Scar management – marrying the practical with the science

Widgerow AD, MBBCh, FCS(SA Plast), MMed(Wits), FACS
Department of Plastic Surgery, University of the Witwatersrand
President AdarScience Inc USA
Correspondence to: Prof Alan Widgerow, e-mail: awidgerow@adarscience.com

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We have come a long way in our understanding of the mechanisms involved in producing an exaggerated scar. One of the important factors to consider is that, as in so many other medical conditions, the answer lies in a multipronged approach. It serves no purpose targeting one area in a cascade of events that result in scarring. Thus we previously published a set of principles that govern the sequential areas of control that we have used to minimise scarring – support, hydration, collagen maturation and controlled inflammation.[1,2] These principles will be elaborated on in respect of new scientific facts and with particular reference to the practical management of different wound sites.

Support

Supporting a scar, particularly a long scar, in areas where vector forces continually pull on the scar, has long been recognised as beneficial to scar outcome.[1,2,3,4] Take for example the presternal chest area – forces are generated on the scar from neck movements, shoulder movements, arm movements and additionally from the weight of breasts in some women (Figure 1). The direct response to such vector forces is increased production of collagen in an effort to keep the wound closed. Using agents such as Vitamin E (especially when used early) can cause major skin sensitivities and it has a collagenase-like effect, which weakens the scar and can have disastrous consequences with stretching and even opening of the scars.[5–8] To quote the literature... *"This study shows that there is no benefit to the cosmetic outcome of scars by applying vitamin E after skin surgery and that the application of topical vitamin E may actually be detrimental to the cosmetic appearance of a scar. In 90% of the cases in this study, topical vitamin E either had no effect on, or actually worsened the cosmetic appearance of scars. Of the patients studied, 33% developed a contact dermatitis to the vitamin E. Therefore we conclude that use of topical vitamin E on surgical wounds should be discouraged."*[5]

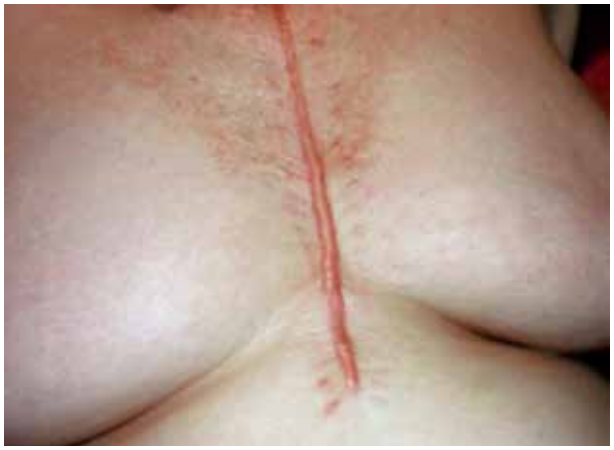

Figure 1: Untreated hypertrophic scar in the presternal area – multiple vector forces working against it

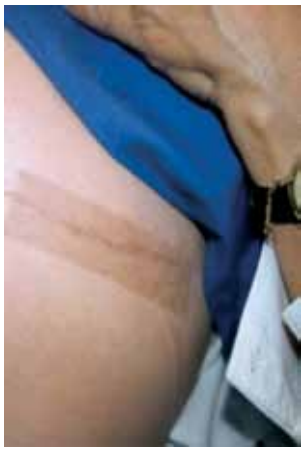

Figure 2: Tape applied longitudinally along direction of scar; white or flesh-tone tape may be used, same effect

The best form of scar support consistently is microporous tape.[2,9,10] The tape must be applied longitudinally along the scar path and not at right angles (Figure 2). This ensures that support is consistent and not intermittent in some areas. Additionally we have found that the tape should not be removed but left in place for days until it spontaneously separates or becomes

