



ASBESTOS IN TALC: A LEADING CAUSE OF OVARIAN CANCER

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ABSTRACT

Talc powder products have been on the market since the 1800s. Pure talc on its own is considered safe, but asbestos-contaminated talc has been a public health concern for decades. Talc and asbestos naturally occur close to each other in the world. If mine, raw talc may they contain asbestos fibers. Talc is often contaminated with amphibole asbestos. Studies finding exposure to five types of asbestos in this category are highly probable leads to asbestos-related diseases. According to the U.S. Food and Drug Administration, questions about asbestos-contaminated talc grown since the 1970s. Studies first emerged in the 1970s linking contaminated talc leads to serious health risks, such as ovarian cancer and other type of cancer. More studies and agencies, including International Agency for Research on Cancer (IARC), have confirmed that contaminated talc is a carcinogen. The powder has been extensively investigated as a potential risk factor for ovarian cancer.

KEYWORDS: Talc, asbestos fibers, ovarian cancer, talcum powder.

INTRODUCTION

Exposure to asbestos-contaminated talc occurs mainly through the use of contaminated talcum powder products, such as talc-based baby powders. However, contaminated talc may also be used for cosmetics and industrial purposes. Historically, the common epithelial ovarian neoplasm has been classified under such familiar pathologic categories as cystadeno carcinoma, papillary carcinoma, and undifferentiated cancer. These symptoms have been shown to be legitimate as any damage from the surface or cell membrane, in many systems, is labeled carcinoma, and is acceptable unless a particular neoplasm exhibits unique properties that distinguish it from other lesions separated under the same common umbrella. The so-called “epithelial tumor” The uterus fulfills a condition that justifies a clear term, as in embryos, historically, and clinically it differs from normal epithelial lesions. There is a rising death rate from ovarian cancer in advanced western countries. By contrast, ovarian cancer is uncommon in less developed areas. Mesotheliomns in asbestosis resemble ovarian cancer in appearance. Intraperitoneal injection of another type of asbestos produces epithelial changes in the guides of guinea pigs and rabbits similar to those observed which are similar to those seen in patient’s ninth early ovarian cancer. Six in twelve patients with malignant early ovarian changes show birefringent crystalline material in the ovaries. This observation is consistent with the theory that asbestos is an etiologic factor in cervical cancer. The use of talcum powder has been extensively investigated as a potential risk factor for ovarian cancer. A meta-analysis of 16 previous studies reported approximately 30% increase in risk of total epithelial ovarian cancer with regular Exposure to talc, and several studies have suggested as strong association with the serous or serious invasive histological subtype. Epidemiologic evidence supports a modest correlation between the use of genital talc and the risk of

ovarian cancer, the association remains controversial due to a lack of a clear dose response and an increase in frequency or duration of talc use, the possibility of confusion or other bias, and uncertainty. Biological approach. Mortality studies among women exposed occupationally to various types of asbestos have reported increased risks for ovarian and cervical cancers. Excess mortality has also been reported for uterine cancer, wherein corpus and cervix were not differentiated. The number of cases of each cancer was small in most cohorts and exposure-response relationships were generally not shown. Examination of the pathologic material, in which it was performed; it was found that some ovarian cancers were malignant mesothelioma of the peritoneum that had not been properly diagnosed. Extreme breast cancer deaths have been reported among women workers in the asbestos fabric factory who are severely exposed that lasts for a time $\gg 2$ years. No studies have investigated the incidence of these cancers among women with asbestos exposure.

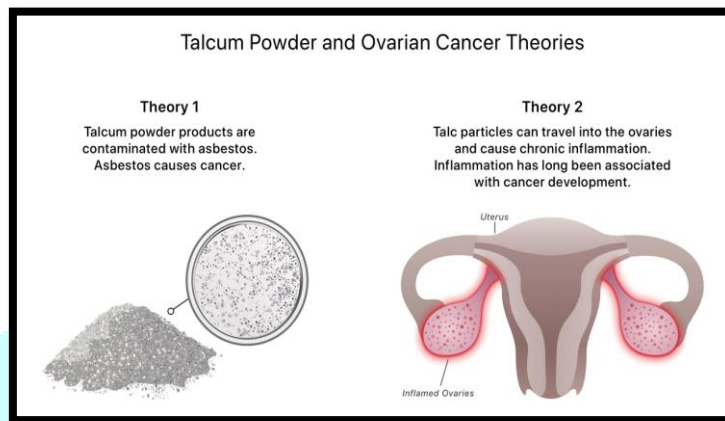


Figure 1 - Effect of talcum powder on ovarian cancer theories

Pathogenesis of ovarian cancer:

