Journal of Cosmetics, Dermatological Sciences and Applications, 2014, 4, 259-267
Published Online September 2014 in SciRes. http://www.scirp.org/journal/jcdsa
http://dx.doi.org/10.4236/jcdsa.2014.44035

Scientific Research

Genital Warts in Infants and Children

—Re-Evaluation of Podophylline 15% as an Effective Topical Therapy

Khalifa E. Sharquie[1,2*], Adil A. Noaimi[1,2], Mohammed N. Almallah[3]

[1]Department of Dermatology, College of Medicine, University of Baghdad, Baghdad, Iraq
[2]Iraqi and Arab Board for Dermatology and Venereology, Baghdad Teaching Hospital, Medical City, Baghdad, Iraq
[3]Department of Dermatology and Venereology, Baghdad Teaching Hospital, Baghdad, Iraq
Email: *ksharquie@ymail.com, adilnoaimi@yahoo.com, vetmed83@hotmail.com

Received 10 January 2014; revised 16 February 2014; accepted 28 March 2014

Abstract

Background: Condylomataacuminata is an infection caused by Human Papilloma Virus, rarely reported in infants and children. Podophylline as a treatment for this condition has been used cautiously in this age group. Objective: To report the cases of anogenital warts including condy lomataacuminata in infants and children and to evaluate the effectiveness and side effects of 15% podophyllin in treatment of genital warts. Patient and Methods: Thirty infants and young children were seen in Department of Dermatology and Venereology—Baghdad Teaching Hospital in this case descriptive and therapeutic trial, in the period from January 2011 to August 2012. Their ages ranged from 8 - 72 (30.43 ± 15.85) months, 20 females and 10 males with a female:male ratio of 2:1. The duration of the disease ranged from 1 - 12 (5.26 ± 4.00) months. All demographics data were recorded in this study. History and examination were carried out to all patients. Family members including mothers were assessed about the presence of any type of viral warts in other location of body. Podophyllin (15%) in tincture benzoin was applied once weekly to all viral warts and the parents advised to wash out after 2 hours of application. The number of applications was repeated until full recovery. Follow-up after recovery was carried out for 6 months to watch for any relapse and to record local or systemic side effects. Results: The clinical pictures were mostly acondylomata acuminata in a form of cauliflower like warts in 20 (73.33%) patients, while in 10 (26.77%) patients there were ordinary verruca vulgaris like warts. The location of warts was perianal in 23 (76.66%) patients, genital only in 2 (6.66%) patients, and mixed in 5 (16.66%) patients. Topical applications of podophyllin 15% gave a full recovery in 27 (90%) patients, while in 3 (10%) patients there was partial response. The number of applications ranged from 1 - 4 (2.7 ± 1.42) applications. Follow up for 6 months after recovery showed relapse in only one patient, and no side effects were reported in any patients. Conclusion: There is upsurge of cases of anogenital warts among infants and children. Podophyllin (15%) in tincture benzoin is an effective therapy and no local or systemic side effects were recorded in any case.

*Corresponding author.

How to cite this paper: Sharquie, K.E., Noaimi, A.A. and Almallah, M.N. (2014) Genital Warts in Infants and Children. *Journal of Cosmetics, Dermatological Sciences and Applications*, **4**, 259-267. http://dx.doi.org/10.4236/jcdsa.2014.44035

Keywords

Genital Warts in Infants and Children, Podophylline, Topical Therapy

1. Introduction

Anogenital warts (AGWs) are caused by HPV. It is an old disease but the incidence of AGWs in children has increased dramatically all over the world since 1990 [1]-[3]. This increase in incidence of AGWs in children is thought to parallel the increase in incidence of AGWs in the adult population [3].

There are over 200 genotypes of Human Papilloma Viruses (HPV), 30 - 40 of which specifically affect the genital tract [4]. Genital types of HPV are divided into high or low risk according to the association with genital tract cancers.

