# Intralesional Mumps, Measles and Rubella Vaccine Injection for the Treatment of Genital Warts

Thesis

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Presented by

***Amira El Sayed Bahgat El Bably***
*M.B.B.Ch., Ain Shams University*

Under Supervision of

**Prof. Dr. Hanan Mohamed Ahmed Saleh**
*Professor of Dermatology, Venereology & Andrology*
*Faculty of Medicine, Ain Shams University*

**Dr. Ghada Fathy Mohamed**
*Assistant Professor of Dermatology, Venereology & Andrology*
*Faculty of Medicine, Ain Shams University*



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# حقن لقاح النكاف والحصبة والحميراء داخل الآفة في علاج الثآليل التناسلية

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توطئة للحصول على درجة الماجيستير

فى الأمراض الجلدية والتناسلية والذكورة


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**الطبيبة / أميرة السيد بهجت البابلي**

بكالوريوس الطب والجراحة

جامعة عين شمس

تحت إشراف

**الأستاذة الدكتورة / حنان محمد أحمد صالح**

أستاذ الأمراض الجلدية والتناسلية والذكورة

كلية الطب – جامعة عين شمس

**الدكتورة / غادة فتحي محمد**

أستاذ مساعد الأمراض الجلدية والتناسلية والذكورة

كلية الطب – جامعة عين شمس



كلية الطب

جامعة عين شمس

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# SUMMARY

Genital warts (Condylomata acuminata, venereal warts, anal warts and anogenital warts) are highly contagious sexually transmitted disease caused by some sub-types of human papillomavirus (HPV). It is spread through direct skin-to-skin contact during oral, genital, or anal sex with an infected partner.

Warts are the most easily recognized symptom of genital HPV infection. They can be caused by strains 6, 11, 30, 42, 43, 44, 45, 51, 52 and 54 of HPV, but types 6 and 11 are responsible for 90% of genital warts cases. It is estimated that 1–2% of the sexually active population between the ages of 15 and 49 is afflicted with these HPV-associated verrucae.

The treatment of warts poses a therapeutic challenge for physicians. No single therapy had been proven effective at achieving complete remission in every patient. As a result, many different approaches to wart therapy exist. These approaches include chemotherapy by (salicylic acid, TCA, podophyllin, podophyllotoxin), cryotherapy mostly by liquid nitrogen, electrosurgery (curettage and cautary), laser therapy and photodynamic therapy. All these previous destructive modalities may be painful, ineffective, costly,


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**Amira El Bably**

# List of Contents

# List of Abbreviations

| | | |
|---|---|---|
| **ALA** | : | Amino-laevulinic acid |
| **APCs** | : | Antigen Presenting Cells |
| **BCA** | : | Bichloroacetic acid |
| **BCG** | : | Bacille Calmette Guerin |
| **BLT** | : | Buschke-Lowenstein tumor |
| **CD** | : | Cluster of differentiation |
| **CDC** | : | Centers for Disease Control and Prevention |
| **CIN** | : | Cervical intraepithelial neoplasis |
| **COX-2** | : | Cyclo-oxygenase 2 |
| **CPG** | : | Cytosine phosphate- guanosine |
| **CTL** | : | Cytotoxic T lymphocytes |
| **DCs** | : | Dendretic Cells |
| **DNA** | : | Deoxyribonuleic acid |
| **E** | : | Early region |
| **EGW** | : | External Genital wart |
| **FDA** | : | Food and Drug Administrations |
| **FISH** | : | Filter in situ hybridization |
| **G** | : | Gap |
| **G-CSF** | : | Granulocyte colony- stimulating factor |
| **HIV** | : | Human immunodeficiency virus |
| **HLA** | : | Human Leukocyte Antigen |
| **HLA-DP** | : | Human Leukocyte Antigen- heterodimer protein/peptide antigen receptor |
| **HLA-DQ** | : | Human Leukocyte Antigen- heterodimer of the MHC class II type |

# List of Abbreviations (Cont.)

| | | |
|---|---|---|
| **HLA-DR** | : | Human Leukocyte Antigen- heterodimer cell surface receptor |
| **HPV** | : | Human Papillomavirus |
| **IL** | : | Interleukin |
| **INF** | : | Interferon |
| **IP 10** | : | Induced Protein 10 |
| **ISH** | : | Tissue in situ hybridization |
| **Kb** | : | Kilo bases |
| **L** | : | Late region |
| **LCR** | : | Long Control region |
| **LCs** | : | Langerhans Cells |
| **LEEP** | : | Loop elecrosurgical excision procedure |
| **LN** | : | Lymph Node |
| **LN2** | : | Liquid Nitrogen |
| **MEM** | : | Minimal Essential Medium |
| **MHC** | : | Major Histocompatibility Complex |
| **MMR** | : | Measles, Mumps and rubella |
| **mRNA** | : | Messenger Ribonucleic acid |
| **Mw** | : | killed Mycobacterium w vaccine |
| **NK** | : | Natural Killer |
| **P 53** | : | Protein 53 |
| **Pap** | : | Papanicolaou |
| **PCR** | : | Polymerase Chain Reaction |
| **PMNs** | : | Polymorphonuclear leukocytes |

