Fat Transplantation

37

Dana L. Ellis and Lisa M. Donofrio

Abstract

The changes that happen as an intrinsic part of aging occur deeper in the subcutaneous tissues and are atrophic in nature (Donofrio, Dermatol Surg 26:1129–1134, 2000). This volume loss can be corrected through several means, including tissue repositioning, implants, synthetic fillers, or autologous tissue (Modarressi, World J Plast Surg 2(1):6–13, 2013). More recently, autologous fat grafting has come to be considered an ideal filler, as fat grafts are biocompatible, nonallergenic, nontoxic, easy to obtain, and synergistic with natural skin (Sinno et al. Plast Reconstr Surg 137:818–824, 2016). Neuber first reported the technique in 1893, followed by Illouz who then pioneered liposuction in the 1980s. In the modern day, Coleman demonstrated techniques for long-term fat graft stability (Sinno et al. Plast Reconstr Surg 137:818–824, 2016). Its first indications were for aesthetic surgery of the face, and more recently in hands (Modarressi, World J Plast Surg 2(1):6–13, 2013). Fat grafting is also useful for tissue loss due to an accident, operation, congenital disease, or lipodystrophy. In addition to a volumizing effect, the injected fat leads to neoangiogenesis, thereby improving the cutaneous elasticity. This technique is also used for wound healing, scar reduction, treatment of radiodermatitis, correction of acne scars, and breast reconstruction and augmentation in plastic surgery (Modarressi, World J Plast Surg 2(1):6–13, 2013).

Keywords

Fat transplantation · Fat grafting · Techniques
Postoperative care · Alternative procedures

Indications for Fat Transplantation

The changes that happen as an intrinsic part of aging occur deeper in the subcutaneous tissues and are atrophic in nature [1]. This volume loss can be corrected through several means, including tissue repositioning, implants, synthetic fillers, or autologous tissue [2]. More recently, autologous fat grafting has come to be considered an ideal filler, as fat grafts are biocompatible, nonallergenic, nontoxic, easy to obtain, and synergistic with natural skin [3]. Neuber first reported the technique in 1893, followed by Illouz who then pioneered liposuction in the 1980s. In the modern day, Coleman demonstrated techniques for long-term fat graft stability [3]. Its first indications were for aesthetic surgery of the face, and

D. L. Ellis
Yale School of Medicine, New Haven, CT, USA

L. M. Donofrio (✉)
Yale University School of Medicine,
New Haven, CT, USA

M. Alam (ed.), *Evidence-Based Procedural Dermatology*,
https://doi.org/10.1007/978-3-030-02023-1_37

more recently in hands [2]. Fat grafting is also useful for tissue loss due to an accident, operation, congenital disease, or lipodystrophy. In addition to a volumizing effect, the injected fat leads to neoangiogenesis, thereby improving the cutaneous elasticity. This technique is also used for wound healing, scar reduction, treatment of radiodermatitis, correction of acne scars, and breast reconstruction and augmentation in plastic surgery [2].

The main advantages of fat grafting include a long-lasting result, especially in comparison to the synthetic resorbable products, avoidance of granulomatous and allergic reactions that are often provoked by the more permanent (synthetic) products, a natural consistency, and improvement of cutaneous and subcutaneous trophicity [2].

Lipoaugmentation has become a staple in aesthetic medicine and surgery, and new technologies are continuously being introduced that support current clinical fat grafting efforts [3].

Effectiveness of Fat Transplantation

Autologous fat transfer offers many qualities of an ideal soft tissue filler. The success of fat grafting is thought to provide an abundant source of regenerative pluripotent cells, specifically adipocyte-derived stem cells (ADCs) [2]. These cells are able to integrate into host tissue and secrete important cytokines and growth factors including vascular endothelial growth factor (VEGF), hepatocyte growth factor (HGF), insulin-like growth factor (IGF), platelet-derived growth factor (PDGF), and transforming growth factor-beta (TGFβ) [4].

