

ASPS® Patient Consultation Resource Book

Smoking and Plastic Surgery

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Introduction

In most medical situations, the effects of tobacco are considered primarily with respect to its production of disease states or neoplasia. Virtually all organ systems including the unborn are affected by exposure to tobacco. Within the specialty of surgery, smoking can dramatically influence the goal of uncomplicated wound healing¹⁻⁸.

The specialty of plastic surgery places great emphasis on both surgical techniques and treatments that promote normal wound healing in order to produce a superior surgical outcome. It has been observed and reported within a variety of different surgical scenarios that smokers have impaired capacity for wound repair and propensity for skin necrosis.

Smoking appears to be a major complicator of surgical procedures, in addition to other known potential risk factors. To this date, it is poorly addressed during informed-consent discussions with patients prior to surgical procedures. The effects of smoking on experimental flap survival have been extensively studied in laboratory animal models⁹.

Both cosmetic and reconstructive surgical procedures have been noted to be adversely affected by smoking. These include: rhytidectomy^{10,42}, abdominoplasty¹¹, reduction mammoplasty, breast reconstruction¹²⁻¹⁶, free-tissue transfer^{17-20,47}, flaps²¹⁻²³, grafts²⁴, and digital replantation²⁵⁻²⁶. Surgery performed in areas of the head where there is a robust blood supply experienced an eight-fold increase in wound healing complications over non-smoking controls⁶. Smoking can impair bone healing and lower extremity wounds²⁷⁻³³.

It is relatively simple to identify a history of smoking during history taking in a non-confrontational manner as it relates to the general health of your patient. It becomes somewhat more difficult to communicate with a smoking patient that this activity places them at an unacceptable level of risk for preventable surgical complications. To many patients, complications following a surgical procedure are not very tangible. Patients seem to place great faith in the wonders of modern medicine to shield them from surgical morbidity and mortality.

Often there is minimal patient insight that activities such as smoking could produce devastating complications. Most patients are intolerant of complications and tend to project blame towards the operating surgeon versus accepting that their smoking has contributed in any meaningful manner. Within this context, it is certainly easier to avoid a devastating complication by refusing to operate on actively smoking patients due to unacceptable risk or require a designated period of complete abstinence from smoking prior to surgery.

Elective Cosmetic and Reconstructive Plastic Surgery

Within the scenario of elective major cosmetic or reconstructive surgery the plastic surgeon certainly has time to discuss with the smoking patient their increased risk of skin necrosis, delayed wound healing, and potential for a poor result. It is additionally possible to identify and address the relevance of other known factors that produce wound healing problems such as diabetes mellitus, chronic steroid use, malnutrition, and prior radiation therapy. Control over patient situations involving elective surgery as to whether or not you choose to operate on any high-risk patient, faced with the increased risk of surgical complications and poor outcome are certainly possible.

Document within your chart notes that you have counseled the patient regarding increased risk of potential complications due to smoking and surgery. Also document your decision with respect to how you choose to manage this issue prior to surgery. This helps avoid a challenge from a plaintiff's attorney alleging that the surgeon knew of the potential for complications due to smoking, yet failed to act in a prudent fashion to prevent these by either advising the patient of increased risk or not performing surgery.

I have found it useful also to address the issue of financial responsibility for expense of treating complications, should they occur. Third party payors generally exclude coverage for complications of cosmetic surgery. There is even resistance on their part to cover revisionary procedures to treat complications after approved reconstructive surgery. I have found that a useful tool in this situation is to then ask your patient would they go

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forth with surgery knowing that their smoking places them at a level of unacceptable financial risk, not to mention surgical risk. Most of the time, the prudent patient will make up their own mind that they should not undergo surgery while smoking. Note: all PCRB informed-consent documents contain a financial informed-consent regarding the patient responsibility for financial expense of surgical complications, additional treatment, and revisionary surgery.

It is important to have a frank discussion regarding the issue of smoking with your patients. Patients may take this matter more seriously if you can portray to them the nature of delayed wound healing or skin necrosis in terms of revisionary surgery, wound debridement, scarring, and emotional distress from a poor surgical result. At the same time, you can certainly become their advocate for offering hope that they can undergo elective cosmetic or reconstructive surgery in the future once they have stopped smoking.

