



**MONASH** University

Medicine, Nursing and Health Sciences

# **The Future in Wound Management**

**Associate Professor Geoff Sussman**  
**Clayton Campus**

## Development of new treatments

The future of wound management will be less dressing focused and more pharmacologically based.

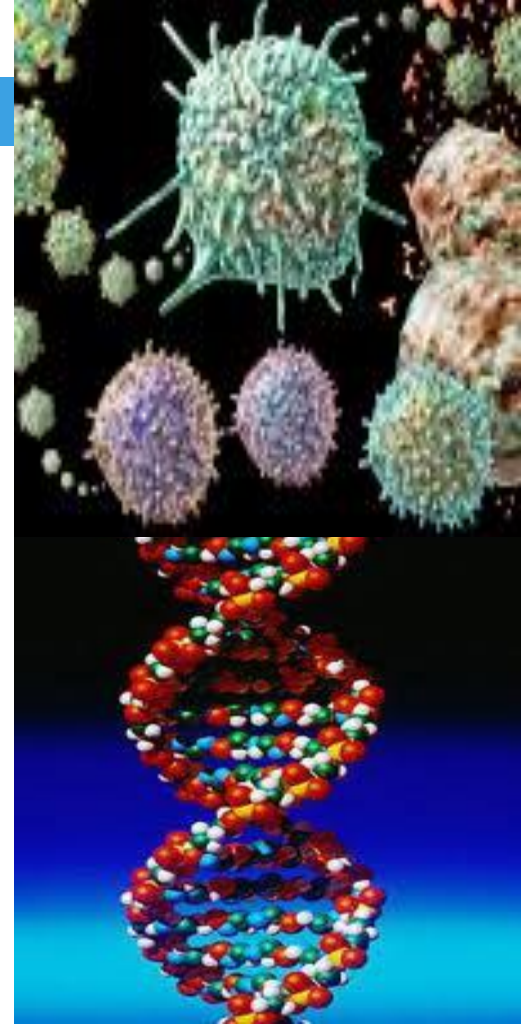
As we increase our understanding of the biology of healing and how cells and tissue react so will our treatments be developed to replace missing elements of healing or to remove or neutralize components slowing or preventing wound healing. This will include Biologicals, Growth Factors, Calcineurin inhibitors Stem cells and Platelet Rich Plasma

## **Development of new treatments**

The next generation of wound products should be smart dressings that provide information on the state of the wound and signal when dressings need to be removed.

# Biologics

- Medicinal products
- Created by biologic processes
- Not chemically synthesized
- Can be
  - Vaccines
  - Viruses
  - Gene therapy
  - Blood or blood components
  - Stem cells, immune cells, tissue or organs
  - **Recombinant therapeutic proteins (main group for new drugs)**



# Monoclonal antibodies

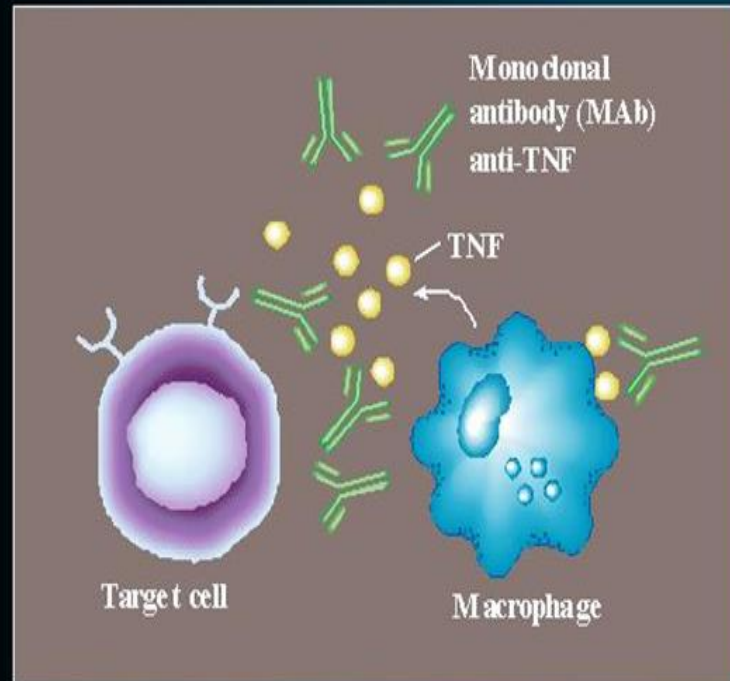
- Similar to natural human antibodies produced by the immune system to fight infections due to bacteria or viruses
- These are “custom-designed” to block or counteract specific substances in the body or to target specific cell types
- Usually aimed at pro-inflammatory proteins, specific immune-mediated cells or identified disease-causing patho-physiological targets

# Chimeric monoclonal antibodies

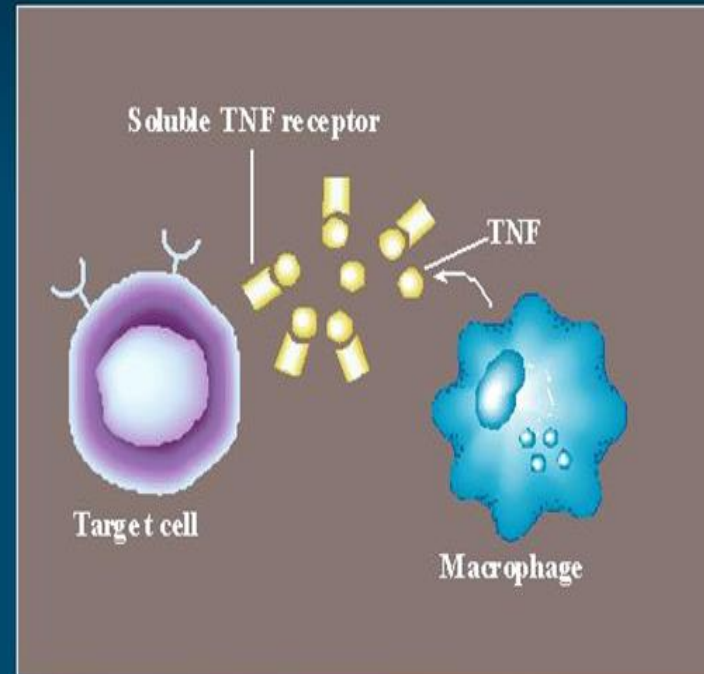
- The first engineered therapeutic antibody drugs were mouse / human chimeric antibodies
- Infliximab (Remicade® - Schering Plough)
- Monoclonal antibody that specifically targets Tumor Necrosis Factor TNF $\alpha$  (pro-inflammatory cytokine).
- TNF is primarily responsible for a range of chronic autoimmune inflammatory conditions

# Rendering TNF Biologically Inactive

Infliximab



Etanercept



# Development of new treatments

## Biologicals -Monoclonal antibodies

They have specific antigenic activity in wounds

MOAB to TNF $\alpha$  have been found useful in healing

Pyoderma Gangrenosum wounds. There are three

TNF- $\alpha$  inhibitors commercially available:

*etanercept (Enbrel)*, *infliximab (Remicade)*, and *adalimumab (Humira)*



# Pyoderma Gangrenosum

## Biologic Therapy: Infliximab (Mab to $\text{tnf}\alpha$ )

*Dini V, Romanelli M, Bertone MS et al. Int J Low Extr Wounds 2007 Jun;6(2): 108-13*



Day 0



After 4 months

# Case 08/10/2009 Adalimumab (Mab to $\text{tnf}\alpha$ )

The patient is a 85yr Lady with a 5 year history of multiple bilateral leg ulcers. She was referred to the wound clinic and a diagnosis of PG was made. She was treated with Immuno-suppressants for three months with little Progress. We commenced Adalimumab ( $\text{tnf}\alpha$ ) 40mg second weekly.





