

Traditional Chinese Medicine: A Viable Alternative to the LEEP Procedure  
in Treating Cervical Dysplasia

By

Myeongae Kang

A Capstone Project

Submitted in partial fulfillment of the requirements for the degree

Doctor of Acupuncture and Oriental Medicine

Yo San University

Los Angeles, California

April, 2013

## Approval Signature Page

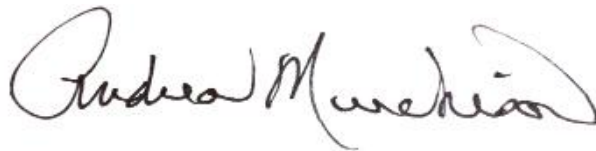
This Capstone Project has been reviewed and approved by:

A handwritten signature in black ink, appearing to read "Lawrence J. Ryan". The signature is fluid and cursive, with a large loop at the end.

Lawrence J. Ryan, PhD., Capstone Advisor *June 10, 2013*

A handwritten signature in black ink, appearing to read "Daoshing Ni". The signature is cursive and elegant, with a large loop at the end.

Daoshing Ni, PhD., L.Ac. Specialty Chair *June 10, 2013*

A handwritten signature in black ink, appearing to read "Andrea Murchison". The signature is cursive and elegant, with a large loop at the end.

Andrea Murchison, DAOM, L.Ac. *June 10, 2013*

## **Abstract**

Cervical dysplasia is a premalignant lesion that can lead to cervical cancer. The LEEP surgical procedure offered by Western medical treatment of cervical dysplasia has been shown to be related to pre-term delivery in pregnancy. Historically, Traditional Chinese Medicine has offered a non-surgical alternative for the treatment of cervical dysplasia. The current research examined data from two case studies that involved the Traditional Chinese Medicine treatment of cervical dysplasia in women who were 28 and 39 years of age. The data were examined regarding similarities and differences in presenting symptoms, treatment procedures and outcomes. Implications for theory and practice were discussed on the basis of the data generated from the case studies, and recommendations for future research were articulated.

## Table of Contents

Chapter 1 : Introduction.....	8
Epidemiology.....	8
Pap Tests.....	9
Limitations of Pap Smear Test.....	10
Coloscopy and Biopsy.....	11
Cone Biopsy.....	11
LEEP Procedure.....	12
Importance of the Current Study.....	12
Glossary of Relevant Terms.....	14
Statement of Research Question.....	16
Chapter 2 : Literature Review.....	17
Overview.....	17
General Considerations.....	17
Epidemiology & Etiology of HPV Disease.....	23
The Medical Burden.....	24
HPV Infection Causes Epithelial Abnormalities.....	24
HPV Infection Can Cause Invasive Cancer.....	25
Risk Factors.....	26
Cervical Dysplasia Treatment.....	31
Electrcauterization.....	31
Cryosurgery and Cryocauterization.....	32

Laser Vaporization or Ablation.....	32
Virology.....	33
Pathogenesis.....	35
Natural History of Cervical Cancer.....	35
Viral Factors.....	38
Nonviral Factors.....	40
LEEP Studies.....	42
Western Medicine Studies.....	45
TCM Considerations.....	45
Herbs to Reduce Stagnation.....	46
Chinese Formulas.....	47
Literature Review Integration.....	50
Chapter 3 : Method.....	52
Designation of Research Method.....	52
Inclusion and Exclusion Criteria.....	53
Data Collection Form.....	54
Procedures.....	55
Human Subjects Ethical Considerations.....	56
Chapter 4 : Results.....	58
Mary's Case.....	58
First Visit: August 13, 2009.....	60
Second Visit: August 20, 2009.....	61
Subsequent Treatments:.....	61

Cathy's Case.....	61
First Visit: April 3, 2010.....	62
Second Visit: April 10, 2010.....	63
Third Visit: April 17, 2010.....	63
Subsequent Treatments.....	64
Western Medicine Treatment for Both	
Cervical Dysplasia Cases.....	64
Traditional Chinese Medicine Treatments.....	65
Chinese Formulas.....	66
Chinese Formulas for Douche.....	67
Mary's Acupuncture Treatment.....	67
Cathy's Acupuncture Treatment.....	70
Acupuncture Points Comparison Between	
the Two Cases.....	71
Comparison of the Chinese Medicine Treatment	
Between the Two Cases.....	71
Acupuncture Comparison Between Mary and Cathy.....	72
Herbal Formula Comparison Between the Two Cases.....	74
Chapter 5 : Discussion.....	76
Implications for Theory and Practice.....	76
Limitations of the Current Study.....	78
Suggestions for Future Research.....	79
Conclusion.....	80

References.....	81
Appendix A : Data Collection Form.....	92
Appendix B: IRB Letter.....	94

### **List of Tables**

Table 1: Summary of Symptoms of Cervical Dysplasia.....	20
Table 2: Human Papillomavirus Gene Functions.....	34
Table 3: Points Protocols for the Two Case Studies.....	73
Table 4: Summary of Background and Treatment Data for the Two Cases.....	75

## Chapter One: Introduction

### Epidemiology

Cervical dysplasia is a premalignant lesion that can progress to cervical cancer that is the second- most common cancer in women age 20 to 39 years (Greelee RT, Hill-Harmon MB, Murray T, Thun M. 2001). Internationally, invasive cervical cancer accounts for 11.6 percent of all cancers. For every case of invasive cancer there are an estimated 50 cases of abnormal cervical smears that require monitoring and follow-up (Franco EL. 1997 ). Currently, evidence suggests the cervical dysplasia lesion is primarily caused by a sexually transmitted infection with an oncogenic strain of the human papillomavirus (HPV). However, this viral genome is found in healthy women, and there is often unhealthy tissue adjacent to neoplastic lesions. As a result factors unique to each individual host appear to contribute to the disease progression and the presence of dysplastic transformation.

Invasive cervical cancer develops from precursor lesions of the cervix called cervical intraepithelial neoplasia (CIN). Progression from normal tissue to invasive cervical cancer occurs through a series of increasing grades of cervical dysplasia. CIN1 represents mild dysplasia and has a high rate of spontaneous remission (60%) and a low rate of progression to carcinoma (insert %). In contrast, approximately 38% of CIN II and CIN III, moderate to severe dysplasia, will spontaneously regress, and 16-36% will progress to invasive cervical cancer (Mitchell, 1996). Because reporting for CIN is not mandatory, the exact incidence is unknown. However, it is estimated that 2.5 million women are diagnosed with low-grade cervical abnormalities annually (Kurman, Henson & Herbst et al., 1994). Routine Pap smear screening is widely credited with



reducing the number of cases of cervical dysplasia. These screenings have resulted in the moving cervical carcinoma from the first leading cause of cancer deaths in the United States to the eighth leading cause. However, the number of deaths attributable to the disease is still high. It is approximately 4,900 annually in the United States (Landis, Murray, Bolden, Wingo, 1998).

### **Pap Tests**

In the 1930's the Greek physician Dr. Papanicolaou developed a test to monitor cervical health, which now known as the Pap smear test. Pap smears discern the appearance of abnormal cells around the cervix. A small brush is used to collect a sample of dead surface cells from the cervix. The brush takes a full sweep of the squamo-columnar junction and upper vagina. Then, cells are placed on a glass slide and sent to the laboratory. The most ideal time for a Pap smear test is around the time of ovulation--10 to 20 days after day one of the menstruation cycle. During ovulation, the cells are flatter and easier to read due to elevated estrogen levels. Having a Pap smear test done right after menstruation is not recommended since there may be too many endometrial cells discharged from the uterus making the test hard to read. To ensure the most accurate Pap reading one should avoid at least two days before the test the use any topical applications such as douches, spermicidal foams and jellies, creams or herbal medicines that will wash away or hide abnormal cells. Medical opinion recommends that every woman over the age of 18, who is sexually active, should have a Pap smear test annually. However, there are mixed opinions about what age to discontinue testing. Some reports suggest discontinuing Pap testing after the age of 65, if 2 consecutive normal smears are obtained. However, contrary studies show that one

in four cases of cervical cancer, and 40% of deaths due to cervical cancer, occur in women 65 years and older (Katolen, 2001) Therefore, it is crucial to continue periodic testing even past age 65 (McCrorry, Matchar, Bastian, Datta & Hasselblad, 1999).

### **Limitations of Pap Smear Test**

There are often errors due to faulty collection procedures that result in a false negative rate in up to one third of all Pap tests. This means that approximately 33% of women actually have cervical abnormalities that the Pap test fails to pick up (McCrorry et al., 1999). A Pap smear test may contain very few cells making grading difficult. Additionally, human error can occur during slide reading, and test grading depends heavily upon personal interpretation. It is possible to have a different interpretation from the same person reading the same slide on different occasions. Readability of a slide depends largely upon the conditions of slide storage, which includes how cell sample was taken and how the subsequent slide was prepared for reading. The Pap test reading is most often the result of a subjective experience rather than scientific methodology. (Barnett, Robin & Fox, 1986).

What is the risk of cervical dysplasia developing into cancer?

Research from the university of Toronto indicates that both mild and moderate cervical dysplasias were more likely to regress than to progress. The trend of mild dysplasia leading into severe abnormalities or cancer was 1% per year (Holowaty, Miller, Rohan & To, 1999).

A review of follow up studies on 3529 women indicated a regression rate of 57% for CIN 1; 32% indicated no change of dysplasia grade; a regression occurred in 43% of cases of CIN 2; and the progression of CIN 1 to invasive cervical cancer was 1%.

Another sample cited in the same study concluded that over a 42 month follow up of 1269 women, spontaneous regression occurred in 53% of cases with CIN 1, and 39% of cases with CIN 2 (Syrianen, 1996).

### **Colposcopy and Biopsy**

Colposcopy is way of looking at cervix through a special magnifying device called a colposcope. It shines through the vagina and onto the cervix. A colposcopy can greatly enlarge the normal view. During colposcopy the abnormal area may be seen more clearly. A biopsy of this area may be need to be done. During biopsy, small piece of abnormal tissue is removed from cervix (American college of OBGYN, 2011).

A colposcopy microscope is a widely used procedure. A 'Schiller test' is performed by painting an iodine or vinegar solution onto the cervix, which turns healthy cells brown. Abnormal cells turn yellow or white resulting in easier identification of irregular tissues. The colposcopy can be connected to a video screen so women can see the cervix on a TV monitor (Barnett, Robiun & Fox et al., 1986)

How to remove cervical tissue for biopsy:

### **Cone Biopsy**

Cone biopsy consists of removing a large cone-shaped piece of tissue to determine whether the abnormal cells have invaded layers of the cervix. Conization is also used to treat carcinoma in situ if the entire lesion can be removed. The cone biopsy removes up to  $\frac{1}{4}$  to  $\frac{1}{2}$  of the face of the cervix and requires a local or general anesthetic procedure. Too much tissue may be removed, increasing the risk of second trimester miscarriage and premature labor. Scar tissue may also make the cervix less elastic and

the endocervical canal less flexible, which may lead to future pain and dysmenorrhea (Northrup & Chrisitane, 1994).

### **LEEP Procedure**

Loop Electro Surgical Excision Curettage (LEEP) removes a thin slice of cervical tissue by using an electric wire loop. This procedure results in immediate cramping and long term tissue scarring (Franco, Duarte-Franco & Ferenczy, 2001).

### **Importance of the Current Study**

High-grade cervical abnormalities are common in young women who could become pregnant. Studies linking laser conization or loop electrosurgical excision procedure (LEEP) to an increased risk for preterm delivery have been inconclusive. Sadler and colleagues investigated the risk of preterm delivery subsequent to treatment of cervical neoplasia. A retrospective cohort study included female patients of a large New Zealand hospital that offered centralized colposcopy and obstetric services. The authors assessed patients who, according to the hospital database, gave birth after at least 20 weeks' gestation and had LEEP or laser procedures for cervical intraepithelial neoplasia (CIN) before becoming pregnant. The study also included a control group of women who visited the colposcopy clinic but did not receive treatment. The authors collected data on demographics, medical history, cervical cytology and histology, colposcopic findings, and obstetric history and complications. Assessment also included vertical height of excised tissue, treatment mode, and number of treatments. The data were adjusted to include risk factors for preterm delivery or premature rupture of membranes not related to CIN treatment. The final analysis included 1,020 of the 9,226 women in the database. About 14 percent (n = 149) had preterm deliveries. Forty-one

were caused by iatrogenic reasons, including induction; 41 occurred spontaneously; and 67 were caused by premature rupture of membranes (PROM) before 37 weeks' gestation. Total preterm delivery rates for treated patients were 14.9 percent compared with 12.2 percent for untreated patients. PROM occurred in 8 percent of treated patients and in 3.5 percent of untreated patients. Spontaneous preterm labor occurred in 4 percent of treated patients and 3.5 percent of untreated patients. CIN treatment did not appear to increase risk for total preterm delivery or spontaneous preterm delivery after data were adjusted for outside risk factors. The adjusted relative risk increased for PROM following laser conization and LEEP treatments (2.7 and 1.9 percent, respectively), but not following laser ablation. The risk of PROM and preterm delivery increased as the height of tissue removed increased. The authors conclude that there is an increased risk of PROM and preterm delivery, but not overall preterm deliveries following laser conization or LEEP. Although PROM leads to preterm deliveries, these were higher in the untreated group after adjustments compared with the treated group. The authors attribute this incongruity to the higher rate of iatrogenic preterm deliveries in the untreated group. The authors suggest careful adherence to CIN management guidelines, avoidance of unnecessary excisions, and appropriate counseling of previously treated women when they become pregnant (Sadler, et al., 2004).

The data generated from the study detailed above highlight the importance of searching for alternatives to the LEEP Procedure. The current study will follow up by exploring Traditional Chinese Medicine procedures as a potential alternative to the LEEP Procedure in the treatment of cervical dysplasia. The next section will provide a list of terms and their definitions relevant to the current study.

## Glossary of Relevant Terms

**ASC:** Atypical squamous cells. One of two choices are added at the end of ASC: ASC-US, which means undetermined significance, or ASC-H, which means cannot exclude HSIL (American College of Obstetricians and Gynecologists, 2010).

**Biopsies:** Biopsies, or tissue samples for examination under the microscope, may be taken of suspicious areas seen during colposcopy. When dysplasia is identified in tissue biopsies of the cervix, the term cervical intraepithelial neoplasia (CIN) is used. CIN is classified according to the extent to which the abnormal, or dysplastic, cells are seen in the cervical lining tissue (American College of Obstetricians and Gynecologists, 2010).

**Cervical dysplasia:** Cervical dysplasia refers to abnormal changes in the cells on the surface of the cervix that are seen underneath a microscope. The cervix is the lower part of the uterus (womb) that opens at the top of the vagina (American College of Obstetricians and Gynecologists, 2010).

**CIN 1** refers to the presence of dysplasia limited to the basal 1/3 of the cervical lining, or epithelium (formerly called mild dysplasia ) (National Cancer institute, 2012).

**CIN 2** is considered to be a high-grade (more serious) lesion. It refers to dysplastic cellular changes confined to the basal 2/3 of the lining tissue (CIN 2 was formerly called moderate dysplasia) (National Cancer institute, 2012).

**CIN 3** is also a high grade lesion. It refers to precancerous changes in the cells encompassing greater than 2/3 of the cervical lining up to and including full-

thickness lesions. These were formerly referred to as severe dysplasia and carcinoma in situ (National Cancer institute, 2012).

**Colposcopy:** Colposcopy, or a procedure that uses a microscope to visualize the cervix during a pelvic exam. Colposcopy can help identify abnormal areas on the cervix and is a safe procedure with no complications other than mild vaginal spotting of blood (National Cancer institute, 2012).