There does not appear to be a consensus regarding how long a smoker should wait to undergo surgery, once they have completely stopped smoking. Within my personal practice, I generally use an arbitrary time of 6 weeks for major cosmetic or reconstructive surgery. This amount of time for a smoker to be away from tobacco is certainly achievable by motivated patients who really want to stop smoking in order to diminish risk factors attributable to smoking. It allows ample time for the patient to succeed at the difficult task of smoking cessation through behavior modification or pharmacological means. This amount of time appears adequate in ferreting out those who lack motivation to stop smoking before surgery.

Although it may be possible to successfully operate on smokers by varying surgical technique such as a deep plane facelift or skin-only facelift with minimal undermining, this approach cannot be applied to other areas of the body where flaps of skin and other tissues are involved. The results from minimized procedures on smokers may not meet their expectations for results when compared with more standard approaches.

Urgent / Emergency Surgery

Situations where “urgent” or “emergency” surgery is needed does not offer the smoking patient adequate time to stop smoking before surgery. The surgeon is faced with the dilemma of having to perform surgery in a situation of combined risk from both the urgent condition/trauma and the effects of smoking.

“Urgent” situations occur, such as a smoking patient with a positive breast biopsy for invasive cancer, who requests an immediate TRAM flap breast reconstruction at the time of mastectomy that is scheduled in three days time. Given this scenario, the patient may already have strong expectations for an immediate reconstruction. The consultation with such a demanding patient can be quite challenging. You literally will have to re-educate her with respect to increased risk of delayed wound healing complications from both the primary procedure, the mastectomy³⁴, not to mention a >4 hour autologous tissue reconstruction. She may not be a suitable risk for any type of an immediate breast reconstruction due to her smoking.

The prudent course of action in this situation may be to just say “no”. There is certainly ample documentation in the medical literature of a variety of smoking-related complications, including increased risk of skin and umbilical necrosis associated with TRAM flap procedures¹¹. Delayed breast reconstruction can be performed electively in the future, once the patient has stopped smoking with less risk of delayed wound healing or skin necrosis complications.

With respect to “emergency” situations, document within the medical record that you have advised the patient of their increased risk for complications attributable both to the trauma and also their history of smoking. Also document that you recommend total cessation of smoking during the peri-operative period. Smoking after surgery can impair circulation in flap and digital replants²⁵.

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Integrating a no smoking policy into your practice means using the following:

- **ASK**

Identify patients with respect to tobacco use status—"never", "former", "active".

- **ADVISE**

In a clear, strong, and personalized manner, urge that your patient stop smoking in order to prevent known surgical complications attributable to smoking such as delayed healing and skin necrosis.

- **ASSIST**

Help the tobacco user who is ready by advising them to develop a plan to quit. Recommend that the patient set a quit date, seek support from friends, family, and coworkers, and remove cigarettes from home and work. A proposed surgical procedure that is desired by a patient such as a reduction mammoplasty or rhytidectomy certainly gives a reason to stop smoking.

- **ARRANGE**

Despite the fact that we are surgeons and do not manage smoking cessation as part of our practice, the reality of the situation is that we are at risk to manage the complications of smoking after surgery. Patients often appreciate your interest in their situation if you offer referral to a cessation specialist, counselor, or support group. Make a follow-up visit to congratulate success in order to reinforce the importance of cessation of smoking prior to surgery.

For example, you can address this issue with your patients by saying, "As your surgeon, I need you to understand that quitting smoking is one of the most important things that you can do to protect your current and future health." Although most patients intellectually agree that smoking is a hazard to one's health and wound healing, the practical aspects of stopping smoking are difficult to master.

Some patients will attempt to bargain with their surgeon in terms of, "Will you do my surgery if I just cut down to one or two cigarettes a day?" Other patients may just tell their surgeon that they have stopped smoking, yet continue surreptitiously (closet smokers). Nicotine is highly addictive and patients may exhibit a variety of behavioral responses when they try to stop smoking. Verify that your patient affirms that they have stopped smoking prior to surgery and will not resume smoking during the post-operative period.

I believe that total abstinence from smoking is necessary prior to major cosmetic and reconstructive surgery. Although nicotine patches and gum may be of some benefit to reduce craving for cigarettes³⁵, these items are still a source for an agent that has been implicated in producing delayed wound healing and skin necrosis. The effect of nicotine patches on wound healing has not been investigated.