# Case 28/01/2010 Adalimumab (Mab to $\text{tnf}\alpha$ )

Within four weeks there was a marked reduction in pain and a significant Reduction in wound size. The s/c administration of Humira was continued secondly weekly.



# Development of new treatments

## Topical and systemic medications

There is evidence that both topically applied and systemic administered medications can improve wound healing

Drugs with a positive effect on wound healing

- Antibiotics (Doxycycline)
- Haemorrheologics
  - Pentoxifylline (Trental®)
  - Other Methyl Xanthines
- Sex hormones
- Retinoids
- Immunosuppressants

# Drugs with a positive effect on wound healing -

## Haemorrheologics

- Pentoxifylline/Oxpentifylline (Trental®)
  - Effectively change flow characteristics of blood
    - Reduce platelet aggregation
    - Reduce leukocyte adhesion
    - Increase RBC membrane flexibility
      - » RBC 8-9µm & capillary 4-5 µm
  - Used to treat PVD
    - Increases blood flow to ischaemic tissue
    - Inhibit TNF- $\alpha$
    - Vasodilator effects
    - Reduce effects of build up of anaerobic metabolites in ischaemic tissue which have effect on tissue as well as RBC cell wall rigidity

# Drugs with a positive effect on wound healing -

## Haemorrheologics

- Pentoxifylline/Oxpentifylline (Trental®)

- Uses in other cerebrovascular disorders
- Well tolerated – A/Es usual suspects

- Cochrane review

Pentoxifylline appears to be an effective adjunct to compression bandaging for treating venous ulcers. There was no cost effectiveness data available and health care commissioners may therefore conclude that it not be considered a routine adjunct. Pentoxifylline in the absence of compression may be effective for treating venous ulcers in the absence of compression, although the evidence should be cautiously interpreted. The majority of adverse effects are likely to be tolerated by patients, and gastrointestinal disturbances are the most frequent adverse effect

- Other Methyl Xanthines

- caffeine, theophylline, theobromine
- Used in 1920s for intermittent claudication but deemed “too unreliable and feeble as a vasodilator to be of value in the treatment of PVD”

# NITRIC OXIDE IN WOUND-HEALING

Nitric oxide is clearly a key modulator of cell responses, both vascular and inflammatory, to various stimuli such as infections, allergens, and wounds. Also, the production of NO is highly regulated by tissue/cell type-specific isoenzymes, allowing for increased control relative to regional tissue demands.

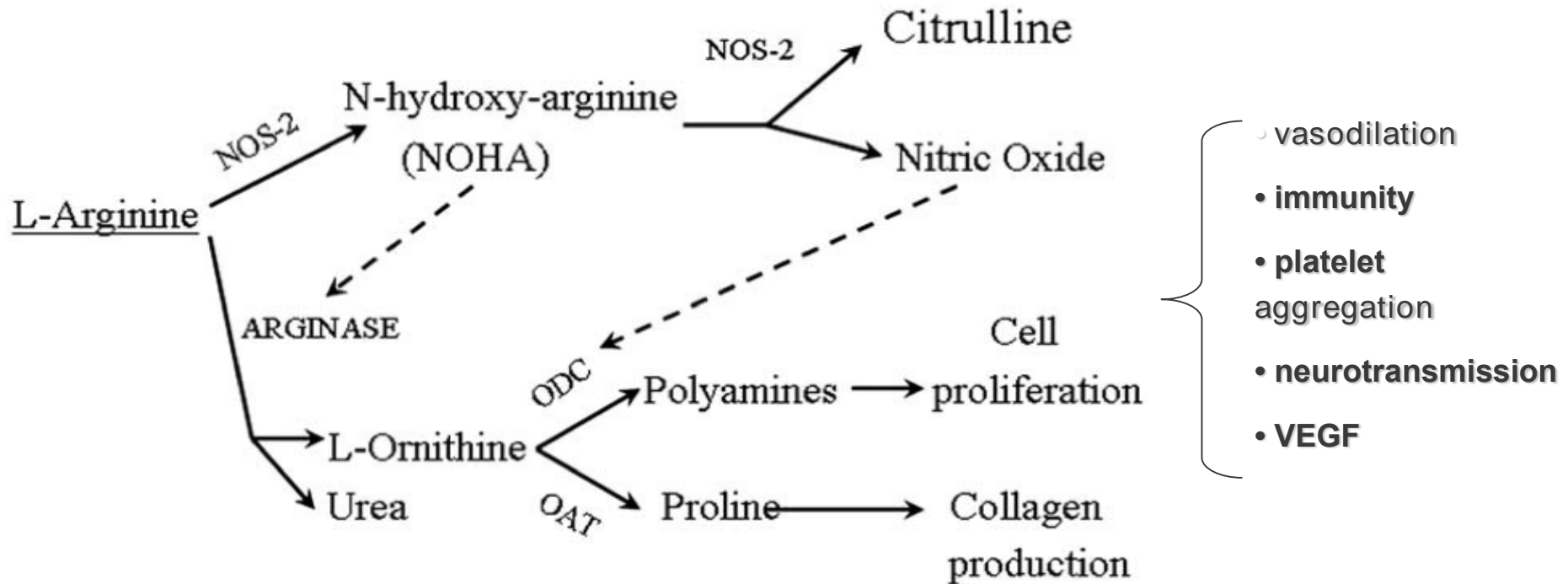
# NITRIC OXIDE IN WOUND-HEALING

In diabetes at least three studies have demonstrated decreased formation of NO metabolites in the wound environment. It is not clear whether this decrease is due to the lesser inflammatory response characteristic of diabetes or to a net decrease in NO formation by all wound cells. L-arginine as well as NO donors can partially reverse the impaired healing of diabetes and in parallel restore wound NO levels toward more normal values



# NITRIC OXIDE IN WOUND-HEALING

## L-Arginine is a Key Substrate



- Kimura H et al. Acta Biochimica Polonica 2003;50:49 (Chiba, Japan)

# NITRIC OXIDE IN WOUND-HEALING

## Examples of Arginine containing Supplements



- Arginaid (4.5 g L-Arginine, Nestle)