Asbestos fibers are known to be strong and can be easily digested or melted after inhaling from the lungs. It was reported that asbestos fibers travel from the lungs to other tissues including the pleural and peritoneal tissues. Asbestos fibers transferred to the mesothelial tissue play an important role in the formation of asbestos related serious disease, such as pleural and peritoneal fibrosis, as well as malignant pleural and/or peritoneal mesotheliomas. High-grade serous ovarian carcinoma (HGS-OvCa) spreads within the peritoneum, causing organ failure with a negative clinical impact related to this disease. Initiation of HGS-OvCa can occur in the epithelium of the fimbriated end of the fallopian tube. Mutation of T P53 in the fimbriae epithelium is considered to be an initiating event in HGS-OvCa pathogenesis, as nearly 100% of serous ovarian tumors harbor these alterations. The distribution of HGS-OvCa involves the discovery of phenotypes that allow carcinoma cells to: (a) release fimbriae into the peritoneal cavity, (b) subjected to proapoptotic pressure caused by separation from the underlying membrane (anoikis) over time for liquid transport of the peritoneal cavity, and (c) attach and wipe the top layer of mesothelium covering the peritoneal cavity organs. And (d) attaches to and clears the superficial layer of the mesothelium that encloses the organs in the peritoneal cavity. Although TP53 mutations are a significant sign of HGS-OvCa, the role played by mutant p53 mutations in the acquisition of these phenotypes is not yet known. Increasing evidence of cells, genes, and clinical evidence suggests that most HGS-OvCa is derived from the fallopian tube (FT) epithelium, which is made up of secretory and ciliated cells. Although dysplastic secretory epithelial cells were reported in FCA mutation-carrying FTs in the early 200's, it was the development of the SEE-FIM protocol (phase and fimbria screening test) that led to the repeated detection of HGS-OvCa precursors in

fimbriated end of the FT. Specifically, A careful examination of FTs from BRCA mutation carriers led to the following observations: (a) Approximately 5% to 10% of fluffy BRCA1 carriers prophylactic surgery will develop premature ulcers, called serous tubal intraepithelial carcinoma (STIC), in their FT fimbria. (b) More than 50% of women with pelvic serous stage III / IV also have STIC (c) Similar TP53 mutations have been identified in STICs and associated serous carcinomas (d) Nonneoplastic FT Asbestos of Chrysotile began to be mined in the province. in Quebec in the late 1870's.

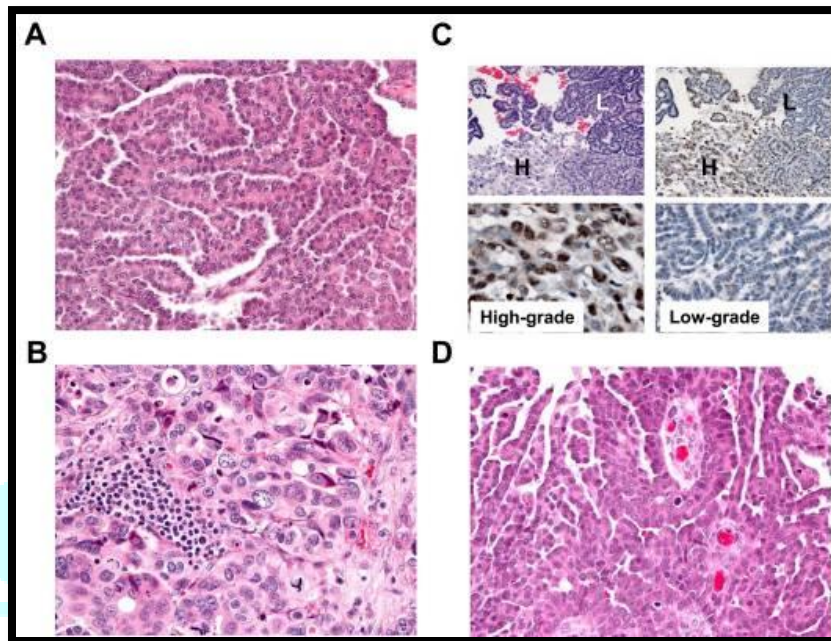


Figure 2 Invasive low-grade micro papillary serous carcinoma. The tumor is characterized by a micro papillary architecture and grade 1 nuclei