Transplanted fat requires contact with living tissue, and these grafts survive by diffusion until the process of neovascularization occurs. As such, one of the major drawbacks to this technique is a somewhat unpredictable long-term survival rate. Long-term results have been documented by operators practicing atraumatic harvesting and multilayer microdroplet infiltration [1]. However, there is difficulty in assessing longevity. First, there are no good objective measurement criteria available. We rely on photographs, but they are a two-dimensional representation of a three-dimensional result and are purposely chosen for their outcome. Second, patients who start with augmentation often supplement their results with other rejuvenation procedures, confounding the effect. Lastly, patients continue to age over the time they are in follow-up [1]. Lasting augmentation is most likely due to neovascularization of the adipocyte grafts; however, volume enhancement may also be caused by replacement fibrosis [1]. Although fat transplantation by structural principles presents a rationale for increased survival, it can occasionally prove to be unreliable, and patients need to be made aware of the often unpredictable nature of fat transplantation [1].

There is a single prospective study on the topic of fat graft longevity to the midface [5]. In this study, 66 patients were grafted with an average of 10 cc of fat using the modified Coleman technique. Using 3D image technology, the authors noted that 32% of the fat grafted to the midface was present at 16 months and concluded that the volumes required to make a visible change in midfacial rejuvenation are considerably less than originally anticipated (4) [5].

This unpredictable long-term survival rate has led to investigations into methods and techniques to increase fat viability and longevity [3].

Preoperative Evaluation

Assessment of the areas of facial atrophy is best accomplished while examining a young photograph. Since the idea that patients need to be filled and not cut is new, it helps to show them visually how they have aged [1]. The areas of future augmentation should be mutually agreed upon and documented. Patients with coagulopathies, a history of deep vein thrombosis, or warfarin intake are excluded. Connective tissue disease warrants caution since theoretically, transfer of an autologous material may stimulate an inflammatory response; however, this has not yet been described [1]. Patients must also be in overall good health with realistic expectations and

acceptance of the gradual sequential nature of the improvement [1]. The procedure works best in patients 30–50 years of age with enough anchoring recipient tissue. Patients with extreme atrophy or advancing age may have limited results or may require numerous transplant sessions [1]. Overweight patients with jowl and neck adiposity may need additional suctioning [1]. The patients should be educated on sun avoidance and textural and pigmentary alterations secondary to photodamage treated with appropriate modalities [1].

Azithromycin 500 mg is initiated on the day before the initial extraction/transplantation procedure and continued at a dose of 250 mg/day for 4 days. All nonsteroidal anti-inflammatory drugs should be discontinued 1 week prior, as well as vitamin E, St. John's Wort, and gingko biloba supplements. Patients should wear dark, loose clothing and bring a snug undergarment such as biking shorts for postoperative compression [1].

Best Techniques and Performance

The donor site should be picked from an area that can benefit cosmetically from fat removal. The outer thighs, buttocks, and abdominal fat have shown to possess the greatest lipogenic activity, and a concerted effort should be made to harvest from these sites [6]. Despite anecdotal reports of differing fat graft quality based on donor site, there are data to suggest no difference exists, as measured by a 2,3-bis-(2-methoxy-4-nitro-5-sulfophenyl)-2H-tetrazolium-5-carboxanilide (XTT) assay, in grafts harvested from four of the most common donor sites: the abdomen, thigh, flank, and knee (4) [7]. Another study reviewed 73 patients who underwent fat grafting for breast reconstruction and showed no difference in longevity between fat harvested from the abdomen or thigh based on three-dimensional imaging (4) [8].

Fat extraction takes place with purely tumescent anesthesia using a modified Klein solution [1]. After prepping and draping the donor area, tumescent anesthesia is infiltrated by hand or pump in a manner previously described [9]. It is best to wait 20–30 min to allow even dispersion of the tumescent fluid and maximum anesthesia. Current practice suggests that the amount of lidocaine used be kept to a minimum, since it is toxic to adipocytes [10]. In actuality, the data regarding the effect of local anesthesia on adipocyte biology is somewhat conflicting. Lidocaine, used for local anesthesia, has been reported to inhibit the growth of adipocytes in culture and slow down glucose transport and lipolysis as evaluated by D-[U-carbon 14]-glucose and spectrophotometric determination of glycerol for lipolysis [11]. Prior studies also suggest that local anesthetic may slow adipocyte metabolism, growth, and viability. These findings only persisted while lidocaine was present. Once the lidocaine was removed, so too were its inhibitory effects [11]. More recent studies show no difference in fat treated with infiltrative anesthetic by counting the number of living fat cells in a 100× field (4) [12].

