

Welcome to the JCAD Aesthetic Complications Guidelines by The Aesthetic Complications Expert (ACE) Group. The ACE Group developed a series of evidence-based, peer-reviewed guidelines that cover complications that can occur in nonsurgical aesthetic practices. The objective of this series is to help dermatologists and other physicians performing aesthetic procedures identify and manage these potential complications. Each guideline was produced after a vast literature review by leading experts in the United Kingdom. We hope these guidelines help raise treatment standards within the medical community and ensure early diagnosis and appropriate management of complications, ultimately improving outcomes for our patients.

This month's guideline:

## Management of Necrosis

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### BACKGROUND

Necrosis is defined as “the death of most or all of the cells in an organ or tissue due to disease, injury, or failure of the blood supply.”<sup>1</sup> Unlike normal cell death, which is a programmed and ordered phenomenon, necrosis is the accidental death of the cell, which can be caused by various mechanisms, such as an insufficient supply of oxygen, thermal or mechanical trauma, or irradiation. Cells that are undergoing necrosis swell and then burst (cytolysis), releasing their contents into the surrounding area. This results in a locally triggered inflammatory reaction characterized by swelling, pain, heat, and redness. The necrotic cells are subsequently phagocytosed and removed by the immune system.

Necrosis is one of the most severe and feared early occurring complications in aesthetic treatments, and can be caused by interruption of the vascular supply, compression of the area around a vessel, obstruction of a vessel with foreign material, and/or direct tissue damage

due to physical, chemical, radiation or laser properties.<sup>2</sup>

### INCIDENCE

Although necrosis can occur during or following many aesthetic treatments, it is most commonly associated with the injection of dermal fillers, including collagen, hyaluronic acid, calcium hydroxylapatite, polymethylmethacrylate beads (PMMA), and fat.<sup>4</sup> The incidence of necrosis related to the injection of collagen has been reported in 9 of every 100,000 cases, and 50 percent of these were in the glabellar region,<sup>3</sup> and in 1 out of every 100,000 cases using other fillers.<sup>5</sup>

Necrosis occurs as a result of injection of all types of dermal filler,

### SIGNS AND SYMPTOMS OF NECROSIS

While many cases of impending necrosis occur immediately following injection, there are several published papers describing delayed necrosis.<sup>5,6</sup> Delayed necrosis is thought to be

caused by compression of a vessel following hyaluronic acid injection, as the filler's hydrophilic properties can cause increased swelling post-treatment. There is also some evidence that delayed necrosis might be due to intra-arterial injection, which can lead to embolism and a subsequent nidus for platelet aggregation with subsequent occlusion in a terminal branch.

**Pain.**<sup>2,3,5,6,7</sup> Severe pain is usually experienced by the patient when necrosis ensues. If local anaesthetic has been used, (topically, as a nerve block, or administered with the product), this symptom can be lessened.

Severe pain is not a reported effect of dermal filler treatments. If a patient complains of severe pain during treatment or during the subsequent hours after treatment, this should alert the practitioner of the risk of impending necrosis and warrant an urgent review.

**Prolonged blanching.**<sup>2,3,5,7</sup> When the vasculature is affected, the area will often initially look very pale, white, or dusky due to

the reduction in blood supply. This color will remain after removal of the needle. The pattern of the blanching is often described as reticulated or irregular, following the same path as the blood supply that has been restricted. This blanching might not be apparent if adrenaline or certain topical anaesthetics have been used.<sup>6,7</sup>

**Dusky, purple discoloration.**<sup>5,7</sup> This usually occurs several hours after treatment when tissue death has already occurred.

**Coolness.**<sup>7</sup> When the blood supply has been affected, the tissues are not being perfused, so the temperature of the skin will be reduced. This will not be apparent immediately following injection.

## AREAS OF CAUTION

There are two main areas of the face that are vulnerable to necrosis following injection of dermal fillers.