Twenty years later, disabling and lethal effects were being reported in workers exposed to dust containing chrysotile asbestos in manufacture, in England, and shortly after in France. For all the growing body of information that accrued subsequently, it was to be a long time before asbestos came to be publicized as an agent that constituted a major 20th century public health problem in urgent need of attention. The sounding of the international alarm that was to initiate the slow retreat from the prodigious use of asbestos, can be dated from a conference hosted by the New York Academy of Sciences in 1964, and in particular its publicizing of the previously reported association between asbestos exposure and lung cancer and malignant mesotheliomas. Asbestos, a generic term for naturally occurring fibrous mineral silicates, is recognized as a carcinogen by the general medical and scientific communities. In 1960, Wagner et al reported a large series of malignant mesotheliomas in individuals who had been exposed to asbestos from South African asbestos mine. It has been demonstrated that all types of asbestos and even brief and low-dose exposures are capable of causing malignant mesothelioma. In the 1970s, several types of cosmetic talcum powder products were shown to contain asbestos. Asbestos fibers in commercial talcum powder have also been shown to be airborne when used, and repeated exposure to cosmetic talc was implicated as a cause of mesothelioma by Gordon et al. Recently, Moline et al, reported a series of 33 subjects with malignant mesothelioma, who's only known exposure to asbestos was cosmetic talc. And presented present 75 additional subjects, with malignant mesothelioma, who's only known exposure to asbestos was cosmetic talc. The use of talc-based powders and their possible health effects has received considerable attention in the print media and in authoritative and consumer-oriented websites. The basis for these concerns is the increased risks of ovarian cancer associated with perineal transport. Despite these concerns, a comprehensive review of talc literature and the scientific and scientific understanding that talc can cause ovarian cancer has not been adequately addressed in medical literature. The current review provides a historical context for the origin of talc and ovarian hypothesis for cancer, how specific speculations on talc carcinogenicity could not be properly understood, and explain the findings of many other details about talc and cancer other than perineal dust associations., concluded with suggestions for new avenues of research in this area with over 22000 new cases diagnosed and about 14000 death survey year in the USA alone, ovarian cancer ranks as the fifth as the cause of neoplastic death among women. It causes more deaths than any other cancer of the female reproductive system, although the incidence has dropped since the mid-1980s (American Cancer Society, 2016). Most cervical cancers are diagnosed over time and have limited treatment prospects. This is due to the lack of a method for testing its early detection and resistance to chemotherapy. The etiology of the disease is not fully understood, although researchers have identified several risk factors, including a family history of ovarian or breast cancer, advanced age, white race, null parity, obesity, education level, and endometriosis. In addition, breastfeeding, tubal ligation, and oral contraceptive use have been reportedly associated with reduced risk. Ovarian cancer is a heterogeneous disease that

