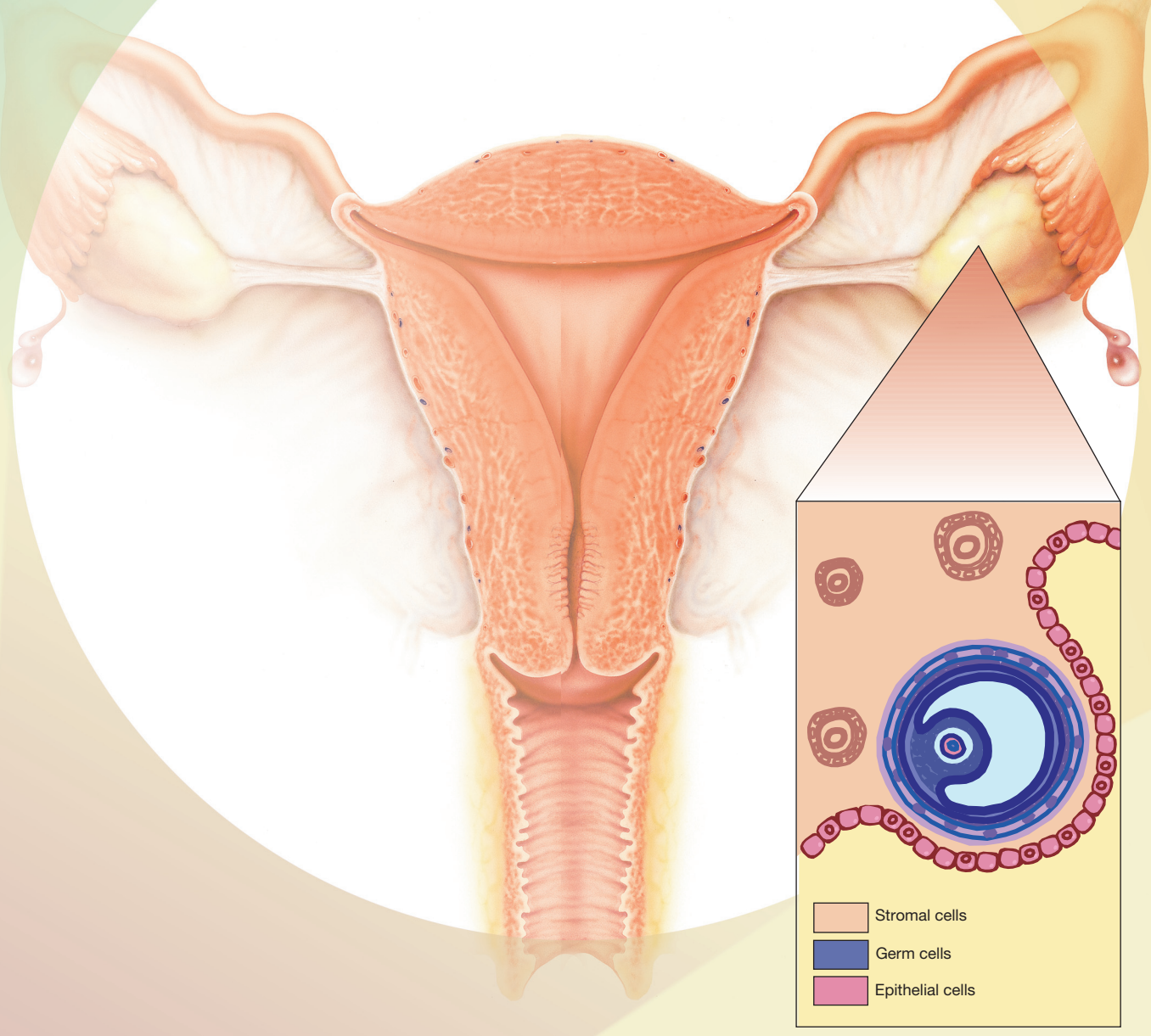
Shining a light on



ovarian cancer

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The author has disclosed that she has no significant relationships with or financial interest in any commercial companies that pertain to this educational activity.

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

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 some 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.

By the numbers

Studies from The American Cancer Society showed that in 2007, 22,430 women in the United States were diagnosed with ovarian cancer and 15,280 women died of the disease. The high number of deaths are 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.

A trio of theories

Why does ovarian cancer occur? Researchers 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 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 causes ovarian cancer. We do know, however, that genetic and endocrine factors raise the risk (see *Where the trouble starts*).

Risky business

The most significant risk factor for ovarian cancer is a positive family history, which is 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:

- never having given birth (nulliparity)
- giving birth for the first time after age 35
- personal history of breast cancer
- age older than 63
- obesity
- early menstruation or menopause after age 50
- use of fertility drugs
- use of estrogen replacement therapy after menopause
- exposure to talc or asbestos
- endometriosis
- pelvic inflammatory disease
- living in a western industrialized country.

