Shining a light on the hidden tumor

Of all the gynecologic cancers, ovarian cancer is the number one killer. But it often goes undetected until it’s too late. We’ll help you understand the signs and symptoms of ovarian cancer, how it’s diagnosed, and what you can do to help your patient manage her illness.

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SHELTERED WITHIN THE depths of a woman’s pelvis, the ovaries are normally hard at work producing ova and secreting hormones, like estrogen and progesterone. But the very environment that protects these solid, slightly nodular, almond-shaped organs also makes them vulnerable—they’re so hidden away that if cancer develops in one of them, it may not be detected until it’s too late.

That’s one reason why ovarian cancer is the deadliest gynecologic cancer in the United States (see By the numbers). The fact that the size, shape, position, and histology of the ovaries change over a woman’s lifetime also contributes to the delay in diagnosis and the high mortality rate.

In this article, I’ll shine a light on this potentially deadly malignancy by discussing possible causes of ovarian cancer and its pathophysiology, clinical presentation, diagnosis, and treatment options. I’ll also tell you what you need to know about screening methods that can lead to earlier detection and treatment.

A trio of theories

Why does ovarian cancer occur? The experts have offered three possible explanations:

- The incessant-ovulation theory focuses on how the monthly ovulatory cycle affects the ovaries. The idea is that the cells in the

By the numbers

Estimates from The American Cancer Society show that in 2006, 20,180 women in the United States will be diagnosed with ovarian cancer and 15,310 women will die of the disease. The high number of deaths is largely due to the fact that more than 70% of women affected have advanced disease when it’s detected. But medical science is gaining ground. Thanks to improved diagnosis, staging, and treatments, 5-year survival has improved from 37% in the 1970s to 45% or higher now. According to the National Comprehensive Cancer Network, the average age at diagnosis is 63. Ovarian cancer is rare in women younger than age 30.

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ovarian cancer,
epithelium may be more likely to mutate with each ovulation, so when the cycle isn’t broken, as with pregnancy, the chance of mutation increases.

The pituitary/gonadotropin hypothesis points to elevated gonadotropin levels as the villain. Normally, the ovarian epithelium turns inward, or invaginates, to form cysts and clefts. Out-of-control gonadotropins may stimulate this process to the extreme, triggering transformation of the cells into a malignancy.

The inflammation theory says that monthly ovulation causes chronic inflammation and mutation in the epithelial cells that lead to ovarian cancer.

Remember, these are theories. We don’t know for sure which one is correct or what really causes ovarian cancer. We do know that genetic and endocrine factors raise the risk (see Where the trouble starts).

Risky business
The most significant risk factor is a positive family history; it’s present in about 10% of women with the disease. Ovarian cancer occurs more commonly in women with one of three hereditary syndromes. Families with these syndromes have a history of early breast and ovarian malignancies or hereditary nonpolyposis colorectal cancer. Also, an inherited mutated breast cancer 1 (BRCA1) or breast cancer 2 (BRCA2) gene is often found in hereditary ovarian cancer. If a woman has the mutated BRCA1 or BRCA2 gene, her lifetime risk for ovarian cancer is estimated at 40% to 50% by age 70. When these genes are normal, they help protect the body from cancer.

Other factors associated with ovarian cancer include:

- age older than 63
- obesity
- early menstruation or menopause after age 50
- fertility drug use
- use of estrogen replacement therapy after menopause
- exposure to talc or asbestos
- endometriosis
- pelvic inflammatory disease
- living in a western industrialized country.

But wait, there’s some good news. Researchers have identified a few seemingly protective factors:

- history of oral contraceptive use
- giving birth before age 25
- tubal ligation
- breast-feeding
- hysterectomy
- anovulatory disorders.

Ovarian cancer usually spreads by hitching a ride with the peritoneal fluid that continuously circulates through the abdomen. Other routes for metastases are through the lymphatic fluid or by direct tumor growth. Metastasis through the bloodstream is rare, and ovarian cancer doesn’t typically spread beyond the abdomen, even when advanced.

Is that a sign?
Don’t be surprised if your patient tells you she had symptoms for a while before she went to her health care provider. Studies indicate that more than 70% of women with ovarian cancer had symptoms for 3 months or longer before diagnosis. The problem is that early signs and symptoms can sometimes be nonspecific:

- increased abdominal size
- bloating
- early satiety (feeling of fullness after eating)
- abdominal pain
- leg or back pain
- indigestion
- vaginal bleeding
- fatigue
changes in bowel and bladder habits.

