**Tendon Biology**

**Tendon Healing**
- Tendons appear inert but nutritional pathways must be maintained/restored for healing to occur.
- Tendon capillaries come from:
  - Musculotendinous junction, bone insertion, vincula.
- Synovial fluid nutrition occurs in sheaths where tendons change direction — intrasynovial tendons:
  - Volar and dorsal wrist.
  - Digital flexor tendon sheath.

**Tendon Vascularity**
- Vincula supply capillaries to dorsal 2/3 of flexor tendons within digital sheath.
- Avascular zone volarly.

**Tendon Vascularity**
- Blood supply to tendon leaves avascular zones between vincula.

**Tendon Vascularity**
- Significant areas of zone 2 tendons have no blood supply and rely on synovial diffusion for nutrition.

**Intrinsic/Extrinsic Tendon Healing**
- Extrinsic healing: Tendons do not have capacity for self-healing, rely on granulation tissue from surrounding areas to invade injury site.
Intrinsic/Extrinsic Tendon Healing

- Intrinsic healing: fibroblasts within tendon can heal injury without granulation from surrounding tissues

Intrinsic Tendon Healing

- Epitenon fibroblasts migrate into laceration site, form collagen fibers, span the injury site.
- Scanning electron microscopy

JHS 10A:632

Intrinsic Tendon Healing

- 3 weeks: migrating fibroblasts
- 9 weeks: gap is filled
- High power
- Low power

Electron microscopy JHS 10A:632

Tendon Healing

- Experimentally, tendons can clearly heal by intrinsic means
- Clinically, tendons likely heal by combination of intrinsic and extrinsic means

Phases of Wound Healing

- I. Hemostasis
- II. Inflammation
- III. Fibroplasia
- IV. Maturation
- Collagen accumulation

Growth Factors Involved in Tendon Healing

- Insulin-like growth factor IGF
- Transforming growth factor TGF
- Platelet-derived growth factor PDGF
- Vascular endothelial growth factor VEGF
- Fibroblast growth factor FGF
- Bone morphogenic proteins BMPs
Growth Factors: Phases of Tendon Healing

Inflammatory
- Fibroblast/imflam cell recruitment to injury site: IGF
- Regulation of cell migration: TGF
- Expression/attraction of other growth factors: PDGF
- Angiogenesis: VEGF, FGF

Proliferative
- Cell proliferation: IGF, PDGF, TGF, BMPs
- Collagen and ECM synthesis: IGF, PDGF
- Cell-ECM interaction stimulation: TGF
- Type III collagen synthesis: TGF, BMPs

Remodelling
- Extra cellular matrix remodelling: IGF
- Termination of cell proliferation: TGF
- Type I collagen synthesis: TGF, BMP

Impact slide: do not dare to remember

"The delivery of necessary factors at the required dosages in a temporal and spatial pattern over the repair phase is critical to a successful treatment." ²

"…current procedures used for repair produce a tissue with biomechanical properties that are inferior to those of normal tendon." ²

Goal of Tendon Healing

- allow tendon-tendon healing
- strong suture, strong technique, strong knot
- minimal interference of vascularity
- avoid tendon-sheath adhesions

Prevention of Adhesions

The Dream
- mechanical barriers
- artificial materials
- sheath closure

The Facts
- ineffective
- obstructive

- pharmacological agents
- anti-inflammatories
- chemical barriers
- collagen degraders
- nonselective

Prevention of Adhesions—The Reality

1 wound, 1 scar.

Tendon Gliding

- accelerates development of tensile strength
- reduces restrictive adhesions
- but forces must be kept below level of suture disruption
A Multitude of Tendon Repair Techniques

- suture material: 3-0 vs 4-0, braided vs. monofilament, nylon vs. many others
- suture technique: 2-strand vs. 4, 6, 8-strand
- tendon grasping maneuvers

Tenofix

Corkscrew-like engagement of tendon fibers

Potential advantages:
quick, strong

Potential disadvantages:
bulky, not suitable for FDS
salvage after failed Tenofix is difficult

Cable Crimp System

2:36 video

Tendon Grafting

- active tendon substitutes
  - Hunter rod with secure biological fixation 1 min video

- conventional donor sites
  - extrasynovial tendons: palmaris longus, plantaris
Tendon Grafting

- Intrasynovial donor tendons (experimental)
- Fewer adhesions (more intrinsic healing)
- Less friction around annular ligaments
- Result: less force required to achieve gliding

Scientific Treatments for Lateral Epicondylitis

- Steroid (injection, phono, ionto [details later])
- No scientific basis since it is not an "itis"
- Autologous blood injection
  - Stimulate an inflammatory response
  - No good studies support its superiority
- Platelet-rich plasma (PRP) injection
  - Rationale: concentrate growth factors

PRP for Tennis Elbow, Rotator Cuff Repair, Achilles Tendinopathy

- Early enthusiasm (Level 4, 5 studies and athlete endorsements)
- Level 1, 2 studies: (no better than whole blood)
- Why no better?
  - Uncontrolled concentration of platelets
  - Timing of growth factor participation
  - Other proteins contributing or inhibiting
- Would it improve a symphony to dump a truckload of instruments on the stage?