But the news isn't all bad. 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 healthcare 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, such as:

- increased abdominal size
- bloating
- early satiety (feeling of fullness after eating)
- abdominal pain
- leg or back pain
- indigestion
- vaginal bleeding
- fatigue

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 cancers*** start in the connective tissue cells that hold the ovaries together and produce female hormones.

• 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 healthcare provider will monitor a premenopausal woman for a few ovulatory cycles and investigate further if the mass doesn't disappear; however, this 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 healthcare provider to see the ovaries. However, the location of the ovaries varies in each woman, so the healthcare provider may order both approaches to be sure.

• *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.

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).

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 (*cytoreduction* or *debulking*). For more about cancer staging, see *Stages of ovarian cancer.*

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 hysterectomy (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 also take multiple

Rating performance

The Eastern Cooperative Oncology Group developed the following scale to rate the effects of cancer and its treatments on the patient.

0 = normal activity, asymptomatic
1 = symptomatic, fully ambulatory
2 = symptomatic, in bed less than 50% of the time
3 = symptomatic, in bed more than 50% of the time but not bedridden
4 = 100% bedridden

samples of the pelvic and para-aortic lymph nodes.

The disease stage is the key factor for determining the prognosis for a woman with ovarian cancer, but 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 over age 69 when diagnosed or who has one of these types of tumors: clear cell, mucinous, or poorly differentiated.

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.

More to follow?

So what happens after surgery? If your patient has well-differentiated stage IA or IB ovarian cancer that's 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 patient will need chemotherapy. 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 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 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. If your patient is one of the lucky ones, she's in complete remission and will 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 patient'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 after less than 6 months, 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 an agent different from the first time around, or your patient 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:

- 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 will 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'll 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 such as 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 (inflammation of the mucous membranes), neuropathy, arthralgia and myalgia (joint and muscle pain), or myelosuppression (bone marrow suppression).

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 important 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, conducted a phase 3 clinical trial for patients with optimally debulked stage III disease. 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 cisplatin 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 penetrate a few millimeters beneath the surface of the tumor, without harming normal tissues. First, I.V. paclitaxel is administered on day 1, followed by intraperitoneal cisplatin on day 2, and then intraperitoneal paclitaxel on day 8. This is repeated for six cycles.

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

Patients with newly diagnosed optimally debulked disease should discuss intraperitoneal therapy with their healthcare provider. This method of delivery isn't right for every patient, so treatment should be individualized.

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. Managing her symptoms, participating in a support group, meeting with a mental health professional, and treatment with an antidepressant or antianxiety medication can help resolve depression and anxiety.

Finally, if cure isn't an option, give your patient and her family support by helping them cope with end-of-life decisions and involving

Clinical trials have shown that combination chemotherapy with paclitaxel and carboplatin works better than a single agent.

the hospice team when the time is right for the patient.

Battling advancing disease

As ovarian cancer advances, it brings with it significant nursing challenges. Let's review assessment findings and management strategies for common problems.

Ascites is an accumulation of fluid in the peritoneal cavity. It occurs when channels 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.

If cure isn't an option, provide support by helping your patient and her family cope with end-of-life decisions.

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 healthcare provider will order an abdominal ultrasound to confirm the diagnosis.

The treatment for ascites is removing the fluid. The oncologist may perform paracentesis (aspiration of fluid) in the office or in the radiology department with ultrasound guidance.

A woman with progressing ovarian cancer is prone to ***intestinal obstruction*** involving the small or large intestine. Peristalsis 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, constipation, and nausea and vomiting.

The first sign of acute intestinal obstruction may be hyperactive bowel sounds as the bowel tries to move digestive contents past the blockage. Teach your patient to recognize problems and to immediately contact her healthcare provider if they occur.

Acute intestinal obstruction may be an indication for admission to the hospital for placement of a nasogastric tube to decompress the bowel. A woman with advanced cancer may already be debilitated, so she'll undergo surgery only if conservative interventions 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. Treatment for DVT 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 as a 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 healthcare 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 healthcare provider will perform a thoracentesis or insert a tunneled indwelling pleural catheter.

On the lookout

You may wonder 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.

Researchers are exploring the natural history of ovarian cancer to develop cost-effective, sensitive screening strategies. They're 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).

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.

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. **LPN**

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On the Web

National Comprehensive Cancer Network: **http://www.nccn.org**
National Ovarian Cancer Coalition: **http://www.ovarian.org**
Ovarian Cancer National Alliance: **http://www.ovariancancer.org**
SHARE: Self-help for Women with Breast or Ovarian Cancer: **http://www.sharecancersupport.org**
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