comprises four major histologic types; serous carcinoma is the most common form (50%), followed by mucinous, endometriosis, and clear cell carcinoma. Each type, with the exception of clear cell carcinoma, is classified as risk factors. On the basis of limited data, there appears to be some variability in the risk factors of certain histological species. A link between asbestos exposure and increased risk of cervical cancer has been reported, but it is not yet clear whether this may indicate improper segregation of peritoneal mesothelioma, a disease associated with severe asbestos exposure, or direct action of asbestos fibers in the uterus. Talc is a naturally occurring mineral that is commonly used in baths and body powders and other cosmetic products. Talc naturally occurs as soft crystals that give it a soft, smooth, absorbing, soft, and resistance to bonding. It is usually used on sanitary napkins, condoms, or underwear, as well as directly on the toilet. To our knowledge, accurate estimates of the widespread use of cosmetic talc in the private area are not available. However, the use of feminine hygiene powders, including body or deodorant powders containing cosmetic talc has been reported to be a shig has 50% in some regions (International Agency for Research on Cancer (IARC), 2010, including parts of North America, Australia, and the UK. Talc was used for the first time by Bethune¹ in 1935 as a pleural sclerosis in agent to avoid pulmonary collapse prior to surgery for tuberculosis. Gaensler in 1956, along with Gobble et al in 1963, reported serious complications after intrapleural injection of talc. However, Weisberg in 1981 stated that “The use of talc in the pleura is safe and effective. It provides excellent relief to patients with pleural effusion and treats it in other groups. Excessive anxiety about complications of using talc is unjustified.” However, recently Lineau et al in 1993, and Kennedy et al in 1994, reported pulmonary in filtrate and respiratory distress syndrome in patients undergoing talc pleurodesis. In the early 1970's, the discovery of asbestos in talc, as well as the discovery of talc mixed with uterine tissue, led to civil strife. For more than 40 years, the talc and manufacturing companies have tried to obscure the value of these findings by keeping the information disclosed behind the business veil and otherwise contributing to the medical knowledge of the health effects and asbestos content of the talc used in cosmetics. Information management is a well-known way in which industries keep selling and avoiding control and legal liability. There are many examples when companies have concealed the presence of hazardous components in products; failed to publish study results indicating that their product presented health risks; and manipulated studies to publish false results that encouraged product use or hid side effects. For example, in 1971, Henderson et al. found talc in an ovarian cancer tissue sample and raised concerns about the relation between talc use and ovarian cancer. Johnson & Johnson hired Arthur Langer, a mineralogist at Mount Sinai, to reexamine the tissue. Langer confirmed the presence of talc, and also found asbestos in ovarian cancer tissue. Evidence shows that Johnson & Johnson successfully dissuaded him from publishing these findings. In 2008, cancer of the ovary represented the second leading cause of gynecologic cancer death worldwide. The geographical distribution of ovarian cancer is characterized by wide international variation. Highest rates are observed in North America and Northern Europe. In the United States, white women have higher incidence and mortality rates than both racial and ethnic groups (Horner et al. 2009). Although The etiology of cervical cancer is poorly understood, recurrence, breastfeeding, oral contraceptive use, and tubal ligation or hysterectomy are associated with risk while only estrogen therapy, smoking, and other environmental factors, function, and genetics are positively associated with ovarian cancer. Approximately 125 million people around the world work in environments in which they are exposed to asbestos, and at least 90,000 people die from asbestos-related lung cancer, mesotheliomas, or asbestosis every year. Asbestos exposure has been identified in some previous reviews as a potential risk factor for cervical cancer. However, the organization was not widely known. The use of talc bacteria, which may in some cases contain asbestiform or talc mineral fibers, has also been linked to ovarian cancer in many studies. The link between the risk of ovarian cancer and asbestos exposure was handled by the Monographs Working Group called March 2009 by the International Agency for Research on Cancer (IARC). After considering the potential role of chance, confounding, and other forms of bias, the working group concluded that the evidence is sufficient for a causal association between occupational exposure to asbestos and ovarian cancer.

Contrary to the research findings and based statistics neither the U.S government nor the talc industry ever banned the presence of asbestos in “cosmetic” talc. In fact, since the 1950s and as recently as October 2019, talc manufacturing companies and the FDA have found asbestos in cosmetic talc products. During perineal and other body applications of cosmetic talc, users inhale talc and asbestos. Inhaled asbestos passes through the lymphatic system to the uterus of the peritoneum and nearby tissues. Exposure during use of cosmetic talc is high enough to cause talcosis in some users. The similarity between ovarian cancer and asbestos causes mesothelioma. Inhaled asbestos is an established cause of mesothelioma, cervical and lung cancer. Peritoneal mesotheliomas and serous ovarian cancer are histologically similar and often difficult to distinguish. The peritoneum, pleura, ovary and fallopian tubes all originate from the mesoderm and their tumors are historically and clinically similar. Mesothelioma and serous ovarian cancer usually indicate p53 chromosomal removal. Asbestos has been shown to induce p53 deletions invitro. Gordon et al. (2019) fund that cosmetic talc contained asbestos was “a causative agent in the development of mesotheliomas, lung tumors, and gastrointestinal tumors.

