Chapter 113
Epithelial Precancerous Lesions

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REFERENCES

1. Cockerell CJ: Histopathology of incipient intraepidermal squamous cell carcinoma ("actinic keratosis"). *J Am Acad Dermatol* ***42***:S11, 2000
2. Freeman RG et al: What is the boundary that separates a thick actinic keratosis from a thin squamous cell carcinoma? *Am J Dermatopathol* ***6***:301, 1984
3. Yantsos VA et al: Incipient intraepidermal cutaneous squamous cell carcinoma: A proposal for reclassifying and grading solar (actinic) keratoses. *Semin Cutan Med Surg* ***18***:3, 1999 [PMID: 10188837]
4. Heaphy MR, Ackerman AB: The nature of solar keratosis: A critical review in historical perspective. *J Am Acad Dermatol* ***43***:138, 2000 [PMID: 10863242]
5. Dubreuilh W: Des hyperkératoses circonscrites. In: *Third International Congress of Dermatology. Official Transactions*, edited by JJ Pringle. London, Waterlow and Sons, 1898, p. 125
6. Freudenthal W: Verruca senilis und keratoma senile. *Arch f Dermat u Syph (Berlin)* ***158***:529, 1926
7. Pinkus H: Keratosis senilis: A biologic concept of its pathogenesis and diagnosis based on the study of normal epidermis and 1730 seborrheic and senile keratoses. *Am J Clin Pathol* ***29***:193, 1958 [PMID: 13520651]
8. Cockerell CJ, Wharton JR: New histopathological classification of actinic keratosis (incipient intraepidermal squamous cell carcinoma). *J Drugs Dermatol* ***4***:462, 2005 [PMID: 16004019]
9. Marks R et al: The relationship of basal cell carcinomas and squamous cell carcinomas to solar keratoses. *Arch Dermatol* ***1224***:1039, 1988
10. Green A, Battistutta D: Incidence and determinants of skin cancer in a high-risk Australian population. *Int J Cancer* ***46***:356, 1990 [PMID: 2394501]
11. Chen GJ et al: Clinical diagnosis of actinic keratosis identifies an elderly population at high risk of developing skin cancer. *Dermatol Surg* ***31***:43, 2005 [PMID: 15720095]
12. Bickers DR et al: The burden of skin diseases: 2004. A joint project of the American Academy of Dermatology Association and the Society for Investigative Dermatology. *J Am Acad Dermatol*. ***55***(3):490, 2006
13. Skin Cancer Foundation: Actinic keratosis and other precancers, http://www.skincancer.org/actinic-keratosis-and-other-precancers.html, accessed Jan 5, 2010
14. Salasche SJ: Epidemiology of actinic keratoses and squamous cell carcinoma. *J Am Acad Dermatol* ***42***:S4, 2000
15. Kwon EJ, Kish LS, Jaworsky C: The histologic spectrum of epithelial neoplasms associated with sorafenib. *J Am Acad Dermatol* ***61***(3):522, 2009
16. Hong DS et al: Multiple squamous cell carcinomas of the skin after therapy with sorafenib combined with tipifarnib. *Arch Dermatol* ***44***(6):779, 2008
17. Lacouture ME et al: Inflammation of actinic keratoses subsequent to therapy with sorafenib, a multitargeted tyrosine-kinase inhibitor. *Clin Exp Dermatol* ***31***(6):783, 2006
18. Wolfe F, Michaud K: Biologic treatment of rheumatoid arthritis and the risk of malignancy: Analyses from a large US observational study. *Arthritis Rheum* ***56***:2886, 2007
19. Marks R et al: The role of childhood sunlight exposure in the development of solar keratoses and nonmelanoma skin cancer. *Med J Aust* ***152***:62, 1990 [PMID: 2296232]
20. Grossman D, Leffell DJ: The molecular basis of nonmelanoma skin cancer. *Arch Dermatol* ***133***:1263, 1997 [PMID: 9382565]
21. Yu RCH et al: A histopathological study of 643 cutaneous horns. *Br J Dermatol* ***24***:449, 1991
22. Zalaudek I et al: Pitfalls in the clinical and dermoscopic diagnosis of pigmented actinic keratosis. *J Am Acad Dermatol* ***53***:1071, 2005 [PMID: 16310072]
23. Cruces Prado MJ, de la Torre C: Jadassohn's intraepidermal epithelioma. *Dermatologica* ***168***:10, 1984

24. Steffan C, Ackerman AB: Intraepidermal epithelioma of Borst-Jadassohn. *Am J Dermatopathol **7***:5, 1985

25. Carag HR et al: Utility of step sections: Demonstration of additional pathological findings in biopsy samples initially diagnosed as actinic keratosis. *Arch Dermatol **136***:471, 2000 [PMID: 10768645]

26. Ackerman AB, Mones JM: Solar (actinic) keratosis is squamous cell carcinoma. *Br J Dermatol **155***:9, 2006

27. Weinstock MA et al: Reliability of counting actinic keratoses before and after brief consensus discussion. *Arch Dermatol **137***:1055, 2001 [PMID: 11493098]

28. Ponsford MW et al: The prevalence and accuracy of diagnosis of non-melanotic skin cancer in Victoria. *Australas J Dermatol **24***:79, 1983 [PMID: 6661117]