**HPV:** Condylomata acuminata; Penile warts; Human papilloma virus (HPV); Venereal warts; Condyloma; HPV DNA test; Sexually transmitted disease (STD) - warts; LSIL-HPV; Low-grade dysplasia-HPV; HSIL-HPV; High-grade dysplasia HPV; HPV (Diaz, 2008).

**HSIL:** High-grade squamous intraepithelial lesion, corresponding to severe precancerous changes (American College of Obstetricians and Gynecologists, 2010).

**Leep electrical surgery:** The loop electrosurgical excision procedure (LEEP) is currently one of the most commonly used approaches to treat high grade cervical dysplasia (CIN II/III, HGSIL) discovered on colposcopic examination. The procedure has many advantages including low cost, high success rate, and ease of use. The procedure can be done in an office setting and usually only requires a local anesthetic, though sometimes a general anesthetic is used (Wikipedia, May 5, 2012).

**LSIL:** Low-grade squamous intraepithelial lesion, or changes characteristic of mild dysplasia (American College of Obstetricians and Gynecologists, 2010)

**Papsmear:** The Papanicolaou test (also called Pap smear, Pap test, cervical smear, or smear test) is a screening test used to detect potentially pre-cancerous and cancerous processes in the endocervical canal (transformation zone) of the female reproductive system (Wikipedia, 2012)

**Preterm delivery:** In humans preterm birth (Latin: partus praetemporaneus or partus praematurus) refers to the birth of a baby of less than 37 weeks gestational age (Wikipedia, May 5, 2012).

**SOAP:** Simple Object Access Protocol, a protocol specification for exchanging structured information in the implementation of Web Services in computer networks. It relies on Extensible Markup Language (XML) Hypertext Transfer Protocol (HTTP) and Simple Mail Transfer Protocol (SMTP), for message negotiation and transmission (Wikipedia, May 5, 2012)

### **Statement of Research Question**

The current study will focus on the exploration of Chinese medicine as an alternative treatment for cervical dysplasia to avoid LEEP surgery. This study will proceed with a literature review, followed by a methods chapter. The case studies will be presented in Chapter Four followed by discussion and implications in Chapter Five.



## Chapter Two Literature Review

### Overview

This chapter will establish the background and foundation for the current study of providing a review of literature that pertain to the leep surgeries causes preterm delivery. The chapter begins by reviewing providing more detail regarding the nature of cervical dysplasia, HPV and treatments current treatment offered by Western medicine studies. Those sections are followed by summaries of studies that have emerged from the field of Traditional Chinese Medicine (TCM) and will include section that specifically address data from use of Chinese herbs and acupuncture. The chapter will conclude with a literature review integration that summarizes the prior studies and leads directly to the need for current studies.

The literature review was conducted primarily using the on-line data bases available through the Yo San Univeristy Library. PubMed and other data bases were found to be especially healpful in this search. The search terms used were “Cervical Dysplasia,” “Cervical Cancer,” “Traditional Chinese Medicine” “Pre-Term Pregnancy,” “LEEP Surgery,” and “Treatments.” These search terms were used individually as well in varying combinations of each other. The researcher also was able to access some articles and sources from the University of California Los Angeles, Bioscience Library as well as the Los Angeles County Medical Society Library.

### General Considerations

Human papillomavirus (HPV) is one of the most common causes of sexually transmitted disease in both men and women worldwide. HPV is associated with a variety of clinical conditions that range from innocuous lesions to cancer. Genital HPV

types are divided into high and low-risk types, according to the oncogenic potential. Molecular and epidemiologic studies have solidified the association between high risk HPV types (especially HPV-16 and HPV-18) and cervical squamous cell carcinoma. HPV infection is often transient and self-limiting but uncommonly, infection persists and progress to high grade lesions and cancer. In addition to persistent high-risk HPV infection, other viral factors such as high viral loads, HPV variants, infections with multiple high-risk HPV types and genetic predisposition contribute to the development of cervical cancer. Although HPV is the primary etiologic agent of cervical cancer, it is not sufficient, and a variety of factors contribute to the cancer development. Risk factors include various aspects of sexual behavior (e.g. number of sexual partners, age of first sexual activity), smoking, long term oral contraceptive use, immunosuppression, and presence of other sexually transmitted agents (Gomez & Santos, 2007).

Papillomavirus are ubiquitous and have been detected in a wide variety of animals as well as in humans. More than 200 types of human papillomavirus (HPV) have been recognized on the basis of DNA sequence. Specific types of HPV tend to show some tissue tropism, and depending on the type of epithelium infected, HPV types are often referred to as "cutaneous" or "mucosal" types. In general, cutaneous types infect the keratinizing epithelium (especially the skin of the hands and feet), while mucosal types infect non keratinizing epithelium, primarily the anogenital tract epithelium, though they can also be found in the oral mucosa, conjunctiva and respiratory tract (Bonnez, Reichman, Mandell & Dolin, 2000).

HPV is associated with a variety of clinical conditions that range from innocuous lesions to cancer. There are seventy classified tyhpes of HPV (Bonnez et al., 2000).

Table 1 shows how the major HPV types have been classified according to their major symptom.

Table 1 Summary of symptoms of cervical dysplasia

<b>Clinical manifestations</b>	HPV type
<b>Plantar warts</b>	1, 2, 4, 63
<b>Common warts</b>	2, 1, 7, 4, 26, 27, 29, 41, 57, 65, 77, 3, 10, 28
<b>Flat warts</b>	3, 10, 26, 27, 28, 38, 41, 49, 75, 76
<b>Other cutaneous lesions</b> (e.g., epidermoid cysts, laryngeal carcinoma)	6, 11, 16, 30, 33, 36, 37, 38, 41, 48, 60, 72, 73
<b>Epidermodysplasia verruciformis</b>	2, 3, 10, 5, 8, 9, 12, 14, 15, 17, 19, 20, 21, 22, 23, 24, 25, 36, 37, 38, 47, 50
<b>Recurrent respiratory papillomatosis</b>	6, 11
<b>Focal epithelial hyperplasia de Heck</b>	13, 22
<b>Conjunctival papillomas/carcinoma</b>	6, 11, 16
<b>Genital warts</b> (condyloma acuminatum)	6, 11, 30, 42, 43, 45, 51, 54, 55, 70
<b>Low-risk cervical intraepithelial neoplasia</b>	6, 11, 16, 18, 31, 33, 42, 43, 44, 45, 51, 52, 74.
<b>High-risk cervical intraepithelial neoplasia</b>	16, 18, 6, 11, 31, 34, 33, 35, 39, 42, 44, 45, 51, 52, 56, 58, 66
<b>Cervical carcinoma</b>	16, 18, 31, 45, 33, 35, 39, 51, 52, 56, 58, 66, 68, 70
<b>Other genital carcinomas</b> (vagina, vulva, penis and anus)	16, 18, 31, 45, 33, 35, 39, 51, 52, 56, 58, 66, 68, 70

(Bonnez et al., 2000).

Most HPV infections are benign. Infection of cutaneous epithelium can cause warts (plantar warts, common warts and flat warts). Skin warts are transmitted by direct contact with an infected tissue or indirectly by contact with virus-contaminated objects. In general, they resolve spontaneously within 1 to 5 years. Epidermodysplasia verruciformis, a rare genetic disease with HPV associated warts on the trunk and upper extremities, can develop into invasive squamous cell carcinoma. Recurrent respiratory papillomatosis is primarily a disease of the larynx in young children but can also occur in adults. The infection in young children is thought to be acquired by passage through an infected birth canal. Respiratory tract lesions may undergo malignant transformation. Focal epithelial hyperplasia of the oral cavity (Heck's disease) tends to regress spontaneously. Conjunctival papillomas associated with HPV have been described. HPV-6 and HPV-11 are the etiologic agents of external anogenital warts (condylomas), which occur in sexually active individuals. Although they are benign, genital warts are a significant problem in sexually active populations. Anogenital cancers are the most important diseases associated with HPV infections. HPV is one of the most common causes of sexually transmitted disease in both men and women worldwide. The incidence of new infections in the United States ranges from 1 million to 5.5 million per year, and the prevalence is estimated to be as high as 20 million (Cates, 1996).

Of the many types of HPV, about 30 infect the genital tract through sexual contact. Genital HPV types infect primarily the cervix, vagina, vulva, penis and anus. These genital-type HPVs are further divided into high and low-risk types, according to the association with genital tract cancer. Low-risk HPV types include types 6, 11, 42, 43, and 44, and usually cause benign anogenital warts. High-risk HPV types include

types 16, 18, 31, 33, 34, 35, 39, 45, 51, 52, 56, 58, 59, 66, 68 and 70, and cause anogenital cancer (Munoz, Bosch, de Sanjose, Herrero, Castellsague & Shah, 2003).

Among the cancers attributable to high-risk HPV infection, cervical cancer has received the most attention. HPV-16, -18, -31, -45 account for more than 90% of cervical carcinomas (Munoz et al., 2003). 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 (Munoz et al., 2003). In addition, high-risk HPV types have been related with other genital cancers, such as carcinoma of vagina, vulva, penis and anus, and their precancerous lesions (Anderson, 2002).

Cervical cancer and premalignant lesions constitute a major problem in women's health. Cervical cancer is the second most common cancer in women worldwide and is the most frequent cancer in many developing countries. Every year, 470,000 new cases of cervical cancer are diagnosed worldwide, and about half of the afflicted women will die (Franco, 1995).

Although cervical screening has dramatically reduced the incidence of this disease in the developed world, it is still estimated that there will be 5,000 deaths from cervical cancer in the U.S. per year (Franco, 1995). In areas of the world where most women do not have access to regular gynecological care and screening, cervical cancer is second only to breast cancer as a cancer-related cause of death (Jin, Cash & Kennedy, 1999). The link between genital HPV infections and cervical cancer was first demonstrated in the early 1980s by Harold zur Hausen, a German virologist. Since then, the link between high-risk HPV types and cervical squamous cell carcinoma has become well known. In 1996, the World Health Association recognized HPV as an

important cause of cervical cancer. HPV has been implicated in 99.7% of cervical squamous cell carcinoma cases worldwide (Walboomers, Jacobs, Manos, Bosch, Kummer & Shah, 1999).

The magnitude of the association between HPV and cervical carcinoma is higher than that for the association between smoking and lung cancer (Franco, 1995).

Adenocarcinomas of the cervix are also related to HPV (especially HPV-18), but the correlation is less pronounced and is age dependent. In women younger than 40 years, HPV was present in 89% of adenocarcinomas, whereas in women aged 60 years and older, HPV was observed in only 43% (Andersson, Rylander, Larsson, Strand, Silversvard & Wilander, 2001).

### **Epidemiology & Etiology of HPV Disease**

Cervical Cancer is the second most common malignancy among women worldwide, with approximately 500,000 new cases diagnosed each year, and about 275,000 deaths per year. Eleven Thousand new cervical cancer cases and 4,000 deaths occur in the United States annually, and 52,000 new cases and 27,000 deaths occur each year in Europe, including new member states from Eastern Europe (Jemal, Siegel, Ward, Hao, Xu & Thun, 2009; Arbyn, 2007). Human papillomavirus (HPV) is the most common sexually transmitted viral disease in the world and is responsible for 99.7% of cervical carcinomas (Walboomers et al., 1999). Over 100 HPV subtypes have been identified, which are divided into low- and high-risk categories, based on the risk that infection evolves to neoplasia and cancer (Bosch et al., 2002).

## **The Medical Burden**

Approximately 291 million women are carriers of HPV at any given time, based on recent estimates (de San José et al., 2007). Of these, 14.7 million live in mature pharmaceutical markets and 78.3 million in emerging pharmaceutical markets. Of approximately 500,000 women worldwide that are diagnosed with having cervical cancer each year, about 70%, or 350,000 patients, carry the DNA of HPV16 and/or 18 (Munoz, 2004; Bosch et al., 2008).

## **HPV infection Causes Epithelial Abnormalities**

Infectious HPV particles introduced into the genital tract upon sexual intercourse can reach the basal cells of the squamous cell epithelium of the cervix uteri through micro-lesions (von Knebel, 2005; Doeberitz, 1994).

Once infection is initiated in the basal cell layer, the viral DNA genome is maintained as a low copy circular episome. Basal cells are the only dividing cells in the epithelium, which generate other basal cells by lateral division and keratinocytes by upward division (Munger et al., 2004). In differentiating keratinocytes in the lower mid-zone, which derive from HPV-infected basal cells, the episomal virus genome expresses early (E) and late (L) genes and amplifies its genome. Once in the upper mid-zone and superficial zone, only late gene expression of the L1 and L2 capsid forming proteins occurs in terminally differentiated squamous keratinocytes (Southern & Herrington, 1994). Subsequently progeny virus is released into the vagina from desquamated cells, which can be further transmitted by intercourse. The presence of the virus in the squamous epithelium causes morphological abnormalities, including



papillomatosis, parakeratosis, and koilocytosis. Such abnormalities correspond histologically to Grade 1 cervical intraepithelial neoplasia (CIN 1).

### **HPV Infection Can Cause Invasive Cancer**

In some keratinocytes in the mid-zone, viral replication does not occur. In this situation, the viral episome persists as either an extra-chromosomal element or becomes integrated into the host cell chromosome at a random site (C. Popescu & J.A. DiPaolo, 1989). Viral integration into the host cell DNA is believed to be a necessary step in cellular transformation of mucosal HPV. The effect is deregulated cell cycle control and uncontrolled cellular proliferation, dependent on constitutive expression of the viral oncogenes E6 and E7 (von Knebel et al., 1994). Through cell division, more and more cells in the epithelium are transformed and form high grade squamous epithelial lesions that histologically correspond to Grade 2 and Grade 3 cervical intraepithelial neoplasia (CIN 2 & CIN 3). This pre-cancer becomes invasive cancer when the lesion disrupts the basement membrane and spreads through the body.

Cervical dysplasia is the abnormal growth of precancerous cells on the surface of the cervix. The condition is classified as low-grade or high-grade, depending on the extent of the abnormal cell growth. Low-grade cervical dysplasia progresses very slowly and often gets better on its own. High-grade cervical dysplasia can lead to cervical cancer. Without treatment, 30 - 50% of cases of severe cervical dysplasia progress to invasive cancer. The risk of cancer is lower for mild dysplasia.

Cervical dysplasia is associated with the human papillomavirus (HPV), a sexually transmitted virus. A vaccine is available to protect against HPV, and regular Pap tests can usually find cervical dysplasia and treat it in its early stage. Currently, 11% of U.S.

women report that they do not have regular Pap tests (Gingelmaier, Grubert & Kaestner, 2007).

Invasive cervical cancer develops from precursor lesions of the cervix called cervical intraepithelial neoplasia (CIN). Progression from normal tissue to invasive cervical cancer occurs through a series of increasing grades of cervical dysplasia (Figure 1). CIN I represents mild dysplasia and has a high rate of spontaneous remission (60%) and a low rate of progression to carcinoma. In contrast, approximately 38 percent of CIN II and III, moderate to severe dysplasia, will spontaneously regress, and 16-36 percent will progress to invasive cervical cancer (Mitchell, Tortolero-Luna & Wright, et.al., 1996). Because reporting for CIN is not mandatory, the exact incidence is unknown. However, it is estimated that 2.5 million women are diagnosed with low-grade cervical abnormalities annually (Kuruman, Henson & Herbst, et.al., 1994).

Cervical dysplasia is a premalignant or precancerous change to the cells of the cervix. There are three types of cervical dysplasia: mild, moderate, and severe. Mild dysplasia is by far the most common, and probably is not a true premalignant disease. Mild dysplasia generally represents a tissue response to the HPV virus. Up to 70% of women with mild dysplasia will have the cells become normal without any treatment. However, even mild dysplasia can progress to more significant disease. Moderate and severe dysplasia are treated when they are discovered, because of their higher rates of turning into cancer (Kuruman et al., 1994).

