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Oral Mucosa Graft

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1. Introduction

Oral mucosa has been used for reconstructing oral and maxillofacial defects for many years (Payne et al., 1998); in repairing the conjunctival mucosa of the eye (Donoff, 1976), in oral pharyngeal reconstructive surgery (Leone, 1995) and in reconstructing vaginal defects (Lin et al., 2003). Since the initial introduction by Humby (1941) and then the re-introduction by Burger, oral mucosa graft has gained widespread use in urethral reconstruction of long segment anterior urethral strictures, hypospadias, epispadias and bladder exstrophy (Barbagli et al., 2006, Martins et al., 2006, Xu et al 2007). Oral mucosal graft, as a free graft for urological reconstruction, has numerous advantages including constant availability, favourable immunological properties, easy harvesting, excellent tissue characteristics; easy handling properties, minimal contracture formation and adaptation to a moist environment (Hensle et al., 2002, Simonato et al.,2006; Chi-Chi & Chi-Yang, 2007)

The purpose of this overview is to provide the reader with an understanding of the biologic characteristics of the oral mucosa and the anatomic features that make it such a versatile tissue for urethral reconstruction. In addition, to report on the technique for oral mucosa graft harvest using sound biologic principles, its clinical applications in urologic reconstruction as well some observed donor site complications will be reviewed.

2. Biology of the oral mucosa

The entire oral cavity is lined by a protective epithelial membrane, the ***oral mucosa.*** Anatomically, the oral mucosa is located between the skin of the outer face and the mucosal lining of the gastrointestinal tract displaying properties of both tissues (Markiewicz et al., 2007). According to standard and accepted dental terminology, the buccal mucosa refers to the oral mucosa overlying the inner cheek of the oral cavity. The labial mucosa refers to the alveolar mucosa of the inner lower lip. The lingual mucosa refers the mucosa overlying the tongue. These are collectively referred to as oral mucosal grafts.

The epithelium of the oral mucosa is stratified squamous and becomes keratinized in areas subject to considerable friction such as the palate. The oral epithelium is supported by a dense collagenous tissue, the lamina propria. In highly mobile areas, such as the soft palate and floor of the mouth, the lamina propria is attached to the underlying muscle by loose submucosal supporting tissue. In contrast, in areas where the oral mucosa is spread over the surface bone, such as the hard palate and tooth-bearing ridges, the lamina propria is firmly bound to the periosteum by a relatively thick fibrous submucosa. Throughout the oral

mucosa, abundant small accessory salivary glands of both mucous and serous varieties are distributed in the submucosa (Burkitt et al., 1993). The oral mucosa is architecturally comparable to the stratified squamous epithelium of the penile and glanular urethra, making it remarkably adaptable for urethral substitution. Oral mucosa consists of a thick non-keratinized stratified squamous avascular epithelium ,slightly vascular underlying lamina propia. These properties contrast with the bladder mucosa and the penile skin, both of which have a thin epithelium and a thick lamina propria. Oral mucosa is approximately 5.0 mm in depth and the thickness is directly associated with male gender and varies indirectly with age (Vandana et al., 2005).

Oral epithelial cells are infused with polymicrobial intracellular and extracellular flora, mainly streptococci, but include other species such as Actinobacillus actinomycetemcomitans, Tannerella orsythensis, Fusobacterium nucleatum, Prevotella intermedia, Porphyromonas gingivalis, Oral Campylobacter species , Eikenella corrodens and Treponema denticola (Rudney, 2005). Despite these harsh microbial exposures, inflammatory infiltrate is seldom witnessed under histological examination of oral mucosa in healthy individuals and the reasons for this are the suppressing activity mediated between polymicrobial flora, production of antimicrobial peptides by the epithelia (defensins, cytokines, etc). Mucosal epithelial cells of the oral cavity impede microflora colonization by sustained exfoliation and by a specialized immune system, the mucosa-associated lymphoid tissue (MALT) (Michael et al., 2007). The lamina propria of a well-defatted oral mucosa graft can be considered a secondary barrier preventing microorganisms from entering adjacent tissue layers and exhibits noteworthy antimicrobial properties including lymphocytes, immunoglobulin-synthesizing plasma cells, monocytes/macrophages ,polymorphonuclear neutrophils , mast cells. Sebaceous glands, where present, are located in the lamina propria and are more widespread in labial than buccal mucosa. It can be demonstrated through immunohistochemical staining that nerve fibers and blood vessels from the submucosa infiltrate into the lamina propria, therefore providing a mechanism for angiogenesis and revascularization of the tissue whilst grafting. Oral mucosa is highly resilient and resistant to recurrent exposure to compression, stretching, and shearing forces. This resilient and resistant can be partially credited to the lamina propria-oral epithelium interface, which consists of widespread projections of connective tissue into the epithelial layer, increasing the surface area of the epithelial-lamina propria interface, and providing the oral mucosa's capacity to resist overlying forces. In contrast to the mucosa of the gastrointestinal tract, oral mucosa has no muscularis mucosae layer between its epithelial and lamina propria layers.

3. Surgical anatomy of the oral mucosa

The morphology of oral mucosa varies from region to region, and is related to the functional demands placed upon it. These regional differences exist in the nature of the submucosa, the morphology of the epithelial-connective tissue boundary the composition of the lamina propria, the thickness of the epithelium and the type of keratinization (Mungadi & Ugboko, 2009).

3.1 Anatomy of the labial mucosa

The upper and lower borders of the mandibular labial mucosal are designated by the vermillion border of the lower lip and the vestibular fold between the lower lip and the

anterior border of the mandible, respectively. The lateral borders are a made up by the outer commissures of the lower lip. Mental nerve, a terminal branch of the inferior alveolar nerve of the mandibular division of the trigeminal nerve, innervates the mandibular labial alveolar mucosa. The mental nerve exits the mandible between the first and second premolar teeth through the mental foreman. The surgeon should plan the incision for a labial mucosa harvest medial to the middle of the canines to evade injuring the mental nerve and compromising sensation to the lower lip. The mandibular labial alveolar mucosa receives its blood supply from the inferior labial artery (a branch of the facial artery), the mental artery (a continuation of the inferior alveolar artery), as well as anastomoses from the buccal artery. The mental and buccal arteries are both branches of the maxillary artery. Both the facial artery and the maxillary artery are divisions of the external carotid artery. The labial mucosa is elastic, thin, resistant and technically easy to harvest and requires no suturing of the harvest site, but the buccal mucosa provides a wider graft and has a more robust quality oral mucosa.