Low-risk HPV types include Types 6, 11, 42-44, and usually cause benign anogenital warts, while high-risk HPV types include Types 16, 18, 31, 33-35, 39, 45, 51, 52, 56, 58, 59, 66, 68 and 70, and cause mostly anogenital cancers, primarily cervical cancer. Low risk HPV 6 and 11 genotypes are the primary causes of condy lomataacuminata, otherwise known as external genital warts [4].

HPV 16, 18, 31, 45 account for more than 90% of cervical carcinomas [5]. Of these types, HPV-16 is the most often found, accounting for about half of the cervical cancer cases in the United States and Europe [5].

Regarding mode of transmission, sexual abuse has been regarded as a possible cause of childhood genital warts associated with mucosal HPV types. The forms of sexual abuse are oral-genital contact, genital-genital contact, genital-anal contact, fondling and digital penetration of the vagina or anus [6] [7].

Reported frequency of sexual abuse varies considerably depending on the series studied [6] [7]. If sexual abuse is suspected in children, examination should always be performed including behavioral indications of abuse, medical examination to identify the physical indications of abuse, microbiological assessment of other STDs, and age-appropriate interviews of the child and caretakers by skilled personnel [8]-[12].

Most data suggest that AGWs among preadolescent children result from non-sexual transmission acquired either perinatally or postnatally [7]. Vertical transmission of HPVs has been reported to be responsible for at least 20% of AGWs in children [3] and occurs by contamination of the newborn descending through the birth canal, or viralascent through the membranes. In utreo, hematogenus transplacental transmission has been debated but has been supported by the fact that HPV16 DNA was detected in cord blood specimens of seven neonates born to mothers with HPV16 DNA in the peripheral blood mononuclear cells [13].

Horizontal transmission by caregivers in the first days of life is another mode of HPVs contamination in newborns. The concordance of HPVs types detected in the newborns and their mothers, reported to be only 57%, further supports this hypothesis [14], as well as the absence of correlation between HPVs on neonatal fore-skin and maternal abnormal Pap smear [15]. The frequency of transmission through inoculation varies with the child population studied [16].

Autoinoculation of HPVs, e.g. by scratching from one site of the body to another, is also possible [6] [7]. HPV type 2 is frequently detected in lesions of the oral mucosa or lips, and it might be acquired by chewing of common warts present on hands [6] [7].

It has also been shown that infants and children can acquire HPV infections by exposure to contaminated fomites such as underwear [17].

Disagreement exists regarding the incubation period of HPVs. Studies have indicated that HPVs can remain dormant for up to 5 years without causing lesions if transmitted vertically. However, other professionals have concluded that 2 years is the longest period that the HPVs lays dormant following vertical transmission [18].

HPV typing alone cannot determine the mode of transmission, because the virus does not display 100% tropism [19].

AGWs in children are associated with both mucosotropic types HPV6 and 11 and cutaneotropic types 1 and 2. [20].

Other HPV types like 3, 27, and 57 can be detected in both cutaneous and mucosal lesions [21].

In Iraq, the AGWs, has been reported as not uncommon problem but its frequency is increasing over the last 10 years.

Seventy-five percent of AGWs resolves spontaneously within months to a few years in children who have healthy immune systems [22]. Those persisting for more than 2 years are less likely to resolve spontaneously or with treatment [23]. But still therapy is strongly recommended in many cases as the disease bothers the parents.

There are no FDA approved treatments for AGWs in children 12 years of age and younger. Treatments can be divided into nonsurgical and surgical. No approach has been shown to be universally successful, and recurrence is common after any form of treatment. Some children may require combination of therapies. Because recurrence is common. Once a child has had AGWs, the appearance of new lesions after spontaneous resolution or treatment does not necessarily indicate a new exposure [24]. One can choose between cryotherapy, electrodessication, podophyllotoxin, or imiquimod [25].

Imiquimod has been effective even for extensive pediatric AGWs, without causing any significant side effects [26]. Podophyllotoxin has also been reported to be effective and safe in children with genital warts [26].