### **Risk Factors**

It is undisputed that infection with sexually acquired HPV is the primary risk factor for cervical cancer and plays a critical role in cervical carcinogenesis (Koutsky, Holmes

& Critchlow, et al. 1992, Schiffman, Bauer & Hoover, et al. 1993). Several other cofactors have been implicated in the progression of low-grade to high-grade lesions and/or the development of cervical cancer, but these remain controversial in clinical trials (Tabrizi, Fairly & Chen, et al., 1999). These include early age at first intercourse, history of multiple sexual partners, oral contraceptive use (The new Zealand Contraception and Health Study Group, 1994), high parity, low socioeconomic status, poor diet, cigarette smoking (Ho, Kadish & Burk, et al., 1998), immunosuppression (Palefsky & Holly, 1995), and promiscuous male sexual partners (Munoz & Bosch, 1989). In one study, with respect to current use, the risk for cervical dysplasia increased for women who had been using oral contraceptives longer than 10 years and dietary deficiencies in Vitamin A, Vitamin B9, Vitamin C and Vitamin E (de Vet, Knipschild & Sturmans, 1993).

HPVs, also called human papillomaviruses, are a group of more than 150 related viruses. More than 40 of these viruses can be easily spread through direct skin-to-skin contact during vaginal, anal, and oral sex (Division of STD Prevention, 1999). HPV infections are the most common sexually transmitted infections in the United States. In fact, more than half of sexually active people are infected with one or more HPV types at some point in their lives. Recent research indicates that, at any point in time, 42.5 percent of women have genital HPV infections, whereas less than 7 percent of adults have oral HPV infections (Hariri, Unger & Sternberg, 2011; Gillison, Broutian & Pickard, 2012,). Sexually transmitted HPVs fall into two categories:

Low-risk HPVs, which do not cause cancer but can cause skin warts (technically known as condylomata acuminata) on or around the genitals or anus. For example, HPV types 6 and 11 cause 90 percent of all genital warts.

High-risk or oncogenic HPVs, which can cause cancer. At least a dozen high-risk HPV types have been identified. Two of these, HPV types 16 and 18, are responsible for the majority of HPV-caused cancers.

High-risk HPV infection accounts for approximately 5 percent of all cancers worldwide (Parkin, 2006). However, most high-risk HPV infections occur without any symptoms, go away within 1 to 2 years, and do not cause cancer. These transient infections may cause cytologic abnormalities, or abnormal cell changes, that go away on their own. Some HPV infections, however, can persist for many years. Persistent infections with high-risk HPV types can lead to more serious cytologic abnormalities or lesions that, if untreated, may progress to cancer (National Cancer Institute, 2012).

The overall HPV prevalence was 26.8% (95% confidence interval [CI], 23.3%-30.9%) among US females aged 14 to 59 years (n = 1921). HPV prevalence was 24.5% (95% CI, 19.6%-30.5%) among females aged 14 to 19 years, 44.8% (95% CI, 36.3%-55.3%) among women aged 20 to 24 years, 27.4% (95% CI, 21.9%-34.2%) among women aged 25 to 29 years, 27.5% (95% CI, 20.8%-36.4%) among women aged 30 to 39 years, 25.2% (95% CI, 19.7%-32.2%) among women aged 40 to 49 years, and 19.6% (95% CI, 14.3%-26.8%) among women aged 50 to 59 years. HPV vaccine types 6 and 11 (low-risk types) and 16 and 18 (high-risk types) were detected in 3.4% of female participants; HPV-6 was detected in 1.3% (95% CI, 0.8%-2.3%), HPV-11 in

0.1% (95% CI, 0.03%-0.3%), HPV-16 in 1.5% (95% CI, 0.9%-2.6%), and HPV-18 in 0.8% (95% CI, 0.4%-1.5%) of female participants.

Genital HPV types are categorized according to their epidemiological association with cervical cancer. Infections with low-risk types, such as HPV types 6 and 11, can cause benign or low-grade changes in cells of the cervix, genital warts, and recurrent respiratory papillomatosis. High-risk HPV types can cause cervical, anal, and other genital cancers. High-risk HPV types are detected in 99% of cervical cancers, and worldwide approximately 70% of cervical cancers are due to HPV types 16 and 17 (Walboomers, Jacobs & Manos MM et al., Bosch & de Sanjose ). Although HPV infection is common, studies suggest approximately 90% of infections clear within 2 years (Moscicki, Shiboski & Broering et al., Franco EL, Villa & Sobrinho et al., 1998). There is no treatment to rid the body of HPV, but 80% of infections are cleared by the body's immune system. For the 20% who develop chronic infection with HPV, the risk of cervical cancer is higher.

Cervical cancer is the second most common cancer in women worldwide. Approximately 500,000 new cases are diagnosed annually worldwide, 83% of which will be in developing countries (estimated 10,370 new cases in the US in 2005). There will be an estimated 273,000 deaths due to the disease annually, three-fourths of these in developing countries.

There are 40 strains of HPV that can affect the anal and genital tracts and these are further divided into low risk and high risk strains. Thirteen strains are considered high risk, or more likely to progress to high grade lesions (HSIL, CIN 2 or 3) and possibly cancer, if not cleared by the immune system. These strains are: 16, 18, 31, 33,

35, 39, 45, 51, 52, 56, 58, 59, and 68. Strains 16 and 18 are by far the most common types, and one or both are present in approximately 70% of cervical cancers worldwide. Only a very small percentage of high risk HPV infections will ever become invasive cancer (estimated at 2%). The time between initial exposure and the development of cancer can vary from months to years, but the average time is thought to be 15 years. The high risk HPV strains do not usually cause any symptoms to alert someone that they have the infection. The low risk strains are not considered a risk for cervical cancer, but they can cause low grade lesions (CIN 1) and several of these strains can cause genital warts (National Cancer Institute, 2012). Over 100 Strains of HPV have no cure including those in the following categories:

Low-risk HPV types (6, 11, 42, 43, 44, 54, 61, 70, 72, and 81) are virtually never found in cancers. Therefore, they are also called non-carcinogenic HPV.

High-risk HPV types (16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 68, 73, and 82) have been identified in cancers of the cervix, vagina, vulva, anus, and penis.

Therefore, they are also called carcinogenic or oncogenic HPV.

Dysplasia that is seen on a biopsy of the cervix is called cervical intraepithelial neoplasia (CIN). It is grouped into three categories:

CIN I -- mild dysplasia

CIN II -- moderate to marked dysplasia

CIN III -- severe dysplasia to carcinoma in situ (National Cancer Institute., 2012).

The high grade lesions (HSIL), CIN 2 and 3, and carcinoma in situ, are almost always caused by the so-called "high risk" HPVs, specially types 16 and 18. In at least 50% of the time they occur without previous documentation of a LSIL lesion. Laura A Koutsky

et al., of the University of Washington, Seattle, in 1992 studied prospectively a cohort of 241 women who presented for evaluation of sexually transmitted disease and had negative cervical cytologic tests. The women were followed every four months with cytologic and colposcopic examinations of the uterine cervix and tests for HPV DNA and other sexually transmitted diseases. Cervical intraepithelial neoplasia grade 2 or 3 was confirmed by biopsy in 28 women. All 24 cases of cervical intraepithelial neoplasia grade 2 or 3 among HPV-positive women were detected within 24 months after the first positive test for HPV ((Koutsky, Holmes, Critchlow Stevens, Paavonen, Beckmann, Derouen, Gallowa, Vernon & Kiviat, 1992; Schwartz, Hadjimichael, Lowell, Merino & Janerich, 1996)

### **Cervical Dysplasia Treatment**

Treatment of cervical dysplasia depends on the severity, the presence of HPV, risk factors, and patient's preference. For ASCUS and mild dysplasia (low-grade SIL/CIN I), the physician may perform HPV typing. If no virus or a low-risk strain is present, Pap smears may be repeated at 4- to 6-month intervals because ASCUS and mild dysplasia often resolve without intervention. If a high-risk strain of HPV is present, colposcopy and biopsy may be indicated and treatment depends on the results of the procedures. High-grade lesions require treatment. There are several methods available to remove the abnormal tissue, including electrocauterization, cryosurgery, laser vaporization, and surgery (Stanley & Swierzewski, 2011).

### **Electrocauterization**

Loop electrosurgical excision procedure (LEEP) emits low-voltage, high-frequency radio waves through a thin loop of wire. Electrical current quickly and safely

cuts away abnormal tissue. The procedure takes about 10 to 30 minutes and is performed in the doctor's office or as an outpatient in the hospital. LEEP allows the removed tissue to be examined by a pathologist to ensure that the lesion was completely removed and to provide an accurate assessment. This type of treatment is typically used in cases of high grade cervical dysplasia (Stanley & Swierzewski, 2011).

### **Cryosurgery and Cryocauterization**

Cryosurgery and Cryocauterization are relatively safe and simple procedures. In cryosurgery, the physician uses a carbon dioxide-cooled probe (also called a cryoprobe) to freeze and kill abnormal cells and the tissue then sloughs off. It is performed in the physician's office. In cryocautery, an electric probe is used to cauterize the abnormal cells. These procedures do not allow abnormal tissue to be saved for pathological examination (Stanley & Swierzewski, 2011).

### **Laser Vaporization or Ablation**

This procedure is performed in the hospital under general or local anesthesia. A laser is used to destroy abnormal surface cells. As with cryosurgery, it is impossible to obtain a specimen for pathologic examination. This procedure may cause less cervical scarring than cryosurgery. Cervical scarring makes the cervix more difficult to visualize. In this study (using retrospective case study method), it will be my objective to demonstrate the effectiveness of acupuncture and Chinese herbal treatments in lowering the CIN level of cases of cervical dysplasia. The purpose of the current research study is to facilitate the inclusion of traditional Chinese medicine treatments into the predominant western medical culture. By examining, quantifying, and evaluating the efficacy of Traditional Chinese medicine through the same methods and



standards of western medicine, we may increase the possibility of its inclusion in western culture. The ultimate goal of this research is to one day give patients suffering from cervical dysplasia a multitude of options that they can not only choose from but live with as well. In the future, it may be possible to expand the number of options the patient has to reflect their specific needs, but their lifestyle and values too.

## **Virology**

Papillomaviruses are members of the Papovaviridae family. HPV is a small, nonenveloped virus, with a diameter of 55nm. It has an icosahedral capsid composed of 72 capsomers, which contain at least two capsid proteins, L1 (major) and L2 (minor). Each capsomer is a pentamer of the major capsid protein. Each virion capsid contains several copies (about 12 per virion) of the minor capsid protein. The HPV genome consists of a single molecule of double-stranded, circular DNA containing approximately 7.900 bp associated with histones (Favre, 1975). The genome is functionally divided into three regions. The first is a noncoding upstream regulatory region (URR). This region contains the p97 core promoter along with enhancer and silencer sequences that regulate DNA replication by controlling the transcription of the “early” and “late” regions. The URR region also contains the highest degree of variation in the viral genome. The second is the “early” region, which include the genes E1, E2, E3, E4, E5, E6, E7 and E8. This region is involved in viral replication and oncogenesis. Expression of the early gene products determines whether an HPV infection is active or latent, or leads to malignant transformation. The third is the “late” region, which encodes the L1 and L2 structural proteins for the viral capsid. HPV gene functions are showed in table 2.

Table 2. Human papillomavirus gene functions

Gene Category	Gene Function
E1	Viral replication
E2	Modulation of transcription and replication
E3	Unknown
E4	Productive viral infections
E5	Transforming properties
E6	Oncoprotein; interaction with p53 protein
E7	Oncoprotein; interaction with pRb protein
E8	Unknown

## Late Gens

L1	Major capsid protein
L2	Major capsid protein

Data from (Anderson, 2002).

A new HPV type is defined as showing less than 90% homology to any of the known types on the basis of the E6, E7, L1 regions. If between 2% and 10% DNA divergence is present, the two viruses are considered subtypes of the same HPV type. When they show less than 2% divergence, the viruses are considered variants (Galloway. In: Holmes, Sparling, Mardh, Lemon, Stamm, Piot & J.N, 1999). Some variants have different biological and biochemical properties important in cervical

cancer. Eighty-six complete genomes of HPV have been characterized and about 120 are partially characterized (de Villiers, 2001).

### **Pathogenesis**

Transmission of HPV occurs primarily by skin-to-skin contact. Basal cells of stratified squamous epithelium may be infected by HPV. Other cells types appear to be relatively resistant. It is assumed that the HPV replication cycle begins with entry of the virus into the cells of the basal layer of the epithelium. It is likely that HPV infection of the basal layer requires mild abrasion or microtrauma of the epidermis. Once inside the host cell, HPV DNA replicates progress to the surface of the epithelium. In the basal layer, viral replication is considered to be non-productive, and the virus establishes itself as a low-copy number episome by using the host DNA replication machinery to synthesize its DNA on average once per cell cycle (Flores & Lambert, 1997). In the differentiated keratinocytes of the suprabasal layer of the epithelium, the virus switches to a rolling-circle mode of DNA replication, amplifies its DNA to high copy number, synthesizes capsid proteins, and causes viral assembly (Flores, Allen, Lee, Sattler & Lambert, 1999).

### **Natural history of cervical cancer**

The pathogenesis of cervical cancer is initiated by HPV infection of the cervical epithelium during sexual intercourse. Even though a high percentage of sexually active young women are exposed to HPV infections, only a very small percentage go on to develop cervical cancer (Elfgren, Kalantari, Moberger, Hagmar & Dillner, 2000). Several studies have suggested that most women successfully clear the HPV infection, presumably through the action of a competent immune system. Approximately, 90% of

lesions regress spontaneously within 12 to 36 months (Chua & Hjerpe, 1996). Other factors such as genetic predisposition, frequency of reinfection, intratypic genetic variation within HPV type, coinfection with more than one HPV type and hormone levels may also influence the ability to clear an HPV infection. The evidence for the importance of the host immune system in preventing the development of cervical disease comes from the analysis of HPV infections in human immunodeficiency virus (HIV)-positive women. HPV infections with high-risk viral types, persistence of HPV infection and the presence of squamous intraepithelial lesions are more common within this immunocompromised group than in immunocompetent women (Cubie, Seagar, Beattie, Monaghan & Williams, 2002).

The host cellular immune response is mediated by cytotoxic T cells and requires the interaction of viral epitopes with histocompatibility class I molecules (Ostor, 1993). A humoral immune response also develops, but local levels of HPV-specific immunoglobulin G (IgG) and IgA in tissue do not correlate with clearance of virus (Ostor, 1993). However, systemic levels of HPV-specific IgA have been correlated with virus clearance. In contrast, systemic levels of HPV-specific IgG have been detected more frequently in patients with persistent HPV infection (Ostor, 1993). The natural history of cervical cancer is a continuous disease process that progress gradually from mild cervical intraepithelial neoplasia (CIN) to more severe degrees of neoplasia (CIN 2 or CIN 3) and finally to invasive cancer (Holowaty, Miller, Rohan & To, 1999).

It is plausible that high-risk HPV infection occurs early in life, may persist, and in association with other factors promoting cell transformation, may lead to a gradual progression to more severe disease (Ho, Burk, Klein, Kadish, Chang & Palan, 1995).

A model for the development of cervical cancer is presented in figure 2. Mild and moderate dysplasias are associated with continued viral replication and virus shedding, and most of these lesions spontaneously regress. Progression to high-grade lesions (CIN 2/3) and ultimately invasive cancer is usually associated with conversion of the viral genome from an episomal form to an integrated form, along with inactivation or deletion of the E2 region and expression of the E6/E7 product genes. Some investigators have correlated HPV type with different degrees of CIN and have suggested that CIN 1 and CIN 2/3 are distinct processes, with CIN 1 indicating a self-limited sexually transmitted HPV infection and CIN 2 or CIN 3 being the only true cervical cancer precursor (Holowaty et al., 1999). Progression to cancer generally takes place over a period of 10 to 20 years. Some lesions become cancerous more rapidly, sometimes within two years (Holowaty et al., 1999).