3.2 Anatomy of the buccal mucosa

The vertical boundary of buccal mucosa is the maxillary and mandibular vestibular folds, whereas its anterior and posterior borders are shaped by the outer commissure of the lips and the anterior tonsillar pillar, respectively. The buccal mucosa is primarily innervated by the long buccal nerve and by the anterior, middle, and posterior superior alveolar nerves of the second division of the trigeminal nerve. Additionally there is limited sensory innervation from the facial nerve(Michael et al.,2007). The blood supply of the buccal mucosa has multiple arteries of origin including the buccal artery(a branch of the maxillary artery), the anterior superior alveolar artery of the infraorbital artery(a branch of the third part of the maxillary artery), the middle and posterior superior alveolar arteries(branches of the maxillary artery) and accessory vessels from the transverse facial artery (branch of the superficial temporal artery). The buccal mucosa is tough, resilient, easy to harvest, easy to handle and **leaves** no visible donor-site scar (Epply et al., 1997; Mahdavi et al.,2006).

3.3 Lingual mucosa

The mucosa covering the inferior lateral surface of the tongue is indistinguishable from that of the lining of the rest of the oral cavity. The mucosal covering the lateral and under surface of the tongue are the same in structure with that lining the rest of the oral cavity(Song et al., 2007). The mucosa covering the tongue has no particular functional features, and like buccal mucosal, lingual mucosa has constant availability, is easy to harvest and has favorable immunological properties (resistance to infection) and tissue characteristics (a thick epithelium, high content of elastic fibers, thin lamina propria and rich vascularization) (Simonato et al., 2006). As the lining of the oral cavity is limited, buccal mucosal graft(BMG) might not be adequate for treating complicated lengthy urethral strictures that require a larger supply of graft tissue. An ideal donor site for substitution urethroplasty will have characteristics comparable to buccal mucosa, but be easier to harvest and provide grafts of sufficient dimensions. Potential complications, although low or absent, in the using buccal mucosal grafts include numbness, difficulty with mouth opening, deviation or retraction,. The lateral aspect of the tongue offers mucosal tracts that are up to 7 to 8 cm long. Two grafts may be available in all patients. The harvesting technique is simple, quick and does

not require nasal intubation or special retraction and, in addition, leaves a concealed donor site scar. The lingual mucosa grafts are similar to the labial grafts. In patients with a small mouth or difficult mouth opening, the tongue represents a good alternative for oral mucosa graft harvest site(Song et al.,2007). Our patients reported only slight oral discomfort at the donor site. For all of these reasons the tongue seems to be a good alternative donor site for graft harvest; however, lingual mucosal grafts are thin and are not as widely used as buccal mucosal grafts.

4. Mucosa graft harvest

4.1 Buccal grafts

The donor site is prepared, and cleaned using solution containing 10% povidone-iodine. Stay sutures are applied to the external edge of the cheek or lip to keep the oral mucosa stretched. The Stensen's duct, located at the level of the second molar, is identified and the desired graft size measured and marked in an ovoid shape(figure 1). Lidocaine HCl, 1% in adrenaline (1:100,000) is injected along the lateral borders of the graft site, to enhance haemostasis(figure 2). Oral mucosa graft is harvested by dissecting the mucosa off the buccinator muscle(figure 3). The oral mucosal donor site was inspected for bleeding and the defect closed with chromic 3/0 suture. This closure is optional(figure 4). When necessary (for longer stricture or extensive graft need) graft is taken from the lip or the other cheek, figure 5. The donor site is packed with a piece of gauze which is removed in the ward.

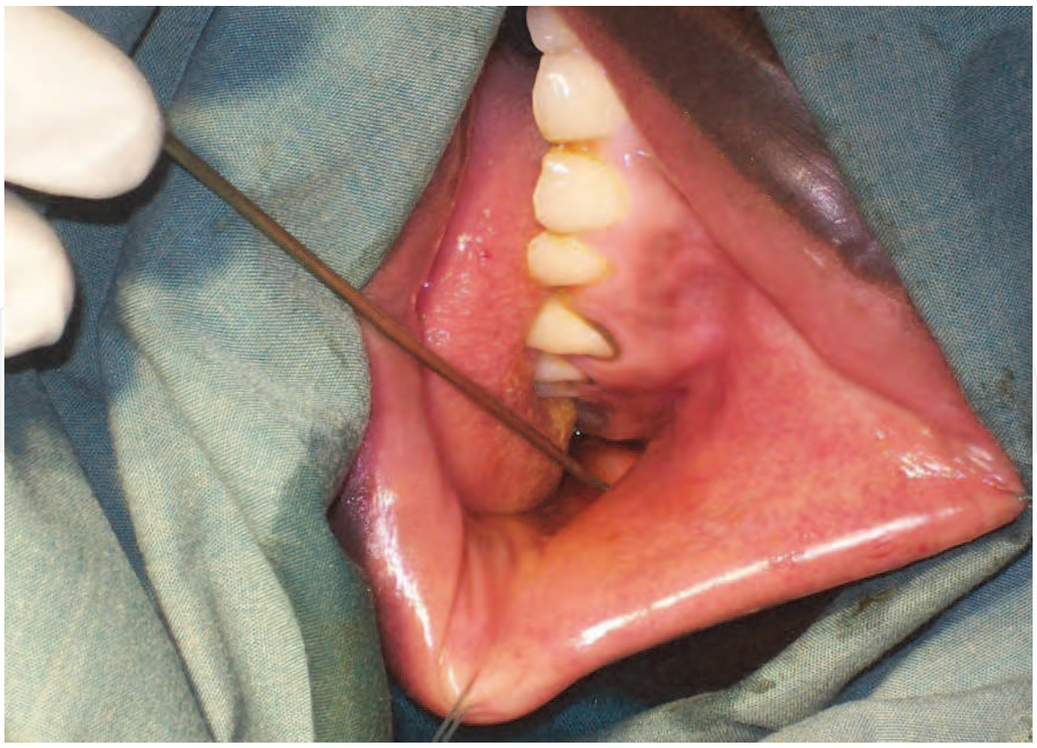

Fig. 1. Exposure of the buccal mucosa graft donor site. The Stensen's duct has been identified by the probe.

