

First Slide!!!!

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Wound healing Physiology: Without the Folklore!!

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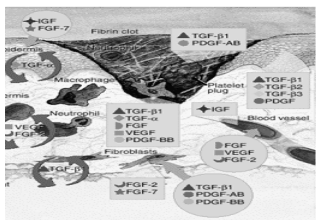


I have no commercial relations relevant to the topic presented!!!

Allen Zagoren DO, MPA

Learning objectives

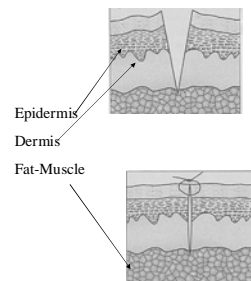
1. At the end of the session the student will be able to identify the basic stages of wound healing (in humans)
2. At the end of the session the student will be able to identify the role the platelet plays in initiating wound healing
3. At the conclusion of the session the student will identify the potential role that impediments to wound healing can play!



The normal wound repair process is a coordinated and predicated series of cellular and biochemical events.....resulting in a *healed wound* with strength and integrity

Primary Intention

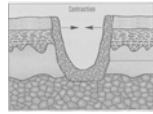
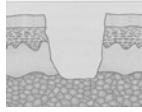
- Little or no loss of tissue
- Edges juxtaposed
- Connective tissue deposited as primary "glue"



Secondary Intention

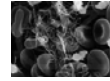
•Edges remain open

•Space needs to be filled in



4 Phases (Old School!)

• Hemostasis



• Inflammation



• Proliferation

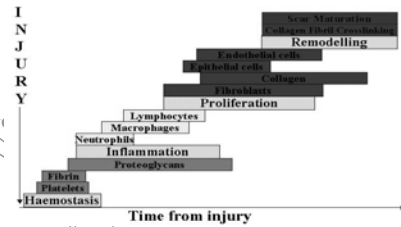


• Maturation

Not So FAST!!!!

Phases of Normal Healing

Towards healing



Wounding

Primary

- coagulation
- inflammatory response
- cellular migration
- epithelialization

Capillary loops {granulation}

Fibroblasts

Myofibrils

Inflammatory cells matrix proteins

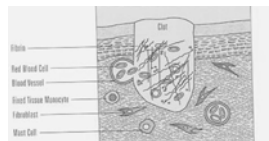


Phases



- INTEGRATION
- ORGANIZATION
- CONTROL

CONTROL



- Injury- (activation)
- Platelet Aggregation
- Coagulation factors
growth factors

Platelet Activation

- Thrombin
- Fibrin → hemostasis
- Clot

Inflammation

- Within hours of injury
- Transient phase 5 -7 days
- Neutrophils
- Macrophages
- Lymphocytes



- Platelets - Growth Factors
- Chemo attractants –stimulate influx of neutrophils and monocytes (pluripotential stem cells)
- Monocytes – phagocytic macrophages



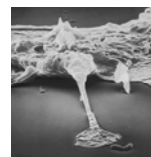
MACROPHAGE



Kill bacteria
Digest damaged tissue

↓ INFECTION

GROWTH FACTOR REGULATOR



Growth Factors

- Platelets —
- Platelets derived growth factor (**PDGF**)
- Epidermal growth factor (**EGF**)
- Transforming growth factor- β (**TGF- β**)
- Heparin binding epidermal growth factor (**HB-EGF**)
- Insulin-like growth factor -1 (**IGF-1**)

Neutrophils Macrophages Inflammatory mediators

- Swelling
- Heat (calor)
- **Redness (rubor)**
- Pain (DOLOR)

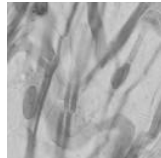


Celsius 200 years ago

Library of Celsus-Epaphasus

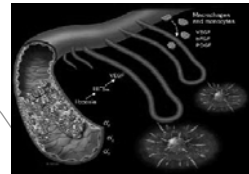
Proliferation (*fibroblasts*)