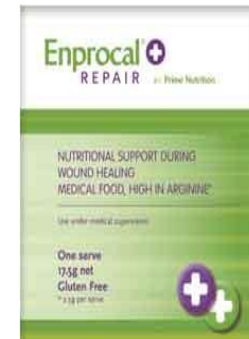
Resource Diabetishield



Resource Arginaid Extra



Cubitan



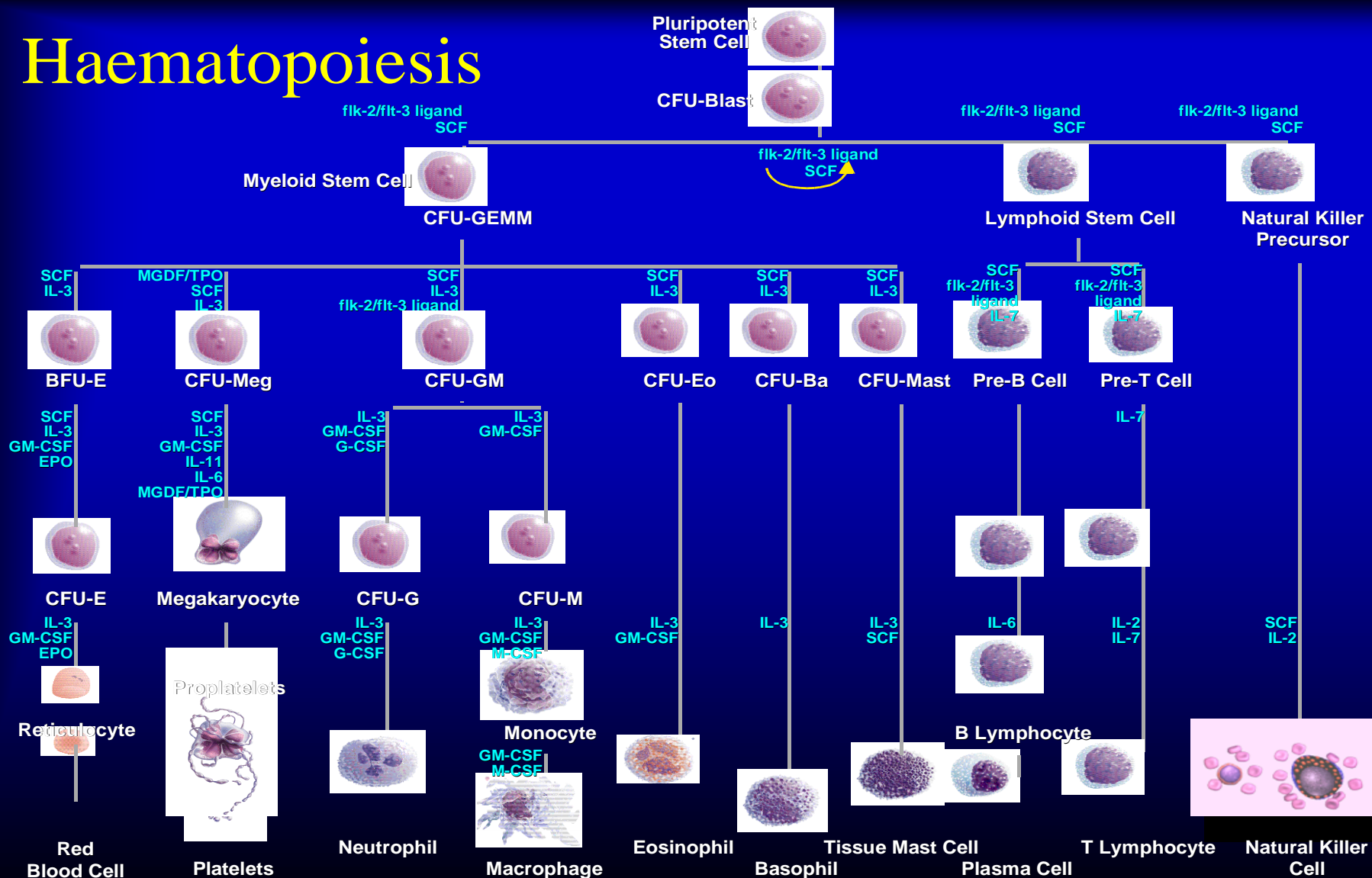
Enprocal Repair

## Haemeopoitic growth factors

These factors include granulocyte colony stimulating factor and the granulocyte macrophage stimulating colony factor and erythropoietin. They have been used particularly in the management of aneamias associated with renal failure patients undergoing haemo-dialysis and as a rescue for patients receiving chemotherapy where they increase the blood cell population. There have been some studies where this type of growth factor has been placed on a wound to improve the healing of such wounds again with some improvement shown.

# Haemeopoitic growth factors

## Haematopoiesis



# PDGF in Necrobiosis Lipoidica Diabeticorum

Patient 40yr Female Type 1 Diabetic with an eight year history of non-healing leg ulcers

Diagnosis: Necrobiosis Lipoidica Diabeticorum

This involves the application of recently Mixed GCSF {Lenograstim} saline. The solution was applied to the wound and left in place undisturbed for 15-20 minutes. The wound was then covered with Mepiex® dressing and held in place with a light tubular bandage. The treatment was repeated in four days



# Necrobiosis Lipoidica Diabeticorum



# Necrobiosis Lipoidica Diabeticorum



**Wound Day 21 of application**



# Necrobiosis Lipoidica Diabeticorum



**Wound Day 49 of application**



## **Tissue Generated Growth Factors PDGF**

Studies have been conducted to evaluate the safety and efficacy of a topical gel containing 0.01% recombinant human platelet-derived growth factor (rhPDGF) for healing of chronic lower-extremity diabetic ulcers.

## Case PDGF in a Diabetic

Patient 70yr Male with NIDDM presented with these wounds the cavity probed to bone he was referred to a Vascular Surgeon for review of possible Osteomyelitis this was confirmed and a decision taken to amputate. The patient requested for us to try to save the leg. After discussion with the Surgeon it was decided to attempt to salvage the leg. Patient was taken to theatre and significant Debridement was performed by the Surgeon. We commenced application of PDGF gel on 13<sup>th</sup> August 2002



