Cancer Association of South Africa (CANSA)

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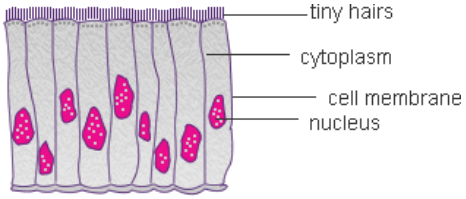
Fact Sheet on Fallopian Tube Cancer

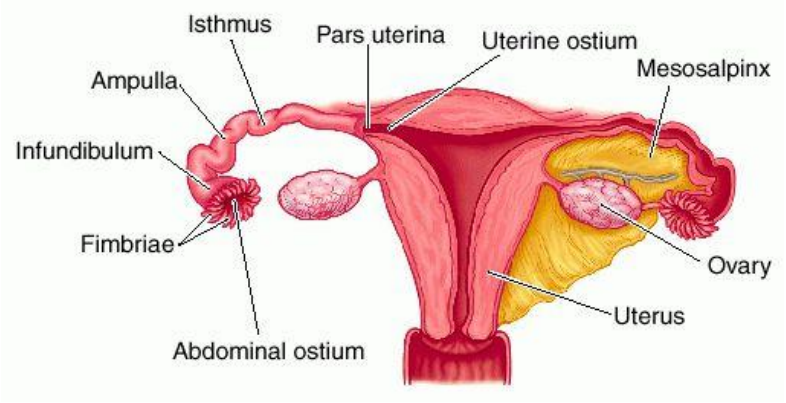
Introduction

The Fallopian tubes, also known as oviducts, uterine tubes, and salpinges (*singular* salpinx) are two very fine tubes lined with ciliated epithelia (cells with fine hair-like structures called cilia which aids to propel ova from the ovaries to the uterus), leading from the ovaries into the uterus, via the utero-tubal junction.



[Picture Credit: Ciliated Epithelium]

[Picture Credit: Fallopian Tubes]



In a woman's body the fallopian tube allows passage of the egg (ovum) from the ovary to the uterus. Its different segments are (lateral to medial):

- The infundibulum with its associated fimbriae near the ovary
- The ampullary region that represents the major portion of the lateral tube
- The isthmus which is the narrower part of the tube that links to the uterus
- The interstitial (also known as intramural) part that transverses the uterine musculature. The tubal ostium is the point where the tubal canal meets the peritoneal cavity
- The uterine opening of the Fallopian tube is the entrance into the uterine cavity, the utero-tubal junction.

The fallopian tubes are named after their discoverer, the 16th century Italian anatomist, Gabriel Fallopius.

[Picture Credit: Gabriel Fallopius]

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Kyo, S., Ishikawa, N., Nakamura, K. & Nakayama, K. 2020.
"Ovarian cancer is the leading cause of gynecologic cancer death in the world, and its prevention and early diagnosis remain the key to its treatment, especially for high-grade serous carcinoma (HGSC). Accumulating epidemiological and molecular evidence has shown that HGSC originates from fallopian tube secretory cells through serous tubal intraepithelial carcinoma. Comprehensive molecular analyses and mouse studies have uncovered the key driver events for serous carcinogenesis, providing novel molecular targets. Risk-reducing bilateral salpingo-oophorectomy (RRSO) has been proposed to reduce the subsequent occurrence of serous carcinoma in high-risk patients with BRCA mutations. However, there is no management strategy for isolated precursors detected at RRSO, and the role of subsequent surgery or chemotherapy in preventing serous carcinoma remains unclear. Surgical menopause due to RRSO provides a variety of problems related to patients' quality of life, and the risks and benefits of hormone replacement are under investigation, especially for women without a previous history of breast cancer. An additional surgical option, salpingectomy with delayed oophorectomy, has been proposed to prevent surgical menopause. The number of opportunistic salpingectomies at the time of surgery for benign disease to prevent the future occurrence of HGSC has increased worldwide. Thus, the changing concept of the origin of serous carcinoma has provided us a great opportunity to develop novel diagnostic and therapeutic approaches."

Fallopian Tube Cancer
Fallopian tube cancer is cancer that occurs in any part of the fallopian tube.