- Restore vascular integrity
- Replace lost or damaged tissue
- Resurface wound

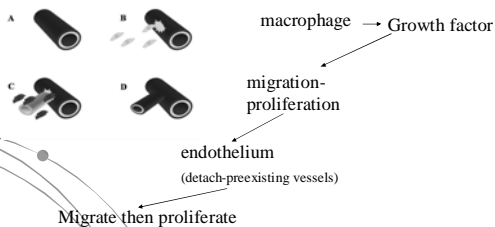


Angiogenesis

- Matrix formation
- Contraction
- Resurface—migrating keratinocytes



Angiogenesis (microvascular-integrity)

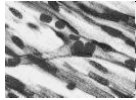
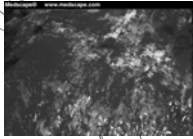


Regulators

- Basic +acidic fibroblastic growth factor (**FGF**)
- Tumor necrosis factor β (**TNF- β**)
- **EGF**
- Wound Angiogenesis factor (**WAF**)

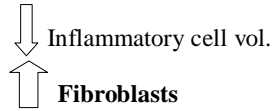
Result:

- Endothelial cells arrange in tubular structures → **capillary sprouts**
- Ultimately a vascular network →
- Extracellular matrix to provide a new vascular membrane



Matrix Formation

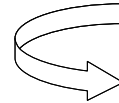
transition ⇒ **Inflammation to proliferation**



TGF-β — **PDGF** ↑ **MACROPHAGES**

1. Macrophage influx---
2. Microbicidal events---(reactive O₂ intermediates)
3. Induction—lipooxygenase-(arachidonic acid cascade)
4. Debridement-synthesis,-secretion-collagenase
5. Prepare for the new matrix!

Growth factors



Fibroblastic proliferation

Counter balance of stimulations

Growth factors—days 5-7



Expression **PDGF, TGF-β**, → **ECM**

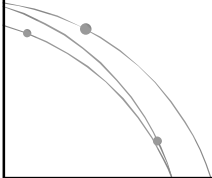
- Fibronectin
- Laminin
- Glycosaminoglycans(GAGS)
- Collagen

Epithelialization



Keratinocytes-migrate to the surface

Epidermis- and supporting basement membrane re-establish to maintain an impermeable barrier.....

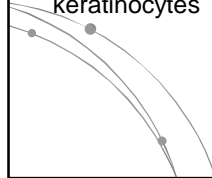


Hours After Injury...

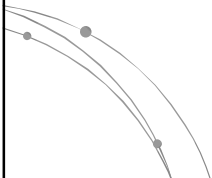


- Migration
- Proliferation
- Differentiation of keratinocytes

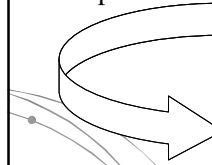
From surrounding epithelial sites. hair follicles, sebaceous glands..



- Epithelial cells migrate as a sheet or in a “leap frog” manner...(epiboly)
- Preserve tight intercellular junction



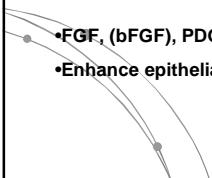
KERATINOCYTES.....secrete membrane Components..



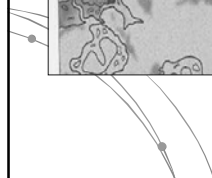
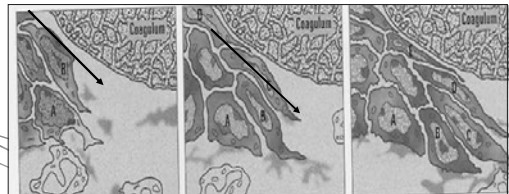
- Fibronectin
- Collagen
- Laminin

Growth factors-aide to stimulate Epithelialization

- EGF, TGF- β \uparrow Rate of Epithelialization
- KGF (FGF-7)—stimulates keratinocyte proliferation
- FGF, (bFGF), PDGF—stimulate connective tissue, Enhance epithelialization