# List of Abbreviations (Cont.)

| | | |
|---|---|---|
| **PPD** | : | Purified Protein derivative |
| **PV** | : | Per Vaginam |
| **RRP** | : | Recurent Respiratory Papillomatosis |
| **S phase** | : | Synthesis phase |
| **SIL** | : | Squamous intraepithelial lesions |
| **STDs** | : | Sexually transmitted diseases |
| **STH** | : | Southern transfer hybridization |
| **STI** | : | Sexually transmitted infection |
| **TCA** | : | Trichloroacetic acid |
| **TGF** | : | Transforming Growth Factor |
| **Th 2** | : | T helper 2 |
| **Th1** | : | T helper 1 |
| **TNF** | : | Tumor Necrosis Factor |
| **VLPs** | : | Viral-like particles |
| **WI-38** | : | Wistar Institute 38 |

# List of Tables

# List of Figures

# List of Figures (cont...)

# INTRODUCTION

Human Papilloma Virus (HPV) is a double-stranded DNA virus that causes cutaneous viral warts, most commonly located on the skin and genitalia ***(Rivera and Tyring, 2004).*** Over 118 types of papillomavirus have been identified, more than 35 types infect the genital tract ***(De Villiers and Fauquet, 2004).***

Types 6 and 11 Human Papilloma Virus (HPV) are associated with low risk anogenital warts, and types 16, 18, 31, 33, 45 and 59 are most commonly associated with squamous cell and adenocarcinomas of the cervix ***(Brotzman, 2005).*** Individuals are likely to be infected by multiple types ***(Vandepapeliere et al., 2005).***

Warts of the genital tract carry a much more pernicious threat for women in particular. It has been estimated that up to 70% of sexually active women become infected during their lifetime with human papillomavirus (HPV) ***(Baseman and Koutsky, 2005).***

Anogenital warts (venereal or condylomata acuminate) occur in the perineum and on the genitalia or in the genital tract and are considered as one of the most common sexually transmitted diseases. They can be an indication of sexual abuse in children under the age of 3, but may be

transmitted to the neonates of infected women ***(Rintala et al., 2005)***.

Approximately 23% of warts regress spontaneously within 2 months, 30% within 3 months and 65% to 78% within 2 years ***(Sterling et al., 2001).*** Previously infected patients have a higher risk for development of new warts than those never infected ***(Allen and Siegfried, 1998).*** The rate of clearance is influenced by factors such as viral type, host immune status, extent and duration of warts ***(Clifton et al., 2003).***

Although there are many destructive and immunotherapeutic options available for the treatment of viral warts, no single treatment has yet proven 100% effective ***(Lipke, 2006).*** Anogenital warts should receive special consideration and warrant vigilance for other sexually transmitted disease ***(Sterling, 2001).***

Destructive therapies include either topical agents, such as salicylic acid, podophyllotoxin, trichloroacetic acid, formaldehyde, 5-flurouracil and photodynamic therapy, or surgical methods such as cryosurgery, laser ablation, electrocautery, and surgical excision. Immunotherapeutic agents include contact sensitizers, imiquimod, intralesional interferons and oral drugs, such as levamisole, cimitidine, and zinc sulphate ***(Dasher et al., 2009)***.

Many observations have suggested that wart proliferation is controlled by the immune system, particularly the cell-mediated immunity ***(Gonc and Donadi, 2004).*** Recently, intralesional immunotherapy by different antigens has been proved effective in the treatment of different types of warts ***(Gupta et al., 2008).***

Intralesional immunotherapy employs the ability of the immune system to recognize certain viral, bacterial and fungal antigens that induce a delayed-type hypersensitivity reaction, not only to the antigen but also against the wart virus, which in turn, increases the ability of the immune system to recognize and clear HPV ***(Maronn et al., 2008).***

Taking the advantage of the vaccination schedule in our country including mumps, measles and rubella (MMR) vaccine, we designed the present study to evaluate the efficacy and safety of this vaccine in the treatment of genital warts.