Where Have We Been?
History of Wound Care

First recorded treatment of wounds in Edwin-Smith Papyrus from ancient Egypt dating from 3000 B.C.
3 Healing “Gestures” of the Egyptians

1. Wash the wound
2. Make a “plaster”-
   (plaster most commonly composed of honey, grease [animal fat] and lint [vegetable fiber])
3. Bandage the wound

Brown, H. A Brief History of Wound Healing, 1998
Among the Earliest Wound Care “Products”

BEER!!

Sumerians brewed at least 19 types
Early Wound Care Product

HONEY

Used in India and Egypt before the time of Christ

Early Venous Ulcer Treatment

“For an obstinate ulcer, sweet wine and a lot of patience should be enough”

Hippocrates describing treatment of a patient with varicose veins and ulcer
Healing Rates of Varicose Ulcer Therapy -- 1964

- 71% healed “at last clinical visit”
- Duration of healing noted to range from 8 weeks to 3 years
- 43% recurrence rate for all therapies
- “Patient could expect to spend 6 to 7 weeks in the hospital.”

Dale AW, Foster JH. Leg Ulcers: Comprehensive Plan of Diagnosis and Management. *Trans South Surg Assoc.* 1964;75:
Treatment of Diabetic Foot Ulcers

- Until 1922 there were essentially NO diabetic foot ulcers
- Banting, Best, and Macleod discovered insulin in 1922
- After insulin, treatment was amputation
Where Is Wound Care Going in the Future?
Do We **Really** Need a Wound Treatment Center?

"I just met the world's greatest salesman!"
What is a “wound treatment center” and why do we need one?

A wound treatment center is a place where physicians and other personnel who are interested and have expertise in wound management come together with the resources needed for appropriate and quality care to treat patients with wounds that are difficult to heal.
HELP!

I'M TRYING TO FIND SOMEONE WHO CAN HELP ME WITH A WOUND PROBLEM.
YOU'RE CLOSE. I'M THE GUY WHO FORWARDS YOUR CALL TO THE WRONG PERSON.
I'D LIKE TO SPEAK WITH YOUR WOUND CENTER, PLEASE I'LL FORWARD YOUR CALL.
WHY A WOUND TREATMENT CENTER?

WHY A WOUND TREATMENT CENTER?

Recurrence Rates

At 6 months
At 12 months

What Does the Future Hold?

• More importance placed on multi-specialty wound care teams
• More specialization for wound care providers
• More wound care physicians practicing full-time wound care
• More advances in care of patients with wounds
• Challenges in reimbursement and cost-effective care
Why Won’t These Ulcers Heal?
Good Therapy?
Why Won’t These Chronic Wounds Heal???

- Do not progress beyond the inflammatory or proliferative phases of healing
- Cellular dysfunction and disregulation in the wound
  1. Hyper-proliferation of cells at wound margins
  2. Failure of epidermal cells to migrate across the wound
  3. Abnormal response of cells to growth factors
  4. Over-expression of matrix molecules
  4. Production of “toxic” wound fluid

Prepare the Wound for Healing

Wound bed preparation is necessary to correct the cellular imbalances present in chronic wounds allowing the wound to heal or be receptive to our therapy.
Optimal Wound Bed Preparation

- Maintenance of optimal moisture balance
- Complete debridement of devitalized and poorly functioning tissue
- Restoration of bacterial balance
- Optimize cellular function
- Treatment of edema / lymphedema

Schultz GS, Falanga V, et. al., Wound Rep Reg 2003;11(Supp):1-28
Effect of Debridement of Chronic Wounds

- Removes necrotic and ischemic tissues
- Removes infected tissues
- Exposes receptors so that growth factors can get to them
- Removes senescent and non-functioning cells
- Stimulates healing
Need for Debridement
Debridement
Diabetic Foot Post Debridement
What’s New in Debridement?
Maggot Therapy
Diabetic Ulcer of Toe
Maggot Therapy

Wound before maggot therapy

Maggots before application to wound
Maggot Therapy

At time of application of maggots

At time of dressing change 3 days later
Maggot Therapy

Wound and maggots at dressing change

Wound after maggot therapy
VERSAJET Hydrosurgery System

Smith & Nephew
Low Frequency, Low Intensity
Ultrasonic Debridement

Mist Therapy
Low Frequency, High Intensity Ultrasonic Wound Treatment System

Sonotrode
Ultrasonic Debridement
Diabetic Foot Ulcer

Before

After
Ultrasonic Debridement
Diabetic Foot Ulcer
INFECTION and BUGS

[Image of various beetles]
Topical Treatments

- Neosporin, Bactroban, other topical antibiotics
- Iodosorb and Iodoflex
- Silvadene
- Silver dressings
New Treatment for Infection?