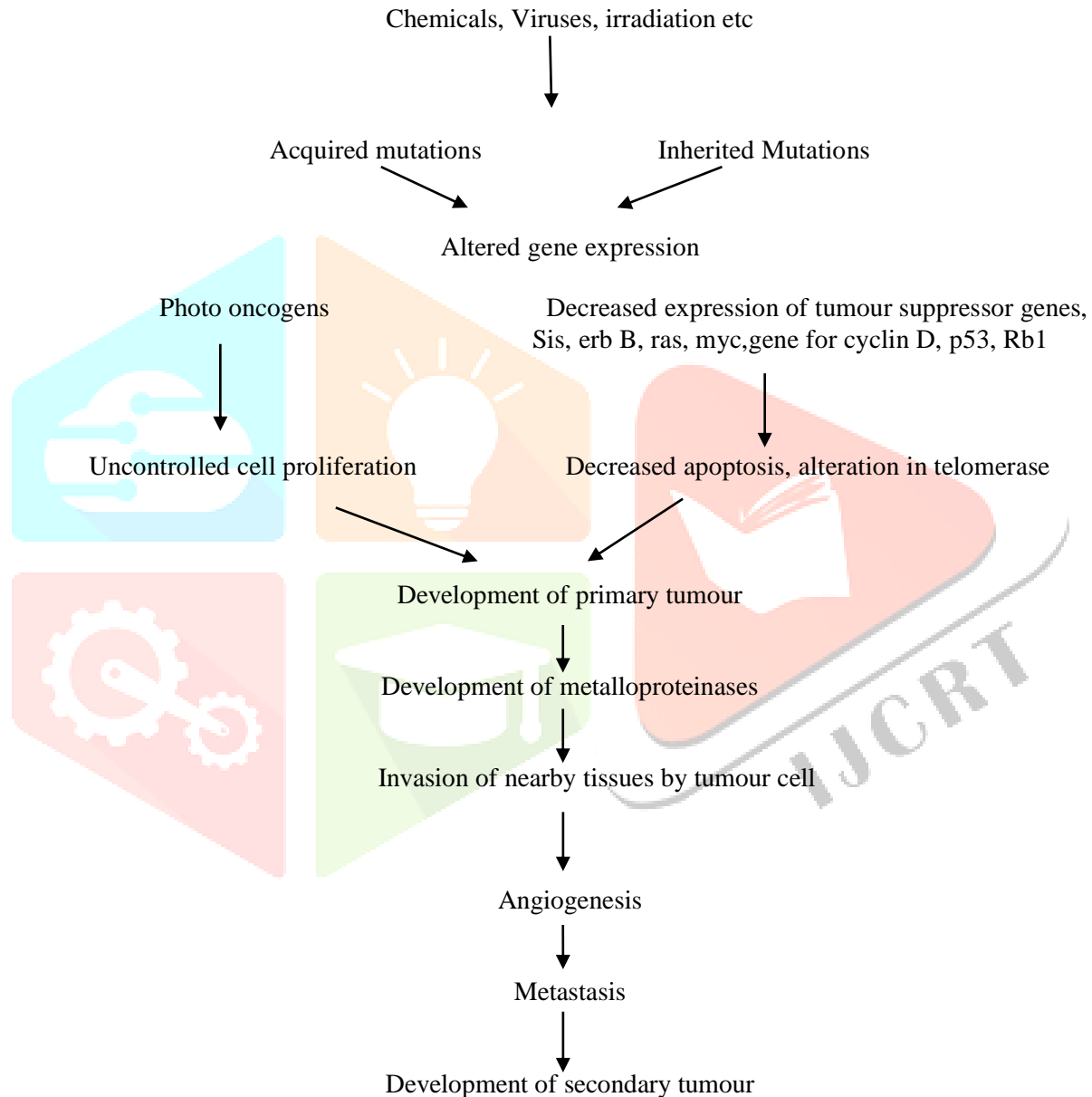


Figure3. Simplified outline of genesis of cancer

It has been demonstrated that both asbestos and talc can and do cause diseases of the pleura. Asbestos has been shown to cause the development of benign lesions in pleura termed pleura plaques. These plaques have become a hallmark for asbestos exposure. These lesions correlated with interstitial fibrosis of the lung parenchyma and the development of lung tumors. These lesions allow for attribution of asbestos as a causative factor in the development of lung tumors in the absence of interstitial fibrosis. Pleural plaques are also lesions that show asbestos exposure in the absence of interstitial fibrosis and / or lung tumors. Asbestos has been shown to be the cause of pleural lining tumors, mesotheliomas. It has been shown that mesotheliomas in men were more common in those men with a history of asbestos exposure. Similarly, it was shown that the females of these exposed men and women with asbestos also developed pleural plaque, interstitial fibrosis and mesotheliomas. It was understood how asbestos caused sores on the pleura of women

