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10th Anniversary of Skin Therapy *Letter*©

Dr Stuart Maddin
Editor-in-Chief

It was 10 years ago this month when we began publishing Skin Therapy *Letter*©.

There have been some changes over the years, not the least of which was the opportunity for Skin Therapy *Letter*© to become the only publication of its kind to be indexed by the US National Library of Medicine and PubMed. We are now an integral part of the SkinCareGuide Network of dermatology-related websites that provide comprehensive information concerning skin therapy for patients and physicians.

In every issue, we have endeavored to bring you articles about current therapies for skin disease that are practical, balanced and have clinical relevance. These peer-reviewed articles are written by contributing authors who provide information drawn from years of clinical experience and pivotal clinical trials. The members of our Editorial Advisory Board are affiliated with leading centers of excellence throughout the world.

I want to take this opportunity to thank you for your support over the past 10 years. We look forward to continuing to provide you with relevant information on dermatological therapies.

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Imiquimod 5% Cream (Aldara®) in the Treatment of Basal Cell Carcinoma

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ABSTRACT

Skin cancer, the most common human cancer, is now a global epidemic. The most prevalent form of nonmelanoma skin cancer is basal cell carcinoma (BCC), the incidence of which continues to increase prompting development of new treatment modalities designed to add or complement current therapies. Although destructive modalities continue to be an important treatment options for BCC, nondestructive measures are a welcome addition to our therapeutic choices. Imiquimod, a topical immune response modifier, belongs to the family of immunostimulators. It enhances both the innate and acquired immune response, and has successfully treated both superficial and nodular basal cell carcinomas through the localized activation of elaborate immune response. Imiquimod can either be used alone or in combination with other treatment modalities. The most common adverse effects of topical use of imiquimod are localized to the site of application and easily managed.

Key Words: *imiquimod, basal cell carcinoma, therapy, skin*

Skin cancer is the most common human cancer, and nonmelanoma skin cancer (NMSC) is now a global epidemic. BCC accounts for approximately 80% of new cases with superficial (sBCC) and nodular (nBCC) BCCs representing the majority of cases reported. The impact of cutaneous malignancies is significant, since they frequently lead to considerable deformities, either from the disease itself or from the resulting therapy. BCCs can destroy tissue through their relentless local growth. New, less invasive, nonsurgical therapies are welcomed as they may offer treatment without the use of destructive modalities.

The immune system plays an important role in the pathogenesis of NMSC. Immunosuppressed patients, such as organ-transplant recipients, have a greater incidence of BCCs. Regressing BCCs are frequently infiltrated with activated T lymphocytes and cytokines including interferon (IFN)-γ, interleukin (IL)-2, and tumor necrosis factor (TNF)-β. Intralesional IFN has been demonstrated to successfully treat BCCs.[1]

Imiquimod (Aldara™, 3M), a topical immune response modifier, enhances both the innate and acquired immune responses, in particular, the cell-mediated immune pathways,[2] and has therefore been studied for the treatment of BCCs.

Mechanism of Action

Imiquimod is a toll-like receptor-7 agonist enhancing both the innate and acquired immune response.[3] It activates the production of numerous compounds, including IFN-α, IL-1, -6, -8, -10, -12, and TNF-α, stimulates natural killer cells and the proliferation of B-cells. It also activates Langerhans cells, the key antigen-presenting cell in the skin, and promotes their migration to the regional lymph nodes. Imiquimod stimulates TH-1 cells to produce IFN-γ, which in turn can activate cytotoxic T lymphocytes. These cells provide long-term immune memory, which can offer future protection against the previously encountered virus or tumor. In animal models, imiquimod use can establish long-term immunity against viruses and certain tumors.[4]

Recently, imiquimod has been shown to promote the expression of cellular receptors that are associated with apoptosis.[5,6] There is mounting evidence that imiquimod antitumor activity *in vivo* stems from the effect it has on the innate and cell-mediated immune response, including cell surface markers.