Given how vague these symptoms are, it’s understandable that a woman might ignore them. That’s where you come in. Teach your female patients to always investigate any of these symptoms if they occur. Tell them not to be embarrassed if it turns out that nothing’s wrong. This is truly a case of better safe than sorry.

When a woman does seek treatment and an ovarian mass is discovered, treatment depends on the clinical findings. The health care provider will probably monitor a premenopausal woman for a few ovulatory cycles, and investigate further if the mass doesn’t disappear; however, that wait-and-see approach doesn’t work with a postmenopausal woman. Any ovarian mass raises a red flag in a postmenopausal woman and must be immediately investigated for cancer.

Let’s look at what happens during that investigation.

Testing, testing…

A patient with suspected ovarian cancer can expect to undergo the following diagnostic tests:

- **Transvaginal and abdominal ultrasound**—Compared with the transabdominal method, a transvaginal approach usually makes it easier for the health care provider to see the ovaries. However, the location of the ovaries varies in each woman, so the health care provider may order both approaches to be sure.

Where the trouble starts

Three major categories of ovarian cancer have been identified, based on which cells are affected.

**Epithelial cancers**, which arise from the cells that line or cover the ovaries, account for 90% of ovarian malignancies. Epithelial cancers are further classified as serous (most common), endometrioid, mucinous, clear cell, and poorly differentiated.

**Germ cell cancers** start in cells that will become ova. **Stromal cell (sex cord) cancers** start in the connective tissue cells that hold the ovaries together and produce female hormones.

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computed tomography (CT) scan of the abdomen and pelvis
blood test for the tumor marker cancer antigen 125 (CA-125)—CA-125 can be elevated in ovarian cancer, but this marker isn’t specific. Although an ovarian mass can trigger a rise in the CA-125 level, so can endometriosis, pregnancy, liver disease, or fibroids. Also, a woman can have ovarian cancer and a normal CA-125 level; it’s elevated in only 50% of women with stage I disease. For this reason, CA-125 isn’t recommended as a screening tool for healthy women, but it can be useful in women with diagnosed ovarian cancer to track response to treatment.

First up, surgery
Exploratory laparotomy, performed by a surgeon who specializes in gynecologic oncology, is typically done to establish a definitive diagnosis, stage the disease if cancer is present, and remove as much of the tumor as possible (known as cytoreduction or debulking). For more about cancer staging, see Stages of ovarian cancer. However, the use of surgery largely depends on how far the cancer has spread, as well as other considerations, such as the patient’s age and general health and whether she plans to have children.

Exploratory laparotomy is extensive. The patient will undergo a total abdominal hys-

Stages of ovarian cancer

Stage I: Tumor limited to the ovaries
IA, limited to one ovary, no tumor on the ovarian surface, no malignant cells in ascites or peritoneal washings, capsule intact
IB, limited to both ovaries, no tumor on the ovarian surface, no malignant cells in ascites or peritoneal washings, capsules intact
IC*, limited to one or both ovaries, tumor on ovarian surface, capsule ruptured, ascites or peritoneal washings containing malignant cells

Stage II: Tumor involving one or both ovaries with pelvic extension
IIA, extension or metastasis to the uterus or tubes, no malignant cells in ascites or peritoneal washings
IIB, extension to other pelvic tissues, no malignant cells in ascites or peritoneal washings
IIC*, pelvic extension, ascites or peritoneal washings containing malignant cells

Stage III: Tumor involving one or both ovaries, peritoneal implants outside the pelvis or regional lymph node metastasis
IIIA, gross tumor limited to the true pelvis, negative nodes, microscopic peritoneal metastasis beyond the pelvis
IIIB, macroscopic peritoneal metastasis 2 cm or less in greatest dimension beyond the pelvis
IIIC, abdominal implants greater than 2 cm in greatest dimension or positive regional nodes

Stage IV: Tumor involving one or both ovaries, metastasis (greater than 2 cm in greatest dimension) beyond the pelvis; if pleural effusion is present, cytologic test results must be positive (parenchymal liver metastasis equals stage IV)

* Knowing whether rupture of the capsule was spontaneous or caused by the surgeon and whether peritoneal washings or ascites was the source of malignant cells helps the clinician decide whether a case should be categorized as stage IC or IIC.