- 9 antibiotic molecules in cockroach brain!
- Kills 90% MRSA on contact
- Kills all gram – bacteria on contact
- Not toxic to human cells (ie. no side effects)

Punch Biopsy Culture Technique
Effect of Local Anesthesia on Wound Bacteria

• EMLA cream has rapid and powerful antibacterial effect (within 30 minutes)
• DO NOT use for anesthesia before culturing tissue samples
• 1% preservative-free lidocaine has antibacterial effect but only after 2 hours
• USE for anesthesia if cultures done within 2 hours of use

Berg JO, Mossner BK, et.al. Antibacterial properties of EMLA and lidocaine in wound tissue biopsies for culturing. Wound Rep Reg 2006;14: 581-585
Looking to the Future in Infection Control

• What will the role of cultures be?
• What wounds are best treated with silver dressings?
• Are there other anti-infectives other than silver?
• What will be available to combat bacterial resistance to antibiotics?
• How important are biofilms in the treatment of chronic wounds?
• What do we have to effectively treat biofilms?
Biofilms

- "Communities" of organisms
- Adhere to solid surfaces (1)
- Organisms are imbedded in an extracellular polysaccharide matrix or glycocalyx (2)
- Imbedded organisms are resistant to antimicrobial agents (1)
- May contain a single or multiple species of organisms, including fungi (2)

Treatment of Biofilms

- Debridement
- Macrolide antibiotic (erythromycin)^
- Treatment with Biofilm-dissolving agents*
- Bioelectric treatment combining antibiotics and electric therapy
- Future therapy?

Ultrasonic Debridement

Before

After
Biofilm Therapy

Pre-treatment

Treated with Biofilm-dissolving Material
Biofilms and Bioelectric Antibiotics
Biofilms and Bioelectric Antibiotics
19 y/o man with sickle cell disease and ulcer for 10 months. Ulcer is unresponsive to therapy.
Bioelectric Administration Device

Battery

Electrodes
Sickle Cell Ulcer with Bioelectric Silver Therapy

Negative electrode

Silver dressing covering wound

Positive electrode
Sickle Cell Ulcer -- Healed

Healed after 36 weeks bioelectric silver therapy
## Bioelectric Silver Therapy

<table>
<thead>
<tr>
<th>Location of Wound</th>
<th>Tissue Silver Levels (PPM)</th>
<th>Pre-Therapy</th>
<th>After 3 weeks of Therapy</th>
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<tbody>
<tr>
<td>Upper level</td>
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<td>.027</td>
<td>.321</td>
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<tr>
<td>(surface to 2mm depth)</td>
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<td>(2mm to 5mm depth)</td>
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Unpublished Data: Institute for Advanced Wound Care, 2006
Vascular Disease in the Chronic Wound Patient
Doppler Study and Ankle Pressure Measurements
What’s New in Vascular Evaluation

Laser Doppler and TcPo2 Evaluation

Scanning Laser Doppler
Treatment of Sickle Cell Ulcer with Nitric Oxide Producing Medication

TcPO2 at ulcer site and control site when treated with Metanx (nitric oxide producing medication) showing marked improvement.
Vascular Bypass

Peroneal Artery Graft

Dorsalis Pedis Artery Graft
Balloon Angioplasty and Stent Placement

Iliac Artery Balloon Angioplasty and Stent Placement
Route of NV1FGF Administration

- Therapeutic genes can be administered by a variety of methods, including systemic injection, local injection into the tissue, or using a gene gun.

- NV1FGF is administered as an intramuscular injection to the patient’s leg.

Source: Applied Molecular Genetics; Miesfeld R; Copyright ©1999 and John Wiley & Sons
This material is used by permission of John Wiley & Sons, Inc.
Therapeutic Angiogenesis for Peripheral Arterial Disease

Example: New collateral blood vessels induced in an ischemic limb by gene transfer of vascular endothelial growth factor (VEGF).