working with asbestos, however, at first it was not understood how the wives or children of the workers started these sores until investigators looked at men's clothing and decided to bring asbestos home and wives or the children were shown washing their clothes. However, only about 30 percent of all mesotheliomas are found in women who may be related to asbestos exposure. The remnants of women with mesotheliomas were considered idiopathic because they were not prone to specific asbestos exposure. Epidemiology Malignant mesotheliomas are an aggressive tumor of serosal surfaces, most commonly involving the pleura followed by the peritoneum. Incidence rate strange between 0.2 and two cases per million in women, versus approximately 6.8 cases per million of serous primary peritoneal cancer of 3300 new diagnoses of mesotheliomas per year in the United States, approximately 10–15% are peritoneal (Good man and Shvetsov, 2009; Surveillance, Epidemiology, and End Results (SEER) Program, 2004), with a mean age at diagnosis of 53. A study of 10,589 cases of mesothelioma reported to the Surveillance, Epidemiology, and End Results (SEER) database between 1973 and 2005 demonstrated that females account for 44% of peritoneal cases compared to 19% of pleural primaries (Surveillance, Epidemiology, and End Results (SEER) Program, 2004; Ovarian involvement in mesothelioma is rare. In a United Kingdom registry encompassing 24 years of data on mesotheliomas, 0.03% of mesothelioma-related deaths had presented with an ovarian mass. Pleural and peritoneal mesotheliomas share many risk factors, the most common of which is exposure to asbestos. In a study of 52 women with malignant mesothelioma, indirect asbestos exposure, as measured by husbands and fathers working in asbestos-related industries, resulted in an increased risk of developing dangerous mesotheliomas. Some women apply a powder to their genitals, directly or through their underwear, clean diapers, diaphragms or tampons. Many powder products include mineral talc. Talc was first investigated as a carcinogen based on its association with asbestos, which has known carcinogenic effects and may be mined in similar areas., all U.S. manufacturers of cosmetic talc agreed to ban asbestos in 1976, and the International Agency for Research on Cancer has concluded that there is only "possible" evidence that the use of perineal talc-based body powder may be is carcinogenic. In the United States, ovarian cancer is the fourth most frequent cause of cancer death among women, following lung, breast, and colorectal cancers. Each year, approximately 26000 women are diagnosed with ovarian cancer and 14000 die of it. Germ line mutations in BRCA1, BRCA2, or other genes have been implicated in a small fraction of cases. It has been suggested that, in many patients, the risk of epithelial ovarian cancer may be associated with " chronic ovulation " (i.e., recurrent formation of stromal epithelial cleft and cysts inserted after ovulation) or in others. a type of hormonal stimulation of the ovarian epithelial cells either on the surface of the ovary or within ovarian inclusion cysts, possibly mediated through excessive gonadotropin secretion. From the evidence to date, the relative importance of these two hypotheses incessant ovulation and gonadotropin stimulation cannot be distinguished. While or both may be contributing to the development of cervical cancer; it seems that a major additional factor should be involved. The purpose of this review is to examine the evidence and contraindications of chronic ovulation and gonadotropin hypotheses, as well as to consider the possibility that ovarian cancer risk may be increased by factors associated with excessive androgenic stimulation of ovarian epithelial cells and may be reduced by progesterone-related factor stimulation. Many features of the evidence bearing on the pathophysiology of ovarian cancer appear to support a connection with androgens and progesterone Voluminous scientific studies in recent years have brought a fundamentally new understanding of the tumor biology of ovarian cancer. It is no longer an issue that the term " cervical cancer " takes a variety of different malignant tumors in terms of important aspects of etiology, pathogenesis, prognosis, pathology, and molecular pathology many medical studies have found very important features. Determining prognosis, as well as their own is now informing therapeutic decisions. In parallel with the FIGO classification for the staging of ovarian cancer the WHO classification was revised and is valid since 2014. Most of the current clinical guidelines of ovarian cancer refer to the previous FIGO and WHO classification systems; therefore we conducted this manuscript to clarify the clinical implications of the news definitions. Both qualities the tumor stage (according to FIGO classification) and the type of tumor (according to WHO classification) are essential criteria for the treatment decision-making process of a differentiated therapy.

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