Primary fallopian tube cancer means the cancer first started to grow in this area. Sometimes cancers that start in other areas, such as the ovaries, womb or cervix, can spread to the fallopian tubes. This is known as a secondary fallopian tube cancer and is treated according to where the cancer started (the primary cancer).

There are different types of fallopian tube cancer. The most common type is adenocarcinoma, which starts in the cells that form part of the lining of the fallopian tubes.

Other types of fallopian tube cancer are very rare and include

- Transitional cell – transitional cells are stretchy cells found in the fallopian tube lining
- Sarcoma – this affects the muscular part of the fallopian tube

Incidence of Fallopian Tube Cancer in South Africa
The National Cancer Registry (2016) does not provide any information on the incidence of Fallopian Tube Cancer.

Risk Factors for Fallopian Tube Cancer?
Given its rarity, the causes and risk factors for developing primary fallopian tube cancer are not clearly defined. There has been some association of the cancer with chronic infection and/or

inflammation of the fallopian tubes (due to untreated sexually transmitted diseases, for example), although a cause-effect relationship has not been definitively established.

Michels, K.A., McNeel, T.S. & Trabert, B. 2019. **Objective:** To clarify associations between metabolic syndrome, its components, and ovarian cancer risk.
Methods: Using a case-control study within the U.S.-based Surveillance, Epidemiology and End Results (SEER)-Medicare linked database, we examined metabolic syndrome, its components (obesity, impaired fasting glucose, hypertension, HDL cholesterol, triglycerides), and ovarian/fallopian tube cancer risk. Cases (n = 16,850) were diagnosed with cancer between age 68-89 from 1994 through 2013. Controls (n = 281,878) were Medicare enrollees without these cancers living in registry areas. We estimated adjusted odds ratios (OR) and 95% confidence intervals (CI) with logistic regression.
Results: Women with metabolic syndrome had reduced ovarian cancer risk compared to women not meeting the diagnostic criteria (OR 0.86, CI 0.82-0.89). Having one or two syndrome components was associated with increased risk, but having ≥3 was not, when compared to women without any components. Impaired fasting glucose, which was highly prevalent among those with metabolic syndrome, was associated with reduced risk (OR 0.90, CI 0.87-0.93). Hypertension and high triglycerides, the most prevalent components among women without metabolic syndrome, were associated with increased risks (OR 1.08, CI 1.04-1.12; OR 1.05, CI 1.01-1.08, respectively).
Conclusions: Specific metabolic syndrome components may have modest associations with ovarian cancer. These associations varied in direction and the prevalence of the components influenced the overall association between metabolic syndrome and ovarian cancer. Evaluating metabolic syndrome as a composite exposure could be misleading in ovarian cancer research, but further study of the syndrome components is warranted.

Signs and Symptoms of Fallopian Tube Cancer
Women with fallopian tube cancer may experience one or more of the following symptoms or signs. Sometimes, women with fallopian tube cancer do not show any of these symptoms. Or, these symptoms may be caused by a medical condition that is not cancer.

- Irregular or heavy vaginal bleeding, especially after menopause or in between periods
- A swollen abdomen
- Occasional abdominal or pelvic pain or feeling of pressure
- Vaginal discharge, which may be clear, white, or tinged with blood
- A pelvic mass or lump

As a tumour in the fallopian tube grows, it can push against the walls of the tube and cause abdominal pain. If untreated, the cancer can spread into and through the walls of the fallopian tubes and eventually into the pelvis (lower abdomen) and stomach areas. This can cause other symptoms as well.

Diagnosis of Fallopian Tube Cancer
Because fallopian tube cancer is so rare, and its symptoms can resemble other problems, it can be difficult to diagnose. Additionally, in some cases, women do not learn they have fallopian tube cancer until a tube has been removed surgically during an operation to treat another illness or problem.

