

3. Successful Management of Viral Infections and Other Dermatoses with Imiquimod 5% Cream

BRIAN BERMAN, ULRICH HENGGE and SIMON BARTON

INTRODUCTION

The immune response modifier imiquimod 5% cream (AldaraTM) is a safe, effective and established treatment for external genital and perianal warts. It is the first member of the family of immune response modifiers, which stimulates innate and cell-mediated immune pathways, inducing potent antitumor, antiviral and immunoregulatory effects (1, 2). Imiquimod stimulates the immune response through induction, synthesis and release of cytokines such as interferon (IFN) α , tumor necrosis factor (TNF) α and interleukin 12 (IL 12) (3, 4). In addition, imiquimod acts to stimulate other components of innate immunity such as natural killer cell activity, secretion of nitric oxide from macrophages and proliferation and differentiation of B-lymphocytes (1). Imiquimod also stimulates the T-helper (Th)-1 cytokine, IFN γ and enhances the migration of Langerhans' cells to the lymph nodes; these cells are important antigen-presenting cells within the epidermis (5). Imiquimod is not only a recommended treatment for anogenital warts (6–8), but has also been shown to be effective in the treatment of other viral infections (9, 10) and epithelial neoplasms (11–13).

IMIQUIMOD FOR THE TREATMENT OF EXTERNAL GENITAL WARTS

Human papillomavirus (HPV) is the most common sexually transmitted infection in many countries. Figures from the World Health Organization (WHO) and Communicable Disease Surveillance Center (CDSC) show that approximately 5.5 million new cases of HPV are reported every year, with 40 million cases in the United States of America (USA). In addition, 1% of sexually active adults in the USA aged between 15 and 49 years develop genital warts. With a steady increase in worldwide incidence, genital warts are the most frequently diagnosed infection in sexually transmitted disease (STD) clinics in both the northern and southern hemispheres (14). Within the UK, HPV-associated anogenital warts account for approximately 25% of total diagnoses at genitourinary medicine (GUM) clinics (15). This increase in the epidemiology of anogenital warts is having a substantial effect on the cost of healthcare services in developed countries, for instance in the UK in 2002 the estimated cost of external anogenital warts was three billion dollars.

HPV is prevalent in many different subtypes with the

clinical manifestation being either anogenital or non-genital. Anogenital warts or condylomata acuminata are clinical conditions of HPV types 6 or 11. High-oncogenic risk anogenital lesions tend to arise from HPV infections of subtypes 16, 18, 31, 33 and 35. HPV types 1, 2 and 3 have clinical manifestations that typify verruca plantaris, verruca vulgaris and verruca planar, respectively (16, 17). In addition to being implicated in many carcinomas of the skin (18), epidemiological studies have underlined that HPVs are the main etiological factor of anogenital cancer (19). Current recommended treatment options for genital warts are patient-applied therapies, which include imiquimod, or podophyllotoxin, an antimitotic agent. Alternative treatment options encompass physician-administered therapies, which may either be ablative, such as surgical excision, cryotherapy, laser therapy, and electrocautery or cytodestructive e.g. trichloroacetic acid (TCA). Guidelines from the Centers for Disease Control and Prevention (USA), Australia and Europe for the management of genital warts strongly recommend patient-applied therapies as a first line treatment option, with physician-administered therapies suggested as alternative strategies (6–8).

Imiquimod is available as a single-use sachet that is applied directly to the lesion three times per week at night and on the following morning, and the area washed with mild soap and water. Treatment duration is recommended until wart clearance is achieved or for a maximum of 16 weeks (20). The importance of ensuring a three times weekly application is highlighted by Gollnick et al. (21) who compared the safety and efficacy of three times weekly and once daily applications of imiquimod 5% cream for the treatment of penile genital warts in uncircumcised men. Both groups showed similar levels of efficacy and the only differences were in the side effects experienced. The most frequently reported local side effects were burning, pruritus, irritation or pain; however, the three times a week dosing regimen was well-tolerated, with a lower incidence of local skin reactions than in the once daily group. The results indicated that the appropriate treatment regimen is three times weekly, which demonstrated higher efficacy with tolerability (21). Additional open-label studies have further established the successful and well tolerated use of imiquimod for treating genital warts in both women and men with low rates of recurrence (22, 23). With any treatment modality, there are possible associated side effects, therefore it is important to highlight these to the

patient prior to commencement of a treatment schedule. Typical local skin reactions with imiquimod are associated with the local inflammatory reaction, including itching, erythema, irritation and ulceration (24). The benefit of imiquimod for the treatment of genital warts is verified by patient preference for this treatment option. In a phase IIIB clinical study conducted by O'Mahony et al. (25), patients expressed greater satisfaction with self-applied imiquimod compared to their previous therapies. In addition, they had specific preference for the length of time of clearance, convenience and lack of associated pain with imiquimod.