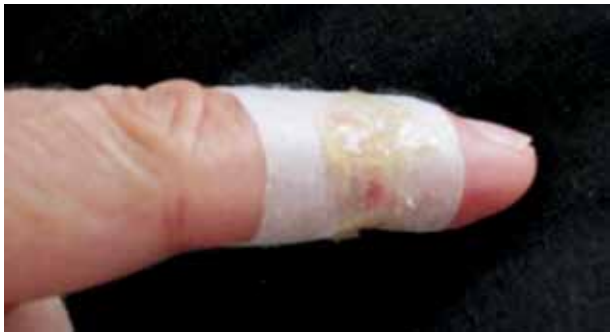

Figure 3: Tape applied over finger cut, one layer, saturated with gel on the surface

tatty. Premature removal results in skin stripping which sets up inflammation with negative consequences on the scar. Although small areas of scars may not need support, some small scars do very well with support – cuts on fingers are continually stressed with forces – applying a single layer of microporous (not plastic, not fabric but breathable porous tape) is ideal to support the scar, avoid maceration as seen with common plasters, and allows the application of additional agents to the tape surface to speed up the maturation process (see later) (Figure 3).

Hydration

Hydration of the scar surface is the basis of action of 90% of scar management systems on the market. Most oils (tissue oils), lotions and creams have beneficial effects on scars purely on the basis of their hydrative capacities.[11,12,13] Although this is obviously beneficial, it is limited in terms of the outcome it can produce and has effect on only one area of scar control. Normal skin has a mature stratum corneum characterised by minimal transepidermal water loss (TEWL). Dehydration of the stratum corneum initiates signalling to keratinocytes. These keratinocytes are stimulated to produce cytokines which activate dermal fibroblasts to synthesise and release collagen. Excessive collagen production leads to abnormal scarring.[14] The most effective barrier to TEWL and stratum corneum breach is silicone, either in the form of sheeting or gels (dimethicone).[14–16] In addition, we have found the gel derived from the plant bulbine frutescens to be effective as a hydrating agent – the glycoproteins of this plant extract are large and remain on the surface of the skin long enough to produce effective hydration of the skin.[2,3]

Scar maturation/collagen modulation

The quicker the scar matures the less chance there is of hypertrophy. Collagen maturation goes through phases with collagen type III being present in greater levels in the early scarring phase. As the scar matures the ratio of type III to type I returns to normal levels.[17] Thus any agent that encourages type I collagen formation and return to stable ratios, is advantageous to scar outcome. Extracts of Centella asiatica have just that effect, increasing levels of mature collagen and encouraging normalising of collagen ratios.[17–19] Purified extracts (triterpenic fractions including asiaticoside) of the Centella plant are essential. Asiaticoside, a saponin component isolated from Centella asiatica, has been shown to induce type I collagen synthesis in human dermal fibroblast cells.[17–19]

TGFβ is the prototype of a protein superfamily that has been recognised as the major fibroproliferative and collagen stimulating agent involved in excess scarring (particularly TGFβ1). Many isoforms of the protein exist with most isoforms sharing the same fibroproliferative properties. One isoform, TGFβ3 however, appears to have a protective effect against excess collagen formation counteracting the TGFβ1 effects.[19] Remarkably, asiaticoside can down-regulate TGF-β1 mRNA and TIMP1 expressions and up-regulate TGF-β3 mRNA expression in post burn hypertrophic scars, and is also capable of decomposing the products of type I collagen, contributing to the reduction of hypertrophic scar formation.[19]

Finally, added laboratory evidence of asiaticoside efficacy, was demonstrated in the rabbit ear model, one of the only consistent animal models producing hypertrophic scarring.[20,21] As opposed to other commonly used anti-scar preparations, asiaticoside could markedly alleviate the scar in the rabbit ear model. Western blotting showed that the asiaticoside could decrease TGFβ1 expression.[20,21] Although we have researched and used the plant extracts for the past decade, the research noted here has only been elucidated in the past few years, making the Centella asiatica plant purified extracts ideal as added components for scar management.

Further collagen modulation – packing the fibres

Having fulfilled the requirement of stimulating new collagen formation, ideally the packaging of the new fibres should be uniform and structured in a non-clumped moiety. The process of fibrillogenesis, new collagen formation, involves the conversion of procollagen to tropocollagen (non helical ends cleaved off) to fibrils arranged uniformly by 'spacers' preventing collagen clumping. These spacers are normally provided by decorin, a proteoglycan macromolecule in the extracellular matrix.[22] Ongoing work that we are doing points to the possibility that bulbine frutescens, when in contact with the skin, elaborates tetrapeptides that resemble those of decorin, mimicking the effects of decorin on collagen spacing.[22]

Inflammation

Inflammation is a necessary sequence in all wound healing mechanisms. However, exaggerated inflammation appears to be the central problem in all chronic (and many acute) diseases, be it cardiac, vascular, diabetic or arthritic. Exaggerated scarring is no exception to this issue – excessive inflammation results in exaggerated scars. Thus controlled inflammation is a sought after principle in scar management.