However, there are several tests that may be performed in order to make a definite diagnosis of the condition. Tests that may be performed include:

- Pelvic Examination - This test involves feeling the uterus, vagina, ovaries, fallopian tubes, bladder and rectum to find any abnormality in their shape or size.
- CA125 Test - This is a blood test that checks levels of a blood protein known as CA125, which is a tumour marker for gynaecological diseases such as fallopian tube cancer. An estimated 85 percent of women with gynaecological disease have increased levels of CA125. However, it is important to note that increased levels of CA125 may not necessarily mean that a woman has cancer, since CA125 levels also may be increased during pregnancy, menstruation, in the presence of other non-cancerous gynaecologic diseases or cancers affecting other parts of the body.
- Computed Tomography (CT) Scan - This imaging test takes a series of detailed pictures of areas inside the body. The pictures are created by a computer, which is linked to an X-ray machine. A special dye may be injected into a vein or swallowed to help the organs or tissues show up more clearly.
- Ultrasound - An ultrasound of the pelvis may be performed. This test involves the use of high-frequency sound waves to create images of organs and systems within the body. These waves, which cannot be heard by humans, create a pattern of echoes called a sonogram. Healthy tissues, fluid-filled cysts, and tumours look different on this picture.
- Transvaginal ultrasound – a special wand is inserted in the vagina which gives off ultrasound waves that can be read on the ultrasound screen.
- Biopsy – Cells are removed from the fallopian tubes and looked at under a microscope. This is the only way to find out for sure if a person has fallopian tube cancer. It usually requires surgery.

PDQ Screening and Prevention Editorial Board. 2020.
"This PDQ cancer information summary has current information about ovarian, fallopian tube, and primary peritoneal cancer screening. It is meant to inform and help patients, families, and caregivers. It does not give formal guidelines or recommendations for making decisions about health care. Editorial Boards write the PDQ cancer information summaries and keep them up to date. These Boards are made up of experts in cancer treatment and other specialties related to cancer. The summaries are reviewed regularly and changes are made when there is new information. The date on each summary ("Date Last Modified") is the date of the most recent change. The information in this patient summary was taken from the health professional version, which is reviewed regularly and updated as needed, by the PDQ Screening and Prevention Editorial Board."

Staging of Fallopian Tube Cancer
Staging of any cancer is very important as the stage of the cancer helps determine the type of anti-cancer treatment that is given.

Treatment of Fallopian Tube Cancer
An optimal treatment regimen should ultimately be individualised as much as possible. It should take into account the patient's stage of disease, other medical history, and personal preference, among other things. Treatment may include:

Surgery - fallopian tube cancer is typically diagnosed with surgery.

Radiation Therapy – Use is made of an external beam.

Chemotherapy - An individual chemotherapeutic regimen should preferably be developed by the oncologist with the patient's specific needs in mind.

Clamp, A.R., James, E.C., McNeish, I.A., Dean, A., Kim, J.W., O'Donnell, D.M., Hook, J., Coyle, C., Blagden, S., Brenton, J.D., Naik, R., Perren, T., Sundar, S., Cook, A.D., Gopalakrishnan, G.S., Gabra, H., Lord, R., Dark, G., Earl, H.M., Hall, M., Banerjee, S., Glasspool, R.M., Jones, R., Williams, S., Swart, A.M., Stenning, S., Parmar, M., Kaplan, R., & Ledermann, J.A. 2019.

Background: Carboplatin and paclitaxel administered every 3 weeks is standard-of-care first-line chemotherapy for epithelial ovarian cancer. The Japanese JGOG3016 trial showed a significant improvement in progression-free and overall survival with dose-dense weekly paclitaxel and 3-weekly carboplatin. In this study, we aimed to compare efficacy and safety of two dose-dense weekly regimens to standard 3-weekly chemotherapy in a predominantly European population with epithelial ovarian cancer.

Methods: In this phase 3 trial, women with newly diagnosed International Federation of Gynecology and Obstetrics stage IC-IV epithelial ovarian cancer were randomly assigned to group 1 (carboplatin area under the curve [AUC]5 or AUC6 and 175 mg/m^2 paclitaxel every 3 weeks), group 2 (carboplatin AUC5 or AUC6 every 3 weeks and 80 mg/m^2 paclitaxel weekly), or group 3 (carboplatin AUC2 and 80 mg/m^2 paclitaxel weekly). Written informed consent was provided by all women who entered the trial. The protocol had the appropriate national research ethics committee approval for the countries where the study was conducted. Patients entered the trial after immediate primary surgery, or before neoadjuvant chemotherapy with subsequent planned delayed primary surgery. The trial coprimary outcomes were progression-free survival and overall survival. Data analyses were done on an intention-to-treat basis, and were powered to detect a hazard ratio of 0·75 in progression-free survival. The main comparisons were between the control group (group 1) and each of the weekly research groups (groups 2 and 3).

