## Keloid Pathogenesis and Treatment

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<table>
<thead>
<tr>
<th>Keloid</th>
<th>Hypertrophic scar</th>
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<tbody>
<tr>
<td>Scar</td>
<td>Invade adjacent normal dermis</td>
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<tr>
<td>Arising</td>
<td>Appear later following the initial scar and then gradually proliferate indefinitely</td>
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<tr>
<td>Fibroblast density</td>
<td>Increased</td>
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<tr>
<td>Fibroblast proliferation rate</td>
<td>Increased</td>
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<tr>
<td>Collagen fiber</td>
<td>Enlarge, thick and wavy than Random orientation mRNA not increased</td>
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<tr>
<td></td>
<td>Increased ratio of type I to type II Collagen</td>
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### Pathogenesis of Keloids

**Altered Growth Factor Milieu**
- Growth factor difference: TGF-β, Plateletes derive growth factor
- Extracellular Matrix Difference: Fibronectin, hyaluronic acid, biglycan.

**Collagen Turnover Hypothesis**
- Collagen produced by mainly fobroblast and endothelial
- Collagen degraded by collagenase produced in fibroblast and inflammatory cell

**Tension Hypothesis**
- Stretch and tension promote collagen production and dictate collagen architecture, orientation and effect of dermal remoldering
- Incisions created parallel to skin tension line rarely form abnormal scar.
- Stretch and tension play a more dominant role in the pathogenesis of hypertrophic scar than keloid formation

**Genetic Immune Hypothesis**

**Sebum Reaction Hypothesis** Keliod could arise from an immune reaction to sebum
Treatment strategies

Steroids
   Triamcinolone
      Inhibit proliferation of normal and keloid fibroblasts
      Inhibit collagen synthesis
      Increase collagenase activity production
      Reduce level of collagenase inhibitors
   Adverse effects
      Subcutaneous atrophy, telangiectasia, pigmented changes (50%)
      Frequently resolve without intervention
      Cushing’s syndrome rarely cases have been reported.
      usually not occur in IL injection of TA

Surgery
   Recurrence rate  40 to 100%
   Subtotal excision along with lateral undermining has been credited with improved outcome
   and fewer recurrences

Radiation
   Its use has been limited by the theoretical risk of inducing malignancy.
   Efficacy rate 65 to 99%
   Radiation therapy is generally administered immediately after keloid excision, using
   fractionated therapy with a total dose of 10 to 15 Gy
   Radiation of keloid damages the fibroblast directly and effects collagen structure and
   Organization

Silicone gel
   The clinical effects of silicone gel
      1. to be mediated by changes in pressure
      2. changes in temperature
      3. changes in oxygenation of the keloids
      4. entry in to the dermis
      5. keeps the skin hydrated
   Needs active compliance from the patient, long term application
   Special challenging on mobile and angled anatomical site

Pressure
   Adjuvant post-operative pressure reduced recurrence rates of keloids excised from various
   part of the body from 67 to 18 %
   Some of therapeutic benefit of pressure therapy might be a result of altered wound tension
   Pressure induced ischemia and promotes collagen degradation and , modulates
   fibroblast activity

Laser
   Laser therapy has been advocated but has not been shown to be effective in keloid
   management, and over 50% recurrence rate
   No advantage over scalpel excision
5 Fluorouracil

Intralesional 5 FU is an experiment therapy of keloids that has been shown some potential in preliminary trials.

5 FU is an antimetabolite inhibit fibroblast proliferation and modestly improve keloidal scarring.

5 FU 50mg/ml injected 0.05 ml/ linear centimeter or until blanching appeared and every 3 weeks upto 10 times.

Excision wounds were exposed to a pledget soaked with 5 FU (50mg/ml) for 5 minutes then closed.

Adverse effects have been rare and include superficial skin irritation without any discernible hematologic change.

Interferon

IL interferon is an experimental therapy with considerable systemic adverse effects.

Its efficacy has not been demonstrated.

Retinoid

An experimental therapy have produced responses in limited clinical trials, but there has not been no general acceptance in clinical practice.

Retinoid enhance epidermal proliferation while inhibiting of fibroblasts and shift the healing process to normal regeneration.

Retinoids also suppress sebum production. (role in keloid pathogenesis)

Adverse effects: photosensitivity

Skin irritation in 50%

Slight skin atrophy in 10% of patient.

Combination therapy

The most effective management of keloids use combination therapy, generally excision with adjuvant therapy

Cure rate exceed 80%

Surgery + steroid

Surgery + silicone gel

Surgery + radiation 65 to 99%

Conclusion

No ideal therapy exists for keloids, reflecting our poor understanding of keloid pathogenesis. Combined treatment appear to decrease recurrence rate as compared with monotherapy. An oral adjuvant therapy (antihistamine, colchicines) to modify host response may improve outcomes.

Ideally, a regimen of surgical excision minimizing tissue trauma, inflammation, and tension could be combined with an injectable modulator, steroids, and 5 FU, external beam radiation when applicable, and hydrating pressure dressing to address the cellular mechanism.