pH ranges. Cooling of the wound surface could result in a reduction of the inflammatory response.

However in a humid unprotected environment growth of micro-organisms can be stimulated leading to unfavourable wound conditions.

Using glycerin in high concentrations, as water soluble humectant in Elasto-Gel™, has a positive effect on the anti-microbial properties of the dressing.
The material does not support growth of any microbe tested.
The material can kill bacteria that are able to survive on inert surfaces.
Only Bacillus subtilus, a gram positive rod that can form spores, is not killed.
Glycerin in high concentrations has a slight but definite anti-microbial action and in this way bacterial growth will be hampered.

Glycerin seems to have immunomodulatory features, influencing the inflammatory response to tissue injury.
Cell cultures of human lymfocytes are hampered to react to foreign epidermal cells in the presence of glycerin in even the slightest amount.
By it's strong negative charge glycerin binds to extra cellular matrix molecules modifying their brake down and subsequently modulating the inflammatory response in this way.
Also frequent dressing changes can lead to impairment of wound healing just by dehydration.

Therefor estimation of the right dressing change regimen in several type of wound healing conditions will be an ultimate requirement for this type of new interactive wound dressing materials.

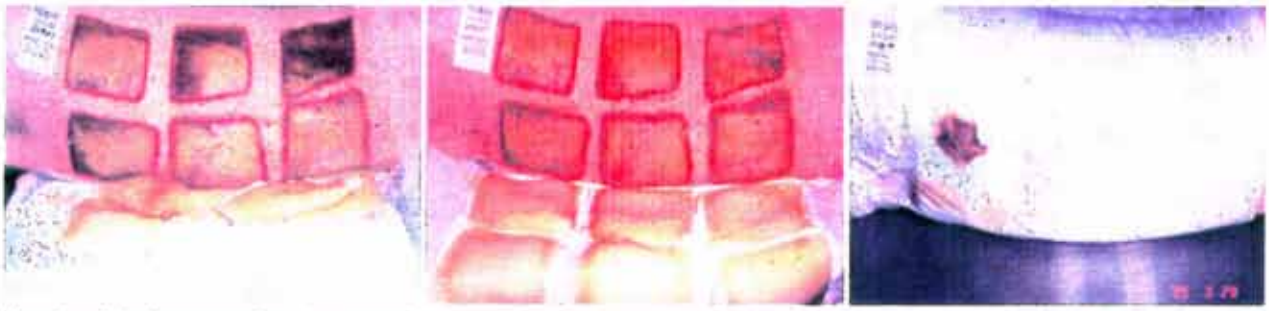
The Yorkshire pig is a reliable model for wound healing. The study design with six contact burns at each flank can give optimal information with a minimal number of animals used.

The reason for using a deep burn wound model is because this type of wounding creates a situation in which healing parameters can be evaluated in a clear and discriminating fashion.

In this study design the average dressing change regimen is comparable to the clinical situation as used for hydrocolloid wound dressing materials, that will be three to four changes on a weekly base.

Study no. 95.626: Elasto-Gel® PBD 0 - 35

Deep partial thickness contact burns just after infliction; de-epidermised white supple eschar at pbd 0; easy dislocation of dressing material during dressing change at pbd 1; white yellow soft supple glycerinized eschar; dislocation of dressing material leading to partial dehydration in some lesions at pbd 4.



Partly dried out eschar in some lesions by dislocation of the dressing material at pbd 6; a typical soft supple glycerinized eschar; no dislocation of dressing material after fixation with Curafix® adhesive bandage; the bandage material shows a blood stain of the excision biopsy wound and a totally rehydrated soft glycerinized eschar in all lesions on pbd 7.

Easy release of the eschar at the wound margins by a humid environment underneath the crust; partly intact and disintegration of the remaining crust at pbd 14; quiet aspect and clean wound bed without any sign of infection after dislodgementof the necrotic tissue; anyhow no dirty smell or other signs of bacterial growth; first signs of contraction at pbd 17.