29. Thompson SC et al: Reduction of solar keratoses by regular sunscreen use. *N Engl J Med **329***:1147, 1993 [PMID: 8377777]

30. Jagdeo J et al: Reliability of the histopathologic diagnosis of keratinocytic carcinomas. *J Am Acad Dermatol **57***(2):279, 2007

31. Berhane T et al: Inflammation is associated with progression of actinic keratoses to squamous cell carcinomas in humans. *Br J Dermatol **146***:810, 2002 [PMID: 12000377]

32. Marks R et al: Malignant transformation of solar keratosis to squamous cell carcinoma. *Lancet **1***:795, 1988 [PMID: 2895318]

33. Montgomery H, Dorffel J: Verruca senilis und keratoma senile. *Arch f Dermatol u Syphilol (Berlin) **166***:286, 1932

34. Glogau RG: The risk of progression to invasive disease. *J Am Acad Dermatol **42***:23, 2000 [PMID: 10607353]

35. Criscione VD et al: Actinic keratoses: Natural history and risk of malignant transformation in the veterans affairs topical tretinoin chemoprevention trial. *Cancer **115***(11):2523, 2009

36. Mittelbronn MA et al: Frequency of preexisting actinic keratosis in cutaneous squamous cell carcinoma. *Int J Dermatol **37***:677, 1998 [PMID: 9762818]

37. Huwitz RM, Monger LE: Solar keratosis: An evolving squamous cell carcinoma: Benign or malignant? [letter]. *Dermatol Surg **21***:184, 1995

38. Guenther ST et al: Cutaneous squamous cell carcinomas consistently show histologic evidence of in situ changes: A clinicopathologic correlation. *J Am Acad Dermatol **41***:443, 1999

39. Lober BA et al: Actinic keratosis is squamous cell carcinoma. *J Am Acad Dermatol **43***:881, 2000 [PMID: 11050603]

40. Czarnecki D et al: The majority of cutaneous squamous cell carcinomas arise in actinic keratoses. *J Cutan Med Surg **6***:207, 2002 [PMID: 11951126]

41. Sellheyer K, Krahl D: Basal cell (trichoblastic) carcinoma common expression pattern for epithelial cell adhesion molecule links basal cell carcinoma to early follicular embryogenesis, secondary hair germ, and outer root sheath of the vellus hair follicle: A clue to the adnexal nature of basal cell carcinoma. *J Am Acad Dermatol **58***(1):158, 2008.

42. Harvey I et al: Nonmelanoma skin cancer and solar keratoses. 1. Methods and descriptive results of the south Wales skin cancer study. *Br J Cancer **74***(8):1302, 1996

43. Frost C, Williams G, Green A: High incidence and regression rates of solar keratoses in a Queensland community. *J Invest Dermatol **115***(2):273, 2000

44. Marks R et al: Spontaneous remission of solar keratoses: The case for conservative management. *Br J Dermatol **115***:649, 1986 [PMID: 3801305]

45. Boddie AW Jr et al: Squamous carcinoma of the lower lip in patients under 40 years of age. *South Med J **70***:711, 1977 [PMID: 877622]

46. Drake LA et al: Guidelines for the care of actinic keratoses. *J Am Acad Dermatol **32***:95, 1995 [PMID: 7529779]

47. Callen JP et al: Actinic keratosis. *J Am Acad Dermatol **36***:650, 1997 [PMID: 9092763]

48. Feldman SR et al: Destructive procedures are the standard of care for treatment of actinic keratoses. *J Am Acad Dermatol **40***:43, 1999 [PMID: 9922011]

49. Thai KE et al: A prospective study of the use of cryosurgery for the treatment of actinic keratoses. *Int J Dermatol **43***:687, 2004 [PMID: 15357755]

50. Burge SM, Dawber RPD: Hair follicle destruction and regeneration in guinea pig skin after cutaneous freeze injury. *Cryobiology **27***:153, 1990 [PMID: 2331888]

51. Bercovitch L: Topical chemotherapy of actinic keratoses of the upper extremity with tretinoin and 5-fluorouracil: A double-blind controlled study. *Br J Dermatol **116***:549, 1987 [PMID: 3555597]

52. Simmonds WL: Topical management of actinic keratoses with 5-fluorouracil: Results of a six year follow-up study. *Cutis* ***10***:737, 1972

53. Weiss J et al: Effective treatment of actinic keratoses with 0.5% fluorouracil cream for 1, 2, or 4 weeks. *Cutis* ***70***:22, 2002 [PMID: 12353677]

54. Loven K et al: Evaluation of the efficacy and tolerability of 0.5% fluorouracil cream and 5% fluorouracil cream applied to each side of the face in patients with actinic keratosis. *Clin Ther* ***24***:990, 2002 [PMID: 12117087]

55. Sachs DL et al: Topical fluorouracil for AKs and photoaging. *Arch Dermatol* ***145***:659, 2009

56. Stockfleth E et al: Low incidence of new actinic keratoses after topical 5% imiquimod treatment: A long-term follow-up study. *Arch Dermatol* ***140***:1542, 2004 [PMID: 15611446]