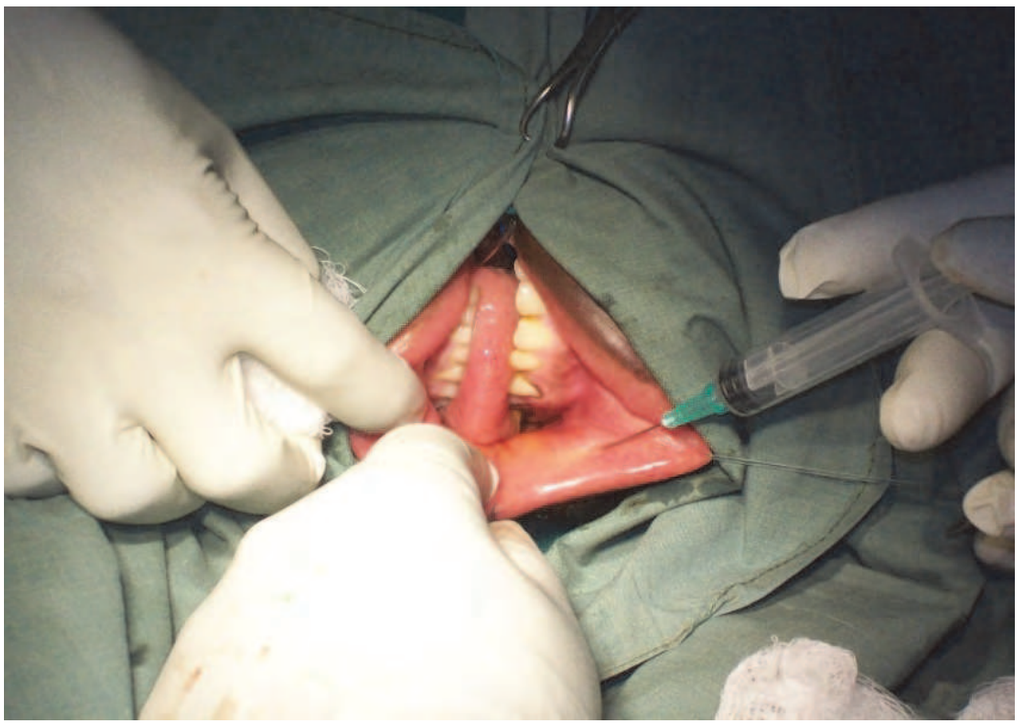

Fig. 2. Submucosal infiltration of donor site with 1% lignocaine in adrenaline to elevate graft and reduce bleeding.

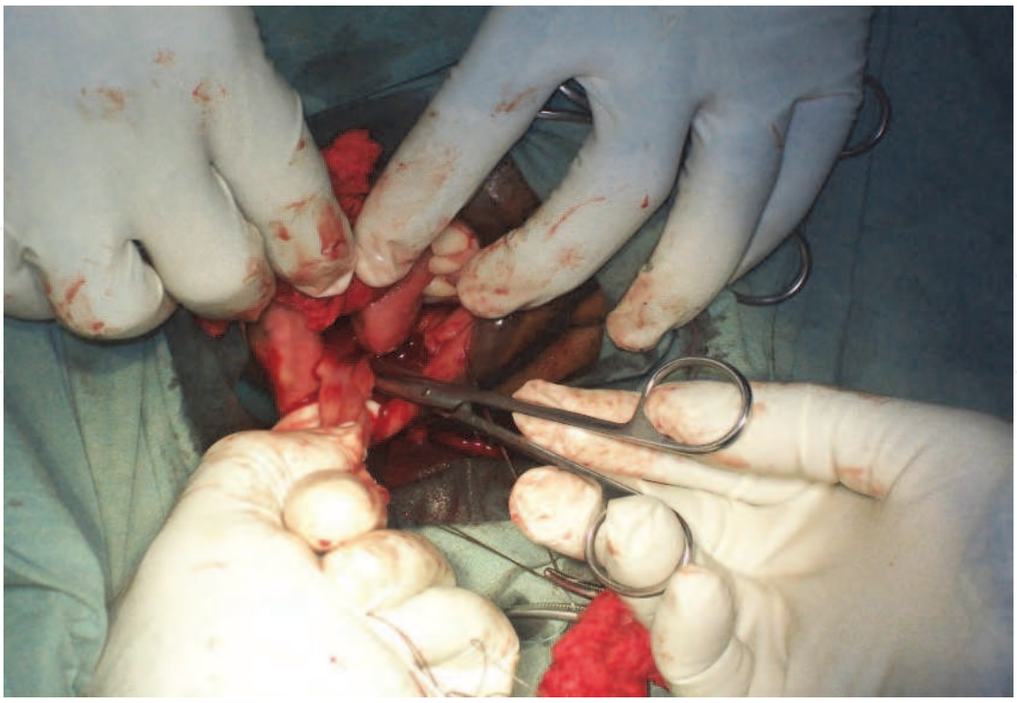

Fig. 3. Buccal mucosa graft being dissected off the cheek.