Clear signs of epithelial outgrowth at pbd 21; still some escharotic remnants and granulation tissue; variable degree of epithelialization at pbd 28; clear wound contraction around pbd 28; typical blister formation and slow down of epithelial outgrowth on base of maceration; typical pale red granulation tissue;

Study no. 95.626: Elasto-Gel® PBD 0 - 35

Deep partial thickness contact burn just after infliction; de-epidermised white supple dry eschar, surrounded by a small hyperaemic zone; soft supple eschar and diminished inflammation in the unburned skin ; no signs of bacterial growth by a (blue-green) discoloration of the dressing material and/or a typical odour.

Soft yellow-white plasticised supple crust; minimal swelling and discoloration of the dressing material; further discoloration of the fully plasticised crust; minimal sign of epithelialization at the wound margins; in other lesions partly disintegration of the crusts in all wounds and a humid wound environment underneath.

Debridement of softened parts of the crust; quiet aspect of a clean wound and skin surface without a foul smell; minimal signs of epithelial outgrowth and beginning contraction; slow loosening of the remaining eschar; more superficial burned lesions show more advanced epithelialization.

Macerated aspect with a mixed pattern of epithelial outgrowth at the wound margins; pale red somewhat hypertrophic granulation tissue; a more advanced epithelialization in all other lesions.

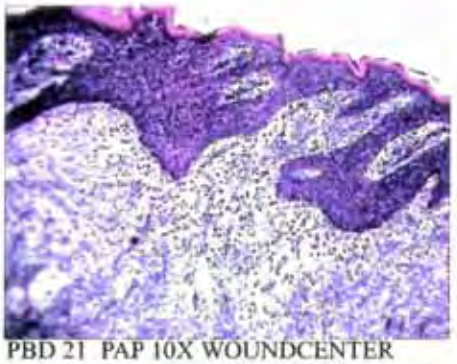
ELASTOGEL 95V626

PBD 7 PAP 2.5X WOUNDCENTER
Intact crust without viable skin appendages
The fatty tissue septa are quiet

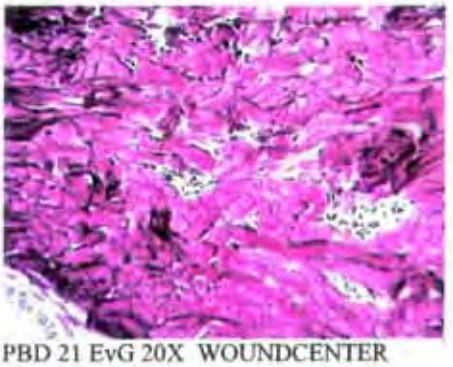
PBD 7 PAP 40X WOUNDCENTER
Superficial hairfollicle. Notice abcense of bacterial colonies

PBD 14 PAP 2.5X WOUNDCENTER
Still intact and demarcated crust. Notice epithelial islands directly below.

PBD 14 PAP 2.5X PARACENTRAL
Re-epithelialization of the surface starting from sub crustal epithelial islands

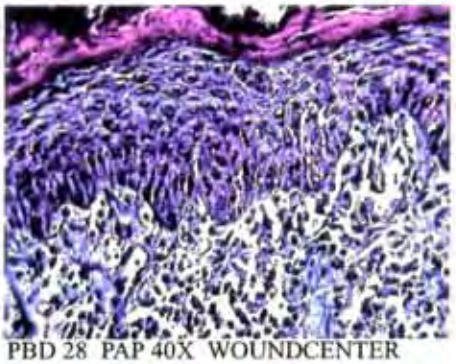


PBD 21 PAP 10X WOUNDCENTER
Part of the surface is covered by acanthotic and spongiotic epithelium



PBD 21 EvG 20X WOUNDCENTER
Sweat gland (bottom left) surrounded with viable dermal remnants with intact elastin

PBD 28 PAP2.5X WOUNDCENTER
Complete re-epithelialisation and superficial perivascular edema