Podophyllin (15%) has been reported in Iraq to be a safe alternative without any side effect or complications [27].

Therefore the aim of present study was to report the upsurge of cases of AGWs among infants and children, and to confirm that podophyllin (15%) could be a safe weapon against HPVs infections of anogenital area.

2. Patients and Methods

This is a case, descriptive, therapeutic trial that was conducted in Department of Dermatology and Venereology—Baghdad Teaching Hospital in the period from January 2011 to August 2012.

A total of 30 infants and children with AGWs were enrolled in this study.

Ages, gender, duration of the disease, clinical type of warts, locations, symptoms, general health, and associated disease were recorded for all children.

AGWs or other types of warts, marital status of the parents, parent's employment status, educational level of the parents were extensively explored.

All patients were examined for any signs of sexual abuse (medical examination, inspection of the genitalia and anus), and the history of the child being placed with relatives and a behavioral history of the child, particularly any unusual behavior, was obtained.

Formal consent was taken from patient's parents following full explanation of the nature of the disease and the procedure of the treatment, and of any possible complications and the need for pre and post treatment photographs. Also, ethical approval was obtained from the Scientific Council of Dermatology and Venereology-Arab Board for Medical Specializations. Fifteen percent podophyllin was prepared by dissolving 15 grams of podophyllum resin (podpphyllin gepulvert, auspodophylumhexandrum, B.P.1973. paul Muggenburg, 2000 HAMBURG1. Ernste Vergiftungsgefahrbeim Verschlucken. Reizt Haut, Augen und Atemwege) in 100 ml benzoinco (COMPOUNlD BENZOIN TINCTURE BP, Friar's Balsam, EVANS, Evans Medical Limited Laughurst Horsham England).

Podophyllin (15%) in benzoin tincture was used in all patients once a week, to applied by a cotton applicator and left on the affected area to dry for a period of time not exceeding 2 hours and after 2 hours it should be washed out. The amount of podophyllin solution did not exceed 1ml/session. The patients were seen once weekly and photographs were taken at each visit.

Follow up was carried out after recovery at month 6 to record any relapse or side effects.

3. Results

Thirty patients with AGWs were included in the study, age ranging from 8 - 72 months with a mean ±SD of 30.43 ± 15.85 months, 20 females and 10 males with a female: male ratio of 2:1 (**Table 1**). The duration of the disease ranged from 1 - 12 months with a mean ± SD of 5.26 ± 4.00 months (**Table 2**). Acuminate lesions (**Figure 1**) were seen in 20 cases whereas in 10 patients ordinary verruca vulgaris like were noted. The location of the lesions was primarily perianal (23/30); 1 boy had lesions on the scrotum; 1 girl had lesions on the vulva; 3 girls had lesions simultaneously on the vulva and perianal area; and 2 boys had simultaneously lesions on the scrotum, penis, and perianal (**Table 3**).

Sexual abuse was not confirmed in any case, both on history and clinical examination. Family history of genital warts was denied among all family members apart from one girl and one boy that their mothers had genital warts. In 6 children, a history of common warts could be elicited by the caregivers, and in 1 girl, common warts

Table 1. Age of patients in months.

Age	No. of patients	Percentage
1st 6 months	0	0
7 - 12	6	20
13 - 18	4	13.33
19 - 24	6	20
25 - 36	6	20
37 - 72	8	26.67
Total	30	100

Table 2. Duration of disease in months.

Duration	No. of patients	Percentage
0 - 3	14	46.66
4 - 6	9	30
7 - 9	2	6.67
10 - 12	3	10
13 - 16	2	6.67
Total	30	100

Table 3. Location of the warts.

Location	No. of patients	Percentage
Perianal	23	76.67
Genital	2	6.67
Both	5	16.66
Total	30	100

Figure 1. Condylomataacuminate in 1-year-old female infant of ano-genital area.

affecting her hand were detected. No urethral or vaginal discharge was noticed in any patient.