Tendon Healing: Key Points

- Tendons have low metabolic demands
- Tendons have low metabolic supply
- Tendons generally heal by combination of intrinsic/extrinsic healing
- Differential gliding of tissues only practical way to modulate adhesion formation
- Ask surgeon how many Newtons the repair can safely resist during early therapy

Reading

- Platelet-rich plasma injection for chronic Achilles tendinopathy: a (double-blinded) randomized controlled trial. JAMA. 2010; 303:144-149

Skin Grafts & Flaps

Prosper Benhaim, MD
Chief Hand Surgery Service
UCLA
DEFINITIONS

**GRAFT**  Detached from its donor site and blood supply. Nourished by recipient site capillaries

**FLAP**  Remains attached to donor site. Nourished through donor site (pedicle)

**FREE FLAP**  Detached from its donor site and blood supply. Nourished by a/v anastomoses near recipient site.

Skin Graft Classifications

**Source**
- Autograft (same person)
- Allograft (different person)
- Xenograft (different species)

**Thickness**
- Split (partial) vs. full
- +/- Meshing

Meshed Split-Thickness Skin Graft

[Image of meshed split-thickness skin graft]

Split-Thickness Skin Graft

[Image of split-thickness skin graft]

Full-Thickness Skin Graft

[Image of full-thickness skin graft]
**Skin Graft Features**

<table>
<thead>
<tr>
<th>Components</th>
<th>Split Thickness</th>
<th>Full Thickness</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Epidermis</strong></td>
<td>epidermis</td>
<td>epidermis</td>
</tr>
<tr>
<td><strong>Part of dermis</strong></td>
<td></td>
<td>entire dermis</td>
</tr>
<tr>
<td><strong>Thickness</strong></td>
<td>.01 - .02 inches</td>
<td>variable</td>
</tr>
<tr>
<td>(thickness of 4 pages = .014&quot;)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Donor sites</strong></td>
<td>multiple, large</td>
<td>limited</td>
</tr>
<tr>
<td><strong>Donor site healing</strong></td>
<td>epithelialization</td>
<td>primary closure</td>
</tr>
</tbody>
</table>

**Skin Graft Healing**

- Rapidity and success inversely affected by graft thickness
  - **Days 0-2**
    - Diffusion of nutrients
    - Fibrin scaffold for graft adherence forms
  - **Days 3-4**
    - Capillaries between bed and graft connect
  - **Day 5-7**
    - New capillaries grow into graft
    - Angiogenic growth factors affect

**Sensory Recovery in Skin Grafts: Incomplete**

- Dependent on innervation density in recipient site
- Axon sprouts follow empty neural sheaths into graft
- Faster in split thickness grafts
- More complete in full thickness grafts
- Pain fibers recover first
- Glabrous (hairless) graft best for fingertips

**Sweat and Sebaceous Gland Function in Skin Grafts**

- Faster and better return in full thickness grafts
- Sweat glands maintain donor site characteristics
- Must lubricate graft until sebaceous glands regain function

**Skin Graft Pigmentation**

- Hyperpigmentation to variable degree
- Affected by pigmentation level at the donor site
- Pronounced in split thickness grafts
- Increases with sun exposure (1-2 years)
Skin Graft Contraction

- **Primary contraction** - elastic recoil of skin
- **Secondary contraction** - combination of graft and host bed contraction
  - controlled by myofibroblasts
  - limited in full-thickness grafts

Recipient Site Preparation

- Requires adequate vascularity
- Contraindications
  - thermal or radiation burn scars
  - exposed bone, cartilage, tendon, nerve
  - necrotic tissue
- No infection
- Excellent hemostasis
- Minimal edema

Recipient Site Preparation

- Requires adequate vascularity
- Contraindications
  - thermal or radiation burn scars
  - exposed bone, cartilage, tendon, nerve
  - necrotic tissue
- No infection
- Excellent hemostasis
- Minimal edema

Skin Graft Preparation

- Sheet vs mesh grafts
- Stabilize graft in awkward places with bolster (here over shoulder)
- Immobilize adjacent joints (here with Kirschner wire)

Donor Site Healing

- Often problematic
- Full thickness donor sites sutured closed
  - stretches adjacent skin, scar may widen
- Split thickness donor sites left open to epithelialize
  - skin cells migrate to surface from hair follicles and divide
  - wound painful and sticky until healed
  - hyperpigmentation possible

FLAP CLASSIFICATION

Choose 1 term from each column

<table>
<thead>
<tr>
<th>Location</th>
<th>Design</th>
<th>Arterial Supply</th>
</tr>
</thead>
<tbody>
<tr>
<td>Local</td>
<td>Transposition</td>
<td>Random</td>
</tr>
<tr>
<td>Regional</td>
<td>Advancement</td>
<td>Axial—pedicled</td>
</tr>
<tr>
<td>Distant</td>
<td></td>
<td>Axial—free</td>
</tr>
</tbody>
</table>