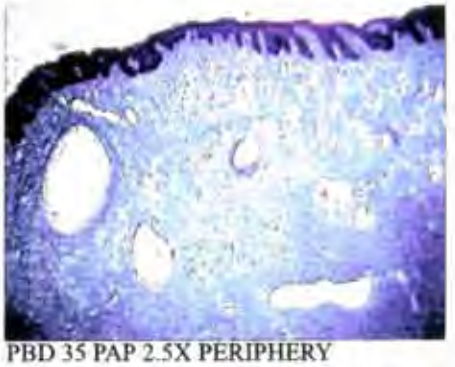


PBD 28 PAP 40X WOUNDCENTER
The neo-epidermis is spongiotic and with parakeratosis

PBD 35 PAP 2.5 X WOUNDCENTER
First location showing complete re-epithelialisation and a relative quiet neo-dermis

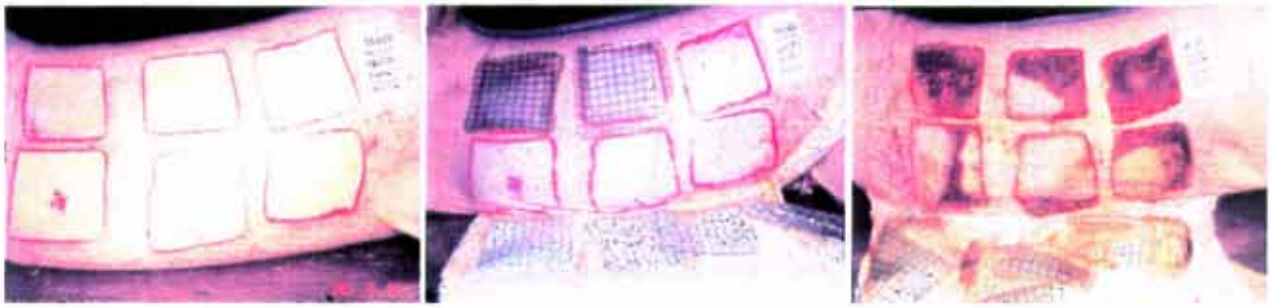
PBD 35 PAP 2.5X PERIPHERY
A few widened vessles are encountered in the middle layers of the granulation tissue

PBD35 PAP 40X WOUNDCENTER
The incomplete neo-epidermis at the second location shows inflammatory infiltration



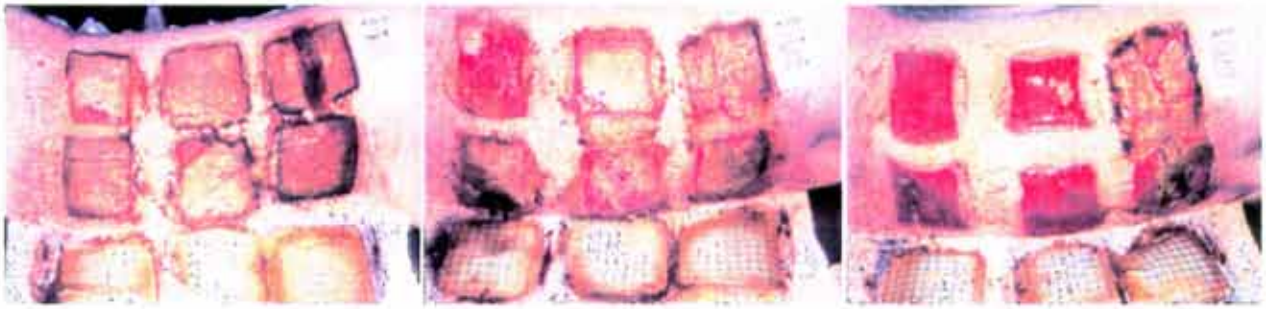
PBD 35 PAP 2.5X PERIPHERY
This second location shows more edema as well as strikening wider vessels.

Study no. 95.626: Visigel® PBD 0 - 35



Deep partial thickness contact burns just after infliction; de-epidermised white supple eschar at pbd 0; supple wet eschar at pbd 1 after change of dressing material; partly dried out eschar by dislocation of dressing material at pbd 4; blue green discoloured dressing material and typical 'pseudomonas' odour.

