

### 3. Keloid

Keloids are benign hyperproliferations of dense connective tissue covered by thin epidermis.<sup>1</sup> Their formation is attributed to abnormal cutaneous wound healing after injury or inflammation. They are distinct from hypertrophic scars in 2 important ways: keloids extend beyond the borders of the original wound or inflammatory process and do not regress spontaneously.<sup>1,2</sup> They present as firm nodules that are either skin-coloured or erythematous, with telangiectases.<sup>1</sup> In addition to cosmetic concerns, keloids can also be painful and pruritic.<sup>3</sup> Keloids might impose psychosocial burdens on the patient and, depending on their location, might also cause functional limitations.<sup>1</sup>

Keloids most commonly appear on the chest, shoulders, upper back, back of the neck, and earlobes.<sup>4</sup> Keloids have also been reported in other locations, such as the genitals.<sup>5-7</sup> Needles do not commonly cause keloids unless the injection stimulates an inflammatory reaction, as in the case of the bacille Calmette-Guérin vaccine.<sup>1,8</sup> Keloids can develop up to 1 year after resolution of the initial injury.<sup>9</sup> Although keloid recurrence is more likely in areas of higher stretch tension, such as the chest wall and the scapular and suprapubic regions,<sup>10</sup> the earlobes, an area of low tension, are a common site for keloid development.<sup>1</sup> Keloids are more prevalent among people of African, Hispanic, and Asian descent,<sup>4</sup> with higher incidence during pregnancy and puberty.<sup>1</sup> While keloids might be slightly more common in women, this is likely attributable to the fact that women are more likely to pierce their earlobes.<sup>11</sup>

The etiology of keloids is believed to involve environmental and genetic factors. Studies of families that show a propensity toward keloid formation have suggested that a degree of genetic susceptibility might exist<sup>12</sup>; however, specific susceptibility genes have not yet been identified.<sup>1</sup> This has raised the possibility of genetic heterogeneity, in which different genes contribute to the formation of keloids in different families.<sup>1</sup> Histologically, keloids contain excess extracellular matrix, particularly glycosaminoglycans and collagen.<sup>13</sup> The collagen of keloidal tissue is arranged in whorls,<sup>8</sup> whereas the collagen of normal tissue is arranged in a regular pattern parallel to the epidermis.<sup>1</sup> The production of excess collagen has been attributed to the fibroblasts found within keloidal tissue.<sup>14,15</sup> Compared with the fibroblasts of normal scar tissue, these fibroblasts produce excess amounts of growth factors and have higher numbers of growth factor receptors on their surfaces, lower growth factor requirements in vitro, lower rates of apoptosis, and lower levels of apoptosis-related genes.<sup>15-17</sup> This causes the tightly regulated process of wound healing to go awry and ultimately leads to keloid formation.<sup>1</sup>



### Prevention

Prevention of keloids is an important consideration. Risk factors include previous keloids, positive family history of keloids, tension at the site of trauma, and dark skin.<sup>11</sup> It is recommended that patients with these risk factors avoid body-piercings and unnecessary or elective surgeries in order to reduce the likelihood of keloid formation over the scar.<sup>1</sup> Postoperatively, the application of a silicone or non-silicone gel patch for 12 hours a day for at least 1 month might decrease the likelihood of keloid formation.<sup>18-20</sup>

### Treatment

While treating keloids is challenging, a number of treatment modalities have been developed. These include intralesional steroid injections (ISIs), surgical excision, cryotherapy, radiotherapy, laser treatment, silicone gel treatment, and immune-response modifiers and anti-metabolites. Combining 2 or more of these modalities is advantageous.<sup>1</sup> Examples are discussed below.

**Intralesional steroid injections.** Intralesional steroid injections flatten, soften, and reduce the symptoms of the keloid, but rarely cause the keloid to resolve completely.<sup>1</sup> Triamcinolone acetonide is a glucocorticoid that is often the agent of choice, and is injected at concentrations of 10 to 40 mg/mL based on the size of the keloid. The injections must be repeated several times, with 4- to 6-week intervals between administrations.<sup>1</sup> While ISI is easy to use, well-tolerated, and effective, the side effects include telangiectases,<sup>1</sup> skin atrophy,<sup>2</sup> and hyperpigmentation or hypopigmentation.<sup>1</sup> Cushing syndrome<sup>21</sup> and anaphylaxis<sup>22</sup> secondary to ISI have been reported. A local anesthetic can be employed to alleviate the injection-associated pain.<sup>1,11</sup> Intralesional steroid injections are often used in combination with other treatments, such as surgical excision, occlusion therapy, cryotherapy,<sup>23</sup> or laser therapy.<sup>24-26</sup> The latter 2 modalities help soften the keloid to make ISI administration easier.<sup>27</sup> Surgical excision is not recommended as a stand-alone therapy owing to the high associated recurrence rates.<sup>27</sup>

