Expert CONSULT

Chapter 24 – Cancer of the Lip

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The lip is the most common site of origin for squamous cell carcinoma of the oral cavity. These cancers are most frequently found on the lower lip. The cause and clinical behavior of carcinoma of the lip, however, more closely parallel squamous cell carcinoma of the skin than they do squamous cell carcinoma of the oral cavity. Occasionally, full-thickness cancer of the lip may have a significant mucosal (oral) component, thus making this distinction more difficult.[1] Carcinoma of the lip occurs most frequently in older white men, with the average age at onset being in the sixth decade of life. It appears that the major risk factors for the development of lip cancer are male gender, a fair ruddy complexion, and an outdoor occupation.[2] In the United States, there is a marked male preponderance (19:1 for cancer of the lower lip and 5:1 for cancer of the upper lip).

Although prolonged exposure to sunlight is believed to be a causative agent,[3] other factors, such as poor dental hygiene, syphilis, chronic alcoholism, and pipe smoking, have been proposed. When pipes were made with clay stems, the high temperature generated within the stem may have caused irritation sufficient to induce malignant degeneration. However, pipes are now made with plastic stems, which are poor conductors of heat and no longer considered a risk factor. A viral etiology has been suggested, particularly oncogenic subtypes of human papillomavirus (types 16 and 18). Carcinoma of the lip has been found to be associated with chronic immunosuppression. The highest rates of cancer occurrence in such patients appear to be in the lip and skin, the former perhaps a variant of the latter.[4] This form of cancer is most prevalent in patients who have undergone renal transplantation.[5]

Other types of cancer occur less commonly on the lip, including malignant melanoma and malignant tumors of salivary gland origin, such as adenoid cystic carcinoma and adenocarcinoma. Basal cell carcinoma occurs infrequently on the lip.

PATIENT SELECTION

Most patients with squamous cell carcinoma of the lower lip consult a physician when the tumor is at a relatively early stage (≤1 cm in diameter) (Fig. 24-1) and because of nonhealing ulceration or bleeding. Although small, most of these lesions have been present in some form for many months, and some have been treated with antibiotic ointment or skin cream. Patients seek medical attention when they see no improvement after this treatment. Some of these cancers have been preceded or accompanied by whitish plaque, ulceration, or erythroplasia.

Figure 24-1 Typical appearance of early squamous cell carcinoma of the lower lip.

A small number of patients are not initially seen until later in the course of the disease, at which time the tumor is characterized by deep invasion of the musculature of the lip (Fig. 24-2), the adjacent skin, the oral mucosa, or the mandible, especially by way of the mental nerve.[2] This may be due to neglect or to a more aggressive tumor phenotype and lack of optimal immune function. A small fraction of patients (approximately 2%) with squamous cell carcinoma will demonstrate perineural involvement. Although occurring infrequently, cancer with perineural spread deserves special attention because it has important therapeutic and prognostic implications, such as a high incidence of local recurrence and nodal metastasis and a 5-year survival rate of 33%, which is strikingly lower than that for most patients with carcinoma of the lip.

Figure 24-2 Advanced cancer of the lip with deep invasion.

Patient selection begins with a thorough history. The presence of other skin changes as a result of exposure to ultraviolet radiation should be noted at this time. The location on the lip, which is highly visible, usually makes the tumor accessible for inspection and palpation. Inspection and measurement of the lesion are important to ensure proper staging. Careful palpation of the lesion between gloved thumb and forefinger is helpful in determining the size and degree of infiltration of the tumor, which may extend beyond the visible ulceration. All patients should be tested for hypoesthesia of the lower lip in the distribution of the mental nerve because of the possibility of perineural involvement. Even in the absence of cortical bone destruction, the tumor may grow along the mental nerve into the medullary portion of the mandible and may even extend as far as the cranial cavity.[2] The neck must be palpated, particularly in patients receiving chronic immunosuppression. Lymphatic drainage of the middle third of the lower lip is primarily into the submental lymph nodes, with secondary drainage into the submandibular and upper internal jugular nodes (Fig. 24-3). Cancer of the lateral third of the lower lip tends to drain into the submandibular lymph nodes. Cancer of the upper lip metastasizes to the submental and submandibular nodal groups. The incidence of regional nodal metastasis has been found to be 5% for T1 lesions, 50% for T2 lesions, and 70% for T3 lesions.[2] Although metastasis to neck nodes has been believed to be related to advanced stage, deeply ulcerated lesions, and mandibular or perineural involvement, Hosal and coworkers concluded that the size of the primary cancer does not correlate closely with predicting the incidence of regional lymph node metastasis.[6] Immunosuppression should lead to heightened concern and search for regional metastasis by palpation and imaging studies.
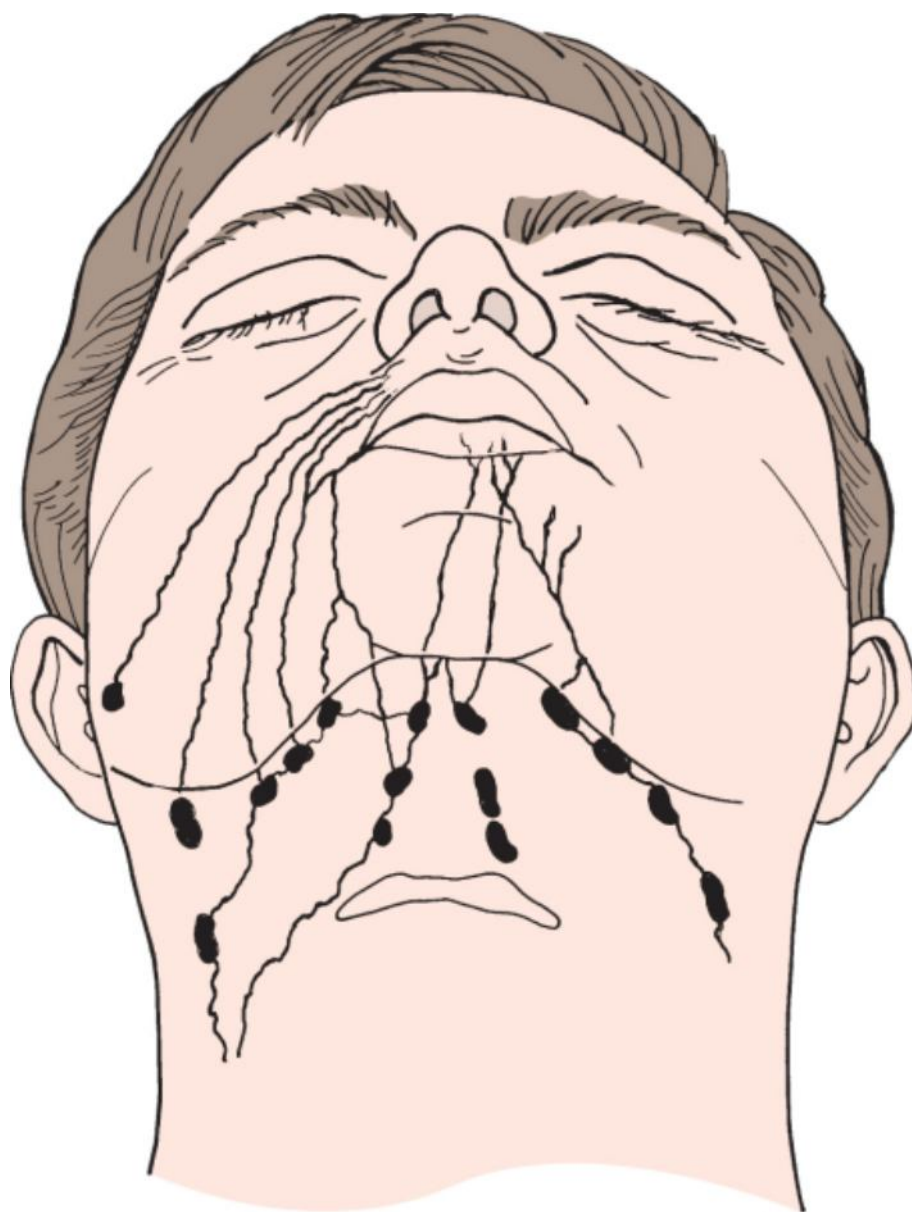
Figure 24-3   Lymphatic drainage of the lip.