Easy dislocation of dressing material and partly dried out eschar at pbd 5 and 6; blue green discoloured dressing material and a dirty smell of putrefaction; better fixation of the dressing material after pbd 6 with Curafix® adhesive bandage;

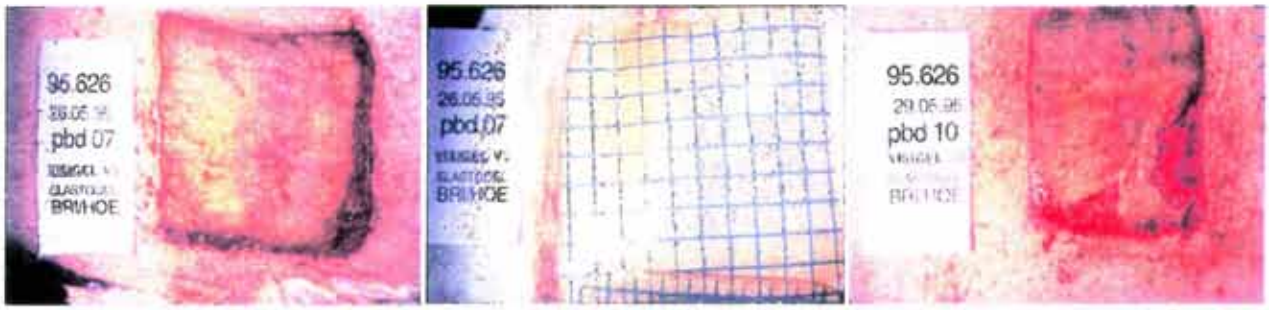


Dirty smell and extremely soft eschar; very friable wound bed with massive blood loss in one lesion by a traumatic tear; profuse bleeding at the biopsy side at pbd 14; quick spontaneous debridement of all remaining eschar; macerated granulating wounds; epithelialization not to judge by transparency and maceration.

Epithelialization also after pbd 21 difficult to judge; very moist aspect; typical small hemorrhagic blisters in all lesions; still a dirty smell perceptible; clear signs of beginning contraction; friable extremely macerated thin epithelium at pbd 35.

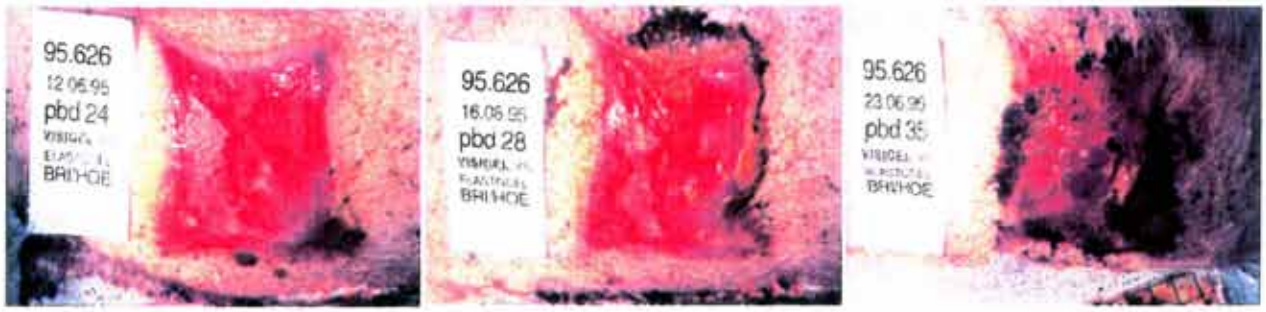
Study no. 95.626: Visigel® PBD 0 - 35

Deep partial thickness burn with a central less deep burned part just after infliction; de-epidermised white supple dry eschar, surrounded by a small hyperaemic zone; after some days a wet soft white and supple light green discoloured eschar and a typical smell (pseudomonas); early deterioration of the central part of the eschar.



Clear deteriorating wet macerated eschar; typical pseudomans like dirty smell and blue green dicolored bandages; easily bleeding spots in some lesions and typical brown-red spots.

