

From Incurable to Preventable, the Success Story of Cancer of the Uterine Cervix

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Abstract: Background: Until late 19th century, cancer of the uterine cervix was deemed incurable due to lack of effective treatment. With the introduction of anesthesia and disinfection surgical management was dared. Around 1895 Professor Wertheim of Vienna, introduced his technique of radical hysterectomy. Around that time X-rays was discovered in 1895 and radium in 1898. Both surgery and radiation therapy became available for the treatment of cervical cancer. Objective: Although in time both surgery and radiation therapy evolved with technical refinement as effective treatment, yet the major impact was in early diagnosis with the introduction of the pap smear cytology. More recently, the discovery of the relationship between human papilloma virus infection and cancer of the uterine cervix resulted in the development of an effective vaccine for preventing the disease. Conclusion: HPV vaccination has almost successfully prevented cancer of the uterine cervix in younger women.

Keywords: Cancer of the Uterine Cervix, Hysterectomy, Human Papilloma Virus, Radiotherapy, Cancer Prevention

1. Introduction

A recent article in JAMA Pediatr [1] reported decreased cervical cancer incidence and mortality among women and girls aged 15 to 24 years after HPV vaccine introduction. The decreases were greater than changes in those aged 25 to 29 years, suggesting associations with HPV vaccination. This confirms the findings of a UK study published by the Lancet. [2].

Until late nineteenth century, cancer of the uterine cervix was virtually untreatable. Cautery to stop the bleeding and other simple measures like packing and ointment applications were all that was available. In 1846 ether was introduced for anesthesia and in 1866, Joseph Lister [3] used carbolic acid sprays in the operating rooms for disinfection. These two events made it possible to perform surgery painlessly and with lower risk of infection. Timid surgical approaches like amputation of the cervix were thus practiced with limited success. More daring surgery was gradually attempted. In late 1870, Freund of Strassburg [4] introduced a surgical procedure for complete resection of the uterus via abdominal route. But a reported surgical mortality of 72% was a nonstarter! In 1893, Schuchardt [5] proposed vaginal

hysterectomy, a technique refined by Schauta [6] who published a report of his experience in 1908. The success of vaginal hysterectomy rested on the extent of the disease and since the iliac nodes were not explored a high percentage of patients had local recurrence.

2. The Evolution of Radical Surgery and Radiation Therapy

Around 1895 Wertheim of Vienna [7], practiced the technique of radical hysterectomy consisting of abdominal hysterectomy with removal of parametrial tissues, upper half of vagina and regional pelvic nodes. In a presentation to the British Medical Association in 1905 (Figure 1) he reported on his experience and stressed the importance of patients' selection to avoid high rates of operative mortality and local failure.

Contemporarily in November 1895, W. C. Roentgen discovered the X-rays and in 1898 Marie and Pierre Curie isolated Radium. Soon after, it was noted that both X-rays and Radium radiations have biological effects on dividing cells. Treatment of cancer with X-rays and Radium radiations

was thus proposed and initiated. As early as 1902 E. W. Caldwell [8] irradiated patients with carcinoma of the cervix by exposing the vulva and cervix to an X-ray tube. The results were disastrous with distressing reactions. In 1903, Alexander Graham Bell the inventor of the telephone, in a letter to Dr. Z. T. Zowers [9] wrote: "... there is no reason a tiny fragment of radium sealed in a fine glass tube should not be inserted into the very heart of a cancer, thus acting directly upon the diseased material." The first reported use of radium for the treatment of cancer of the cervix was in September 1903 by Dr. Margaret Cleaves [10] of New York.

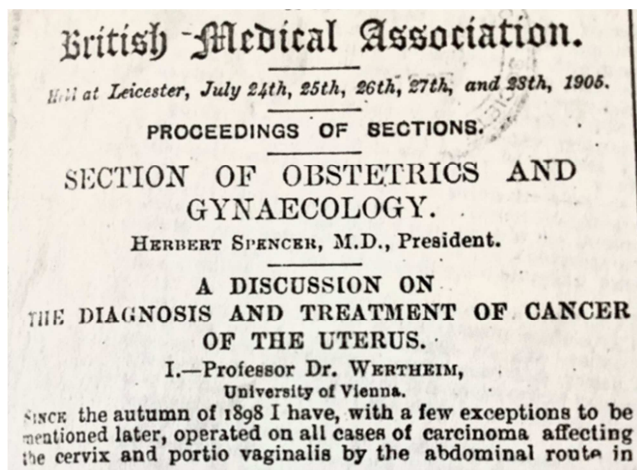


Figure 1. BMA publication of Wertheim's Presentation in 1905 of his radical hysterectomy.