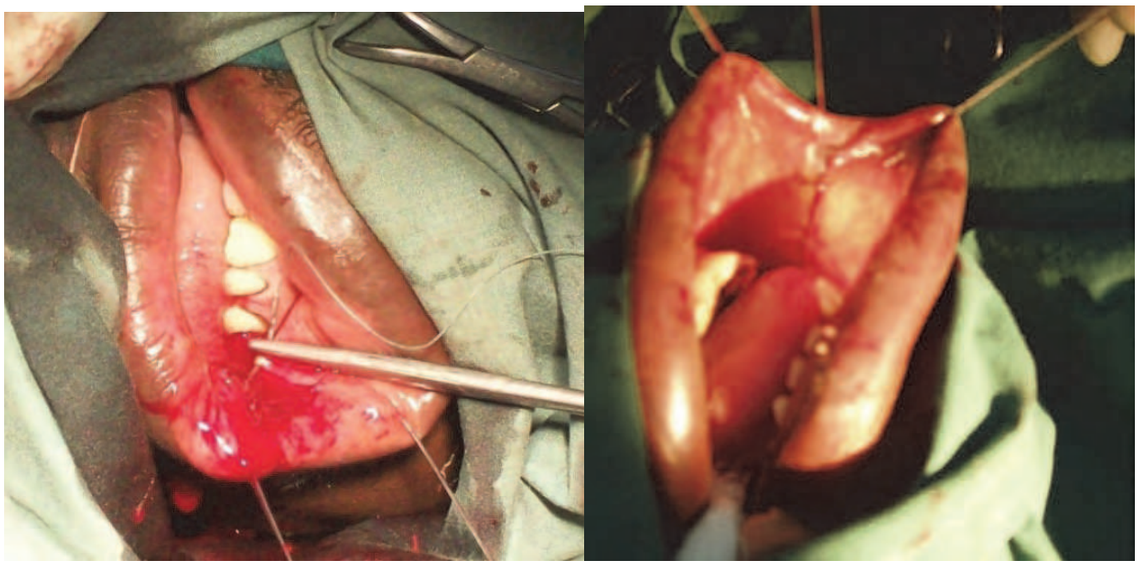

Fig. 4. Closure of buccal mucosa donor site. This is optional

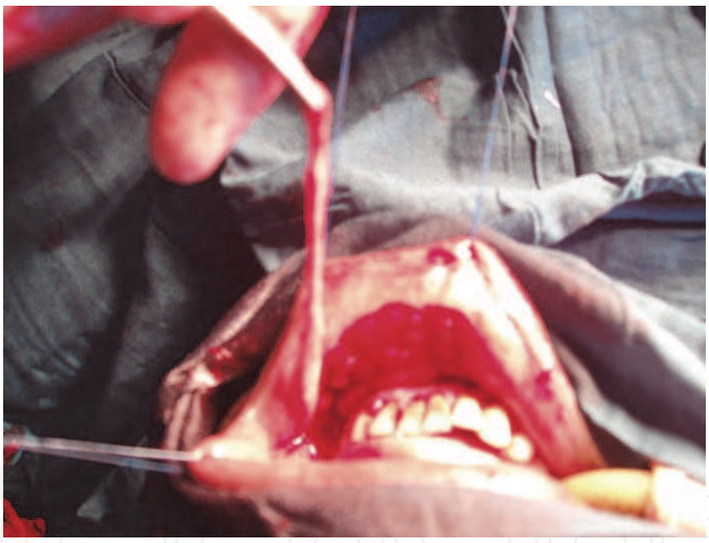

Fig. 5. Oral mucosa harvest from the lower lip

4.2 Lingual mucosa graft harvest

The mucosa covering the inferior lateral surface of the tongue is identical to the lining of the rest of the oral cavity.

For lingual graft harvest, the mouth is opened with a mouth opener. The apex of the tongue is passed through with a suture for traction or direct traction with a Babcock clamp to expose the ventrolateral surface of the tongue. The location of the harvest graft is the ventrolateral mucosal surface of the tongue, below the lining that separates the dorsum, where the papillae are situated, from the sublingual mucosa. The required graft (which may be infiltrated with lignocaine in adrenaline solution) is measured and marked with a surgical pen after identification of the opening of the parotid duct. The graft edges are

incised with a scalpel and a full-thickness mucosal graft is harvested using sharp instruments beginning at the anterior land mark of the graft, figures 6 and 7. A 4-0 traction stitct may be useful to better handle the graft. The donor site is carefully examined for bleedinsg and easily closed with interrupted polyglactin 3-0 sutures

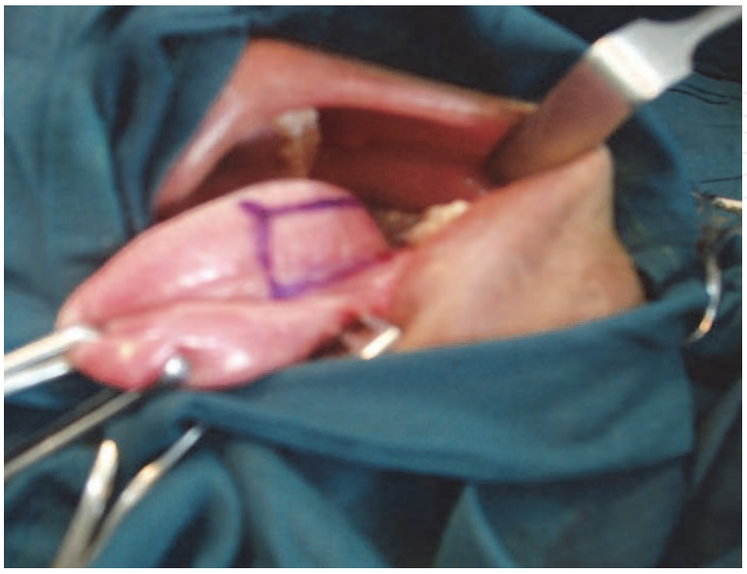

Fig. 6. Lingual mucosa donor site exposed.

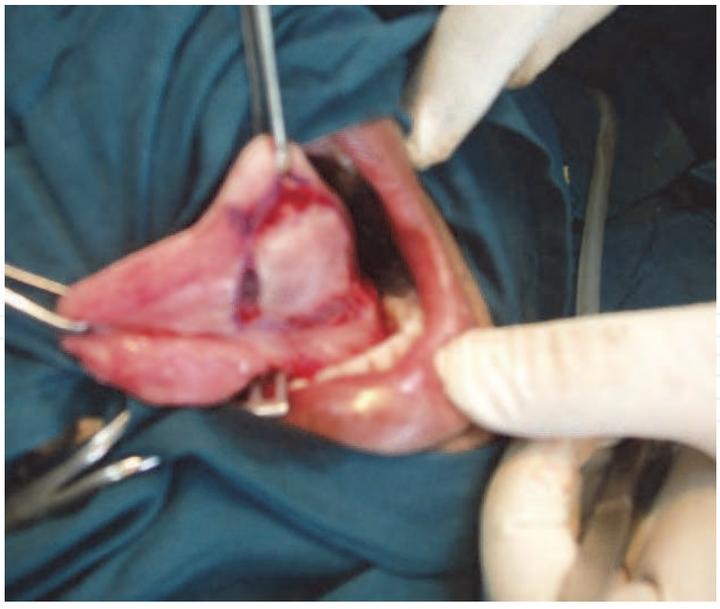

Fig. 7. Limgual graft being havested

4.3 Handling of the oral mucosa grafts

The harvested graft is immediately placed in isotonic saline and kept wet, thus preventing dessication especially in our tropical hot climate.The graft is then defatted to remove any

remnants of fatty tissue and strands of muscle. The fatting process can be accomplished after pinninig the graft on a board or can be done while rolling it on the finger as illustrated(Figure 8). We find this defatting easy to accomplish on the finger using tenotomy scissors. The graft is fenestrated so as to create openings that may allow egress of serum after the graft has been fixed on the recipient site.