Examples follow …
Flap Classification:
Location of Feeding Artery

- Random
  - just capillaries
- Cutaneous
  - artery in sub q
- Fasciocutaneous
  - artery in fascia
- Musculocutaneous
  - artery in muscle

Random, transposition, random flaps
Example: cross finger flap

Regional, transposition, random
Example: radial forearm flap

Regional, transposition, axial
Example: radial forearm flap

Distant, transposition, axial (free)
Example: fibula and skin

Distant, transposition, axial (pedicle) and random
Example: groin flap

49 local, transposition, random flaps

50 regional, transposition, random
Example: cross finger flap

51 distant, transposition, axial
Example: radial forearm flap

52 regional, transposition, axial (free)
Example: fibula and skin
Reconstructive Ladder: Fingertip Injuries

- Primary closure

- Granulation/contraction

• split thickness skin graft

• full thickness skin graft

• Regional random flap
  • Cross finger
  • Thenar

Local V-Y advancement flap
Reconstructive Ladder:
Fingertip Injuries
Distant random flap, pedicled
• cross-arm, chest wall, groin

Reconstructive Ladder:
Distant, axial, free: partial/whole toe transfer

Skin Grafts and Flaps: Key Points
• skin grafts—depend entirely on recipient bed for nutrition
• split vs. full thickness
• flaps—bring some blood supply to recipient bed
• local, regional or distant
• transposition or advancement
• random or axial (pedicled or free)
• choose simplest method that will solve problem

Vessel Biology
Vascular Histology, Physiology and Healing
Pressing Questions:
1. How does blood normally get around?
2. What's it delivering?
3. Why isn't it getting around now?
   a. cut and clot
   b. constriction
   c. compression
   d. congestion

Pressing question #1:
How does blood normally get around?

Arterial System
• arteries and arterioles
  • layers
  • adventitia
  • media
  • intima
  • diameter
  • 2 cm diameter
  • .01 mm
  • (terminal arteriole)
Capillaries
- diameter .003-.007 mm
- red cell diameter .006 mm (6 microns)
- maximum 2 cells thick
- endothelial cells
- pericytes

Veins
- postcapillary venules .008-.03 mm
- 1st site of infirm, allergy, fluid leakage
- collecting venules (.05 mm)
- Veins:
  - thin walls compared to arteries
  - valves
  - travel with arteries (venae comitantes)

We can grow new capillaries: angiogenesis
1. growth factors activate endothelial cell
2. cell makes enzymes that digest extracellular matrix
3. endothelial cell invades matrix space and divides
4. new endothelial cells divide again
5. spaces form within the new cells
6. spaces join to form lumen of new capillary

Lymphatics
- Capillary
- Extracellular fluid
- Lymphatics

Lymph: filtered through nodes above medial epicondyle and in axilla, reenters blood stream in chest:
- right lymphatic duct and thoracic duct

Kinesiotape: related to lymphatics?
Pressing question #2:

What's the blood delivering?
Oxygen!!
Is more better?

Hyperbaric oxygen
100% oxygen under increased atmospheric pressure
Increase oxygen levels 10-20 times
Increase oxygen diffusion from capillaries

HYPERBARIC OXYGEN THERAPY

“Oxygen is an antibiotic.”

- Stimulates fibroblasts (+collagen), osteoblasts, osteoclasts, and white cells
- Stimulates angiogenesis
- Stimulates white cell activation and efficiency

HYPERBARIC OXYGEN THERAPY

Clear Indications for Systemic Problems
(where oxygen carrying capacity is restricted)

- Diminished oxygen carrying capacity
  - carbon monoxide and cyanide poisoning
  - extreme anemia
- Air bubbles in tissues or in vessels
  - decompression sickness—the “bends”
  - air embolism

HYPERBARIC OXYGEN THERAPY

+/- Indications for Local Problems

- Acute, traumatic ischemia
- Crush injury, compartment syndrome
- Gas gangrene, necrotizing fasciitis
- Compromised skin grafts and flaps
- Radiation burns, scarring
- Thermal burns
- Diabetic ulcers

(If no blood is getting to area, even highly oxygenated blood won’t help)

Pressing question #3:

Why isn’t blood getting there now?
(And how can we change that?)