“Leap Frog”



Remodeling

- Excess collagen and matrix are removed (collagenase)
- Proteolytic enzymes

Matrix remodeling ⇌ Fibroblasts--collagen

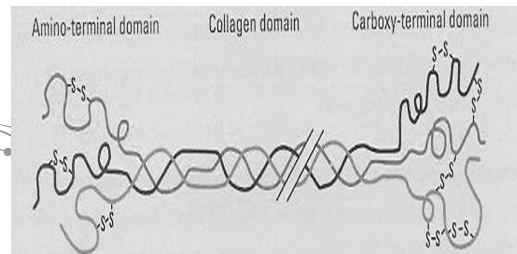
- **Hydroxyprolene, hydroxylysine—specific locations**
- **Requires O₂**
- **Vit. C**

Collagen

- 19 different types
- 3-peptide chains
- Triple helix
- lengthy lumen
- Flexible
- Semi-flexible

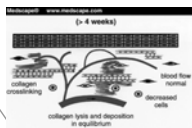


Triple –helix Collagen



Degradation-collagen

- Collagenase (metallo-proteinase) {MMP}
- Critical for remodeling



- Collagen turnover

↓
Cleaves collagen fiber into 2 components

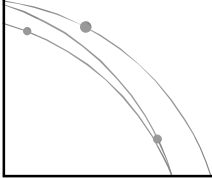
TCa-----TCb

Wound repair

- Collagen synthesis



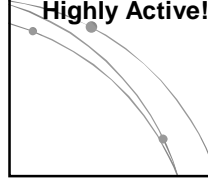
- Degradation rate



Chronic wounds

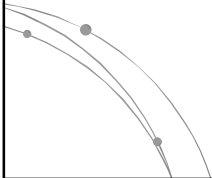
- MMP8—(collagenase produced by neutrophils)

Highly Active!



Remodeling

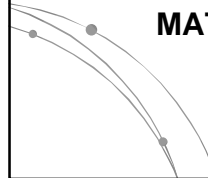
- Regulators: **TGF- β** , **PDGF**, **FGF**
Insulin-like growth factor
interleukin-1(IL-1)
TNF- β
interferon- γ



Remodeling—2 year process

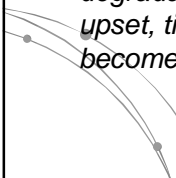
- Fibroblast induced collagen synthesis
- Breakdown by collagenase
- Regression of inflammatory cells

MATURE SCAR!



Remodeled tissue is never as strong as the original!

When balance between degradation and synthesis is upset, tissue integrity can become severely disrupted



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Key Non-Nutrition Factors Affecting Wound Healing



I have no commercial relationships
to disclose

Learning Objectives

- Identify key non-nutrition factors that affect wound healing
- Differentiate factors that can be corrected from those factors that cannot be corrected
- Describe three effective principles of wound management

Learning Assessment Questions

1. Key non-nutrition factors that affect wound healing include:
 - a. Age
 - b. Thermoregulation
 - c. Circulation/oxygen
 - d. All of the above

Learning Assessment Questions

2. The three principles of wound management are:
 - a. Address the wound etiology, support the host, and maintain a physiological local wound environment
 - b. Debridement, control of infection, and exudate control
 - c. Establish treatment goal, wound cleansing and physiological local wound care
 - d. Assessment of the host, debridement and physiological local wound care

Learning Assessment Questions

3. Which of the following criteria is used to optimally select a wound dressing?
- Product availability and cost
 - Functions of the dressing
 - Characteristics of the wound
 - Number of dressing changes required daily

Non Nutrition Factors that Affect Wound Healing

- Circulation/Oxygen
- Bacterial Burden/Necrotic Tissue
- Age
- Co-morbid Conditions
- Thermoregulation
- Hydration/Fluid Balance

Determine Goals of Wound Management

- Healing
 - Underlying pathology can be corrected
 - Systemic problems can be corrected
- Maintenance
 - Underlying pathology cannot be corrected
 - Systemic problems cannot be corrected
 - Terminal Illness
 - Pain control
 - Odor control