57. Chen K et al: Short course therapy with imiquimod 5% cream for solar keratoses: A randomized controlled trial. *Aus J Dermatol* ***44***:250, 2003 [PMID: 14616490]

58. Korman N et al: Dosing with 5% imiquimod cream three times per week for the treatment of actinic keratosis: Results of two phase 3, randomized, double-blind, parallel-group, vehicle-controlled trials. *Arch Dermatol* ***141***:467, 2005 [PMID: 15837864]

59. Harrison LI et al: Pharmacokinetics and safety of imiquimod 5% cream in the treatment of actinic keratoses of the face, scalp, or hands and arms. *Arch Dermatol* ***296***:6, 2004 [PMID: 15083310]

60. Hadley G et al: Imiquimod for actinic keratosis: Systematic review and meta-analysis. *J Invest Dermatol* ***126***:1251, 2006 [PMID: 16557235]

61. Stockfleth E et al: A randomized double-blind vehicle-controlled study to assess 5% imiquimod cream for the treatment of multiple actinic keratoses. *Arch Dermatol* ***138***:1498, 2002 [PMID: 12437457]

62. Lebwohl M et al: Imiquimod 5% cream for the treatment of actinic keratosis: Results from two phase 3 randomized, double-blind, parallel group, vehicle-controlled trials. *J Am Acad Dermatol* ***50***:714, 2004 [PMID: 15097955]

63. Szeimies RM et al: Imiquimod 5% cream for the treatment of actinic keratosis: Results from a phase 3 randomized, double-blind, vehicle-controlled clinical trial. *J Am Acad Dermatol* ***51***:547, 2004 [PMID: 15389189]

64. Lee PK et al: Long-term clinical outcomes following treatment of actinic keratosis with imiquimod 5% cream. *Dermatol Surg* ***31***:659, 2005 [PMID: 15996416]

65. Ulrich C et al: Topical immunomodulation under systemic immunosuppression: Results of a multicentre, randomized, placebo-controlled safety and efficacy study of imiquimod 5% cream for the treatment of actinic keratoses in kidney, heart, and liver transplant patients. *Br J Dermatol* ***157***(Suppl. 2):25, 2007

66. Benson E: Imiquimod: Potential risk of an immunostimulant. *Australas J Dermatol* ***45***(2):123, 2004

67. An KP et al: Cyclooxygenase-2 expression in murine and human NMSCs: Implications for therapeutic approaches. *Photochem Photobiol* ***76***:7380, 2002

68. Wolf JE Jr et al: Topical 3% diclofenac in 2.5% hyaluronan gel in the treatment of actinic keratoses. *Int J Dermatol* ***40***:709, 2001 [PMID: 11737438]

69. Lawrence N et al: A comparison of the efficacy and safety of Jessner's solution and 35% trichloroacetic acid vs 5% fluorouracil in the treatment of widespread facial actinic keratoses. *Arch Dermatol* ***131***:176, 1995 [PMID: 7857114]

70. Witheiler DD et al: Long-term efficacy and safety of Jessner's solution and 35% trichloroacetic acid vs 5% fluorouracil in the treatment of widespread actinic keratoses. *Dermatol Surg* ***23***:191, 1997 [PMID: 9145962]

71. Lawrence N et al: A comparison of the efficacy and safety of Jessner's solution and 35% trichloroacetic acid vs 5% fluorouracil in the treatment of facial actinic keratoses. *Arch Dermatol* ***131***:176, 1995 [PMID: 7857114]

72. Iyer S et al: Full face laser resurfacing therapy and prophylaxis for actinic keratoses and nonmelanoma skin cancer. *Lasers Surg Med* 34:114, 2004 [PMID: 15004822]

73. Trimas SJ et al: The carbon dioxide laser: An alternative for the treatment of actinically damaged skin. *Dermatol Surg* ***23***:885, 1997 [PMID: 9357496]

74. Jiang B et al: YAG laser for the treatment of actinic keratoses. *Dermatol Surg* ***26***:437, 2000 [PMID: 10816231]

75. Ostertag JU et al: Recurrence rates and long-term follow-up after laser resurfacing as a treatment for widespread actinic keratoses on the face and scalp. *Dermatol Surg* ***32***:261, 2006 [PMID: 16442048]

76. Nestor MS et al: The use of photodynamic therapy in dermatology: Results of a consensus conference. *J Drugs Dermatol* ***5***:140, 2006 [PMID: 16485882]

77. Jeffes EW et al: Photodynamic therapy of actinic keratoses with topical aminolevulinic acid hydrochloride and fluorescent blue light. *J Am Acad Dermatol* ***45***:96, 2001 [PMID: 11423841]

78. Kurwa HA et al: A randomized paired comparison of photodynamic therapy and topical 5-fluorouracil in the treatment of actinic keratosis. *J Am Acad Dermatol* ***41***:414, 1999 [PMID: 10459115]

79. Piacquadio DJ et al: Photodynamic therapy with ALA topical solution and visible blue light in the treatment of multiple actinic keratoses of the face and scalp: Investigator-blinded, phase 3, multicenter trials. *Arch Dermatol* ***140***:41, 2004 [PMID: 14732659]

80. Szeimies RM, Matheson RT, Davis SA: Topical methyl aminolevulinate photodynamic therapy using red light-emitting diode light for multiple actinic keratoses: A randomized study. *Dermatol Surg* ***35***(4):586, 2009