The cardinal principle of structural augmentation involves the atraumatic and gentle harvesting of intact fat cylinders. This is accomplished with a 3-mm open-tipped cannula attached to a 10-ml syringe. Most dermatologic practices avoid the use of suction machines in this procedure because they generate damaging negative pressures [1]. However, there is evidence to suggest that no difference exists in cell viability between syringe aspiration and liposuction-assisted aspiration. One study using human fat, grafted into severe combined immunodeficient mice, argued that there was no difference between a 10-cc syringe or a Byron liposuction pump when comparing the specimen weights and metabolic assays of 12-week-old graft explants (4) [13].

When using a syringe, the plunger of the syringe is withdrawn slowly 1 ml at a time. The to-and-fro motion of the open-bore cannula is enough to fill the syringe with clean yellow fat tissue. A total of 10–20 syringes are filled in this manner, depending on the projected volume and number of transplants required. The collected 10-ml syringes are then spun down in a centrally sterile centrifuge for 20 s to separate the fat cells from the triglycerides and tumescent fluid. Once done, the watery infranate is released from the syringe, and the fat is transferred to 1-ml syringes

with a 16-gauge female-female adapter, stopping short of the oily supernate [1].

The reported rates of fat cell survival vary greatly in the medical literature (10–90%). Different techniques of harvesting and processing the fat cells are so claimed to be responsible for these differences, without any agreement concerning the best way to process [2]. Various studies have assessed the impact of centrifugation on fat transfer, and most have concluded that, unless conducted at very high speeds, in vernal centrifugation does not adversely affect adipocyte viability (3b) [14, 15] Coleman et al. suggest 3000 rpm for 3 min, but 1 min of centrifugation is as efficient with less harm to fat cells [16].

Although many authors may advocate for one fat preparation protocol over another, there are no objective data to support these claims. There is in fact evidence to suggest no difference in graft outcome between several fat preparation protocols. Of note, a previously cited study found no difference in end graft survival of fat without treatment, with centrifugation, with washes of normal saline, with washes of lactated Ringer solution, and with combinations of centrifugation and washes, where graft survival was estimated using explant weights and with an XTT cell viability assay (3b) [13].

Many properties of fat begin to change after processing. Glycerol-3-phosphate dehydrogenase activity, which is a measure of adipocyte destruction, increases linearly until 4 h [3]. Stem cells can be harvested up to 4 h at room temperature and up to 24 h at 4 °C [17]. Therefore, although fat preparation protocols may vary from one operator to another, there is evidence to support the notion that fat transfer should be undertaken as soon as possible after harvesting [3].

After extraction and preparation of the fat, the patient is placed in an upright position and the areas requiring augmentation sketched onto the skin with a sterile marking pen. The face is then prepped with an antiseptic wash and the table reclined. Facial anesthesia is in the form of blocks and local infiltration to effectively cover all the planned areas of augmentation. Entry sites are most often made with an 18-gauge Nokor needle tip in areas affording access and are best hidden at the hairline and in the base of rhytides. All infiltration is by way of a blunt cannula [1]. The large diameter ensures that the fat may pass in intact tissue parcels, and the blunt end prevents perforation or tearing of underlying structures [1]. There are experimental data supporting the notion that low-shear devices maintain fat structural integrity. Specifically, one study used computed tomographic (CT) volume measurements at 4 weeks to show a significantly increased fat viability and significantly lower lipolysis with a low-shear device [18]. This same study noted significantly higher fat volume retention in addition to healthier appearing fat on histologic evaluation in an animal model after delivery through a low-shear device (5) [18].

Optimal cannula diameter for fat injection is a minor topic of debate. One particular study found viability to be greatest with use of a 2.5-mm (~10–11 gauge) cannula compared with smaller cannulas as evaluated by counting live cells using a hemocytometer under 40× magnification [18]. The authors concluded that by increasing the diameter of aspiration and injection cannulas, trauma is minimized and viability and graft survival are improved (5) [18]. Another study stated the best results were achieved with the no. 14 cannula, as compared with smaller ones [19]. A third study found no difference between 14-, 16-, and 20-gauge cannulas. In this study, viability of the fat grafts was evaluated by fat cell isolation with collagenase digestion and staining and subsequently counted with a hemocytometer (5) [20].