Principles to Guide Topical Therapy Choices for Wound Healing

- Topical therapy (choosing a proper dressing) is only one component of the management regime
- Must consider measures to address etiologic and systemic factors

Principles to Guide Topical Therapy Choices for Wound Healing

- Assess and remove impediments to healing from the wound bed
- Maintain optimal environment in the wound bed for wound healing

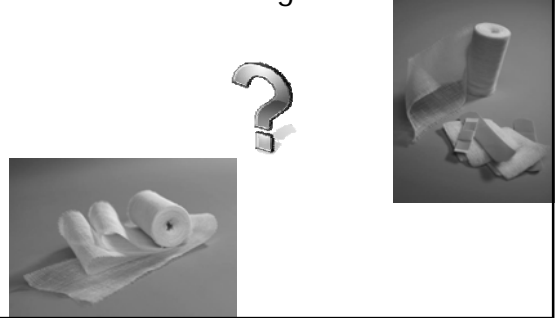
Remove Impediments to Healing

- *Debride necrotic tissue
 - Surgical
 - Autolytic
 - Mechanical
 - Enzymatic
- * *Stable non infected wound with poor circulation should not be debrided*
- Identify and treat infection
- Absorb excess wound exudate
- Fill wound "dead space"
- Open or excise closed wound edges: Epibole

Optimal Local Environment for Wound Healing

- Maintain moist wound surface
- Protect wound from trauma and secondary infection
- Insulate the wound bed

Decisions, Decisions, Decisions How do I choose the right dressing?



Topical Wound Care: Match the Dressing to the Wound

- Purpose of the dressing
- Volume of wound exudate
- Wound Size
- Occlusive or Non-occlusive
- Adhesion to the wound bed
- Cost/usage/availability

Wound Dressings

- Purpose
 - Absorb exudate/wick fluid from wound tunnels
 - Maintain moist wound surface
 - Insulate
 - Provide a bacterial barrier
 - Atraumatic dressing removal: yes or no

Wounds and Wound Dressings

- Volume of wound exudate
 - None
 - Small
 - Moderate
 - Large
- Wound Size
 - Length, width and depth
 - Presence/absence of tunnels, tracks, undermining or ledges

Wound Dressings

- Occlusive/ Semi-occlusive or non-occlusive
- Adhesion to wound bed: yes or no
- Cost/usage/availability of wound dressing

Topical Wound Care: Match the Dressing to the Wound

- Purpose of the dressing
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- Cost/usage/availability

Wound Dressings

■ Definition of Terms

– Primary Dressing

– Secondary Dressing

Wound Dressing Examples General Categories

Gauze Dressings

- Woven and Nonwoven
- Plain and/or impregnated with various products: petrolatum, iodides and antimicrobials
- Generally used on draining wounds, wounds requiring debridement, packing, or a cover
- Fills tunnels, dead space
- Primary or secondary dressing
- Examples: Kling, Kerlix, AMD gauze, 4x4s, TELFA , Island Dressings

Gauze Dressings

- | | |
|---|---|
| <ul style="list-style-type: none">■ Advantages<ul style="list-style-type: none">– Readily available– Many forms and sizes– Can be combined with other topical products– Less expensive | <ul style="list-style-type: none">■ Disadvantages<ul style="list-style-type: none">– Fibers can shed or adhere to the wound bed– Needs a secondary dressing– Requires more frequent changing to adhere to principles of moist wound healing– Poor thermoregulation |
|---|---|

Transparent Films

- Made of a copolymer or polyurethane membrane
- Porous adhesive layer: allows oxygen to pass through to the wound, impermeable to bacteria
- Allows moisture water vapor to cross the barrier
- Examples: Tegaderm, Opsite