81. Pariser D et al: Topical methyl-aminolevulinate photodynamic therapy using red light-emitting diode light for treatment of multiple actinic keratoses: A randomized, double blind, placebo-controlled study. *J Am Acad Dermatol* ***59***(4):569, 2008

82. Moloney EJ, Collins P: Randomized, double blind, prospective study to compare topical 5-aminolaevulinic acid methylester with topical 5-aminolaevulinic acid photodynamic therapy for extensive scalp keratosis. *Br J Dermatol* ***157***(1):87, 2007

83. Krawtchenko N et al: A randomized study of topical 5% imiquimod vs. cryosurgery in immunocompetent patients with actinic keratoses: A comparison of clinical and histological outcomes including one-year follow-up. *Br J Dermatol* ***157***(Suppl. 2):34, 2007

84. Gold MH: Pharmacoeconomic analysis of the treatment of multiple actinic keratoses. *J Drugs Dermatol* ***7***(1):23, 2008

85. Drake LA et al: Guidelines of care for actinic keratoses. Committee on guidelines of care. *J Am Acad Dermatol* ***32***(1):95, 1995

86. Stockfleth E, Kerl H; Guideline Subcommittee of the European Dermatology Forum: Guidelines for the management of actinic keratoses. *Eur J Dermatol* ***16***(6):599, 2006

87. Siller G et al: PEP 005 (ingenol mebutate) gel, a novel agent for the treatment of actinic keratosis: Results of a randomized, double blind, vehicle-controlled, multicentre, phase IIa study. *Australas J Dermatol* ***50***(1):16, 2009

88. Huyke C et al: Treatment of actinic keratoses with a novel betulin-based oleogel. A prospective, randomized, comparative pilot study. *J der Deutsch Dermatol Gesellsch* ***7***(2):128, 2008

89. Szeimies RM et al: A phase II dose-ranging study of topical resiquimod to treat actinic keratosis. *Br J Dermatol* ***159***(1):205, 2008

90. Weinstock MA, Moses AM: Skin cancer meets vitamin D: The way forward for dermatology and public health. *J Am Acad Dermatol* ***61***:720, 2009

91. Ananathaswamy HN et al: Inhibition of UV-induced p53 mutations by sunscreens; implications for skin cancer prevention. *J Investig Dermatol Symp Proc* ***3***:52, 1998

92. Darlington S et al: A randomized, controlled trial to assess sunscreen application and beta carotene supplementation in the prevention of solar keratoses. *Arch Dermatol* ***139***(4):451, 2003

93. van der Pols JC et al: Prolonged prevention of squamous cell carcinoma of the skin by regular sunscreen use. *Cancer Epidemiol Biomarkers Prev* ***15***(12):2546, 2006

94. Green A et al: Daily sunscreen application and betacarotene supplementation in prevention of basal cell and squamous cell carcinomas of the skin: A randomized controlled trial. *Lancet* ***354***(9180):723, 1999

95. Black HS et al: Effect of a low-fat diet on the incidence of actinic keratosis. *N Engl J Med* ***330***:1272, 1995

96. Hughes MCB et al: Food intake, dietary patterns, and actinic keratoses of the skin: A longitudinal study. *Am J Clin Nutr* ***89***:1246, 2009

97. Black HS: Influence of dietary factors on actinically induced skin cancer. *Mutat Res* ***422***:185, 1998 [PMID: 9920444]

98. Jaax S et al: General guidelines for a low-fat diet effective in the management and prevention of nonmelanoma skin cancer. *Nutr Cancer* ***27***:150, 1997 [PMID: 9121942]

99. Odom R: Managing actinic keratoses with retinoids. *J Am Acad Dermatol* ***39***:574, 1998

100. Peck GL: Topical tretinoin in actinic keratosis and basal cell carcinoma. *J Am Acad Dermatol* ***15***:829, 1986 [PMID: 3534022]

101. Cho S et al: Long-term treatment of photoaged human skin with topical retinoic acid improves epidermal cell atypia and thickens the collagen and the papillary dermis. *J Am Acad Dermatol* ***53***:769, 2005 [PMID: 16243124]

102. Weinstock MA et al: Topical tretinoin and prevention of keratinocyte carcinoma. *J Invest Dermatol* ***129***(Suppl. 1):S65, 2009

103. Weinstock MA et al: Topical tretinoin therapy and all cause mortality. *Arch Dermatol* ***145***(1):18, 2009

104. Rook AH et al: Beneficial effect of low-dose systemic retinoid in combination with topical tretinoin for the treatment and prophylaxis of premalignant and malignant skin lesions in renal transplant recipients. *Transplantation* ***59***:714, 1995 [PMID: 7886798]

105. George R et al: Acitretin for chemoprevention of non-melanoma skin cancers in renal transplant recipients. *Australas J Dermatol* ***43***(4):269, 2002

106. Kraemer KH, DiGiovanna JJ, Moshell AN: Prevention of skin cancer in xeroderma pigmentosum with the use of oral isotretinoin. *N Engl J Med* ***318***(25):1633, 1988