Phenol compounds in newly pressed olive oils confer anti-inflammatory activity. Beginning in the early nineteenth century, medical journals began to report that the bitter tea brewed from olive leaves was an effective treatment for malaria. Many patients improved using this therapy, but further work on this natural antibiotic and antiviral agent was to wait for another 100 years before the true extent of olive leaf extract healing potential would be discovered. Later in that century, biochemists isolated a crude powdered extract from olive leaves, which contained oleuropein, which was considered to be the source of the olive tree's powerful disease and pest-resistant properties.[23–25] Oleuropein can be found in most parts of the tree, but is especially rich in the leaves. More recently a

host of publications have demonstrated that the topical application of the olive oil compounds produced a significant degree of anti-inflammatory and antimicrobial effects.[23–25] Oleuropein has also been demonstrated to stimulate proteasome function and fibroblast formation of new collagen.[25] Proteasomes mop up fragmented protein particles including fragmented collagen, a process critical to the prevention of clumped collagen. Thus stimulation of proteasomes and inhibition of inflammation is extremely advantageous to the process of scar maturation.

Thus combining the Centella, bulbinela and oleuropein components results in a significant collagen modulation preparation – this is patent pending and trademarked under the name Moducoll.

Putting it all together.....

It seems so obvious in retrospect but the process of application of the cream/gel on the surface of the tape has been patented by us. This now creates the ideal occlusive dressing for scars. The gel with its active agents is absorbed through the tape within two minutes but the saturated tape continues to work as a scar dressing. So all principle requirements are accomplished – support, hydration, scar maturation through collagen modulation and controlled inflammation. The tape remains in place during bathing, it is only replaced once spontaneous separation takes place (3–5 days usually), gel is applied to the surface of the tape twice a day and the routine is continued until scar maturation (white colour) takes place. The tape component may be stopped anywhere from six weeks of application if the scar is seen to be maturing well – gel is then applied directly to the scar. This modification was made (tape was previously used up to six months) when results with the new formulation showed more rapid scar maturity.[2]

As some areas are not conducive to taping and support may not be critical to the smaller scars, taping can be left out of the routine. To compensate for this a further modification was made to the formulation whereby a thin film/crust has been planned to form when the gel dries – this provides a certain amount of support to the scar but more importantly serves as a barrier from outside contamination, irritation from sun, cosmetics etc.

As with all theoretic postulations, these need to be subject to scientific validation. An intensely comprehensive trial was undertaken assessing 170 scars in different clinical situations; some scars were followed in the same patient with different treatments, and a multitude of differing factors were introduced. Assessments were made by surgeons, independent observers and patients and a fully documented analysis of the clinical trial was accepted and published in Aesthetic Plastic Surgery.[2] In a nutshell, this trial demonstrated that if scar management is dealt with conscientiously with adherence to the principles elucidated above, hypertrophy could be prevented in greater than 80% of cases (Figure 3). This contrasts

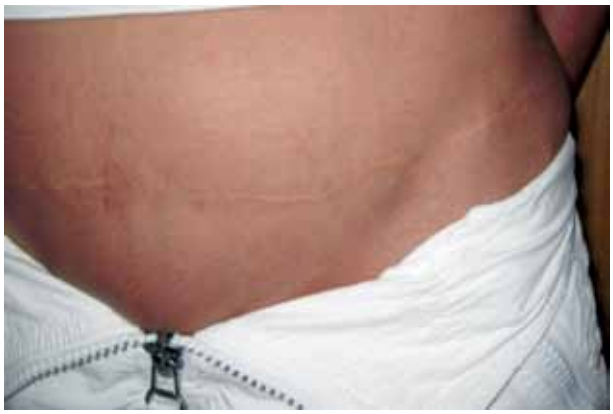

Figure 4: Mature treated abdominal scar – flat, white, non-reactive (note, it is normal for most scars to hypopigment to some extent). Contrast this to the untreated scar in Figure 1

sharply with reported series on scar outcome where hypertrophy and exaggeration of the scar is anticipated in 60–80% of cases where no management of the scar is undertaken (Figure 4).[26]