In Paris, France, working at Laboratoire Biologiques du Radium, H. Dominici [11] introduced the principle of radium filtration to optimize its therapeutic effect by eliminating the undesirable particulate radiation and utilizing the ultra-penetrating gamma radiation.

In France, Chiron, and R. Duval [12] published an article in 1910 about obtaining local control in 18 of 50 patients with inoperable cervix carcinoma treated with radium. In 1913 The German Congress of Gynecologists took place at Halle, Germany. Extensive reports were presented on successful treatment of uterine cervix carcinoma patients with radium applications. Wertheim was scheduled at that meeting to present a comprehensive account of his operative results. However, he was so impressed with the successful radium treatments that he cancelled his announced lecture. It was told that he confided to one of his colleagues saying: "It is tragic that my life's work on the radical operation is now surpassed and deemed unnecessary!"

The same year 1913, Robert Abbe [13] of New York published his 8-years' experience of treating cervix carcinoma with radium.

Slowly but surely treatment of cervix carcinoma by intracavitary radium insertions took off in Europe as well as in the USA. In Stockholm, Forsell [14] treated patients with cervix cancer at the Radiumhemmet hospital which was established in 1914.

In 1919 Regaud and Lacassagne [15] inaugurated the Paris school of radium technology.

1927, J. Heyman [16] of Stockholm reported that the radiological treatment as practiced at Radiumhemmet was superior to surgical treatment in respect to absolute results of the treatment of cancer of the uterine cervix. In the same year, the Cancer Commission of the League of Nations appointed a sub-commission on the radiotherapy of uterine cervix cancer. In 1929, this sub-committee allocated staging system according to anatomic-clinical extent of the cancer. In 1938, Margret Todd and Meredith, W. [17] of Manchester introduced a radium dosage system based on precalculated cancericidal dose delivered to a geometrical area referred to as the paracervical triangle.

J. V. Meigs [18] of the Memorial Hospital, N. Y. revived interest in radical hysterectomy by reporting superior results of treating a series of cases of Stage I and II cancer of the uterine cervix.

In 1960, Henschke [19] introduced the first after-loading radium applicator for the treatment of carcinoma of the cervix.

For some time, a silent competition existed between the radiation oncologist armed with better intracavitary and high energy external beam radiation techniques [20, 21] and the oncology gynecologist supported by better anesthesia, asepsis, surgical and post-operative advances. Through clinical trials this competition was settled by evidence-based indications for radiation, surgery, and where needed chemotherapy.

3. Early Detection and Prevention

In the meantime, several milestone developments improved the early detection and diagnoses of cancer of the uterine cervix. The question of prevention rested on the attempt to understand the etiology of cancer of uterine cervix. Intelligent observations of its epidemiology lead to identifying risk factors. Rigoni-stern [22], a surgeon from Padua, Italy noted in 1842 that celibate nuns do not get cancer of uterine cervix. However, cervical cancer was prevalent among prostitutes, those who have multiple sexual partners and those whose husbands have multiple sexual partners. In 1924 Hans Hinselmann [23] of Germany, invented the Colposcope for the early detection of cervical cancer. An important development in the quest for early detection was launched by George Papanicolaou [24] who in 1928 described the cytological characterization of cervical cancer based on the microscopic examination of exfoliative cytology. This became a routine test known as the Pap smear that helped save the lives of many women.

A breakthrough in the identification of the etiology and the prevention of cervical cancer came in 1976 when H. zur Hausen [25] and L. Gissmann successfully isolated and cloned HPV-6 DNA from genital warts. In 1983 they were able to isolate HPV-16 in 50%, and HPV-18 in 20% of cervical cancer biopsies.

Based on this breakthrough two vaccines were developed and successfully tested for safety and efficacy. It was

determined that cervical cancer is a sexually transmitted disease. It can thus be prevented by vaccination of females aged 9-13 years of age.

4. Conclusion

The story of cervical cancer had a grim beginning but a happy conclusion: it can be prevented, diagnosed early, and treated effectively with surgery, radiation, chemotherapy and immunotherapy with excellent results and minimal side-effects!

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