Pharmacokinetics

Imiquimod is applied topically to the affected areas and its clinical effects are primarily localized to the skin. It has minimal percutaneous absorption in healthy skin, the skin of genital warts, and in sun damaged skin. When imiquimod was applied 3 times per week for 16 weeks in 58 patients with actinic keratoses (AKs), the mean peak serum levels at the end of week-16 were very low, measuring approximately 0.1-3.5ng/ml depending whether one packet (12.5mg) was used or up to six packets (75mg) were used. The half-life of topically applied imiquimod is approximately 26 hours with urinary recovery of less then 0.6%.

Clinical Trials

The most common indications for the topical use of imiquimod are the treatment of external anogenital warts, AKs, and sBCCs. In this review, we will concentrate on the evidence for BCC therapy.

In one of the first studies, Beutner and colleagues evaluated the response of BCCs (87% of treated sites were sBCCs) to the topical application of imiquimod.[7] The best response (100% histologic clearance) was

Study	Design	No. of Patients	Duration (wks)	Application frequency	Results (clearance)
Beutner et al.[7]	Rand, DB, VC, sBCCs and nBCCs	35	16	b.i.d. q.d. 3x/wk 2x/wk 1x/wk	b.i.d. (100%) q.d. (100%) 3x/wk (100%) 2x/wk (60%) 1x/wk (50%)
Marks et al.[8]	Rand, OL, sBCCs	99	6	b.i.d. q.d. b.i.d. 3x/wk q.d. 3x/wk	b.i.d. (100%) q.d. (88%) b.i.d. 3x/wk (73%) q.d. 3x/wk (70%)
Geisse et al.[9]	Rand, DB, VC, sBCCs	128	12	b.i.d. q.d. 5x/wk 3x/wk	b.i.d. (100%) q.d. (87%) 5x/wk (81%) 3x/wk (52%)
Shumack et al.[10]	Rand, OL, nBCCs	99	6	b.i.d. q.d. b.i.d. 3x/wk q.d. 3x/wk	b.i.d. (not reported) q.d. (71%) b.i.d. 3x/wk (42%) q.d. 3x/wk (59%)
	Rand, OL, nBCCs	92	12	b.i.d. q.d. b.i.d. 3x/wk q.d. 3x/wk	b.i.d. (not reported) q.d. (76%) b.i.d. 3x/wk (70%) q.d. 3x/wk (60%)
Sterry et al.[11]	Rand, OL, sBCCs	93	6	3x/wk 3x/wk (occl) 2x/wk 2x/wk (occl)	3x/wk (76%) 3x/wk (occl) (87%) 2x/wk (50%) 2x/wk (occl) (43%)
	Rand, OL, nBCCs	90	6	3x/wk 3x/wk (occl) 2x/wk 2x/wk (occl)	3x/wk (50%) 3x/wk (occl) (65%) 2x/wk (57%) 2x/wk (occl) (50%)
Geisse et al.[12]	Rand, DB, VC, sBCCs	364	6	5x/wk 7x/wk	5x/wk (82%) 7x/wk (79%)

Table 1: Summary of the key published studies assessing efficacy of topical imiquimod in the treatment of basal cell carcinomas.
Abbreviation: Rand – *randomized*, DB – *double-blind*, VC – *vehicle controlled,* OL – *open-label*, b.i.d. – *twice per day*, q.d. – *once per day,* occl – *under occlusion*

seen in the b.i.d., q.d. and 3x/week groups. In the first multicenter, randomized, open-label, dose-response trial, 99 patients were randomized to apply imiquimod b.i.d. every day, q.d., b.i.d. 3 times per week, or just once per day, 3x/week for 6 weeks. In an intent-to-treat analysis, the histologic clearance rates were highest in the b.i.d. every day regimen (100%) and lower in the 3x/week regimen (69.7%).[8] In a second multicenter, prospective, randomized double-blind, vehicle-controlled study, 128 patients with sBCC were randomized to 12 weeks of imiquimod b.i.d., q.d., 5x/week and 3x/week. Once again, the complete clearance rates varied based on the frequency of drug application from 100% in the b.i.d. group to 51.7 % in the 3x/week group.[9]

The treatment of nBCC using imiquimod was also assessed with or without occlusion using 6- and 12-week protocols.[10,11] Once daily dosing produced the highest clearance rates with 71% and 76% of cancers showing clearance in the 6- and 12-week studies, respectively. Occlusion did not have a clinically significant effect on the treatment of either sBCC or nBCC. The data suggested that a 6-week treatment protocol would be as effective as a 12-week long regimen.