Metastasis from cancer of the upper lip may occur more frequently than that of the lower lip.[4] Likewise, cancer involving the commissure metastasizes more frequently than that of the midportion of the lip. A complete examination of the head and neck should be performed to rule out a second primary cancer of the head and neck.

PREOPERATIVE PLANNING

All lesions suspected of being malignant or premalignant should undergo biopsy. If the lesion is ulcerated, as with most squamous cell carcinomas, a punch biopsy under local anesthesia may be performed, preferably on the edge of the lesion and including some normal tissue. In lesions manifested as submucosal nodules, such as salivary gland cancer, an incisional biopsy, again taking some normal tissue, is necessary for diagnosis.

Cancer of the lip is staged as follows:
- T1—Tumor less than 2 cm in greatest diameter
- T2—Tumor between 2 and 4 cm in greatest diam-eter
- T3—Tumor larger than 4 cm in greatest diameter
- T4—Tumor larger than 4 cm in greatest diameter with deep invasion, including muscle, bone, or other structures

Patients who have any history or physical finding suggestive of perineural spread, mandibular involvement, or palpable lymph nodes should undergo imaging of the neck with computed tomography (CT) or magnetic resonance imaging (MRI). This group should also include any patient who is chronically immunosuppressed. These studies

should encompass the entire head and neck because perineural involvement can be discovered in the mental and inferior alveolar nerves, as demonstrated by widening of the foramen, or as far proximal as the intracranial cavity. MRI may demonstrate tumor involvement of the inferior alveolar nerve before bone erosion is visible on CT. In more advanced cases, there is an increased probability of lymph node metastasis. Imaging is useful in planning treatment by identifying cervical lymph nodes that meet the criteria for malignancy. Combined positron emission tomography (PET)/CT may be useful in such situations, particularly for evaluating bilateral or contralateral spread to the neck and for staging purposes before forming a plan of management.

Modalities that have been used successfully in the treatment of carcinoma of the lip include surgical excision alone, radiation therapy alone (external beam, intensified implants, or both), or combined surgical excision and radiation therapy.[2] The management program selected usually depends on a number of factors, including the size and location of the lesion; the patient's age, general medical condition, and needs; and the experience and skill of the surgeon and radiation oncologist.

T1 and T2 invasive squamous cell carcinoma and the more infrequently occurring basal cell carcinoma may be treated successfully by either surgery or radiation therapy. The results are cosmetically acceptable with either technique. In advanced lesions, surgical excision or a combination of surgery and radiation therapy is preferred.

Radiation therapy may consist of interstitial, external, or contact beam therapy (or any combination). Application of external beam radiation is disadvantageous to patients who will return to occupations requiring sun exposure because sensitivity of the treated area to thermal actinic stimuli is said to be increased. Because many of these patients live in rural or remote areas, access to radiation therapy over a long period may be inconvenient or impossible. Radiation is also not useful in more advanced forms of cancer with deep infiltration, perineural involvement, mandibular destruction, or positive lymph nodes. Although radiation therapy is not generally as invasive and carries a lower risk of treatment-related morbidity, it is more time consuming and expensive in most cases. Even successful radiation therapy frequently leaves a tissue defect that may need to be reconstructed or an atrophic scar at the site of the original primary lesion. It also provides unpleasant side effect such as xerostomia and loss of taste.

The mainstay of treatment of cancer of the lip is surgical excision. Radiation therapy is typically reserved for patients who refuse surgery or those whose physical or mental condition may not permit surgery. It can also be used in programs of combined therapy in patients with advanced lesions.[7] Neck dissection should be undertaken only if palpable nodes are present, if imaging suggests abnormal nodes meeting the criteria for malignancy, or for a large or bulky cancer in which the risk of local metastatic disease is increased. Sentinel node biopsy may be used to determine the presence of metastasis and lymphatic drainage patterns to assist in management of the neck, particularly in high-risk patients.[8]

SURGICAL TECHNIQUE

Surgical management of carcinoma of the lip should accomplish the following objectives:

- Adequate excision of the cancer
- Preservation of lip function (speech, chewing, oral competence, and retention of saliva)
- Satisfactory cosmetic appearance
- Rapid rehabilitation
- Minimal cost

Because of the low probability of a coexisting second primary cancer in the upper digestive tract, routine preoperative panendoscopy is not performed. However, if the patient has oropharyngeal symptoms, physical findings on examination of the head and neck, or abnormal imaging studies, endoscopy is warranted. The key to the successful treatment of affected patients is removal of the cancer in its entirety. Surgical margins are close (5 mm), so pathologic examination is mandatory. We systematically perform intraoperative frozen section examination of surgical margins to decrease the likelihood of re-excision later.[9] If permanent section reveals positive margins, re-excision is mandatory because recurrence and often metastasis are distinct risks related to subtotal excision of the tumor.