In a recent open-label clinical trial, imiquimod has also shown promise as a treatment for other HPV-associated conditions. Hengge and colleagues have reported the successful use of imiquimod for the treatment of common warts (9). A total of 50 patients suffering from nongenital cutaneous warts, located on the hands, feet and face were treated with imiquimod 5% cream. In this patient population there were four children under the age of 16 years, 12 HIV-infected patients (mean CD4 count reading 323) (Fig. 1a) and 3 allograft recipients. Imiquimod was applied once daily for five consecutive days per week. The application schedule was intensified, compared to the recommended three times a week application as used for the treatment of genital warts, because of the higher degree of keratinization of the skin. Results showed that 30% of

patients with warts achieved total clearance (Fig. 1b) while 26% demonstrated a >50% reduction in wart size. A common side effect observed was erythema, but this was generally mild and transient (9).

To exemplify the successful use of imiquimod for an HPV-associated condition, we report a case of an 84-year-old female with Heck's disease, who presented with a papule on the posterior aspect of the upper gum, located under her prosthesis. A physical examination demonstrated many white coalescing papules (Fig. 2a). She was instructed to topically apply imiquimod 5% cream to the lesion, under her prosthesis. Following three applications there was significant improvement in her condition, with no indication of the papules or the intraepithelial hyperplasia (Fig. 2b). These documented findings clearly highlight the therapeutic benefits of imiquimod in treating HPV-associated skin lesions.

IMIQUIMOD FOR THE TREATMENT OF MOLLUSCUM CONTAGIOSUM

Another common benign viral infection of the skin is molluscum contagiosum (MC), which can closely resemble warts in appearance. It is caused by one of three poxviruses (MCV I, MCV II, MCV III) (26), which are large double-stranded DNA viruses that replicate within the cytoplasm of keratinocytes. Within the host cell, the virion colony is encased and isolated

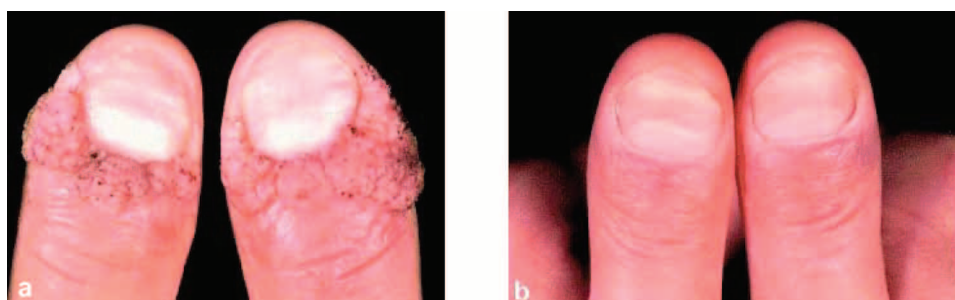


Fig. 1. A human immunodeficiency virus-positive patient with a 12-month history of extensive periungual warts caused by human papilloma-virus 42 (HPV 42) on 10 fingers is shown before (a) and after 8 weeks of therapy (b). Hengge UR, et al. *Br J Dermatol* 2000;**143**(5):1026–1031.