Podophyllin 15% in tincture benzoin was used once weekly and the number of applications ranged from 1 - 4 applications with a mean ± SD of 2.7 ± 1.42 applications (**Table 4**). The response to therapy was obvious after one week and full recovery was achieved after 4 weeks, apart from 3 cases with partial response (**Figure 2**, **Figure 3**). The cure rate was 90%.

Acuminate lesions had more rapid response to therapy, necessitated less number of applications, and full recovery was seen in all cases, while ordinary viral warts had slow response to therapy, need more applications, and full recovery was seen in 7 out of 10 cases.

In all patients, a slight irritation and swelling of the lesion was noticed after the first application, which did not occur after subsequent applications. No child had any signs of toxicity during the course of therapy and follow up period.

No recurrences were noted apart from one case at 6-month follow-up period.

Table 4. Number of treatment sessions.

No. of sessions	No. of patients	Percentage
1	3	10
2	6	20
3	13	43.33
4	8	26.67
Total	30	100

Figure 2. (a) One and a half-year-old female before podophyllin treatment; (b) After 3 sessions of podophyllin treatment.

Figure 3. (a) One and a half-year-old male before podophyllin treatment; (b) After 3 sessions of podophyllin treatment.

4. Discussion

The incidence of anogenital warts in infants and children has increased dramatically all over the world since 1990 [1]-[3]. This is thought to parallel the increase in incidence of AGWs in the adult population [3].

These reasons might explain the increase in the frequency of AGWs in Iraqi infants and children or there might be other contributory.

In children with AGWs, reports of sexual abuse have varied from 0% to 80% [19] [28]. In our study, we did not document any case of sexual abuse by history or physical examination.

However, evaluation is complex, because most children who have been sexually abused will not show carriage of the virus, nor will have evidence of physical trauma [29] [30].

The presence of warts or HPVs DNA alone without supporting social and clinical information is not diagnostic of sexual abuse. An epidemiological study of 124 children with clinical HPVs infection concluded that many children over 2 years of age acquired HPVs from non-sexual contact. The positive predictive value of the presence of AGWs for sexual abuse was 37% for children aged 2 - 12 years, and increased with age (70% for children over 8 years of age) [22]. But still sexual abuse needs to be considered in every case of AGWs, particularly in those over 2 - 3 years of age.

Vertical transmission of HPVs has been reported, HPVs transmission can occur inutero through semen, ascending infection from the mother's genital tract, or transplacentally [3]. Vertical transmission of the HPVs does not mean that warts must be present at birth or shortly after birth. HPVs is a latent virus and can reside in the skin and mucous membranes without causing warts. The warts may not appear until months or even years after birth [18].

Horizontal transmission by caregivers and autoinoculation of HPVs, e.g. by scratching from one site of the body to another, is another possibility of infection [3].

It has also been shown that infants and children can acquire HPVs infections by contaminated fomites such as underwear [17].

HPVs typing does not offer any help to determine whether genital warts in children are sexually transmitted or not [19].

Most of AGWs disappear spontaneously within months to a few years in children who have good immune system [23]. Those persisting for more than 2 years are less likely to resolve spontaneously or with treatment [24].

The decision to treat or not AGWs in children lies on the physician. However, the overwhelming parent's anxiety and the problems that AGWs may cause, such as bleeding or infection, usually lead to a form of treatment.

Many treatments have been used in infants and children, one can choose cryotherapy, electrodessication, podophyllotoxin, or imiquimod [26].

After the discovery of podophyllum resin in 1835 by John King [31], it was put to numerous innovative therapeutic uses over the next century ranging from a laxative to treatment of cancers. However, in the 1940s, it has been used topically for treatment of various skin lesions, especially for venereal warts, and also has antineoplastic effect, as it has been shown in a very recent study

Podophyllin resin is an antimitotic and caustic agent with antiviral activity [32] [33]. The possible mechanism of action is that it arrests cellular mitosis in metaphase, accomplished by reverse binding to tubuline which is the protein subunit of the spindle microtubules at a site that is the same of overlaps with the colchicines binding site thereby preventing polymerization of tubuline into microtubules. So it will disturbs the cellular cytoskeleton; it blocks oxidation enzymes in tricaboxylic acid cycle, and interferes with nutrition of cells; it inhibits axonal transport, protein, RNA, and DNA synthesis and also inhibits mitochondrial activity and reduction of cytochrome oxidase activity [34] [35].