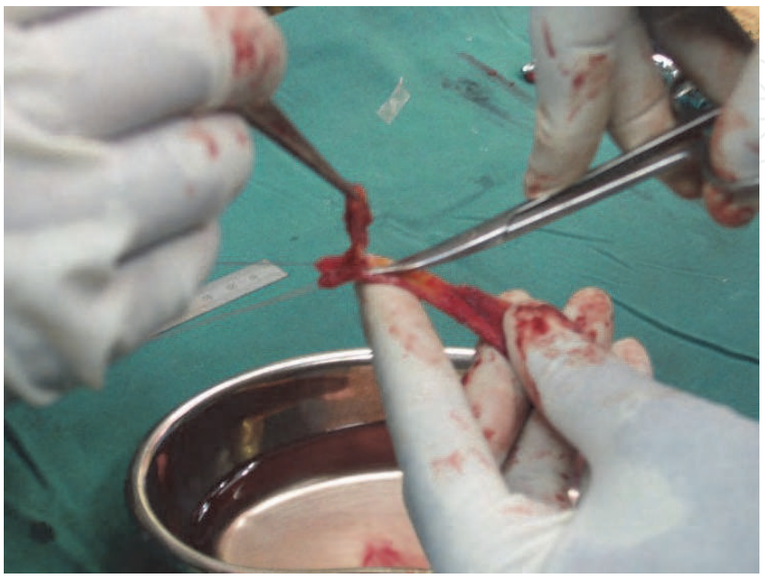

Fig. 8. Oral mucosa is defatted before application

5. Clinical applications of oral mucosa grafts in urology

Clinical application of oral mucosa grafts consists of autologous transplantation of non-keratinized oral mucosa for
repair of a variety of acquired and congenital urethral defects such as urethral strictures, hypospadias and epispadias.

5.1 Use of oral mucosa grafts in urethral reconstruction for stricture disease

Surgical options for urethral stricture disease are based primarily on the location of the stricture and the technique used and include excision and primary anastomosis, on-lay repairs, stricture excision and augmented anastomosis, flap based repairs and staged repairs (McAninch et al., 2008).
In situations where simple excision and primary anastomosis is not appropriate to maintain urethral continuity, some form of substitution urethroplasty will be necessary. Substitution urethroplasty is the gold standard for treatment of strictures of the male urethra not amenable to excision and primary anastomosis. This involves augmentation or replacing the circumference of the urethra using a patch or tube respectively of suitable material which may be genital or extra- genital tissues (Andrich & Mundy 2001; Turner-Warwck 1989). This involves the transfer of tissues in the form of a free graft or flaps (Weasells & McAninch 1996; Fischer,1997). The term graft implies that tissue has been excised and transferred to a graft host bed where a new blood supply develops by a process of take. This requires about

96 hours and occurs in two phases: The initial phase is imbibitions and during this phase the graft survives by absorbing nutrients from the host bed. The second phase is termed inosculation and this is when the microcirculation is established in the graft (Fischer, 1997).
On the other hand, a flap implies that a tissue is excised and transferred with the blood supply either preserved or surgically re-established at the recipient site. Until recently, flaps have been favoured to grafts for substitution urethroplasty because of the theoretical benefit that they carry their blood supply, and therefore , their viability is more secure (Andrich & Mundy, 2001). Flap construction is time- consuming with extensive dissection and redeployment of dartos fascia and have a tendency to cause penile deformity and scarring (Mungadi & Mbibu, 2006).
There has been a recent surge in the use of grafts for urethral reconstruction in the last decade because of the outstanding success of free grafts (especially oral mucosa) which are technically more efficient (Myers & Morey, 2008). The types of grafts used for urethral reconstruction include full thickness skin grafts, the split- thickness skin graft from the scrotum, penis and extra-genital sites, bladder epithelial grafts and oral mucosal grafts (Bhargava & Chapple, 2004; Weasells & McAninch, 1996). Other graft materials that have been used for substitution urethroplasty and include tunica vaginalis (Foinquinos et al., 2007), tunica albuginea (Mathur et al., 2009), colonic mucosa (Xu et al., 2009), small intestine submucosa (Donkov et al., 2006) and human dura matter (Maverich et al., 1998)
The scrotal skin has been used for two-stage urethroplasty as it provides a large quantity of easily accessible graft but its keratinized epithelium and split- thickness depth increases susceptibility to post-operative contracture, hyperkeratosis leading to graft failure in the wet environment of the urethra and the increased risk of diverticulum formation . In addition, scrotal skin is usually hair -bearing and may form hair balls in the urethra.
Non- hirsute full thickness grafts from the penis were initially found to provide satisfactory results in urethral reconstruction for stricture, but donor- site problems such as penile scarring , torsion of the penis, stricture recurrence and the high likelihood of failure in the presence of balanitis xerotica obliterans led to the hunt for a better urethral substitute (Greenwall et al., 1999)
Bladder mucosa grafts theoretically may be well suited for contact with urine but its use has been associated with many complications including meatal stenosis, prolapse and granulomatous reaction at the urethral meatus. Besides, bladder mucosa is difficult to harvest especially in patients who had previous bladder surgery, extrophy, chronic cystitis or neurogenic dysfunction and is weak to handle and liable to shrinkage (El- Sherbny et al., 2002)
Unlike bladder mucosa and skin, oral mucosa has a thick, non- keratinized epithelial layer and a well vascularised thin lamina propria favouring early inosculation (Duckett et al., 1995; Weasells and McAninch,1996; Duckett et al.,1995). Among reconstructive urologists, oral mucosa is emerging as the ideal substitute for the urethra with medium term results comparable to penile skin flaps.

5.1.1 One-stage oral mucosal graft meatoplsty

This technique is used in patients with hypospadias or ischaemic urethral stricture within the glans. The external urethral meatus and fossa navicularis are fully opened. The oral mucosa graft is sutured to the left side of the opened urethra. The graft is rotated over the urethral plate and sutured to the right of the urethra. The glans is closed over the graft and a Foley silicone catheter left in place for one week (Barbagli et al 2003b).

5.1.2 Dorsal oral mucosal graft urethroplasty

Dorsal oral mucosal grafts are suggested for repair of penile urethral strictures only in patients with normal corpus spongiosum. A circumcoronal foreskin incision is made with complete degloving of the penis, the penile urethra is exposed and the strictured tract fully opened by a ventral midline incision. The oral mucosa graft is sutured and quilted on the bed of the dorsal urethral incision with interrupted 6/0 sutures (Figure 9). The urethra is closed and tubularized. A dartos fascial flap is obtained to cover the urethral repair.