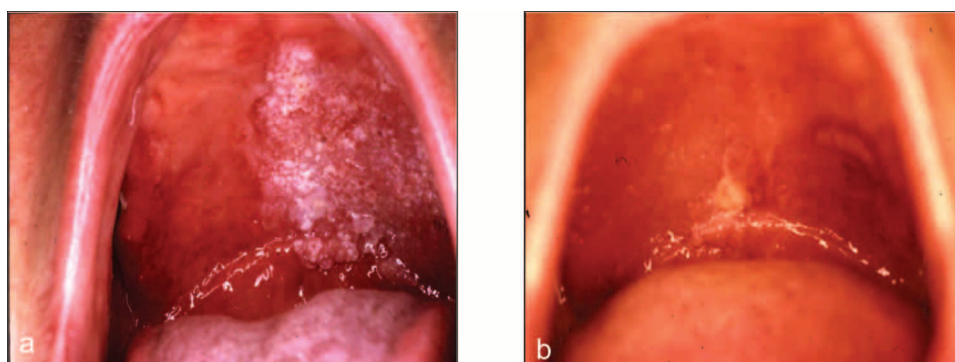


Fig. 2. (a) White coalescing papules on the posterior aspect of the upper gum in an 84 year old woman. (b) Clinical clearance of the papules (intraepithelial hyperplasia), following 3 applications of topically applied imiquimod 5% cream.

in a protective sac, thereby preventing activation of the host's cell-mediated immune response (27, 28). Transmission of the virus is facilitated by mechanical trauma (29). Although MC is frequently thought of as a childhood disease, the incidence of MC in sexually active adults has shown a marked increase over the past few decades (28). Data collected by the national Disease and Therapeutic Index Survey between 1966 and 1983 showed a statistically significant increase in the number of patients above 15 years of age who were diagnosed with MC. There was a greater incidence among patients aged 20 to 29 years, with a slight male dominance (30). Recently, the prevalence of MC or 'giant' MC has been documented in patients with primary immunodeficiencies or HIV infection (31). Conventional treatments for MC encompass topical application of caustic agents such as silver nitrate, TCA or cantharidin curettage. Alternatively, lesions may be excised or treated by cryotherapy. These treatments are often painful and not always feasible for larger or widespread lesions (26).

The proposal to treat MC with imiquimod followed initial findings by Hourihane et al. (32), who reported the successful treatment of MC in immunodeficient children with subcutaneous injections of IFN α . Based on these findings researchers proposed that treatment of this condition may be possible with imiquimod 5% cream. The unique immunostimulatory properties of imiquimod have resulted in its documented use in treating MC in young children and HIV-infected patients, as well as for recalcitrant MC (33, 34). In the same open-label trial that investigated imiquimod for common warts conducted by Hengge et al. (9), they documented the successful use of imiquimod for MC lesions. Inclusion criteria specified patients who had previous failed treatments with an average of three different therapy modalities. Imiquimod was applied once daily for five days a week. Of the total patient population, 15 patients presented with molluscum contagiosum, which included seven children (all

under 16 years of age) and three HIV-infected patients. Of the 93% of the patients with MC who completed the trial, 53% achieved total clearance while 27% showed a >50% reduction in molluscum size. In addition, six of the seven children demonstrated complete regression of their MC. Fig. 3 shows the typical response of MC to imiquimod application. The average time to clearance was between 8 and 12 weeks (9). Recently, Barba et al. (26) conducted an open-label safety study of topical imiquimod cream for treating MC in children. An acceptable degree of localized irritation was observed with no systemic toxicity. Clinical resolution was observed in a third of patients. However, this study did not address drug efficacy, therefore highlighting the need for further studies to determine imiquimod's efficacy and optimal dosing regimen.

It appears conclusive that imiquimod is an important addition to the therapeutic modalities available for the treatment of MCV-associated infections, as well as providing clinicians with a powerful tool in the arsenal against HPV.

IMIQUIMOD FOR THE TREATMENT OF VULVAL INTRAEPITHELIAL NEOPLASIA

Another HPV-associated condition is vulval intraepithelial neoplasia (VIN), best described as dysplasia of the squamous epithelium of the vulva (35). Vulval intraepithelial neoplasia is divided into three histological grades that encompass a spectrum of lesions of increasing severity: VIN I (mild dysplasia), VIN II (moderate dysplasia) and VIN III (severe dysplasia/carcinoma *in situ*). VIN III is the most common presentation and may be unifocal or, more likely, multifocal (36, 37). The etiology of VIN III has been linked to HPV types 16 and 18 (38).