Side effects include local erythema, tenderness, burning, erosions, and edema [36]. If podophyllin is used in an extensive area or injected or ingested, central nervous system toxicity and respiratory depression may result [35].

Experimental studies in animals have clearly demonstrated that podophyllin is embryotoxic and has a strong growth retarding effect on pregnancy [36] [37]. Fetal anomalies suspected to have been induced by podophyllin include preauricular skin tags, limb malformations, simian crease, septal heart defects and polyneuritis [38] [39]. Intrauterine death has also followed the application of podophyllin on vulvarwarts [40].

Bargman [41] has reviewed the whole subject of systemic toxicity to podophyllin including its reported tera-

togenicity. He noted that in almost all cases there were factors (such as alcohol or drug abuse, recent surgical procedures, general anaesthesia) which may have potentiated the toxicity of podophyllin. Since nearly all reported cases have been blacks, he also considered the possibility of an unsuspected racial susceptibility. He concluded that the dangers of podophyllin toxicity have been overplayed, and that it is an extremely safe drug when used properly.

Accordingly, podophyllin has been widely used in Iraq in the treatment of genital warts among infants and children, and proved to be a safe drug when applied cautiously and wisely. Its safety has been well documented by an Iraqi study in 2006 among infants and children with AGWs, where in 18 patients with conylomata acuminate were treated with podophyllin 15% during the period from January 1996 to January 2000, effectively with a cure rate 100%, and no side effects were reported during therapy and follow up [28].

In this study, a greater number of patients were included for a shorter study duration indicating a possible increase in incidence.

We had also proved that podophyllin application is an effective therapy for genital warts in infants and children and no case showed any symptoms and signs of toxicity. The cure rate was 90% and was more effective in acuminate lesions.

Sundharam in 2011 put precautions based on the recommendations of Fisher [42], Miller [43] and others [38]-[40], so the following precautions are considered obligatory in this table:

Precautions No.	Precautions
1	Podophyllin should be applied only by the physician.
2	The drug should be applied only to small areas of intact skin. Biopsies if taken, should be allowed to heal completely before the application of podophyllin.
3	Alcohol should be avoided before and for several hours after the application. General anaesthesia and central nervous system depressant drugs should be avoided.
4	The drug should be avoided in the oral cavity.
5	It should not be used in pregnant women.
6	Initially, a test application should be left on for a period of one hour. If there is no irritation, subsequent applications should be allowed to remain for 4 - 6 hours.
7	The volume of liquid applied should be kept to the minimum (von Krogh [44] recommends a volume not exceeding 0.4 - 0.5 ml for *P. emodi* based podophyllin and 0.9 -1.2 nil for *P. peltatum* based podophyllin).
8	The drug should be stored in narrow-mouthed bottles, otherwise undue evaporation might lead to an increased concentration of podophyllin. Preparations containing a sludge or precipitate and old, dried, gritty preparations should be discarded.

But our practice doesn't agree with many of these precautions, and we recommend the following guidelines of therapy:

1) The drug should be applied by physician or by very careful parents.

2) Podophyllin should be used in low concentrations not above 15% and kept for not more than 2 hours, possibly half an hour is enough, and then washed away.

3) The drug used once a week and could be repeated according to the response.

4) Infants and children should be kept under clinical supervision to watch any side effect, and laboratory test like liver function test, renal function test, complete blood picture might be needed.

These recommendations agrees with bargman who concluded that the danger of podophyllin toxicity have been overplayed and could be used safely when used in correct way.

After the use of podophyllotoxin, which is much safer and less irritating than podophyllin, podophyllin has been largely replaced. However, it is a useful alternative and its use should not be completely abandoned.