During injection, the fat is deposited in minuscule strands of less than 0.1 ml amounts on the withdrawal phase of the motion [1]. The fat is woven in a three-dimensional design starting at the most stable plane (next to bone when available) and working up through the subcutaneous fat. Every attempt should be made to place the fat in virgin tunnels, avoiding excessive positive pressure on the syringe and globular deposits [1]. If at any time the infiltrator becomes clogged, it should be withdrawn and cleared. The purpose of this is to anchor the fat and allow enough room

between adipocytes for survival through respiratory diffusion [1].

Safety

Patients need to consent to all possible developments before the procedure. Expected sequelae are bruising and edema lasting 2–10 days, depending largely on the aggressiveness of the augmentation. Pre-icing as well as post-icing of the face and intramuscular betamethasone decrease this side effect. Other possible complications include local infection, asymmetry, lumpiness and fat cysts, entry site scars or discoloration, perforation of the orbital septum, marginal mandibular injury, parotitis, and reabsorption of fat. Most if not all of these can be avoided with experience and conservative, meticulous technique [1].

Postoperative Care and Follow-Up

Since the conditions favorable to fat cell survival are poorly understood, repeat staged transplants give an added advantage by providing more chances for the fat to take, and healing from initial treatments may increase vascularity and fibrosis in the recipient tissue [1].

Initial transfer procedures use 15–30 ml of the freshly harvested fat. The extra fat syringes are then labeled with name, date, and social security number and stored in a plasma freezer at 30° C. Patients return for additional augmentation procedures at 4–6-week intervals over the course of a year. At these visits, 8–12 ml of fat is placed in areas requiring further augmentation, adhering to the placement principles described above. There is usually no downtime from these smaller treatments, and the patient can put on makeup right after the session and return to work. Viability of thawed adipocytes has been previously demonstrated, and many believe that frozen fat "takes" better than fresh fat [10]. This may be due to dehydration of the tissue with freezing, leaving a more concentrated adipocyte suspension [1].

Alternative Procedures and Modifications

Animal models have proven that a number of tissue scaffolds can improve the longevity of grafted fat. One group of authors used a recently reported protocol to suspend harvested fat in Growth Factor-Reduced Matrigel (BD Biosciences, San Jose, Calif.) [21]. This biological matrix has been shown to improve early angiogenesis [22]. It has also been hypothesized that suspending the purified cells in the resorbable matrix helps to optimize graft viability by meeting the high metabolic demand of lipocytic tissue. This procedure was tested in a murine model that compared harvested fat alone to harvested fat suspended in Growth Factor–Reduced Matrigel. The matrix-assisted fat showed greater maintenance of volume and adipocyte cellularity at 3 months (5) [21].

Although there are numerous studies that focus on improving the harvest and preparation of fat, the recipient site is often forgotten when attempting to optimize the outcome. Microneedling has been proven beneficial in increasing skin vascularity and skin quality, but there have been few studies specifically investigating whether this technique is beneficial for increasing fat graft survival [3]. However, one study showed significantly more vascularity, higher graft survival, and better graft integrity with less fibrosis (by histomorphometric and immunohistochemical evaluation) after preconditioning with microneedling 1 week before grafting in an animal model (5) [22].

Again, there is no consensus concerning the best way to process the harvested fat before reinjection. Based on the recent literature, adding platelet-rich plasma (PRP) to fat preparation may be a means of improving fat survival and rendering a more predictable result [2]. Platelets work via the degranulation of their α-granules, which contain synthesized and prepacked growth factors [3], the most potent ones being PDGF, TGFβ, IGF, VEFG, and endothelial growth factor (EGF). Released growth factors stimulate angiogenesis, cell differentiation, and proliferation, leading to

the reconstitution of the tridimensional matrix that allows the rearrangement of adipocytes into the correct 3D organization. This approach is completely autologous and immediately employed without any type of in vitro preconditioning or media complement [2].