**Cryotherapy.** Cryotherapy can be used to treat small keloids<sup>27</sup> and has been shown to have a synergistic effect when used in combination with triamcinolone acetonide ISI.<sup>23</sup> Multiple treatments are needed<sup>28</sup> and a 15- to 30-second freeze-thaw cycle is typically employed.<sup>27</sup> The associated pain can be prevented with local anesthetic. Darker-skinned individuals might experience depigmentation; in such cases cryotherapy should generally be avoided.<sup>28</sup>

**Radiotherapy.** This treatment modality is especially effective when used immediately after surgical excision of the keloid.<sup>29</sup> Several techniques are used, including superficial x-ray therapy, an electron beam, and low- or high-dose-rate brachytherapy.<sup>1</sup> Owing to the risk of carcinogenesis, radiotherapy for keloids should be undertaken with caution in patients younger than 21 years of age.<sup>1</sup>

**Laser therapy.** While earlier attempts to use lasers produced unacceptably high recurrence rates, the 585-nm pulsed-dye laser has shown more promise.<sup>24</sup> In some cases, it is used to soften the keloid in preparation for ISI<sup>25,26</sup> or, more commonly, used afterward to deal with residual erythema.

**Silicone gel dressings.** These should be applied immediately after surgical excision and worn for 12 hours a day for at least a month. The dressings occlude and hydrate the scar and appear to be somewhat beneficial in preventing keloid recurrences.<sup>9,30</sup>

Other treatments that are still under investigation include an immune response modifier (ie, imiquimod) and 2 antimetabolites (ie, 5-fluorouracil and bleomycin). Two small studies used imiquimod after surgical excision of a keloid and reported low recurrence rates over a 24-week follow-up period.<sup>31,32</sup> Antimetabolites are administered intralesionally and have also shown varying levels of efficacy in small trials,<sup>33-35</sup> although they have yet to be investigated with larger randomized controlled trials.

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#### Competing interests

None declared

#### References

- Robles DT, Berg D. Abnormal wound healing: keloids. *Clin Dermatol* 2007;25(1):26-32.
- Griffith HB. The treatment of keloids with triamcinolone acetonide. *Plast Reconstr Surg* 1966;83(3):202-8.
- Lee SS, Yosipovitch G, Chan YH, Goh CL. Pruritus, pain, and small nerve fiber function in keloids: a controlled study. *J Am Acad Dermatol* 2004;51(6):1002-6.
- Bayat A, Arscott G, Ollier WE, Ferguson MW, Mc Grouther DA. Description of site-specific morphology of keloid phenotypes in an Afrocaribbean population. *Br J Plast Surg* 2004;57(2):122-33.
- Gürnlüoğlu R, Bayramiçi M, Numanoglu A. Two patients with penile keloids: a review of the literature. *Ann Plast Surg* 1997;39(6):662-5.
- Gürnlüoğlu R, Dogan T, Numanoglu A. A case of giant keloid in the female genitalia. *Plast Reconstr Surg* 1999;104(2):594.