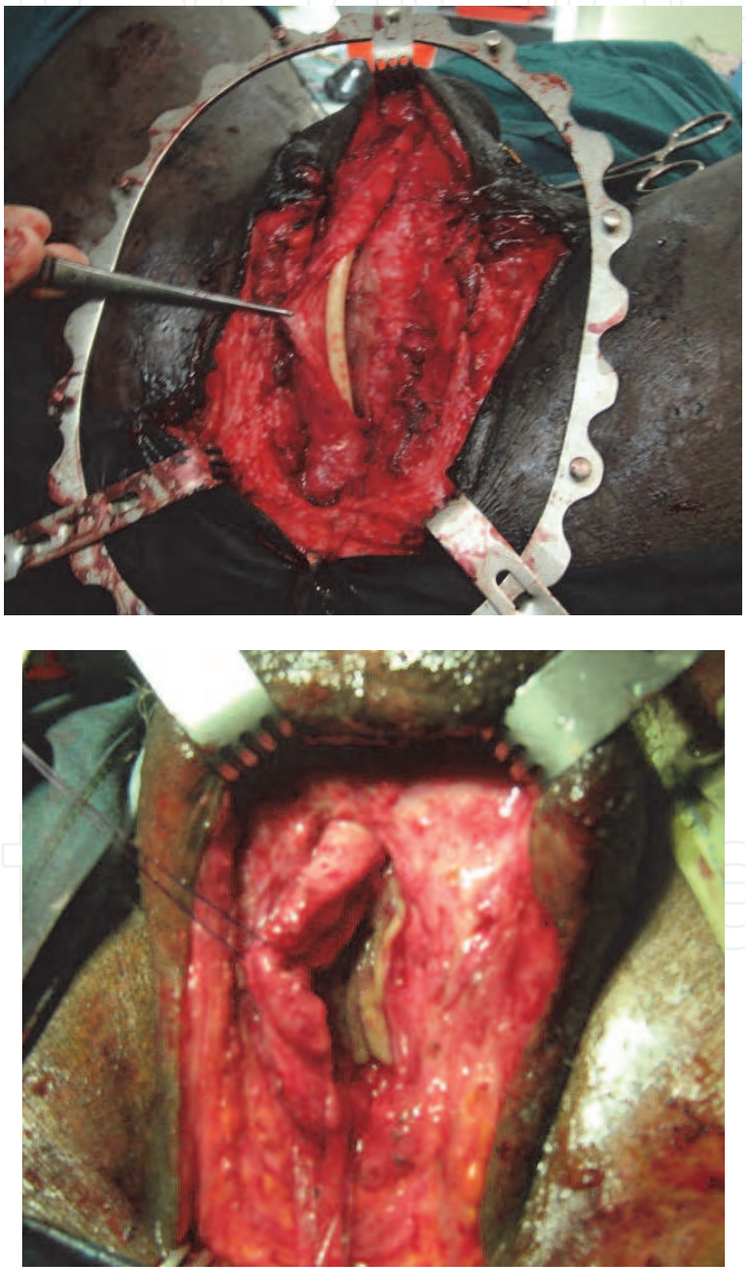

Fig. 9. Buccal mucosa applied for dorsal onlay urethroplasty

5.1.3 Staged oral mucosal graft urethroplasty

Staged oral mucosa graft urethroplasty is advocated for patients with complex penile or bulbar strictures in which a long stricture is associated with adverse local conditions such as fistula, periurethral inflammation, perineal abscess and extensive local scarring, balanitis xerotica obliterans(BXO) or previous failed urethroplasties (Bhargava & Chapple,2004; Greenwall et al.,1998; Barbagli et al.,2003;Joseph et al., 2002; Palminteri et al.,2002; Pansadoro et al.,1999) . Such adverse local tissue conditions will not favour graft take, thus requiring staging of the operation. In the first stage, the urethral plate is removed, the glans fully opened and oral mucosa graft splayed and quilted over the tunica albuginea. Six months later, after the graft has fully taken, the urethra is tubularized.

5.1.4 Augmented anastomotic urethroplasty

Augmented anstomotic urehroplasty combines stricture excision and urethral floor (or roof) strip re-anastomosis with augmentation of the anastomotic area using either a penile skin flap or a full- thickness graft (oral mucosa). The urethra is approached as for a standard anastomotic repair, being transected at the distal limit of the stricture and the strictured portion of the urethra is opened proximally on its dorsal surface (MacDonald et al., 2005; Datta et al., 2007). Strictures amenable to augmentation anastomotic repair are long bulbar strictures (>2cm) in which excision and primary anastomosis may result in a short urethra and chordee formation(figure 10).

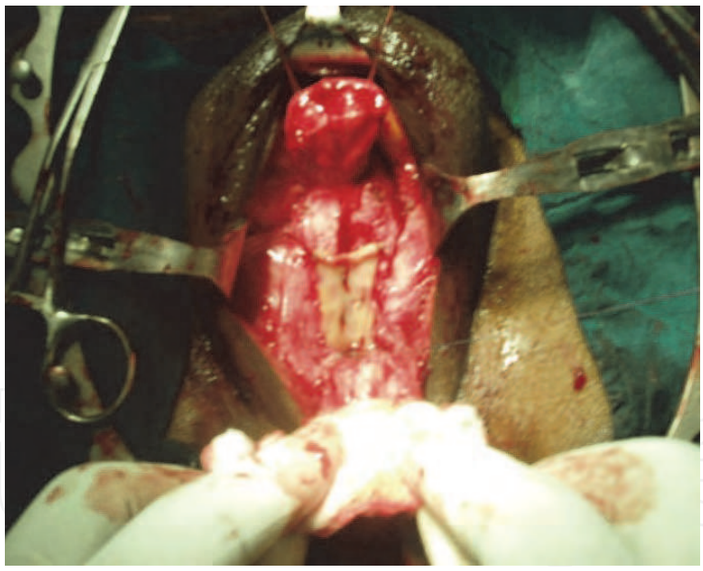

Fig. 10. Buccal mucosa applied for augmented anastomotic urethroplasty

5.1.5 Onlay graft orientation

There is controversy over placement of oral mucosa grafts- either dorsally, ventrally or laterally on the urethra (Morey, 2005; Datta et al.,2007; Barbagli et al., 1998; Morey 2005). Traditionally, grafts have been placed on the ventral aspect of the urethra because it allows easier access to the urethra and a better visualization of the stricture. Some authors have espoused that use of oral mucosa grafts as ventral onlay grafts and gives good outcomes (Gupta et al., 2004; MacLaughlin et al., 2006)