Source: Federation Internationale de Gynecologie et d’Obstetrique (International Federation of Gynecology and Obstetrics).
terectomy (removal of the uterus) and bilateral salpingo-oophorectomy (removal of the fallopian tubes and ovaries). To determine the extent of the cancer, surgery typically includes scraping the abdominal surface of the diaphragm, peritoneal cytology, an omentectomy (removal of the fatty tissue layer that covers abdominal contents like an apron), and peritoneal and random biopsies. The surgeon will take multiple samples of the pelvic and para-aortic lymph nodes, too.

Look at the disease stage as the key factor for determining prognosis for a woman with ovarian cancer, but know that other factors influence outcome as well. These include how much cancerous tissue is left after surgery (suboptimally debulked disease, residual tumor less than 1 cm; optimally debulked disease, residual tumor less than 2 cm), the histologic type and grade of the tumor, the woman’s age, and her overall condition or performance status (see Rating performance). If your patient has a performance status of 0 to 2, she’s more likely to respond to chemotherapy, experience less toxicity from treatment, and have a better outcome. On the other hand, you can expect a poorer prognosis in a patient who’s older than age 69 when she’s diagnosed or who has one of these types of tumors: clear cell, mucinous, or poorly differentiated.

More to follow?

So what happens after surgery? If your patient has well-differentiated stage IA or IB ovarian cancer that has been surgically removed, she’s considered to be at low risk for metastasis and she won’t need further treatment. The oncologist will determine a follow-up plan.

Stage IA or IB ovarian cancer with a poorly differentiated tumor and stage IC, II, III, or IV disease are classified as high risk for metastasis, and the woman will need chemotherapy. We’re still looking for the optimal regimen, but evidence from clinical trials indicates that combination therapy with a taxane, such as paclitaxel (Taxol), and a platinum compound, such as cisplatin or carboplatin, is better than a single agent. The National Comprehensive Cancer Network guidelines recommend the paclitaxel/carboplatin combination. The frontline Gynecologic Oncology Group trials that are currently open are studying either intravenous (I.V.) paclitaxel and cisplatin with or without bevacizumab for patients with suboptimally debulked disease, or I.V. paclitaxel plus intraperitoneal therapy with paclitaxel and cisplatin for patients with optimally debulked disease (see Frontline chemotherapy: What are the options?).

Good news and not-so-good news

Complete remission from cancer means all signs and symptoms have disappeared; remission after initial therapy that lasts 5 years may be considered a cure. Let’s say your patient is one of the lucky ones: she’s in complete remission. She’ll likely undergo regular CA-125 monitoring and periodic abdominopelvic CT scans to check for recurrence. In most cases of recurrent disease, the CA-125 level rises above normal before symptoms develop. But an elevated CA-125 level doesn’t necessarily translate into quicker action. Most oncologists don’t start chemotherapy unless a pelvic exam or results of an abdominopelvic CT scan indicate disease recurrence. Otherwise, it would be too hard to identify a response.

What happens when the news isn’t...
good? If a woman’s cancer recurs, her response to initial chemotherapy and the length of time until recurrence help determine the next step in therapy. There are two possibilities:

- If she achieved complete remission and didn’t have a recurrence for more than 6 months after completing initial therapy, her disease is considered **drug sensitive** and she’ll probably receive the same regimen.
- If she achieved complete remission and had a recurrence less than 6 months after, her disease is considered **drug resistant**. If the cancer doesn’t respond to initial therapy at all, it’s labeled **drug refractory**. Drug-resistant or drug-refractory disease is typically treated with a different agent than the first time around, or the woman may be offered the option of participating in a clinical trial. Some of the agents used to treat recurrent disease include liposomal doxorubicin (Doxil), topotecan (Hycamtin), gemcitabine (Gemzar), oral etoposide (VePesid), tamoxifen (Nolvadex), and hexamethylmelamine (Hexalen).

When recommending a treatment approach for recurrent disease, the oncologist considers several factors, including the patient’s:
- prior responses
- quality of life
- toxicity profile
- current symptoms
- disease volume
- ability of the gastrointestinal system to absorb drugs
- age
- other illnesses
- social issues.

Radiation therapy may be part of the equation in a palliative treatment plan and may help if the patient has uncontrolled vaginal bleeding or pain. A radiation oncologist should outline a treatment plan. The goal of all palliative treatment is to balance toxicity with quality of life.

**A helping hand**
The more a woman feels threatened or harmed by cancer, the more education and support she’s going to need. With ovarian cancer, she might be facing tremendous psychosocial and physical issues, such as advanced disease at diagnosis, repeated cycles of aggressive treatment, little respite from therapy, and a poor chance of survival. You’ll be facing the challenge of addressing her psychosocial needs while preparing her for treatment and helping her manage adverse reactions to treatment, like infection, bleeding, and fatigue.