Sexual activity at an early age also have an increased risk of HPV infection, as does a history of other sexually transmitted diseases, genital warts, abnormal Pap smears or penile cancer in an individual or sexual partner (Franco, Duarte & Ferencz, 2001). Condom usage may not adequately protect individuals from exposure to HPV since the virus can be transmitted by contact with infected tissues that are not protected by a condom. In addition to sexual activity, age is an important determinant of risk of HPV infection. Most cervical cancers arise at the squamocolumnar junction between the columnar epithelium of the endocervix and the squamous epithelium of the ectocervix. At this site, there are continuous metaplastic changes. The greatest risk of HPV infection coincides with greatest metaplastic activity. Greatest metaplastic activity occurs at puberty and first pregnancy and declines after menopause. The HPV

prevalence reaches its peak in young adults (18 to 30 years of age) and declines at older ages (Burk, Kelly, Feldman, Bromberg, Vermund & Deltovitz, 1996). As many as 46% of college women may have an HPV infection of the genital tract (Bauer, Ting, Greer, Chambers, Tashiro & Chimera, 1991). However, cervical cancer is more common in women older than 35 years, suggesting infection at a younger age and slow progression to cancer (Gomez & Lopez Santos, 2007).

### **Viral factors**

Persistent cervical infection (often defined as an infection that is detected more than once in an interval of 6 months or longer) with an oncogenic HPV type (especially HPV-16 and HPV-18) is the most important risk factor for progression to high-grade dysplasia and invasive cancer (Ho, Burk, Klein, Kadish, Chang & Palan, 1995).

The risk of progression depends on the HPV type. A 4-6 year follow-up of 1.643 women with normal cytology showed that women with a positive PCR high-risk HPV DNA test at baseline were 116 times more likely to develop CIN 3 than women with a negative DNA test (Rozendaal, Walboomers, van der Linden, Voorhorst, Kenemans & Helmerhorst, 1996).

The risk of progression for HPV-16 and HPV-18 is greater than for other HPV types, approximately 40% (Kiviat & Koutsky, 1993). It has been proposed that the viral load correlates directly with the severity of disease. Studies using quantitative type-specific PCR for high-risk HPV and low-risk HPV have shown that HPV-16 can reach much higher viral loads than the other types, and that only for HPV-16 high viral loads correlate with increased severity of cervical disease (Swan, Tucker, Tortolero, Follen, Wideroff & Unger, 1999).

Other studies using Hybrid Capture IITM (Digene Diagnostics, Gaithersburg, MD) have shown an increased viral load of high-risk HPV types in high-grade lesions (Tena, Garrido, Menéndez, Delgado, Romanyk & González-Palacios, 2005). However, high-risk HPVs are able to induce malignant tumors even when they are present at low levels. An important emerging factor in the development of cervical neoplasia is the role of HPV variants. HPV variants differ in biological and chemical properties and pathogenicity (Giannoudis & Herrington, 2001).

The oncogenicity of specific HPV variants appears to vary geographically and also with the ethnic origin of the population studied. Based on sequence variation of L1, L2 and URR regions of HPV-16, five variants have been defined for HPV-16: European (E), Asian (As), Asian-American (AA), African-1 (Af1) and African-2 (Af2). Asian-American variants might have enhanced oncogenic activity compared to European isolates due to an increased transcriptional activity (Quint, Scholte, van Doorn, Kleeter, Smits & Lindeman, 2001).

Several studies have shown that infections with multiple types of HPV can occur (Quint, Scholte, van Doorn, Kleeter, Smits & Lindeman, 2001), (Kleeter, van Doorn, Schrauwen, Molijn, Sastrowijoto & Terscheget, 1999). The majority of multiple infections contain two HPV types, but samples with two, three, four or five types were also seen (Quint et al., 2001). The presence of multiple HPV types tended to increase with the severity of cervical disease. Multiple HPV types, usually with at least one type classified as high-risk, were found in 12% of patients with normal cytology and in 35% of patients with mild or moderate dysplasia (Kleeter et al., 1999).

## **Nonviral factors**

The primary immune response to HPV infection is cell mediated; therefore, conditions that impair cell-mediated immunity such as renal transplantation or HIV disease, increase the risk of acquisition and progression of HPV (Sun, Kuhn, Ellerbrock, Chiasson, Bush & T.C, 1997).

The URR region of HPV contains sequences similar to the glucocorticoid responsive elements that are inducible by steroid hormones such as progesterone (the active component of oral contraceptives). Long-term use of oral contraceptives is a significant-risk factor for high-grade cervical disease according to some studies (Adam, Berkova, Daxnerova, Icenogle, Reeves & Kaufman, 2000). Cervical cancer risk also seems to be independently influenced by other variables including current smoking and parity (Adam et al., 2000). Local immune suppression induced by smoking and the mutagenic activity of cigarette components have been demonstrated in cervical cells, and may contribute to persistence of HPV or to malignant transformation similar to that seen in the lung (Yang, Jin, Nakao, Rahimtula, Pater & Pater, 1996).

It appears that smoking is the most important risk factor independent of HPV infection for higher grades of cervical disease (Adam, Berkova, Daxnerova, Icenogle, Reeves & Kaufman, 2000). Multiple pregnancies were a significant independent risk factor among women with histopathologic evidence of HPV infection in biopsy specimens and among women with CIN 2/3 (Adam et al., 2000). Other factors such as alcohol consumption and diet have not been well established. There has been some suggestion that sexually transmitted viruses may serve as cofactors in the development



of cervical cancer. It has been postulated that coinfection with herpes simplex virus type 2 may play a role in the initiation of cervical cancer (zur Hausen, 1992).

Cytomegalovirus (CMV), human herpesvirus 6 (HHV-6) and HHV-7 have also been detected in the cervix. Coinfection offers the opportunity for these viruses to interact with HPV. Recent studies using PCR to detect CMV, HHV-6 and HHV-7 in women with abnormal cytologic test results indicate that these viruses are only bystanders rather than cofactors in the development of cervical cancer (Chan, Chan, Li, Chan, Cheung & Cheung, 2001). Chlamydia trachomatis infection has been associated with cervical cancer, but the meaning of this association remains unclear. Some authors have suggested that the association between C. trachomatis infection and cervical cancer may be due to an effect of Chlamydia infection on persistence of high-risk HPV (Samoff, Koumans, Markowitz, Stemberg, Sawyer & Swan, 2005).

Genetic predisposition was found to be a great component in cervical cancer (Magnusson, Lichtenstein & Gyllenstein, 2000). Genetic heritability was found to account for 27% of the effect of underlying factors for tumor development. Heritability could affect many factors contributing to the development of cervical cancer, including susceptibility to HPV infection, ability to clear HPV infection, and time to development of disease. The effect of shared familial environment was shown to be small at 2% and was found only between sisters and not between mother and daughter (Magnusson et al., 2000).

## LEEP Studies

The study done by Noehr, Jensen, Frederiksen, Tabor and Kjaer, (2009), to investigate the association between cone depth of the loop electrosurgical excision procedure (LEEP) of the cervix and subsequent risk of spontaneous preterm delivery. The method included all deliveries in Denmark over a 9-year period, 1997-2005, with information obtained from various public health registries. Of the 552,678 singleton deliveries included in the study, 19,049 were preterm and 8,180 were subsequent to LEEP. Of the 8,180 deliveries with prior LEEP, 273 were subsequent to two or more LEEPs. Of the deliveries subsequent to only one LEEP, we extracted information about cone depth on 3,605 deliveries, of which 223 were preterm (6.2%). Logistic regression analyses were used to evaluate association between cone characteristics and the subsequent risk of preterm delivery, with simultaneous adjustment for potential confounders.

The results showed increasing cone depth was associated with a significant increase in the risk of preterm delivery, with an estimated 6% increase in risk per each additional millimeter of tissue excised (odds ratio 1.06, 95% confidence interval 1.03-1.09). Severity of the cone histology and time since LEEP were not associated with the risk of preterm delivery. Having had two or more LEEPs increased the risk almost fourfold for subsequent preterm delivery when compared with no LEEP before delivery, and almost doubled the risk when compared with one LEEP before delivery. The conclusion was that increasing cone depth of LEEP is directly associated with an increasing risk of preterm delivery, even after adjustment for several confounding factors.

The study done by Nøhr, Tabor, Frederiksen and Kjaer (2007) investigated the association between loop electrosurgical excision procedure (LEEP) and other potential risk factors, and subsequent preterm delivery (<37 weeks), using data from a large cohort study of Danish women. The Danish prospective cohort study was initiated in 1991, with the original aim of investigating the role of human papillomavirus in the natural history of cervical neoplasia. The study included 11,088 women aged 20-29. The cohort was invited for 2 follow-up examinations in 1993-1995 and 1999-2000, respectively. At all 3 examinations, the women answered questions about a number of different lifestyle variables. We assessed the relationship between preterm delivery and potential risk factors, such as previous LEEP treatments, smoking during pregnancy, age, parity and previous preterm delivery. The cohort was followed until 2004, through linkages with the nationwide Pathology Data Bank and the Medical Birth Registry. The results were the 14,982 deliveries in the cohort during follow up, 542 were preterm (21-37 weeks). Among deliveries with no previous LEEP, 3.5% ended as a preterm delivery, whereas this applied to 6.6% among deliveries following a LEEP, yielding a significantly increased risk of preterm birth after LEEP (OR=1.8; 95% CI: 1.1-2.9). The strongest risk factor for preterm delivery was a previous preterm delivery (OR=2.3; 95% CI: 1.4-3.7). Other significant risk factors were smoking during pregnancy and low educational status. The study showed an almost 2-fold increase in the risk of preterm delivery after LEEP treatment. Thus, women in their reproductive age should be informed about the increased risk of preterm delivery, if treated with LEEP.

In a study completed by Sadler, Saftlas, Wang, Exeter, Whittaker and McCowan (2004), it is unclear whether treatments for cervical intraepithelial neoplasia (CIN)

increase the subsequent risk of preterm delivery. Most studies have lacked sufficient sample size, mixed heterogeneous subtypes of preterm delivery, and failed to control for confounding factors. This study was to determine whether cervical laser and loop electrosurgical excision procedure (LEEP) treatments increase risk of preterm delivery and its subtypes. The retrospective cohort study conducted among women evaluated at a colposcopy clinic serving Auckland, New Zealand (1988-2000), comparing delivery outcomes of untreated women (n = 426) and those treated (n = 652) with laser conization, laser ablation, or LEEP. Record linkage using unique health identifiers identified women who had subsequent deliveries. It was total preterm delivery and its subtypes, spontaneous labor and premature rupture of membranes before 37 weeks' gestation (pPROM). It was concluded the overall rate of preterm delivery was 13.8%. The rate of pPROM was 6.2% and the rate of spontaneous preterm delivery was 3.8%. Analyses showed no significant increase in risk of total preterm delivery (adjusted relative risk [aRR], 1.1; 95% confidence interval [CI], 0.8-1.5) or spontaneous preterm delivery (aRR, 1.3; 95% CI, 0.7-2.6) for any treatment. Risk of pPROM was significantly increased following treatment with laser conization (aRR, 2.7; 95% CI, 1.3-5.6) or LEEP (aRR, 1.9; 95% CI, 1.0-3.8), but not laser ablation (aRR, 1.1; 95% CI, 0.5-2.4). Moreover, risk of pPROM and total preterm delivery increased significantly with increasing height of tissue removed from the cervix in conization. Women in the highest tertile of cone height ( $\geq$  1.7 cm) had a greater than 3-fold increase in risk of pPROM compared with untreated women (aRR, 3.6; 95% CI, 1.8-7.5). This showed LEEP and laser cone treatments were associated with significantly increased risk of pPROM. Careful consideration should be given to treatment of CIN in women of reproductive

age, especially when treatment might reasonably be delayed or targeted to high-risk cases.

### **Western Medicince Studies**

The study of Flaws (1990) contains the western etiologies of cervical dysplasia, HPV description, and diagnosis, also western treatment of HPV infection in women. The remedial TCM treatment of cervical intraepithelial neoplasia (CIN), complications during remedial treatment of CIN, and the preventive treatment of CIN during remission. While Western medicine has made gains in preventing cervical dysplasia via HPV vaccinations, the treatment options remain limited. Prevention may be the best policy, but treatment options for those who are suffering now must improve and expand as well. The LEEP surgery procedure, although effective, carries significant risks such as subsequent preterm pregnancies. The nature of this surgery results in permanent damage to the cervical wall and there is no known remedy to this side effect. This research hopes to illuminate effective alternatives, such as Traditional Chinese medicine, that can provide just as much treatment to the cervical dysplasia while avoiding the damaging side effects of surgery. Through the application of acupuncture techniques and herbal prescriptions, Traditional Chinese medicine seeks to focus the body's own natural resources and abilities to treat the illness directly without the side effects of drugs or surgeries.

### **TCM Considerations**

Traditional Chinese Medicine considers the whole body when looking at disease and disharmony. A detailed intake process helps Chinese medicine practitioners understand the root of the disharmony. The initial intake process considers the patient's

internal condition as well as looking at their lifestyle, environment, and habits.

Additionally, the diagnosis process relies upon palpation of the pulse and abdomen and observation of the tongue. Chinese medicine practitioners use all of this information to diagnose the root cause and pathway of the disharmony, based on TCM pattern diagnosis. Once a diagnosis has been made the practitioner will develop a treatment plan that is based upon the individual constitution of the patient. Drawings of tumors have been found on turtle shells and "oracle bones" dating from the eleventh century B.C. Medical texts dating from 200 B.C. have detailed descriptions of tumors and their causes. Cancer is well known and well documented in Chinese medical literature. Yet there is no word for cancer in Traditional Chinese Medicine (TCM). This is because Chinese medicine has always regarded cancer as several different diseases rather than a single disease. Ironically, modern physicians are beginning to recognize this as well. Perhaps in our search for "the cure", we can find a measure of help in the vast experience of Chinese medicine. Chinese holistic herbal medicine for cancer is based on the principle of Fu Zheng Gu Ben. "Fu Zheng" means strengthening what is correct. "Gu Ben" means regeneration and repair. Treating cancer with Chinese herbs requires diagnosing according to the four examinations. The aim of treatment is to harmonize the patient as well as to attack cancer.

### **Herbs to Reduce Stagnation**

The accumulation (tumor) is attacked with strong blood breaking and anti-cancer herbs. Herbs will differ according to the location of the cancer. Because many patients receive chemotherapy, and because toxicity may be a disease factor, anti-toxic herbs are often added (Kawai, 2008).

## Chinese Formulas

The following Chinese formulas have been used to treat cervical dysplasia:

Reishi Mushroom

Shitake Mushroom

Colorious Mushroom

Maitake Mushroom

Agaricus Mushroom

Medicinal mushrooms and mushroom extracts are used worldwide to fight cancer and enhance and modulate immune response. *Lentinula edodes* (shiitake), *Grifola frondosa* (maitake), *Ganoderma lucidum* (mannentake), and *Cordyceps* have a history of medicinal use for millennia in parts of Asia. Research has indicated mushrooms have possible anti-cancer, antiviral, anti-inflammatory and liver-protective activities. These are six of the most well-researched anti-cancer mushrooms rich in polysaccharides and beta glucans, the primary active immune-enhancing constituents (Xu, Towers & Li, 2006).