Other types of medications such as Zyban (bupropion) may be of benefit in helping curb nicotine addiction³⁶⁻⁴⁰. Zyban may offer a theoretical advantage for surgical patients over nicotine preparations as this approach does not rely upon the addictive agent (nicotine) for smoking cessation. Successful cessation of smoking in patients can be a challenging experience. This may require a variety of approaches from both a behavioral and pharmacological standpoint. There is a high incidence of recidivism in patients who attempt to stop smoking. Make certain that your message to your patients is that you require complete abstinence from tobacco and nicotine during the peri-operative period.

I have found it helpful to enlist the assistance of other physicians who deal with the medical management of smoking cessation and behavior modification. This approach of using other physicians or support groups to help patients successfully stop smoking is a good strategy. It allows the smoker to receive ample care and support by medical personnel that are experienced in dealing with smoking cessation.

Minimum abstinence time from nicotine and reversal of nicotine-induced wound healing risks

There has not been a controlled study that demonstrates a specific minimum time for the reversal of nicotine-induced wound healing risks when exposure to nicotine ceases⁴⁶. Nicotine exposure can occur in non-smoking ways through trans-dermal patches, nicotine-containing gum, nasal spray, or smokeless tobacco products in patients who "no longer smoke". Manassa et Al found that although patients report smoking cessation, 85.3% actually continue smoking before surgery and 58.8% afterwards⁴³. Wound healing problems appear unrelated to actual number of cigarettes smoked, but on the basis of exposure to tobacco smoke and

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its products. There is no minimum safe amount of cigarettes on a daily basis⁴⁴. Second-hand smoke exposure also exposes a patient to the harmful effects of nicotine.

Laboratory testing for cotinine, a metabolite of nicotine may be a way to determine compliance with recommended smoking cessation prior to elective surgery. Consider this simple test for urinary or serum cotinine as a way to screen patients for compliance⁵⁴.

Strategies

The pre-operative medication information form that is part of the PCRFB has a passage that asks patients to disclose their smoking status and warns about alternative forms of exposure to nicotine. This form offers a way to have patients attest to their smoking status and for this to be noted prior to surgery. Such disclosures offer protection if a patient willingly misrepresents smoking and then has a smoking-related wound healing problem after surgery⁴⁵.

Smoking, Second-Hand Smoke Exposure, Nicotine Products (Patch, Gum, Nasal Spray) -

Patients who are currently smoking, use tobacco products, or nicotine products (patch, gum, or nasal spray) are at a greater risk for significant surgical complications of skin dying and delayed healing. Individuals exposed to second-hand smoke are also at potential risk. These are attributable to nicotine exposure. Please indicate your current status regarding these items below:

_____ I am a non-smoker and do not use nicotine products. I understand the potential risk of second-hand smoke exposure.

_____ I am a smoker or use tobacco / nicotine products.

Date: _____ Signature: _____

Conclusion

Total abstinence from smoking during the peri-operative period still remains the best course of management in order to reduce the negative effects of smoking on wound healing and propensity towards skin necrosis. Unfortunately, there does not exist any magic pill or treatment otherwise that will serve as an antidote for the effects of smoking on surgical wounds⁴¹.

Although we as physicians seek to please our patients by following their requests for elective cosmetic or reconstructive surgery, avoid becoming trapped in going forth with surgery on a smoking patient because you do not want to anger them with respect to addressing the issue of their smoking. As a surgeon, you certainly have the upper hand both with respect to knowledge of increased risk that smoking plays in surgical complications and control with respect to choice in your decision to operate on this patient. A visual aid of an abdominoplasty flap in a smoker that has undergone a full thickness slough and remains unhealed 8 weeks after surgery due to subdermal fat necrosis represents a graphic patient education tool that will help a patient understand the magnitude of nicotine-induced wound healing problems.

Although there is intense competition for major cosmetic or reconstructive cases, avoid compromising your good surgical judgment by operating on smokers due to economic considerations. Don't assume unnecessary risk by failing to ignore the potential for demise in performing surgery on smokers. In such a situation, you literally cannot afford to operate from the perspective of your future economic costs of follow up care for complication management and expected free revisionary surgery to "make it right".

