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#### 4 **Abstract**

5 Human Papilloma Virus (HPV) is a miniature DNA (deoxy ribonucleic acid) virus of the  
6 family Papovaviridae which primarily access the squamous cells. The categories of HPV  
7 exceed a 100(11). Histological transformation and infiltrative malignant neoplasm in the vulva  
8 and anogenital area such as Condyloma, Verrucous lesions, tiny Papules or Plaque like  
9 modification and Vulvar Intraepithelial Neoplasia (VIN) are elucidated with various HPV  
10 classes. Condylomata acuminatum is a classic, well differentiated lesion which exemplifies  
11 acanthosis, hyperkeratosis, parakeratosis, dyskeratosis with koilocytosis(2). Bowenoid  
12 papulosis comprises of multiple, red - brown genito-anal papules with epidermal adaptations  
13 identical to the Bowen's disease on histology. Malignant conversion has been scripted in what  
14 is essentially a benign disease(10). Female companions of males contaminated with the virus  
15 display an enhanced probability of cervical cancer(4). Histopathology and Serological  
16 investigations may be required as the clinical elucidation may be inadequate. Classification of  
17 the high risk genotypes of HPV is desirable due to the affiliation with cervical cancer and  
18 bowenoid papulosis. Anogenital warts (condylomata acuminatum) are a viral disorder with a  
19 frequent sexual transmission. Women are implicated in two-thirds of the patient population,  
20 though both sexes are afflicted.

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#### 22 **Index terms—**

23 Genitive Communication -Anogenital Warts -Condylomata Acuminatum Anubha Bajaj I. Preface uman  
24 Papilloma Virus (HPV) is a miniature DNA (deoxy ribonucleic acid) virus of the family Papovaviridae which  
25 primarily access the squamous cells. The categories of HPV exceed a 100 (11) . Histological transformation  
26 and infiltrative malignant neoplasm in the vulva and anogenital area such as Condyloma, Verrucous lesions,  
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34 risk genotypes of HPV is desirable due to the affiliation with cervical cancer and bowenoid papulosis. Anogenital  
35 warts (condylomata acuminatum) are a viral disorder with a frequent sexual transmission. Women are implicated  
36 in two-thirds of the patient population, though both sexes are afflicted.

#### 37 **1 II. Causatum and Prospects**

38 Condylomata acuminatum commences from the Human Papilloma Virus (HPV), a family of highly contagious  
39 double stranded DNA viruses, essentially exhibiting a sexual transmission. Lesions appear in 3 weeks to 8  
40 months after initial exposure. Majority of the infections are transitory and dissipate within 2 years. Almost 35  
41 sub-categories of HPV are limited to the anogenital epithelium with a probability of malignant conversion such  
42 as cervical and anal cancer (5) . High risk serotypes 16 and 18 collaborate with low risk subtypes of HPV such as  
43 6 & 11 to elucidate benign condylomas and low grade intra epithelial neoplasia without incorporating in the host  
44 genome. Intermediate risk HPV subtypes delineate a high grade dysplasia which may persevere with negligible  
45 evolution and invasion.

## 5 VI. DETERMINANTS

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46 Author: e-mail: anubha.bajaj@gmail.com Condylomata emerge from sexual activity Digital / anal, oral /  
47 anal and digital / vaginal contact possibly disperses the virus besides various fomites. Immune suppression  
48 predisposes to the disorder. The contamination in women is largely transmitted by vaginal intercourse. Anal  
49 condyloma may evolve from vulvar or perineal infections or by recipient anal intercourse. Numerous sexual  
50 participants enhances the occurrence of the disease (condylomata 7 times frequent and recurrent condylomata  
51 12 times) in contrast to a singular partner with equivalent predisposition in both the genders. Previous exposure  
52 to a sexually transmitted disorder or oral herpes is concordant with a possible condyloma. The cavity of the  
53 prepuce or the penile shaft is implicated in the heterosexual or homosexual process. Heterosexuals may elucidate  
54 perianal lesions, although these are usually encountered in the homosexuals. Condylomas are preponderant in  
55 the HIV (human immune deficiency virus) infected individuals besides those with variants of STD (7%) and  
56 may evolve into a squamous cell carcinoma if the contamination persists. Diminished CD4 T lymphocyte count  
57 (<500 cells/ $\mu$ l) and frequent administration of drug injections may elucidate a vulvovaginal or perianal lesion.  
58 Efficacious antiretroviral therapy reduces the incidence of these lesions.

## 59 2 III. Scientific Indications

60 Condylomata acuminatum manifests clinically contingent to various lesions with pertinent locations. A  
61 smattering of warts frequently lack characteristic features. However patients exhibit itching, bleeding, burning,  
62 localized tenderness, pain and vaginal discharge (in females). Occasionally, exophytic and extensive warty clusters  
63 are evidenced which may impede defecation, intercourse or vaginal delivery. Proximal anal canal configurations  
64 may incite a stricture.