Reishi Mushroom, AKA Ling Zhi, or Mannentake, "The Mushroom of Immortality," is one of the great longevity tonics of Chinese Medicine used in cancer treatment in Traditional and Modern Chinese Medicine to improve vitality, strength, stamina, and to prolong life. Reishi enhances immune response, alleviates chemotherapy side effects such as nausea and kidney damage, and protects cellular DNA by raising antioxidant capacity (Chilkov, 2012). Reishi contains polysaccharides that are effective in suppressing cancer cells. Research by Dr. Fukumi Morishiga at the Linus Pauling Institute of Science and Medicine took a hot water extract of Reishi (which concentrates

the active ingredients) and showed that when used in conjunction with vitamin C (which humans, unlike animals, cannot make), macrophage activity was greatly stimulated. In his paper he showed that all manner of cancers from brain tumours to breast cancer regressed over time (Chilkov, 2012).

Shiitake (*Lentinula edodes*), AKA Black Forest Tree Mushroom, or Xiang Gu (Fragrant Mushroom) is a tender and tasty mushroom found in many Asian cuisines. It is considered both a delicacy and a medicinal mushroom. Shiitake contains a glucan called AHCC (Active Hexose Correlated Compound) and is widely used in alternative and complementary treatment of cancer in Japan due to its immune-enhancing functions. Lentinan, a compound found in Shiitake, is used as an intravenous anti-cancer drug with antitumor properties. Clinical studies have associated lentinan with a higher survival rate, higher quality of life and lower recurrence of cancer (Chilkov, 2012). Shiitake has been used in medicine for years as a blood “balancer” and particularly for lowering cholesterol levels. The National Cancer Center in Tokyo isolated lentinan, one of the active ingredients, and showed that the extract could reduce tumours in mice by 80 to 100 percent (Chilkov, 2012).

*Coriolus versicolor* (*Trametes versicolor*), AKA "Turkey Tail Mushroom" or Yun Zhi is one of the most well-researched medicinal mushrooms in the world. It is a biological response modifier. Turkey Tail has been used in Chinese Medicine as a tonic for centuries. Studies show that it improves survival rates and acts as an immune modulator with immune stimulating and anti-tumor properties. Some studies show that it can enhance the effects of chemotherapy cancer treatment and reduce the side effects of radiation therapy (Chilkov, 2012).



Maitake (*Grifola Frondosa*), AKA Cloud Mushroom, or Hui Shu Hua, is used in traditional Chinese and Japanese medicine to enhance the immune system. It is one of the major mushrooms in Japanese cooking. Studies have shown that it can enhance both the innate immune response to fight infections as well as adaptive immune response conferring long-term immune enhancement. Maitake also protects cells with its antioxidant properties and decreases the inflammatory factor COX2 enzyme; the enzyme common in cancer physiology. Studies have also shown that Maitake has potential anti-metastatic properties inhibiting the proliferation and spread of cancer (Chilkov, 2012).

*Cordyceps Sinensis*, AKA Chinese Caterpillar Fungus, or Dong Chong Xia Cao, acts as an immune stimulator by raising cancer- and virus-fighting T Cells and Natural Killer Cells and prolongs the life of white blood cells, improving resolution of infections. It has demonstrated anti-tumor properties and also protects the kidneys from chemotherapy side effects. It is one of the most widely used tonics in anti-cancer formulas in Chinese Medicine (Chilkov, 2012).

Agaricus Mushroom (*Agaricus blazei murill*), or Ji Song Rong, is a mushroom that originated in the rainforests of Brazil. The mushroom thrives in certain tropical areas of China and the Chinese have become the premier growers of Agaricus for the world. Agaricus is traditionally known as "God's Mushroom" because of its near miraculous curative benefits to a wide range of disorders. People have used it to overcome numerous diseases and disorders relating to the immune system, cardiovascular system, digestion, and for weight management, diabetes, chronic and

acute allergies, cataracts, hearing difficulties, stress syndrome, chronic fatigue, diarrhea, constipation, and disorders of the liver (Kaphle, Wu, Yang & Lin, 2006).

The researcher uses these mushroom formulas to promote the functions of the immune system. The human immune system is a network of cells, tissues, and organs that work together as well as independently to defend the body against illness caused by microbes, bacteria, parasites, and fungi that cause infection (NISD, 2012). A strong immune system promotes quick cell development and regeneration. Only through swift regeneration can damaged cells be replaced with healthy, fully-functioning, proper operating cells (NISD, 2012). To combat the serious infection of the Human papillomavirus, Traditional Chinese medicine offers remedies to promote the immune system through the use of these mushrooms.

### **Literature Review Integration**

There are a number of studies that demonstrate the application of Western medicine in the etiology treatment of cervical dysplasia (Rozendaal et al., 1996; Sweann et al., 1999; Giannoudis & Herrington, 2001; Quint et al., 2001; Moliijn et al., 1999,) LEEP surgical techniques have been utilized in many cases to treat cervical dysplasia (Noerh et al., 2009; Tabor et al., 2007; Sadler, et al., 2004). While Traditional Chinese Medicine has a long history in the treatment of cervical dysplasia, accounts of those treatments have been published only relatively recently (Chilkov, 2012; Kaphle et al., 2006). As a result the published evidence pertaining to the Traditional Chinese Medicine treatment of cervical dysplasia is limited, and a gap exists in the literature. It will be the purpose of the current research study to further fill that gap in the literature by

providing the details of two systematic cases of cervical dysplasia treated with Traditional Chinese Medicine.

### **Chapter Three: Method**

In this retrospective case study it will be the researcher's objective to demonstrate the effectiveness of acupuncture and Chinese herbal treatments in lowering the CIN level of cases of cervical dysplasia. The purpose of this research study is to facilitate the inclusion of traditional Chinese medicine treatments into the predominant western medical culture. By examining, quantifying, and evaluating the efficacy of Traditional Chinese medicine through the same methods and standards of western medicine, we may increase the possibility of its inclusion in western culture. The ultimate goal of this research is to one day give patients suffering from cervical dysplasia a multitude of options that they can not only choose from, but live with as well. In the future it may be possible to expand the number of options the patient has to reflect not only their specific needs, but their lifestyle and values too.

#### **Designation of Research Method**

Case study is an ideal methodology when a holistic, in-depth investigation is needed (Feagin, Orum, & Sjoberg, 1991). A case study is a research method based on an in-depth investigation of a single individual, group, or event. Case studies have been used in varied investigations, but increasingly in instruction as well (Shepard, 2003). Research methodologists, who have wide experience in this method, have developed robust procedures. Whether the study is experimental or quasi-experimental because of the focus on specific variables and factors, data collection and analysis methods often do not provide for the articulation of many important details. Case studies, on the other hand, are designed to bring out a multitude of details by using multiple sources of data (Stake, 1995).

The case study format and qualitative research approach is an effective way to document the full range of experience of women with cervical dysplasia who choose to treat with TCM to avoid LEEP surgery. Case study method allow for the description and discussion of many aspects of the process from diagnosis to treatment to results. The current study entailed the collection and analysis of data from two medical charts.

### **Inclusion and Exclusion Criteria**

Charts were selected on the following predetermined inclusion and exclusion criteria. The inclusion criteria for the case studies engaged in the current study specified a number of factors. Those factors include the following:

The case study subjects must be females.

The case study subjects have never be pregnant

The case study subjects must be between ages 21 to 43.

The case study subjects must have history of cervical dysplasia

The case study subjects must have CIN stage between II to III

The case study subjects must be use same Chinese herbal formula for treatment

The case study subjects have never had traditional western medicine treatment including any surgeries

The case studies must be instances of cervical dysplasia diagnosed by abnormal pap smear and biopsy by their OBGYN.

Depending on the lab terminology used, the CIN lesions observed are subdivided into dysplasias (mild, moderate, severe); cervical intraepithelial neoplasias (CIN I, II, and III); or low-grade and high-grade squamous intraepithelial lesions (LGSILs and HGSILs).

The case study subjects must be suggested LEEP surgery by their OBGYN.

The exclusion criteria were carefully selected through the case study subjects and include the following:

The case study subjects must not be males

The case study subjects cannot be females with no history of cervical dysplasia

The case study subjects should not have any fertility problem.

The case study subjects not have any health issue besides cervical dysplasia.

The case study subjects must not be on any medication.

The case study subjects must have no history of prior acupuncture or Chinese herbal medicine treatment.

### **Data Collection Form**

A data collection form was developed which provided a systematic means for recording data from the two charts. The following variables were included on the data collection form:

Age

Family Background (Married/Single/Divorced etc)

Occupation

Ethnicity

Number of treatments

Acupuncture points

CIN Grading

Herbals

A copy of the data collection form is included in Appendix A.

## Procedures

The current study included the collection and analysis of data from two medical charts from the researcher's practice office. The current study compared and contrasted two cases using same method of TCM treatment of cervical dysplasia. The two charts were reviewed and chosen as appropriate since they met both the inclusion and exclusion criteria. The charts include the cases of a 28 year old female, and a 39 year old female.

In this study, data were collected from medical charts based on SOAP intake in the researcher's office. The SOAP note (an acronym for "subjective, objective, assessment, and plan") is a method of documentation employed by health care providers to write out notes in a patient's chart, along with other common formats, such as the admission note. Documenting patient status in the medical record is an integral part of practice workflow starting with patient appointment scheduling, to writing out notes, to medical billing. Prehospital care providers such as EMTs may use the same format to communicate patient information to emergency department clinicians (Wikipedia., Jun 6, 2012).

The SOAP note format is used to standardize medical evaluation entries made in clinical records. The SOAP note is written to facilitate improved communication among all involved in caring for the patient and to display the assessment, problems and plans in an organized format. Many Electronic Health Records (EHR) systems are capable of producing SOAP Notes. The actual notes and other information contained within the EMR are commonly referred to as Electronic Medical Records or EMRs (Physicianssoapnotes., Jun 6, 2012).

Data were reported in charts showing differences and similarities between the two cases, their use of acupuncture, and Chinese herbal prescriptions to treat cervical dysplasia. The charts included age, race, marital status, diagnostic criteria, height and weight, and time spent for the acupuncture and Chinese herbal treatment. The charts include Chinese herbal formulas and acupuncture points. Data were also reported in the form of case descriptions for both patients.

Each case study was systematically reviewed with data being entered on the data collection instrument form as appropriate for each patient. Review of all case data collection forms to discern similarities and differences in the course of each patient's illness and the impact of TCM treatments.

### **Human Subjects Ethical considerations**

The current study was engaged exclusively by collection and analysis of data collected from the archived charts of the designated case study patients. No new data were collected, nor were any additional interviews or observation of the patients made. Additionally, all data were collected, managed and reported anonymously with no possibility of identification of the case study subjects. In the reporting of the data in this document fictitious names were used to identify each of the cases. As a result, this study qualified for exempt status from Institutional Review Board (IRB) procedures. The proposal for this research project was presented to Yo San University IRB in April 2012. The Yo San University IRB review resulted in a response letter which affirmed the exempt status of the study. A copy of the IRB response letter is included in Appendix B. In terms of risk to benefit ratio, this study resulted in more benefit than risk. The research process was entirely retrospective chart review involving no additional



gathering of data or interviewing of patients. It assumed that the conclusions that might be drawn from these case studies have a potential benefit to a large population of patients and practitioners. TCM treatment would help avoid LEEP surgery for women who suffer from cervical dysplasia. As for risks in this retrospective case studies, case charts and patients names' were carefully handled with caution. To minimize risk, in this study patients names were coded to initials, and no charts were copied or taken outside of the researcher's office.

## **Chapter 4 : Results**

This chapter will present the results of the current research study which used case study method to study the impact of acupuncture and Chinese herbal medicine on patients who have cervical dysplasia. The chapter will proceed with the presentation of data from the two case studies chosen for this research project. Each case study will begin with a brief description of the patient followed by her medical history, followed by the course of treatment in the researcher's office using Traditional Chinese Medicine. At the end of each case study a summary of the data collection form for each patient will be presented. After both case studies have been summarized, a table will be presented which highlights the similarities and differences between the two case studies.

This retrospective study employed qualitative analytic methods, such as finding themes within the data, categorizing the variables, and finding and discussing similarities and differences. Only two patient charts were evaluated for this study. The patients are referred to as Mary and Cathy. Descriptions of each case follow.

### **Mary's case**

Mary, a 39 year-old Asian women, presented cervical dysplasia after several biopsy tests by her OBGYN in July 2009. Her OBGYN recommended LEEP surgery to prevent cervical cancer, however she wanted to avoid LEEP surgery. She visited me in July of 2009 to receive acupuncture and herbal treatments as an alternative to LEEP surgery. Mary had her first pap smear test in March 2008 and it came back abnormal. She had a biopsy test 3 weeks later and the results pointed to cervical dysplasia. Her OBGYN recommended her to have LEEP surgery but she refused. She went to see a different OBGYN and had a pap smear test again in May 2008; the results were

negative. She went back to an annual pap smear test in June 2009; this time the results were positive. She underwent a biopsy 2 weeks later and she was diagnosed moderate level (CIN2) of cervical dysplasia. Her OBGYN suggested cryosurgery procedure. She accepted and underwent the procedure 3 weeks after the biopsy test. A month after cryotherapy procedure she had another biopsy test; the results were positive and her OBGYN strongly recommended LEEP surgery as soon as possible.

Mary has been married for 7 years and has worked for a bank for 10 years. Her job was very stressful, working long hours and usually sitting all day. She exercised regularly 2-3 times a week, including jogging or yoga. Sometimes it was hard to stay sleep even though she feels very tired. She had frequent urination and was prone to urinary tract infections. She has severe allergies in spring time such as congestion and itchy eyes.

Menarche was at age 14. She had never taken birth control pills. Her menstruation was irregular. The irregularity of her menstrual cycle was such that her periods came anywhere between 32 days to 90 days. When she turned 32 she started getting acupuncture treatment for back and knee pain regularly for 2 years and her menstrual cycle became regular, anywhere between 30 days to 34 days. The color was red on the first day and was typically heavy. There were some clots and dysmenorrhea. The second day was heavier and there were clots but cramps decreased. By day three and four, the flow had lightened up considerably. Premenstrually, Mary was moody, irritable, craved sugar, experienced decreased appetite, sleepiness, and retained water. She has never detected the signs or symptoms of ovulation, and did not know if

or when she ovulated. She had a normal libido, good lubrication, no sexual difficulties, no pelvic inflammatory disease, and no sexually transmitted disease.

There were no problems regarding her thyroid, skin, heart, lungs, breasts, urination or bowel movements. Her abdomen was soft, non-tender, non-distended, and without mass. Her external genitalia, vagina, uterus and ovaries were all within normal limits. There was no edema, and no fibroids.

### **First Visit: August 13th, 2009**

Mary presented slightly red and puffy tongue, scanty coating, teeth mark on the side, and red color tip. Her pulse was slippery and wiry. Left kidney pulse was weak. Her TCM diagnosis was phlegm-damp accumulation with heat and kidney yin deficiency. Points used were RN17, RN12, ST25 SP15, RN6, RN4, RN3, RN2, ST29, Zi Gong Xue, LI11, ST36, ST 40, SP6, SP9, KD3, Ying Tan. Ear points used were Uterus, Shen Men, Heart.

The herbal formula used was in powder form. It contains Reishi mushroom (3g), Maitake mushroom (3g), Shitake mushroom (3g), Agaricus mushroom (4g), Colorious mushroom (3g) 15 gram for 3 times a day on an empty stomach. I recommended douche 2-3 times a day with decoction containing Huang Qin, Huang Lian, Huang Bai. After douche, I recommended her to raise both her legs leave for 30 minutes. Her treatment plan included acupuncture treatments once a week, taking Chinese herbal formula everyday, and douching 2-3 times per week. After 3 months of treatment she took the biopsy test again.