Barbagli et al (2003a) championed dorsal placement of the buccal mucosa grafts adducing that the dorsal approach to strictures of the bulbar urethra to be anatomically superior to ventral, requiring less extensive opening of the spongy tissue and reducing significant bleeding from the corpus spongiosum and mechanical weakening of the graft with better outcome. Dorsal placement of the graft on the urethra is simpler and safer in the distal part of the bulbar urethra whereas ventral placement of the graft is more efficacious in the proximal part of the bulbar urethra, where the spongiosum tissue is thicker and has better vascularise. In addition, a dorsally placed graft is more stable and is mechanically supported (by the corporal bodies) than a ventral graft. The take is reliable and out-pouching of the graft with increased intra-urethral pressure on voiding is prevented (Heinke et al., 2003).

5.1.6 Combined tissue transfer

Extensive, focally dense or panurethral strictures involving more than one segment of the anterior urethra, present a very challenging condition because sufficient oral mucosa may not be present to complete the repair. One of the reconstructive options in this case is the use of a combination of oral mucosa and a genital skin island flap to reconstruct the long urethral defect. Thus, dorsal on-lay oral mucosa grafts may be combined with various substitute materials like preputial skin, pedicled flaps, labial mucosa and human urethral mucosa from corpse (Rajiv et al., 2002). This makes it possible for one-stage reconstruction of urethral strictures avoiding the problems associated with hair bearing flaps and two-stage procedures (Elliot et al 2003)

5.1.7 Oral mucosa as tube graft

Tubularized grafts in urethral reconstruction failed mainly due to inadequate graft take as they are circumferentially surrounded by vascularised tissue. The use of oral mucosa onlay grafts are superior to tubularized grafts(El-Sherbny et al.,2002)

5.2 Use of oral mucosa grafts in hypospadias repair

Surgical treatment of hypospadias remains a challenge to the paediatric urologist due to the variation in the nature of the anomaly and availability of a multitude of techniques for repair. The surgical techniques have continued to evolve over the years. The goals of hypospadias repair include creating a straight penis, reconstructing a slit-like meatus at the tip of the penis, a urethra of adequate length and uniform calibre, symmetry in appearance of the glans and penile shaft and normalization of erection thereby restoring confidence on the child; (Bhat, 2008). The majority of hypospadias cases are mid shaft or distal. Here the axial integrity of the urethral plate can be conserved and hypospadias can be corrected with native tissue by means of either the well established techniques of tubularized incised plate urethroplasty or meatal advancement with glanuloplasty (Snodgrass, 2008; Goyal et al.,2010; Braga et al., 2008). In a number of patients there is a scarcity of local tissue to utilize for reconstruction, usually due to complications from earlier hypospadias surgery. In these patients a source of extra-genital tissue is frequently necessary for urethral reconstruction, and a number of tissues have typically been used (Hensle et al., 2002; Catti et al., 2008). Oral mucosa graft is a versatile substitute and a useful alternative in salvage situations. Whether harvested from the cheek, lip or tongue, it is currently the most widely used alternative to the inner prepuce skin and is an excellent urethral substitute as it leaves no visible scar with no significant donor- site morbidity and no danger of intra- urethral hair growth (Bracka, 2008).

Oral mucosa can be used for either urethral plate augmentation as a ventral or dorsal graft, or complete substitution (1-stage tube graft or 2-stage Bracka repair). Conventionally. OMG has been used as a ventral onlay graft with the advantage of easier placement. Barbagli (1998), introduced the dorsal onlay OMG for stricture urethroplasty with proposed advantages of better mechanical support, better blood supply to the graft, and hence, better chances of take and less chance of urethral diverticula. The dorsal placement of the oral mucosa graft can be applied in hypospadias repair can be used as one or two- stage procedure depending on the prevailing penile tissue.

Outcome following use of oral mucosa graft for hypospadias repair has been good with durable results; although, some complications may be observed. Hensle and colleagues (2002), reported complication rate of 32% in their series and observed that oral mucosa grafts do not have higher success rate than vascularized pedicle flaps.

5.3 Use of oral mucosal grafts for ureteral replacement.

Surgical correction of complicated, long-segment ureteral defects resulting from congenital malformations, retroperitoneal fibrosis, specific and non- specific inflammation, trauma, iatrogenic injuries and malignancy can be challenging (Selzman et al., 1996). Options for ureteral replacement traditionally include psoas hitch, boari flap, the Monti tube, use of the appendix, reconfigured colon or ileal segment (Brandes et al., 2004; Mathews &Marshal,1997; Ali-El-Dein&Ghoneim,2003; Jeffrey et al.,2000; Armatys et al.,2009; Pope&Koch,1996). Ureteral defects too long to be treated by excision and spatulated end-to-end anastomosis can be treated by use of oral mucosa grafts. Naude (1999) treated 4 patients with long segment ureteral loss using oral mucosa grafts applied as a patch wrapped with omentum. However, Badawy and co-workers(2010) reported a series of five patients who presented with extensive ureteral strictures who had oral mucosa grafts laid and fixed to the ureteral adventitia and tubularized over a double –J stent (Badawy et al., 2010). Although there is paucity of this application of oral mucosa grafts in the literature at the present, increasing use of this will increase.

5.4 Use of oral mucosa grafts for vaginal reconstruction

Vaginal reconstruction is indicated in congenital absence of the vagina as found in Mayer-Rokitansky- Kuster- Hauser syndrome, isolated vaginal agenesis in children, in adults following pelvic exentration for malignancy, patients who had undergone sex re-assignment and in those undergoing feminizing genitoplasty for congenital adrenal hyperplasia (Gupta et al., 2002; Hensle&Reily, 1998; Fleighner, 1994; Leslie et al, 2009; Gollu et al,2007).