107. Harwood CA et al: Low dose retinoids in the prevention of cutaneous squamous cell carcinomas in organ transplant recipients: A 16 year retrospective study. *Arch Dermatol* ***141***:456, 2005

108. Brown VL et al: Safety and efficacy of 5% imiquimod cream for the treatment of skin dysplasia in high-risk renal transplant recipients: Randomized, double-blind, placebo-controlled trial. *Arch Dermatol* ***141***:985, 2005 [PMID: 16103328]

109. Amadori S et al: Use of arsenic trioxide in haematological malignancies: Insight into the clinical development of a novel agent. *Curr Med Res Opin* ***21***:403, 2005 [PMID: 15811209]

110. Schwartz RA: Arsenic and the skin. *Int J Dermatol* ***36***:241, 1997 [PMID: 9169318]

111. Khandpur S et al: Chronic arsenic toxicity from ayurvedic medicines. *Int J Dermatol* ***47***(6):618, 2008

112. Chakraborti D et al: Arsenic toxicity from homeopathic treatment. *J Toxicol Clin Toxicol* ***41***(7):963, 2003

113. Blejer HP, Wagner W: Case study 4: Inorganic arsenic—Ambient level approach to the control of occupational carcinogenic exposures. *Ann N Y Acad Sci* ***271***:179, 1976 [PMID: 1069501]

114. Tchounwou PB, Centeno JA, Patiolla AK: Arsenic toxicity, mutagenesis, and carcinogenesis-a health risk assessment and management approach. *Mol Cell Biochem* ***255***(1-2):47, 2004

115. Travis LB, Arndt KA: Occupational skin cancer. *Postgrad Med* ***79***:211, 1986 [PMID: 3703756]

116. Col M et al: Arsenic-related Bowen's disease, palmar keratosis, and skin cancer. *Environ Health Perspect* ***107***:687, 1999 [PMID: 10417369]

117. Jackson R, Grainge JW: Arsenic and cancer. *Can Med Assoc J* ***113***:396, 1975 [PMID: 125622]

118. Pershagen G: The carcinogenicity of arsenic. *Environ Health Perspect* ***40***:93, 1981 [PMID: 7023936]

119. Hsu C-H et al: Mutational spectrum of p53 gene in arsenic-related skin cancers from the blackfoot disease endemic area of Taiwan. *Br J Cancer* ***80***:1080, 1999 [PMID: 10362120]

120. Banerjee M et al: Polymorphisms in the ERCC2 codon 751 is associated with arsenic-induced premalignant hyperkeratosis and significant chromosome aberrations. *Carcinogenesis* ***28***:672, 2007

121. Wong SS et al: Cutaneous manifestations of chronic arsenicism: Review of 17 cases. *J Am Acad Dermatol* ***38***:179, 1998 [PMID: 9486671]

122. Graham JH: Selected precancerous skin and mucocutaneous lesions. In: Neoplasms of the skin and malignant melanoma: a collection of papers presented at the Twentieth Annual Clinical Conference on Cancer, 1975, at the University of Texas System Cancer Center, M.D. Anderson Hospital and Tumor Institute, Houston, Texas. (Editors: Susan B. Freitag and Diane L. Culhane)

123. Son SB, Song HJ, Son SW: Successful treatment of palmoplantar arsenical keratosis with a combination of keratolytics and low-dose acitretin. *Clin Exp Dermatol* ***33***(2):202, 2008

124. Yerebkan O et al: Treatment of arsenical keratosis and Bowen's disease with acitretin. *Int J Dermatol* ***41***(2):84, 2002

125. Boonchai W: Treatment of precancerous and cancerous lesions of chronic arsenicism with 5% imiquimod cream. *Arch Dermatol* ***142***(4):531, 2006

126. Arrington JH III, Lockman DS: Thermal keratoses and squamous cell carcinoma in situ associated with erythema ab igne. *Arch Dermatol* ***115***:1226, 1979 [PMID: 507871]

127. Chatterjee S: Erythema ab igne from prolonged use of a heating pad. *Mayo Clin Proc* ***80***:1500, 2005 [PMID: 16295029]

128. Bachmeyer C, Bensaid P, Begon: Laptop computer as a modern cause of erythema ab igne. *J Eur Acad Dermatol Venereol* ***23***(6):1736, 2009

129. Shahrad P, Marks R: The wages of warmth: Changes in erythema ab igne. *Br J Dermatol* ***97***:179, 1977 [PMID: 911679]

130. Iacocca MV et al: Mixed Merkel cell carcinoma and squamous cell carcinoma of the skin. *J Am Acad Dermatol* ***39***:882, 1998 [PMID: 9810922]

131. Boffetta P et al: Cancer risk from occupational and environmental exposure to polycyclic aromatic hydrocarbons. *Cancer Causes Control* ***8***:444, 1997 [PMID: 9498904]

132. Pott P: Cancer scroti. In: *Chirurgical Works of Percivall Pott*. Dublin, James Williams, 1775, p. 403

133. Letzel S, Drexler H: Occupationally related tumors in tar refinery workers. *J Am Acad Dermatol* ***39***:712, 1998 [PMID: 9810887]

134. Götz H: Tar keratosis. In: *Cancer of the Skin: Biology—Diagnosis—Management*, edited by R Andrade et al. Philadelphia, WB Saunders, 1976, p. 492