## Day One

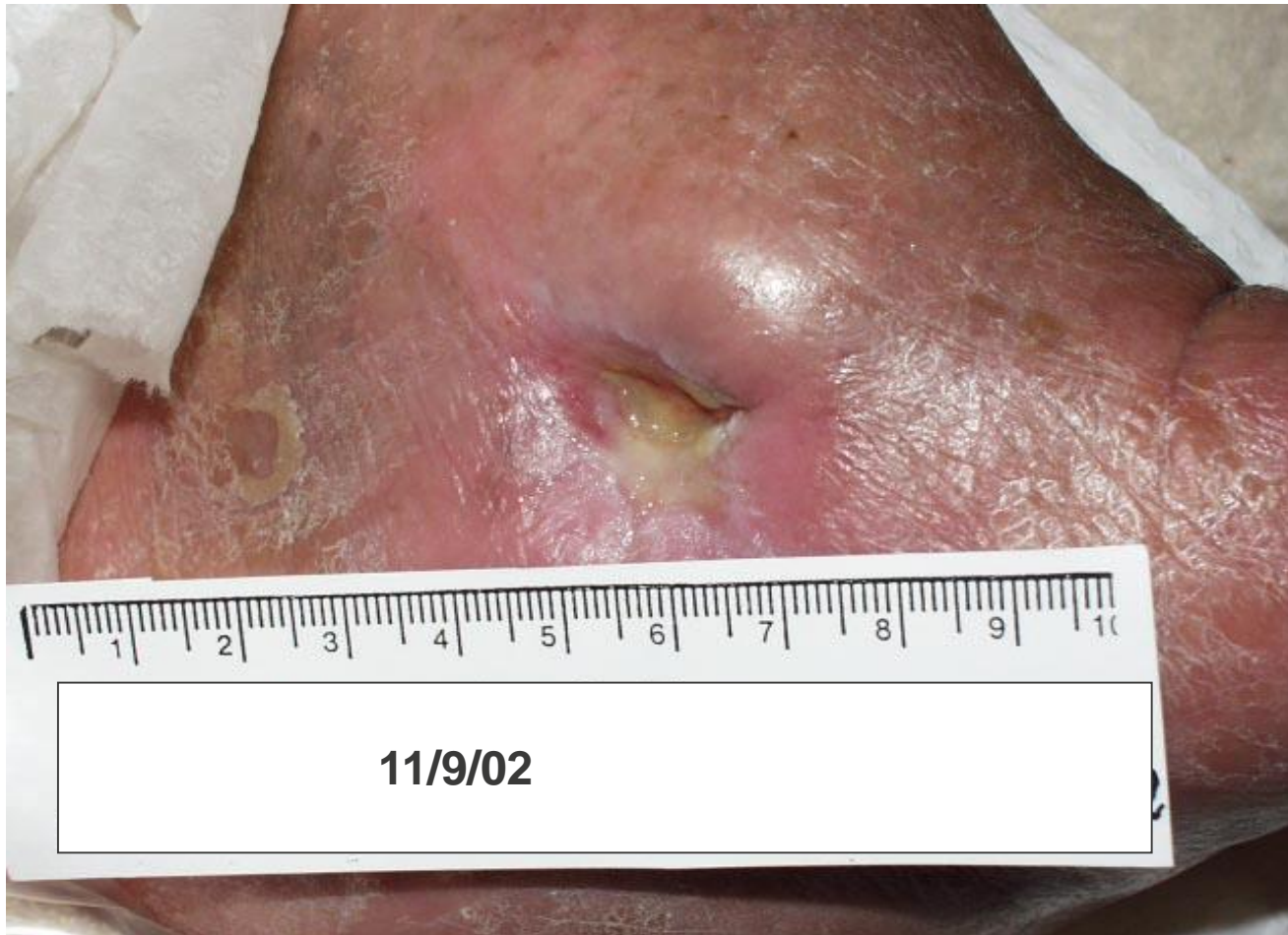


**Day 11**





**Day 29**



**11/9/02**

Day 31



# **Immuno suppressive drugs either systemic or Topical Topical administration**

Topical tacrolimus has been used in the management of a number skin diseases. These include vitiligo, inflammatory skin diseases such as atopic dermatitis, contact dermatitis and alopecia and facial erythematous lesions of Cutaneous lupus erythematosus and dermatomyositis, and pyoderma gangrenosum

## Topical tacrolimus

Topical tacrolimus exerts important immunosuppressive effects during induction of contact hypersensitivity. Moreover, a recent study showed that tacrolimus ointment is highly effective in the treatment of atopic dermatitis. Our observation indicates that the destructive skin inflammation characterising pyoderma gangrenosum may also be successfully treated with topical tacrolimus.



# Necrobiotic xanthogranuloma

Necrobiotic xanthogranuloma (NXG) is a rare, chronic granulomatous disorder characterized by indurated plaques and nodules of the skin.<sup>1</sup> Necrobiotic xanthogranuloma initially presents with yellowish papules and nodules that coalesce into indurated plaques, usually 0.5 to 2.0 cm. Lesions often show superficial telangiectasias and scar and ulcerate in 40% to 50% of patients. Skin lesions can recur rapidly, and lesion size typically increases with recurrence. Despite these potential complications, incisional biopsy is recommended to confirm the diagnosis when NXG is suspected clinically. Most NXG skin lesions (60%-70%) first appear on the trunk or extremities.

# Topical tacrolimus in NXG

Patient was a 55yr Male with a history of diagnosed NXG had a number of different treatment with limited success. We commenced treatment with topical Tacrolimus in January 2013

**17<sup>th</sup> January 2013**



**14<sup>th</sup> February 2013**



**14<sup>th</sup> March 2013**



# Pyoderma Gangrenosum

PG is an inflammatory skin disease resulting in painful, enlarged, ulcerated nodules.

The ulcer is irregular, raised, with Reddish borders and undermined edges with necrotic base. A Rare condition destructive, non-infective ulceration of the skin. It is associated with Inflammatory Bowel diseases and immune system abnormalities.

The ulcers are painful rapidly Enlarging with undermined bluish and purplish red margins.

# Pyoderma Gangrenosum

PG is difficult to diagnose and is Mostly obtained by exclusion. Wound Biopsy will often help to exclude other cases. It is often the Case that if a biopsy is taken that the Wound will enlarge. PG is Difficult to treat this involves

Pain management, Moist Environment, Systemic use of Steroids, Cyclosporin, Dapsone.

# Topical tacrolimus in PG

9<sup>th</sup> June 2016





# Topical tacrolimus in PG

23rd June 2016



# Topical tacrolimus in PG

21st July 2016



# Protease inhibitors

In chronic wounds the level matrix Metalloproteinases (MMP's) is high and this contributes to the delay in wound healing. In addition the exudate rich in MMP's will damage the peri-skin around a wound. One suggested method of management is to apply a protease inhibitor to neutralize The excess amounts of MMP's. Normally the tissue produce a neutralizing agent tissue immobilizing MMP's (TIMPS) but in a chronic wound these are insufficient to keep the wound in balance.



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# Protease inhibitors

## Urgo Start

- TLC (Technology Lipido-Colloid) combined with NOSF (Nano-Oligo Saccharide Factor) is a patented innovative technology which in contact with wound exudate forms a gel and creates a moist environment enabling the key cells involved in the repair process (fibroblasts, keratinocytes, macrophages) to exert their action.
- TLC-NOSF interacts with the wound micro-environment of the wound by preventing the detrimental effect of Matrix Metallo Proteases (MMPs) which in excess in chronic wounds creates a continuous degradation of the extra-cellular matrix.




## PROMOGRAN® PROMOGRAN PRISMA®

PROMOGRAN® is sterile, freeze-dried composite of 55% collagen and 45% oxidised regenerated cellulose (ORC). PROMOGRAN® is designed to promote an optimal healing environment

Promogran Prisma wound balancing matrix is a version of Promogran that includes silver. This provides protection against bacteria, while allowing healing to progress

Enhances the deposition of new collagen and reduces wound contraction Collagen fragments can attract cells into the wound area and induce cell proliferation Collagen peptides break down to amino acids, which can be reused by the cells to help build new proteins Reduces MMP activity, an effect that helps control the proteolytic environment in the chronic wound





Doxycycline, a member of the tetracycline family of antibiotics that inhibits metalloproteinases, was evaluated in vitro for inhibition of tumor necrosis factor-alpha (TNF $\alpha$ ) converting enzyme (TACE) and for inhibition of protease activities in human chronic wound fluid. In addition, topical doxycycline treatment was evaluated in a pilot, randomized, controlled trial of chronic, diabetic, lower-extremity foot ulcers.