Orientation of the specimen can be problematic, especially if the pathologist is not familiar with head and neck procedures. We believe that asking the pathologist to come into the operating room to visualize the specimen and the defect and to speak with the surgeon directly is the best method to enhance communication so that the patient's chance for cure is not compromised. Debate about whether frozen section margins should be removed from the tumor specimen or from the patient is ongoing.

Small Cancers of the Upper or Lower Lip (Excision of Less Than One Third of the Lip)

Anatomically, the facial aesthetic unit of the lips is bounded by the nasal base superiorly and centrally, the

melolabial crease laterally, and the labiomental crease inferiorly. As much as possible, particularly with smaller defects, one tries to stay within these anatomic boundaries. Furthermore, the relaxed skin tension lines (RSTLs) are oriented in radial fashion around the upper and lower lips, much like the spokes of a wheel. Orienting incision lines parallel to the RSTLs will ultimately help provide optimal scar camouflage.

The excision is generally performed with the patient under local anesthesia with intravenous sedation. If the surgery is performed under general anesthesia, a nasotracheal tube should be used to avoid distortion of the lower lip from an orotracheal tube. Excision margins should be marked on the patient with methylene blue or a marking pen before infiltration of local anesthetic to prevent distortion of tissues. With the scalpel blade, the vermilion border is marked on each side of the lip adjacent to the margins of excision (Fig. 24-4). Included in the incision, in addition to the cancer, should be approximately 5 mm of normal-appearing tissue to be certain that the margins of resection are free of tumor. We inject 1% lidocaine with 1:100,000 epinephrine through a no. 30 needle to obtain anesthesia and vasoconstriction. The injection is carried out along the previously marked lines of incision so that if the lines are erased during preparation of the skin, the needle marks will still provide an accurate line of incision. Mental (lower lip) or infraorbital (upper lip) nerve blocks can be helpful for additional anesthesia. The skin of the entire face is prepared with povidone-iodine (Betadine) solution, and the entire face is draped into the sterile field. Ten minutes should elapse after the completion of infiltration to obtain maximal vasoconstriction.
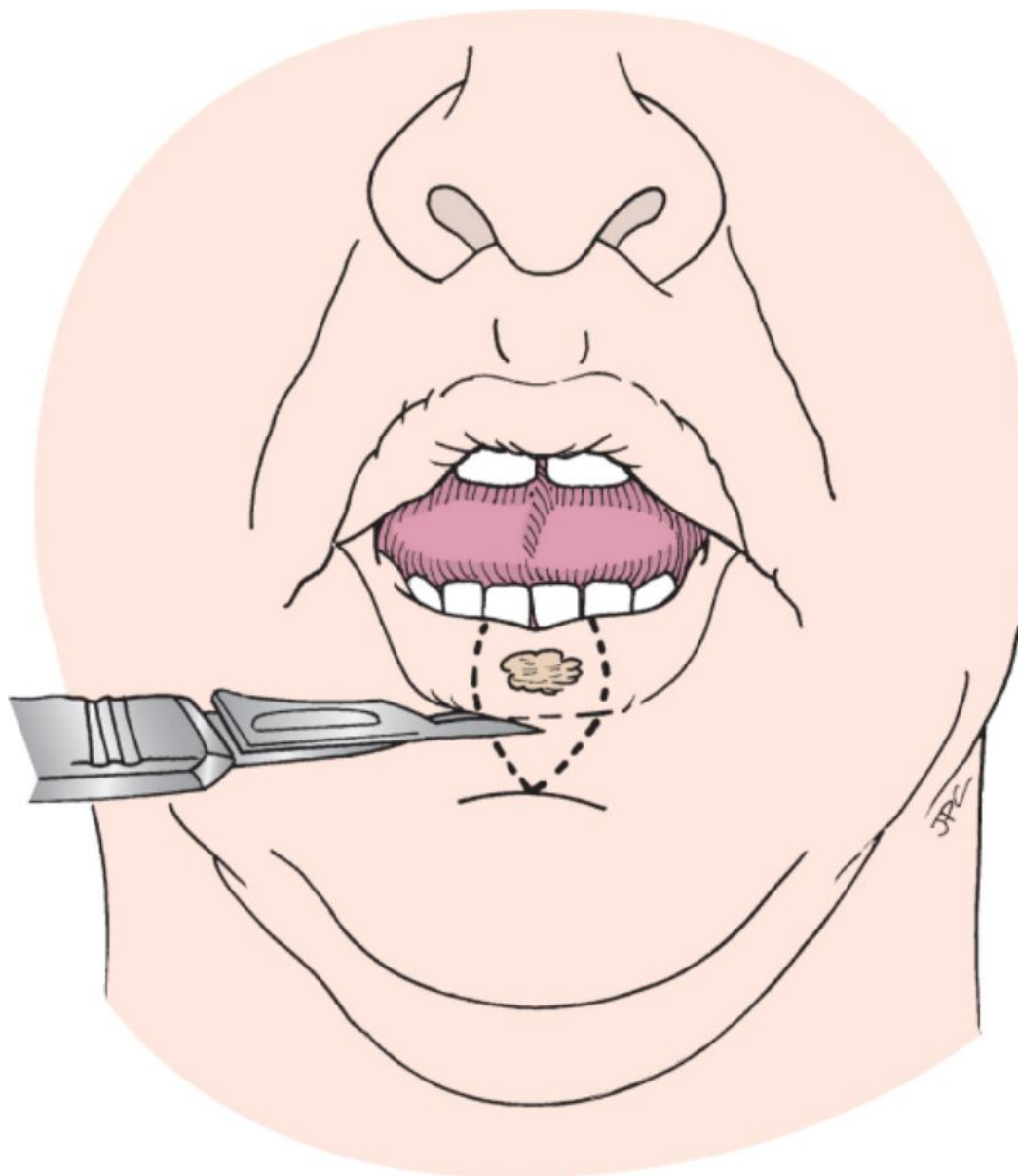

Figure 24-4 The incision is marked on the skin, and the vermilion border is marked with a scalpel to ensure accurate realignment.