## 65 3 IV. Interpretation

66 Visual inspection of the site of involvement is recommended. Smooth, flattened, skin coloured or pink papules  
67 or verrucous papillae may be encountered. Anoscopy, Sigmoidoscopy, Colposcopy and/or a Vulvovaginal  
68 examination is indicated to evaluate the magnitude of the disease. High resolution anoscopy is frequently  
69 employed to augment tissue visualization. Application of 5% acetic acid produces a pearly white H lesion  
70 which simplifies the recognition of the lesion, though the measure is non-specific.

## 71 4 V. Histopathology

72 Condylomata acuminatum or venereal warts (commonly an HPV 6 genesis) develop in the vicinity of the anus,  
73 vulva, glans penis and mucosal membranes such as the oral cavity. Focal epidermal hyperplasia is substantiated  
74 by hyperkeratosis, parakeratosis, varying or extensive acanthosis and papillomatosis. Trichilemmal type of  
75 keratinisation may emerge (13) . Vacuolated cells may be visualized in the upper malpighian layer in the early  
76 lesions. Atypical cells, characterized by abundant, eosinophilic cytoplasmic accumulations may be demonstrated.  
77 Miniature vacuolated cells and pyknotic nuclei are exhibited in the thick, basal stratum corneum (13) . Ancient  
78 verrucae may emerge as papillomas or keratoses. Flat warts with involution display a degenerative epidermis and  
79 a prominent mononuclear dermal or intra-epidermal inflammation. The viral nuclear inclusions are basophilic.  
80 They can be established with immunohistochemistry and in-situ hybridization procedures. The eosinophilic  
81 aggregates in the cytoplasm are indicative of aggregated tonofilaments. In concordance with the HPV induced  
82 lesions, benign or malignant skin tumours or tumour like conditions manifest, such as seborrheic keratosis, bowen's  
83 disease, invasive squamous cell carcinoma and epidermodysplasia verruciformis. The keratinocytes reveal altered  
84 keratin on account of the viral infection and further alterations ensue with malignant conversion. A biopsy may  
85 be contemplated with ambiguous lesions, in the patients refractory to therapy, in immune-deficient individuals,  
86 with extensive lesions or lesions which elucidate atypical components. A routine biopsy can be advocated to  
87 investigate a dysplasia.

## 88 5 VI. Determinants

89 Detection of the subtypes of the contaminant HPV is essential to specify the patients which may progress to  
90 squamous cell carcinoma. Anogenital tumours induced by HPV may be clinically challenging and troublesome  
91 to diagnose and treat. Determination of the virus incorporates In situ hybridization (ISH), Southern blot  
92 hybridization method, Dot blot hybridisation, Polymerase Chain Reaction (PCR) and real-time PCR. However  
93 the technique of ISH for diagnosing the HPV is inferior and insensitive. Besides PCR and real time PCR require  
94 valuable machinery such as a thermal cycle (8) . A Hybriobio geno array test for HPV genotyping can be utilized  
95 as a commercial kit. It is an expeditious, efficacious, specific and sensitive technique to ascertain the HPV DNA.  
96 The test displays a decisive concordance which exceeds that of 95% with the interpolation of the commercial  
97 kit and the viral DNA sequencing. The concurrence of the real time PCR and viral DNA sequencing is around  
98 95%. Viral DNA sequencing is the gold standard. The real time PCR is a dependable, sensitive and a specific  
99 investigation to discover the infections created by the high risk and low risk HPV genotypes (6) .

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## 100 **6 VII. Distinguishing Diagnoses**

101 Condylomata acuminatum requires distinction from condylomata lata, a pattern of condyloma which develops  
102 in secondary syphilis. Condylomata lata delineates flat and velvety lesions. Generally, micropapillomatosis of  
103 the vulva ensues. A solitary base abuts each individual papillary projection, in contrast to the condylomata  
104 acuminatum where multiple papillae emerge from a singular base. Verrucous lesions, which are painful and  
105 perianal, develop in concurrence with the contamination of Herpes Simplex virus and HIV infection. Anogenital  
106 squamous cell carcinoma may coincide with condylomata acuminatum. Ulcerated and ambiguous lesions require  
107 a biopsy. Lesions with three previous treatment protocols or if unresolved within six months of therapy require  
108 a histological re-assessment. Immune-deficient patients, those beyond 40 years of age, pigmented, anomalous  
109 lesions also necessitate a re-evaluation. Demarcation is also required from disorders such as hymenal remnants,  
110 vulvar intraepithelial neoplasia (in women), molluscum contagiosum, skin tags and angiofibromas.