# Treatment of Chronic Wounds With a Protease Inhibitor - Doxycycline

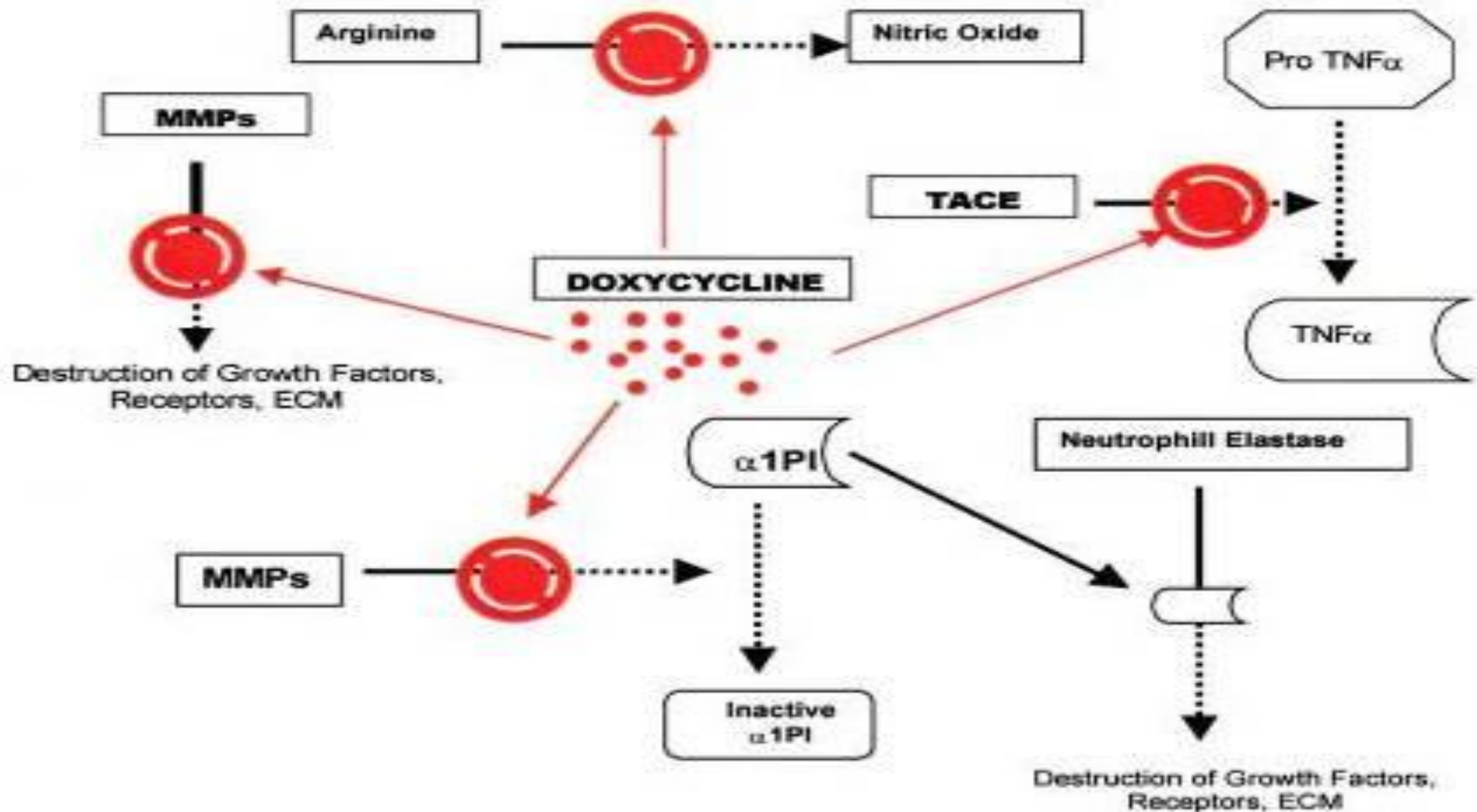
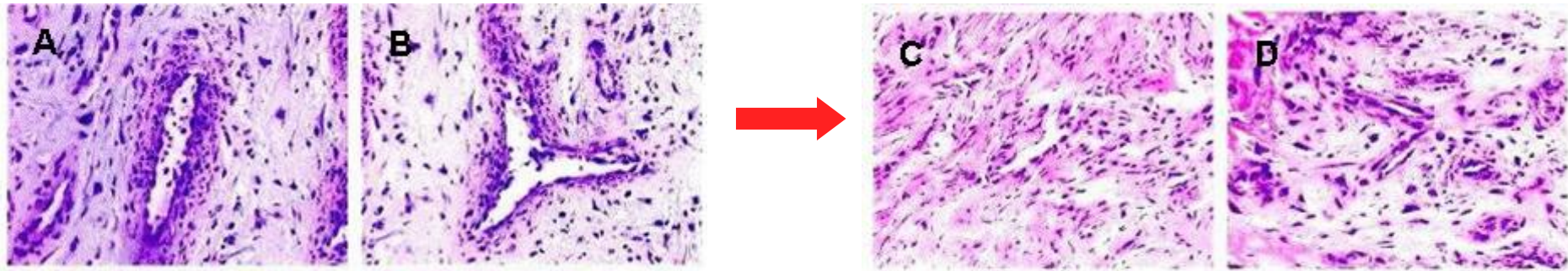


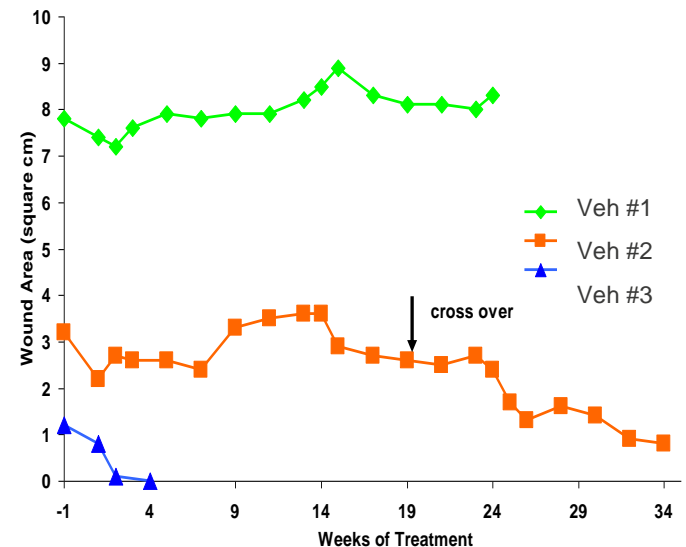
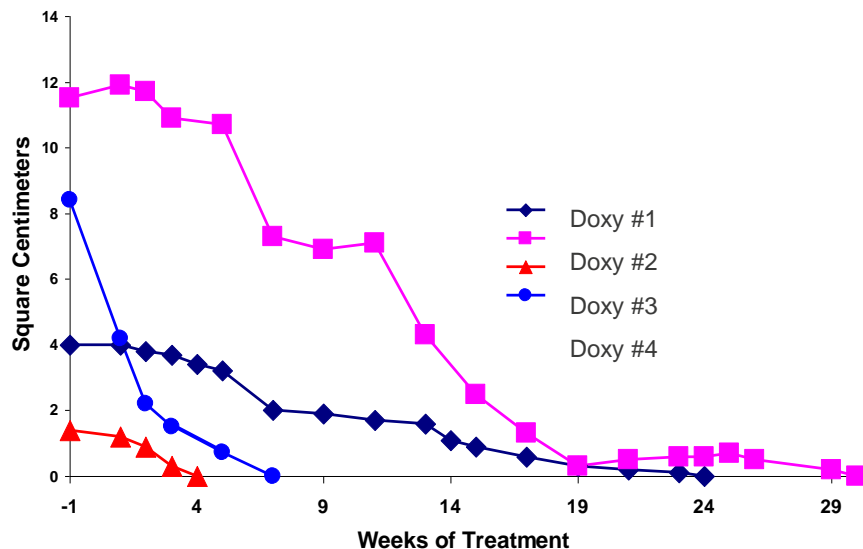
Figure 2. Doxycycline directly inhibits the matrix metalloproteinases (MMPs), the TNF $\alpha$  converting enzyme (TACE), the nitric oxide synthase, and indirectly inhibits the serine protease, neutrophil elastase by preventing degradation of its inhibitor,  $\alpha$ 1-PI by MMPs.



# Doxycycline Inhibits MMP Activity and TNF $\alpha$ Release and Promotes Healing of Chronic Diabetic Foot Ulcers



Two weeks of ORAL DOXYCYCLINE treatment decreased inflammatory cells and increased extracellular matrix (panels C and D) compared to biopsies of pressure ulcer taken before treatment (panels A and B). Diegelmann, Schultz





## **Gene Therapy in the Treatment of Lower Extremity Wounds**

Gene therapy is a new and emerging technology that has been catalyzed by the progress of the Human Genome Project. It employs the process of manipulating genes to achieve a clinically beneficial alteration in gene product. Wound healing lends itself to the application of gene therapy by virtue of the vast array of proteins involved in its complex cascade. Several clinically effective proteins have been identified that can be used in gene therapy approaches to improve the healing of chronic wounds.

# Stem Cells

The use of Mesenchymal Stem Cells and adipose-derived stem cells in tissue repair is a new form of therapy being studied in animal models and in clinical studies. There are a limited number of published studies with very low patient numbers.

Maxon et al described the action of stem cells with multiple mechanisms are involved in MSC-mediated wound healing, including anti inflammatory and antimicrobial, immuno-modulative, and tissue reparative activities

## Stem Cells

Dash et al conducted a RCT with 24 patients targeting non-healing ulcers of lower extremity in human through autologous bone marrow-derived mesenchymal stem cells.