Transparent Films

- Advantages
 - Transparent
 - Impermeable to external fluid/bacteria
 - Maintains moist wound environment
 - Promotes autolytic debridement
 - Prevents/reduces friction
 - Many sizes, conforms
 - Primary and secondary dressing
 - 5-7 day wear time
 - Disadvantages
 - May stick to some wounds
 - May damage surrounding skin when removed
 - Most do not absorb moisture*: not indicated for draining wounds
 - Fluid retention under dressing can cause periwound skin maceration
- *newer films have limited absorptive qualities

Hydrogels

- Water or glycerin based amorphous gels
- Water in a gel matrix
- High water content: 80-99%
- Examples: Aquasorb, Carrasyn Gel, IntraSite, SoloSite, SAF-Gel, DuoDerm Hydroactive Gel, Curasol, Curagel, Restore Hydrogel

Hydrogels



Courtesy of ConvaTec

Hydrogels

- Advantages
 - Rehydrate wound bed
 - Reduce wound pain
 - Promote autolytic debridement if needed
 - Nonadherent
 - Easy to remove
- Disadvantages
 - Require a secondary dressing as is nonadherent and dehydrates if not covered
 - Reduced absorptive qualities
 - May macerate periwound skin

Hydrocolloids

- Composed of gelatin, pectin and carboxymethylcellulose
- Occlusive or semioclusive
- Provides moist healing milieu for clean wounds to granulate and autolytic debridement for necrotic wounds
- Can be a primary or secondary dressing
- Examples: Duoderm, RepliCare, Restore, Comfeel

Hydrocolloids



Courtesy of ConvaTec

Hydrocolloids

- Advantages
 - Impermeable to contaminants
 - Thermal insulation
 - Self adherent/molds well
 - Facilitate autolytic debridement if needed
 - Minimize skin trauma/healing disruption
 - Light/moderate absorption of drainage
 - Dressing changes up to 5-7 days
- Disadvantages
 - Not transparent: wound assessment difficult
 - Light/moderate drainage absorption
 - Some types adhere
 - May become dislodged with heavy exudate/curl and bunch up: additional trauma potential
 - Residue left in wound from dressing mistaken for infection
 - Odor is produced that maybe mistaken for infection

Foam Dressings

- Absorptive dressing made of hydrophilic polyurethane or film coated gel
- Non-occlusive, non-adherent, non-linting
- May be a primary or secondary dressing
- With and without adhesive borders
- Examples: Allevyn, COPA, Hydrofera Blue, LYOFoAM, Mepilex, POLYDERM, PolyMem

Foam Dressings

- Advantages
 - Many sizes, shapes, forms available
 - Conformable, easy to apply/remove
 - May repel contaminants
 - Absorb light to heavy drainage
 - Frequency of change dependent on wound drainage amount
 - Ok to use under compression
- Disadvantages
 - Ineffective on non draining wounds or eschar
 - May/may not be used on infected wound or wounds with tunnels
 - Secondary dressing, tape, wrap or net may be needed to secure
 - Periwound skin macerates if foam not changed appropriately

Alginates

- Derived from brown seaweed
- Composed of soft non woven fiber ropes or pads
- Interacts with wound exudate to form a soft gel
- Can absorb up to 20 times its weight
- Examples: KALTOSTAT, Curasorb

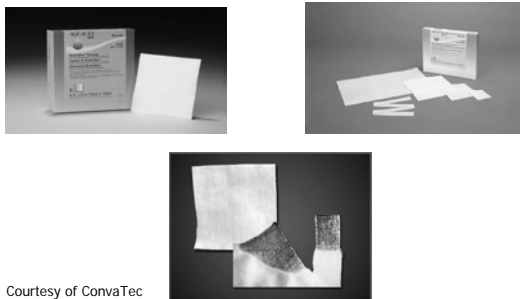
Alginates

- Advantages
 - Highly absorptive
 - Forms soft gel: moist wound healing and atraumatic removal
 - Gently conforms to all wound walls
 - Fills dead space
 - Easy to apply and remove
- Disadvantages
 - Not recommended for wounds with small drainage amounts or dry eschar
 - Can dehydrate a wound
 - Requires a secondary dressing