135. Helm KF et al: Radiation keratosis associated with exposure to a gold ring. *Cutis* ***57***:435, 1996 [PMID: 8804849]

136. Yamada M et al: Prevalence of skin neoplasms among the atomic bomb survivors. *Radiat Res* ***146***:223, 1996 [PMID: 8693072]

137. Peter RU et al: Chronic cutaneous damage after accidental exposure to ionizing radiation: The Chernobyl experience. *J Am Acad Dermatol* ***30***:719, 1994 [PMID: 8176010]

138. Pierard GE et al: Emerging therapies for ionizing radiation-associated skin field carcinogenesis. *Expert Opin Pharmacother* ***10***(5):813, 2009

139. Marjolin JN: Ulcère. In: *Dictionnaire de Médecine*, vol 21. Paris, Béchet, 1828, p. 31

140. Phillips TJ et al: Burn scar carcinoma. *Dermatol Surg* ***22***:561, 1998

141. Dupree MT et al: Marjolin's ulcer arising in a burn scar. *Cutis* ***62***:49, 1998 [PMID: 9675536]

142. Arons MS et al: Scar tissue carcinoma: A clinical study with special reference to burn scar carcinoma. *Ann Surg* ***161***:170, 1965 [PMID: 14260013]

143. Novick M et al: Burn scar carcinoma: A review and analysis of 46 cases. *J Trauma* ***17***:809, 1977 [PMID: 909123]

144. Dubina M, Goldenberg G: Viral-associated nonmelanoma skin cancers. A review. *Am J Dermpath* ***31***(6):561, 2009

145. Lloyd KM: Multicentric pigmented Bowen's disease of the groin. *Arch Dermatol* ***101***:48, 1970 [PMID: 5416792]

146. Kopf AW, Bart RS: Tumor conference. No 11. Multiple bowenoid papules of the penis: A new entity? *J Dermatol Surg Oncol* ***3***:265, 1977 [PMID: 874134]

147. Wade TR et al: Bowenoid papulosis of the genitalia. *Arch Dermatol* ***115***:306, 1979 [PMID: 434846]

148. Bleeker MC et al: Penile cancer: Epidemiology, pathogenesis and prevention. *World J Urol* ***27***(2):141, 2009

149. Obalek S et al: Bowenoid papulosis of the male and female genitalia: Risk of cervical neoplasia. *J Am Acad Dermatol* ***14***:433, 1986 [PMID: 3007587]

150. Descamps V et al: Topical cidofovir for bowenoid papulosis in an HIV-infected patient. *Br J Dermatol* ***144***:642, 2001 [PMID: 11260042]

151. Wigbels B et al: Imiquimod: A new treatment possibility in bowenoid papulosis? *Hautarzt* ***52***:128, 2001 [PMID: 11244890]

152. Petrow et al: Successful topical immunotherapy of bowenoid papulosis with imiquimod. *Br J Dermatol* ***145***:1022, 2001 [PMID: 11899127]

153. Loo WJ, Holt PJA: Bowenoid successfully treated with imiquimod. *J Eur Acad Dermatol Venereol* ***17***:363, 2003 [PMID: 12702095]

154. Goorney BP, Polori R: A case of bowenoid papulosis of the penis successfully treated with topical imiquimod 5% cream. *Int J STD AIDS* ***15***:833, 2004 [PMID: 15601490]

155. Matuszewski M et al: Topical treatment of bowenoid papulosis of the penis with imiquimod. *J Eur Acad Dermatol Venereol* ***23***(8):978, 2009

156. Ricart JM et al: Extensive genital bowenoid papulosis responding to imiquimod. *J Eur Acad Dermatol Venereol* ***21***(1):113, 2007

157. Ramoz N et al: A susceptibility locus for epidermodysplasia verruciformis, an abnormal predisposition to infection with the oncogenic human papillomavirus type 5, maps to chromosome 17qter in a region containing a psoriasis locus. *J Invest Dermatol* ***112***:259, 1999 [PMID: 10084299]

158. Ramoz et al: Mutations in two adjacent novel genes are associated with epidermodysplasia verruciformis. *Nat Genet* ***32***:579, 2002 [PMID: 12426567]

159. Rogers HD et al: Acquired epidermodysplasia verruciformis. *J Am Acad Dermatol* ***60***(2):315, 2009

160. Bowen JT: Precancerous dermatoses: A study of two cases of chronic atypical epithelial proliferation. *J Cutan Dis* ***30***:241, 1912

161. Kossard S, Rosen R: Cutaneous Bowen's disease: An analysis of 1001 cases according to age, sex, and site. *J Am Acad Dermatol* ***27***:406, 1992 [PMID: 1401276]

162. Reizner GT et al: Bowen's disease (squamous cell carcinoma in situ) in Kauai, Hawaii: A population-based incidence report. *J Am Acad Dermatol* ***31***:596, 1994 [PMID: 8089285]

163. Arlette JP: Treatment of Bowen's disease and erythroplasia of Queyrat. *Br J Dermatol* ***149***:43, 2003 [PMID: 14616349]

164. Meyer T et al: Importance of human papillomaviruses for the development of skin cancer. *Cancer Detect Prev* ***25***:533, 2001 [PMID: 12132874]