**Glabellar region.** Fifty percent of necrosis cases occur as a result of injection of dermal fillers in the glabellar region due to the poor collateral circulation in this watershed area.<sup>2,3,4,8</sup>

**Nasal tip and alar triangle.** The nasal tip and alar triangle are also commonly affected because blood is supplied to these areas by an end artery with no collateral blood flow. The angular artery turns sharply within the alar triangle and is prone to external compression or inadvertent injection leading to necrosis.<sup>3,4,7</sup>

## MINIMIZING THE RISK OF NECROSIS

Clinicians should do the following to minimize risk of necrosis:

1. Have a strong understanding of the anatomy of the area being treated.<sup>7,9</sup>
2. Perform aspiration prior to injection in order to ensure that the injection is not intravascular, although beware, as aspiration might not always be possible, even if the needle tip is within a vessel.<sup>5,7,8,10</sup>
3. Maintain good injection technique with the filler delivered at the appropriate depth and tissue plane.<sup>2,5</sup>
4. Use the smallest possible volume of filler to achieve the desired effect and avoid overfilling the area. If more product is required, a repeat treatment in 7 to 14 days might be safer and more appropriate.<sup>2,7,8</sup>
5. Avoid bolus injections in areas at risk of necrosis.<sup>7</sup>
6. Avoid using products containing adrenaline, as this can mask the blanching produced by occlusion.<sup>6</sup>
7. Be aware that injection of local anaesthetic or lidocaine pre-mixed with a dermal filler might lessen or block any pain experienced from an impending necrosis.
8. Do not inject into the tip of the nose.
9. Use caution when injecting into the glabellar region.<sup>2</sup> Injections should be placed superficially and medially.<sup>8</sup>
10. Be aware that the use of blunt-ended cannulas are less likely to penetrate vessels and lead to an inadvertent intravascular injection.<sup>7</sup>
11. Carefully consider patient selection. Be cautious when treating patients who have undergone rhinoplasty<sup>3</sup> or other surgical procedures, as the anatomy and vasculature might have been altered. Extra caution is required when injecting over existing fillers.
12. Pay attention when injecting—look for warning signs and listen to your patient.
13. Be aware that necrosis is more common when using denser or more permanent fillers.

## TREATMENT OF NECROSIS (FIGURE 1)

Necrosis can result from arterial occlusion by direct injection into an artery or embolization of product, typically presenting immediately with acute pain and blanching. It can also occur due to venous occlusion from external compression of a vessel by dermal filler or subsequent edema and compression, more often with hyaluronic acid fillers. Venous occlusion usually presents later with dull pain and dark discoloration of the skin.<sup>2</sup>

**Immediately stop treatment.**<sup>2-6,8,9</sup> As soon as the practitioner suspects the blood supply has been compromised (marked by pain and blanching in an at-risk area), the most important step is to immediately discontinue injecting any further product and if possible aspirate any product when withdrawing the needle.

**Massage the area.**<sup>2-6,8,11</sup> Massage will help to encourage blood flow and can remove any obstruction caused by dermal filler compressing a vessel. Massage might be required for several minutes.

**Apply heat.**<sup>2-6,8-11</sup> Heat will encourage vasodilatation and increase blood flow to the area.

**Tap the area.** Tapping over an area can dislodge intra-arterial emboli either at the site or further up in the vessel.<sup>10</sup>

**Inject with hyaluronidase.**<sup>2-5,9,10,11</sup> When hyaluronic acid fillers are the culprit of necrosis, injecting with hyaluronidase might relieve the problem before complications even occur (Refer to the Aesthetic Complications Expert Group document on Hyaluronidase). Test patching is not required if hyaluronidase is used for impending necrosis, as the risk of necrosis is generally greater than the risk of anaphylaxis. As with any aesthetic treatments, it is important to have appropriate resuscitation available to deal with any potential complications.<sup>7</sup> Some evidence suggests that using hyaluronidase when a nonhyaluronic acid dermal filler has been injected can lessen the subsequent necrosis.<sup>4</sup> A study conducted by Deok-Woo Kim et al<sup>11</sup> demonstrated significantly reduced areas of necrosis when hyaluronidase was administered within four hours of a hyaluronic acid dermal filler injected into the auricular arteries of rabbits; however no improvements were shown after 24 hours. Hyaluronidase has also been shown to diffuse into the lumen of blood vessels even when injected external to it; for potential cases of necrosis due to intravascular deposition of hyaluronic acid, it is not essential to inject directly into the vessel— injection into the surrounding area is also likely to result in dissolution of the product.