## 111 **7 VIII. Therapies Numero Uno**

112 Three major modalities are instituted: Chemical or Physical destruction, Immune therapy and Surgical excision.  
113 Topical anti microbial agents have a restricted collusion. The number and magnitude of lesions dictate the mode  
114 of therapy. However, the therapeutic interventions for genital warts may be inadequate as the reoccurrence is  
115 up to 30-70 % within 6 months. Spontaneous retrogression may occur within 3 months in 20-30 % cases. An  
116 exceptional or a pertinent treatment option for the entire panorama of warts is nonexistent. Trichloracetic acid  
117 or podophyllin may be applied to the warts. Imiquimod, podophyllin or( D D D D )

118 C extended patient analysis is then required. Self application of imiquimod or podofilox is beneficial in  
119 the absence of trichloracetic acid or podophyllin. Surgical intervention is recommended for enormous lesions.  
120 (Gynaecologic / Anorectal surgery).

121 Chemical agents incorporate podophyllin, trichloracetic acid or 5 fluorouracil / epinephrine gel. Podophyllin  
122 is a decoction of podophyllum peltatum, comprising of an anti mitotic agent podophyllotoxin which arrests the  
123 cell cycle in metaphase with consequent cell demise. A 0.5% concentration of podofilox / podophyllotoxin can be  
124 employed. Reoccurrence occurs in 43% individuals in 12 weeks. Trichloracetic acetic (TCA) decimates the wart  
125 by protein coagulation in 80 to 90% cases. 5 Flurouracil / Epinephrine gel is a pyrimidine antimetabolite that  
126 mediates in DNA synthesis, arrests the methylation of deoxy uridylic acid thereby resulting in cellular demise.  
127 Intra-lesion injection of epinephrine enhances the resolution of the warts, particularly with integrated therapy.  
128 At 3 months 50-60% lesions tend to reoccur.

## 129 **8 IX. Immune Modulation**

130 Imiquimod and interferon alpha are dual immune modulating agents which can be utilized. Imiquimod is an  
131 immune transformer which activates local cytokines. Vulval and Anal intraepithelial neoplasia may be managed  
132 with the same. Interferon Alpha, when employed with for systemic therapy comprehensively remedies the anal  
133 condyloma in 25-80% individuals. Ancillary alpha interferon therapy in conjunction with the 5 fluorouracil cream  
134 or laser ablation elucidates a reoccurrence of 6% in contrast to a figure of 24% with no additional treatment.

## 135 **9 X. Surgery**

136 Excision or surgical ablation is optimal with the non performance of medical therapy and for warts susceptible to  
137 surgery. Cryotherapy is an outpatient technique which employs liquid nitrogen spray. Laser therapy necessitates  
138 an operation theatre or a mobile surgical and anaesthetic service. The warts are disposed of in a 100% cases (33),  
139 nevertheless reoccurrence ensues in 45%. Surgical intervention is an exorbitant procedure for treating warts.

## 140 **10 XI. Excision Modalities**

141 Knife or scissor excision requires anaesthesia. Infection and haemorrhage may probably emerge. Complete  
142 eradication occurs in 36% cases. Condylomata acuminatum treated with excision requires evaluation for squamous  
143 cell carcinoma. Antimicrobials can be topically adopted inclusive of Cidofovir and Bacille Calmette Guerin  
144 (BCG). Cidofovir competitively restricts the viral Deoxy Ribonuclease (DNA) by incorporating viral DNA  
145 polymerase. The drug mediates and prevents the extension of the DNA. Bacille Calmette Guerin (BCG) elucidates  
146 a partial or a negligible recovery.

## 147 **11 XII. Infrared Coagulation**

148 Tissue coagulation is attained by a narrow beam of infra red light focussed within a probe. Hemorrhoids, tattoos,  
149 chronic rhinitis, ablation of common warts and anogenital condylomata (82%) are benefitted by the modality.  
150 Reoccurrence can be managed with excision or fulguration. A partial biopsy is required for evaluating malignant  
151 conversion. Cryotherapy may be employed subsequent to recovery. Ancillary treatment with imiquimod cream  
152 is recommended.