The implant group had significant improvement in pain-free walking distance and reduction in ulcer size as compared to those in the control group. The present study documented that autologous implantation of BM-derived MSCs is a simple, safe, and effective therapy for chronic non-healing ulcers.

## Stem Cells

Rigotti et al conducted an open study on 20 patients clinical treatment of radiotherapy tissue damage by lipoaspirate transplant: A healing process mediated by adipose-derived adult stem cells.

Clinical outcomes led to a systematic improvement or remission of symptoms in all evaluated patients, including otherwise untreatable patients exhibiting initial irreversible functional damage.



## Stem Cells

Significantly larger studies need to be conducted to clearly identify the role and place of Stem Cells in non-healing wounds.

The current published study show promise

But much more needs to be done. The study on repair of radio-necrosis injury is important and needs follow up studies as these wounds are almost unhealable.

## Platelet Rich Plasma

Platelet-rich plasma contains seven known growth factors including : platelet derived growth factor aa (PDGFaa), PDGFbb, PDGFab, transforming growth factor beta-<sub>1</sub> (TGF-b<sub>1</sub>), TGF-b<sub>2</sub>, vascular endothelial growth factor (VEGF), and epithelial growth factor (EGF).

The growing evidence for the use of platelet-rich plasma on diabetic chronic wounds this included a Cochrane search (1978–2015) was performed and all studies assessing the clinical effect of PRP on the healing of diabetic chronic wounds and found that homologous PG was effective for the enhancement and acceleration of diabetic lower extremity wounds healing.

## Platelet Rich Plasma

Driver et al conducted a Prospective, Randomized, Controlled Trial of Autologous Platelet-Rich Plasma Gel for the Treatment of Diabetic Foot Ulcers in 75 patients.

PRP gel is safe for use in the treatment of nonhealing diabetic foot ulcers. Treating wounds with PRP or saline gel resulted in healing in approximately 6 weeks, but in the most common wound sizes, almost twice as many PRP treated wounds healed in that timeframe

Ostomy Wound Manage. 2006;52(6):68-87.

## Platelet Rich Plasma

Picard et al published a review of the growing evidence for the use of platelet-rich plasma on diabetic chronic wounds. This review included data from 210 patients. On six randomized studies included, five found significant benefits for the use of PRP on diabetic chronic foot ulcers and the sixth randomized study did not publish a statistical analysis but found favorable outcomes. The two other controlled studies included found significant benefits regarding the healing rate and the four uncontrolled studies included showed high rates of healing with the adjunction of PRP. 87.5% of controlled studies found a significant benefit for the adjunction of PRP to treat chronic diabetic wounds. As PRP may be beneficial, we suggest using PRP on diabetic ulcers which remain unhealed after standard treatment.

## Platelet Rich Plasma

Mehta and Watson also published a review of Platelet Rich Concentrate: Basic Science and Current Clinical Applications included were studies of 192 patients. Research has revealed that the role of platelets is much more involved than simply “plug” formation; they are responsible for actively extruding growth factors, which initiate soft tissue healing, bone formation, and stem cell recruitment.

These growth factors and cytokines are proteins stored in the alpha granules of the platelets, which are expressed with trauma or surgery.

They concluded that The application of autologous PRP can enhance wound healing

. J Orthop Trauma. 2008;22(6):432-8.



## Platelet Rich Plasma

Kontopodis et al conducted an open study with 72 they sought to investigate the effect of autologous platelet-rich plasma (PRP) on the healing rate of diabetic foot ulcers in patients with diabetes and concomitant peripheral arterial disease (PAD) Diabetic patients with foot ulceration presenting with PAD who were treated with local growth factors in a single center, during a 24-month period from May 2009 to April 2011, were retrospectively reviewed. Ulcer area reduction >50% was observed in 58/72 patients while reduction >90% was achieved in 52/72 patients. There were 14 (19%) major and minor amputations, whereas the limb salvage rate was 89%.

PRP could serve as a useful adjunct during management of diabetic foot ulcers even in diabetic patients with unreconstructable arterial disease.

*The International Journal of Lower Extremity Wounds* March 2015 1-7

## Platelet Rich Plasma

There are very few good RCT's and clinical studies on PRP there needs to be significant ongoing research to fully explain PRP and its role in wound healing



# Development of new treatments

## Tissue Matrix

Extracellular matrix (ECM) interact with growth factors and are important to wound healing. The ECM and can induce growth factor expression and stimulates synthesis of platelet-derived growth factor.

There are several collagen and Keratin matrix products available this will be an important product type to speed up the healing of Deeper wounds.

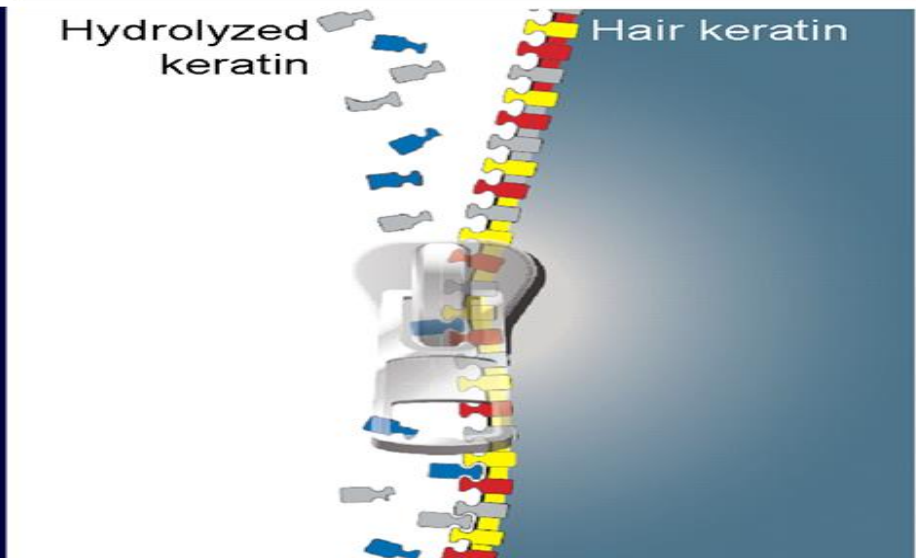
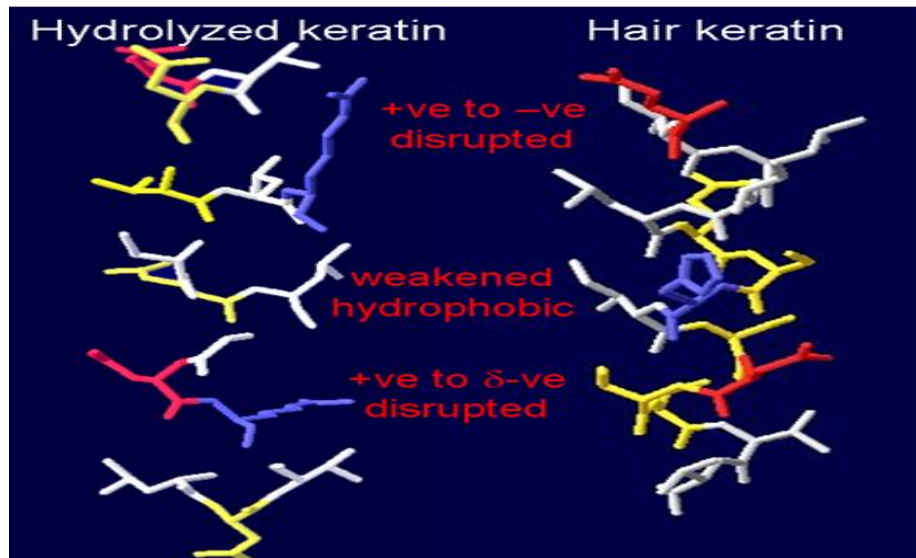
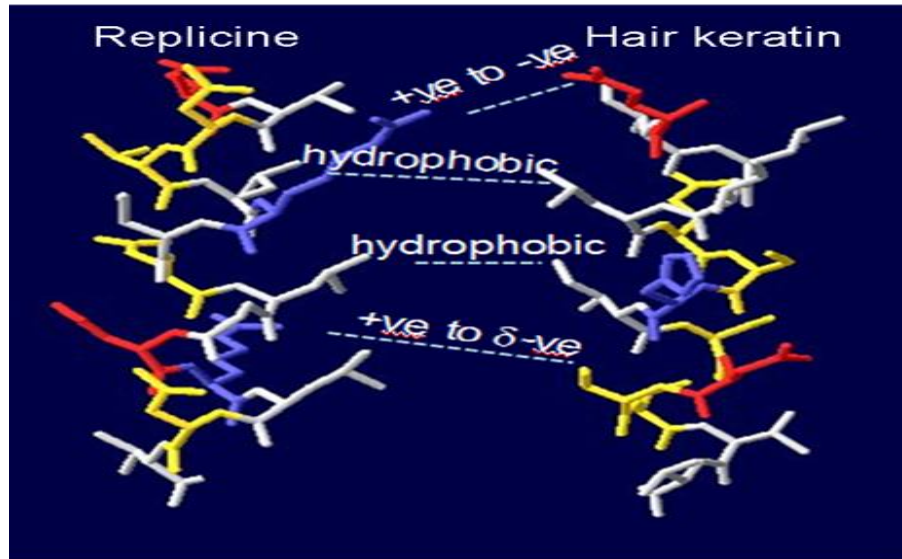