165. McGrae JD et al: Multiple Bowen's disease of the fingers associated with HPV type 16. *Int J Dermatol* ***32***:104, 1993 [PMID: 8382665]

166. Ragi G et al: Pigmented Bowen's disease and review of 420 Bowen's disease lesions. *J Dermatol Surg Oncol* ***14***:765, 1988 [PMID: 3292613]

167. Civatte J: Pseudo-carcinomatous hyperplasia. *J Cutan Pathol* ***12***:214, 1985 [PMID: 4019860]

168. Kao GF: Carcinoma arising in Bowen's disease. *Arch Dermatol* ***122***:1124, 1986 [PMID: 3767398]

169. Jaeger AB et al: Bowen's disease and risk of subsequent malignant neoplasms. A population-based cohort study of 1147 patients. *Arch Dermatol* ***135***:740, 1999

170. Ragnarsson B et al: Carcinoma in situ of the vulva: Long-term prognosis. *Acta Oncol* ***26***:277, 1987 [PMID: 3689581]

171. Sideri M et al: Squamous vulvar intraepithelial neoplasia: 2004 modified terminology, ISSVD vulvar oncology subcommittee. *J Reprod Med* ***50***:807, 2005

172. Joura EA et al: Trends in vulvar neoplasia. Increasing incidence of vulvar intraepithelial neoplasia and squamous cell carcinoma of the vulva in young women. *J Reprod Med* ***45***:613, 2000

173. Hart WR: Vulvar intraepithelial neoplasia: Historical aspects and current status. *Int J Gynecol Pathol* ***20***(1):16, 2001

174. van Seters M, van Beurden M, de Craen AJ: Is the assumed natural history of VIN III based on enough evidence? A systematic review of 3322 published patients. *Gynecol Oncol* ***97***:645, 2005

175. Le T et al: Final results of a phase 2 study using continuous 5% imiquimod cream application in the primary treatment of high grade VIN. *Gynecol Oncol* ***106***:579, 2007

176. Mathiesen O, Buus SK, Cramers M: Topical imiquimod can reverse VIN: A randomized, double-blinded study. *Gynecol Oncol* ***107***:219, 2007

177. van Seters M et al: Treatment of VIN with topical imiquimod. *N Engl J Med* ***358***:1465, 2008

178. Sillman FH, Sedlis A, Boyce JG: A review of lower genital intraepithelial neoplasia and the use of topical 5 fluorouracil. *Obstet Gynecol Surv* ***40***:190, 1985

179. Krupp PJ: 5 fluorouracil topical treatment of in situ vulvar cancer. *Obstet Gynecol* ***51***:702, 1978

180. Joura EA et al: Efficacy of a quadrivalent prophylactic HPV (types 6, 11, 16, 18) L1 virus-like-particle vaccine against high-grade vulvar and vaginal lesions: A combined analysis of 3 randomized trials. *Lancet* ***369***:1693, 2007

181. Kenter GG, Welters MJP, Valentijn ARPM: Vaccination against HPV-16 oncoproteins for vulvar intraepithelial neoplasia. *N Engl J Med* ***361***:1838, 2009

182. Srodon M et al: The distribution of low and high-risk HPV types in vulvar and vaginal intraepithelial neoplasia. *Am J Surg Pathol* ***30***:1513, 2006

183. Hampl M et al: Effect of HPV vaccines on vulvar, vaginal, and anal intraepithelial lesions and vulvar cancer. *Obstet Gynecol* ***108***:1361, 2006

184. Solomon D et al: The 2001 Bethesda System: Terminology for reporting results of cervical cytology. *JAMA* ***287***:2114, 2002

185. Mahto M, Nathan M, O'Mahony C: More than a decade on: Review of the use of imiquimod in lower anogenital intraepithelial neoplasia. *Int J STD AIDS* ***21***(1):8, 2010

186. Palefsky JM et al: A trial of SGN-00101 (HspE7) to treat high-grade AIN in HIV positive individuals. *AIDS* ***20***:1151, 2006

187. Micali G et al: Penile cancer. *J Am Acad Dermatol* ***54***(3):369, 2006

188. Queyrat L: Erythroplasie du gland. *Bull Soc Fr Dermatol Syphiligr* ***22***:378, 1911

189. Wieland U et al: Erythroplasia of Queyrat: Coinfection with cutaneous carcinogenic human papillomavirus type 8 and genital papillomaviruses in a carcinoma in situ. *J Invest Dermatol* ***115***:396, 2000 [PMID: 10951274]

190. Cubilla AL, Velasquez EF, Young RH: Epithelial lesions associated with invasive penile SCC: A pathologic study of 288 cases. *Int J Surg Pathol* ***12***(4):351, 2004

191. Graham JH, Helwig EB: Erythroplasia of Queyrat: A clinicopathologic and histochemical study. *Cancer* ***32***:1396, 1973

192. Oliver RTD: Circumcision and/or vaccination against HPV in the male to prevent infection with HIV: An early surrogate endpoint for the later prevention of penile, prostate, anal, and oral cancer. *BJU* ***104***(6):753, 2009

193. van der Waal I: Potentially malignant disorders of the oropharyngeal mucosa: Terminology, classification, and present concepts of management. *Oral Oncol* ***45***:317, 2009