In the two recent double-blind, vehicle-controlled clinical studies, 364 patients with primary sBCCs were treated with imiquimod or vehicle 5 or 7x/week for 6 weeks.[12] Twelve weeks following the treatment, histologic clearance rates were 82% and 79% for the 5 and 7x/week groups, respectively. Since the response rates were similar in both groups and the frequency of adverse effects was lower in the 5x/week protocol, the authors recommended that patients with sBCC be treated 5x/week for 6 weeks.

Imiquimod can also be used in combination with other treatment modalities. In particular, it has been studied as an adjunct modality with Mohs surgery,[13] electrodesiccation & curettage as well as curettage alone.[14]

Treating BCC with imiquimod prior to Mohs surgery reduces the size of the tumor and results in a smaller surgical defect. The use of curettage, one of the most common physical treatment modalities, and imiquimod (an immunological agent) allows for the ability to manually debulk the cancer and to ascertain its extent in addition to allowing subsequent application of the topical immune response modifier.

Dosage

The recommended dosing frequency for the treatment of sBCC is 5x/week for 6 weeks prior to normal sleeping hours. In addition to the tumor itself, a 1cm area of normal skin around the tumor needs to be treated. This allows for application to the site of subclinical tumor extensions. When imiquimod is used in combination with curettage, it can be started 1-week postcurettage up to 5x/week and continued for up to 6 weeks. Rest periods can be used as required to manage local skin reactions.

Adverse Effects

Application site reactions, which were the most common adverse effects, were seen in up to 87% of patients treated for sBCCs with imiquimod applied 5x/week for 6 weeks. The most common application site reactions were erythema, edema, induration, erosion, scaling, crusting, pruritus and burning sensations. Only 2% of patients discontinued the treatment due to the local skin reactions. Some patients may require a rest period if the local reaction severity warrants temporary cessation of treatment. From the clinical point of view, it appears that a patient's local reaction correlates with the treatment success rate. The incidence of distant reactions, i.e., at sites other than the site of application, is low. Distant reactions include erythema, fatigue, myalgia, arthralgia as well as lymphadenopathy.

Conclusion

Topical, non-invasive, patient-administered modalities continue to expand our options for treating a variety of skin conditions including skin cancers. Less patient discomfort, favorable cosmetic outcome and documented efficacy against BCCs make imiquimod an attractive treatment choice. In addition, patients who are poor surgical candidates (i.e., patients who are elderly, anticoagulated or who have implanted cardiac pacemakers) would benefit from this non-invasive, self-administered topical therapy. Its usefulness as an adjunct to surgical modalities, such as curettage or surgical excision, allows us to combine immunological-based treatment with surgical intervention.

Imiquimod stimulates innate and cell-mediated immune pathways, which are critical components of the body's defence mechanisms against both viruses and tumors. The clinical potential of this new family of compounds is growing. What started as a treatment for external anogenital warts has already evolved into an excellent treatment choice for selected skin malignancies.

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~ Conference News ~

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Combining Chin-Jowl Implants With Local Anesthesia Facial Rejuvenation

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ABSTRACT

Mandibular implantation is an outpatient procedure that can be used in combination with other minimally invasive cosmetic interventions. Specifically, silastic chin implants can help create a strong chin and smooth the jawline in carefully selected patients. A standard surgical excision tray plus a few additional simple instruments are required, and a variety of commercially available implants are available for placement via an intraoral or submental approach. Meticulous technique minimizes the small risk of nerve injury and numbness. Chin-jowl implants may be preceded by neck liposuction and immediately followed by a face-lift to achieve overall facial enhancement.