# Keratin Matrix Products

The amino acids in keratins are linked in a particular sequence. Within keratin materials, such as hair and skin, these sequences coil together like small bundles of rope, to build strong protein networks.

The particular amino acids in the coil link, like teeth in a zipper, to lock the structure in place.

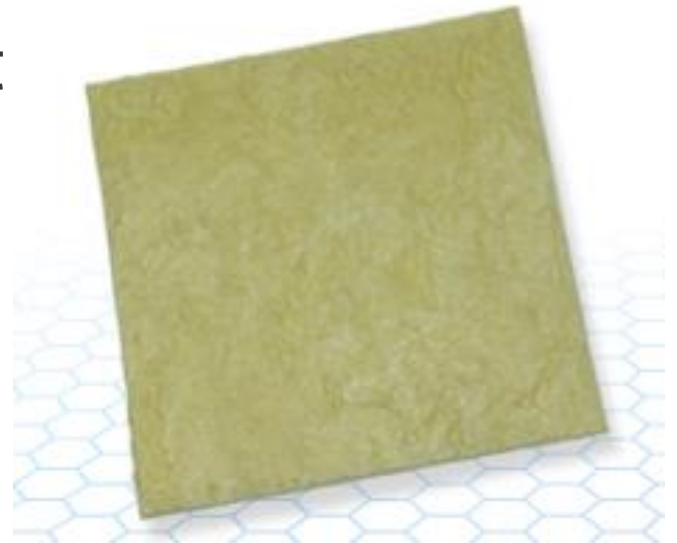
# Keratin Matrix Products





# Keramatrix

Keramatrix is a robust keratin matrix designed for medium exudate wounds, or for use as an interface with negative pressure wound therapy. As the wound heals the keramatrix is absorbed into the wound area and does not removed at dressing change.



# Keragel & Keragel T

Keragel is a keratin-rich gel designed for chronic dry wounds, acute wounds and skin disorders. Keragel provides moisture to a dry wound as well as a keratin environment to encourage cell growth, leading to an excellent healing outcome. Keragel T is formulated for convenient application to delicate skin, keragel T is used in the management of the skin disorder epidermolysis bullosa (EB).



# Development of new treatments

## Keratin Tissue Matrix





# Keratin Tissue Matrix





# Keratin Tissue Matrix Gel



**02.04.13**



**04.04.13**



**11.06.13**



**12.06.13**



**16.08.13**

**post CABGS Part of the suture line dehiscd we applied the Keragel to the cavity.**

**The wound was healed in 14 weeks.**

# Development of Devices

.Over the past few years there has been a major shift and development of  
A number of devices used in wound management including;

1. Negative pressure wound therapy
2. Ultrasonic Debridement
3. Hydrosurgery
4. Hyperbaric Oxygen
5. Epidermal Skin Graft device
6. Electrostimulation Device



# Negative pressure wound therapy

- Negative pressure wound therapy has become an increasingly important part of wound management. Over the last decade, numerous uses for this method of wound management have been reported, ranging from acute and chronic wounds, to closure of open sternal and abdominal wounds, to assistance with skin grafts. The biophysics behind the success of this treatment largely have focused on increased wound blood flow, increased granulation tissue formation, decreased bacterial counts, and stimulation of wound healing pathways through shear stress mechanisms. The overall success of negative pressure wound therapy has led to a multitude of clinical applications

# Negative pressure wound therapy





Stage 4 pressure ulcer before treatment



Stage 2 pressure ulcer after 96 days treatment with TNP



Surgical Wound Breakdown



Post VAC

# Negative pressure wound therapy





# Non Healing Leg Ulcer JG

**Tx Iodosorb / Allevyn 30/8 to 22/8 PICO 22/8 to 25/8/**



**Traumatic wound in a 80 yr old female on Warfarin after debridement and Iodine**  
**Was treated with topical negative pressure disposable unit**

# Ultrasonic Debridement

Low frequency ultrasonic therapy occurs when an electrical current converts into sound waves at frequencies that range from 20 to 40 kHz. The primary mechanisms for the function of ultrasonic debridement devices are “acoustic streaming” and “cavitation –

The irrigation fluid (sterile saline) is required as a coupling medium to transmit the mechanical vibration to the tissue and to rinse out the necrotic cell fragments and bacteria.

The hand piece has to be moved continuously and gently over the wound surface.

Different handpieces were developed to assure an optimized treatment result for all individual wound situations.



# Ultrasonic Debridement



# Sonoca – typical case

## Non-healing Diabetic foot



**Fig. 4a & 4b—Scheduled for amputation, the foot belonged to a diabetic with complicating inhibitors including alcoholism and a smoking dependency. After five 30-minute treatments, the wound is healing nicely.**

# Epidermal Skin Graft device

Epidermal Skin Grafting is Minimally invasive procedure that can be performed in outpatient setting. It Does not require donor site anaesthetic, is minimal scarring at donor site uses Autologous grafts.

Keratinocytes are sufficient for graft acceptance the process is well tolerated by patients and is cheaper than skin substitutes

The Control Unit creates and regulates the vacuum and warming required to raise the epidermal microdomes. The Vacuum Head and tubing deliver the vacuum and warming from the Control Unit.