The lip is grasped on each side of the line of incision with a thumb and finger (for hemostatic control) or a Lahey clamp, and the tumor is excised in a wedge shape. While frozen sections are being carried out, hemostasis is obtained by electrocautery or ligatures as needed. A Prolene suture is loosely applied in the area marking the

edges of the vermilion border and the lips drawn together (Fig. 24-5). A three-layer closure follows, starting at the apex of the wedge in the mucosal area, working out with interrupted 3-0 chromic catgut suture, and ending at the vermilion border. Absorbable suture, either chromic catgut, Vicryl, or PDS, is used to close the defect in the orbicularis muscle. The same material is used for the subcutaneous layer, and the skin is approximated with either running or interrupted 5-0 or 6-0 nylon or Prolene monofilament suture. Steri-Strips are applied over the suture line in such a way that the area of incision is relaxed and without tension. Patients are discharged from the hospital the same day and return to the office in approximately 7 days for removal of the sutures. Chronically immunosuppressed patients have delayed wound healing and may require additional time before the sutures are removed.
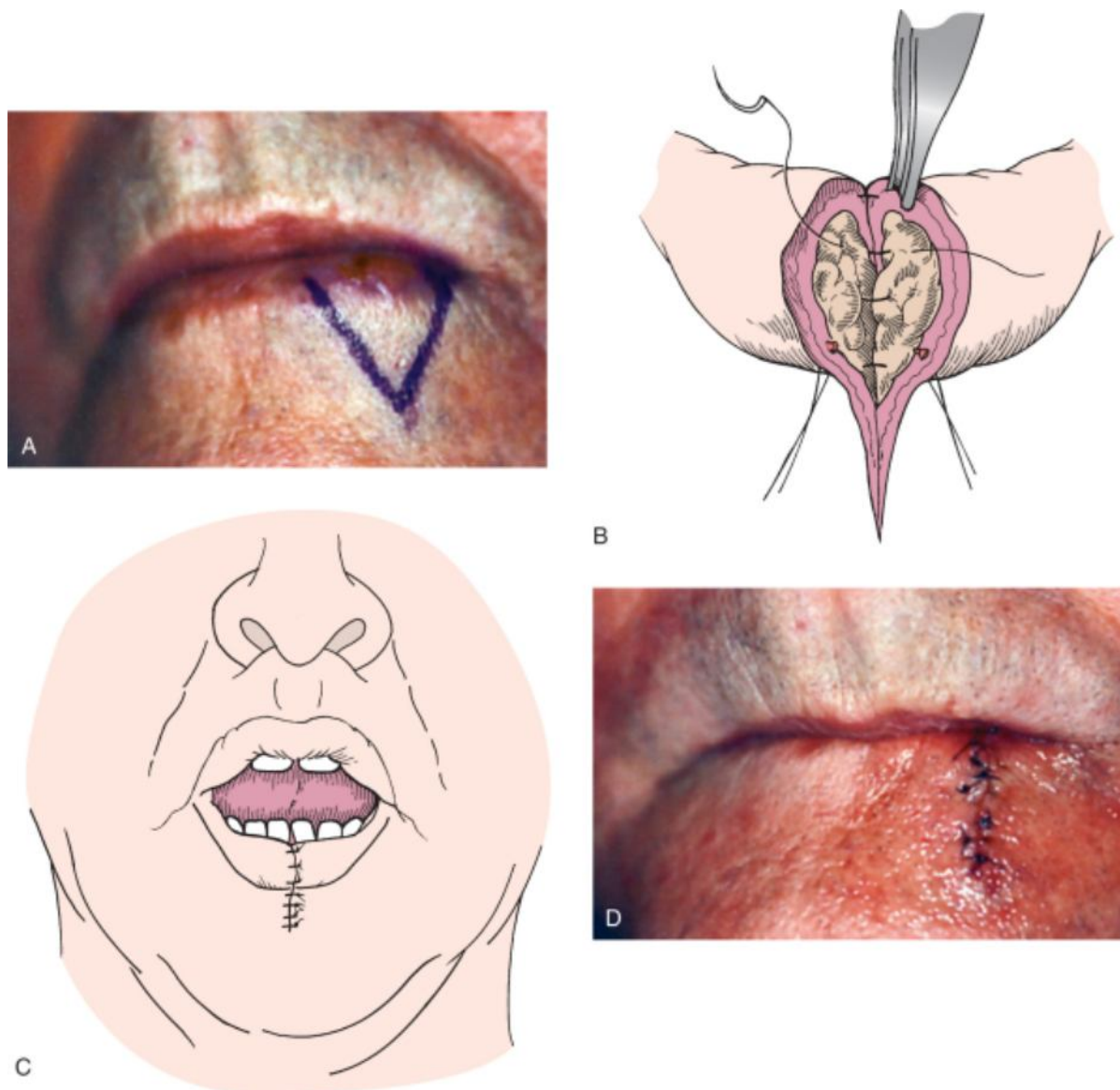

Figure 24-5 **A,** A wedge incision is used for excision of a small cancer of the lower lip. **B,** The skin, muscle, and mucosa are closed without tension. A temporary Prolene suture may be used to approximate the vermilion or gray line while the deeper layers are closed. **C,** Closure includes accurate restoration of the vermilion border. **D,** Wound is closed.