Key Words: *chin, jowl, implant*

The Concept

Today's educated patients seek cosmetic procedures with less downtime, risk, and cost, yet they still expect a dramatic outcome typical of traditional techniques under general anesthesia. As experts in less aggressive skin surgery using local anesthesia, dermatologists must be innovative to produce rejuvenation results that appeal to this patient population. Often when smaller, less invasive techniques are combined, synergistic outcomes can be achieved that satisfy those patients looking for the level of improvement produced by traditional surgery. One example of procedural synergy is the combination of chin-jowl implants with neck liposuction and minimally invasive lifting procedures.

A weak chin, whether congenital or acquired through the normal age-associated resorption of the mandible, causes blunting of the cervicomental angle, a fleshy appearing neck, and an irregular mandibular border, and makes the nose appear proportionately larger.[1-5] These facial features are negative physical attributes that suggest weakness, submissiveness, and lack of beauty. In contrast, a balanced and proportional chin is a positive physical attribute associated with strength, assertiveness, and youth.[3] For example, our society does not generally elevate men with weak chins into positions of power; our political leaders, corporate leaders, and famous male actors typically have powerful chins and jawlines. The goal of chin augmentation is to increase the volume of the mandible to restore a natural and balanced relationship between lower third (mouth and chin), middle third (lower eyelids, cheeks, and nose), and upper third (forehead, eyebrow, and upper eyelids) of the face.

Chin-jowl implants are easily combined with local anesthesia face and neck liposuction, and lifting procedures. By providing volume replacement of the lower face, these subperiosteal implants create a more dramatic and permanent rejuvenation with minimal additional surgical time, risk, or downtime (Table 1). The analysis and correction of the recessed chin and irregular mandibular border is critical for a youthful and natural facial rejuvenation outcome. It requires an understanding of the anatomical changes of the mandible during the aging process, the ideal facial proportions for your patients, the esthetic value of a strong chin and smooth jawline, and proper selection of the numerous mandibular implants available for augmentation.

Restoration of facial balance
Decreased cervicomental angle
Improved anterior chin projection
Correction of prejowl sulcus
Anterior stretch of submental neck skin

Box 1: Benefits of Chin Augmentation

Anatomical Considerations

During the normal aging process, the mandible loses vertical height and anterior projection causing an

alteration of the normal balance of the lower third with the upper two-thirds of the face. Progressive bony atrophy of the mid-lateral mandible, located between the chin and jowl, and its overlying soft tissue results in the formation of the prejowl sulcus and an irregular mandibular border (Figure 1).[1,3] This sulcus accentuates the aging jowl and eventually becomes the inferior aspect of the marionette line.

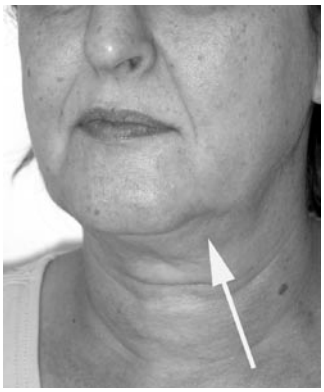


Figure 1: Prejowl sulcus

Despite the loss of mandibular vertical height, the mental foramina maintain a relatively fixed distance of at least 8 mm from the inferior border of the mandible.[3] This 8-10mm zone serves as a safe zone for the formation of subperiosteal pockets for extended chin implants that extend from the central chin to the mid-lateral mandible (Figure 2).[1,3] The mental nerve exits the foramen in a superior direction surrounded by a fibrous sheath approximately 2.5cm from the midline. This tough sheath protects the mental nerve from injury however, aggressive pocket formation or placement of larger implants may stretch the nerve resulting in transient numbness of the lower lip. The sheath also prevents upward migration of the lateral wings of the chin-jowl implant to prevent migration.[3]