5. Conclusion

Podophyllin (15%) in tincture benzoin is an effective therapy for AGWs in infants and children and no adverse effects were noted in any case.

References

[1] Cohen, B.A. (1997) Warts and Children: Can They Be Separated? *Contemporary Pediatrics*, **14**, 128-149.

[2] Siegfried, E., Conley, R., Cook, J., Leonardi, C. and Monteleone, J. (1998) Human Papillomavirus Screening in Pediatric Victims of Sexual Abuse. *Pediatrics*, **101**, 43-47. http://dx.doi.org/10.1542/peds.101.1.43

[3] Syrjänen, S. and Puranen, M. (2000) HPV Infections in Children: The Potential Role of Maternal Transmission. *Critical Reviews in Oral Biology Medicine*, **11**, 259-274. http://dx.doi.org/10.1177/10454411000110020801

[4] Garland, S. (2002) Human Papillomavirus Update with a Particular Focus on Cervical Disease. *Pathology*, **34**, 213-224. http://dx.doi.org/10.1080/00313020212469

[5] Muñoz, N., Bosch, F.X., de Sanjosé, S., Herrero, R., Castellsagué, X., Shah, K.V., *et al.* (2003) Epidemiologic Classification of Human Papilloma Virus Types Associated with Cervical Cancer. *New England Journal of Medicine*, **348**, 518-527.

[6] Syrjänen, K. and Syrjänen, S. (2000) Papillomavirus Infections in Human Disease. Wiley & Sons, New York, 1-615.

[7] Syrjänen, S. (2003) HPV Infections in Children. Invited Review. *Papillomavirus Report*, **14**, 93-110. http://dx.doi.org/10.1179/095741903235001425

[8] Hornor, G. (2004) Ano-Genital Warts in Children: Sexual Abuse or Not? *Journal of Pediatric Health Care*, **18**, 165-170. http://dx.doi.org/10.1016/j.pedhc.2003.01.001

[9] Gutman, L.T., Claire, K., Herman-Giddens, M.E., Johnston, W.W. and Phelps, W.C. (1992) Evaluation of Sexually Abused and Non-Abused Young Girls for Intravaginal Human Papillomavirus Infection. *American Journal of Diseases of Children*, **146**, 694-699.

[10] Gutman, L.T., Claire, K.K., Everett, V.D., Ingram, D.L., Soper, J. and Johnston, W.W. (1994) Cervical-Vaginal and Intra Anal Human Papillomavirus Infection of Young Girls with External Genital Warts. *The Journal of Infectious Diseases*, **170**, 339-344. http://dx.doi.org/10.1093/infdis/170.2.339

[11] Gutman, L.T. (1990) Sexual Abuse and Human Papillomavirus Infection. *Journal of Pediatrics*, **116**, 495-496. http://dx.doi.org/10.1016/S0022-3476(05)82863-X

[12] Muram, D. (1989) Anal and Perianal Abnormalities in Prepubertal Victims of Sexual Abuse. *American Journal of Obstetrics & Gynecology*, **161**, 278-281. http://dx.doi.org/10.1016/0002-9378(89)90498-5

[13] Tseng, C.J., Lin, C.Y., Wang, R.L., Chen, L.J., Chang, Y.L., Hsieh, T.T. and Pao, C.C. (1992) Possible Transplacental Transmission of Human Papillomaviruses. *American Journal of Obstetrics & Gynecology*, **166**, 35-40. http://dx.doi.org/10.1016/0002-9378(92)91825-U

[14] Alberico, S., Pinzano, R., Comar, M., Toffoletti, F., Maso, G., Ricci, G. and Guaschino, S. (1996) Maternal-Fetal Transmission of Human Papillomavirus. *Minerva Ginecologica*, **48**, 199-204.