4 “C” issues:

a. cut and clot
b. constriction
c. compression
d. congestion

INJURED VESSELS RESPONDS WITH HEMOSTASIS

(smooth muscle in media—vasoconstriction: restricted in stiff vessels, partial lacerations, veins
endothelium—provide clotting factors, fibronectin, contractile proteins, platelet adherence
platelets—adhere to exposed collagen
clotting factors (eg, VIII missing in hemophilia)
later capillaries regenerate by angiogenesis)
Clot (hemostasis can be a bad thing)

Anticoagulants
- aspirin—permanently blocks platelet function
- other COX 1 inhibitors—temporarily block platelets
  - (COX 2s: no effect on platelets)
- heparin—blocks clotting at multiple steps
- dextran—decreases platelet adhesiveness
- hirudin—potent, from leech, relieves venous sludging

Disruption of arteries and veins: restore continuity

Neural Control of Blood Flow
- cardiovascular homeostatic reflexes
- atrial volume receptors
- carotid artery pressure receptors
- sympathetic fibers
  - alpha: vasoconstrictive
  - beta: vasodilatory
- norepinephrine at smooth muscle motor end plates increases intracellular calcium thereby enhancing constriction

Vascular Flow Dynamics

Ohm’s Law:

\[
\text{blood flow} = \frac{\text{pressure gradient}}{\text{resistance}}
\]

Poiseuille’s Law:

\[
\text{circulatory resistance} = \frac{\text{viscosity} \times \text{vessel length}}{\text{radius}^4}
\]

Therefore:

\[
\text{blood flow} = \frac{\text{pressure gradient} \times \text{radius}^4}{\text{resistance} \times \text{viscosity} \times \text{vessel length}}
\]

Rheologic Agents (increase flow)

- dextran—decreases blood viscosity
- pentoxifylline (Trental)—increases red cell deformability and flexibility in capillaries
**Arteriovenous Anastomoses (glomus apparatus)**
- AV shunts that bypass capillary beds
- Intermediate segment of smooth muscle and thickened adventitia
- Nerve plexus controls dilation
- Provide temperature regulation

**AV Shunt Control of Blood Flow**
- Half of all blood flow to skin is to hands, feet and head (high density of AV anastomoses)
- If patient is cold in hand therapy, glomus is going to shunt blood to vital organs and away from hand

**Hand Ischemia Large Differential Diagnosis**
- Atherosclerosis
- Embolism
- Compression
- Aneurysm
- Thrombosis
- Raynaud’s disease/syndrome
- Vasospasm
- Nicotine, cold, etc.
- Vasculitis

See last 4 slides for some details on these conditions

**Pressure**
- When pressure on capillaries exceeds 30 mm Hg:
  - For seconds: Blanch and fill
  - For minutes: Reactive hyperemia
  - For hours: Necrosis

What does 30 mms of mercury (Hg) feel like?

**How much pressure is 30 mm of mercury (Hg)?**
When you do the math….

30 mm of Hg = .58 pounds per square inch
= roughly 2 sticks of butter on end

**Pressure is an unavoidable issue when splinting**
- Static & dynamic splinting produce pressure at contact areas
- As the area of contact decreases the amount of pressure increases
- Pressure > 30 mmHg exceeds capillary perfusion pressure
  - Tolerated over minutes
  - Uncomfortable over an hour
  - Necrosis over a day
Artery                Capillary                Vein
90 mm Hg             ≤ 30 mm Hg             0-5 mm Hg

Increased Compartment Pressure
Artery  Compartment  Artery  Capillary  Vein
• 90  20                  70 ≤ 30  0-5
• 90 30 muscle ≤ 60 ≤ 30 0-5
• 90 dies 0 0 0 0

but distal pulse & cap fill persist, masking diagnosis!

Untreated Compartment Syndrome Leads to Volkman’s Ischemic Contracture

Venous Congestion
- Cellular nutrition
- Threat to arterial inflow
- Edema

To Decrease Venous Pressure
- Elevate
- Relieve constrictions
- Straighten elbow
- Loosen clothes
- Loosen bandages/splints
- Contract muscles
- Pump blood past valves
- Massage
- Use elastic wrap, elastic garment
- Kinesiotape?

Pressure as a Modality for Edema Reduction
Reactive hyperemia (ischemia) likely to be followed by edema
Reactive hyperemia is a warning that skin was ischemic during pressure application: OK for a few minutes, not OK overnight
Bottom line: be careful that pressure for edema reduction does not produce edema

Does dependent position in whirlpool increase venous pressure and edema?
Fluid presses proportionate to its vertical "thickness"
Since water and blood are ~ equal density, water pushes up and in with a force equal to the force of venous blood pushing down and out
Net effect: the limb is only as dependent as the vertical distance from heart to surface of whirlpool.