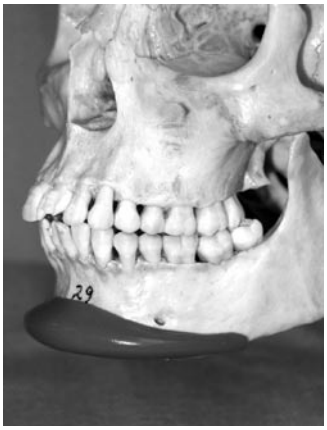


Figure 2: Extended chin-jowl implant

Patient Selection

A large percentage of patients seeking facial rejuvenation surgery are candidates for chin augmentation and/or correction of the prejowl sulcus. In a retrospective review of facial rejuvenation patients over a 12-month period, 24/121 (20%) of this author's neck liposuction (n=55) and facelift (n=66) patients underwent simultaneous mandibular implant placement.[6] Only 5% of these patients were aware that they were candidates for chin-jowl augmentation at the time of their consultation. During a facial rejuvenation consultation when the patient is unaware of his/her recessed chin and is a candidate for an implant, this author first discusses the primary procedures for which the patient initially requested the consultation appointment. When discussing the anticipated benefits of the neck or facial rejuvenation procedure, the limitations created by the patient's weak chin or prominent prejowl grooves on the overall outcome is reviewed to set proper expectations. A discussion of the anatomy, the functional role of the chin in shaping the face and neck, and the importance of a smooth mandible for a youthful appearance is usually successful in orienting the patient to mandibular augmentation. Most patients are receptive to the suggestion of a mandibular implant because the long-term benefit of this procedure far outweighs the minimal risk. The author's patients were polled 6 months post-procedure, and in the 95% of patients who were unaware of the mandibular implant option prior to surgery, all reported that the addition of the chin implant was a "very important" (18/19) or "somewhat important" (1/19) procedure to achieve their desired facial rejuvenation outcome.

Mandibular implants are ideally indicated for patients with age-related resorption of the chin, microgenia (small chin resulting from underdevelopment of the mandibular symphysis), micrognathia (small chin resulting from underdevelopment of components of the jaw), and prominent prejowl grooves when normal or near normal dental occlusion is present. A hypoplastic chin (microgenia) is the most common indication for chin augmentation. A simple method to assess the ideal anterior projection of the chin involves dropping a vertical line from the lower lip vermillion border of the closed mouth. In men, anterior chin projection that falls behind this vertical line, and in women, chins that recede more than 2mm behind this line are candidates for chin augmentation when normal or near-normal dental occlusion exists.[2] When there is more than 2cm of recession of the chin behind this vertical line or significant dental malocclusion, referral for orthognathic surgery is indicated prior to implant placement. In patients with malocclusion who undergo evaluation and ultimately refuse jaw advancement surgery, chin implants are an option however, custom implants or modifications of commercial implants are frequently necessary to achieve proper augmentation.

The assessment for augmentation of the prejowl sulcus is based primarily on the aesthetic interpretation of the physician. Patients with a weak chin seeking facial rejuvenation surgery typically have a prominent prejowl sulcus and are candidates for an extended implant that augments both areas. Patients who have normal chin projection with a prominent prejowl sulcus are candidates for the prejowl implants for selective augmentation of the mid-lateral mandible.

Implant	Sizes	Features
Extended anatomical chin	4	Full lateral arms blend into mandible
Flowers mandibular implant	5	Provides directional tilt of central chin
Mittelman prejowl chin	4	Adds variable correction to prejowl sulcus
Mittelman prejowl implant	4	Prejowl sulcus augmentation without chin projection
Terino square chin	4	Square profiles for a masculine chin

Table 1: Most common types of silastic extended chin implants

Implant Selection

Chin augmentation with alloplastic implants has been practiced since the late 1950s and has increased in popularity as our understanding of the anatomy of the aging face and mandible has been followed by improvements in facial implant form and function.[3,5]

This author prefers extended chin-jowl implants over central chin implants. The central chin implant is easier to place, however it does not have a correct anatomical shape and is prone to displacement.[1] As the patient with a central implant ages, the lack of mid-lateral mandible augmentation results in an accentuation of the prejowl sulcus and the irregular jawline. In contrast, the extended chin-jowl implants provide both central chin augmentation and correction of the prejowl sulcus, resulting in a more natural transition from the chin to the mid-lateral mandible.[1-3]

There are numerous commercially available silastic implants with different configurations and sizes (Table 1).[1-3,5] Each of these implants provides an effective augmentation, so implant choice is dependent on physician preference after discussing the patient's desired correction. To ensure correct sizing, each implant style has a sizer set that allows for intra-operative comparison of 3-4 different sizes prior to placement of the actual implant. Each of these implants can be customized intraoperatively with a scalpel or scissors for patients with asymmetry or for sizes and shapes not available commercially.

