Managing Chronic Wounds:
Past Success and Future Challenges

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Course Content

- The Wound Healing Cascade: Cytokines & Growth Factors
- The Integument and Extracellular Matrix
- Risk Factors & Chronic Wounds
- Differential Diagnosis of Chronic Wound
- Moist Wound Healing Principles and Choice of Dressing
- Adjunctive Treatment Measures in Treatment of Chronic Wounds
- Advances in Wound Care – Directions of Future Research

The Role of Physical Therapists in Wound Care

"I dressed the wound – God healed it"
- Ambroise Pare (French Military Surgeon, 1510-1590)

- Identification of risk factors

- Wound care assessment
  Acute wounds

  Chronic wounds: 90% of all chronic wounds are [1]
  - » Vascular wounds: arterial ulcers, venous stasis ulcers
  - » Pressure ulcers
  - » Neuropathic ulcers: diabetic wounds

  Chronic wounds affect more than 7 million people in the United States [2]

- Treatment planning, reassessment and revision

Physical Therapy Interventions in Wound Care

- EDUCATION!!
- Patient education
- Family/ caregiver education
- Sharing information/ collaborating with the health care team
- Maximizing mobility and function: therex, transfer training, gait training, etc.,
- Positioning, pressure relief, offloading
- Wound cleansing and debridement
- Supportive modalities and proper choice of dressing
- Phototherapy
- Electrotherapy
- Hyperbaric Oxygen
- Negative Pressure Wound Therapy
- Ultrasound

The Integumentary System

- Epidermis – outer layers of epithelial cells, .06 to 6 mm thick
- Basement membrane
- Dermis: blood vessels, lymphatics, cutaneous nerve endings
- Subcutaneous tissues: adipose, fascia, muscle, bone

Characteristics of Healthy Skin

- Acid mantle (pH of 4.5 to 5.5)
- Elastic and well hydrated
- Waterproof barrier
- Sensory organ – largest organ of the body
- Functions in thermoregulation

Skin Changes with Aging

- Thinning of epidermis and adipose layer
- Decrease in collagen and elastin – decreased turgor
- Slower rate of regeneration
- Decreased moisture
- Texture – "onion skin"
- May be partially due to reduced estrogen production and function [4]

The Effect of Estrogens on Skin

- Estrogen receptors are located in fibroblasts, macrophages, endothelial cells and epidermal cells [4]
- Estrogen action in skin [4]
    - Increases mitosis in epidermal cells
    - Enhances angiogenesis
    - Modulates inflammatory response
    - Accelerates re-epithelialization
    - Regulates proteolysis
    - Stimulates wound contraction

Risks of Estrogen Deficiency

- Reduced phagocytosis – increased risk of infection [4]
- Increased levels of elastase – accelerated and excessive tissue breakdown [4]
- Decreased expression of PDGF and TGF-beta [4]

Possible Treatment Options

- Systemic hormone replacement therapy
  - Estrogen as a carcinogen? [4]
- Topical estrogen application
- Dose, duration of treatment?
- Administration of an androgen precursor, e.g. – DHEA [4]

The Wound Healing Cascade: Phases of Wound Healing

- Inflammation
- Proliferation
- Remodeling/ Maturation

Inflammatory Phase

- Mast cells release heparin – maintains balance of perfusion during hemostasis [6]
- Clotting releases thrombin
- Thrombin induces platelet degranulation
- Platelet degranulation releases cytokines
  - PDGF
  - TGF-beta
  - TNF
  - IL-1
- Cytokines attract phagocytes to region of injury [7]

Phagocyte Activity

- Clean up debris [2]
- Secrete proteinases & reactive oxygen species [2]
- Monocytes are activated as macrophages [2]
- Macrophages express growth factors [2]
    - CSF-1 (colony stimulating factor)
    - TNF-alpha (tumor necrosis factor)
    - PDGF (platelet derived growth factor)
    - VEGF (vascular endothelial growth factor)

VEGF: Vascular Endothelial Growth Factor

- Potent stimulator of angiogenesis
- Plays an important role in nervous tissue regeneration [9]
- Decreased expression of VEGF is noted in people with diabetic neuropathy [9]

Transition from Inflammation to Proliferation

- May be initiated by mast cells – negative feedback mechanism [6]
- Degranulation of mast cells may result in activation of bFGF [6]

Formation of the Extracellular Matrix

- Fibroblasts and endothelial cells migrate into clot to form the ECM & granulation tissue [2]
- Fibronectin – adhesive component – aids cell chemotaxis and attachment [7]
- Proteoglycans are incorporated [7]
    - Chondroitin sulfate
    - Hyaluronic acid
- Migration of keratinocytes from wound margins [2]

The Role of Nitric Oxide (NO)

- Signaling molecule for epithelialization [6]
- NO may be synthesized by intact basal keratinocytes [6]
- NO amplifies production of VEGF [6,11] and plays role in angiogenesis [11]

The Role of Oxidative Stress

- Respiratory burst of inflammatory cells in early stages of injury leads to free radical production [12]
- Free radicals produce oxidative stress:
  - Lipid peroxidation/ tissue breakdown [12]
  - DNA breakage [12]
  - Enzyme inactivation [12]
  - Prolonged inflammation [11]

Wound Assessment:The Guide to Physical Therapy Practice

- Integumentary System – Practice Patterns 7A – 7E
- Arranged by preventative measures (7A)
- Partial to full thickness (7B – 7E)

Taking a Patient History

- Wound etiology
- Barriers to wound healing:
  - Medical issues
  - Psychosocial issues – living and working environment, support system
  - Demographics – age, PLF
- Past or present treatment of the wound and results of treatment
- Patient's level of mobility & function
- Equipment use and/ or need – transfer & assistive devices, prosthetics and orthotics …

Physical Exam

- Wound Appearance:
    - Size and shape
    - Color, presence of necrotic debris
    - Odor
    - Drainage/ exudate

- Appearance of surrounding skin, hair and nails

- Circulation:
    - peripheral pulses, skin color & temp, capillary refill, ABI

ABI: Ankle Brachial Index

Peripheral Pulses

- 0 = no pulse felt

- 1+ = barely felt

- 2+ = diminished

- 3+ = normal pulse

- 4+ = bounding (aneurismal)

Testing Capillary Refill

- Observe response to pressure at distal toe

- Apply pressure until area blanches, hold 5 sec and release

- Normal refill time < 3 sec

- Longer refill times may indicate arterial insufficiency

Pitting Edema

- 0 = not present
- 1+ = minimal
- 2+ = moderate
- 3+ = severe

Sensory Testing:

- Semmes-Weinstein monofilaments (sensitivity & reliability?)[15]

Anthropometric testing:

- body weight, BMI

Presence and degree of pain

High Frequency Ultrasound [11]

- 20-40 MHz devices
- Can be used to image/ assess wound bed, peri-wound skin and underlying soft tissue

Characteristics of Wounds

- Size
- Shape
- Location
- Depth – partial thickness, full thickness
- Grading Scales–
    - Pressure Ulcers (NPUAP Grading Scale)
    - Diabetic (neuropathic) ulcers (Wagner Scale)
- Wound margins
    - Undermining
    - Tunneling
    - Sinus formation
    - Epiboly
    - Discoloration, maceration, callus formation, induration…
- Wound bed appearance
    - Granulating
    - Presence of debris and/ or necrotic tissue
- Exudate (drainage)

    Amount: scant, moderate, copious

    Color
    - Serous
    - Sanguinous
    - Serosanguinous
    - Purulent – green, yellow, white

    Consistency: thick, thin

    Odor
    - Present/ absent
    - Foul
    - Fruity (pseudomonas)
    - Ammonia (proteus)
    - Wet cardboard (malignancy)

Wound Measurement

- Ruler based measurements:
    - approximate surface area – length X width

- Wound depth at deepest region

- Clock method:
    - document location and measurement of undermining
    - 12:00 usually corresponds to patient's head
    - 3:00
    - 6:00
    - 9:00

- Planimetry:
    - wound tracing (sterile film), graph paper to count square mm [21]