Surgical techniques for vaginal reconstruction include use of myocutaneous flaps, partial and full thickness skin grafts and use of intestinal segments (Leslie et al., 2009; Johnson et al., 1991; Michal et al 2007; Rajimwale et al., 2004; Franz, 1996). The neo-vagina created by flap and graft vaginoplasty call for constant dilatation and are prone to stenosis but the intestinal neo-vaginas do not require frequent dilatations but generate mucus which may be plentiful to make patients put on sanitary pads. However, all these techniques entail abdominal procedures and visible scars. Oral mucosa grafts have been applied for vaginal reconstruction in selected patients. Samuelson et al (2006) performed autologous buccal mucosa graft vaginoplasty in a post-pubertal patient with adrenogenital syndrome who had excellent functional and cosmetic outcome. Muxin and colleagues (2009) reported of a

series of 9 patients presenting with vaginal agenesis who had construction of neo-vagina that was lined with autologous micromucosa . Both reports corroborate the advantages of oral mucosa grafts in vaginoplasty which include wet, non-keratinized neo-vaginal mucosa with excellent color and texture matching to the genital and vaginal skin. In addition, OMGs leaves no visible surgical scars, avoids abdominal bowel surgery and do not produce excess mucus. Buccal mucosa may be a replacement for the female vulva and vaginal glabrous skin and be an excellent adjunct or alternative in challenging reconstruction.

6. Donor-site morbidity in oral mucosa graft harvest.

Serious complications from oral mucosal graft harvest are uncommon. Possible adverse effects of harvesting oral mucosa include intra-operative haemorrhage, post-operative infection, pain, swelling, injury to the parotid duct, limitation of oral opening and loss of or altered sensation of the cheek or lower lip through nerve damage (Dublin &Stewart, 2004; Markiewcz et al., 2007)

Wood et al (2004) noted reduction of sensation in the oral cavity in the region of the site of graft harvest in 68% of patients which persisted in 26% at, or further than, six months follow-up. This complication is more frequent when the graft is harvested from the lower lip (Kamp et al., 2005). The neurosensory deficit of the long buccal and mental nerves could be explained by individual variations in the location and nature of branching of these two nerves. This may happen with short and thin patients especially when the amount of available buccal mucosa tissue is small or a larger graft is harvested.

Tulstunov et al (1997) in a more detailed study of twelve patients reported that all patients had only mild oral discomfort at the end of the first week and by the third week, no patient had oral discomfort. Dublin et al (2004), found that 10% of the patients had moderate-to-severe pain on discharge but after about three weeks the pain resolved. Wood et al(2004) found that the daily pain score was higher in those patients with donor- site closure than in those in whom the donor-site was left open.

Damage to surrounding structures can be avoided by careful marking of the cheek mucosa before harvesting. It is recommended that the dissection should be at least 1 cm from the opening of the parotid duct and care should be taken during suturing of the wound. Parasthesia after harvesting a buccal mucosal graft is the most common complication in our patients.

7. Role of tissue engineering in urethral reconstruction.

The main constraint in use of oral mucosa grafts for extensive urologic reconstruction is the limited amount of graft available for harvest in patients as a result of previous dental procedures, trauma, infection, malignancy or prior oral mucosa grafts.

Tissue engineering encompasses a multidisciplinary approach that applies the principles and methods of engineering and life sciences geared for the development of tissue and organs as biological substitutes to restore and preserve normal function in diseased or injured tissues (Cross et al., 2003). Tissues that are engineered using the patient's own cells or immunologically inactive allogenic or xenogenic cells have the potential to overcome current problems of replacing function (Saxena, 2005). Bhargava and colleagues (2004) developed a technique to increase the amount of tissue available for harvest called tissue-engineered buccal mucosa (TEBM). Izumi and colleagues (2003) reported clinical study

using ex vivo produced human oral mucosa composed of both epithelial dermal component for intraoral grafting procedures. Tissue engineering has a principal advantage over organ transplantation and circumvents organ shortage. Tissues that match the patient's requirements can be reconstructed from readily available biopsies and then re-implanted with minimal or no immunogenicity.

Tissue engineering in urology is a rapidly emerging field with researchers and clinicians world-wide in search of 'off- the- shelf' replacements for the bladder and urethra. Buccal mucosa has been successfully tissue-engineered by culturing oral keratinocytes and fibroblasts. These cells were applied to de-epidermised dermis to obtain full-thickness tissue-engineered oral mucosa for substitution urethroplasty (Bhargava et al., 2004, Lavick & Langer, 2004; Li et al., 2008). De Fillipo et al (2002) demonstrated in rabbit models that collagen matrices seeded with cells from normal urethral tissue can be used for tubularized replacement.

The success of tissue engineered grafts is dependent on the ability to provide a suitable environment for regulating cell behaviour such that adhesion, proliferation, migration and differentiation eventually result in a graft composed of a population of cells similar in morphology and phenotype to the desired tissue(Fransis et al., 2009). Engineered buccal mucosa will offer a useful addition in urethral reconstruction, thus creating sufficient tissue for urethroplasty with minimal donor-site morbidity and quicker surgery for longer and complex procedures such as those associated with balanitis xerotica obliterans and two-stage circumferential urethral replacements (Lavick et al., 2004).

8. Conclusion

Oral mucosa is an excellent substitute to skin whenever reconstruction is required with a non hirsute and non keratinized skin. This requirement had previously posed an immense challenge to urologic, pediatric and plastic surgical reconstruction. As skin substitute, oral mucosal grafts are reliable with long term results comparable to that of penile skin flaps. Oral mucosa is more resistant to infection and has a micro-vasculature that encourages inosculation. Oral mucosa grafts are easier to harvest compared with penile flaps and are not attended with potential complications of scaring, cordee and torsion. This is also an ideal substitute in patients with Lichen sclerosis. In addition to urethral reconstruction in adult and children, OMGs can be used for glans reconstruction and resurfacing, clitoral reconstruction, ureteral repair and vaginal reconstruction. The graft volume can be improved with tissue engineering making it potentially available for wider coverage

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The procedure of skin grafting has been performed since 3000BC and with the aid of modern technology has evolved through the years. While the development of new techniques and devices has significantly improved the functional as well as the aesthetic results from skin grafting, the fundamentals of skin grafting have remained the same, a healthy vascular granulating wound bed free of infection. Adherence to the recipient bed is the most important factor in skin graft survival and research continues introducing new techniques that promote this process. Biological and synthetic skin substitutes have also provided better treatment options as well as HLA tissue typing and the use of growth factors. Even today, skin grafts remain the most common and least invasive procedure for the closure of soft tissue defects but the quest for perfection continues.

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