**Apply nitroglycerin paste.**<sup>2-12</sup> Nitroglycerin (glyceryl trinitrate) induces vasodilatation and increases blood flow to the area. Nitroglycerin paste (Rectogesic rectal paste, used off label) can be applied under an occlusive dressing for several days. It is recommended to apply for 12 hours and then remove for 12 hours until clinical improvement is seen<sup>8</sup> or until it is no longer tolerated. Nitroglycerin can lead to skin reactions, irritation, and erythema.

**Aspirin.**<sup>7</sup> One article encouraged the use of aspirin until the necrosis had resolved, in order to limit platelet aggregation, clot formation, and further compromise the area where a blood vessel has already been impeded. The case study recommended

immediate treatment with two 325mg enteric-coated aspirin.<sup>7</sup> However, the evidence for the use of aspirin in cardiovascular disease, which follows a similar mechanism of action, recommends a stat dose of 300mg followed by 75mg a day, when there are no contraindications to the use of aspirin, until the necrosis has resolved.<sup>13</sup>

**Antibiotics.**<sup>2,3</sup> Necrosis consists of dead cells and dead tissue and is prone to secondary opportunistic infection. Depending on the extent of necrosis, topical and/or oral antibiotics might be required to promote healing and to prevent further complications developing. Anti-herpetic medication may be considered if necrosis occurs in a perioral distribution in a susceptible patient.<sup>4</sup>

**Superficial debridement.**<sup>2,3,5,8,9</sup> Referral to a plastic surgeon might be required for removal of dead tissue to promote healing.

**Wound care management.**<sup>3,8</sup> Apply appropriate dressings and perform wound care to encourage healing.

**Refer.** It is always sensible to involve other practitioners who are experienced in the management of necrosis for further advice and/or treatment.

**Speak to your medical defense organization.** Necrosis can cause significant scarring and distress to patients. Practitioners should be prepared for the possibility that a patient will file a malpractice claim.

**Additional recommendations.** Hyperbaric oxygen therapy has been successfully used in nasal tip graftin, following cases of cancer or trauma, with positive results on revascularisation, although there is not enough evidence to recommend this for necrosis secondary to aesthetic procedures.<sup>2,3,14</sup>

The use of low molecular weight heparin<sup>4</sup> has been used to prevent thrombosis and embolisation in one case report,<sup>15</sup> although there is not enough evidence to recommend this as a standard treatment. Oral vasodilators including cGMP-specific phosphodiesterase type 5 (PDE5) inhibitors have also been advised for the treatment of necrosis, but evidence is lacking for their wider use for this indication.<sup>4</sup>

Pain management should be considered when managing necrosis, which can be very painful. While over-the-counter analgesics might be adequate in some cases, opioids might be required in cases of severe pain.