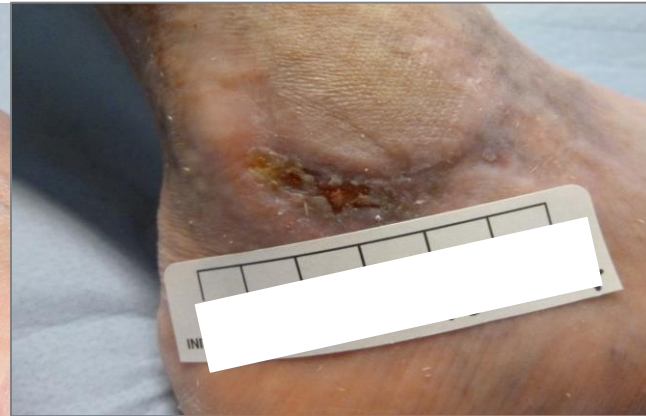
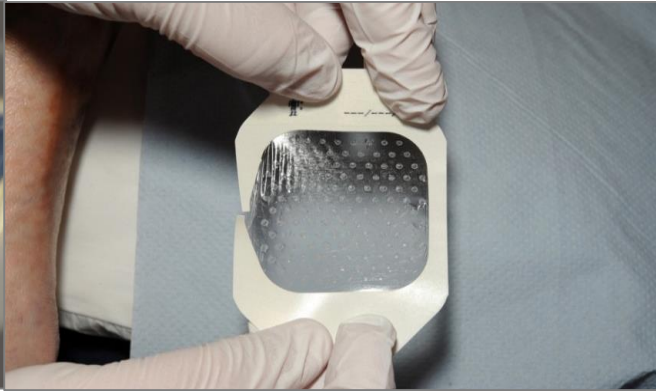
# Epidermal Skin Graft device

## CelluTome™ Epidermal Harvesting System | KCI





# Epidermal Skin Graft device



## Electrostimulation Device Body Flow

Early studies indicate that this device has a tendency to increase venous velocity and blood flow in deep veins of some normal individuals tested <sup>1</sup>. Mild electrical stimulation of the lymphatic and skeletal musculature is an effective adjunct in the treatment of lymphoedema with outcomes dependant on the lymphoedema stage, indicating a need to target treatment to achieve either fluid or tissue volume changes. Irrespective of these, subjective improvements are consistent leading to improved quality of life and ability to undertake activities of daily living.<sup>2</sup>

1.Parsi et al Blood flow,fibrinolysis and anti-procoagulant activity after treatment with a portable Electrostimulation device (Bodyflow) in healthy subjects Australasian College of Phlebology conference Sept 2007

2.Piller et al Results of a single blinded placebo controlled trial of Bodyflow technique for the treatment of Lymphoedema of the legs subjects Australasian College of Phlebology conference Sept 2007



## Electrostimulation Device Body Flow

We conducted a study at our wound clinic. Three case studies were undertaken with people with leg ulcers of primarily venous aetiology who were using no compression therapy or low compression therapy to assess adherence to the BodyFlow™ Therapy and wound progress. The case series found that concordance with the electrical stimulation treatment was achieved although none to the recommended schedule and with variation observed between and within clients. The treatment was well accepted by clients. Positive healing trends were observed for two of the three case studies.

Miller S McGuiness W Woodward M Boo E Client concordance and wound healing using the BodyFlow™ electrostimulation device: case series Wound Practice and Research Volume 22 Number 3 – September 2014 145-154

## Electrostimulation Device Body Flow

A single, blinded randomised controlled trial (RCT) pilot study will commence in 2014 to further appraise the clinical effectiveness and client concordance with electrical stimulation therapy for people with venous leg ulcers. We4 will present the results at the Wounds Australia Conference in Melbourne November 2016.

Miller S McGuiness W Woodward M Boo E Client concordance and wound healing using the BodyFlow™ electrostimulation device: case series Wound Practice and Research Volume 22 Number 3 – September 2014 145-154

## Electrostimulation Device Body Flow



Mrs J #1: left leg 12 April 2013



Mrs J #2: right leg 12 April 2013



Mrs J #3: left leg 9 May 2013



Mrs J#4: right leg 9 May 2013





# **The need to develop diagnostic tests to identify and the defining of the underlying cause of the wound.**

Inflammatory Cytokines

MMP's

TIMP levels

Wound Ph

Auto immune antibodies

# WOUNDCHEK™ Protease Status

**Chronic wounds with elevated protease activity (EPA) have a 90% probability they won't heal<sup>1</sup>** (without appropriate intervention)

Developed to aid wound assessment and help clinicians target advanced wound care therapies more effectively, **WOUNDCHEK™ Protease Status** is able to detect EPA. As there are no visual cues for EPA, wounds with EPA have so far gone undetected<sup>2,3</sup>. **WOUNDCHEK™ Protease Status** will help clinicians establish within minutes which wounds may most benefit from a protease modulating therapy, ensuring appropriate and targeted use of these therapies.





WOUNDCHEK™ Bacterial Status is an *in vitro* chromatographic test for the **qualitative assessment of bacteria-derived protease activity (BPA)** from the most common bacterium in non-healing wounds<sup>1</sup> directly from a wound fluid swab sample collected from a chronic wound.

**A chronic wound** is a wound that **fails to progress through a normal, orderly, timely sequence of repair** and where co-morbidities interfere with the normal healing process.<sup>2</sup> This encompasses wounds described as delayed, stalled, hard to heal, recalcitrant, difficult, complex, or failing to respond and could include acute wounds that have healing problems. **Chronicity is not necessarily dependent on the time since the wound was first formed.**<sup>3</sup>

WOUNDCHEK™ **Bacterial Status is intended for diagnostic use, at the point of care**, as an aid in the healthcare professional's assessment of whether a wound may be non-healing due to the presence of elevated bacterial protease activity.

1. Gardner SE, Frantz RA. Wound bioburden and infection-related complications in diabetic foot ulcers. *Biol Res Nurs*. 2008;10(1): 44-53

2. Lazarus GS, Cooper DM, Knighton DR, et al. Definitions and guidelines for assessment of wounds and evaluation of healing. *Arch Dermatol*. 1994;130(4):489-493.

3. Using a Diagnostic Tool to Identify Elevated Protease Activity Levels in Chronic and Stalled Wounds: A Consensus Panel Discussion. *Ostomy Wound Manage*. 2011;57(12):36-46.



### Use of WOUNDCHEK™ Bacterial Status Test: Case Study

This patient had a diabetic foot ulcer to the right plantar aspect. The wound had no signs of clinical infection when reviewed at Week 0 and Week 4, but tested positive on the test for BPA on both occasions. By Week 5, the patient had a number of signs of infection and had been referred to surgery for amputation. NB: This case was part of a clinical study protocol requiring the treating clinician to be 'blinded' to the BPA test results until study completion.

#### Week 0:

- No clinical signs of infection
- However, the wound tested positive for BPA
- Treatment provided: silicon polyurethane foam dressing and silicone non-adherent contact

#### Week 4:

- No clinical signs of infection
- However, the wound tested positive for BPA
- Treatment provided: absorbent gelling fibre dressing

#### Week 5:

- Patient was bedridden with chills and pains
- Foot was swollen and there was increased odour
- Third digit purple with a 9cm x 8cm area of redness on dorsal foot
- Patient referred to surgery for amputation



Week 0



Week 4

### Use of WOUNDCHek™ Bacterial Status Test: Case Study

This patient had a diabetic foot ulcer to the right lateral plantar. The wound had no signs of clinical infection when reviewed at Week 0 and Week 4, but tested positive on the test for BPA on both occasions. By Week 13, the patient had a number of signs of infection and had been referred to surgery for amputation. NB: This case was part of a clinical study protocol requiring the treating clinician to be 'blinded' to the BPA test results until study completion.

#### Week 0:

- No clinical signs of infection
- Positive for BPA
- Treatment: Aquacel

#### Week 4:

- No clinical signs of infection
- Positive for BPA
- Treatment: Calcium alginate

#### Week 8:

- AFM Ag (antimicrobial dressing applied)

#### Week 13:

- Foot swollen and warm
- Patient claims temperature 100.6 °F the previous evening
- Patient referred to surgery for amputation



# CONCLUSION

The future hold much potential with considerable basic wound research around the world. The Next step must be to translate this research into Potential new treatments and to test them in a clinical setting.

This will require a synergy between the scientist, the clinician and industry.

Combined with our ever increasing knowledge and understanding of the mechanism of tissue repair new treatments with ensure a faster and more successful outcome for our patients.