The above described routine deals with scars relating to trauma, surgery, acne, insect bites, most acute and chronic wounds and chicken pox. Regrettably, it is not ideal as a sole agent for large surface area scarring such as burn scars. We would still suggest using silicone sheeting and pressure in these situations, with the gel where necessary. New interactive 'scar dressings' are being investigated for this type of widespread scar.

Scar management discussions would not be complete without discussing the concept of keloid scars. These are often confused with hypertrophic scars and arise from completely different circumstances. Keloid scarring is usually a genetic phenomenon where collagen type1 is produced in a tumour-like fashion with uncontrolled growth of scar tissue. The history usually involves a wound well managed, without infection or any discernable problem that progressively increases in size and reactivity and overflows the boundary of the wound (Figure 5). It may be painful, sensitive and extremely uncomfortable and treatment today (often radiotherapy) is unpredictable and unsatisfactory. The principles described above

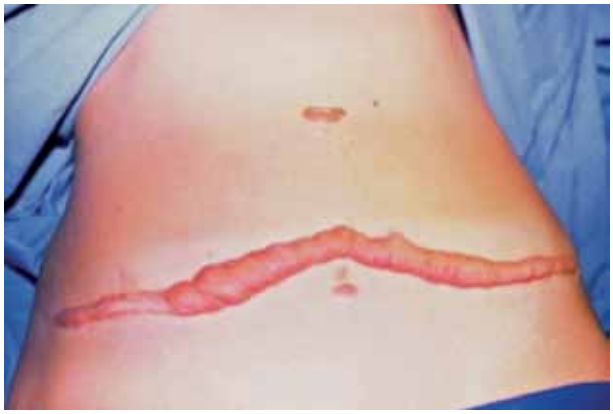

Figure 5: Keloid scarring – grows like a tumour, flows over the scar boundary, occurs wherever the skin is breached; different pathogenesis and treatment to hypertrophic scars

do not relate to keloid scarring and it is important to recognise that. Any company making claims of prevention and treatment of keloids and hypertrophic scar with the same preparation are displaying ignorance and casting great doubt on the efficacy of that product. These are different mechanisms of scarring and need to be dealt with as such.

Special areas – ACNE

One of the most exciting advancements in scar management has been the application to acne scarring. Acne scarring involves a complicated process of hormonal, infective, genetic and environmental factors that combine to produce devastating outcomes in many patients. The most feared outcome of the process is the ultimate scarring that may result. The formulation described above is non-comedogenic but is not being used to control acne. Rather it is specifically used as an adjunct to the normal anti-acne routine. Thus when the pustule is free of pus and advances to an inflammatory lesion, the gel is used on each individual lesion. This is a phased approach where each lesion is treated individually depending on its state in the acne evolution. The best results appear to be those that are initiated as soon as the infective episode is under control and inflammation predominates.

Trials are currently underway in the USA and SA where each lesion treated is graded according to redness, surface indent filling, hypertrophy, irritation and so forth and patients are graded on an anti-acne scale. Thus far preliminary results have demonstrated great efficacy at scar prevention, alleviation of redness and surface filling. Results are to be published in the near future, but this indication is proving to be excellent in the scar control arena.

Summary

Scar control is an area that has received much attention from a patient perspective and fortunately from a research perspective too. Much of the guesswork involved in scar formation and exaggeration has been eliminated and the principles involved have been well defined. It is clear that control needs to come from a number of areas and no single modality will be adequate to ensure good outcome. Thus the combination of proven factors relating to support, hydration, collagen modulation, controlled inflammation and barrier film formation have proved extremely efficacious in the clinical trials conducted to date. Scar control should be an important aspect of all wound management and can now be scientifically directed to varying clinical situations that may present themselves.

Disclaimer

Prof Widgerow is consultant to Omnimed, Smith & Nephew, Southern Medical, Sirius, Litha, Syneron and Thebe.

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