- Photography:
    - Include reference for scale (ruler)
    - Obtain consent

- Computer assisted analysis of planimetry or photography [21]

***ALWAYS CLEAN WOUND BEFORE MEASURING

Challenges in Ruler Based Measurements

- Measurements tend to overestimate actual size but can be reliable as long as the point of measurement is kept consistent
    e.g. – longest width and longest length perpendicularly [21]

- Accuracy may be improved by taking 3 measurements and calculating average [21]

- Ruler based measurements are least reliable in wounds greater than 5 cm^2 [(25)]

Transcutaneous Pressure of Oxygen

- TcPO2 less than 30 mm Hg – wound will not heal[1]

- Greater than 30 mm Hg, wound should heal, safe for debridement [1]

- Measurements not reliable in patients with swelling or infection [1]

Chronic Wound Characteristics and Delayed Healing

- Wound "gets stuck" in the inflammatory phase, possible causes include:
  - Wound clogged by necrotic tissue
  - Wound contaminated by debris &/or bacteria

- Other possible causes for delayed closure:
  - Lack of circulation/ proper oxygenation
  - Complicating factors such as DM, venous or arterial insufficiency, smoking, poor nutrition, repetitive trauma, poor sensation (e.g. – SCI), age, meds

Factors Affecting Healing of Chronic Wounds

- Wound Hydration:
  - Dessication – wound bed too dry, blocks epithelial migration
    reduces electrical potential (current of injury)
    reduces level of active growth factors

  - Maceration – too much moisture, can extend area of damage, promote infection

- Need to strike a healthy balance, maintain adequate moisture, prevent maceration

- Mechanical stress - pressure, friction, shearing

- Age

- Lifestyle – ETOH, tobacco use

- Medications
  - Chemo
  - Long term steroids use – pulmonary problems, RA …
  - NSAIDs

Reperfusion Injuries and Delayed Healing

Effects of cyclic ischemia and reperfusion:

- Decreased expression of bFGF [26]
- Increased production of proinflammatory cytokines [1, 26]
- Increased levels of matrix metalloprotienases (MMPs) [26]
- Decreased levels of tissue inhibitors of MMPs [26]

Bacterial Contamination or Infection

- Bacteria may produce proteases that degrade tissues and growth factors [27,28]
- Endotoxin production may result in prolonged elevation of proinflammatory cytokines [28]
- BUT … low levels of bacteria may actually be beneficial in accelerating wound healing through granulation and collagen formation [28]

Edema

- Increases distance between vascular bed and cellular structures [1]
- Can impair capillary diffusion [1]

Differential Assessment:Vascular Wounds

Arterial Ulcers

Risk Factors for Arterial Insufficiency/ Atherosclerosis

- Males > females
- Tobacco use
- HTN
- Hyperlipidemia
- Obesity
- DM
- Age

Signs of Arterial Insufficiency

- Intermittent claudication
- Rest pain – worse with elevation, better in dependent position
- Rubor of dependency
- Trophic changes to skin – thin, shiny, absence of hair
- Trophic changes to nails – thick, brittle, discolored

Medical Diagnostic Exams

- Segmental blood pressure:
  - Measures systolic BP at dorsalis pedis or post tibial artery using Doppler probe
  - BP cuff inflated at three segments: thigh, below the knee, above the malleoli
  - pressure drop of >20 mm Hg is indicative of significant blockage at or below that segment
- Arteriogram: use of radiopague dye and standard imaging to identify blockage
- MRA: magnetic resonant arteriogram

Long Term Risks of Atherosclerosis

- Ulcerations
- Gangrene
- Amputation

Characteristics of Arterial Ulcers

- Negligible edema
- Minimal drainage or bleeding
- Dryness/ dessication
- Black eschar typical (may be yellow if dressing retains moisture)
- Pale wound base if no necrotic tissue
- Mummification
- Gangrene

Circulatory Assessment

- Skin temperature
- Transcutaneous pressure of O_2
- Peripheral pulses
- Capillary refill
- Rubor of Dependency Test

Rubor of Dependency Test

- pt supine, examine color of soles of feet
- elevate foot about 60 degrees for one minute & examine color
- normal = little or no color change on elevation
- pale = arterial insufficiency
- foot returned to resting position supine, note time for color to return
- normal = pink within 15 to 20 sec
- abnormal = dependent rubor

Wound Assessment: Characteristics of Arterial Ulcers

- Typically, round borders
- Can have very steep margins
- Slow to show signs of infection – check for subtle erythema at wound margins

Treatment of Arterial Ulcers

- Keep wound dry and protected
- Never wet/ soak arterial wounds – can increase tissue damage, cause maceration
- Position for comfort – no elevation
- No compression
- Medical Rx of infection (IV antibiotics)
- Surgical consult for revascularization
- After revascularization, follow principles of moist wound healing

Patient Education

- Protect surrounding skin from trauma:
  - Proper foot care
  - Friction – tight shoes
  - Adhesives
  - Compression – socks and LE clothing
- Behavior modification
  - Smoking
  - Diet
- Signs and symptoms requiring immediate attention & intervention
  - Recognizing gangrene and infection

Surgical Approaches

- Angioplasty
- Angioplasty with stents
- Vascular bypass

Venous Stasis Ulcers

Characteristics of Venous Stasis Ulcers

- Due to vascular congestion, chronic edema and impaired venous return (VENOUS HYPERTENSION)
- Typically located below the knee: "gaitor area"
- Account for 70-90% of all LE ulcers
    - Effects ~1% of population as a whole
    - Increased incidence in elderly population: ~3.5% of people over 65
- Increased intravascular pressure promotes edema and reduces reabsorption
- Impaired microvascular level diffusion due to pericapillary cuffing of fibrin and macroglobulins [32]
- Extravasation of white blood cells and large plasma proteins can initiate damage leading to ulceration
- Leakage of fibrogen, macroglobulin and albumin may contribute to growth factor depletion [2]
- Proteases overwhelm anti-proteases [32]
- Presence of proteases decreases with elevation and edema reduction [32]
- Fluctuations in edema can contribute to repeated reperfusion injury[1]

Lower Extremity Venous System

- Mirrors the arterial system
- Thinner walls and larger lumen when compared with arteries
- System of valves that open towards the heart and prevent backflow

Venous Return

- Calf muscle pump responsible for ~90% of blood returning from the lower extremities
- Gastrocsoleus complex contracts and puts pressure on the veins; as the muscle relaxes, veins fill again
- Immobility and weakness may significantly impair venous return

Causes of Venous Insufficiency

- Ineffective calf pump (weakness)
- Inactivity
- Valvular incompetence
- Prior injury – trauma, DVT
- Obesity
- Pregnancy
- Infection
- Congenital defects
- Pelvic tumors

Differential Medical Diagnosis

- R/o CHF – bilateral LE edema, breath sounds, chest films
- R/o ESRD – labs, output, etc.,

Changes Due to Venous Insufficiency

- Itchy, dryness – eczema
- Atrophie blanche – off-white plaques or raised lesions in skin
- Pitting edema
- Pt may c/o heavy dull aching in lower extremities alleviated on elevation and/or compression

Characteristics of Venous Stasis Ulcers

- Occur within the "gaitor area"
- Irregular shape
- Shallow
- Often have crusted edges and beefy red wound base
- Hemosiderin staining as a sign of chronic venous congestion
- Generalized edema
- Nail changes – prone to fungal infections
- Tend to drain heavily
- Periwound tissue may be macerated
- Skin surrounding wound may exhibit fibrotic changes (champagne glass) scaly dermatitis (lipodermatosclerosis)
- Wound may be covered by yellow or grey film, stringy necrotic tissue

Patient Assessment:Venous Filling Time

- Examine veins in dorsum of foot with patient positioned supine
- Elevate leg 60 degrees for 1 minute, or until veins drain by gravity
- Place LE in dependent position and record time for refilling
- Normal = 5 to 15 sec
- Immediate filling may indicate venous insufficiency
- Prolonged filling may be predictive of arterial insufficiency