153 **12 XIII. Conclusion**

154 Human Papilloma Virus (HPV) appertains to the Papillomaviridae family, a divergent class of viruses which  
155 contaminate the skin and the mucosal epithelium of numerous vertebrate species. Forty kinds of HPV pertaining  
156 to the genus papillomavirus have been identified. These contaminate the epithelium and mucosal lining of the  
157 anogenital tract (1) . HPV subtypes are categorized as per the probability of malignant transformation as low  
158 risk or high risk. Low risk HPV subtypes (HPV 6 & 11) produce common genital warts such as condylomata  
159 acuminatum, benign hyperproliferative lesion and a controlled development of malignancy. Condylomata  
160 acuminatum are discovered with HPV 6 or 11 or both in 90% individuals and with HPV11/18 in about 4%  
161 cases. Concomitant infection by dual DNA subtypes can be detected by Hybrizio HPV geno array test or viral  
162 DNA sequencing. Numerous HPV genotypes are ascertained with the Bowenoid Papulosis consisting of HPV  
163 16,18,31,35,39,42 and 48(5). HPV 16 contamination is particularly connected with the squamous cell carcinoma  
in situ of the external genitalia such as Bowen's disease and Erythroplasia of Queyrat (9) . <sup>1 2</sup>

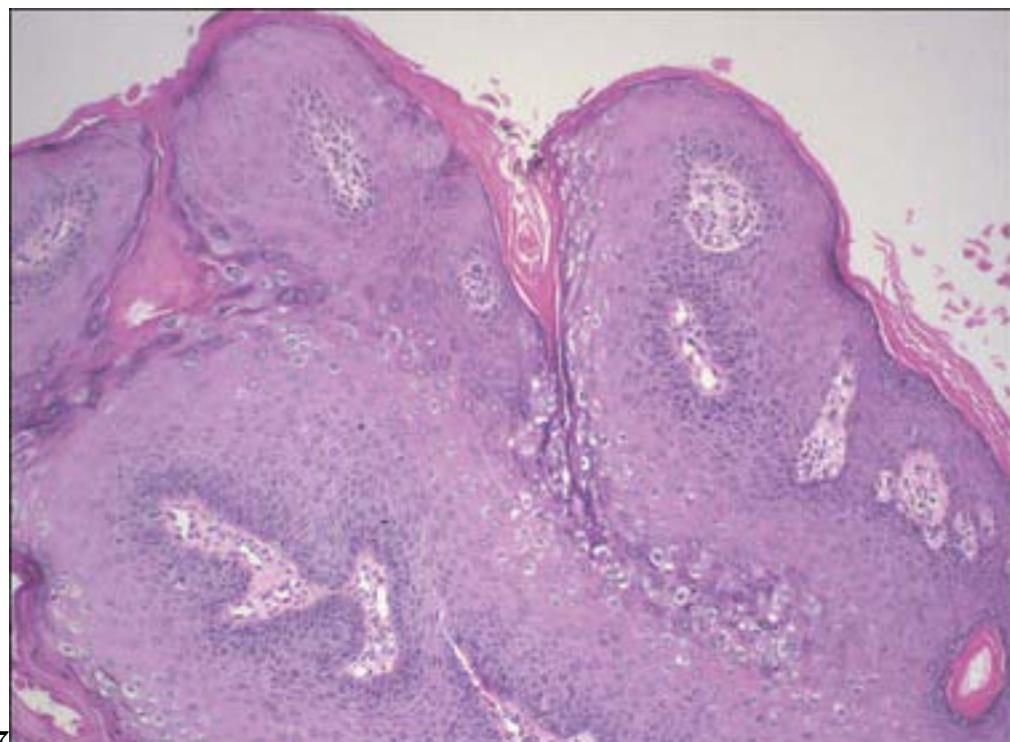


Figure 1: Fig. 1 :Fig. 2 :Fig. 3 :Fig. 4 :Fig. 5 :Fig. 6 :Fig. 7 :

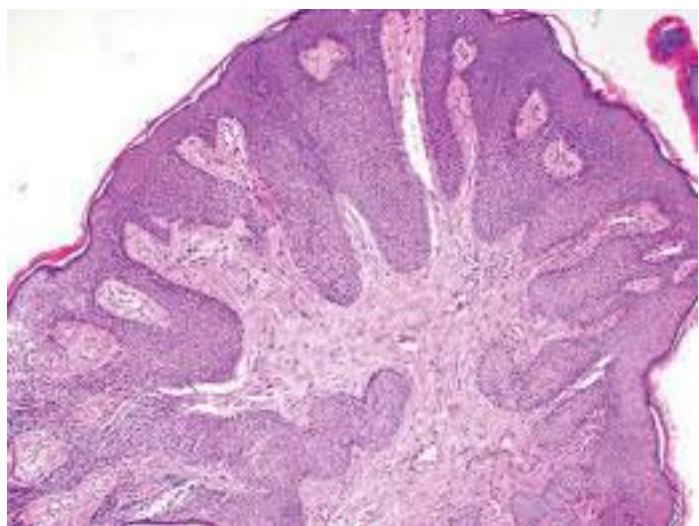


Figure 2:



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