When the surface area of the cancer is somewhat larger (occasionally up to half the lip) but it remains relatively superficial rather than infiltrating deeply, a variation of the wedge excision in terms of a W excision and closure is useful. This incision essentially "inverts" the V of the wedge to reduce the distance that the incision must extend below (or above) the lip, thus helping keep excision lines within the boundaries of the aesthetic unit. Preparation, anesthesia, and performance of this incision are similar to those described earlier. The closure, however, is somewhat more complex (Fig. 24-6).
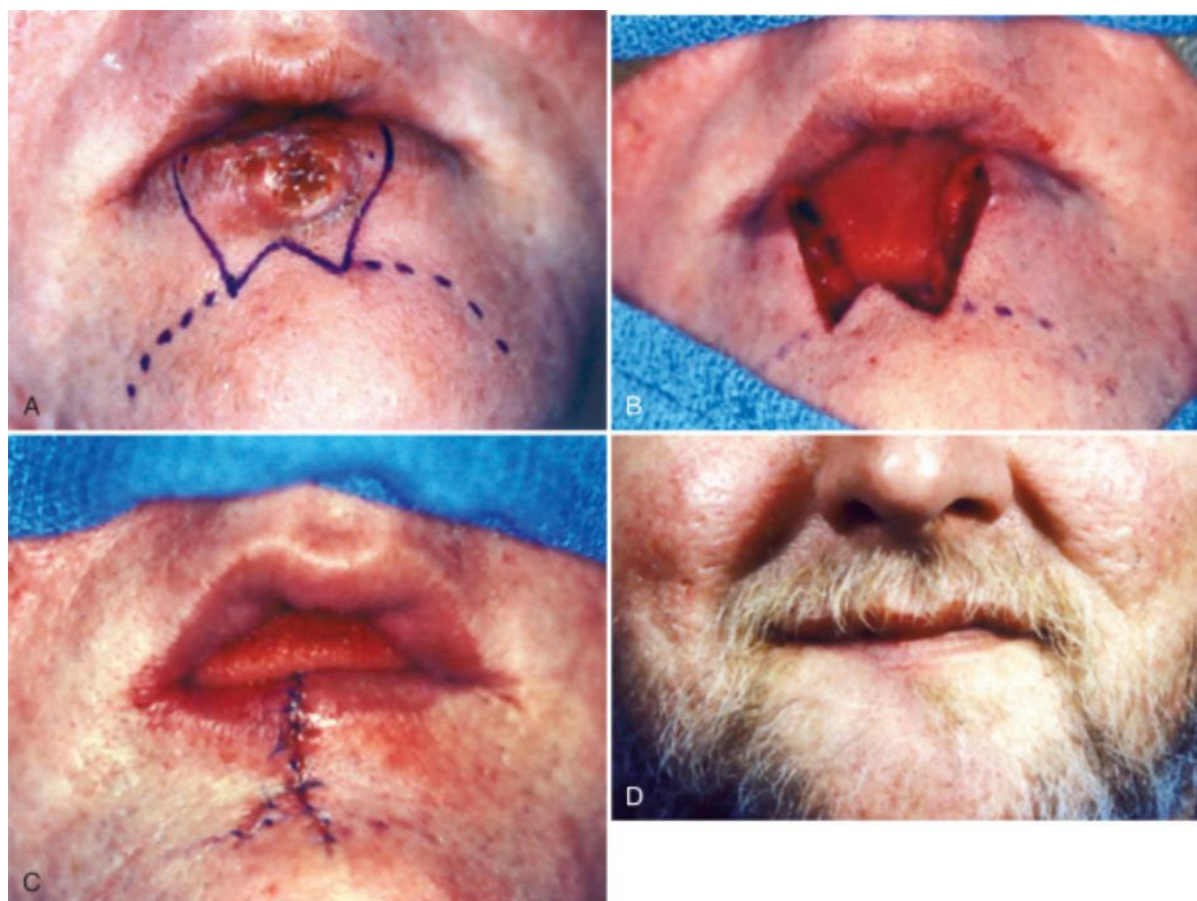
Figure 24-6 **A,** The W excision is outlined. **B,** The defect is shown. **C,** Wound closure. **D,** Wound is completely healed with good cosmetic result.

Larger Cancers of the Upper and Lower Lips

More extensive cancer involving the upper or lower lip, in which more than one third of the lip must be excised, cannot generally be closed primarily. Such defects will result in unsightly distortion of the oral commissure and difficulty with oral intake and articulation if they are closed primarily. Additional local tissue must be advanced into the defect. Usually, this takes the form of simple advancement flaps with or without some type of lip switch procedure to achieve a functional unit. The mucosa under the lip must be incised to release the tissue and advance the flaps properly.

Excision of the cancer is carried out in a manner similar to that described earlier, except that rather than planning the excision in the shape of a V (see Fig. 24-5), the rectangular block is shaped to incorporate the incisions required for advancement (Fig. 24-7). The transverse incision must be situated in the sulcus at the junction between the upper lip and chin to incorporate this natural skin fold for camouflage of the scar. Two through-and-through vertical incisions are made to encompass the cancer with adequate margins. A horizontal connecting incision is made in the melolabial crease where the chin and lip intersect. After excision and confirmation of adequate margins with frozen section, relaxing incisions are made laterally. These incisions permit mobilization of two opposing rectangular advancement flaps, which can then be advanced. The wound is once again closed in layers.
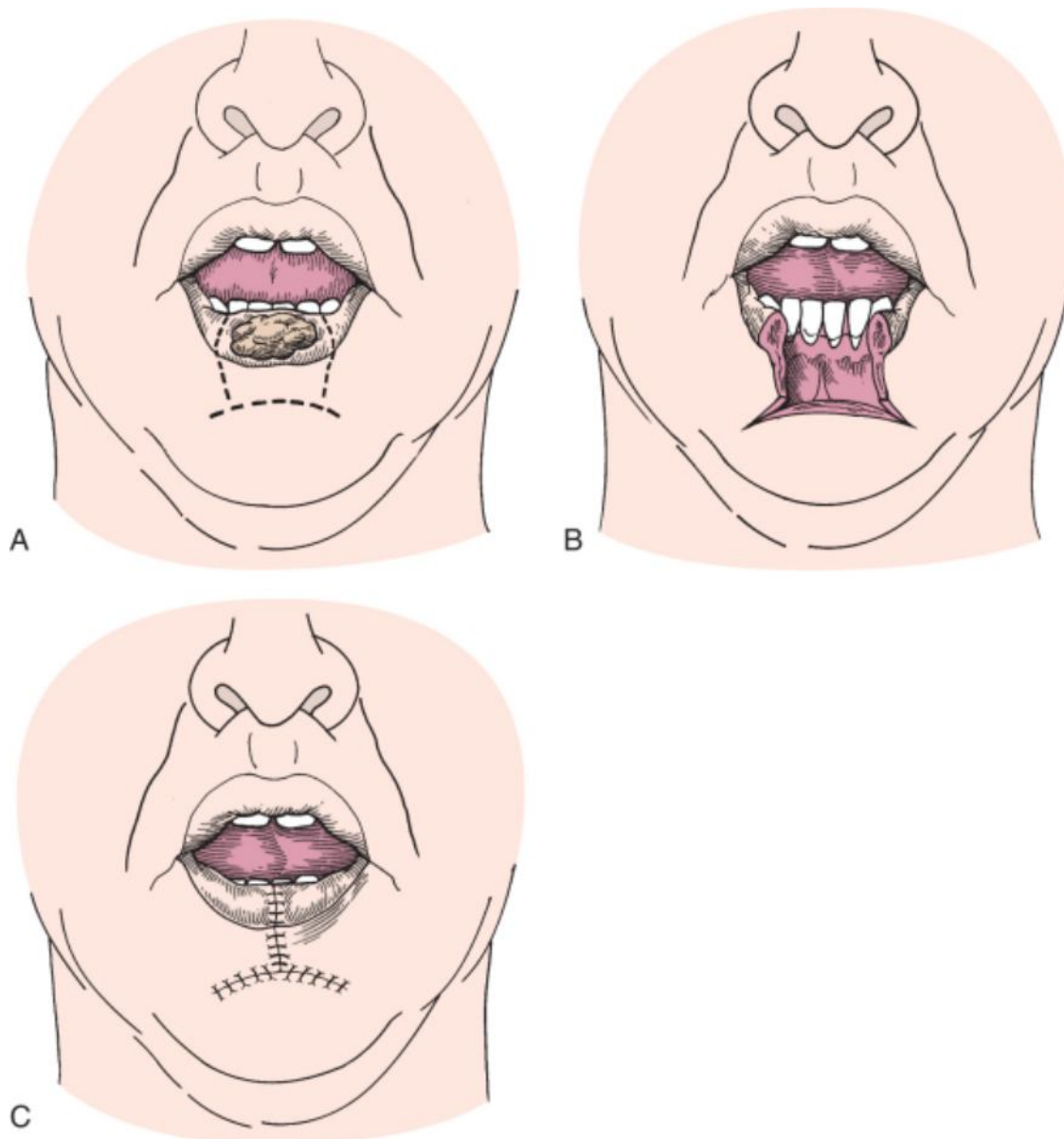
Figure 24-7 **A,** The wedge/block excision is shown with the advancement flaps outlined. A central lower lip cancer is removed, with optional relaxing incisions for residual lip mobilization. **B,** The defect is shown with the advancement flaps outlined. **C,** Wound closure.