The benefit and safety of PRP are documented in more than 5000 studies where the authors observed enhancement of bone regeneration [23–25], wound healing [26–28], tendon and cartilage healing [29–31], corneal healing [32], and skin rejuvenation [33]. PRP is so used more and more often in the plastic, reconstructive, and aesthetic surgery fields [34–36].

In a series of in vitro studies, it has been demonstrated that PRP increases fat cells' survival rate and stem cells' differentiation [34, 37]. One study showed that fat graft survival rates were significantly increased in rats treated with PRP (4) [38]. There are also some successful cases of facial reconstruction with fat grafting and PRP [39], and this association has also been described for aesthetic cases [2].

Observations and Recommendations

Evidence-based summary: Grading of Recommendations Assessment, Development and Evaluation (GRADE)

Findings	Grade score: quality of evidence
Evidence does not support that abdominal fat demonstrates superior viability to that of other anatomic areas	C
Evidence does not support that infiltrative anesthesia affects the viability of fat from donor sites	C
There is limited evidence to support that liposuction pump aspiration yields fat as viable as that by syringe aspiration	D
There is no evidence to support that washing or centrifugation of fat improves graft survival	B
Evidence does not support an optimal cannula or needle diameter for fat reinjection	C
There is some evidence to support that injecting fat with a low-shear device preserves fat integrity	D
There is evidence to support that fat should be injected as soon as possible after harvesting	D
There is some evidence to support that the viability of thawed adipocytes is better than that of fresh fat	D
There is evidence to support the long-term efficacy of fat grafting to the midface	C
There is evidence to support tissue engineering techniques for improving fat longevity	D
There is some evidence to support that preconditioning the recipient site improves fat graft survival	D
There is evidence that demonstrates that PRP increases fat cell survival rates	C
There is no gold standard that exists for quantifying fat viability after transplant	N/A

References

1. Donofrio LM. Structural autologous lipoaugmentation: a pan-facial technique. Dermatol Surg. 2000;26:1129–34.
2. Modarressi A. Platlet rich plasma (PRP) improves fat grafting outcomes. World J Plast Surg. 2013;2(1):6–13.
3. Sinno S, Wilson S, Brownstone N, Levine SM. Current thoughts on fat grafting: using the evidence to determine fact or fiction. Plast Reconstr Surg. 2016;137:818–24.
4. Kim WS, Park BS, Sung JH. Protective role of adipose-derived stem cells and their soluble factors in photoaging. Arch Der- matol Res. 2009;301:329–36.
5. Meier JD, Glasgold RA, Glasgold MJ. Autologous fat grafting: long-term evidence of its efficacy in midfacial rejuvenation. Arch Facial Plast Surg. 2009;11:24–8.
6. Lilleth H, Boberg J. The lipoprotein-lipase activity of adipose tissue from different sites in obese women and relationship to cell size. Int J Obes. 1978;2:47–52.
7. Rohrich RJ, Sorokin ES, Brown SA. In search of improved fat transfer viability: a quantitative analysis of the role of centrif- ugation and harvest site. Plast Reconstr Surg. 2004;113:391–5. discussion 396
8. Small K, Choi M, Petruolo O, Lee C, Karp N. Is there an ideal donor site of fat for secondary breast reconstruction? Aesthet Surg J. 2014;34:545–50.