[15] Roman, A. and Fife, K. (1986) Human Papillomavirus DNA Associated with Foreskins of Normal Newborns. *Journal of Infectious Diseases*, **153**, 855-861. http://dx.doi.org/10.1093/infdis/153.5.855

[16] Handley, J., Hanks, E., Armstrong, K., Bingham, A., Dinsmore, W., Swann, A., Evans, M.F., McGee, J.O.D. and O'Learj, J. (1997) Common Association of HPV 2 with Anogenital Warts in Prepubertal Children. *Pediatric Dermatology*, **14**, 339-343. http://dx.doi.org/10.1111/j.1525-1470.1997.tb00976.x

[17] Bergeron, C., Ferenczy, A. and Richart, R. (1990) Underwear: Contamination by Human Papillomaviruses. *American Journal of Obstetrics & Gynecology*, **162**, 25-29. http://dx.doi.org/10.1016/0002-9378(90)90813-M

[18] Frazier, L. (1998) Genital Warts in Children. *The American Professional Society of the Abuse of Children Advisor*, **11**, 9-12.

[19] Armstrong, D.K. and Handley, J.M. (1997) Anogenital Warts in Prepubertal Children: Pathogenesis, HPV Typing and Management. *International Journal of STD & AIDS*, **8**, 78-81. http://dx.doi.org/10.1258/0956462971919598

[20] Joyasinghe, Y. and Garland, S.M. (2006) Genital Warts in Children: What Do They Mean? *Archives of Disease in Childhood*, **91**, 696-700. http://dx.doi.org/10.1136/adc.2005.092080

[21] Singlair, K., Woods, C., Kirse, D. and Sinal, S.H. (2005) Anogenital and Respiratory Tract Human-Papillomavirus Infections among Children: Age Gender and Potential Transmission through Sexual Abuse. *Pediatrics*, **116**, 815-825. http://dx.doi.org/10.1542/peds.2005-0652

[22] Culton, D.A., Morrell, D.S. and Burkhart, C.N. (2009) The Management of Condyloma Acuminata in the Pediatric Population. *Pediatric Annals*, **38**, 368-372. http://dx.doi.org/10.3928/00904481-20090622-05

[23] Allen, A.L. and Siegfried, E.C. (1998) The Natural History of Condyloma in Children. *Journal of the American Academy of Dermatology*, **39**, 951-955. http://dx.doi.org/10.1016/S0190-9622(98)70268-3

[24] Sinclair, K.A., Woods, C.R. and Sinal, S.H. (2011) Venereal Warts in Children. *Pediatrics in Review*, **32**, 115-121.

http://dx.doi.org/10.1542/pir.32-3-115

[25] Stefanaki, C., Barkas, G., Valari, M., Bethimoutis, G., Nicolaidou, E., Vosynioti, V., Kontochristopoulos, G., Papadogeorgaki, H., Verra, P. and Katsarou, A. (2012) Condylomata Acuminata in Children. *The Pediatric Infectious Disease Journal*, **31**, 422-424.

[26] Moresi, J.M., Herbert, C.R. and Cohen, B.A. (2001) Treatment of Anogenial Warts in Children with Topical 0.05% Podophilox Gel and Imiquimod Cream. *Pediatric Dermatology*, **18**, 448-450. http://dx.doi.org/10.1046/j.1525-1470.2001.1980a.x

[27] Sharquie, K.E., Al-Waiz, M.M. and Al-Nuaimy, A.A. (2005) Condylomata Acuminata in Infants and Young Children. Topical Podophyllin an Effective Therapy. *Saudi Medical Journal*, **26**, 502-503.

[28] Moscicki, A. (1998) Genital Infections with Human Papillomavirus (HPV). *Pediatric Infectious Disease Journal*, **17**, 651-652. http://dx.doi.org/10.1097/00006454-199807000-00014

[29] Atabaki, S. and Paradise, J. (1999) The Medical Evaluation of the Sexually Abused Child: Lessons Learned from a Decade of Research. *Pediatrics*, **104**, 178-186.