Similar advancement flaps can be created after block resection of cancer of the median portion of the upper lip (Fig. 24-8A and B). Flaps similar to those described earlier are created by removing Burrow's triangles just lateral to the nasal ala (see Fig. 24-8C and D). This provides two flaps that can be advanced to the midline without producing the unsightly bunching effect that would otherwise take place (see Fig. 24-8E). This type of simple reconstruction provides excellent cosmetic results.
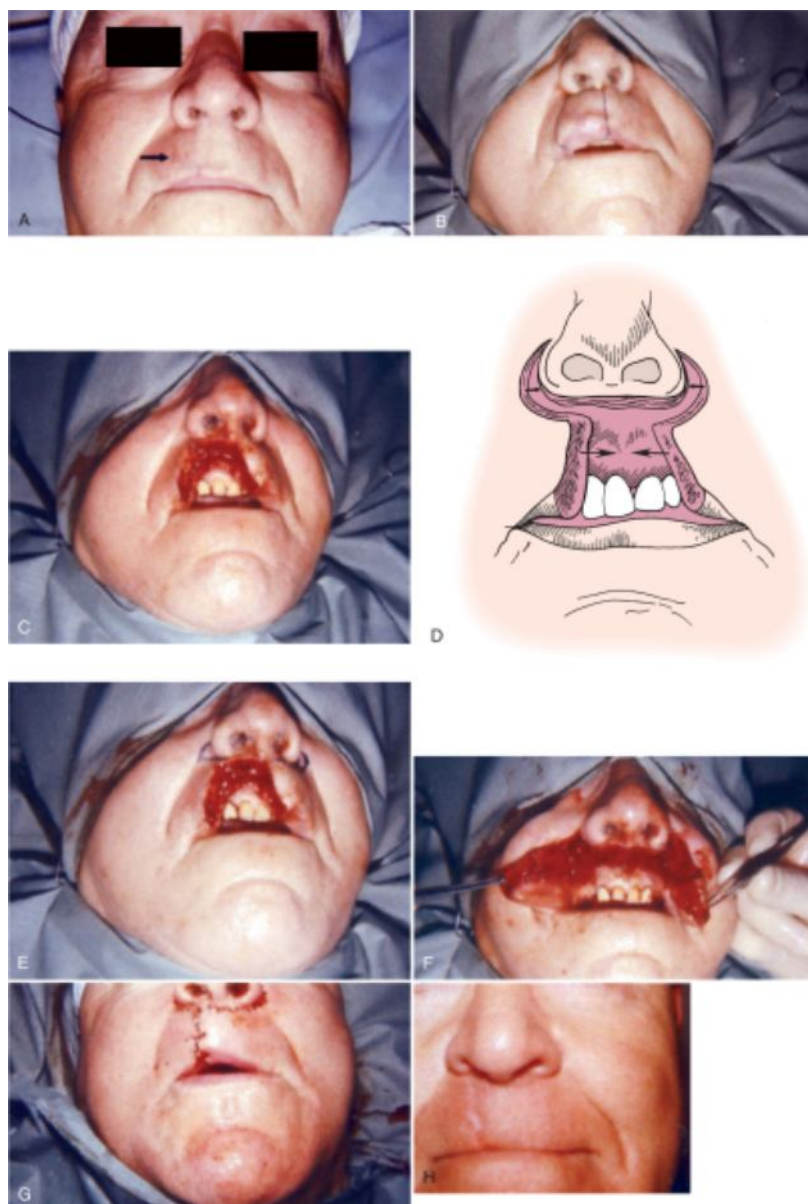
Figure 24-8 **A,** Cancer of the upper lip *(black arrow).* **B,** The excision is outlined. **C,** The defect after excision. **D,** Diagram of reconstruction. **E,** Burrow's triangles outlined. **F,** Excision of Burrow's triangles and bilateral advancement flaps. **G,** Wound closure. **H,** Postoperative appearance.

For resection defects up to one half to two thirds of the lip, closure will generally require a full-thickness pedicled flap from the opposite lip (the "lip switch" flaps—Abbé or Estlander) or larger perioral advancement flaps such as the Karapandzic flap.