Venography

- Use of radiopague dye to produce image of LE venous system

Treatment of Venous Hypertension

- Leg elevation
  - Must be at least 18 cm above level of heart
  - 20-30 min at a time for a total of 2 hrs a day

- Compression garments
  - approx 40 mm Hg at the ankle, 12-17 mm Hg @ infrapatellar notch
  - Higher compression for people who are ambulatory and less for those who aren't (18-24 mm Hg)
  - Should be worn at all times unless bathing or sleeping

- Mechanical intermittent compression

- Manual lymphatic drainage (MLD)

- Medications – fibrinolytics - e.g. – Trental, pentoxifylline

Treatment of Venous Ulcers

- Must address LE edema
  - Use of Diuretics** - may cause volume depletion, increase uric acid
  - Compressive dressings (UNNA boot), garments
  - Mechanical compression
  - Elevation
  - Exercise to improve muscular pump

- Removal of necrotic debris
  - Mechanical debridement
    - caution with W/P
  - Selective sharp debridement
  - Autolysis

- Rx of infection, if applicable

- Control of exudates
  - Alginates
  - Absorbent dressings

- Use of topical agents

- Adjunctive modalities
  - E-stim, US, Phototherapy

Unna Boot

- Paste bandage
- Gauze impregnated with zinc and calamine
- May also contain glycerin, petrolatum
- Goes on wet like a cast, dries firm to provide compression while dressing soothes skin and reduces eczema

Diabetic Ulcers

- AKA neuropathic ulcers
- Stem from damage/ deterioration of the sensory, autonomic and motor nerves in the distal LEs
- Affect 1 in 20 patients with DM [1]
- More common in men and people over 60 [(15)]
- Primary noxious stimulus is repeated axial pressure and shear [32]

Pathogenesis of Diabetic Peripheral Neuropathy

- Persistent hyperglycemia causes increase in intracellular sorbitol and fructose in n fibers leading to edema and degeneration [36, 37]
- May involve an autoimmune process [38]: antineuronal antibodies have been found in the serum of some diabetic patients [36]
- Prevalence of DPN increases with age, duration of diabetes and fluctuations/ suboptimal control of blood glucose levels [39]

Denervation and Nerve Growth Factor

- Reduction of NGF in diabetes [40, 36]
- Symbiotic relationship with skin cells: lower turnover of keratinocytes, lower production of NGF [40]
- NGF is structurally similar to insulin and may also be affected in DM [40]

Denervation & Neuropeptides

- Substance-P (SP)& calcitonin gene-related peptide (CGRP) is reduced in denervation
  - Both found in nerves which innervate blood vessels [41]
  - SP found in C-fibers
  - CGRP found in C and A-delta fibers [40]
- SP stimulates leukocyte chemotaxis, assists activation of neutrophils [40,41], upregulates synthesis of transforming growth factor-alpha [40]
- CGRP stimulates proliferation of keratinocytes [40]
- Both have potent effects on microvascular tone and permeability [41]

Reinnervation & Diabetic Foot Ulcers

- Reinnervation may be possible through decompression of multiple lower extremity peripheral nerves [40]
  - E.g. – tarsal tunnel release
- Effects of decompression on small fiber damage?
  - Diabetic neuropathy primarily effects small diameter fibers [37]

Sensory Neuropathy

- Loss of protective sensation
- Decreased awareness leading to inadvertent trauma and injury
- Delay in seeking medical intervention for injury or infection due to absence of pain and discomfort [42]
- Up to 50% of patients with neuropathy never experience symptoms [42] – can be hard to identify risk of wounds
- Diabetic patients with sensory loss have a seven-fold increased incidence of developing foot ulcers vs. diabetic patients without sensory loss [15]

Autonomic Neuropathy

- Decreased perspiration and sebaceous secretions in the distal lower extremities and feet
- Skin prone to dryness, cracks, callus formation and breakdown
- Disturbances is vasomotor responses
  - Vasoconstriction may result in ischemic damage
  - Prolonged vasodilation increases blood flow to bone and may contribute to osteopenia [43]
  - Foot may stay warm due to distention of dorsal veins even in presence of microvascular pathology [15]

Motor Neuropathy

- Weakness in intrinsic muscles of the foot
- Muscle imbalances may contribute to foot deformities, increased heel and plantar forces, microfractures and ligamentous laxity [15]
- Impairments in ROM at the foot and ankle result in substituted movement patterns that perpetuate foot deformities
- Muscle atrophy reduces padding to pressure points
- Weakness, foot deformities limit patient's mobility
  - exacerbates weight problems
  - reduces function,
  - impacts control of blood sugar

Common Foot Deformities

- Plantarflexion contractures
- Hallux valgus
- Forefoot varus or valgus
- Net result = increased plantar pressures at metatarsal heads (common location for neuropathic ulcers)

Charcot Foot

- AKA – "rocker bottom foot"
- Bone deterioration and pathologic fractures lead to deformity
- Abnormal pressure & weight bearing areas increases risk of ulceration[15]

Concomitant Impairments

- Diabetic retinopathy:
  - difficulty in skin assessment and wound care
- Obesity:
  - contributes to pressure on feet, reduced activity
- Delayed healing due to hyperglycemia:
  - reduces rate of fibroblast proliferation, angiogenesis & collagen synthesis
  - reduced tensile strength and risk of wound dehiscence
- Delayed immune response:
  - increased risk of infection due to slower rates of phagocytosis in lymphocytes
- Increased risk of PVD & renal problems

Neurological Assessment

- Loss of large and small fibers [45]
  - Test vibration using 128 Hz tuning fork as a marker[15]
  - Test touch/ pressure using 10g monofilament as a marker[45]
- Reduced proprioception
  - Unsteadiness may result in repetitive minor traumas and increased risk of wound formation[15]

Circulatory Assessment

- Peripheral pulses may be normal: can have microvascular changes without large vessel disease [45]
- ABI**
- Capillary refill
- Skin color and temperature

Foot Assessment

- Calluses are potential sites of breakdown [39]
  - Metatarsal heads
  - Interdigital areas

- Cracks and fissures are potential avenues for infection and further skin deterioration

- Toe nails are prone to fungal infections and deformities and can injure adjacent skin

New Assessment Methods

- High frequency diagnostic ultrasound
  - examines reduced subcutaneous tissue/ padding in high pressure areas and/ or region of bony deformities [39]

Preventative Measures in DM

- Wearing shoes in the home – compliance reduced to 15% [(45)]

- Therapeutic footwear (extra depth, etc.,) & orthotics
  - Pressure mapping [15]
  - Protection from inadverntent trauma
  - Cushioning and/ or relief of pressure
  - Load transfer from vulnerable sites to other areas [39]

- Socks
  - May be used as added padding, must not be restrictive [39]

- Behavior modification for wt loss, ETOH, smoking

- Encourage exercise and control of blood glucose levels

- Daily inspection of shoes and feet

- Proper cutting of toe nails

- Awareness of sensory deficits – limiting exposure to heat, cold

- Maintain moisture/ lubrication of skin to avoid cracking and drying (avoid lotions between toes – powders for fungal infections

Wound Assessment: Grading Scale

- Practice Guide – by wound depth (partial vs full thickness)

- Wagner Scale
  - Grade 0 – deformities or callus present without ulceration (Pattern 7A & 7B)
  - Grade 1 – superficial ulcer (Pattern 7C)
  - Grade 2 – deep ulcer, exposed tendon, joint capsule or bone (Pattern 7E)
  - Grade 3 – deep ulcer, exposed tendon, joint capsule or bone with osteomyelitis or infection (Pattern 7E)
  - Grade 4 – Localized gangrene – no more than 2 digits (Pattern 7E)
  - Grade 5 – gangrene of foot or greater than 2 digits (Pattern 7E)

Characteristics of Diabetic Wounds

- Location: Plantar aspect of foot or toes, between toes, dorsum and lat border of foot if abnormal pressures

- Callused wound margins

- Round shape

- Minimal drainage

- Generally painless or with minimal pain due to sensory neuropathy

- Patient may be unaware of cause of wound – cannot identify precipitating incident

Diabetic Wound Care

- Debridement of wound

- Debridement of callus???