Devastating complications attributable to the effects of smoking now become your problem since you have assumed this risk by going forth with surgery. The best combination still remains that of prudent surgeon, prudent patient, and prudent surgery.

Once the ever-downward spiral of complications, poor result, disfigurement, emotional distress, and out of pocket financial expense has started, the end result could be a claim for damages based on professional liability. Consider the effects of smoking from both the viewpoint of wound healing and risk-management⁴⁷⁻⁵¹.

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References

1. Fawcett A. Shembekar M. Church JS. Vashisht R. Springall RG. Nott DM.
Smoking, hypertension, and colonic anastomotic healing; a combined clinical and histopathological study [see comments].
Comment in: Gut 1996 Dec;39(96):889-90
Gut. 38(5):714-8, 1996 May
2. SMITH JB. Fenske NA.
Cutaneous Manifestations and consequences of smoking [see comments]. [Review] [311 refs].
Comment in: J Am Acad Dermatol 1997 Jun;36(6 Pt 1):1029
Journal of the American Academy of Dermatology. 34(5 Pt 1):717-32; quiz 733-4, 1996 May.
3. Viehbeck M. McGlynn J. Harris S.
Pressure ulcers and wound healing: educating the spinal cord injured individual on the effects of cigarette smoking.
Sci Nursing. 12(3):73-6, 1995 Aug.
4. Frick WG. Seals RR Jr.
Smoking and wound healing: a review. [Review] [24 refs]
Texas Dental Journal. 111(6):21-3, 1994 Jun.
5. Peat BG. Bell RS. Davis A. O'Sullivan B. Mahoney J. Manktelow RT. Bowen V. Catton C. Fornasier VL. Langer F.
Wound-healing complications after soft-tissue sarcoma surgery.
Plastic & Reconstructive Surgery. 93(5):980-7, 1994 Apr.
6. Jones JK. Triplett RG.
The relationship of cigarette smoking to impaired intraoral wound healing: a review of evidence and implications for patient care.
Journal of Oral & Maxillofacial Surgery. 50(3):237-9; discussion 239-40, 1992 Mar.
7. Silverstein P.
Smoking and wound healing. [Review] [10 refs]
American Journal of Medicine. 93(1A):22S-24S, 1992 Jul 15
8. Jensen JA. Goodson WH. Hopf HW. Hunt TK
Cigarette smoking decreases tissue oxygen.
Archives of surgery. 126(9):1131-4, 1991 Sep.
9. Nolan. J., Jenkins, R., Kurihara, K., Schultz, R.
The Acute Effects of Cigarette Smoke Exposure on Experimental Skin Flaps
Plastic & Reconstructive Surgery. 75(4):544-49, April 1985.
10. Netscher DT. Clamon J.
Smoking: adverse effects on outcomes for plastic surgical patients.
Plastic Surgical Nursing. 14(4):205-10, 1994 Winter.
11. Kroll SS.
Necrosis of abdominoplasty and other secondary flaps after TRAM flap breast reconstruction.
Plastic & Reconstructive Surgery. 94(5):637-43, 1994 Oct
12. Takeishi M. Shaw WW. Ahn CY. Corud LJ.
TRAM flaps in patients with abdominal scars
Plastic & Reconstructive Surgery. 99(3):713-22, 1997 Mar
13. Banic A. Boeckx W. Greulich M. Guelickx P. Marchi A. Rigitti G. Tschopp H.
Late results of breast reconstruction with free TRAM flaps: a prospective multicentric study.
Plastic & Reconstructive Surgery. 95(7):1195-204; discussion 1205-6, 1995 Jun.
14. Watterson PA. Bostwick J 3rd. Hester TR Jr. Bried JT. Taylor GI.
TRAM flap anatomy correlated with a 10-year clinical experience with 556 patients (see comments).
Plastic & Reconstructive Surgery. 95(7):1185-94, 1995 Jun.
15. Jacobsen WM. Meland NB. Woods JE.
Autologous breast reconstruction with use of transverse rectus abdominis musculocutaneous flap: Mayo clinic experience with 147 cases.
Mayo Clinic Proceedings. 69(7):635-40, 1994 Jul.
16. Shrotria S. Webster DJ. Mansel RE. Hughes LE.
Complications of rectus abdominis myocutaneous flaps in breast surgery (see comments).
Comment in: Eur J Surg Oncol 1993 Jun; 19(3):309
European Journal of Surgical Oncology. 19(1):80-3, 1993 Feb.