Source: Reprinted with permission from Elsevier (The Lancet 1996;348: 370)
Neuropathy In The Diabetic Patient

“Neuropathy is the single most important factor leading to ulceration in the diabetic patient.”
Neurosensory Testing
Monofilament Test for Neuropathy
Testing for Neuropathy with Ballpoint Pen

Ballpoint Pen with Point Extended

Barely Indent Skin and Note Sensation
# Monofilament vs Ballpoint Pen in Diagnosing Neuropathy

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<th>Neuropathy</th>
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<th>Pen</th>
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</tr>
</tbody>
</table>

Data – Institute for Advanced Wound Care, 2009
Tuning Fork Testing for Diabetic Neuropathy

Apply Tuning Fork to IP Joint of Great Toe
Neuropathy in Diabetics

- Sensory
- Autonomic
- Motor
Treatments for Diabetic Peripheral Neuropathy

- Tricyclic antidepressants (Elavil, Pamelor)
- Antiepileptic medications (Dilantin, Neurontin, Lamictal, Lyrica)
- Local anesthetic / antiarrhythmia medications (Mexitil)
- Pain medications (Ultram, Ultracet, Percodan, Tylox, Oxycontin)
- Metanx
New Therapies for the Treatment of Peripheral Neuropathy
MIRE Therapy: Monochromatic Near-infrared Photo Therapy

Anodyne Therapy
Possible Cause of Diabetic Peripheral Neuropathy

Role of PKC? Activation and Action of LY333531

- Diabetes
- Advanced glycosylation end products (AGE)
- Diacylglycerol (DAG) generation
- Oxidative stress

PKC? activation

Microvascular damage
- Retinopathy
- Neuropathy
- Vision loss
- Ulcers, Amputation

LY333531

Nephropathy
- Renal failure
Improvement of Diabetic Peripheral Neuropathy Treated with LY333531

NTSS-6 = Neuropathy Total Symptom Score-6

LY333531 Improves NTSS-6

Mean Change in NTSS-6 for Symptomatic DPN Patients

*Negative change value indicates improvement.
†P = 0.017 vs placebo. ‡P = 0.064 vs placebo. §P = 0.014 vs placebo.

Peripheral Nerves Involved by Neuropathy
Peripheral Nerves Before and After Treatment with Topiramate (Topamax)

Treatment of Peripheral Neuropathy

• Metanx
Treatment of Peripheral Neuropathy

- Bone marrow stem cells
- Umbilical cord stem cells

What’s Next?

Hum…
Where do I go from here?
SKIN “SUBSTITUTES” and CELL THERAPY

• Acellular skin “substitutes” – AlloDerm, Biobrane, Integra, Dermagraft-TC, Oasis, Promogran, Puraply, Graft-jacket, Biovance

• Single-layer skin “substitute” – Epicel, Dermagraft, Vitrex, InterCytex

• Bilayered, living skin construct – Apligraf, OrCel
Tissue Engineered Skin Products: The Ideal Therapy for Chronic Wounds?

• Provide cells responsive to the wound environment
• Provide a "living factory" producing numerous growth factors, cytokines, and matrix proteins
InterCytex Dermal Matrix

Fibroblasts in Gel Matrix
Composite Cultured Skin
“OrCel”
OrCel vs Human Skin

OrCel

Human Skin
Photomicrographs of hematoxylin-eosine-stained cross-sections of APLIGRAF® (left) and human skin (right) ×250.
What Evidence Is There That These Products Work?
# FDA Approval Status

<table>
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<tr>
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<th>Apligraf</th>
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<th>Regranex</th>
<th>Oasis</th>
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## FDA Product Indications

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<td>Other</td>
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</table>
“Smart Therapy”

- “Cultured skin…acts as a ‘smart material’ responding to its environment to bring about the desired effect.”

DIABETIC FOOT ULCER

Pre Apligraf
DIABETIC FOOT ULCER

12 Weeks Post Apligraf
DIABETIC HEEL ULCER

Heel ulcer before debridement

Heel after debridement
DIABETIC HEEL ULCER

APPLICATION OF APLIGRAF
DIABETIC HEEL ULCER

16 WEEKS POST APLIGRAF
Venous Ulcer
Venous Ulcer

8 weeks post application

Healed at 33 weeks
Looking for The Evidence??
ILLITERATE?
WRITE FOR FREE HELP.
ILLITERACY FOUNDATION
806 MAIN STREET

www.StrangeCosmos.com