With the "lip switch" flaps, tissue is rotated from the upper to the lower lip or from the lower to the upper lip, depending on circumstances. These flaps lend themselves to satisfying rehabilitation in this area because the neurovascular supply is retained. They are preferable because they are local flaps and afford an excellent match in skin color and texture and the availability of vermilion and mucous membrane. The flaps should be designed so that the height of the flap equals the height of the defect. The width of the flap should be one half that of the resected segment so that both lips are reduced in width proportionately.[1,9]

The Estlander flap is based on branches of the labial artery and is used to reconstruct defects in the lateral aspect of the lip and oral commissure (Fig. 24-9A). Effort should be made to terminate the incision at the nasolabial fold to incorporate the scar into this natural structure. Accurate approximation of the vermilion border of the flap with that of the defect will ensure a good cosmetic result (see Fig. 24-9B and C). The surgeon should recall that the vermilion border is an important guide, because the labial artery runs just deep to the muscle at the level of the vermilion border. The flap, once developed, is transposed into the defect, and after hemostasis is achieved, a four-layer closure is performed as described earlier, including mucosa, muscle, subcutaneous tissue, and skin. The only unfortunate aspect of this reconstruction is the creation of a rounded commissure. Although this does not produce any functional problems, the patient may request revision for cosmetic appearance at a later date.
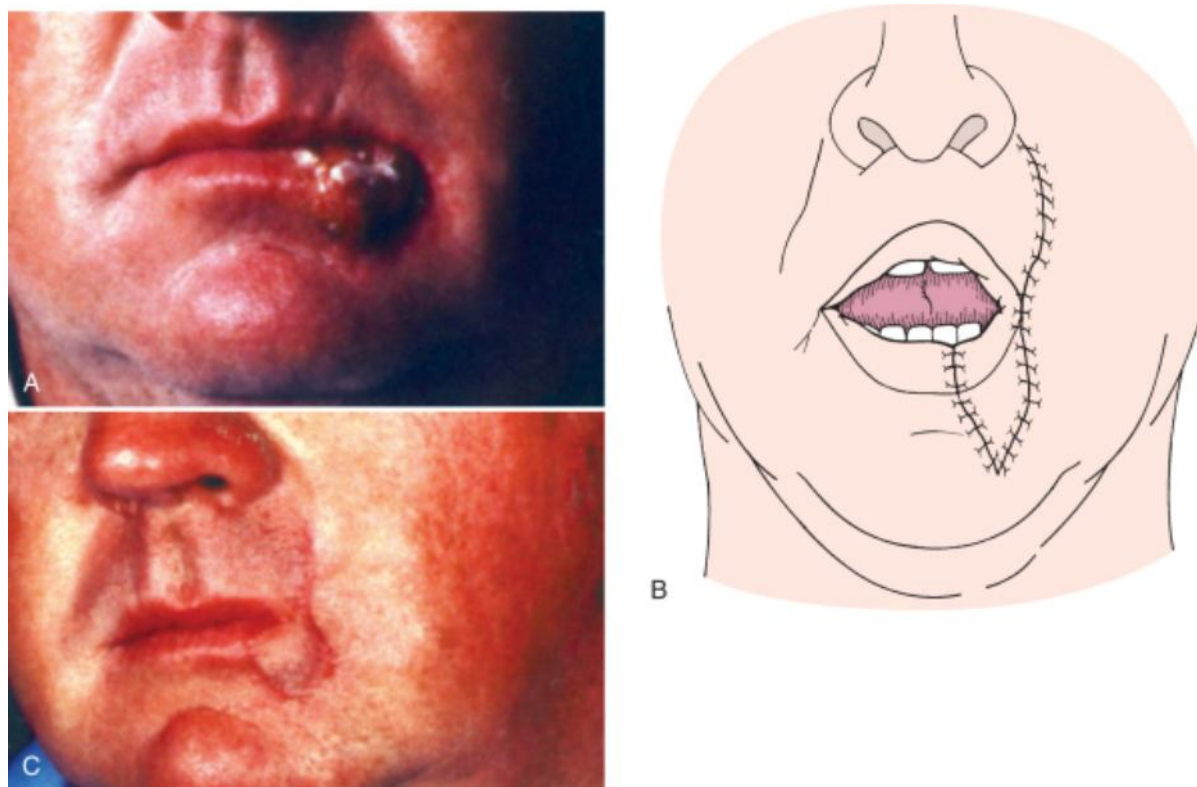
Figure 24-9 A, Recurrent squamous cell carcinoma of the lower lip. **B,** Scheme for an Estlander flap. **C,** Acceptable cosmetic and functional results at the commissure with an Estlander flap.

An Abbé flap based on the opposite lip is, in principle, similar to an Estlander flap except that it is used to reconstruct defects away from the oral commissure. It may be used if tumor resection includes an area that is too large for primary closure and yet not large enough to require Karapandzic advancement flaps. A wedge-shaped defect is created by tumor resection, and the surgeon then makes a full-thickness incision in the opposite lip in the shape of a wedge, pedicled on the labial artery on one side. Precautions in dissecting the labial artery and preserving the pedicle are carried out as described earlier. The flap is transposed into the defect, and a four-layer closure is carried out (Fig. 24-10). The donor site is also closed in layers. The patient is fed a liquid diet by straw over the next 14 to 21 days, at which time the pedicle is divided and the flaps inset, with special care taken to approximate the vermilion border on both sides.

Figure 24-10 **A,** Extensive cancer of the upper lip. **B,** The defect after excision of the cancer. **C,** The defect reconstructed with an Abbé flap and cheek advancement flaps facilitated by the use of Burrow's triangles. **D,** Appearance after release and inset of the Abbé flap.

The Karapandzic flap provides an excellent method of reconstructing larger defects while still preserving a functional, albeit smaller oral stoma. This may cause difficulty with feeding, oral hygiene, and insertion of dentures. Bilateral oral commissure revision can be performed at a later date to obtain more definition of the oral commissure. This is not only functionally beneficial to the patient but is also an important cosmetic consideration.