Before surgery, teach your patient and her family about the procedure and what to expect afterward. Explain that after surgery, you’ll monitor her for infection, circulatory complications, fluid and electrolyte imbalances, and pain.

If she’s scheduled to receive chemotherapy, teach her and her family about the major adverse reactions. Tell them how to prepare and respond if she develops fatigue, nausea, vomiting, hair loss, diarrhea, constipation, mucositis, neuropathy, arthralgia and myalgia, or myelosuppression.

Understandably, depression and anxiety are common when a patient faces a serious illness like ovarian cancer. Your patient may need help coping with such issues as premature menopause; loss of fertility; altered body image, sexual function, and family relationships; impaired functional capacity; financial problems; and loss of spiritual well-being.

Assess her for mood changes, feelings of worthlessness, inability to concentrate, fatigue, insomnia, impaired functioning, agitation, restlessness, and apprehensiveness.

Review her medical history, current medications and treatments, nutritional status, pain rating, elimination pattern, and sexual history for factors that may contribute to depression.

Listen to your patient’s concerns and refer
her to support services as appropriate. Man-
aging her symptoms, participating in a sup-
port group, meeting with a mental health
professional, and treatment with antidepres-
sant or antianxiety medication can help
resolve depression and anxiety.

Finally, if cure isn’t an option, you can
give your patient and her family tremendous
support by helping them cope with end-of-
life decisions and involving the hospice team
when the time is right.

Battling advancing disease
As ovarian cancer advances, it brings with
it significant nursing challenges. Let’s re-
view assessment findings and management
strategies for common problems.

Ascites is an accumulation of fluid in the
peritoneal cavity, which occurs when chan-
nels that normally remove fluid are blocked
or when cancer cells prevent absorption of
peritoneal fluid. Symptoms include early
satiety, dyspnea, increased abdominal girth,
constipation, and pain.

You should suspect ascites if your patient
has a protuberant abdomen with bulging
flanks, an everted umbilicus, diminished
bowel sounds, shiny or taut abdominal skin,
and dullness to percussion in dependent
areas of the abdomen. The health care
provider will order an abdominal ultra-
sound to confirm the diagnosis.

The treatment for ascites is removing the
fluid. The oncologist may perform paracen-
tesis in the office or in the radiology depart-
ment with ultrasound guidance.

A woman with progressing ovarian can-
cer is prone to intestinal obstruction in-
volving the small or large intestine. Peri-
stalsis is impaired if tumor growth in the
abdomen or adhesions causes a partial or
complete blockage. An obstruction can be
acute or chronic. Signs and symptoms of
acute obstruction include acute abdominal
distension and pain and projectile vomiting.
Symptoms of chronic obstruction include
abdominal distension and discomfort, con-
stipation, and nausea and vomiting.

Frontline chemotherapy: What are the options?
The current standard regimen for ovarian cancer is I.V. paclitaxel (Taxol)
with I.V. carboplatin. Docetaxel (Taxotere) is sometimes used in place of
paclitaxel, and cisplatin may be ordered in place of carboplatin. It’s impor-
tant to consider the toxicity of the prescribed regimen.

Recently, intraperitoneal delivery of paclitaxel and cisplatin has been
studied as an alternative to I.V. delivery. The Gynecologic Oncology
Group, a research group funded by the National Cancer Institute, conduct-
ed a phase 3 clinical trial for patients with optimally debulked stage III dis-
ease. Patients were given either I.V. paclitaxel with I.V. cisplatin or I.V.
paclitaxel with intraperitoneal paclitaxel and cisplatin. The results are
promising: I.V. paclitaxel followed by intraperitoneal paclitaxel and cis-
platin improved patients’ overall survival rate, and reduced the risk of
death by 25%.

The idea behind intraperitoneal delivery is to expose the tumor site (the
peritoneum) to high concentrations of antitumor agents, which only pene-
trate a few millimeters beneath the surface of the tumor, without harming
normal tissues. First, I.V. paclitaxel is administered on day one, followed
by intraperitoneal cisplatin on day 2, and then intraperitoneal paclitaxel on
day 8. This is repeated for 6 cycles.

The challenges with intraperitoneal therapy are catheter-related infec-
tions and a lower quality of life during treatment than with I.V. delivery.
Patients may experience abdominal pain related to the infusion and possi-
bile toxicity. Researchers are experimenting with using intraperitoneal car-
boliplatin instead of cisplatin to reduce toxic effects and improve tolerance.