- Pressure relief
  - Total contact casting – RCT shows 90% of patients healed within 12 weeks [39]

- Choice of dressing to promote moist wound healing

- Medical management of infection

Total Contact Casting

- Should be changed at least once every week, or at maximum, every 2 weeks [15]

- Disadvantages [15]:
  - Need for expertise in application
  - Use of time and monetary resources
  - Inability to examine wound daily (window?)

- Contraindications [15]:
  - Significant PVD
  - Infected wounds
  - Osteomyelitis

Novel Approaches to Pressure Redistribution

- Liquid silicone injected under high pressure areas [39]

- May help replace fat padding that is displaced by bony deformities, e.g. – claw toes, charcot foot [39]

- May reduce callus formation [39]

- Benefits maintained at 12 month follow-up [39]

Physical Therapy Intervention

- Gait training – use of assistive device as needed

- Therex for improved flexibility, ROM and strength

- Encourage weight loss if indicated, therex to assist control of glucose levels

Pressure Ulcers

Etiology

- Tissue necrosis due to ischemia
- Soft tissue is compressed between an external surface and underlying bone impeding circulation
- When pressure applied exceeds capillary closing pressure (13 – 32 mm Hg), damage occurs**
- Also depends on type of pressure, duration of exposure, location of the body and intrinsic factors (health and stature of patient)
- Abnormal pressure may lead to multiple microvascular thrombi [50]
- Pressure and shear applied over a prolonged period of time stretches the skin & small blood vessels leading to microvascular trauma [50]
- Reperfusion injury [51]
- Use of anticoagulants may prevent ulceration by protecting the microvasculature [50]

Pressure Distribution Cone

- Iceberg effect
- Visible damage represents the "tip of the iceberg"
- Most of the tissue damage lies in deeper layers beneath the surface of the skin

Prevalence and Risk Factors

- 15% of all hospital residents (acute care) nationwide [43]
- Greatest risk in patients with impaired mobility
- Malnutrition – including obesity (53% of patients with pressure ulcers are obese)
- Can lead to serious complications, risk of death
- Preventable**** and mostly treatable

Risk Factors

- Positioning: pressure, friction and shear
- Re-positioning: repeated ischemia-reperfusion which may be more damaging than ischemia alone [1]
- Moisture:
  - Wound drainage
  - Perspiration
  - Incontinence – urine acidity, bacterial content
- Impaired mobility:
  - Musculoskeletal weakness, depression, impaired cognition, sedatives
  - Contractures
  - Spasticity
- Hydration
- Nutrition
- Low diastolic BP – takes less pressure to impede circulation
- ETOH, tobacco use and DM – leads to microvascular changes
- Improper fitting braces, casts, orthotics, etc.,
- Aging skin
- Previous history of pressure ulcer – never fully regain skin thickness

Risk Assessment Tools

Braden Scale:

Six Subscales, scored 1 – 4, greatest to least impaired

- Mobility – can pt control and change body position?
- Activity – e.g. – ambulatory, able to transfer OOB?
- Sensation
- Skin moisture
- Nutritional status
- Friction and shear – ability to move without sliding

Score indicates risk:

- Less than 13 = high risk
- 13 to 14 moderate risk
- 15 to 18 mild risk

Should be administered upon admission, weekly for one month, then quarterly [52]

Re-administered with change in status/ illness [52]

Norton Pressure Ulcer Scale:

Looks at 5 categories scored 1 to 4 (worse to better)

- Physical condition
- Mental condition
- Activity
- Mobility
- Incontinence

Norton "Plus" Scale also takes into account DM, HTN, HCT, hemoglobin, albumin, fever

Preventative Measures

- Team Approach:
  - Patient
  - Family/ caregivers
  - Hospital staff

- Risk factor reduction through education:
  - Proper skin care
  - Turning and positioning
  - Skin assessment

Turning & Positioning Schedule

- Every 15 minutes sitting up
- Every 2 hrs lying down
  - Should be individualized based on patient need and support surface

Positioning in Side-Lying

- Avoid direct pressure on trochanter
- Patient should be inclined laterally approx 30 degrees

Pressure Relieving Support Surfaces

- Specialized beds and mattresses [53]
  - Low air-loss therapy
  - Fluidized air or high air-loss therapy
  - Alternating pressure air mattress
  - Kinetic therapy (passive motion) – bed frame may move or cushions in mattress inflate and deflate

- Reimbursement issues
  - Medicare B – must be stage 3 or 4, resident of long term facility or permanent home

Pressure Wound Assessment

Patient History

- Screen for risk factors - may affect prognosis as well as treatment plan
    - Comorbidities – cardiovascular, renal, endocrine …
    - Smoking/ ETOH
    - Incontinence
    - Mobility
    - Social history – occupational stresses, home environment, support structure
    - Nutritional status – labs, calorie count ..
    - Hydration
    - Sensation
    - Age
    - Past history of ulceration

Staging System

Stage I Pressure Ulcer

- Not yet an open wound
- Nonblanchable erythema – first sign of underlying skin damage
- In darker pigmented skin, may appear purple, blue, or violet
- May also see changes in skin texture and consistency: "boggy"
- Can present with elevated skin temperature, stinging, itching, numbness
- May be reversible if pressure is alleviated soon enough
- May develop into an open area

Stage II Pressure Ulcers

- Superficial ulcer – partial thickness
- Epidermis, sometimes part of dermis
- Also includes blisters
- Guide to Physical Therapy Practice – Pattern 7C – "Impaired Integumentary Integrity Associated with Partial-Thickness Skin Involvement and Scar Formation"

Stage III Pressure Ulcer

- Deep ulcer, extensive necrosis
- Full thickness
- Epidermis, dermis and subcutaneous tissue involved – extends to BUT not through the subcutaneous fascia
- Guide to Physical Therapy Practice – Pattern 7D – "Impaired Integumentary Integrity Associated with Full Thickness Skin Involvement and Scar Formation"

Stage IV Pressure Ulcer

- Full thickness
- Deep ulceration, may have undermining
- Involves epidermis, dermis, subcutaneous tissue through the fascia to muscle, tendon, joint capsule and sometimes bone
- High risk of osteomyelitis
- Guide to Physical Therapy Practice – Pattern 7E – "Impaired integumentary integrity associated with skin involvement extending into fascia, muscle or bone and scar formation"

Limitations of Staging System

- No reverse staging – e.g. – Stage IV DOES NOT heal and become a Stage II
- Cannot stage a wound that is covered by eschar – must be able to accurately assess wound depth

Pressure Ulcers vs Incontinence Associated Dermatitis

- Correct identification essential for proper treatment
- Misidentification of IAD as a pressure ulcer may result in loss of revenue under the Deficit Reduction Act/ Hospital Acquired Conditions (CMS)

Surgical Wound Closure: Skin Grafts

- Autologous/ homogenous (autograft)
- Hetergeneous (xenograft or allograft)
- Cultured epidermal autografts (CEAs)
- Synthetic skin substitutes/ engineered tissue

Surgical Wound Closure: Musculocutaneous Flaps

- For closure of Stage IV ulcers
- Muscle helps pad defect and prevent future ulcerations
- Muscle has good vasculature/ muscle flow
- Donor sites include
    - Gluteus max
    - TFL
    - Latissimus dorsi
- Transposition vs. free flap

Principles of Wound Management

Wound Contamination vs Wound Infection

Development of infection depends on [28]

- Total bacterial count
- Type of species present - virulence
- Number of different species present – synergistic interaction
- Immune response of host
- No "magic" number – previous standard was to maintain a bacterial level below 10^5/ gram of tissue on tissue biopsy
- Biopsies are preferable to wound culture in terms of accuracy [15]
- Clean before culturing

Diagnosis of Infection

- Clinical signs and symptoms [28]:
    - Increased pain
    - Change in exudate
        - » Increased amount
        - » Odor
        - » Change in color or consistency

- Signs of infection may be diminished in certain conditions [28]:
    - » Steroid tx
    - » Ischemia
    - » Malnutrition
    - » Neuropathy