Traditional treatment modalities consist of either medical, (e.g. 5-fluorouracil (5-FU), IFN α) surgical (e.g. cryotherapy, surgical vulvectomy) or photodynamic

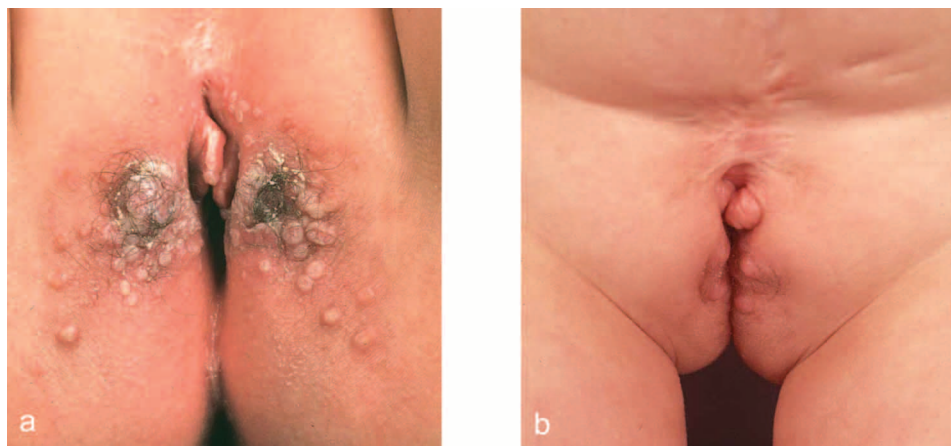


Fig. 3. 9-year old girl with genital mollusca shown (a) before and (b) after 6 weeks of therapy with imiquimod 5% cream. Hengge UR, et al. *Br J Dermatol* 2000;143(5):1026–1031.

therapy (36). All these treatment modalities, although effective, are associated with limited success and recurrence (36, 37). Based on findings that have implicated HPV as a contributing factor in the development of VIN, and the successful use of imiquimod in treating HPV-associated anogenital warts (20, 22), imiquimod has been proposed as a possible treatment option for VIN. Davis et al. (39), were the first to report the successful use of self-administered topical imiquimod for treating VIN III lesions associated with HPV-16. Imiquimod was applied three times a week for a total of six weeks. This preliminary study has led to further studies being conducted to determine the potential use of imiquimod for treating VIN. Such studies include those by Jayne et al. (40) and Todd et al. (41) who demonstrated either complete clinical clearance or greater than 50% reduction in the size of the VIN lesions within their patient population following treatment with imiquimod. These initial studies have highlighted another therapeutic benefit of imiquimod 5% cream, an already accepted therapy option for the treatment of viral and oncogenic pathologies of the skin.

IMIQUIMOD FOR THE TREATMENT OF KELOIDS

As imiquimod affects both innate and cell-mediated immunity, it is possible to speculate about its use for treating conditions where the immune systems plays a role in disease regression, or in conditions where IFNs have been previously used as treatment options. Keloids are an example of such a dermatological condition. These are best described as an overgrowth of fibrous tissue that occurs on the site of a scar of a previous injury and it is thought that tension plays a major pathophysiological role. Proliferative scars are characterized by increased collagen and glycosaminoglycan content, as well as an increase in collagen turnover (42). Traditional therapeutic treatments encompass occlusive dressings, compression therapy, intralesional corticosteroid injections, cryosurgery, excision, radiation, laser and therapies directed at collagen synthesis (42, 43). An additional treatment option is the therapeutic use of

IFNs. IFNs are antiviral agents that possess anti-angiogenic, anti-proliferative, anti-cancer activities as well as immunomodulatory activity. In addition to this, IFNs are able to regulate the expression of native functioning p53, a tumor suppressor protein, as well as enhancing apoptosis. IFNs act by increasing keloidal collagenase activity, reducing both glycosaminoglycan synthesis and keloidal fibroblast synthesis of collagens. These properties of IFNs all contribute to its anti-keloidal and antifibrotic effects.