9. Klein JA. The tumescent technique. Anesthesia and modified liposuction technique. Dermatol Clin. 1990;8:425–37.
10. Moore JH, Kolaczynski JW, Morales LM, et al. Viability of fat obtained by syringe suction lipectomy: effects of local anesthesia with lidocaine. Aesthet Plast Surg. 1995;19:335–9.
11. Moore JH Jr, Kolaczynski JW, Morales LM, et al. Viability of fat obtained by syringe suction lipectomy: effects of local anes- thesia with lidocaine. Aesthet Plast Surg. 1995;19:335–9.
12. Kim IH, Yang JD, Lee DG, Chung HY, Cho BC. Evaluation of centrifugation technique and effect of epinephrine on fat cell viability in autologous fat injection. Aesthet Surg J. 2009;29:35–9.
13. Smith P, Adams WP Jr, Lipschitz AH, et al. Autologous human fat grafting: effect of harvesting and preparation techniques on adipocyte graft survival. Plast Reconstr Surg. 2006;117:1836–44.
14. Kurita M, Matsumoto D, Shigeura T, Sato K, Harii K, Yoshimura K. Influences of centrifugation on cells and tissues in lipo- suction aspirates: optimized centrifugation for lipotransfer and cell isolation. Plast Reconstr Surg. 2008;121:1033–41.
15. Condé-Greena A, Ferreira N, de Amorima G, Pitanguya I. Influence of decantation, washing and centrifugation on adipocyte and mesenchymal stem cell content of aspirated adipose tissue: a comparative study. J Plast Reconstr Aesthet Surg. 2010;63:1375–81.
16. Coleman WP. Autologous fat transplantation. Plast Reconstr Surg. 1991;88:736.
17. Matsumoto D, Shigeura T, Sato K, et al. Influences of preser- vation at various temperatures on liposuction aspirates. Plast Reconstr Surg. 2007;120:1510–7.
18. Chung MT, Paik KJ, Atashroo DA, et al. Studies in fat graft- ing: part I effects of injection technique on in vitro fat viability and in vivo volume retention. Plast Reconstr Surg. 2014;134:29–38.
19. Fournier PF. Liposculpture: the syringe technique. Paris: Arnette Blackwell; 1991.
20. Erdim M, Tezel E, Numanoglu A, Sav A. The effects of the size of liposuction cannula on adipocyte survival and the optimum temperature for fat graft storage: an experimental study. J Plast Reconstr Aesthet Surg. 2009;62:1210–4.
21. Piasecki JH, Gutowski KA, Moreno KM, Lahvis GL. Purified viable fat suspended in matrigel improves volume longevity. Aesthet Surg J. 2008;28:24–32.
22. Kleinman HK, Martin GR. Matrigel: basement membrane matrix with biological activity. Semin Cancer Biol. 2005;15:378–86.
23. Marx RE, Carlson ER, Eichstaedt RM, Schimmele SR, Strauss JE, Georgefff KR. Platelet-rich plasma: Growth factor en- hancement for bone grafts. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 1998;85:638–46.
24. Garg AK. The use of platelet-rich plasma to enhance the success of bone grafts around dental implants. Dent Implantol Updat. 2000;11:17–21.
25. Mooren RECM, Merkx MAW, Bronk- horst EM, Jansen JA, Stoelinga PJW. The effect of platelet-rich plasma on early and late bone healing using a mixture of par- ticulate autogenous cancellous bone and bio-Oss: an experimental study in goats. Int J Oral Maxillofac Surg. 2010;39:371–8.
26. Villela DL, Vera Lucia C, Santos G. Evi- dence on the use of platelet-rich plasma for diabetic ulcer: a systematic review. Growth Factors. 2010;28:111–6.
27. Pallua N, Wolter T, Markowicz M. Platelet- rich plasma in burns. Burns. 2010;36:4–8.
28. Lacci KM, Dardik A. Platelet-rich plasma: support for its use in wound healing. Yale J Biol Med. 2010;83:1–9.
29. Lubowitz JH, Poehling GG. Shoulder, hip, knee, and PRP. Arthroscopy. 2010;26:141–2.
30. Peerbooms JC, Sluimer J, Bruijn DJ. Go- Sens T. positive effect of an autologous platelet concentrate in lateral epicondylitis in a double-blind randomized controlled trial: platelet-rich plasma versus corticosteroid injection with a 1-year follow-up. Am J Sports Med. 2010;38:255–62.
31. Creaney L. Platelet-rich plasma for treat- ment of Achilles tendinopathy. JAMA. 2010;303:1696–8.
32. Tayfun TS, Altintas YN, Yildiz O, Kursat D, Ender S, Yusuf C. The effect of sub- conjunctival platelet-rich plasma on cor- neal epithelial wound healing. Cornea. 2010;29:664–9.
33. Kau E, Kagami H, Kato R, Yamada Y, Ueda M. Regenerative medicine for anti-aging. Nippon Rinsho. 2009;67:1402–6.
34. Cervelli V, Gentile P, Scioli MG, Gri- maldy M, Casciani CU, Spagnoli LG, Or- landi A. Application of platelet-rich plasma in plastic surgery: clinical and in vitro evaluation. Tissue Eng Part C Methods. 2009;15:625–34.
35. Adler SC, Kent KJ. Enhancing wound healing with growth factors. Facial Plast Surg Clin North Am. 2002;10:129–46.
36. Man D, Plosker H, Winland-Brown JE. The use of autologous platelet-rich plasma (platelet gel) and autologous platelet-poor plasma (fibrin glue) in cosmetic surgery. Plast Reconstr Surg. 2001;107:229–37.
37. Natsuko K, Tatsuya M, Toshihito M, Sato- shi K, Zefanya NF, Kenji K. Proliferation- promoting effect of platelet-rich plasma on human adipose-derived stem cells and hu- man dermal fibroblasts. Plast Reconstr Surg. 2008;122:1352–60.
38. Shinichiro N, Masayuki I, Megumi T, Kaoru M, Satoko K, Shingo N, Satoshi Y, Sa- toshi K, Naoto Y, Tomoharu K. Platelet- rich plasma (PRP) promotes survival of fat-grafts in rats. Ann Plast Surg. 2010;65:101–6.
39. Cervelli V, Gentile P. Use of cell fat mixed with platelet gel in progressive hemifacial atrophy. Aesthet Plast Surg. 2009;33:22–7.