- In some ulcers, the only sign of infection is a failure to heal [28]

Biofilm

- Communities of aggregate bacteria imbedded in a self-secreted extracellular matrix [28]

- Become more complex as they mature and may include channels for transport of water, nutrients and waste [28]

- Biofilm increases bacterial resistance by forming a diffusion barrier, reducing effectiveness of antibiotics & action of phagocytotic cells [28]

- Biofilm may act as a mechanical barrier to wound closure and contribute to epiboly [1]

- Removal of film may be assisted by enzymatic debriders [28]

- Erythromycin may inhibit growth and propagation of biofilms [28]

Infection Control

Common Modes of Transmission

- Door knobs
- Handrails
- Patient charts
- Pens
- Neckties

Elements Of Effective Infection Control

- Standard precautions
- Sterile or clean technique as indicated
- Use of Personal Protective Equipment

Standard Precautions

- Aka – Universal Precautions
- All blood and body fluids are treated as potential contaminants
- Wearing gloves, washing hands before and after gloves are used

PPE: Personal Protective Equipment

- Gloves:
  - Clean
  - Sterile
  - Non-latex
- Protective Eyewear/ face shield
- Gowns
- Masks
- Bonnet/ OR cap
- Shoe covers

Wound Cleansing

Wound Irrigation Methods

- Bulb syringe
- Water pik
- Shower
- Spray bottle
- Pulsed lavage
- Normal saline is most commonly used irrigant

Pulsed Lavage

- AKA pulsatile irrigation: with or without suction
- Safe, effective irrigation pressure is between 4 and 15 psi
- Higher pressure may be used operatively to drive out wound contaminants – risk of trauma to tissues, driving bacteria deeper or into blood stream (questioned by lit review – Bierbaum)
- Cleanses surface debris and reduces bacterial load [58]
- Promotes granulation and epithelialization
- Can be used when whirlpool is inaccessible or contraindicated
- Can be more time efficient for therapist
- May cause less trauma to wound bed than whirlpool (at low psi)
- Decreased length of stay
- Decreased risk of cross-contamination

Precautions for Pulsed Lavage

- Decreased sensation
- Barriers to communication
- Anticoagulation therapy
- Wounds with tunnels or undermining
- Wounds near major vessels – e.g. – groin, axilla
- Exposed nerve, tendon, bone
- Skin grafts, muscle flaps
- Facial wounds
- PPE required for therapist
- One device per patient – (Most are single use)

Treatment Parameters

- Usually once a day
- Twice a day if significant necrosis (>50%), purulent drainage and/ or odor
- Less often in conjunction with other treatment modalities, e.g. - with NPWT at dressing changes

Treatment Procedure

- Adjust height of Rx surface to allow proper body mechanics
- Place towels and/ or fluid-resistant pads around affected body part
- All other points of entry – e.g. – catheter, drains, IVs – should be covered with a clean towel
- Sterile field for equipment and dressings
- Patient should be treated in a closed area (doors – not curtains)
- No one in Rx area without PPE

Personal Protective Equipment

- Protects against aerosolization and splashing
- Mask
- Hair cover – including ears
- Face shield or goggles
- Fluid proof gown
- May need shoe covers

Guidelines for Discontinuing Treatment [59]

- Wound closure
- Once wound is clean – if no increase in granulation in 1 week
- If no change in necrosis in 1 week

Topical Agents &Wound Cleansing

- Antiseptics – may assist in early wound cleansing, but can later impede healing [53]
- Common cytotoxic agents include:
    - Hydrogen peroxide
    - Chlorazine
    - Iodine

Wound Debridement

Debridement Methods

- Selective Debridement
- Non-selective Debridement
- Mechanical Debridement
- Autolytic Debridement
- Enzymatic Debridement
- Sharp Debridement
- Biological Debridement

Enzymatic Debridement

- Collagenase (santyl)
- Papain/ urea (accuzyme, panafil)
- Fibrinolysin/ deoxyribonuclease (elase)
- Travase – water soluble mix of enzymes

**Contraindicated in wounds with exposed tendons, ligaments, joint capsule, blood vessels, nn, bone

Biological Debridement

- The use of sterile maggots to remove necrotic tissue

Advantages of Biological Debridement

- Maggots will not damage healthy tissue
- Maggots secrete enzymes which liquify necrotic tissue, fight infection and stimulate healing [60]
- Necrosis is ingested by maggots and maggots are disposed
- Maggots excrete ammonia and salts and help maintain an alkaline wound pH which facilitates action of collagenases [61]
- Excretion also contains urea – stimulates granulation [61]
- Excretion may also contain cytokines [61]

DISADVANTAGES

Treatment Procedure [60]

- Measure hydrocolloid dressing to size of target area
- Cut hole the shape of the wound
- Hydrocolloid prevents "tickling sensation" and escape
- Place maggots in wound bed – usually approx 5 – 8 maggots per cm^2
- Cover hydrocolloid and maggots with a nonocclusive dressing – fine mesh or gauze
- Top layer of gauze changed every 4 to 8 hrs, as needed, due to large amounts of drainage
- Change dressing and remove engorged maggots – usually every three days
- Used maggots are placed in airtight container and disposed as biohazardous waste

Biobag [61]

- New advance – maggots are encased in a commercial dressing: sponge netting and small cube of spacer material
- Maggots feed through the dressing and secretions reach the wound
- No mechanical irritation of wound edges by the maggots
- No risk of escape

Moist Wound Healing Principles

Advantages of Moist Healing

- Allows progression of healing cascade
- Moist enviroment aids epithelialization [62]
- Facilitates synthesis and retains growth factors at site of injury [62]
- Can promote autolytic debridement
- Supports current of injury [62]

Current of Injury

- Voltage gradient between wound and intact skin (Dubois-Raymond) [63]
- Intact epidermis (-) with respect to underlying tissue [63]
- Exposed tissue layers give open wounds a (+) charge [64]
- Generated by sodium-potassium pump [63]
- Current stimulates proper healing mechanisms
- Magnitude of current is approximately 1mA for each millimeter of wounded epidermis
- Current of injury decreases as wound size decreases

Nutritional Support for Wound Healing

Changes in Nutritional Demands

- Body's initial response to trauma is a decrease in metabolic rate
- Metabolic rate will rise again to initiate healing if supported by adequate nutrition/ protein intake [64]

Glucose & Carbohydrates

- Used in inflammatory stage to fuel infiltration of leukocytes and macrophages [64]
- Supplies energy for fibroblast production and collagen synthesis [64, 65]

Fatty Acids

- Needed for maintaining and restoring cell membrane structure and function [64]
- Omega 3s may reduce incidence of infection and contain micronutrients, e.g. – zinc, iron, copper [64]
- Metabolism of fatty acids produces prostaglandins and leukotreines
    - Vasodilatory effects
    - Antinflammatory actions [64]
- May need to monitor/ adjust intake of fatty acids to modulate chronic inflammation in certain wounds [64]

Protein

- Deficiency can prolong inflammation [64] by decreasing phagocytic activity and antibody levels [65]
- Deficiency can also contribute to edema formation [66]
- Low levels impair collagen synthesis and may contribute to wound dehiscence [64, 65]
- Wound exudate may be protein laden increasing dietary needs [64]

Vitamin C

- Needed for collagen synthesis [64, 65]
- May increase activity and migration of macrophages and leukocytes during inflammatory phase [64]
- Needed for angiogenesis [65]
- Deficiency may increase risk of wound infection [65]
- Greatest risk of deficiencies are in elderly, alcoholics and drug abusers [66]

Vitamin A

- Helps fight infection[64]
- Aids in fibroblast differentiation and collagen synthesis[64, 65]
- Topical use may enhance epithelialization[64] and reverse suppressive effects of steroids[65]

Vitamin K

- Needed for clotting/ hemostasis[64]
- Deficiency may lead to hematoma formation & increase susceptibility to wound infection[65]

Vitamin B Complex

- Important in formation of collagen matrix[64]
- May enhance host immune response[65]