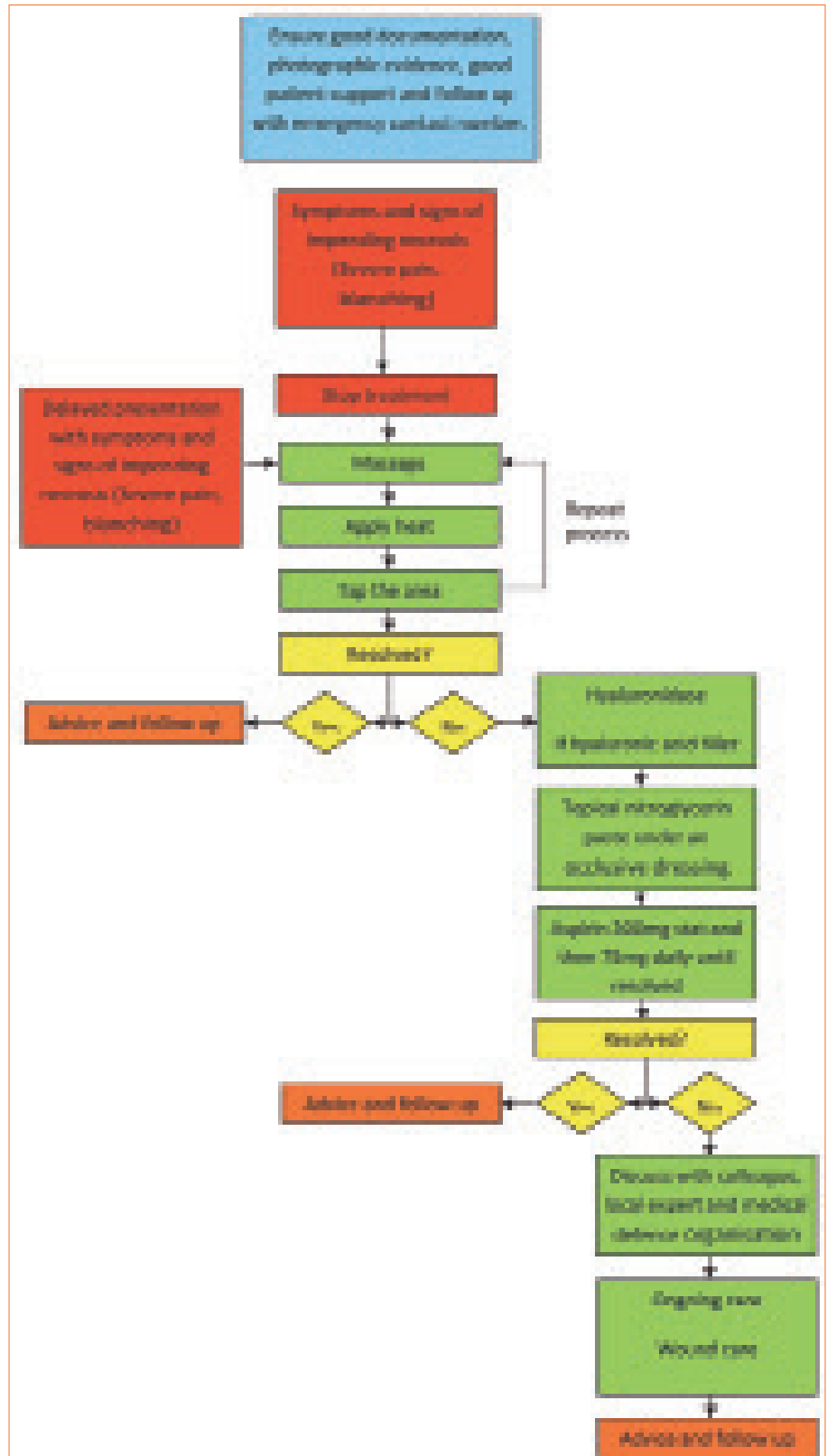


FIGURE 1. Management of necrosis

## MANAGEMENT OF NECROSIS

An Aesthetic Complications Expert (ACE) Group Consensus Paper

### FOLLOW-UP

All patients presenting with necrosis need follow-up until the problem has completely resolved; this should be on a day-by-day basis initially. Immediate follow-up is required when a delayed onset of necrosis is suspected. The Aesthetic Complications Expert Group advocates an emergency telephone number where the practitioner can be contacted after office hours. Good follow-up and patient support are the best approach to preventing a medical malpractice claim.