Dirty wound surface and extremely weakened crusts; very weakened soft granulation tissue with pocket formation and massive blood loss by minimal insult; stil a clear penetrating dirty smell of pseudomonas; also profuse bleeding at the biopsy site; minimal sign of contraction; progress of epithelialization difficult to judge.



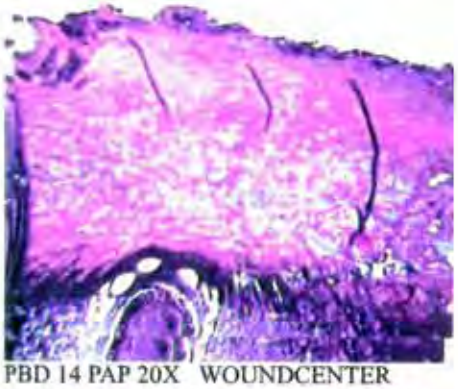
Typical blister formations in a partly epithelialised wound bed; epithelialization difficult to judge; very friable macerated epithelium; clear contraction in all lesions; easyly hemorrhagic tissue.

VISIGEL 95V626

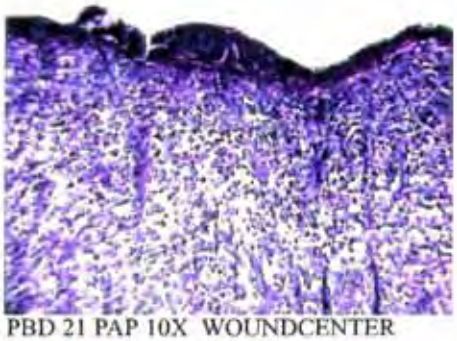
PBD 7 PAP2.5X WOUNDCENTER
Eroded crust surface with micro-organisms. Notice early thickening of fat tissue septa

PBD7 PAP 20X WOUNDCENTER
Bacterial colonies both superficial and in hair follicle remnants

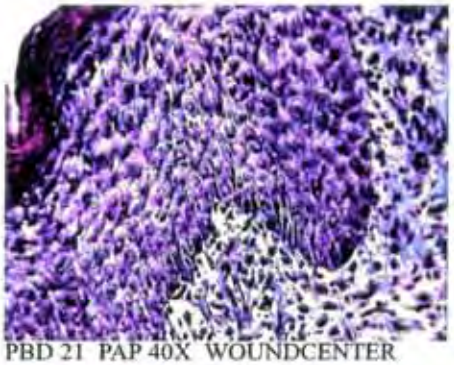
PBD 14 PAP 2.5X WOUNDCENTER
Eroded loosely attached crust undermined by focal abcesses



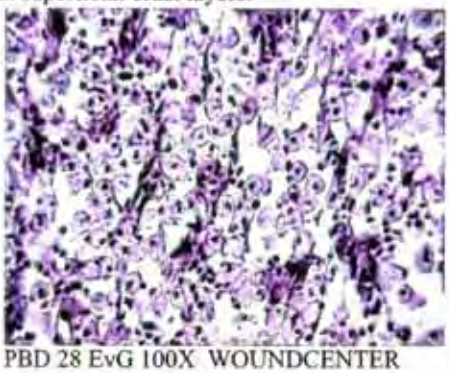
PBD 14 PAP 20X WOUNDCENTER
Notice bacterial colonies staining dark blue in superficial crust layers.



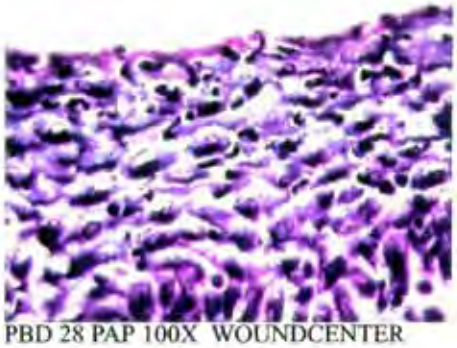
PBD 21 PAP 10X WOUNDCENTER
Bandlike superficial inflammation with foamy histiocytes