Answer: No
Key Points: Vascular System
• arteries—muscular
• capillaries—leaky
• veins—thin, low pressure
• circulation controlled by neural, hormonal, chemical and thermal factors
• small change in vessel diameter greatly affects flow
• clotting and angiogenesis complex mechanisms
• vascular disease multifactoral, difficult to treat
• hyperbaric O₂ can help when some circulation is present

Key Points: Pressure Mechanics
• capillary perfusion = 30 mg Hg
• pressure = .58 pounds / square inch
• prolonged pressure > capillary perfusion pressure causes cell death
• venous pressure
  • increased causes edema — stiffness,
  • decrease with carefully controlled external pressure and active motion

Appendix
some clinical details on:
• Types of vasculitis
• Raynaud's disease vs. syndrome
• Scleroderma

Types of Vasculitis
• collagen vascular disease
• systemic lupus erythematosis
• rheumatoid arthritis
• scleroderma
• polyarteritis nodosa
• thromboarteritis obliterans (Buerger's disease)
• hypersensitivity
• polycythemia

Raynaud's Disease
exaggerated response to cold, emotion
local vasospasm, associated numbness, pain
no identifiable underlying pathology
typical sequence
white (no blood)
blue (deoxygenated blood)
red (reactive hyperemia)

A Myriad of Possible Diseases Underly Raynaud's Syndrome
• scleroderma
• atherosclerosis
• Buerger's disease
• vasculitis
• myositis
• recurrent trauma
• cold injury
• multiple myeloma
• cts, thoracic outlet synd.
• multiple sclerosis
• metal poisoning
• drugs (ergot, beta blockers)
• cryoglobulinemia
Scleroderma

adventitial stripping helps:
local sympathectomy?
allow arterial dilation?

Journal Club
See Article PDFs

Limb Transplantation

Presentation originally prepared by
Kenneth R. Means, Jr., M.D.
Curtis National Hand Center @
MedStar Union Memorial Hospital
Baltimore, MD

History
• 1964 - Ecuador
  • 1st Hand transplant
  • Failed due to acute rejection
  • Limited immunosuppressive therapy available

Modern Transplants
• 1998 - Lyon, France
  • Hand removed 2001 (pt request)
  • Pt non-compliance
• 1999 - Louisville, KY
  • Successful hand transplant using modern protocols
  • 70+ in 40+ pts since 1998
  • 10 countries

Animal Models
• Cyclosporine A alone
  • Late rejection
• Addition of Mycophenolate Mofetil
  • Rejection free
Pre-operative Considerations

Recipient Inclusion Criteria

- Dominant or bilateral hand amputee
- Age 18 - 60
- Strong motivation to proceed with transplant
- Accepts dedicating >2 years to postoperative rehabilitation
- Elapsed injury to transplant time >6 months, <15 years
- Reports suboptimal outcome with myoelectric prosthesis for >6 months, verified by occupational therapist

Recipient Exclusion Criteria

- Single, non-dominant hand amputee
- Record of poor compliance
- Inability to receive adequate follow up care and/or immunosuppression
- Inability to follow strict postoperative rehabilitation regimen
- Documented psychiatric disorder(s)
- Impaired renal and/or hepatic function
- Severe cardiopulmonary dysfunction
- Active cancer w/ or w/o metastases within past 5 years

Donor Screening

- Allograft recovery
  - Wrap in sterile gauze
  - Ice (~ 4 degrees)
  - Infuse with University of Wisconsin solution

Hand Allograft Rejection

- Hyperacute Rejection
  - Occurs w/in seconds to minutes
  - Eliminated by pre-op screening
  - anti-ABO
  - negative cross-match

- Acute (Immediate) Rejection
  - 86% have at least one episode
  - Most T-cell mediated
  - Dermatitis or edema
  - Treat with steroids, increased immunosuppression, photopheresis, etc.

- Chronic Rejection
  - Most common cause of rejection in solid organ transplant
  - No cases of graft-vs-host disease in CTA
Maintenance Protocol

- Most common combination:
  - Tacrolimus, MMF, and corticosteroids

- Antibiotics:
  - IV broad spectrum antibiotics and antivirals (+/- antifungals) given perioperatively
  - Oral antibiotics for ~18 months

Rehabilitation

- Begins pre-operatively
- Dynamic/static casting or bracing
- Scar management
- Electrical muscular stimulation for improved tendon gliding

Complications

- Systemic/Vascular complications
  - Partial skin necrosis
  - Arterial thrombosis
  - A-V fistulas
  - Chronic headaches
  - Serum sickness
  - Ulnar artery thrombosis

- Infections
  - CMV reactivation
  - Papilloma virus
  - C. difficile
  - Ulnar osteomyelitis

- Metabolic complications
  - Cushion syndrome
  - Weight gain
  - Hyperglycemia
  - Renal insufficiency
  - Dermatitis
  - Hip AVN

Results at 15 years

- 85% have had episode of acute rejection within 1st year
- All resolved with immunosuppressive boost therapy
- 96% of transplants have survived
- Failures due almost exclusively to medical noncompliance
- Early post-transplant infection risk reported to be 11% (primarily hospital acquired organisms)
- Time window not yet sufficient to comment on downstream malignancies
- Minimal reported long-term endocrine derangement