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17. Chang LD. Buncke G. Slezak S. Buncke HJ.
Cigarette smoking, plastic surgery, and microsurgery. [Review] [79 refs].
Journal of Reconstructive Microsurgery. 12(7):467-74, 1996 Oct.
18. Al Qattan MM. Bowen V.
Effect of pre-existing health conditions on the results of reconstructive microvascular surgery. [Review] [94 refs]
Drug Safety. 8(1):49-56, 1993 Jan.
19. Gu YD. Zhang GM. Zhang LY. Li FG. Jiang JF.
Clinical and experimental studies of cigarette smoking in microvascular tissue transfers.
Microsurgery. 14(6):391-7, 1993.
20. Reus WF 3d. Colen LB. Straker DJ.
Tobacco smoking and complications in elective microsurgery.
Plastic & Reconstructive Surgery. 89(3):490-4, 1992 Mar.
21. Lovich SF. Arnold PG
The effect of smoking on muscle transposition
Plastic & Reconstructive Surgery. 93(4):825-8, 1994 Apr.
22. Kroll SS. Goepfert H. Jones M. Guillaumondegui O. Schusterman M.
Analysis of complications in 168 pectoralis major myocutaneous flaps used for head and neck reconstruction.
Annals of Plastic Surgery. 25(2):93-7, 1990 Aug.
23. Erdmann MW. Court-Brown CM. Quaba AA.
A five year review of islanded distally based fasciocutaneous flaps on the lower limb.
British Journal of Plastic Surgery. 50(6):421-7, 1997 Sep.
24. Goldminz D. Bennett RG.
Cigarette smoking and flap and full-thickness graft necrosis.
Archives of dermatology. 127(7):1012-5, 1991 Jul
25. Gu YD. Li JF. Jiang JF.
Circulatory crisis caused by cigarette smoking in tissue transfer. Clinical and experimental studies.
Chinese Medical Journal. 106(9):682-7, 1993 Sep.
26. Van Adrichem LN. Hovius SE. van Strik R. van der Meulen JC.
Acute effects of cigarette smoking on microcirculation of the thumb.
British Journal of Plastic Surgery. 45 (1):9-11, 1992 Jan.
27. Haverstock BD. Mandracchia VJ
Cigarette smoking and bone healing: implications in foot and ankle surgery.
Journal of Foot & Ankle Surgery. 37(1):69-74; discussion 78, 1998 Jan-Feb.
28. Marsh DR. Shah S. Elliott J. Kurdy N.
The Ilizarov method in nonunion, malunion and infection of fractures.
Journal of Bone & Joint Surgery – British Volume. 79(2):273-9, 1997 Mar.
29. Gualdrini G d. Zati A. Degli Esposti S.
The effects of cigarette smoke on the progression of septic pseudarthrosis of the tibia treated by Ilizarov external fixator.
Chirurgia Degli Organi di Movimento. 81(4):395-400 hl, 1996 Sep-Dec.
30. Kwiatkowski TC. Hanley EN Jr. Ramp WK
Cigarette smoking and its orthopedic consequences. [Review] [112 refs]
American Journal of Orthopedics. 25(9):590-7, 1996 Sep.
31. Whitesides TE Jr. Hanley EN Jr. Fellrath RF Jr.
Smoking abstinence. Is it necessary before spinal fusion?
Spine. 19(17):2012-4, 1994 Sep 1.
32. Lind J. Kramhoft, M. Bodtker S.
The influence of smoking on complications after primary amputations of the lower extremity.
Clinical Orthopaedics & Related Research, (267):211-7, 1991 Jun.
33. Sherwin MA. Gastwirth CM.
Detrimental effects of cigarette smoking on lower extremity wound healing. [Review] [12 refs]
Journal of Foot Surgery. 29(1):84-7, 1990 Jan-Feb.
34. Vinton AL. Traverso LW. Jolly PC.
Wound complications after modified radical mastectomy compared with tylectomy with axillary lymph node dissection.
American Journal of Surgery. 161(5):584-8, 1991 May