194. Axell T et al: International collaborative group on oral white lesions: Oral white lesions with special reference to precancers and tobacco-related lesions: Conclusions of an international symposium held in Uppsala, Sweden, May 18–21, 1994. *J Oral Pathol Med* ***25***:49, 1996 [PMID: 8667255]

195. Reibel J: Prognosis of oral premalignant lesions: Significance of clinical, histopathological and molecular biological characteristics. *Crit Rev Oral Biol Med* ***14***:47, 2003 [PMID: 12764019]

196. Scheifele C, Reichart PA: Is there a natural limit of the transformation rate of oral leukoplakia? *Oral Oncol* ***39***:470, 2003 [PMID: 12747971]

197. Petti S: Pooled estimate of world leukoplakia prevalence: A systematic review. *Oral Oncol* ***39***:770, 2003 [PMID: 13679200]

198. Baric JM et al: Influence of cigarette, pipe, and cigar smoking, removable partial dentures, and age on oral leukoplakia. *Oral Surg Oral Med Oral Pathol* ***54***:424, 1982

199. Maserejian NN et al: Prospective study of alcohol consumption and risk of oral premalignant lesions in men. *Cancer Epidemiol Biomarkers Prev* ***15***:774, 2006

200. Bagan JV et al: Lack of an association between proliferative verrucous leukoplakia and HPV infection. *J Oral Maxillofac Surg* ***65***:46, 2007

201. Campisi G et al: HPV DNA in clinically different variants of oral leukoplakia and lichen planus. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* ***98***:705, 2004

202. Fornatora M et al: HPV-associated oral epithelial dysplasia (koilocytic dysplasia). An entity of unknown biologic potential. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* ***82***:47, 1996

203. Scully C et al: Progress in determining the malignant potential of oral lesions. *Oral Pathol Med* ***32***:251, 2003 [PMID: 12694347]

204. Miller CS, Johnstone BM: Human papillomavirus as a risk factor for oral squamous cell carcinoma: A meta-analysis, 1982–1997. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* ***91***:622, 2001 [PMID: 11402272]

205. Dietrich T et al: Clinical risk factors of oral leukoplakia in a representative sample of the US population. *Oral Oncol* ***40***:158, 2004 [PMID: 14693239]

206. van der Waal I, Axell T: Oral leukoplakia: A proposal for uniform reporting. *Oral Oncol* ***38***:521, 2002

207. Greenspan D, Jordan RCK: The white lesion that kills—Aneuploid dysplastic oral leukoplakia. *N Engl J Med* ***350***:1382, 2004 [PMID: 15070786]

208. Kramer IR et al: The clinical features and risk of malignant transformation in sublingual keratosis. *Br Dent J* ***144***:171, 1978 [PMID: 272896]

209. Schepman KP et al: Malignant transformation of oral leukoplakia: A follow-up study of a hospital-based population of 166 patients with oral leukoplakia from the Netherlands. *Oral Oncol* ***34***:270, 1998 [PMID: 9813722]

210. Holmstrup P et al: Long-term treatment outcome of oral premalignant lesions. *Oral Oncol* ***42***:461, 2006 [PMID: 16316774]

211. Epstein JB et al: Advances in the diagnosis of oral premalignant and malignant lesions. *J Can Dent Assoc* ***68***:617, 2002 [PMID: 12410942]

212. Pindborg JJ et al: *Histological Typing of Cancer and Precancer of the Oral Mucosa*. Berlin, Springer-Verlag, 1997

213. Lodi G et al: Interventions for treating oral leukoplakia. *Cochrane Database Syst Rev* (4), CD0018292006

214. Sudbø J et al: The influence of resection and aneuploidy on mortality in oral leukoplakia. *N Engl J Med* ***350***:1405, 2004 [PMID: 12455964]

215. van der Hem PS et al: The results of CO_2 laser surgery in patients with oral leukoplakia: A 25-year follow-up. *Oral Oncol* ***41***:31, 2005

216. Bouquot JE, Ephros H: Erythroplakia: The dangerous red mucosa. *Pract Periodontics Aesthet Dent* ***7***:59, 1995 [PMID: 9002888]

217. Reichart PA, Philipsen HP: Oral erythroplakia—Review. *Oral Oncol* ***41***:551, 2005 [PMID: 15975518]

218. Hashibe M et al: Chewing tobacco, alcohol and the risk of erythroplakia. *Cancer Epidemiol Biomarkers Prev* ***9***:639, 2000 [PMID: 10919731]

219. Trock B: Out of the mouth of babes: Oral premalignant lesions and use of alternative tobacco products. *Cancer Epidemiol Biomarkers Prev* ***9***:637, 2000 [PMID: 10919730]

220. Tomar SL et al: Oral mucosal smokeless tobacco lesions among adolescents in the United States. *J Dent Res* ***76***:1277, 1997 [PMID: 9168861]

221. Shafer WG, Waldron CA: Erythroplakia of the oral cavity. *Cancer* ***36***:1021, 1975 [PMID: 1182656]

222. Mashberg A, Samit A: Early detection, diagnosis, and management of oral and oropharyngeal cancer. *Cancer* ***39***:67, 1989 [PMID: 2495159]