Hydrofibers

- Derived from sodium carboxymethylcellulose +/- Silver
- Available in ribbons, pads
- Similar advantages/disadvantages as alginates
- Silver impregnated dressing grey in color/broad spectrum antimicrobial properties: kills MRSA, VRE, prevents colonization in dressing and effective barrier to bacterial penetration
- Examples: AQUACEL, AQUACEL AG

Hydrofibers



Courtesy of ConvaTec

Antimicrobials

- Topical dressings derived from silver, polyhexamethylene biguanide (PHMB) and iodine.
- Deliver antimicrobial or antibacterial action to the wound
- Provide barrier to specific organisms
- Inhibit growth of bacteria within dressing
- Examples: Acticoat, Kerlix AMD Gauze, IODOFLEX, IODOSORB

Other Topical Treatments

- Enzymatic Debriding Agents
 - Collagenase Santyl Ointment
 - Accuzyme*
 - Panafil*
 - *Banned by FDA/no longer available
- Negative Pressure Wound Therapy (NPWT)
 - Examples: KCI VAC Therapy, Blue Sky, Prospera, VISTA

Negative Pressure Wound Therapy



Learning Assessment Questions

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 - b. Thermoregulation
 - c. Circulation/oxygen
 - d. All of the above

Learning Assessment Questions

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 - c. **Characteristics of the wound**
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Remember

- Wounds are not static entities
- Needs change as wounds progress or deteriorate
- Dressings appropriate in the early phases of wound healing will be inappropriate in the later phases
- Continued assessment of the wound is critical for successful management

Choose a dressing that meets the needs of the wound



References

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- Ovington, L (2001) Hanging Wet-to Dry Dressings out to Dry. Home Healthcare Nurse. 19 (8): 477-483.

Nutrition: An Opportunity to Promote Wound Healing

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1

Learning Objectives

- Identify the role of specific macro- and micronutrients in wound healing
- Examine clinical guidelines for recommendations concerning the role of nutrients in healing



Critically Reviewing the Evidence on Wound Healing

- Surrogate markers vs complete wound healing as endpoints in nutrient interventions studies
 - Hydroxyproline content
 - Wound tensile strength
 - Wound surface area
- Nutrition interventions
 - Hypoalbuminemia \neq malnutrition
 - Correcting nutrient deficit \neq \uparrow healing
 - EN & PN may mask benefit of nutrition



3

Critically Reviewing the Evidence on Wound Healing

- Small sample sizes
- Heterogeneous populations
- Type and severity of wound
 - Surgical wound
 - Trauma
 - Pressure ulcers



4

Critically Reviewing the Evidence on Wound Healing

- Underlying disease states/conditions
- Diverse treatment regimens
- Healing vs risk of developing a wound
- Caveats of laboratory measurements



5

*Most wounds heal even
in the sickest patients.*

*A slow healing wound
can heal completely.*

6

Healing is a matter of time, but it is sometimes a matter of opportunity

Hippocrates

7

Mini Nutritional Assessment & Screening Tool

- Easy to use and accurate in elderly patients
- Screening portion: weight, appetite, mobility, psychological stress, neuropsychological problems, BMI
- Assessment portion: includes screen portion + anthropometrics, global problems, dietary issues, and self-assessment

<http://www.mna-elderly.com>

8

MNA Assessment

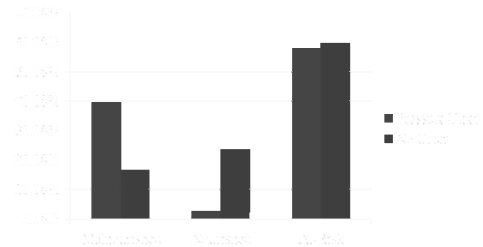
Langkamp-Henken, et al. *JADA* 2005;105:1590-1596

