ELASTO-GEL AND WOUND HEALING

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Contents:

- I. REDUCTION /MODULATION OF INFLAMMATION REACTION
- II. BACTERIOSTATIC EFFECT
- III. NO TOXIC SIDE EFFECTS

Results

I. Investigations with topical therapeutics to which glycerine is added in increasing concentrations (5-15-30%) show increasingly a reduction of inflammation reaction. At high concentrations though, this can lead to a considerable slowing down of wound healing. Biomaterials to which glycerine is added appear to be more difficult to break down. This was observed a.o. with glycerine treated Soft Dura[™](Braun Medical, Melsungen, Germany) and collagen. After implantation, these products, which are generally easily degradable biological polymers, are found nearly intact after a prolonged period.

In a first pilot study with Elasto-GelTM (Southwest Technologies, Inc., Kansas City, MO) during which the dressing is changed regularly(aprox. daily), a strong reduction of inflammation reaction was noted as well as a concurrently slower healing rate.

During cell-breeding research using T-lymphocytes collected from human tonsils, it appears that allogeneic epithelial cells, which still contain traces of glycerine, strongly exert a negative influence on the reaction of these lymphocytes to the "alien" epithelial cells. Thus glycerine appears in vitro to possess clear immuno-modulating properties.

II. By comparison with conventional hydrogels, no microscopically visible infections are seen during a treatment with Elasto-GelTM. Specifically, the <u>absence</u> of odor on the site treated with Elasto-GelTM is evidence as well as the <u>absence</u> of blue-green discoloration(associated with pseudomonas) on the dressing.

This seems due to the intrinsically bacteriostatic properties of high concentrations of glycerine. Glycerine is not a quick and highly effective antibacterial agent, but because no bacterial growth is possible, eventually all bacteria will disappear (data available from the research group at Beverwijk).

In the presence of 15% water, spores too(Bacillus subtilis) will disappear. Besides that, glycerine possesses clearly demonstrable antifungal and antiviral properties(publication by research group at Beverwijk).

ELASTO-GEL AND WOUND HEALING (translation)

III. Glycerine is not demonstrably toxic. In the early 1950's this was investigated at length by Billingham & Medawar for the purpose of using glycerine during deep-freezing of human cells. Even when glycerol(glycerine) is used in increasing concentrations, no significant toxicity can be demonstrated, although, at higher concentrations cells die as a result of dehydration.

Considering the arguments presented under I, II, and III, it seems that a dressing containing glycerine, definitely has its place in the therapeutic arsenal for wound treatment.

There is need for:

- -- topical therapeutics with an intrinsic antibacterial(and antiviral) effect:
- -- topical therapeutics with little or no toxic effects to human cells:
- -- topical therapeutics with immunomodulation and inflammation reducing properties for wounds, whereby excessive inflammation leads to a poor quality scar tissue, such as in burn wounds, traumatic wounds and a multitude of surgical wounds.

Based on the observation that regular changes with Elasto-GelTM can lead to a strong reduction of inflammation reaction, but also to a strong slow down of the wound healing process, it is to be accepted that for treatment of different wounds a matching treatment protocol will have to be established. Experimental research on animals will give a good insight and clinical trials will eventually have to provide a final answer.

As a proposal for treatment of acute, traumatic, surgical and burn wounds, one might for instance propose the following scheme:

PROTOCOL FOR TRAUMATIC WOUNDS AND BURN WOUNDS

- Day 0 7: apply Elasto-Gel dressing; regularly inspect wound, but in general do not change the dressing, unless it is fully saturated with wound exudate and/or leakage or maceration occurs.
- A: If after 1 week, if the wound heals well:

 do nothing different, that is continue to apply a new
 Elasto-GelTM dressings as they become fully saturated with exudate.
- B: If after 1 week the wound heals moderately:

 possibly stop using Elasto-GelTM and change to a product that stimulates healing, such as a hydrocolloid:
- C: If after 1 week the wound heals hardly or not at all: stop using Elasto-GelTM and change to an inflammatory stimulating therapy, including for instance a hydrocolloid, or surgical intervention(skin graft).

ELASTO-GEL AND WOUND HEALING (TRANSLATION)

CHRONIC WOUNDS

The healing of a number of chronic wounds can also be positively influenced by using a dressing containing glycerine on the basis of the above mentioned properties such as the antibacterial and immuno-modulating effects of Elasto-GelTM. Specifically, when facing irritated chronic granulating defects that have been treated for a long time with various topical chemotherapeutics application of Elasto-Gel can be beneficial.

Glycerine has an astringent effect and it extracts exudate together with many inflammation factors from the wound bed. Because of this "detoxifying" effect of the dressing, quality of wound healing can be improved.

Also, because of the strong hygroscopic effect of glycerine, deepening of the wound bed will occur, which goes often hand in hand with initiation of wound healing in non-healing ulcers.

On the other hand, too strong of a dehydration can lead to cell necrosis and a slow down or an arrest of the healing process. In many cases of "low grade" bacterial infections, these infections will be reverted further, which can lead to the start of the healing process in poorly healing wounds and ulcers. Because a stable equilibrium can quickly be disturbed, here too, the "dosage" of using Elasto-GelTM will be of paramount importance for a successful treatment. "Dosage" is to be understood as the number of dressing changes that will lead to the desired therapeutic effect. Therefore, the effective use of interactive wound dressing material will increasingly correspond, in this respect, with dosages in force for topical chemotherapeutics.

Comments
by Dr. Ed Stout, PhD
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Note that much of the previously reported data, which supports the effects of Elasto-GelTM on wound healing, has been obtained from the application of solutions of glycerine in water to the wound, in which the total concentration of glycerine in that solution is immediately inter-acting with the cells in the wound site. In contrast, when applying Elasto-GelTM dressings, the glycerine is slowly released from the dressing as the wound exudate is absorbed. This gives a slower build up of the concentration of the glycerine in the wound site and the amount of glycerine "seen" by the human cells is relatively lower. The cells, which are on the surface of the tissue, are constantly bathed or fed new fluid from the underlying tissue, and are not exposed to the total concentration of the glycerine in the surrounding wound fluid. However, frequent dressing changes without cleansing the wound site could lead to high concentrations of glycerine, but will always be less than 65%, which is the concentration in the Elasto-GelTM dressing.

Note that preliminary results indicate application of Elasto-GelTM wound dressings increases the concentration of the growth factors in the wound site by absorption of the water from the exudate but not the growth factors. That is, Elasto-GelTM acts as a filtering medium to leave behind the growth factors as the fluid is absorbed into the gel matrix. Frequent dressing changes with wound cleansing would remove or dilute this high concentration of growth factors and potentially slow the rate of healing. Therefore, as recommended here by Dr. Hoekstra, the results all indicate that we do not want to change the dressing unless it is nearly fully saturated and to only cleanse the wound when it is absolutely necessary.

The results here and in related clinical studies, have shown the elimination of bacterial growth in the wound site when Elasto-GelTM is used as the wound dressing. Thus, the growth factors deposited in the wound site by the normal healing process are available for human cell growth rather than being used for bacterial cell growth. This may be the explanation that frequent reports are received from

clinical nurses and patients that non-healing wounds of 10, 12, even 16 years duration begin healing within a few days after application of Elasto-GelTM dressings. Many diabetic ulcers have also been reported to heal after applying Elasto-GelTM dressings.

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