Vitamin E

- Maintains and stabilizes cell membrane integrity[65]
- May play a role in reducing excessive scar tissue formation[65]

Trace Elements

- Copper –
  - needed for formation of collagen matrix [64,65]
  - Needed for RBC production [64]
- Iron –
  - Needed for oxygen transport, RBC synthesis and function [64]
  - Needed for hydroxylation of proline in collagen production [65]
- Magnesium –
  - Cofactor for many enzymes required for protein & collagen synthesis [65]
- Zinc –
  - Involved in DNA synthesis, cell replication and proliferation [65]
  - Deficiencies can occur with prolonged steroid use and lead to decreased collagen synthesis, wound tensile strength and delayed epithelialization [65]

Choice of Dressing

Characteristics of An Effective Wound Dressing

- Protects wound from trauma
- Maintains a clean environment – prevents infection
- Supports moist wound healing – optimal fluid balance
- Assists in maintaining tissue temperatures conducive to healing (at least 37 degrees Celsius)
- Free from particulates or toxic contaminants
- Nonadherent – does not cause pain or tissue damage during dressing changes

Types of Dressings

- Dry, protective dressings, e.g. – plain gauze
- Basic saline moistened gauze (NOT wet to dry)
- Inert dressings
- Moisture retentive
- Absorbent
- Moisture added (hydrative)
- Compressive garments (remodeling, edema)
- Charcoal dressings for odor control
- Dressings to help fight infection – dressings containing topical antibiotics, silver impregnated dressings

Inert Dressings

- Petrolatum gauze
  - Petroleum or paraffin
  - Used with superficial wounds and burns
  - Used with skin grafts and donor sites to prevent adherence and/ or dryness
  - Need to be changed frequently
  - Require a secondary dressing
  - E.G. – xeroform

- Emulsified gauze
  - Contain oil or silicone
  - E.G. – adaptic

Film Dressings

- Semipermeable – let O2 in, CO2 and water vapor out
- Transparent
- Nonabsorbent
- Elastic and extensible
- Promote autolytic debridement
- Can be used as a secondary dressing with hydrogels and alginates
- Not recommended in deep cavity wounds or full thickness wounds
- Must be discontinued if wound is too moist (maceration) or if infection is present
- Can remain in place for 1 week – change sooner as needed

Foam Dressings

- Absorbent
- Optimal choice for moderate to heavy exudate (Eaglstein)
- Single or multi layer polyurethane
- Cushion and protect
- Provide thermal insulation
- May be used with hydrogel to promote autolysis
- Can come with charcoal to control odor
- Change every 1 to 4 days, 7 days max
- Change every day if wound is infected
- Use alternate dressing if exudate soaks through in less than 24 hrs
- Come in nonadherent sheets if skin trauma is a concern
- E.G. – hydrasorb, allevyn, curafoam, polyderm, mitraflex, lyofoam

Hydrogels

- Hydrative – add moisture
- Amorphous gels – used to fill cavities
- Can also come as a thin, flexible sheet
- Non adherent
- Assist autolytic debridement
- Can stay in clean wound up to 3 d – remove gel by flushing with sterile water or saline
- No sheet hydrogels in infected wounds***
- E.G. – Carasyn, Intrasite, Curagel, Elastogel,Saf-Gel

Hydrocolloids

- Somewhat absorbent – slow rate – not for bleeding wounds
- Contain a gel forming polymer
- Usually applied as a sheet, but also available as powder, granules and paste
- Provide thermal insulation
- Occlusive – not for use in infected wounds
- Change every 5 to 7 days, sooner if strike-through
- Dressing can leave a foul smell – do not confuse with infection
- E.G. – duoderm, comfeel, tegasorb

Alginates

- Absorbent
- Look like felt – made from seaweed
- Exchanges Ca++ ions from dressing for sodium ions in wound
- Can be used to control bleeding
- Can be used in infected wounds, non-occulsive
- Require secondary dressing (film)
- Do not premoisten
- Do not use on exposed tendon, bone or joint capsule
- D/C if not enough exudate to saturate dressing
- Change daily if infected, no more than 7 days, sooner if saturated
- E.G. – algoderm, curosorb, kalostat, caloflex, sorbsan, kalginate, calgicare, kutinova

Hydroactive Dressings

- Absorb but do not form a gel like an alginate
- Good for use over joints
- Can stay in place up to 7 days
- Do not use on infected or dry wounds
- E.G. – Cutinova, Biotane

Dressings for Controlling Odor

- Cadexomer iodine (not the same as betadine)
    - Screen patients for iodine allergies
    - Not for use in patients with thyroid dz
    - Comes as a powder, paste or sheet
    - Initially brown, but turns white when interacting with exudate
    - Do not use in patients under 12 y.o.
    - No more than 50g at a time, 150 g per week
- Charcoal

Hyaluronan (Hyalofill)

- Creates a thick gel in wound bed that releases hyaluronic acid
- Hyaluronic acid may promote keratinocyte migration and increase rate of wound closure [67]

Adjunctive Treatment Interventions
Physical Agents and Wound Care

Effects of Electrical Current on Wound Healing

Electrical Stimulation for Wound Healing

- Open wounds – electrodes may be placed around or over the wound using sterile technique

- E-stim may also be applied underwater using sterile technique

- Commercial dressings are also available – used in combination with e-stim Rx
    - Both water and glycerin based hydrogels can act as a conducting medium [64]
    - Alginates may also be conductive once wet [64]

General Effects of Electrical Current

- Either positive or negative charge increases local blood flow [64,68]

- Alternating polarity periodically during Rx may optimize results [69]

- Improves transcutaneous oxygen content [64]

- May increase number of mast cells and mast cell degranulation [69]

- Stimulation of growth factor receptors [69]

- Increased formation and release of VEGF[11]

- Metanalysis showed a 144% net increase in healing as compared with control [68]

- HVPC to fibroblasts in culture increased DNA production and protein synthesis [70]

Anodal Stimulation (+)

- Uses the positive pole of the circuit as the active electrode(s)
- Magnifies the current of injury to enhance body's natural healing process
- Enhances migration of macrophages & fibroblasts (proliferative phase)
- Stimulates migration of neutrophils, macrophages and epidermal cells [64, 63] - galvanotaxis
- May encourage fibroblast migration [64] and increased collagen density
  May allow collagen to be deposited in a more regular pattern – increased elasticity
- Can also be used to enhance tendon & ligament healing:
  - Improved collagen synthesis
  - Increased tensile strength
- Enhances ion transport, amino acid uptake, protein and ATP production [64]
- May decrease vascular congestion [64]
- These effects greatest during the proliferative stage [64]

Cathodal Stimulation (-)

- Uses the (-) pole of circuit as the active electrode
- May be placed around or over the wound site using sterile technique, commercial dressings
- May also be done underwater using sterile technique
- Bacterialcidal effects [64,63]
- Enhances blood flow/ increases circulation
- May repel plasma proteins (-) to decrease acute edema formation [69, 11]
- May reduce hypertrophic scarring

Waveforms for Wound Healing

- Waveforms/ polar effects can be combined with TENS protocols to alleviate pain & encourage healing

- Ideally, low total current – less potential for skin irritation & pt discomfort
    - Guidelines for setting amplitude: Average current of 22 mA/ cm or more but below the threshold of pain [64]

- Protocols may include use of the cathode for first 3-5 days to reduce bacterial load, then anode to accelerate tissue repair [68]

Waveforms for Wound Healing: Polar Effects

- Monophasic pulsed current: HVPC*, MENS

- Diadynamic current

- Unbalanced assymetrical biphasic pulsed current

- Straight DC/ galvanic stim –
  Caution: high total current, must be kept at very low amplitude
  Potential for injury
  Tendency for sensory accomodation

Effects of HVPC

- May induce release of vasoactive substances by nerve endings [32]

- Increased production of nitric oxide by endothelial cells
    - Promotes improved microcirculation [32]
    - May protect against reperfusion injury [32]

Contraindications to Electrical Stimulation in Wound Healing

- Wounds that contain metallic residue [32]
- Proximity to cancerous tissue [32]
- Near a gravid uterus [32]
- Near a cardiac pacemaker [32]