It has been reported that keloids have an approximate 50% recurrence rate (44). This rate, however, falls to 19% in patients treated with post-operative injections of IFN- α 2b into the suture line at the time of excision and again a week later (44). As imiquimod induces both a constant and high level of IFN α at the site of application, we undertook a study to evaluate its role in treating keloids following surgical excision and to assess the rate of recurrence. In a small study, 12 patients displaying a total of 13 keloids located on the mid back (one) and earlobe (twelve) were enrolled. The keloids were surgically excised and primarily closed and patients were instructed to topically apply imiquimod 5% cream directly to the suture line once a night, initiated on the day of surgery, for a total of eight weeks. Patients were assessed at 4, 8, 16 and 24 week intervals post surgery for adverse reactions at the site of application as well as any side effects that may have arisen from systemic IFN toxicity. In total, 10 of the 12 patients completed the six month study. For these 10 patients, none of the 11 keloids showed signs of recurrence (Fig. 4). In addition, there were no systemic symptoms of IFN toxicity; however, six patients demonstrated hyperpigmentation that resolved spontaneously over 4–5 months and two patients showed mild eczematous erythema at the site of application, which resolved spontaneously with dose reduction (45). In addition to these findings, there is currently a double-blind, randomized, vehicle-controlled study being conducted of 30 patients with keloids that have not been excised but are being treated with imiquimod or vehicle cream, once daily for eight weeks. Although longer follow-up and active comparator studies are needed, early



Fig. 4. Keloid lesion located on the ear-lobe of a female patient, (a) before treatment with imiquimod 5% cream; (b) following treatment with imiquimod cream after surgical excision, there was sustained clearance of the keloidal lesion.

indications suggest that imiquimod may be a safe and effective treatment to minimize the recurrence of keloids following surgical excision.

CONCLUSION

The clinical benefits of imiquimod 5% cream are primarily attributed to stimulation of innate and cell-mediated immunity. Following its approval as an effective treatment option for external genital warts, it has also been successfully used in clinical practice for the treatment of a range of other cutaneous viral infections such as VIN, MC, reported here, and for skin tumors such as basal cell carcinoma and actinic keratosis (discussed in more detail in this supplement). It is essential that further studies accurately identify the most appropriate method and frequency of application of imiquimod for optimal clinical benefits for many cutaneous infections and malignancies.