Procedure

Equipment

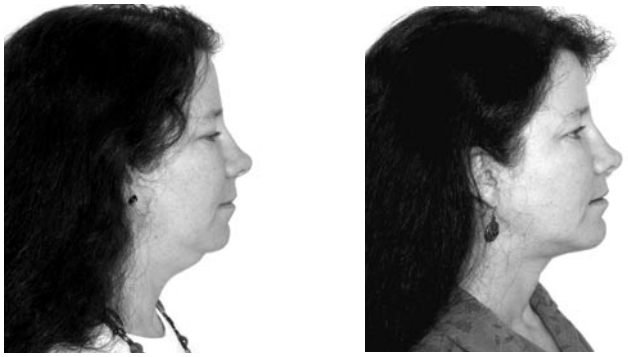
A standard skin surgical excision tray will contain all of the instruments necessary, except for a periosteal elevator and an implant sizer set. The periosteal elevator should be no wider than 6mm to optimize subperiosteal pocket formation without traumatizing the mental nerve. The Freer elevator, commonly used for nail elevation or periosteal elevation by dermatologists, is a readily available instrument with a narrow blade. Gentamicin sulfate injection 80mg/2ml solution is added to the saline solution and placed in a small bowl for the irrigation of the incision and soaking of the implant. The implant sizer is set prior to placement.

Surgical Technique

This procedure can be performed with local anesthesia alone via an intra-oral or submental approach. When combined with facelifts, these implants are placed following neck liposuction and platysma plication through the pre-existing submental incision. The facelift procedure immediately follows implant placement.

While in a seated position prior to surgery, the inferior border of the mandible, the prejowl sulcus, the midline of the chin, and the incision located anterior to the submental crease are marked with a marker. Intraoral mental nerve blocks are obtained with Lidocaine 1% with 1:1,000,000 epinephrine followed by direct infiltration along the footprint of the implant at the level of the periosteum. Neck liposuction and optional submentoplasty are performed first. The 1.5-2cm submentoplasty incision, just anterior to the submental crease, is retracted cephalad over the central chin and the incision is carried down through muscle and periosteum to bone. After elevating the periosteum 1.5cm superiorly off the mentum, the subperiosteal dissection is directed posterolaterally along the inferior border of the mandible in both directions. The free hand palpates the inferior border of the mandible to ensure that the lateral pocket does not extend below the inferior border of the mandible. The subperiosteal dissection is carried out approximately 5.5cm laterally in each direction. Once the pockets are formed, the different sizes of the sizer implants can be used to determine the degree of desired augmentation.

Prior to implant placement, the pockets are irrigated generously with the Gentamicin solution to minimize infection. The implant is placed by inserting one wing with a hemostat into the subperiosteal pocket and advancing the implant slowly to ensure its placement along the inferior border of the mandible. The implant is folded over on itself to allow insertion of the other arm into the contralateral subperiosteal pocket. Once



Figures 3a and 3b: Patient pre and post chin-jowl implant and neck liposuction.

inserted with its lateral arms flush with the mandible without curling of the ends, the implant is moved horizontally with a hemostat or forceps until the blue line present at the implant midline is aligned with the patient's midline.

Two 4.0 Vicryl® (Ethicon) sutures are placed to fix the inferior border of the central portion of the implant to the inferior edge of the chin periosteum to prevent cephalad movement of the implant immediately post-operatively. If possible, the periosteal flap created above the mentum is dissected free from the overlying muscle and reapproximated to the inferior periosteal remnant. Meticulous closure of the muscular layer and skin is performed with 4.0 Vicryl® interrupted, buried sutures and 5.0 running, interrupted, or subcuticular nylon sutures.