Therapeutic Ultrasound in Wounds Healing

Ultrasound in the Inflammatory Stage

- Low intensity US can inhibit release of histamine: decreased edema formation
- Moderate intensity can stimulate release of histamine
- Can facilitate early end to inflammatory stage
- Can stimulate release of chemical mediators that attract neutrophils and monocytes to remove debris

Ultrasound in the Proliferative Phase

- Release of growth factors by neutrophils and macrophages is facilitated by US [11]
- US may enhance peripheral nerve healing [70]
- Later in healing, US encourages presence of fibroblasts and can stimulate increased collagen production: ground substance, angiogenesis, wound contraction [11]

Ultrasound in the Remodeling Phase

- US can increase collagen content making scar tissue less fragile
- US can encourages more regular pattern of collagen fibers – increased elasticity of scar tissue [11]

Low Frequency Ultrasound

- MIST therapy by Celleration
- Has been shown to increase angiogenesis & collagen deposition in diabetic mice [11]
- May enhance formation and/ or release of nitric oxide [11]: NO plays role in formation VEGF and angiogenesis

Phototherapy in Wound Healing

Effects of Laser and Low Intensity Light Therapy

- Increased expression of interleukins [71]
- Increased cellular metabolism:
    - Increased light absorption by mitochondria
    - Increased rate of cell division
    - Increased rate of DNA/ RNA synthesis
    - Increased rate of fibroblastic activity [72]

Effects of Lasers and LILT on Scar Tissue Formation

- More uniform alignment of collagen fibers
- Smaller scars
- Less incidence of contractures

Effects of Ultraviolet C

- UV-C: 200-280 nm, e.g. – cold quartz
    - Increased blood flow [11]
    - Bacterialcidal effects [11]
        - » Kill rate of 99.9% at 5 sec, 100% at 90 sec for MRSA
        - » Kill rate of 99.9% at 4 sec for group A strep (causes necrotizing fascitis)
    - Production & release of interleukin 1 by keratinocytes: enhanced epithelialization, enhanced fibroblastic activity [11]
    - Fibronectin release – promotes cell migration [11]

Systemic Hyperbaric Oxygen Treatment

- Three phases:
    - Compression to prescribed pressure level
    - Prescribed treatment time/ administration of oxygen
    - Decompression from treatment pressure to normal atmospheric pressure
- FDA approval 2002 for use in Rx of diabetic ulcers [73]

Purpose of HBO Therapy

- Tissue oxygenation can be increased from 3 to 5X beyond normal content at sea level
- Increased oxygenation speeds healing, reduces necrosis and secondary tissue death
- Bacterialcidal effects: treatment of necrotizing infections & osteomyelitis [73], especially effective for anerobic agents [6]

Benefits of HBO

- Decreased local edema [73]
- Improved cellular metabolism [73]
- Improved local tissue oxygenation [73]
- Enhanced leukocytic activity [73]
- Increased effectiveness of antibiotics[73]
- Increased uptake of PDGF [73]
- Increased rate of angiogenesis [73]
- Improved epithelial migration [73]
- May have a synergistic effect with concurrent application of topical growth factors [1]

Contraindications for HBO Therapy

- Untreated pneumothorax [73]
- Concomittant chemotherapy Rx [73]
- Relative contraindications [73]:
    - Known malignancy
    - Pregnancy
    - PPM
    - URI
    - Chronic sinusitis
    - Seizure disorders
    - Emphysema
    - Hyperthermia
    - History of thoracic surgery

Precautions for HBO Therapy

- Patient should wear natural fabrics, e.g. – 100% cotton to reduce potential for sparks
- Avoid alcohol based products, e.g. – hairspray
- Avoid petroleum based products
- Need for patient to equilize pressure in middle ear during compression stage (e.g.- Valsalva)
- Pt may feel too warm during compression, too cold during decompression

Negative Pressure Wound Therapy: NPWT
Also known as VAC: Vacuum Assisted Closure

- Wound dressing/ apparatus:
    - Foam
    - Semipermeable film
    - Suction apparatus & tubing
    - Collection canister
    - Control panel: constant or intermittent pressure/ suction in mm Hg

Benefits of Negative Pressure Wound Therapy

- Increases healing rates [1, 74]
  - Applied stretch increases mitotic rate of keratinocytes [74]
- Facilitates removal of exudates – promotes fluid balance/ moist wound healing [1], decreases bacterial load [74]
- Increases blood flow, reduces ischemia [74, 58]
- Stimulates production of VEGF [74]
- Reduces inflammation [1], decreases edema and shortens distance for diffusion [74]
- Limits cyclic ischemia-reperfusion [1]
- Mechanical effects promote wound contraction
- Decreases length of stay
- Results in fewer dressing changes
- May reduce overall pain level and decrease need for pain medication
- Less extensive surgical procedures required for wound closure for larger defects

Indications for Negative Pressure Wound Therapy

- Acute or traumatic wounds
- Chronic ulcers – vascular, diabetic, pressure ulcers
- Dehisced surgical wounds

Guidelines for Negative Pressure Wound Therapy

- Patient must be hemodynamically stable (low risk of hemorrhage)
- Patient must be able to tolerate Rx at least 22 hrs/ day
- Wound must be free of necrotic tissue and/ or malignancy
- Wound must not have communication/ proximity to major blood vessels or organs

Application of Wound VAC

- Wound cleansed (one study used pulsed irrigation)
  Baptist Hospital, Nashville, TN
- Cut sponge(s) to fit the wound – fill all spaces including tunneling and undermining
- If using more than one sponge, be sure to document # for subsequent dressing change
- Sponges must touch each other so that they collapse evenly under pressure
- Apply sponge(s) & cover with transparent wound dressing – avoid overfilling wound
- Secure tubing to computerized unit
- Keep tubing away from skin, pressure areas and bony prominences
- If there are two wounds in close proximity, can use Y adapter or bridging technique
- May use envelope technique for digits: fingers/ toes

Potential Difficulties in Treatment with Wound VAC

- Pain – sponges adhere to wound bed at dressing change
  - Moisten with normal saline, can add lidocaine
  - Do not use topical anesthetics with epinephrine (vasoconstrictor)
- Unable to achieve airtight seal – unit alarm will sound
- Pt reports "stinging" sensation – can reduce pressure slightly to improve pt comfort
- Choice of foam – white foam hydrophilic, less adherent and can be removed easier from tunnels and sinuses – may need to adjust pressure

Surgical Approaches to Wound Closure

- Sutures/ staples (Direct closure)
- Adhesives
- Skin grafts – STSG, full thickness skin graft
  allograft
  autograft
- Muscle flaps

Direct Closure

- Primary or delayed primary closure
- Wound must be clean of debris and necrotic tissue
- Must be closed from deepest layers first to prevent abscess formation

Wound Adhesives

- Histoacryl blue (n-butyl-1,2-cyanoacrylate)
- Dermabond (2-octyl-cyanoacrylate)
- Indermil (enbucrylate)
- Actions – binds superficial layers of epidermis, provides approximation of wound margins to facilitate healing and reduce deficit
- Peels off in 5 to 10 days
- Risk of dehiscence for deeper wounds, larger wounds, or wounds subjected to high tension (e.g. – across a joint surface)
- Forms a water resistant seal – usually no additional dressing needed
- Do not apply topical antibiotics – can break bond/ degrade polymer
- Can cleanse area with water, but should not be soaked

- Bruns and Worthington, Using Tissue Adhesive for Wound Repair: A Practical Guide to Dermabond. American Family Physician. 20(61):1383-8

Skin Grafts: Autografts

- Split-thickness – meshed, covers larger area, heals with "pebble" appearance
- Full-thickness – can only cover 1/3 of the area as a meshed graft
- Donor site – heals by re-epithelialization in 10 -14 days

Skin Grafts: Allografts

- Cadaver skin – temporary biological dressing, eventually rejected by host [75]

Benefits of Skin Grafts [76]