REFERENCES

1. Miller RL, Gerster JF, Owens ML. Imiquimod applied topically: a novel immune response modifier and new class of drug. *Int J Immunopharmacol* 1999; 21: 1–14.
2. Hengge UR, Benninghoff B, Ruzicka T, Goos M. Topical immunomodulators: progress towards treating inflammation, infection and cancer. *Lancet Infect Dis* 2001; 1: 189–198.
3. Reiter M, Testerman T, Miller R. Cytokine induction in mice by the immunomodulator imiquimod. *J Leukocyte Biol* 1994; 13: 71–76.
4. Gibson S, Imberston L, Wagner T. Cellular requirements for cytokine production in response to the immunomodulators imiquimod and S27609. *J Interferon Cytokine Res* 1995; 58: 365–372.
5. Suzuki H, Wang B, Shivji GM. Imiquimod, a topical immune response modifier, induces migration of Langerhans' cells. *J Invest Dermatol* 2000; 114: 135–141.
6. Centres for Disease Control and Prevention (CDC). 2002 Guidelines for treatment of sexually transmitted diseases. Morbidity and Mortality Weekly Report (MMWR) 2002; 51(RR 6): 53–56.
7. Professional Advisory Board (PAB) of the Australia and New Zealand HPV Project, Guidelines for the Medical Management of genital HPV and/or genital warts in Australia and New Zealand. 2002; 1–22.
8. von Krogh G, Lacey CJ, Gross G, Barrasso R, Schneider A. European Course on HPV Associated Pathology (EHPV), European Branch of the International Union against Sexually Transmitted Infection and the European Office of the World Health Organization. European guidelines for the management of anogenital warts. *Int J STD and AIDS* 2001; 12: 40–47.
9. Hengge UR, Esser S, Schultewolter T, Behrendt C, Meyer T, Stockfleth E, Goos M. Self-administered topical 5% imiquimod for the treatment of common warts and molluscum contagiosum. *Br J Dermatol* 2000; 143: 1026–1031.
10. Muzio G, Massone C, Rebora A. Treatment of non-genital warts with topical imiquimod 5% cream. *Eur J Dermatol* 2002; 12: 347–349.
11. Beutner KR, Geisse JR, Helman D, Fox TL, Ginkel A, Owens ML. Therapeutic response of basal carcinoma to the immune response modifier imiquimod 5% cream. *J Am Acad Dermatol* 1999; 41: 1002–1007.
12. Smith KJ, Germain M, Skelton H. Squamous cell carcinoma in situ (Bowen's disease) in renal transplant patients treated with 5% imiquimod and 5% 5-fluorouracil therapy. *Dermatol Surg* 2001; 27: 561–564.
13. Schroeder TL, Sengelmann RD. Squamous cell carcinoma in situ of the penis successfully treated with imiquimod 5% cream. *J Am Acad Dermatol* 2002; 46: 545–548.
14. Koutsky L. Epidemiology of genital human papillomavirus infection. *Am J Med* 1997; 102: 3–8.
15. Scottish ISD (D) 5 Collaborative groups Trends in the sexually transmitted infections in the United Kingdom 1990–1999. Public health laboratory services (PHLS), London: 2000.
16. von Krogh G, Lacey CJ, Gross G, Barrasso R, Schneider A. European course on HPV-associated pathology: guidelines for primary care physicians for the diagnosis and management of anogenital warts. *Sex Trans Infect* 2000; 76: 162–168.
17. Brentjens MH, Yeung-Yue KA, Lee PC, Tying SK. Human papillomavirus: a review. *Dermatol Clin* 2002; 20: 315–331.
18. Aboulafia DM, Gibbons R. Penile cancer and human papillomavirus (HPV) in a human immunodeficiency virus (HIV)-infected patient. *Cancer Invest* 2001; 19: 266–272.
19. zur Hausen H. Papillomavirus and cancer: from basic studies to clinical application. *Nat Rev Cancer* 2002; 2: 342–350.
20. Edwards L, Ferenczy A, Eron L, Baker D, Owens ML, Fox TL. Self-administered topical 5% imiquimod cream for external anogenital warts. *Arch Dermatol* 1998; 134: 25–30.
21. Gollnick H, Barasso R, Jappe U, Ward K, Eul A, Carey-Yard M, Milde K. Safety and efficacy of imiquimod 5% cream in the treatment of penile genital warts in uncircumcised men when applied three times weekly or once per day. *Int J STD AIDS* 2001; 12: 22–28.
22. Buck HW, Fortier M, Knudsen J, Paavonen J. Imiquimod 5% cream in the treatment of anogenital warts in female patients. *Int J Gynaecol and Obstet* 2002; 77: 231–238.
23. Garland SM, Sellors JW, Wikstrom A, Peterson CS, Aranda C, Aractingi S, et al. Imiquimod 5% cream is a safe and effective self-applied treatment for anogenital warts: results of an open-label multicentre Phase IIIB trial. *Int J STD AIDS* 2001; 12: 722–7229.
24. Beutner KR, Spruance SL, Hougham AJ, Fox TL, Owens ML, Douglas JM, Jr. Treatment of genital warts with an immune-response modifier (imiquimod). *J Am Acad Dermatol* 1998; 38: 230–239.
25. O'Mahony C, Law C, Gollnick HPM, Marini M. New patient-applied therapy for anogenital warts is rated favourably by patients. *Int J STD AIDS* 2001; 12: 565–570.
26. Barba AR, Kapoor S, Berman B. An open label safety study of topical imiquimod 5% cream in the treatment of molluscum contagiosum in children. *Dermatol Online J* 2001; 7: 20.
27. Williams LR, Webster G. Warts and molluscum contagiosum. *Clin Dermatol* 1991; 9: 87–93.
28. Brown TJ, Yen-Moore Y, Tying SK. An overview of sexually transmitted diseases. Part II. *J Am Acad of Dermatol* 1999; 41: 661–677.
29. Buller RM, Palumbo GJ. Poxvirus pathogenesis. *Microbiol Rev* 1991; 55: 80–122.
30. Becker TM, Blount JH, Douglas J, Judson FN. Trends in molluscum contagiosum in the United States, 1966–1983. *Sex Trans Dis* 1986; 13: 88–92.