Self-Assessment Questions

1. Which of the below is false?
   Repeat staged transplants give an added advantage by:
   (a) Providing more chances for the fat to take
   (b) Increasing vascularity in the recipient tissue
   (c) Increasing fibrosis in the recipient tissue
   (d) Increasing elasticity in the recipient tissue
   (e) Decreasing fibrosis in the recipient tissue
2. Which of the below are true?
   The main advantages of fat grafting include:
   (a) A long-lasting result
   (b) Avoidance of granulomatous reactions
   (c) Avoidance of allergic reactions
   (d) A natural consistency
   (e) Improvement of cutaneous and subcutaneous trophicity
   (f) All of the above
3. The success of fat grafting is based largely on the provision of an abundant source of regenerative stem cells, specifically:
   (a) Embryonic stem cells
   (b) Pluripotent stem cells
   (c) Hematopoietic stem cells
   (d) Epidermal stem cells
   (e) Epithelial stem cells
4. Lasting augmentation is most likely due to:
   (a) Fibrosis of the adipocyte grafts
   (b) Neovascularization of the adipocyte grafts
   (c) Stimulation of neoadiposity
   (d) Nature of underlying facial anatomy
   (e) Inosculation of the grafts
5. Which are absolute contraindications to autologous fat transfer? (Can pick more than one)
   (a) History of coagulopathies
   (b) History of deep vein thrombosis
   (c) Current use of warfarin
   (d) Current use of statin drug
   (e) Diabetes

Correct Answers

1. e: Since the conditions favorable to fat cell survival are poorly understood, repeat staged transplants give an added advantage by providing more chances for the fat to take, and healing from initial treatments may increase vascularity and fibrosis in the recipient tissue.
2. f: The main advantages of fat grafting include a long-lasting result, especially in comparison to the synthetic resorbable products, avoidance of granulomatous and allergic reactions that are often provoked by the more permanent (synthetic) products, a natural consistency, and improvement of cutaneous and subcutaneous trophicity.
3. b: The success of fat grafting is based largely on the provision of an abundant source of regenerative pluripotent cells, specifically adipocyte-derived stem cells (ADCs). These cells are able to integrate into host tissue and secrete important cytokines and growth factors including vascular endothelial growth factor (VEGF), hepatocyte growth factor (HGF), insulin-like growth factor (IGF), platelet-derived growth factor (PDGF), and transforming growth factor-beta (TGFβ).
4. b: Lasting augmentation is most likely due to neovascularization of the adipocyte grafts; however, volume enhancement may also be caused by replacement fibrosis.
5. a, b and c: Patients with coagulopathies, a history of deep vein thrombosis, or warfarin intake are excluded from autologous fat grafting procedures. Connective tissue disease warrants caution since theoretically, transfer of an autologous material may stimulate an inflammatory response; however, this has not yet been described. Patients must also be in overall good health with realistic expectations and acceptance of the gradual sequential nature of the improvement.