**Second Visit: August 20th, 2009**

Her condition was same as first visit Points used were UB20, 23, 25, 28, UB31, UB32, UB33, UB34, GB20, 21, SP6, SP4, KD3 ,KD2, PC6, HT7, DU20. She continued to take same formula and douche. She received one treatment per week for 15 weeks. She took Chinese herbal formula every day. She douched every day except during menstruation periods. Treatment involved alternating anterior and posterior acupuncture points every week

**Subsequent Treatments**

After 15 weeks of treatment, she followed-up with her OBGYN; her CIN level has dropped from CIN2 to CIN1. She continued acupuncture treatment twice a month as well as continued taking Chinese herbal treatment. She also continued douche treatment twice a week. She receives Pap smear test every 6 months and monitors her cervical condition. Her cervical dysplasia has never progressed since.

**Cathy's case**

Cathy, a 28 year-old Latina woman, presented cervical dysplasia after biopsy tests in April 2010. She had a normal pap smear in March 2009. However she was found to have an abnormal pap smear April 2010. She had a biopsy, and it was positive with a moderate level (CIN2) of cervical dysplasia. Her OBGYN recommended LEEP surgery to prevent cervical cancer, however she wished to avoid LEEP surgery. Her friend recommended to her to pursue eastern medical treatment. She visited me in April 2010 to receive acupuncture and herbal treatments as an alternative to LEEP surgery.

Cathy is single and works for private clinic as a nurse. She had a boyfriend for almost six months, but separated in March 2010.

Menarche began at age 11. She had been taking birth control pills since age 18. Her menstrual cycle was 28 days. The color was red on the first 3 days with small clots and by day three and four, the flow had lightened up. She normally has abdominal cramps for the first two days. Premenstrually, Cathy was moody and irritable, suffered from fatigue, and sleepiness as well as retained water. She normally detected the cervical mucus during ovulation. Quality of cervical mucus is white and sticky. She had a normal libido, good lubrication, no sexual difficulties, no pelvic inflammatory disease. However she got a yeast infection in August of 2009. She saw her OBGYN and took medication.

There were no problems regarding her thyroid, skin, heart, lungs, or breasts. She has tendency to be constipated after ovulation periods. Her abdomen was tight, distended, and cold. Her external genitalia, vagina, uterus and ovaries were all within normal limits. There was no edema, and no fibroids.

**First visit: April 3rd, 2010**

Cathy was very nervous and emotional. She cried during intake. She presented pale purple tongue with thin sticky white coating, teeth mark on the side, and red tips. Her pulse was slightly rapid, and wiry slippery. Her TCM diagnosis was liver qi stagnation, spleen qi deficiency and phlegm- damp accumulation.

Points used were Ren17, Ren12, Ren9, Ren4, Ren3, Ren2, SP15, SP9, SP6, SP4, Zi Gong Xue, ST29, ST 36, ST40, LV3, LI4, PC6, Yin Tang, DU20, GB20.

The herbal formula used was in powder form. It contains Reishi mushroom (3g), Maitake mushroom (3g), Shiitake mushroom (3g), Agaricus mushroom (4g), Colorious mushroom (3g) 15 gram for 3 times a day on an empty stomach. I recommended douche 2-3 times a day with decoction containing Huang Qin, Huang Lian, Huang Bai. After douche, I recommend her to raise both her legs leave for 30 minutes.

### **Second Visit: April 10th 2010**

Cathy was calmer than first visit but still worried. She had a stressful week because of her work. She presented pale purple puffy moist tongue, white sticky coating on the roots of tongue, teeth mark on the side, and red tip. Her TCM diagnosis was liver qi stagnation, spleen qi deficiency, and phlegm- damp accumulation. Points used were RN17, RN12, RN6, RN4, RN3, RN2, SP15, SP9, SP6, SP4, Zi Gong Xue, ST29, ST 36, ST40, LV3, LI4, PC6, Yin Tang, GB20, Si Shen Chong. Ear points used were Uterus, Shen Men, Heart. I added Xiao Yao San for her herbal prescription. She continued to take same formula and douche.

### **Third Visit: April 17th, 2010**

Cathy was much calmer than at last treatment, however, she still had a lot of stress from her work. She presented pale purple moist tongue, white coating on the roots, teeth mark on the side, and red tip. Her TCM diagnosis was liver qi stagnation, spleen qi deficiency and phlegm- damp accumulation. Points used were UB15, UB17, UB18, UB20, UB23, UB25, UB28, UB31, UB32, UB33, UB34, GB20, 21, SP6, SP4, PC6, HT7, DU20. Cathy continued to take same formula and douche as second visit. She received one treatment per week for 19 weeks. She took the Chinese

herbal formula every day. She douched 3 times a week. Treatment involved alternating anterior and posterior acupuncture points every week.

### **Subsequent Treatments**

After 19 weeks of treatment, she has been cured completely. She monitors her cervical condition with Pap smear test (twice in for the first six months, now once annually.) She did not have any recurrence and has yet to detect any new abnormalities.

### **Western Medicine Treatment for Both Cervical Dysplasia Cases**

Cervical intraepithelial neoplasia (CIN), also known as cervical dysplasia and cervical interstitial neoplasia, is the potentially premalignant transformation and abnormal growth (dysplasia) of squamous cells on the surface of the cervix (Kumar, Abbas, Fausto, Nelson & Mitchell, 2007). Depending on several factors, such as the type of HPV and the location of the infection, CIN can start in any of the three stages, and can either progress or regress (Kumar et. al., 2007). The least risky type is CIN 1, representing only mild dysplasia, or abnormal cell growth. It is confined to the basal 1/3 of the epithelium. This type corresponds to infection with HPV and typically will be cleared by immune response in a year or though can take several years to clear (Agorastos, Miliaras, Lambropoulos, Chrisafi, Kotsis, Manthos & Bontis, 2005). CIN 2 is defined as moderate dysplasia confined to the 2/3 of the epithelium and CIN 3 is defined as severe dysplasia that spans more than 2/3 of the epithelium and may involve the full thickness. This lesion may also be referred as cervical carcinoma in situ (Agorastos. et al., 2005).



Mary was diagnosed with CIN 1 for two years and progressed to CIN 2. Cathy had never be diagnosed any cervical dysplasia before she was diagnosed with CIN 2. Mary had a pap smear test every 6 months after being diagnosed with CIN 1 for two years. Cathy had an annual pap smear test every year since she was 22 years old. Treatment for higher grade CIN involves removal or destruction of the neoplastic cervical cells by cryocautery, electrocautery, laser cautery, loop electrical excision procedure (LEEP), or cervical conization. Therapeutic vaccines are currently undergoing clinical trials. The lifetime recurrence rate of CIN is about 20%, but it isn't clear what proportion of these cases are new infections rather than recurrences of the original infection (Murthy & Mathew, 2000). Both of their doctors recommended to them LEEP surgery, however they refused and decided to have TCM treatment.

### **Traditional Chinese Treatment for Both Cervical Dysplasia Cases**

Both Mary and Cathy decided to not take LEEP surgery and received only Traditional Chinese Medicine treatment, including both acupuncture and Chinese herbs. We set forward with three months treatment and updated pap smear tests to check progress. Mary's TCM diagnosis was phlegm-damp accumulation with heat and kidney yin deficiency. Cathy's TCM diagnosis was liver qi stagnation, spleen qi deficiency and phlegm-damp accumulation. It is typical to see women with the same Western diagnosis of Cervical Dysplasia have different TCM diagnosis and different treatment plans (Lyttleton, 2004).

The first reference to virus infectious disease appeared in *Huang Di Nei Jing* (Yellow Emperor's Inner Classic), compiled in the first or second century CE. This text discussed *re bing* (hot disease), which refers to the various types of virus infectious

disease (Gilbert, Moellering & Sande, 1999). According to the theory, warm and hot disease plagued everyone, starting "from one person to the entire household, from one household to the entire street, and from one street to the entire village." The disease first affects the exterior of the body and progresses to the interior, following the patterns of wei (defensive), qi (energy), ying (nutritive) and xue (blood) levels (Wen Re Lun, 1745-1766). Furthermore, the cause of these warm and hot diseases have "no sound nor smell, and no shape nor shadow." In addition, the warm and hot disease may be transmitted from one person to another via "heaven (airborne)" or "earth (direct contact)," and affect individuals with low immunity (Wen Yi Lun, 1642). Prevention of the progression of virus infectious disease is certainly no exception since virus tend to adversely affect those who have weakened immune systems. Traditional Chinese medicine treats *wen bing* with heat-clearing herbs. Many of these herbs have remarkable antibiotic and antiviral effects, therefore I used exactly same Chinese formula for both of them to treat their cervical dysplasia CIN 2.

### **Chinese formulas**

The following Chinese formulas have been used in Traditional Chinese Medicine to treat cervical dysplasia and were used in both case studies examined in this research:

Reishi Mushroom

Shiitake Mushroom

Coriolus Mushroom

Maitake Mushroom

Agaricus Mushroom (Chilkov, 2012)

The researcher uses these mushroom formulas to promote the functions of the immune system. The human immune system is a network of cells, tissues, and organs that work together as well as independently to defend the body against illness caused by microbes, bacteria, parasites, and fungi that cause infection (NISD, 2012). A strong immune system promotes quick cell development and regeneration. Only through swift regeneration can damaged cells be replaced with healthy, fully-functioning, properly operating cells (NISD, 2012). To combat the serious infection of the Human papillomavirus, Traditional Chinese medicine offers remedies to promote the immune system through the use of these mushrooms.

### **Chinese Formula for Douche**

The following formula was used for douching: Huang Lian, Huang Bai, Huang Qin. This formula removes pernicious Heat and Toxins from the Three Burners. It is used to help a person who has Heat in all the Three Burners.

### **Mary's Acupuncture Treatment**

Mary presented slightly red and puffy tongue, scanty coating, teeth mark on the side, and red color tip. Her pulse was slippery and wiry. Left kidney pulse was weak. Her TCM diagnosis was phlegm-damp accumulation with heat and kidney yin deficiency. Mary's diagnosis explains the use of LI11 and SP9, clear damp heat and phlegm-damp accumulation. Since she tended toward heaviness sensation with heat, phlegm-damp with heat and kidney yin deficiency were present. Phlegm-damp accumulation with heat is one of the most common patterns in clinical practice. As her age Kidney yin deficiency is present. KD3 and 2 help her to tonify kidney yin. KD2 has action as cool the blood, clear deficiency-heat, invigorate the yin heel vessel. KD3

tonifies the kidney, regulate the uterus, benefit the essence, strengthen the lower jiao. Since KD3 is the yuan-source points of the kidney and decline of the kidney dictates aging. KD3 tonifies the both kidney yang and yin which suffers deficiency with age (Maciocia, 1998). ST25 is used as four door treatment with RN12 and Rn6 which regulates qi and warm the abdominal area (Maciocia, 1998).

Lower jiao points and lower back shu points such as Ren6, Ren4, Ren3, Ren2, SP15, ST29, Zi Gong Xue, UB20, UB23, UB25, UB28, UB31, UB32, UB33, and UB34 to promote circulate qi and good blood flow in uterus and cervical area. Mary's points included eight points on the Urinary Bladder channel: UB20, 23, 25, 28, 31, 32, 33, and 34. UB20 resolve dampness and nourish the blood. UB23 is the back-shu point of kidney, widely treat in many types of conditions. UB23 is located at the same level as DU4 which is called as life gate. They both are approximately at the same level as RN8 where the umbilical cord attaches as our lifeline until birth which easily helps to explain the broad range of applications. UB23 resolves dampness, nourish blood, strengthen the kidney, nourish kidney essence and strengthen lower area. UB23 is also stimulate the kidney to receive qi. UB25 is promote function of large intestine, relieve fullness and swelling, also strengthen lower back. UB28 uses as clear heat from lower jiao, resolve dampness, eliminate stagnation, open water passages in the lower jiao, and strengthen the lower back. UB32 treats the lower abdomen and uterus which widely treats for gynecological issue. UB32 also uses for strengthen lower jiao, regulate the lower jiao, and nourish the kidney (Maciocia, 1998).

Mary's points included four points in the Ren Channel: RN2, 3, 4, 6, 12, and 17. RN2 is uses for irregular menstruation, prolapse of uterus, and cystitis. RN3 is

important point for gynecological treatment especially problem due to blood stasis. RN3 also uses as clear heat and resolve damp-heat from lower jiao, and promote UB function of transforming qi. RN4 nourishes yin and blood, regulate uterus, strengthen yang, benefit of yuan qi, tonify the kidney, calm the mind, and root of the ethereal soul. RN4 is translated as vital gate. To needle RN4 treats kidney yin deficiency and with moxa increases kidney yang and yuan qi. RN6 uses for tonify qi and yang, regulate qi, strengthen yuan qi and resolve dampness. RN12 also resolve dampness. it can use to regulate stomach qi and tonify stomach and spleen. RN17 regulates and tonify qi and resolve phlegm (Maciocia, 1998).

Mary's points protocol included two spleen points: SP4 and 6. SP4 uses as strengthen the stomach and spleen, control penetrating channel, regulate menstruation, resolve obstruction from the channel, dispel fullness. SP6 is often used for the gynecological disorders. SP6 treats strengthen spleen, resolve dampness, regulate the uterus and menstruation, promote liver function and sooth the flow of liver qi, nourish the kidney, invigorate the blood, remove stasis, cool the blood, stop pain, and calm the mind (Maciocia, 1998).

ST36 is called Zu San LI which translates to "Leg Three Miles." It means to walk for three extra miles even when exhausted. ST36 is the most vital acupuncture points by Ma Dan Yang who was the great physician of the Jin dynasty. It tonifies stomach and spleen, harmonize stomach and spleen. ST36 is used to treat supporting qi, reviving yang, strengthen yin, nourish blood, and resolving dampness. Because it is a vital acupuncture point, using ST36 can treat all kind of disease by Qin Cheng zu of the

Song dynasty (Deadman & Al-khafaji, 2001). Mary had total of fifteen acupuncture treatments and alternated front and back treatment every other week.

### **Cathy's Acupuncture Treatment**

Cathy presented pale purple tongue with thin sticky white coating, teeth mark on the side, and red tips. Her pulse was slightly rapid, and wiry slippery. Her TCM diagnosis was liver qi stagnation, spleen qi deficiency and phlegm-damp accumulation. The following acupuncture points were used throughout her treatments: RN17, RN12, RN4, RN3, RN2, SP15, SP9, SP6, SP4, Zi Gong Xue, ST29, ST 36, ST40, LV3, LI4, PC6, Yin Tang, DU20, GB20, UB15, UB17, UB18, UB20, UB23, UB25, UB28, UB31, UB32, UB33, UB34, GB20, 21, SP6, SP4, PC6, HT7, DU20. Many of these points were also used in Mary's treatment. Points that were the same for both cases include: RN17, RN12, RN6, RN4, RN3, RN2, SP15, SP9, SP6, SP4, ST29, ST36, ST40, PC6, Zi Gong Xue, Yin Tang, Du20, GB20, UB20, UB23, UB25, UB28, UB31, UB32, UB33, and UB34. Points that were unique to Cathy's case include: ST40, LV3, LI4.

Cathy's diagnosis explains the use of LV3 and LI4, clear liver stagnation. She was moody and irritable and easy to get angry. LV3 and LI4 is often used as paired which treats expel interior wind, promote the smooth flow of liver qi, subdue rising liver yang, and calm the mind. ST40 treats all types of phlegm even visible or invisible, all disorders caused by phlegm. In TCM, all chronic diseases are caused by phlegm or blood stasis. ST40 can be used for any chronic disease caused by phlegm. It resolves dampness and phlegm, clear heat, and calm the mind (Maciocia, 1998).