Functional Recovery

**TABLE 8. Independent Functional Assessment of Eleven Hand Transplants**

<table>
<thead>
<tr>
<th>Motor/Sensory Function</th>
<th>Range of Motion (ROM)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wrist extension</td>
<td>40 degrees</td>
</tr>
<tr>
<td>Wrist flexion</td>
<td>33 degrees</td>
</tr>
<tr>
<td>Total finger flexion</td>
<td>174 degrees</td>
</tr>
<tr>
<td>Finger extension lag</td>
<td>35 degrees</td>
</tr>
<tr>
<td>Pulp-to-distal palmer crease</td>
<td>3.7 cm</td>
</tr>
<tr>
<td>Digital localization</td>
<td>6/10</td>
</tr>
<tr>
<td>Two-point discrimination</td>
<td>&gt;15 mm, 8/10HTs</td>
</tr>
</tbody>
</table>

Back to Work

- 8 of 9 returned to work one year post-transplant
- 9 of 11 returned to modified job tasks

Satisfaction

- Satisfied: 4/11
- Less function than hoped for: 4/11
- Medication side effects: 3/11
- Prolonged rehab: 2/11
- Unsatisfied: 1/11


The Science of Modalities

Roy A. Meals, MD

People instinctively accept information to which they are exposed and must work actively to resist believing falsehoods. They tend to think that familiar information is true. They cherry-pick data to support their existing views. Humans have a tendency to steer clear of facts that would force their brains to work harder.

Therapeutic Modalities to Discuss

- heat
  - superficial
  - deep (including phonophoresis)
- cold
- electricity
  - tens, fes, iontophoresis
- magnets
- low level laser

Heat: Basic Science

Rat Tail Collagen Studies

- at normal temperatures, collagen is elastic
- at 41-45°C, collagen becomes viscous, plastic
- stress results in permanent elongation
- “therapeutic tissue temperature”
- 20% reduction in stiffness at 45°C
- increased stiffness with cooling

Effects of Heat

- proven: increases collagen extensibility at 41-45°C (“therapeutic tissue temperature”)
- generally agreed:
  - decreases joint stiffness
  - relaxes muscles
  - dilates blood vessels
  - reduces ischemia and ischemic pain
  - releases endorphins (feels good!)
  - flushes pain mediators (histamine, prostaglandins)
  - alters membrane permeability
  - decreased edema relieves stretch-related pain
Heat Modalities

- differ in pattern, rate, depth
  - superficial heat (best for ≤ 2 cm deep)
    - conduction: packs, pads, paraffin
    - convection: fluidotherapy, hydrotherapy
    - radiation: infrared heat lamp
  - deep heat: ultrasound, microwave, shortwave
  - US best: depth, safety, ease, effectiveness

Superficial Heat

The Science in the Books

Original Paper
the beginning temperature for studied tissues was 33-34°C, therefore

- at 5 mm deep in hand
  - 6°C increase in joint capsule (34°C → 40°C)
  - 4°C increase in muscle (34°C → 38°C)
- at 20 mm deep in hand
  - 1°C increase (34°C → 35°C)

Conclusion: superficial heat does not bring hand tissues into therapeutic tissue temperature range.

Deep Heat: Ultrasound

- acoustic energy
  - audible sound 30-20,000 Hz (aka cycles/sec)
  - therapeutic ultrasound .5 - 3 million Hz
- dose determination difficult
  - power settings and timers often inaccurate
  - affected by coupling medium
  - patient feedback inadequate
  - deep tissues lack temperature receptors
Ultrasound Variability

• beam orientation
  • muscle fibers parallel to beam receive 4x energy of those perpendicular to beam
• lower frequencies penetrate deeper
• higher frequencies spread out less
• heat production tissue dependent
  • for instance cancellous bone > joint capsule
• tissue interfaces are heated more than tissues

Ultrasound: Non-Thermal Effects

• beneficial effect?
  • high frequency "massage"
• detrimental effects (causing cell membrane and metabolic damage) (echo analogies)
  • cavitation (bubbles)
• streaming: fluid flow from high to low pressure areas
• standing waves: result in local hot spots

Ultrasound: The Science

• most reports have flawed methodology
  • placebo effect, uncontrolled variables, faulty/absent controls
• meta-analyses conclude principal effect from concomitant exercise regimen
• randomized, double-blinded, placebo-controlled study for pain control (Faulkoner): no difference
• low-intensity ultrasound hastens fracture/tendon healing
  This frequency not possible with OT/PT machines

Ultrasound + Drug = Phonophoresis

• common medications: corticosteroids, salicylates, local anesthetics
• potential advantages
  • avoid injection
  • adjust dosage during treatment
• avoid degradation of oral meds by GI tract, liver
  • provide local and systemic effects
• most basic research focuses on non-human living studies or cadaver skin

Phonophoresis

Ideal  Theoretical  Actual

target  target  target

capillary circulation

The Best Science Available!
Physical Therapy, 75:539-553, 1995

Summary: "... Most studies documented that phonophoresis was associated with an increase in drug diffusion at the subcutaneous level. There were inconsistent findings for successful drug delivery beyond the subcutaneous level. Most studies did not find increased penetration at the level of the muscle or the joint."
Well-Known Effects of Cold