Patients with newly diagnosed optimally debulked disease should dis-
cuss intraperitoneal therapy with their health care provider. This method of
delivery isn’t right for every patient, so treatment should be individualized.

The first sign of acute intestinal obstruc-
tion may be hyperactive bowel sounds as the
bowel tries to move digestive contents past
the blockage. Teach your patient to recog-
nize problems and to immediately contact
her health care provider if they occur.

Acute intestinal obstruction may be an
indication for admission to the hospital for
placement of a nasogastric tube to decom-
press the bowel. A woman with advanced
cancer may already be debilitated, so she’ll
undergo surgery only if conservative inter-
ventions fail or she’s in acute distress.

Three factors—prolonged immobility,
tumors that decrease or obstruct blood flow,
and hypercoagulability—put all cancer
patients at risk for deep vein thrombosis.
(DVT). Watch your patient for unilateral leg edema or pain accompanied by tenderness, warmth, and erythema. DVT treatment includes anticoagulation therapy and, possibly, placement of a filter in the inferior vena cava.

One of the greatest challenges for a woman with ovarian cancer is malnutrition. She may have little appetite—the result of treatment or advancing disease—causing her to lose weight. This wasting syndrome is called cancer cachexia, an advanced state of protein-energy malnutrition. Besides weight loss, signs of cancer cachexia include decreased subcutaneous tissue, edema, abdominal distension, dry skin, and behavioral changes like irritability. Cancer patients with weight loss generally have poor performance status, poor response to chemotherapy, and median survival; they may also be at greater risk for infection.

Certain measures can be taken to protect your patient from malnutrition, such as treating the underlying problems, delaying chemotherapy, getting a nutrition consult, and giving medications to improve appetite (such as corticosteroids, oxandrolone [Anavar], or megestrol [Megace]).

Advise your patient to eat small, frequent meals served at room temperature. She should also eliminate disagreeable food odors, get help with food preparation, and use nutritional supplements.

Lymphedema is an accumulation of lymphatic fluid in the interstitial tissue that occurs when the tumor blocks the lymphatic system or when lymph nodes have been removed. Lymphedema associated with ovarian cancer affects the legs. When edema develops, the patient’s range of motion (ROM) decreases and her skin will feel tight; however, she’ll still have sensation in her leg.

Refer your patient to a health care provider who’s knowledgeable in lymphedema management. The severity and grade of lymphedema determine the interventions, which may include:

- ROM exercises
- meticulous skin care to reduce the risk of skin breakdown
- elevation
- massage or physical therapy to manually aid drainage
- compression bandaging
- sequential pump therapy.

Pleural effusion occurs when the rate of pleural fluid production exceeds its removal rate from the pleural space. This can happen when a tumor invades the thoracic duct or when ascites fluid seeps through the diaphragm. You may note dyspnea, decreased or absent breath sounds, decreased tactile fremitus, or dullness to percussion in a patient with pleural effusion. To drain the fluid, the health care provider will perform a thoracentesis or insert a tunneled indwelling pleural catheter.

On the lookout
You may be asking, “If ovarian cancer is so deadly, why not screen all women for it?” The answer is that current screening methods aren’t sensitive enough or specific enough for routine use. However, a woman with a positive family history should have a formal risk assessment with an extensive family history, education, risk estimation, risk counseling, optional genetic testing, and specific screening and prevention strategies. Screening strategies often include a rectovaginal pelvic exam, a CA-125 blood test, and transvaginal ultrasound.

Scientists are exploring the natural history of ovarian cancer to develop cost-effective, sensitive screening strategies. Researchers studying cell proteins are developing and testing a test that tracks trends in multiple tumor markers specific for ovarian cancer. Clinical trials are currently under way in proteomics (the large scale study of proteins).

But let’s back up and look at how ovarian cancer can be prevented in the first place. Prevention strategies may include a prophylactic bilateral oophorectomy in high-risk women who’ve finished childbearing. Other
prevention strategies being studied in clinical trials include administering such drugs as acetaminophen and the synthetic retinoid fenretinide.

**Evening the odds**

Patient outcomes for ovarian cancer are getting better as detection and treatment methods improve. Don’t forget your role in improving outcomes. Educate your female patients about the signs and symptoms of ovarian cancer. Emphasize the importance of reporting “insignificant” symptoms that could be early warning signs because early detection and treatment offer the best chance for survival.

And, remember, when you care for a woman with ovarian cancer, give her the education and support she needs to boost her ability to fight this insidious disease.

**Learn more about it**