### **Acupuncture Points Comparison Between the Two Cases**

Acupuncture points typically have multiple actions and often influence on more than one channel. A comparison chart of the acupuncture points used in Mary and Cathy's cases shows how these points can affect multiple channels (see table). Points used in both cases are similar which focuses on increasing blood circulation in the uterus and lower jiao area to regenerate tissues and resolve dampness from the lower jiao area. Both cases focused on removing phlegm-damp from the lower jiao area, however Mary has phlegm-damp with heat symptoms presented. Cathy was accumulating phlegm-damp in the lower jiao without heat symptoms. Mary presented yin deficiency symptoms because of her age. Cathy has liver stagnation symptoms presented from high stress.

As discussed above, in both cases the Ren, Urinary Bladder, Spleen, Stomach points are frequently used. In Mary's case, additionally used Kidney and Large Intestine points to tonify kidney yin and resolve heat. In Cathy's case, additionally used Smooth Liver, promote and circulate liver qi such as LV3 and LI4 combination.

### **Comparison of the Chinese medicine treatment between the two cases**

Both Mary and Cathy chose to receive Chinese medical treatment instead of LEEP surgery. There were similarities and differences. Mary received cryosurgery procedure before starting Chinese medical treatment but Cathy didn't. Mary was diagnosed CIN3, and Cathy was diagnosed CIN2. Even though they had the same Western diagnosis, they had different TCM diagnoses. Mary's TCM diagnosis was phlegm-damp accumulation with heat and kidney yin deficiency. Cathy's TCM

diagnosis was liver qi stagnation, spleen qi deficiency and phlegm-damp accumulation.

Each Patient received a combination of acupuncture and Chinese herbs.

### **Acupuncture comparison between Mary and Cathy**

Both Mary and Cathy received acupuncture once a week during their Chinese herbal treatment and douche treatment. Mary received cupping five times during her 15 weeks of treatment due to her shoulder and neck pain, and Cathy did not. Many acupuncture points were different between the cases, but the following points were used in both cases:

Front treatment: RN17, RN12, RN6, RN4, RN3, RN2, SP15, SP9, SP6, ST29, ST36, ST40, Zi Gong Xue, Yin Tang.

Back treatment: UB20, UB23, UB25, UB28, UB31, UB32, UB33, UB34, GB20, GB21, PC6, HT7, SP6, SP4, DU20.

Comparing acupuncture points in both cases, seven points were used on the Ren channel, four points were used on the Spleen channel, four points were used in Urinary bladder channel, two points were used in Gall Bladder channel, two points were used in the Stomach channel, three points were used in Extra channel, and one point was used in the DU channel. There were two Kidney points in Mary's point protocol, but none in Cathy's. There were LV3 and LI4 points in Cathy's point protocol, but not in Mary's. There were three ear points in Mary's case, but none in Cathy's. A comparison chart of the acupuncture points used in Mary and Cathy's point protocols shows how the points influenced multiple channels (see table # 3)



Table # 3 Comparison of acupuncture points for the two cases

Acupuncture Points Used	Channels Accessed by Mary's Points Protocol	Channels Accessed by Cathy's Points Protocol
Ren 17	SP, SI, KD, SJ, DU	SP, SI, KD, SJ, DU
Ren 12	Ren, ST, SP	Ren, ST, SP
Ren 6	Ren, KD	Ren, KD
Ren 4	Ren, SP, LV, KD	Ren, SP, LV, KD
Ren 3	Ren, SP, LV, KD	Ren, SP, LV, KD
Ren 2	Ren, LV	Ren, LV
SP 15	SP	SP
SP 9	SP	SP
SP 6	SP, LV, KD	SP, LV, KD
SP 4	N/A	
ST 29	ST	ST
ST 36	ST, SP	ST, SP
ST 40		
KD 2		N/A
KD 3	KD, LU	N/A
HT 7		
DU 20	DU, UB, GB, SJ, LV	DU, UB, GB, SJ, LV
GB 20	GB, SJ	GB, SJ
PC 6	PC, HT, SP, ST, LU, LV	PC, HT, SP, ST, LU, LV
UB 15	N/A	
UB 17	N/A	
UB18	N/A	
UB20		
UB23		
UB25		
UB25		

UB28		
UB31	UB, GB	UB, GB
UB32	UB, GB	UB, GB
UB33	UB, GB	UB, GB
UB34	UB, GB	UB, GB
LI4	N/A	LI
LV3	N/A	LV

### **Herbal Formula Comparison Between two cases**

The same herbal formula was given to each women over the course of their treatment. They both took a powder formula. Cathy was given Jia Wei Xiao Yao pill formula for first four weeks with herbal formula given to each of them. The formulas given to both of them were Reishi mushroom (3g), Maitake mushroom (3g), Shiitake mushroom (3g), Agaricus mushroom (4g), Colorious mushroom (3g). Both of them took the same dosage

Table 4 provides a summary of the background and treatment of the two cases engaged in this research study.

Table 4 Summary of background and treatment data for the two cases

	M	C
Age	39	28
Race	Asian	Hispanic
Marital Status	Yes	No
Previous Sexual Partner	6	3
CIN	2	2
Pop Smear Test	3 times since a year ago	Every year since 21 years old
Previous Treatment	Cryocauterization	none
Smoking	none	none
TCM Diagnosis	Phlegm-damp accumulation with heat and kidney yin deficiency	Liver qi stagnation, spleen qi deficiency and phlegm- damp accumulation
Acupuncture Treatment	15 weeks	19 weeks
Chinese Herbal Treatment	15 weeks	19 weeks
Douched	Everyday for 15 weeks except during menstruation periods	2-3 times a week for 19 weeks except menstruation periods

## Chapter 5 : Discussion

This study contrasts and compares two cervical dysplasia cases. Only Eastern medicine was used to treat cervical dysplasia for both Mary and Cathy. The patients were treated by Traditional Chinese Medicine with combination of acupuncture and Chinese herbs.

Women with cervical dysplasia can be treated on a consistent basis with weekly acupuncture treatment and daily herbal intake for at least three months to lessen the dysplasia condition and avoid LEEP surgery. Mary had fifteen weeks of weekly acupuncture treatment and daily Chinese herbal treatment. Cathy had nineteen weeks of weekly acupuncture treatment and daily Chinese herbal treatment. Mary douched daily with Chinese herbal decoction except during menstruation periods. Cathy douched two to three times a week with Chinese herbal decoction except during menstruation periods.

Both patients were diagnosed with CIN 2, But Mary had cryocautery treatment before starting TCM treatment. Both of them had a regular menstruation cycle. Mary had a 32 day menstruation cycle and Cathy had a 28 day menstruation cycle. Mary did not experience menstruation cramps during menstruation periods, but Cathy had severe menstruation cramps for first two days during menstruation periods.

### **Implications for Theory and Practice**

This study includes two case studies of two women treated for cervical dysplasia using acupuncture and Chinese herbal medicine for three to four months avoiding LEEP surgery. This study showed how acupuncture and Chinese herbal medicine can be effective to treat cervical dysplasia without using Western treatment even in a period of

only three to four months. This short period of treatment could have significant implication for practice because more Western practitioners might be more open to include a Traditional Chinese Medical adjunct into their protocols.

Mary and Cathy used same Chinese herbal treatment. However, Mary and Cathy were not treated with the exact same acupuncture points through their treatments. Therefore, it is difficult to ascertain if acupuncture or Chinese herbal medicine or a combination of the two were responsible for their successful outcome. If future studies were to look into these scenarios further, successful protocols might come to light and advance the relationship between Western and Eastern medicine.

This study can be benefit to individual practitioners of both Eastern and Western medicine. Western practitioners might get a better impression of TCM theory and practice by learning how it can be treated cervical dysplasia without just monitoring or surgical procedures. They may come to understand how acupuncture and Chinese herbal medicine can complement Western cervical dysplasia treatment, and they might discover various acupuncture and Chinese herbal treatment that can be used in cervical dysplasia treatment protocols.

TCM practitioners may gain an understanding of how gynecologists treat women with cervical dysplasia. They can understand how the course of events or treatments that is the most likely to occur when their cervical dysplasia patients are treated by gynecologists. They will come away with better understanding of cervical dysplasia is treated with LEEP surgery, as well as the pros and cons of various procedures.

## **Limitations of the Current Study**

The primary limitation of the present study was the limited sample size. It was a small study comparing only two cases. Another limitation is that the two patients were of different ages, 28 and 39 years old. This is a weakness because the results of the study cannot be extrapolated to other age groups, whether older or younger. However, the two women being of different ages can be considered a strength, since in spite of the difference in age, the same treatment outcome was observed—the remission of the condition of cervical dysplasia. In a small, qualitative study such as the current study, one must be careful about generalizing and extrapolating results to other age groups. However, since both patients had positive outcomes with treatment via similar acupuncture points, the exact same Chinese herbal medicine, and same acupuncturist, there is reason to consider further controlled studies examining the treatment protocol used in the current limited case studies.

While the data collected and analyzed regarding the subject was diverse, extensive and in-depth, the nature of qualitative case study research method is limited as there are no average data across a number of subjects that can be engaged for comparison. The factor of Chinese herbal treatment raises a further limitation of the current study. The relationship between TCM diagnosis and Western diagnosis and prescribed Chinese herbal medicine is, in most cases, just beginning to approach the level of science.

A limitation of the current study as well as in all acupuncture research models is the issue of points locations, points prescription, and the methods of insertion. The different locations, different levels of insertion and different stimulation lead to different

results. Because of the spectrum of styles that result from a range of theory and training models in TCM, it must be kept in mind that treatment is likely to differ when engaged by different acupuncturists.

### **Suggestions for Future Research**

For future research, a retrospective case study series that would offer more than two case studies would be advisable. Such a study would need to use cases that had more detailed documentation than those available in the current study. Additionally, a more controlled trial study with treatment and control groups would provide the best possible scenario to investigate this subject further.

In the current study, it was hypothesized that women with cervical dysplasia who are treated with weekly acupuncture treatments and daily Chinese herbal medicine intake for at least three months will effect lowering CIN level or cure without using any Western treatment such as LEEP surgery. However, comparison of these two cervical dysplasia cases did not completely confirm the hypothesis. While these two particular cases showed the benefit of traditional Chinese medicine, it cannot be postulated that all cases of cervical dysplasia can be treated by TCM alone. Mary had fifteen weeks of TCM treatment and a lowering CIN level. Compared to Mary, Cathy had total of nineteen weeks of TCM treatment and her cervical dysplasia symptom had completely disappeared.

The next step might be to to conduct large number of case studies that engage the same factors that were explored in the current study using more controlled empirical quantitative methods. Such studies should be carried out with randomization, blind, and double blind controls in effect to explore the same variables engaged in the current

study. The more advanced approach, the randomized controlled trial (RCT) is suggested for future research.

More specific research is also warranted regarding the impact of acupuncture, Chinese herbal intake, and Chinese herbal douches on the process to reducing CIN level or eliminate cervical dysplasia. The further controlled research is needed regarding the impact of acupuncture and Chinese herbal medicine on treating cervical dysplasia causing from Human Papilloma Virus. All of the above mentioned potential research studies will continue the important research path regarding women with cervical dysplasia research at a higher and more conclusive level than characterized by the preliminary and tentative conclusion of the current study.

### **Conclusion**

As demonstrated from analysis of two case studies chart review data, the combined use of Acupuncture and Chinese herbal medicine appears to have potential to treat women with cervical dysplasia to avoid Western treatment such as LEEP surgery. However further studies that engage controlled randomized clinical trial methods are needed to further affirm the observations that emerged from the current study.



## References

- Adam E, Berkova Z, Daxnerova Z, Icenogle J, Reeves WC & Kaufman RH. (2000).  
*American Journal of Obstetrics and Gynecology* 182, 257.
- Agorastos T, Miliaras D, Lambropoulos A, Chrisafi S, Kotsis A, Manthos A, & Bontis J. (2005). "Detection and typing of human papillomavirus DNA in uterine cervixes with coexistent grade I and grade III intraepithelial neoplasia: biologic progression or independent lesions?". *Eur J Obstet Gynecol Reprod Biol* **121** (1): 99–103.
- Anderson AM. (2002). *Clinical Microbiology Newsletter* 24, 113.
- Andersson S, Rylander E, Larsson B, Strand A, Silfversvard C, & Wilander E. (2001).  
*European Journal of Cancer* 37, 246.
- Arbyn M, Autier P, & Ferlay J. (2007). Burden of cervical cancer in the 27 member states of the European Union: estimates for 2004. *Ann Oncol.* 18: 1425-7.
- Barnett R & Fox R. (1986). *A Feminist Approach to Pap Tests*. Vancouver, B.C.: The Vancouver Women's Health Collective, Press Gang.
- Bauer HM, Ting Y, Greer CE, Chambers JC, Tashiro CJ, & Chimera J. (1991). *Journal of the American Medical Association* 265, 472.
- Bonnez W & Reichman R. (in: GL Mandell, G Bennett, & R Dolin [eds]). (2000).  
Principles and Practice of Infectious Diseases. Philadelphia, PA: Churchill Livingstone.
- Bosch FX, Burchell AN, Schiffman M, Giuliano AR, de Sanjose S, & Bruni L. (2008).  
Epidemiology and natural history of human papillomavirus infections and type-specific implications in cervical neoplasia. *Vaccine.* 26 Suppl 10: K1-16.

- Bosch FX & de Sanjose S. (2003). Chapter 1: human papillomavirus and cervical cancer-burden and assessment of causality. *J Natl Cancer Inst Monogr.* ((31)):3-13.
- Bosch FX, Lorincz AT, Munoz N, Meijer CJ, & Shah KV. (2002). The causal relation between human papillomavirus and cervical cancer. *J Clin Pathol.* 55: 244-65.
- Burk RD, Kelly P, Feldman J, Bromberg J, Vermund SH, & Deltovitz JA. (1996). *Sexually Transmitted Diseases* 23, 333.
- Cates W. (1996). HPV. *Sexually Transmitted Diseases* 26, S2. Cervical cancer in adolescents: screening, evaluation, and management. (2010). Committee Opinion No. 463. American College of Obstetricians and Gynecologists. *Obstet Gynecol.* 116:469–72.
- Chan PK, Chan MY, Li WW, Chan DP, Cheung JL, & Cheung AF. (2001). *Journal of Clinical Pathology* 54, 48.
- Chua KL & Hjerpe A. (1996). *Cancer* 77, 121.
- Cubie HA, Seagar AL, Beattie GJ, Monaghan S, & Williams AR. (2002). *Sexually Transmitted Diseases* 76, 257 .
- Deadman P, & Al-khafaji, M. (2001). A Manual of Acupuncture (pp.151-552). East Sussex: *Journal of Chinese Medicine Publications.*
- de Sanjose S, Diaz M, Castellsague X, Clifford G, Bruni L, & Munoz N. (2007). Worldwide prevalence and genotype distribution of cervical human papillomavirus DNA in women with normal cytology: a meta-analysis. *Lancet Infect Dis.* 7: 453-9.
- de Vet HC, Knipschild PG, & Sturmans F. (1993). The role of sexual factors in the aetiology of cervical dysplasia. *Int J Epidemiol.* 22:798-803.

- de Villiers EM. (2001). *Papillomavirus Report* 12, 57.
- Diaz ML. (2008). Human papilloma virus: prevention and treatment. *Obstet Gynecol Clin North Am.* 35(2):199-217.
- Division of STD Prevention (1999). Prevention of genital HPV infection and sequelae: report of an external consultants' meeting. Atlanta, GA: *Centers for Disease Control and Prevention*. Retrieved January 4, 2012.
- Doeberitz M, Rittmuller C, Aengeneyndt F, Jansen-Durr P, & Spitkovsky D. (1994). Reversible repression of Papillomavirus oncogene expression in cervical carcinoma cells: consequences for the phenotype and E6-p53 and E7-pRB interactions. *J Virol* 68. 2811-2821.
- Dunne EF, Unger ER, Sternberg M, McQuillan G, Swan D, Patel SS, & Markowitz L. (2007). Prevalence of HPV Infection Among Females in the United States *JAMA.* 297(8):813-819
- Elfgrén K, Kalantari M, Moberger B, Hagmar B, & Dillner J. (2000). *American Journal of Obstetrics and Gynecology* 183, 561.
- Favre M. (1975). *Journal of Virology* 15, 1239.
- Flaws B. (1990). Blue poppy press, *Cervical Dysplasia & Prostate Cancer HPV, A Hidden Link?*, 1-185.
- Flores ER & Lambert PF. (1997). *Journal of Virology* 71, 7167.
- Franco E. (1997). Understanding the epidemiology of genital infection with oncogenic and nononcogenic human papillomaviruses: a promising lead for primary prevention of cervical cancer. *Cancer Epidemiol Biomarkers Prev.* 6:759-761.