• beneficial
  • reduces muscle spasticity and tone
  • increases muscle strength/endurance
  • increases pain threshold
    • diminished nerve function, muscle relaxation, counterirritation?
  • detrimental
    • increased vasoconstriction/reduces edema

Cold Therapy
The Science for Pain Control

• 15 prospective, randomized, controlled studies for post-surgical pain 1993-97 (Bissell)
  • 7 showed no benefit
  • 3 showed some benefit
  • 5 showed substantial benefit

• literature probably biased in favor of reporting positive results (publication bias)

Contrast Baths

• Finnish sauna—feels good?
  • Excuse to drink?
• No science to support efficacy
• Rationale for use in hand therapy unclear

Electrical Stimulation

• FES: functional electrical stimulation
• TENS: transcutaneous electrical nerve stimulation
• Iontophoresis

Spinal Anatomy

FES: effective in upper motor neuron diseases because axon is still connected to motor cell body in anterior horn

FES: ineffective in lower motor neuron diseases because axon is disrupted from its cell body
Electricity: FES

- useful in upper motor neuron diseases (stroke, spinal cord injury, etc.)
  - muscle strengthening, re-education, edema reduction
  - great future for implanted neurostimulators
- ineffective in lower motor neuron disease (anterior horn disease (Lou Gerhig), laceration, peripheral neuropathy, etc.)
  - muscle reinnervation not enhanced by FES
  - axon sprouting may be suppressed by FES

Electricity: TENS

- stimulation of large sensory nerve fibers blocks noxious stimuli coming into dorsal root ganglion from small pain fibers
- efficacy generally accepted
- placebo controlled studies impossible
- physiologic tolerance develops

TENS + Drug = Iontophoresis

- electrically-charged molecule (a.k.a. ion) is driven away from electrode of same charge
- effectiveness related to
  - ion size and charge, concentration of substance
  - current density, duration of treatment
- skin (stratum corneum layer) is dense barrier
- effect related to medication or to TENS?
- good studies are sparse

Iontophoresis: Think about it!!

Ionto-driven medications are absorbed in dermal capillaries and circulated systemically rather than sent to the targeted tissue

Magnetic Field Therapy

- touted benefits
  - increase blood flow
  - why then no erythema?
  - iron in hemaglobin unaffected by magnets
  - ease pain
  - blinded studies difficult
Magnetic Field Therapy

• static fields
  • difficult to compare strength, frequency, and application mode of magnetic fields in different studies
  • study results mixed
• pulsed fields
  • sets up electric current in tissues—tried for bone healing (mimicking piezoelectric forces)
  • study results mixed

Therapeutic magnets too weak to penetrate skin
Paracelsus (1493-1541) used lode stones
Thin, flexible magnets into clothing, mattresses
With magnets it is difficult to do a blind study
One good study does not clear up the question
Therapeutic magnets ~600 Gauss, refrigerator magnets ~300 Gauss

Low-Level Laser/Cold Laser

“available literature not supportive, at best palliative; data are inconsistent/conflicting”

Comparison of splinting and splinting plus low-level laser therapy in idiopathic carpal tunnel syndrome. Clin Rheumatol 2009


Effects of low-level laser therapy on proliferation and differentiation of mesenchyme bone marrow cells into osteoblasts and osteoclasts. Lasers Surg Med, 2009


Beware: high risk of publication bias!

Therapeutic Modalities


Key Points: Heat and Cold

• heat clearly makes joints and other tissues more supple
• unlikely that heated tissues ever reach "therapeutic range" for plasticity of collagen
• no good science for cold or contrast baths
• ultrasound and phonophoresis
  • no good science
  • local tissue concentrations of drugs? doubtful
  • potentially damaging non-thermal effects


http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3445200/
Key Points: Electricity/Magnetism/Light

- TENS: it works!!!
- FES: it works for upper motor neuron diseases
- Iontophoresis
  - no good science
  - local tissue concentrations? doubtful
- Magnets: unlikely
- Cold laser: I’m doubtful

Tissue Engineering
Prosper Benhaim, MD

Tissue Disturbances

- Congenital malformation, absence
- Aging, atrophy
- Tumor excision
- Trauma
- Impaired wound healing

Incidence of Tissue Loss or Organ Deficiency

<table>
<thead>
<tr>
<th>Tissue</th>
<th>Proc/Yr</th>
</tr>
</thead>
<tbody>
<tr>
<td>Skin</td>
<td>2,750,000</td>
</tr>
<tr>
<td>Bone</td>
<td>1,343,000</td>
</tr>
<tr>
<td>Cart/ten/lig</td>
<td>1,253,000</td>
</tr>
<tr>
<td>Vessels</td>
<td>1,360,000</td>
</tr>
<tr>
<td>Liver</td>
<td>205,000</td>
</tr>
<tr>
<td>Pancreas</td>
<td>728,000</td>
</tr>
<tr>
<td>Intestine</td>
<td>100,000</td>
</tr>
<tr>
<td>Kidney</td>
<td>600,000</td>
</tr>
<tr>
<td>Neuromus.</td>
<td>200,000</td>
</tr>
<tr>
<td>Hernia</td>
<td>290,000</td>
</tr>
<tr>
<td>Breast</td>
<td>261,000</td>
</tr>
<tr>
<td>GU</td>
<td>139,000</td>
</tr>
</tbody>
</table>