[30] Berenson, A.B., Chacko, M.R., Wiemann, C.M., Mishaw, C.O., Friedrich, W.N. and Grady, J.J. (2000) A Case-Control Study of Anatomic Changes Resulting from Sexual Abuse. *American Journal of Obstetrics & Gynecology*, **182**, 820-834. http://dx.doi.org/10.1016/S0002-9378(00)70331-0

[31] Zakon, S. (1952) Discovery of Podophyllum Resin. *JAMA Dermatology*, **65**, 620-622. http://dx.doi.org/10.1001/archderm.1952.01530240112022

[32] Sharquie, K.E. and Noaimi, A.A. (2012) Basal Cell Carcinoma: Topical Therapy versus Surgical Treatment. *Journal of the Saudi Society of Dermatology and Dermatologic Surgery*, **16**, 41-51. http://dx.doi.org/10.1016/j.jssdds.2012.06.002

[33] United States Pharmacopeia Committees (2004) Podophyllin. In: *Drug Information for the Health Care Professional*, 24th Edition, Rev. US Convention Inc., Thomason Micromedex, 2341-2348.

[34] Oslen, D.G. and Dart, R.C. (2004) Skin and Mucous Membrane Agents. In: *Medical Toxicology*, 3rd Edition, Vol. 165, Walters Kluwer Company, Philadilphia, 1003-1004.

[35] Moore, M.M. and Strober, B.E. (2008) Topical and Intralesional Cytotoxic Agent. In: Wolff, K., Goldsmith, L.A., Katz, S.I., Gilchrest, B.A., Paller, A.S. and Leffell, D.J., Eds., *Fitzpatrick's Dermatology in General Medicine*, 7th Edition, McGraw-Hill-Company, New York, 220, 224.

[36] Thiersch, J.B. (1963) Effect of Podophyllin and Podophyllotoxin on the Rat Litter in Utero. *Proc. Soc. Exp. Biol. Med.*, **113**, 124.

[37] Joneja, M.G. and Leliever, W.C. (1974) Effects of Vinblastine and Podophyllin on DBA Mouse Fetuses. *Toxicology and Applied Pharmacology*, **27**, 408-414. http://dx.doi.org/10.1016/0041-008X(74)90211-7

[38] Cullis, J.E. (1962) Congenital Deformities and Herbal "Slimming Tablets". *Lancet*, **280**, 511-512. http://dx.doi.org/10.1016/S0140-6736(62)90387-2

[39] Karol, M., Conner, C., Watanabe, A.S. and Murphrey, K. (1980) Podophyllum: Suspected Teratogenicity from Topical Application. *Clinical Toxicology*, **16**, 283-286. http://dx.doi.org/10.3109/15563658008989950

[40] Chamberlein, M.J., Reynolds, A.L. and Yeoman, M.B. (1972) Toxic Effect of Podophyllum Application in Pregnancy. *British Medical Journal*, **3**, 391-392. http://dx.doi.org/10.1136/bmj.3.5823.391

[41] Bargman, H. (1988) Is Podophyllin a Safe Drug to Use and Can It Be Used in Pregnancy? *JAMA Dermatology*, **124**, 1718-1729. http://dx.doi.org/10.1001/archderm.1988.01670110074020

[42] Fisher, A. (1981) Sever Systemic and Local Reaction to Topical Podophyllin Resin. *Cutis*, **28**, 233-236.

[43] Miller, R.A. (1985) Podophyllin. *International Journal of Dermatology*, **24**, 491-498. http://dx.doi.org/10.1111/j.1365-4362.1985.tb05535.x

[44] Von Krogh, G. (1983) Condylomata Acuminate 1983 an Updated Review. *Semin Dermatol*, **2**, 109-129.

Scientific Research Publishing (SCIRP) is one of the largest Open Access journal publishers. It is currently publishing more than 200 open access, online, peer-reviewed journals covering a wide range of academic disciplines. SCIRP serves the worldwide academic communities and contributes to the progress and application of science with its publication.

Other selected journals from SCIRP are listed as below. Submit your manuscript to us via either submit@scirp.org or Online Submission Portal.