31. Schwartz JJ, Myskowski PL. Molluscum contagiosum in patients with human immunodeficiency virus infection. *J Am Acad Dermatol* 1992; 27: 583–588.
32. Hourihane J, Hodges E, Smith J, Keefe M, Jones A, Connett G. Interferon alpha treatment of molluscum contagiosum in immunodeficiency. *Arch Dis Children* 1999; 80: 77–79.
33. Liota E, Smith KJ, Buckley R, Menon P, Skelton H. Imiquimod therapy for molluscum contagiosum. *J Cut Med Surg* 2000; 4: 76–82.
34. Buckley R, Smith K. Topical imiquimod therapy for chronic giant molluscum contagiosum in a patient with advanced human immunodeficiency virus I disease. *Archives of Dermatology* 1999; 135: 1167–1169.
35. Wilkinson EJ, Kneale B, Lynch PJ. Report of the ISSVD terminology Committee. *J Reprod Med* 1986; 31: 975–986.
36. Jebakumar S, Wooley PD, Bhattacharyya MN. Vulval intraepithelial neoplasia. *Int J STD AIDS* 1996; 7: 10–13.
37. Kurwa HA, Barlow RJ, Neill S. Single-episode photodynamic therapy and vulval intraepithelial neoplasia type II resistant to conventional therapy. *Br J Dermatol* 2000; 143: 1040–1042.
38. Ochiai T, Honda A, Morishima T, Sata T, Sakamoto H, Satoh K. Human papillomavirus types 16 and 39 in a vulval carcinoma occurring in women with Hailey-Hailey disease. *Br J Dermatol* 1998; 140: 509–513.
39. Davis G, Wentworth J, Richards J. Self-administered topical imiquimod treatment of vulvar intraepithelial neoplasia. A report of four cases. *J Reprod Med* 2000; 45: 619–623.
40. Jayne CJ, Kaufman RH. Treatment of vulvar intraepithelial neoplasia 2/3 with imiquimod. *J Reprod Med* 2002; 47: 395–398.
41. Todd RW, Etherington IJ, Luesley DM. The effects of 5% imiquimod cream on high-grade vulval intraepithelial neoplasia. *Gynecol Oncol* 2002; 85: 67–70.
42. Berman B, Flores F. The treatment of hypertrophic scar and keloids. *Eur J Dermatol* 1998; 8: 591–595.
43. Berman B, Bielek HC. Adjunct therapies to surgical management of keloids. *Dermatol Surg* 1996; 22: 126–130.
44. Berman B, Flores F. Recurrence rates of excised keloids treated with postoperative triamcinolone acetonide injections or interferon alfa-2b injections. *J Am Acad Dermatol* 1997; 37: 755–757.
45. Berman B, Kaufman J. Pilot study of the effect of postoperative imiquimod 5% cream on the recurrence rate of excised keloids. *J Am Acad Dermatol* 2002; 47 (Suppl 4): S209–211.

QUESTIONS AND ANSWERS

Question: *Erythema is typically observed at the point of regression of molluscum contagiosum, isn't this a type of immune response that is typically observed during imiquimod treatment?*

Professor Hengge: I agree that spontaneous regression of this cutaneous lesion is accompanied by erythema.

In addition, I would like to add that the side effects observed during the treatment of molluscum contagiosum with imiquimod include erythema and tend to be greater than those observed for cutaneous warts.

Question: *You mention that HIV-positive patients have more HPV-associated lesions, does that imply that disease management and treatment, in terms of biopsies and follow-up, should be different with these patients compared to non HIV-infected patients?*

Dr Johnson: The treatment of this group of patients has changed considerably as our understanding of HPV infections is that they frequently become highly malignant in HIV-infected patients. This has necessitated early biopsies and both constant and regular follow-ups, which is important in establishing whether the HPV infection is of a low or high oncogenic subtype. This is particularly important for the management of HPV in the genital area.

Question: *What would be the first line of treatment for multiple warts in children and is there any evidence for the treatment of resistant and recurrent beard warts in males with imiquimod?*

Professor Hengge: When treating children, the best line of therapy is the one with minimal pain and trauma. I suggest imiquimod, because unlike conventional treatments it is self-administered and is not associated with unnecessary pain, although this would depend on the consent of the parents and the extent of the disease. With reference to beard warts, I have little research experience with this cutaneous pathology. It appears that conventional methods of shaving these lesions causes the generation of micro trauma which will probably result in the spread of the virus.

Question: *Warts located within the urethra and mouth mucosa have proved difficult to treat, could you suggest the best method of treating lesions at these sites?*

Professor Hengge: Lesions located in these areas are difficult to treat with a topically applied cream, as the cream is likely to wash off. Therefore a combination of therapies may be required. Physical removal by the most appropriate means, depending in the location, can be coupled with topical application of imiquimod to create immunity against viral infection and prevent recurrence.