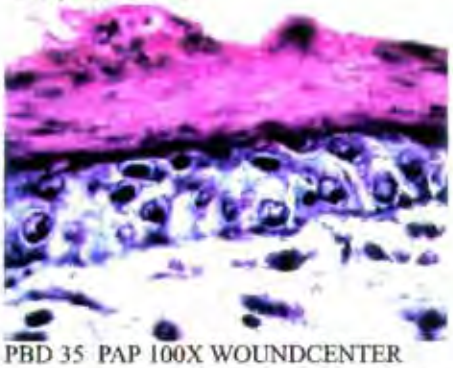
PBD 21 PAP 40X WOUNDCENTER
The neo-epidermis is spongiotic, acanthotic and parakeratotic.



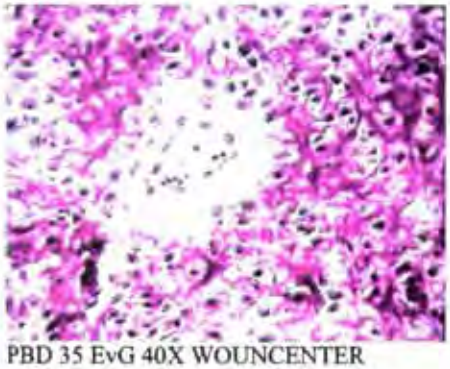
PBD 28 EvG 100X WOUNDCENTER
Detailed view on "foamy histiocytes" in superficial layers



PBD 28 PAP 100X WOUNDCENTER
The neo-epidermis is very spongiotic and infiltrated with inflammation

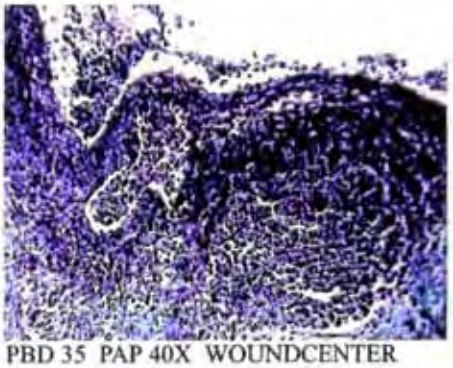


PBD 35 PAP 100X WOUNDCENTER
Macerated neo-epidermis showing spongiosis and parakeratosis



PBD 35 EvG 40X WOUNCENTER
Perivascular edema

PBD 35 PAP 2.5X WOUNDCENTER
Subepidermal blister formation draining on the woundsurafce



PBD 35 PAP 40X WOUNDCENTER
Blister wall with necrosis and inflammation

PRELIMANARY CONCLUSIONS:

There is a striking difference in bacterial colonization between Elasto-Gel™ and Visigel™ treated wounds.

Unless the fact that Visigel™ treated wounds show many bacterial colonies in the top of the necrotic layer and underneath leading to abcess formation, no bacterial colonization can be observed at the Elasto-Gel™ treated side.

Elasto-Gel™ treated wounds have an intact necrotic layer without erosions and no early deterioration of the eschar as seen in Visigel™ treated wounds.

All treated wounds show a slow epithelialization pattern.
The neo-epidermis is striking normal in total epithelialised Elasto-Gel™ treated wounds and shows some inflammatory infiltration in partially epithelialised wounds.

Also there is a quiet neo-dermis in fully epithelialised wounds and some perivascular edema in partially epithelialised wounds.

In contrast to Elaso-Gel™ treated wounds the epidermis in Visigel™ treated wounds is macerated and infiltrated with many inflammatory cells.
The neo-dermis shows extensive perivascular edema with subepidermal blister formation and inflammatory infiltrates.

As an early conclusion it can be stated that Elasto-Gel™ is a far superior dressing material in contrast to Visigel™ as a result of the high glycerine content.

Although highly concentrated glycerol in a hydrogel matrix also creates a moist wound environment, its discourages bacterial growth in the dressing material as well as in the wound bed.

Epithelialization isn't retarded in superficial wounds with a surplus epithelial remnants.

In deeper wounds Elasto-Gel™ creates a status quo situation by protecting the wound bed against bacterial infection causing extensive inflammation and multiple abcesses.