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35. Hughes JR.
Risk-benefit assessment of nicotine preparations in smoking cessation. [Review] [43 refs]
Drug Safety. 8(1):49-56, 1993 Jan.
36. Hurt, R.D. and Others
A Comparison of Sustained Release Bupropion and Placebo for Smoking Cessation
New England Journal of Medicine. 337(17): 1195-1202, 1997 October 23.
37. Benowitz, N.L.
Treating Nicotine Addiction- Nicotine or No Nicotine?
New England Journal of Medicine. 337(17): 1230-31, 1997 October 23.
38. Goldstein, Michael, G.
Bupropion Sustained Release and Smoking Cessation
J Clinical Psychiatry. 59(Suppl 4): 66-72, 1998:59.
39. Settle, Edmund C., Jr.
Bupropion Sustained Release:Side Effect Profile
J Clinical Psychiatry. 59(Suppl 4): 342-36, 1998:59.
40. Davidson, Jonathan , Connor, Kathryn, M.
Bupropion Sustained Release: A Therapeutic Overview
J Clinical Psychiatry. 59(Suppl 4): 25-31, 1998:59.
41. Davies, Brian, Lewis, Robert, Pennington, Gary
The Impact of Vasodilators on Random-Pattern Skin Flap Survival in the Rat Following Mainstream Smoke Exposure
Annals of Plastic Surgery. 40(6): 630-6, 1998
42. Rees, Thomas, Liverett, David, Guy, Cary
The Effect of Cigarette Smoking on Skin-Flap Survival in the Face Lift Patient
Plastic and Reconstructive Surgery. 73(6):911-915, 1984
43. Manassa, Edouard, Hertl, Catherine, Olbrisch, Rolf-Ruediger,
Wound Healing Problems in Smokers and Nonsmokers after 132 abdominoplasties
Plastic and Reconstructive Surgery 116(6):2082-2087:2003.
44. Rohrich, Rod, Coberty, Dana, *Discussion: Wound Healing Problems in Smokers and Nonsmokers after 132 abdominoplasties*
Plastic and Reconstructive Surgery 116(6):2088-2089:2003.
45. Gorney, Mark, Martello, Jeanette, *The Genesis of Plastic Surgery Claims,*
Clinics in Plastic Surgery 26:1:123-131:1999
46. Rohrich, Rod, Coberly, Dana, Krueger, Jeffrey, Brown, Spencer, *Planning Elective Operations on Patients Who Smoke: Survey of North American Plastic Surgeons*
Plastic and Reconstructive Surgery: 109:1:350-355:2002.
47. Chang, Lawrence, Buncke, Greg, Slezak, Sheri, Buncke, Harry, *Cigarette Smoking, Plastic Surgery, and Microsurgery.*
Journal of Reconstructive Microsurgery: 12:7: 467-474:1996
48. Rohrich, Rod, *Cosmetic Surgery and Patients Who Smoke: Should We Operate?,*
Plastic and Reconstructive Surgery: June 2000, 137-138.
49. Rosenthal, Jeffrey, *The Responsibility of Plastic Surgeons To Help Patients Stop Smoking,*
Plastic and Reconstructive Surgery: Letter to the Editor, 109:3 1201-1202,:2002
50. Rayatt, Sukh, *Smoking and Elective Surgery: A Survey of United Kingdom Plastic Surgery Consultants*
Plastic and Reconstructive Surgery: Letter to the Editor:114:2 605-606: 2004.
51. Krueger, Jeffrey, Rohrich, Rod, *Clearing the Smoke: The Scientific Rationale for Tobacco Abstinence with Plastic Surgery*
Plastic and Reconstructive Surgery: 108:4: 1063-1075 (includes discussion by Tom Mustoe, M.D.) 2001.
52. Akoz, Tayfun, Akan, Mithat, Yidirim, Serkan, *If You Continue to Smoke, We May Have a Problem:Smoking Effects on Plastic Surgery,*
Aesthetic Plastic Surgery: 26:477-482, 2002.
53. Ziegler, Ulrich, Kauczok, Jens, Dietz, Ulrich Andreas, Reith, H. Bernd, Schmidt, Karsten, *Clinical Correlation Between the Consumption of nicotine and Cotinine Concentrations in Urine and Serum by Competitive Enzyme-Linked Immunosorbent Assay,*
Pharmacology: 72:254-259:2004.