The excision is performed as necessary to accommodate the large size of the cancer. In most cases this will, for all practical purposes, entail sacrificing most of the lower lip (Fig. 24-11A). Incisions are made in the nasolabial folds and carried down through subcutaneous tissue (see Fig. 24-11B). The incisions should be made sharply through the dermis and subcutaneous tissue, but the remainder of the dissection must be carried out bluntly with the use of blunt dissecting scissors to avoid devascularizing and denervating the flap (see Fig. 24-11C). The tissues are spread along the course of the facial artery and its branches to identify and preserve these vessels. Soft tissue should be preserved around the neurovascular bundle to maintain the integrity of the vasa vasorum and vasa nervorum. Dissection should be carried down to but not through the mucosa. Care must be taken to preserve branches of the facial nerve if one hopes to maintain a functional unit. Flaps are mobilized to obtain the desired skin coverage. As tension is applied to the flaps, the mucosa is incised incrementally for a distance sufficient to allow the flaps to come together with sufficient mucosal coverage. Flaps should be approximated with subcutaneous absorbable catgut suture in the mucosa and 4-0 Vicryl or Dexon suture to bring the orbicularis oris muscles together. The submucosal and dermal layers can be closed with 4-0 chromic catgut suture, the mucosa is closed with 3-0 chromic catgut, and the skin is closed with 5-0 or 6-0 interrupted silk suture (see Fig. 24-11D and E). Steri-Strips are applied to minimize tension on the suture lines. This technique produces a functional oral commissure with acceptable, if not outstanding cosmetic results.
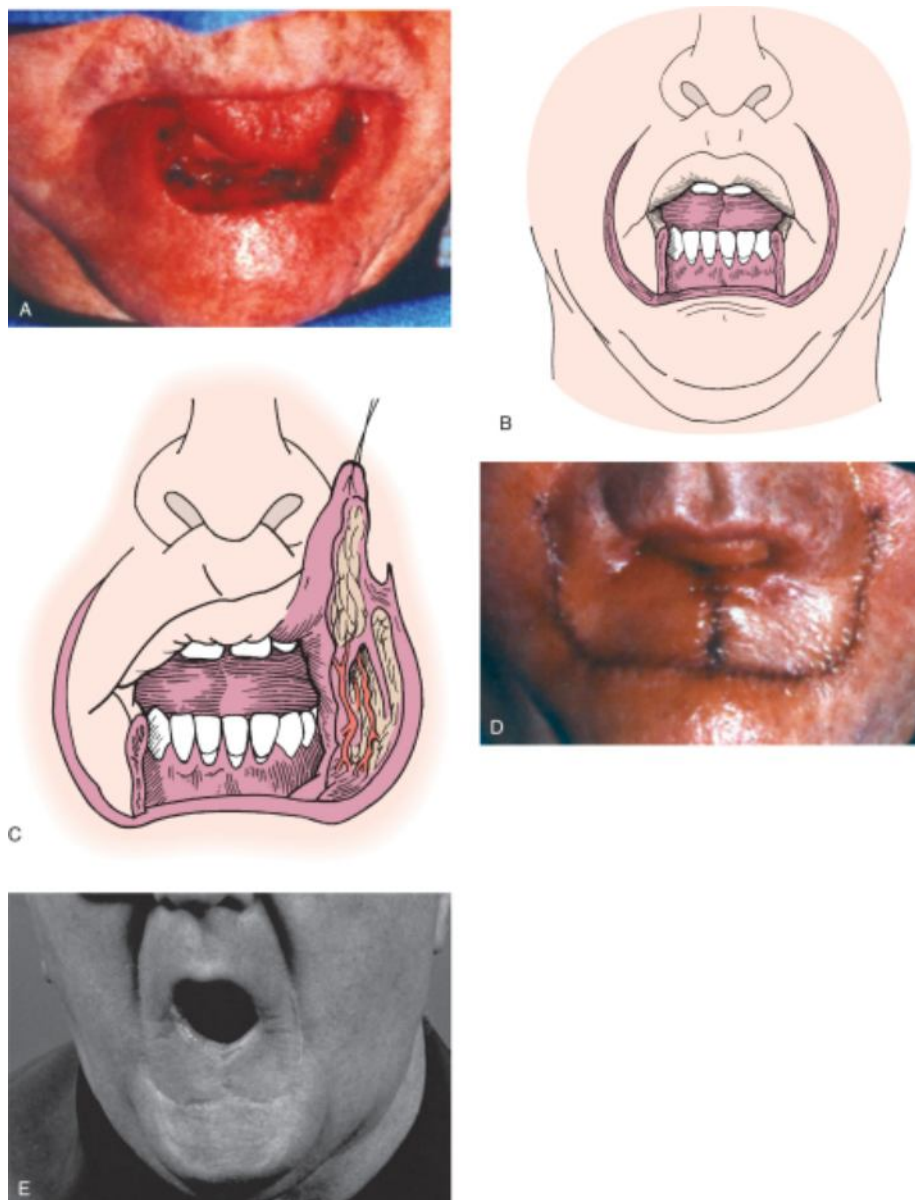
Figure 24-11 **A,** The defect after excision of a large cancer of the lower lip. **B,** The Karapandzic flaps incised. **C,** The flaps incorporate new vascular components. **D,** The flaps are advanced and closed in multiple layers. **E,** Good functional and cosmetic results are shown.

In certain types of defects that do not allow closure by either straight advancement flaps or local flaps, a combination of flaps may be necessary. Such a situation is demonstrated in Figure 24-10. Massive tumors requiring excision of blocks of tissue too large to reconstruct with local flaps may require reconstruction with free flaps or a regional pedicle flap.

POSTOPERATIVE MANAGEMENT

We routinely administer intravenous antibiotics perioperatively for 24 hours and then have the patient continue oral medication for a total of 1 week because these wounds are technically contaminated by oral cavity flora. Postoperative care includes both local and general considerations. It is important to keep the suture line clean and well lubricated. The suture line itself is cleaned of dried blood and crusts with peroxide two or three times a day, and antibiotic ointment, such as bacitracin ointment, is applied to the skin of the lip. The Steri-Strips used to reduce skin tension are removed in 1 week. The sutures are removed in 10 days to 2 weeks.

Consideration must be given to the patient's diet. In patients who have undergone only excision and primary closure, a liquid diet for the first 48 hours, particularly with use of a straw, is helpful. A soft diet is prescribed for the following week because it requires less chewing and therefore less movement of the lips, thereby preventing tension on the suture line. Patients with an Abbé flap should be maintained on a liquid diet through a straw until division of the pedicle can be accomplished.

PEARLS

- Wound infection can be prevented by good local wound care and the administration of antibiotics.
- Vascular compromise in the pedicle, which may destroy the viability of the flap, can be avoided by meticulous attention to surgical technique.
- Nonabsorbable sutures should be used for up to 2 weeks, until wound strength is sufficient to counteract the strong muscular force exerted by the oral commissure.
- Uneven bites of tissue must be taken while suturing the midportion of the lip, which is thick, to the thinner, lateral portion of the commissure.
- The degree of microstomia is proportional to the extent of tumor resection, and it is a necessary tradeoff for using lip tissue for reconstruction after lip resection.

PITFALLS

- Tension on the pedicle will lead to severe complications such as tissue necrosis in the cross-lip and local flap operations.
- Not accurately marking the vermilion border before excision for careful approximation of the vermilion margins will lead to poor cosmetic results.
- Distortion of the oral commissure may occur, particularly with use of the Estlander flap, and should be corrected at a revision procedure.
- Drooling may result from injury to the neuromuscular components of the lip in either excision or reconstruction of the defect. A secondary revision procedure in these areas may be required.