- Mastrolorenzo A, Rapaccini AL, Tiradritti L, Zuccati G. A curious keloid of the penis. *Acta Derm Venereol* 2003;83(5):384-5.
- Lee JY, Yang CC, Chao SC, Wong TW. Histopathological differential diagnosis of keloid and hypertrophic scar. *Am J Dermatopathol* 2004;26(5):379-84.
- Brissett AE, Sherris DA. Scar contractures, hypertrophic scars, and keloids. *Facial Plast Surg* 2001;17(4):263-72.
- Ogawa R, Mitsuhashi K, Hyakusoku H, Miyashita T. Postoperative electron beam irradiation therapy for keloids and hypertrophic scars: retrospective study of 147 cases followed for more than 18 months. *Plast Reconstr Surg* 2003;111(2):547-53.
- Kelly AP. Medical and surgical therapies for keloids. *Dermatol Ther* 2004;17(2):212-8.
- Mameros AG, Norris JE, Olsen BR, Reichenberger E. Clinical genetics of familial keloids. *Arch Dermatol* 2001;137(11):1429-34.
- Berman B, Flores F. The treatment of hypertrophic scars and keloids. *Eur J Dermatol* 1998;8(8):591-5.
- Fujiwara M, Muragaki Y, Ooshima A. Keloid-derived fibroblasts show increased secretion of factors involved in collagen turnover and depend on matrix metalloproteinase for migration. *Br J Dermatol* 2005;153(2):295-300.
- Mameros AG, Krieg T. Keloids—clinical diagnosis, pathogenesis, and treatment options. *J Dtsch Dermatol Ges* 2004;2(11):905-13.
- Messadi DV, Le A, Berg S, Huang G, Zhuang W, Bertolami CN. Effect of TGF-beta 1 on PDGF receptors expression in human scar fibroblasts. *Front Biosci* 1998;3:a16-22.
- Sayah DN, Soo C, Shaw WW, Watson J, Messadi D, Longaker MT, et al. Downregulation of apoptosis-related genes in keloid tissues. *J Surg Res* 1999;87(2):209-16.
- Mustoe TA, Cooter RD, Gold MH, Hobbs FD, Ramelet AA, Shakespeare PG, et al. International clinical recommendations on scar management. *Plast Reconstr Surg* 2002;110(2):560-71.
- De Oliveira GV, Nunes TA, Magna LA, Cintra ML, Kitten GT, Zarpellon S, et al. Silicone versus nonsilicone gel dressings: a controlled trial. *Dermatol Surg* 2001;27(6):721-6.
- Chang CW, Ries WR. Nonoperative techniques for scar management and revision. *Facial Plast Surg* 2001;17(4):283-8.
- Liu MF, Yencha M. Cushing's syndrome secondary to intralesional steroid injections of multiple keloid scars. *Otolaryngol Head Neck Surg* 2006;135(6):960-1.
- De Souza BA, Bantick G. Anaphylactic reaction to intralesional steroid injection. *Plast Reconstr Surg* 2006;117(1):336.
- Sharma S, Bhanot A, Kaur A, Dewan SP. Role of liquid nitrogen alone compared with combination of liquid nitrogen and intralesional triamcinolone acetonide in treatment of small keloids. *J Cosmet Dermatol* 2007;6(4):258-61.
- Alster TS, Williams CM. Treatment of keloid sternotomy scars with 585 nm flashlamp-pumped pulsed dye laser. *Lancet* 1995;345(8959):1198-200.
- Kumar K, Kapoor BS, Rai P, Shukla HS. In-situ irradiation of keloid scars with Nd:YAG laser. *J Wound Care* 2000;9(5):213-5.
- Manuskiatti W, Fitzpatrick RE. Treatment response of keloidal and hypertrophic sternotomy scars: comparison among intralesional corticosteroid, 5-fluorouracil, and 585-nm flashlamp-pumped pulsed-dye laser treatments. *Arch Dermatol* 2002;138(9):1149-55.
- Mutalik S. Treatment of keloids and hypertrophic scars. *Indian J Dermatol Venereol Leprol* 2005;71(1):3-8.
- Har-Shai Y, Amar M, Sabo E. Intralesional cryotherapy for enhancing the involution of hypertrophic scars and keloids. *Plast Reconstr Surg* 2003;111(6):1841-52.
- Ragoowansi R, Comes PG, Moss AL, Glees JP. Treatment of keloids by surgical excision and immediate postoperative single-fraction radiotherapy. *Plast Reconstr Surg* 2003;111(6):1853-9.
- Borgognoni L. Biological effects of silicone gel sheeting. *Wound Repair Regen* 2002;10(2):118-21.
- Berman B, Kaufman J. Pilot study of the effect of postoperative imiquimod 5% cream on the recurrence rate of excised keloids. *J Am Acad Dermatol* 2002;47(4 Suppl):S209-11.
- Berman B, Villa A. Imiquimod 5% cream for keloid management. *Dermatol Surg* 2003;29(10):1050-1.
- España A, Solano T, Quintanilla E. Bleomycin in the treatment of keloids and hypertrophic scars by multiple needle punctures. *Dermatol Surg* 2001;27(1):23-7.
- Gupta S, Kalra A. Efficacy and safety of intralesional 5-fluorouracil in the treatment of keloids. *Dermatology* 2002;204(2):130-2.
- Saray Y, Güleç AT. Treatment of keloids and hypertrophic scars with dermojet injections of bleomycin: a preliminary study. *Int J Dermatol* 2005;44(9):777-84.

