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AMERICAN CANCER SOCIETY'S
SCIENCE WRITERS' SEMINAR

Vacation Village Hotel, San Diego, Calif.

March 22-27, 1968

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OVARIAN CANCER, DETECTION & ETIOLOGY

John B. Graham, M.D.
Gynecologic Department
Roswell Park Memorial Institute
School of Medicine
State University of New York
at Buffalo
Buffalo, New York

# OVARIAN CANCER, DETECTION & ETIOLOGY

John Graham and Ruth Graham

Gynecologic Department
Roswell Park Memorial Institute
School of Medicine, State University
New York at Buffalo

Cancer of the ovary is a serious and growing problem. In New York State it ranks third in cancer deaths of women. If the cancer is recognized when it is apparently confined to the ovary, the five-year cure rate is 90%. About 20% of more advanced cases are cured. Unfortunately, the majority (80%) of cases are advanced which results in a poor overall cure rate (25-30%).

Early diagnosis could increase the salvage but symptoms and signs are unreliable until the tumor is far advanced. Cytology has been effective in cervical cancer and may have comparable value in ovarian cancer. A sample of peritoneal fluid, which contains cells shed from the ovary, can be obtained with a needle passed through the upper vagina into the pouch of Douglas. This is done in the office or clinic with only mild discomfort. The sample is processed much like a vaginal smear.

In 22 cases with malignant cells in the cul-de-sac fluid and normal physical examination the ovaries were removed. In two, there were small invasive cancers and in the remainder, there was malignant epithelium on the surface. The non-invasive malignant epithelium is referred to as a borderline lesion and is regarded as comparable to carcinoma in situ of the cervix. Borderline lesions are composed of malignant cells, i.e., they have an irregular chromatin pattern in the nucleus. This type epithelium is found in and adjacent to clinical ovarian cancers. The frequency that borderline lesions progress to clinical cancer is unknown. That needs to be studied by biopsy and protracted follow-up without treatment. We are currently following fifteen of this type case.

We regard cul-de-sac aspiration as useful in the high risk or diagnostic problem patient. These include all who come to examination under anesthesia for vaginal bleeding without an obvious cause, those with pelvic masses of uncertain character, and those with vague pelvic or abdominal discomfort. It also could be used in the patient scheduled for pelvic laparotomy where preservation of the ovaries is contemplated to avoid leaving those with malignant proclivity.

Ovarian cancer has quadrupled since the turn of the century in this country. A hundred years ago it was relatively rare in Western Europe and North America. Now it is common and increasing. In other parts of the world such as Latin America, Japan and China ovarian cancer is still uncommon. This suggests some etiologic element in modern western life. Women with asbestosis frequently have mesotheliomas and ovarian cancer. Some mesotheliomas due to asbestos are indistinguishable from ovarian cancer.

We have injected finely divided asbestos intra-peritoneally in guinea pigs and rabbits. Weekly injections are followed by malignant changes on the ovarian surface. These are seen as early as seven weeks. By a year, half of the guinea pigs and all of the rabbits show these changes. But none showed invasive cancer. However, if stibestrol is given after a course of intra-peritoneal asbestos, invasive cancer resulted in one of three guinea pigs and four of six rabbits. The guinea pig received asbestos for ten months and 5 mg./week of stibestrol for four months. The rabbits had received asbestos for eight to thirteen months and stibestrol 10 mg./week for two weeks to three months. Two of the cancers are sarcomas and three carcinomas. Two probably are ovarian in origin. The

site of origin of the others is less certain.

Asbestos fibers are demonstrable in non-neoplastic tissues of exposed animals and man but are rarely found in the cancer itself. We have looked for asbestos fibers in ovarian cancers without success. Histologic sections of ovaries of 12 patients with borderline lesions or microinvasive lesions were examined under polarized light. In six, bi-refringent crystalize material was found near the abnormal epithelium. These crystals could be asbestos but have not been identified.

Until recently, laparotomy and gross inspection were needed to make or exclude the diagnosis of ovarian cancer. (Endoscopy is used in some clinics for this purpose.) Cul-de-centesis offers a method of excluding cancer diagnosis if normal peritoneal fluid is found and of recognizing preclinical cancer.

The prevention of ovarian cancer is preferred to its early detection. Our evidence suggests; but by no means proves, that there may be an etiologic relation between asbestos and ovarian cancer. The lesions on the ovarian surface elicited by asbestos in guinea pigs and rabbits are similar to those found in patients with borderline lesions and adjacent to clinical cancer. It is of interest that invasive cancer was only found after the addition of stibestrol. This implys a two-step process.

The use of asbestos has increased a thousand fold since the turn of the century. It is ubiquitous in our environment. It is virtually undestructable. It can be fragmented into ever smaller particles but is still there. The smaller particles (less than five microns) readily pass into

the tissues by way of the respiratory tract and possibly by the intestinal tract as well. The home, the automobile, the office and industry all provide exposure. We think that asbestos may be a factor that predisposes to ovarian cancer and that it deserves further investigation.