### NECROSIS CAUSED BY SCLEROTHERAPY

The incidence of necrosis following the injection of sclerosant when treating veins is 1 in 100 to 500 cases,<sup>17</sup> a considerably greater frequency than incidence of necrosis caused by dermal filler treatments. In these cases, necrosis can be mild and result in a small ulcer that completely heals without scarring, or the necrosis can be severe and result in significant tissue death. Necrosis can occur following the inadvertent injection of sclerosant into an artery or arteriole or due to excessive injection pressure leading to retrograde flow of sclerosant into the arterial capillary vasculature (low volume and low pressure are desirable). The type of sclerosant used can have an impact on the incidence of necrosis. Certain sclerosants, such as hypertonic saline, have greater inherent risk, but the proper concentration of product for the size of the vein should also be considered. Certain patients, such as smokers or patients with underlying vasculitis, are at a higher risk for necrosis. The presentation is similar to what has previously been described, and key features

include pain, pale skin, and discoloration within the first 24 hours following treatment. Dermal sloughing occurs 24 to 72 hours after the ischemic event, and an ulcer often subsequently develops.

Treatment is supportive and includes measures to improve perfusion to the area, compression, and occlusive dressings. If wound infection occurs, antibiotics might be required. Appropriate wound management, including superficial debridement, might also be necessary. Once the area has healed, dermal scarring should be addressed. Prognosis is very good when the extent of necrosis is minimal.

### REFERENCES

1. Necrosis. Oxford Dictionaries site. 2016. Oxford University Press. <https://en.oxforddictionaries.com/definition/necrosis>. Accessed 12 July 2018.
2. Sclafani A, Fagien S. Treatment of injectable soft tissue filler complications. *Dermatol Surg*. 2009;35: 1672–1680.
3. Grunebaum L, Allemann I, Dayan S, et al. The risk of alar necrosis associated with dermal filler injection. *Dermatol Surg*. 2009;35:1635–1640.
4. Ozturk CN, Li Y, Tung R, Parker L, Peck Piliang M, Zins JE. Complications following injection of soft-tissue fillers. *Aesthet Surg J*. 33(6):862–877.
5. Tracy L, Ridgway J, Nelson JS, et al. Calcium hydroxylapatite associated soft tissue necrosis: a case report and treatment guideline. *J Plast Reconstr Aesthet Surg*. 2014;67:564–568.
6. Narins RS, Jewell M, Rubin M, et al. Clinical conference: management of rare events following dermal fillers—rocal necrosis and angry red bumps. *Dermatol Surg*. 2006;32: 426–434.
7. DeLorenzi C. Complications of injectable fillers, part 2: vascular complications. *Aesthet Surg J*. 2014;34: 584–600.
8. Glaich AS, Cohen JL, Goldberg LH. Injection necrosis of the glabella: protocol for prevention and treatment after use of dermal fillers. *Dermatol Surg*. 2006;32:276–281.
9. Nettare K, Maas C. Facial filler and neurotoxin complications. *Facial Plast Surg*. 2012;28: 288–293.
10. Cohen JL. Understanding, avoiding, and managing dermal filler complications. *Dermatol Surg*. 2008;34:592–599.
11. Deok-Woo K, Eul-Sik Y, Yi-Hwa J, et al. Vascular complications of hyaluronic acid fillers and the role of hyaluronidase in management. *Plast Reconstr Aesthet Surg*. 2011;64:1590–1595.
12. Kleydman K, Cohen JL, Marmur E. Nitroglycerin: a review of its use in the treatment of vascular occlusion after soft tissue augmentation. *Dermatol Surg*. 2012;38:1889–1897.
13. Antithrombotic therapy: a national clinical guideline. SIGN Guideline No. 36. Scottish Intercollegiate Guidelines Network. March 1999.
14. Impending necrosis after injection of hyaluronic acid and calcium hydroxylapatite fillers: report of 2 cases treated with hyperbaric oxygen therapy. *Dermatol Surg*. 2014; 40:9:1049–1052.
15. Schanz S, Schippert W, Ulmer A, et al. Arterial embolization caused by injection of hyaluronic acid (Restylanes). *Br J Dermatol*. 2002;146: 928–929.
16. Graiche J. Overview of complications of sclerotherapy. Australian College of Phlebology 2007 Scientific meetings and workshops.
17. Consensus paper on venous leg ulcer. The Alexander House Group. *Journal of Dermatologic Surgery & Oncology*. 1992;18(7):592–602. ■

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