- MNA correlated with BMI, calf circumference, Hgb, Hct, fat-free mass, body cell mass index & fat mass index in patients with pressure ulcers
- Hepatic proteins did not correlate with MNA
 - Prealbumin negatively correlated with ESR – a marker of inflammation

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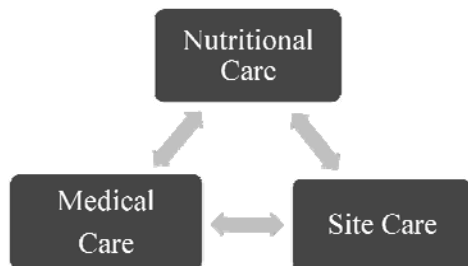
MNA Assessment

Hengstermann et al *JPEN* 2005;31:288-294



10

Nutrition is One Aspect of Care



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Nutrition & Healing

- Fluid
 - 30-40 mL/kg are normal requirements^{4,6}
 - 10-15 mL/kg additional fluids with air-fluidized beds set at high temperatures^{5,6}
- Energy
 - All patients with PU: 30-35 kcal/kg/d^{1,2,6}
 - Underwt/losing wt: 35-40 kcal/kg/d^{3,6}
- Protein
 - 1.25-1.5 g/kg/d^{1,6}
 - 1-1.5 g/kg/d²

¹AHCPR, ²EPUP, ³NPUAP, ⁴ASPEN, ⁵Ayello, ⁶ADA NCM

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Nutrition & Healing

- Vitamins/Minerals
 - Daily vitamin & mineral supplement^{1,6}
 - Supplement cautiously when giving > ULs⁶
 - Glutamine
 - Efficacy not demonstrated. Not recommended^{4,6}
 - Arginine
 - Maximum safe dose not identified. Not recommended^{4,6}
- ¹AHCP, ²EPUP, ³NPUAP, ⁴ASPEN, ⁵Ayello, ⁶ADA NCM

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A.S.P.E.N. Practice Guidelines for Adult Patients with Burns (JPEN 2002)

- Provide adequate kcal and increased protein (20-23% total kcal) to severely burned patients (A)
- No current role for routine use of specific nutrients or anabolic agents (B)
- Initiate EN ASAP in moderate/severe burns (A)
- Initiate PN when EN not tolerated or unlikely to meet needs within 4-5 days (B)

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Wounds, Inflammation & Malnutrition



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Anti-Inflammatory Nutrients

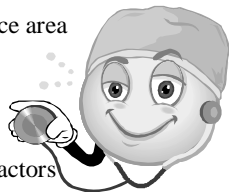
- Anabolic steroids
- Modular protein
- Glutamine
- Arginine
- OKG
- Fish oil
 - EPA
 - GLA
- Vitamins
 - Vitamin A
 - Vitamin C
 - Vitamin E
 - Vitamin K
- Trace Elements
 - Copper
 - Selenium
 - Zinc



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Monitor Outcomes

- Decreased wound surface area
- Improved weight
- Improved appetite
- Glycemic control
- Reduction in negative factors
- Complete wound healing



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*The presence of passion
does not replace
the absence of data*

Buchman, AL. *Am J Clin Nutr* 2001

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*Absence of evidence
is not
evidence of absence*

MacFie J. *Nutr* 2000

19

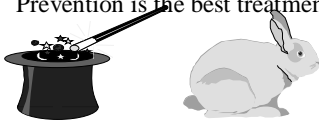
Prevention of Pressure Ulcers

- Monitor patients at risk
 - Consume < 50% of meals served
 - NPO/CL > 5 days
- Provide supplements and assistance with meals and snacks
- Collaborate with members of the healthcare team to reduce risk

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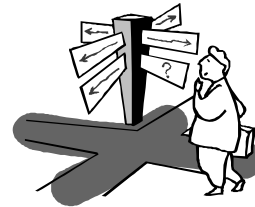
Nutrition Support Pearl

Wound healing takes time
Chronic wounds don't happen overnight
Nutrition is only one aspect of care
Provide consistent, adequate nutrition
Prevention is the best treatment!



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Thank You



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