Findings: Between June 6, 2011, and Nov 28, 2014, 1566 women were randomly assigned to treatment. 72% (365), completed six protocol-defined treatment cycles in group 1, 60% (305) in group 2, and 63% (322) in group 3, although 90% (454), 89% (454), and 85% (437) completed six platinum-based chemotherapy cycles, respectively. Paclitaxel dose intensification was achieved with weekly treatment (median total paclitaxel dose 1010 mg/m^2 in group 1; 1233 mg/m^2 in group 2; 1274 mg/m^2 in group 3). By February, 2017, 1018 (65%) patients had experienced disease progression. No significant progression-free survival increase was observed with either weekly regimen (restricted mean survival time 24·4 months [97·5% CI 23·0-26·0] in group 1, 24·9 months [24·0-25·9] in group 2, 25·3 months [23·9-26·9] in group 3; median progression-free survival 17·7 months [IQR 10·6-not reached] in group 1, 20·8 months [11·9-59·0] in group 2, 21·0 months [12·0-54·0] in group 3; log-rank p=0·35 for group 2 vs group 1; group 3 vs 1 p=0·51). Although grade 3 or 4 toxic effects increased with weekly treatment, these effects were predominantly uncomplicated. Febrile neutropenia and sensory neuropathy incidences were similar across groups.

Interpretation: Weekly dose-dense chemotherapy can be delivered successfully as first-line treatment for epithelial ovarian cancer but does not significantly improve progression-free survival compared with standard 3-weekly chemotherapy in predominantly European populations.

Funding: Cancer Research UK, Medical Research Council, Health Research Board in Ireland, Irish Cancer Society, Cancer Australia.

Taylor, S.E., Chu, T., Elvin, J.A., Edwards, R.P. & Zorn, K.K. 2019.

Background: Recurrent ovarian, fallopian tube, and peritoneal cancers have limited potential for cure with traditional therapies. Preliminary results from a phase I study of everolimus and bevacizumab in advanced solid tumors showed it to be a promising combination. The primary

objective of this study was to evaluate the 6-month progression-free survival for everolimus and bevacizumab in recurrent ovarian, peritoneal, and fallopian tube cancer. Secondary objectives included evaluation of efficacy and safety.
Methods: In this open-label, single-institution, phase II trial, patients received everolimus 10 mg/day by mouth and bevacizumab 10 mg/kg intravenously every 14 days on a 28-day cycle. Treatment continued until disease progression or adverse event.
Results: Fifty patients were enrolled. Median age was 60.5 years (range 28-82). Forty-six (92%) subjects had measurable disease. Thirteen (26%) (24% adjusted) were progression-free at 6 months (95% CI 16.67-42.71%). One patient had a complete response, while six had a partial response and 35 had stable disease as their best response. Patients with both platinum-sensitive and -resistant disease demonstrated responses, as did some prior bevacizumab exposure. There were two grade 4 and 31 grade 3 toxicities noted in 25 distinct patients. The most common reported toxicities included oral mucositis, fatigue, diarrhea, hypertension, pain, nausea and anorexia. Thirty-eight (76%) patients came off study because of disease progression. Unique molecular profiles were identified in long-term responders.
Conclusions: Combining everolimus and bevacizumab does not distinctly improve response compared to bevacizumab alone, but further study of selected patients with alterations in the PI3K/mTOR pathway may document benefit.

Hormonal Therapy - the role of hormonal treatment for fallopian tube cancer is not clear, although both varying degrees of success has been shown with various methods.

Combined Modality - the latest in combined modality approaches for advanced disease consists of cryoreductive surgery, post-surgical chemotherapy to reduce remaining tumour burden to microscopic levels, and possible radiation to the abdomen and pelvis following chemotherapy.

About Clinical Trials
Clinical trials are research studies that involve people. They are conducted under controlled conditions. Only about 10% of all drugs started in human clinical trials become an approved drug.

Clinical trials include:
- Trials to test effectiveness of new treatments
- Trials to test new ways of using current treatments
- Tests new interventions that may lower the risk of developing certain types of cancers
- Tests to find new ways of screening for cancer

The South African National Clinical Trials Register provides the public with updated information on clinical trials on human participants being conducted in South Africa. The Register provides information on the purpose of the clinical trial; who can participate, where the trial is located, and contact details.

For additional information, please visit: www.sanctr.gov.za/

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