Troubleshooting

Complications are temporary and are minimized by careful preoperative counseling, ensuring a sterile environment, careful execution of the periosteal pocket formation, and correct sizing of the implant (Box 2). Once the dermatologic surgeon is experienced, this procedure is accomplished in less than 30 minutes with minimal complications.

A follow-up survey undertaken 6 months postoperatively by this author revealed that 60% of patients experienced post-operative complaints including swelling (9/12), tenderness (9/12), and numbness (1/12). All problems resolved within 3 months.[6] No episodes of extrusion, displacement, nerve injury, or infection occurred. Permanent nerve injury is rare due to the anatomical considerations. Patient dissatisfaction can be corrected by implant removal with the option of placing a different size.

Conclusion

Just as dermatologic surgeons evolved to become the primary providers of facial skin cancer excision and reconstruction, we are now poised to revolutionize facial rejuvenation surgery with local anesthesia

Nerve injury (temporary)
- Motor (marginal mandibular nerve)
- Sensory (mental nerve)
  - Up to 20%-30%[1,3]

Muscle injury
- Creates speech impediment
- Swelling or surgical injury

Infection (1%-5%)[1,3,5]
Displacement (rare)
Hematoma (very uncommon)
Bone resorption beneath implant
Swelling
Scarring
Asymmetry
Changes in chin cleft or dimples
Dissatisfaction

Box 2: Side-effects and complications

procedures combining lasers, liposuction, mandibular implants, and minimally invasive lifting techniques. This evolution of cosmetic dermatologic surgery coincides with an enlarging patient population desiring natural rejuvenation results equivalent to the traditional techniques, but without the prolonged healing period, risk, and expense.

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Class	Name/Company	Approval Dates and Comments
Antipsoriatic Agent	**Infliximab** *Remicade®* Centocor/Schering-Plough	The US FDA approved this monoclonal antibody in May 2005 for the treatment of psoriatic arthritis. This is the ninth new indication for this product.
Health Advisory	**Cyproterone Acetate/ Ethinyl Estradiol** *Diane-35®* Berlex	TPP Canada issued a Health Advisory in May 2005 informing consumers of a new version of the product monograph agreed upon by Berlex and TPP Canada that includes the following information: • This product must not be used in women with thrombohebitis, thromboembolic disorders, or a history of these conditions. • Some published studies show that Diane-35® users appear to have an elevated risk of blood clots compared with users of combination oral contraceptives. • Diane-35® should not be prescribed for birth control alone. • Oral contraceptives should not be taken during treatment with Diane-35®. • Diane-35® should be discontinued 3-4 months after signs of acne have completely resolved. • Consumers should be aware that cigarette smoking increases the risk of serious adverse effects on the heart and blood vessels from Diane-35® use. Any occurrences of thromboembolic disorders (blood clots) or other serious and/or unexpected adverse reactions in patients taking Diane-35® should be reported to TPP Canada.

Drug News

Antipsoriatic Agent	Biogen Idec and Fumapharm AG in April 2005, announced results from a multicenter, double-blind, placebo-controlled Phase III study designed to evaluate the efficacy and safety of BG-12, an oral fumerate, in the treatment of moderate-to-severe psoriasis. The trial met the primary endpoint and patients receiving BG-12 demonstrated a statistically significant clinical improvement as measured by a lower median psoirasis severity score after 16 weeks of treatment compared with patients receiving placebo. The median PASI was 5.8 for the BG-12 group and 14.2 for the placebo group. Median percentage reduction from baseline PASI was 68% for patients receiving BG-12 and 10% for patients receiving placebo.
Hair Dye	In an article recently published in *Journal of the American Medical Association**, a meta-analysis of the scientific evidence looking at the association between cancer and hair dye use has found no strong evidence of increased risk. Although the authors report that there is a borderline effect for hematopoietic cancers (e.g., leukemia and multiple myeloma). However they say that the evidence of a causal effect is too weak to represent a major public health concern. **JAMA* 293:2516-25 (2005).

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