Evolution of Surgical Treatment

- Excision/ablation of diseased/injured tissue
- Reconstruction of structural defects
- Replacement/transplantation of missing or deficient parts
- Induction or regeneration of missing or deficient parts

Options for Reconstruction

- Primary healing
- Autologous tissue transplantation
- Allogenic tissue transplantation
- Biomaterials
- Tissue induction/engineering
TISSUE ENGINEERING
Definition
- Manipulation of a cell’s or group of cells’ genome or environment
- Manufacturing or induction of the growth of a ‘tissue construct’
- Correction of pathologic process or functional deficit

Engineered Tissue Components
- Cells: (e.g. Epicel)
- Scaffold/matrix
  - Biologic, synthetic, hybrid
  - Optimized cell/scaffold combination (e.g. Integra)
- Bioreactive factors
  - Proteins: bFGF, TGFβ, IGF, KGF, etc. (e.g. Regranex)
  - Cytokines, hormones
  - Transcriptional control factors
- Host integration
  - Vasculogenesis (VEGF)
  - Biomechanical stability
- Flap prefabrication and prelamination

General Process of Tissue Regeneration/Engineering

Gene Therapy
- Transfer of a particular gene into a cell so that the cell transcribes the gene into messenger ribonucleic acid (mRNA)
- The cell’s ribosomes then translate the mRNA into a protein (cytokine)
- Often uses a viral vector (FDA and safety issues)

Cells for Tissue Engineering
- fully differentiated cells (skin, bone, cartilage)
- progenitor cells
- stem cells
  - autologous (sparse but no immunity problems)
  - human embryos (controversial, immunity problems)

Autologous Stem Cells: Problems
- not isolated for all tissues
- present in minute quantities
- numbers may decrease with age
- difficult to isolate and purify
Mesenchymal Stem Cells

- expand in tissue culture
- possibly modify gene to produce specific protein or tissue type
- seed onto matrix
- implant to correct defect

Matrix/Scaffold Considerations

- structurally sound
- biodegradable
- permeable

Scaffolds

<table>
<thead>
<tr>
<th>Scaffold type</th>
<th>Advantages</th>
<th>Disadvantages</th>
</tr>
</thead>
<tbody>
<tr>
<td>host tissue</td>
<td>no foreign body</td>
<td>donor site morbidity</td>
</tr>
<tr>
<td>(meniscus, muscle)</td>
<td>responsive cells</td>
<td>limited quantity</td>
</tr>
<tr>
<td>natural polymers</td>
<td>remodeling potential</td>
<td>purity?</td>
</tr>
<tr>
<td>(collagen, hyaluronate)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>synthetic polymers</td>
<td>mass production</td>
<td>foreign body, infection</td>
</tr>
<tr>
<td>(PLA, PGA)</td>
<td>custom-designed</td>
<td>inflammatory reaction?</td>
</tr>
</tbody>
</table>

Currently Available Tissue Engineered Products

- cartilage for knee defects
- Autologous Chondrocyte Implantation
- skin for burns, pressure sores

Adipose or Muscle Derived Stem Cells

- Fat
- Bone
- Cartilage
- Nerve
- Muscle

Engineered Musculoskeletal Products on Horizon

- ligaments
- vascularized bone
- vertebral disc
- digital joint
- tendons
- vessels
Engineered Bone with Blood Supply

- bone mesenchymal cells
- placed on collagen sponge
- wrapped around artery and vein
- covered with membrane

Engineered Bone in Rat Model

Key Points

- Tissue engineering has vast potential
- Use fully differentiated cells, progenitor cells, stem cells
- Matrix considerations and vascularity are major

Accessing Valid Information On-Line for Professionals and Patients


TIP: Always take a few minutes to review the site before accessing any health-related information other than original journal articles.

Key points:
- How do they know? Are there alternative explanations?
- Commercial interest?

Referred journal article sources

- www.pubmed.org: can purchase articles through loansome doc; $11 per article (cheapest available)
- www.emedicine.com: abstracts are free
- www.cochrane.org: abstracts are free
- www.amedicine.com: full text articles up to 90 days old

Information for patients and families

- www.webmd.com: info for patients, sources cited, reviewed by MD cited
- www.orthoinfo.aaos.org: American Academy of Orthopedic Surgeons
- www.nih.gov: National Institutes of Health
- www.nih.gov: links to many other sites
- www.amedicine.com: useful for fact checking, authors may have an agenda

Cancer

- www.cancer.gov: National Cancer Institute
- www.cancer.gov: Congenital differences, support groups

- www.nlm.nih.gov: links to various other sites—good for patients

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