- Franco E, Duarte-Franco E, & Ferenczy A. (2001). Cervical Cancer: Epidemiology, Prevention and role of human papillomavirus infection, *Canadian Medical Association Journal*. 164 (7) 1017-1025.
- Franco EL. (1995). *Journal of the National Cancer Institute* 87, 779.
- Franco EL, Duarte E, & Ferencz A. (2001). *Canadian Medical Association Journal* 164, 1017.
- Franco EL, Villa LL, & Sobrinho JP. (1999). Epidemiology of acquisition and clearance of cervical human papillomavirus infection in women from a high-risk area for cervical cancer. *J Infect Dis*. 180:1415-1423 - PubMed
- Flores ER, Allen BL, Lee D, Sattler CA, & Lambert PF. (1999). *Virology* 262, 344.
- Giannoudis A & Herrington C. (2001). *Journal of Pathology* 193, 295.
- Gilbert D, Moellering R, & Sande M. (1999). *The Sanford Guide to Antimicrobial Therapy*. 29th Edition. Hyde Park, Vt.: Antimicrobial Therapy, Inc.,
- Gillison ML, Broutian T, & Pickard RK. (2012). Prevalence of oral HPV infection in the United States, 2009–2010. *JAMA*. 307(7):693–703.
- Gingelmaier A, Grubert T, & Kaestner R. (2007). High recurrent rate of cervical dysplasia and persistence of HPV infection in HIV-1-infected women. *Anticancer Research*. 27(4A): 1795-1798.
- Gomez D & Santos J. (2007). Human papillomavirus infection and cervical cancer: pathogenesis and epidemiology. *Pathogenesis and Epidemiology*, 1 Section of Microbiology. 2 Service of Clinical Analysis. University Hospital of Guadalajara. C/. Donante de sangre s/n. 19003. Guadalajara, Spain, 2007.

- Greelee R, Hill-Harmon M, Murray T, & Thun M. (2001) Cancer statistics-2001. *Journal of Clinical Cancer*. 51: 15-36.
- Hariri S, Unger ER, & Sternberg M. (2011). Prevalence of genital human papillomavirus among females in the United States, the National Health and Nutrition Examination Survey, 2003–2006. *Journal of Infectious Diseases*. 204(4):566–573.
- Hildesheim A, Herrero R, Wacholder S, Rodriguez AC, Solomon D, Bratti MC, Schiller JT, Gonzalez P, Dubin G, & Porras C, (2007). Effect of human papillomavirus 16/18 L1 viruslike particle vaccine among young women with preexisting infection: a randomized trial. *JAMA* 298, 743-753.
- Ho GY, Burk RD, Fleming I, & Klein RS. (1994). *International Journal of Cancer* 56, 788.
- Ho GY, Burk RD, Klein S, Kadish AS, Chang CJ, & Palan P. (1995). *Journal of the National Cancer Institute* 87, 1365.
- Ho GY, Kadish AS, & Burk RD. (1998). HPV 16 and cigarette smoking as risk factors for high-grade cervical intra-epithelial neoplasia. *Int J Cancer*. 78:281-285.
- Holowaty P, Miller A, Rohan T, & To T. (1999). Natural History of Dysplasia of the Uterine Cervix. *Journal of the National Cancer Institute*. 91 (3) 252-258.
- Hung CF, Ma B, Monie A, Tsen SW, & Wu TC. (2008). Therapeutic human papillomavirus vaccines: current clinical trials and future directions. *Expert Opin Biol Ther* 8, 421-439.
- Jemal A, Siegel R, Ward E, Hao Y, Xu J, & Thun MJ. (2009). Cancer statistics, 2009. *CA Cancer J Clin*. 59: 225-49.

- Jin XW, Cash J, & Kennedy AW. (1999). *Clinical Journal of Medicine* 66, 533.
- Kaphle K, Wu LS, Yang NY, & Lin JH. (2006). *Herbal medicine research in Taiwan*. eCAM. 3(1):149-155.
- Kawai K. (2008). *Treatment for women health*. Ikuhousya, Japan.
- Kiviat N & Koutsky LA. (1993). *Journal of the National Cancer Institute* 85, 934.
- Kleter B., van Doorn J., Schrauwen L., Molijn, A., Sastrowijoto, S., & Terscheget, J. (1999). *Journal of Clinical Microbiology* 37, 2508.
- Koutsky LA, Holmes KK, Critchlow CW, Stevens CE, Paavonen J, Beckmann AM, Derouen TA, Galloway DA, Vernon D, & Kiviat NB. (1992). A cohort study of the risk of cervical intraepithelial neoplasia grade 2 or 3 in relation to papillomavirus *Infection*. 327: 1272-1278.
- Kumar V, Abbas AK, Fausto N, & Mitchell RN. (2007). *Robbins Basic Pathology* (8th ed.). Saunders Elsevier. pp. 718–721. ISBN 978-1-4160-2973-1.
- Kurman RJ, Henson DE, & Herbst AL. (1992) Interim guidelines for management of abnormal cervical cytology. The 1992 National Cancer Institute Workshop. *JAMA* 1994;271:1866-1869.
- Landis S, Murray T, Bolden S & Wingo P. (1998) *Cancer statistics, 1998*. CA Cancer J Clin 1998;48:6-29. Loop Electrical Surgery, retrieved May 5, 2012. Wikipedia Website:  
[http://en.wikipedia.org/wiki/Loop\\_electrical\\_excision\\_procedure#cite\\_ref-0](http://en.wikipedia.org/wiki/Loop_electrical_excision_procedure#cite_ref-0)

- Lowy DR & Howley PM. (2001). Papillomaviruses, in: Fields Virology, D.M. Knipe, P.M. Howley, D.E. Griffin, R.A. Lamb, M.A. Martin, B. Roizman and S.E. Straus. eds, Lippincott, Williams & Wilkins.
- Lyttleton J. (2004). *Treatment of infertility with Chinese medicine* (pp.xvi-361). Edinburgh: Churchill Livingstone.
- Maciocia G. (1998). *The foundation of Chinese medicine* (pp.15-146). Edinburgh: Elsevier Churchill Livingstone.
- Magnusson PKE, Lichtenstein P, & Gyllenstein UB. (2000). *International Journal of Cancer* 88, 698.
- McCrary DC, Matchar DB, Bastian L, Datta S, & Hasselblad V. (1999). "Evaluation of cervical cytology. Evidence report/technology assessment no 5," AHCPH publ no 99 E010. Rockland (MD): *Agency for Health Care Policy and Research*.
- Mitchell MF, Tortolero-Luna G, & Wright T. (1996). Cervical human papillomavirus infection and intraepithelial neoplasia: a review. *J Natl Cancer Inst Monogr.* 21:17-25.
- Moscicki AB, Shiboski S, & Broering J. (1998). The natural history of human papillomavirus infection as measured by repeated DNA testing in adolescent and young women. *J Pediatr.* 132:277-284 - PubMed.
- Munger K, Baldwin A, Edwards KM, Hayakawa H, Nguyen CL, Owens M, Grace M, & Huh K. (2004). Mechanisms of human papillomavirus-induced oncogenesis, *J Virol* 78. 11451–11460.
- Munoz N & Bosch FX. (1989). *Epidemiology of cervical cancer*. IARC Sci Publ. 94:9-39.

Munoz N, Bosch FX, Castellsague X, Diaz M, de Sanjose S, & Hammouda D.(2004).

Against which human papillomavirus types shall we vaccinate and screen?

The international perspective. *Int J Cancer*. 111: 278-85.

Muñoz N, Bosch FX, de Sanjosé S, Herrero R, Castellsagué X, & Shah KV. (2003). *Ne*

*England Journal of Medicine* 348, 518. National Cancer Institute at the

NationalInstitutes of Health, retrieved April 20th, 20012.

<http://www.cancer.gov/cancertopics/causes/hpv/hpv-prevalence0308>

Murthy NS & Mathew A. (February 2000). "Risk factors for pre-cancerous lesions of the

cervix". *European Journal of Cancer Prevention* 9 (1): 5–14.N. Chilkov. (2012).

Six Cancer-Fighting Medical Mushrooms., Huffpost Healthy Living., (2012).

Noehr, B., Jensen A, Frederiksen K, Tabor A, & Kjaer SK. (2009). Loop electrosurgical

excision of the cervix and the subsequent risk of preterm delivery. *Obstet*

*Gynecol*. 114(6):1232-8.

Northrup, C. (1994). *Women's bodies, Women's Wisdom*. Bantam Books, New

York, New York. pg. 262.

Ostor, A.G. (1993). *International Journal of Gynecological Pathology* 12, 186.

Palefsky, J.M. & Holly, E.A. (1995). Molecular virology and epidemiology of human

papillomavirus and cervical cancer. *Cancer Epidemiol Biomarkers Prev*.

4:415-428.

Parkin, D.M. (2006). The global health burden of infection-associated cancers in the

year 2002. *International Journal of Cancer* ; 118(12):3030–3044.

Peyton, C.L., Gravitt, P.E., Hunt, W.C., Hundley, R.S., Zhao, M, & Apple, R.J. (2001).



Piot & Wasserheit JN (eds). (1999). Sexually Transmitted Diseases. *McGraw-Hill*, New York, pp. 335-346.

Popescu NC & DiPaolo JA. (1989). Preferential sites for viral integration on mammalian genome, *Cancer Genet Cytogenet* 42, 157–171. Preterm delivery, retrieved May 5, 2012. Wikipedia Website:  
[http://en.wikipedia.org/wiki/Preterm\\_birth](http://en.wikipedia.org/wiki/Preterm_birth)

Quint WGV, Scholte G, van Doorn LJ, Kleeter B, Smits PHM, & Lindeman J. (2001). *Journal of Pathology* 194, 51.

Rozendaal L, Walboomers JM, van der Linden JC, Voorhorst FJ, Kenemans P, & Helmerhorst T. (1996). *International Journal of Cancer* 68, 766.

Sadler L, Saftlas A, Wang W, Exeter M, Whittaker J, & McCowan L. (2004). Treatment for cervical intraepithelial neoplasia and risk of preterm delivery. *JAMA*. 5;291(17):2100-6.

Sadler L, Saftlas A, Wang W, Exeter M, Whittaker J, & McCowan L. (2009). Depth of cervical cone removed by loop electrosurgical excision procedure and subsequent risk of spontaneous preterm delivery. *Obstet Gynecol*. 114(6):1232-8.

Samoff E, Koumans EH, Markowitz LE, Stemberg M, Sawyer MK, & Swan D. (2005). *American Journal of Epidemiology* 162, 668.

Schiffman MH, Bauer HM, & Hoover RN. (1993). Epidemiologic evidence showing that human papillomavirus infection causes most cervical intraepithelial neoplasia. *J Natl Cancer Inst*. 85:958-964.

- Schwartz PE, Hadjimichael O, Lowell DM, Merino MJ, & Janerich D. (1996). The Connecticut experience. *Am J Obstet Gynecol.* 175: 1105-1109. SOAP. Retrieved May 5, 2012. Wikipedia Website: <http://en.wikipedia.org/wiki/SOAP>
- Southern SA & Herrington CS. (1998). Differential cell cycle regulation by low- and high-risk human papillomaviruses in lowgrade squamous intraepithelial lesions of the cervix, *Cancer Res* 58. 2941–2945.
- Stake, R., (1995). *The art of case study research*. Thousand Oaks, CA: Sage.
- Sun XW, Kuhn L, Ellerbrock TV , Chiasson MA, Bush TJ, & Wright TC. (1997). *New England Journal of Medicine* 337, 1343.
- Swan DC, Tucker RA , Tortolero G , Follen M, Wideroff L, & Unger ER. (1999). *Journal of Clinical Microbiology* 37, 1030.
- Swierzewski III SJ. (2011). Treatment of cervical dysplasia. Health.com. <http://www.healthcommunities.com/physicianboard.shtml>
- Syrianen KJ. (1996). “Spontaneous evolution of intraepithelial lesions according to the grade and type of the implicated human papillomavirus (HPV), *European Journal of Obstetrics Gynecology and Reproductive Biology*;65 (1).
- Tabrizi SN, Fairley CK, & Chen S. (1999).Epidemiological characteristics of women with high grade CIN who do and do not have human papillomavirus. *Br J Obstet Gynaecol.* 106:252-257.
- Tena D, Garrido N, Menéndez JM, Delgado JJ, Romanyk J, & González-Palacios J. (2005). *Enfermedades Infecciosas y Microbiología Clínica* 23, 474.

- Von Knebel, Vachani C. (2005). Some Cause Genital Warts, Some Invade Epithelial Cells HPV and Cervical Cancer. *The Abramson Cancer Center of the University of Pennsylvania*. 2-29-7.
- Walboomers JM, Jacobs MV, & Manos MM. (1999). Human papillomavirus is a necessary cause of invasive cervical cancer worldwide. *J Pathol*. 189:12-19.
- Wen Re Lun* (Discussion of Warm and Hot Disorders) by the apprentices of Ye Gui, 1745-1766.
- Wen Yi Lun* (Discussion of Epidemic Warm Disease) by Wu You-Xing, 1642.
- WHO (1993). Collaborative Study of Neoplasia and Steroid Contraceptives. *International Journal of Cancer* 55, 228.
- Yang XG, Jin G, Nakao Y, Rahimtula M, Pater MM, & Pater A. (1996). *International Journal of Cancer*. 65, 338.
- Yardley K. (2001). Understanding Cervical Dysplasia: A holistic Treatment Protocol. *British Journal of Phytotherapy*, Vol. 5 No. 4, ISSN 0959-6879.
- Xu W, Towers AD, & Li P. (2006). Traditional Chinese medicine in cancer care: perspectives and experiences of patients and professionals in China. *European Journal of Cancer Care*. 2006;15:397-403.
- zur Hausen H. (1992). *The Lancet ii*, 1370.
- zur Hausen H. (2000). Papillomaviruses Causing Cancer: Evasion From Host-Cell Control in Early Events in Carcinogenesis. *J Natl Cancer Inst*. 92: 690-8.

**Appendix A: Data Collection Form**

**Copy of Data Collection Form**

Was the patient treated for cervical dysplasia with Chinese herbs and acupuncture?	Yes	No
Was the patient diagnosis of cervical dysplasia previously?	Yes	No
Did the patient have Leep surgery previously?	Yes	No
Is this treatment for recurrent condition?	Yes	No
Was the patient treated by Western treatment?	Yes	No
Did modified the formula according to constitution?	Yes	No
Did modified the acupuncture points according the constitution?	Yes	No

**Appendix B: IRB Approval Letter**

April 25, 2012

Myeongae Kang, L.Ac.  
825 Chehalis Road  
La Canada, CA 91011

Dear Myeongae,

Your Claim for Exemption from the Institutional Review Board (IRB) has been reviewed. Your research proposal has been approved, with no recommendations effective April 1, 2012 through March 31, 2013.

Should there be any significant changes that need to be made which would alter the research procedures that you have explained in your proposal, please consult with the IRB coordinator prior to making those changes.

Regards,

Debra Jean Rawdin  
IRB Coordinator