- Require less synthesis of new tissue
- Formation of granulation tissue limited to thin layer between underside of skin graft and base of original wound defect
- Granulation tissue formation secures the graft and allows infiltration of blood vessels from wound base to graft

Musculocutaneous Flaps

- Used for closure of stage IV pressure ulcers, severe diabetic foot ulcers, traumatic wounds
- Muscle is harvested from donor site and transplanted to defect with vasculature intact
- Muscle transplant provides padding and improves circulation to the recipient site
- May help reduce risk of future breakdowns/ wound recurrence

Donor Sites for Muscle Flaps

- Free flap or transposition
- Glut max – common donor site for sacral & ischial ulcers
- TFL – common donor site for ulcers over greater trochanter

Post-Operative Precautions and Preventative Management

- Factors that can threaten graft survival include:
    - infection
    - mechanical stress: weight bearing & shear forces
    - venous congestion
    - Malnutrition
    - Poor glycemic control
    - Location of surgical site – tension on the flap, inadequate immobilization

Prognosis and Treatment Planning in Wound Healing

- Use known markers to assess potential for healing

- Prognostic factors in order of decreasing predictive value [77]:
    - Wound size
    - Patient age
    - Elapsed time from wound appearance to initiation of treatment
    - Width to length ratio
    - Location
    - Type of treatment

- Monitor rate of wound closure
    - Reduction in size of 10-15% per week represents normal rate of healing [78, 79]

Back to the Future

Revisiting Past Success and Reviewing New Developments in Wound Care

Silver Dressings

- Broad spectrum anti-microbial properties : bacteria, fungi and viruses [80]

- Inhibits oxidative enzymes and interferes with bacterial replication [80]

- Binds to bacterial cell membranes and induces apoptosis [80]

- Reports of silver-resistant bacteria: e. coli, enterobacter, klebisella, salmonella, pseudomonas [80]

- Silver ions in dressing can be inactivated by saline ions in irrigant or exudate [80]

- May inhibit uptake of skin grafts [81]

Homeopathic Remedies

- Honey dressings
- Sugar as a wound healing agent
- Topical application of papaya

Use of Honey in Wound Healing

- Dates back to ancient Greece and Egypt [82]
- Seen in Ayurvedic medicine [82]
- Described in the Koran [82, 83], Bible and Torah [83]

Therapeutic Honey

- Raw – no heat treatment like culinary honeys – heat would reduce the antibacterial action by destroying the enzyme responsible for production of hydorgen peroxide [82](Glucose oxidase)
- Sterilization by gamma irradiation [82]
- Examples (derived from tea trees)[82]:
  - Medihoney (Australia)
  - Active Manuka Honey (New Zealand)

Challenges

- Frequency of application
- Source of honey
- Method of application – direct topical application vs.gauze or occlusive dressings soaked in honey

Properties of Honey

- Production of hydrogen peroxide – slow, low level production inhibits bacteria without damaging tissue [82]
    - Hydrogen peroxide also aids debridement
- High sugar content and acidic pH inhibits growth of pathogens [82]
- Promotes moist wound environment [82]

Effects of Honey [82]

- Reduced infection
- Decreased inflammation and swelling
- Alleviates pain
- Controls odor
- Reduces necrotic tissue
- Speeds granulation & re-epithelialization
- Minimizes scarring
- Improves uptake of skin grafts
- Non-adherent
- pH creates good environment for fibroblast activity: migration, proliferation and organization of collagen

Application of Sugar in Wounds

- Used in Brazil – crystalline sugar as wound packing material
- Decreases odor by inhibiting bacterial growth [83] – lowers wound pH and fights infection
    - Effective against pseudomonas and e coli, staph aureus and klebisella
    - No effect against proteus & enterobactus
- Reduces drainage and moisture [83]
- Dilates small blood vessels and enhances nutrition of healing tissues [83]

Application of Papaya in Wound Healing

- Used in Brazil to facilitate debridement
- Green papaya contains papain and chemopapain
- 10% solution for tissue with black necrosis, more dilute for slough or granulating tissue
- Can cause allergic reactions in patients who are latex sensitive [8]

Skin Equivalents

- Cultured epidermal autografts (CEAs)
    - Autogenic
    - Can provide permanent coverage
    - Requires a skin biopsy (sample) for cultivation
    - Take 3 weeks to cultivate
    - Can be cryopreserved and banked
    - Not presently available commercially [84]
    - Lack of dermal component – unstable attachment
    - Sometimes preceded by cadaveric graft to allow dermal propagation prior to application of CEAs
    - High cost: Epicel, approx $825 for a 50 cm^2 sheet
    - Future developments – allogenic grafts derived from newborn foreskin

Tissue Engineered Skin

- Various types [84]
    - Made mainly of cells
    - Extracellular matrix materials only
    - Combination of cells and matrices

- **Integra**: Bilayer: artifical dermis - nonliving extracellular matrix of collagen and chondroitin-6-sulfate, artificial epidermis: disposable silicone sheet

- **Alloderm**: acellular dermal matrix & intact basement membrane can be used to improve uptake of CEAs, or for use of thinner autograft

- **Dermagraft**: living dermal fibroblasts grown on a degradable scaffold

- **Transcyte**: temporary skin replacement - human dermal fibroblasts

- **Apilgraf**: living bilayered artifical skin equivalent with keratinocytes, fibroblasts and bovine collagen, can be applied as outpatient procedure

- **Oasis**: porcine small intestinal submucosa acellular collagen matrix, contains growth factors

- **Orcel**: keratinocytes seeded over nonporous collagen gel, fibroblasts on the underside of a porous sponge

Topical Growth Factors

- Recombinant epidermal growth factor (EGF)
- Fibroblast growth factor (bFGF)
- Platelet derived growth factor (PDGF)
    - FDA approval for diabetic foot ulcers [26, 32]
    - Beclaplermin – regranex gel [32]
    - Procuren [89]

Challenges to Use

- High cost ($400/ tube) [32]
- Chronic wound environment –
  - Increased levels of proteases may impair function of topical growth factors [26, 2]
- Topically applied factors may not reach intended target: only 1-9% of applied dose reached depth of 1 to 3 mm [2]
- May be possible to use gene transfer for improved delivery [26]
- Topical growth factors may have mitogenic properties – malignancy? [26]
- Topical growth factors may increase risk of hypertrophic scarring, e.g. – FGF? [26]
- Growth factor timing and delivery
- Use of isolated factors not as effective as synergistic action [2], delivery in combination

Gene Therapy: Promising Results [2]

- Animal study (Deodato, et al & Galeano, et al)
- Delivery of VEGF-A by adenovirus
- Accelerated healing
- Well-structured granulation, greater vascularization as compared to control
- Genetically modified keratinocytes transplanted as an epithelial sheet in mice
- PDGF-A production and release was enhanced leading to increased granulation

Future Research and Development

- Gene therapy may help overcome difficulty in planning timed release of topically applied growth factors [90]
- Future research and development may focus on combination of gene therapy and artifically engineered skin substitutes: GAM – gene-activated matrices [90]

Methods of Application:Electroporation

- Use of an electric field to assist gene delivery
- Studies show use with TGF-beta1 DNA and keratinocyte growth factor DNA for increased rate of collagen synthesis and angiogenesis in rats [2]

Methods of Application:Direct Injection

- Direct injection of "naked" DNA/ RNA into recipient cell/ target area
- Microseeding

Stem Cell Research in Wound Care

- Possibilities for re-establishing sweat glands, hair follicles in full-thickness wounds [26]
- May be possible to harvest embryonic stem cells without destroying the embryo [75]
- Embryonic stem cell use comes with concerns regarding neoplasia [75]
- Stem cells may have potential to act as vehicles for gene transfer [90]

Adult Stem Cells

- Human mesenchymal stem cells (hMSCs) - derived from bone marrow [91]
- Capable of differentiating into multiple cells and tissues – developmental plasticity [75, 90]
- During the inflammatory process, bone marrow contributes granulocytes and monocytes (macrophages) [75]
- hMSCs plus bFGF accelerated wound healing and hMSCs transdifferentiated into epithelium [75]
- hMSCs increases angiogenesis [75]