Kate O'Hanlan, M. D.
F. A. C. O. G., F. A. C. S.

Gynecologic Oncology, Surgery and Endoscopy
4370 Alpine Road
Portola Valley, CA 94028-7927
Phone: (650)-851-6669 **FAX: (650) 851-9747**

Regarding Ovarian Cancer, Ca 125 and Ultrasound

My practice entails the surgical care of women with endometrial, ovarian, cervical and vulvar cancer, as well as benign pelvic surgery and laparoscopic surgery. My focus on cancer prevention by patient education led me to write this response to an email that has been widely disseminated about a woman who developed peritoneal cancer after her ovaries had been removed. She felt that she was a victim of failed medical care. In reality, she developed one of the rarest cancers that we Gynecologic Oncologists see, and her story is truly sad.

In this monograph, I wish to respond to each point made or suggested in her story in order to maximize appropriate response by other women with further testing, or provide appropriate reassurance that no testing (and no worry) is needed.

First, it is important to understand the difference between screening tests and diagnostic tests. **Screening tests** are the familiar procedures that are recommended for all healthy people, such as pap smears for all women, cholesterol assay, dental exams, blood pressure checks for all adults, etc. Screening tests are cheap and easy to do, and they have, by definition, been proven to save lives because they detect common mild or early abnormalities that, if treated, prevent bigger problems such as cervical cancer, heart attack tooth loss, stroke etc. The screening test does not provide much information in itself other than to say that further investigation of the situation by **diagnostic testing** is needed to see if a real problem exists and to see what treatment may be needed.

A **diagnostic test** is prescribed in response to an abnormal finding from a screening test or for a patient with a significant symptom or significant abnormal finding on an exam by a clinician. Most blood tests, x-rays, and procedures are considered diagnostic tests and the results must then be reviewed in the context of a long list of possible abnormalities.

The Ca-125 blood test, an ultrasound, and the "total body scan" are all considered diagnostic tests, not screening tests, because they don't provide highly useful information when used by the larger population which has no abnormal finding of a screen, abnormal finding on an exam or abnormal symptom. Administering diagnostic tests to the larger population has been shown to provide few people value because of the low likelihood of finding an abnormality, often results in many false positive findings, and costs much. One example would be taking a trip to Las Vegas in order to make money by gambling. Most everyone loses money, but one or two find great wealth. The tree test mentioned above have been researched well as **proposed screening tests** for the larger healthy population, and the results consistently show that there is little value *to most* in their use without symptoms, exam findings, or screening test indications. Many women find value in the reassurance that the above tests if normal will provide, and they can afford to pay the fee for this reassurance. Most people have fun in Las Vegas and are happy to afford the trip, and expect to lose money gambling for fun. The research shows that there are likely to be very few revelations by diagnostic tests used in a screening context that will save peoples lives or result in dramatic benefit. Everyone knows of some one person, from thousands taking the Total Body Scan, in whom a mass is found and whose subsequent surgery saved their life.

In the email being sent to many, one woman has told her story about being misdiagnosed with a gastro-intestinal problem, when in fact she had a peritoneal malignancy (a cancerous growth in the lining of her abdomen). Years earlier, her reproductive organs — including ovaries — had been removed, yet a malignancy appeared later in her abdomen identical to an ovarian carcinoma. In other words, she had an ovarian cancer like syndrome, but it had grown from her abdominal lining.

Primary ovarian cancer — which starts in the ovaries — occurs in 1 in 70 women, or 1.7%. Primary peritoneal cancer, which grows from the lining of the peritoneum, occurs in 1 in 2,000 women, or .05%. It is thus rare upon rare.

Her intestinal symptoms, in the absence of any ovaries, should have been tested out with colonoscopy and upper GI Endoscopy, study of her gall bladder and ruling out of colitis and irritable bowel syndrome. It is most reasonable to suspect bowel problems in a woman who has abdominal bloating, swelling and constipation/diarrhea, because intestinal problems and even intestinal cancer are more common than ovarian cancer, and cause the same symptoms. It is actually said, "the road to the diagnosis of ovarian carcinoma is paved with Pepto-Bismol."

Since the emailing woman had had her gynecologic organs removed, few doctors would immediately suspect that she might have such a rare type of carcinoma as peritoneal carcinoma (.16%), when colon cancer strikes about 8% of women, colitis much more, irritable bowel syndrome many more. But if all these tests were done and they were all normal, a CT Scan of her abdomen would be the next study to perform. This would have revealed the peritoneal cancer. Ca 125 and ultrasound were **not indicated** in her case. Ca125 tests for gynecologic problems, and ultrasound is the best test to measure the gynecologic organs: uterus, tubes, and ovaries, none of which she had.

If she still had her gynecologic organs and developed bloatiness and other GI symptoms, the a complete evaluation of the **abdomen and pelvis** would likely have been performed In addition, any woman who has new symptoms from her intestinal tract or gynecologic organs or new findings on her pelvic exam should definitely be evaluated by an ultrasound exam of the pelvis and serum Ca125. Additionally, whenever a pelvic or abdominal mass or fluid distension of the abdomen (called ascites) are observed, a Ca-125 and CEA blood test should be obtained.

Perhaps some of the tumors she had could possibly have been felt by pelvic examination. One of the lessons here is that every woman, whether she has had a hysterectomy or not, needs a pelvic exam on a yearly basis. Many women forego this exam after their uterus, tubes and ovaries have been removed. Sometimes the primary care provider doesn't do pelvic exams, but women should then see a gynecologist for a yearly pelvic exam. While the annual pelvic exam itself does not have screening value (believe that or not, it is true! Pap of the cervix qualifies as a screen, but not pap of the vagina or palpation of the pelvis), it can reveal a pelvic mass that the patient may not have noticed. The pelvic should also include rectal exam in every woman over age 40 to feel for polyps and check for hidden blood in the stool (fecal blood testing over age 40 qualifies as a screening test)

Ca-125: Good for Diagnosis, Not useful in Screening

The story circulating on the Internet encourages women to insist that their doctors test the levels of the protein Ca-125 in their blood. However, all the medical studies have shown that the Ca-125 test is not an effective screening tool in the general population of menstruating women.

Among menstruating women, the Ca125 has been shown to be frequently elevated if they have fibroids, adenomyosis, endometriosis, diverticulitis, and many benign, non-surgical entities that are not a problem. Broad testing of healthy reproductive-aged women has been

shown to result in many high Ca-125 counts, which then lead to much worry, much testing, and even many surgeries for benign masses, which will find very few otherwise undetectable cancers. This is because many benign tissues secrete Ca-125. By definition, in a pre-menopausal woman, the uterine lining is actively growing and the ovaries are actively secreting, thus many perfectly normal women will have elevated Ca125's fluctuating every month. For these reasons, the Ca-125 is ordered for pre-menopausal women only when symptoms or pelvic exam findings have raised concern. If the results show an elevated Ca-125 level, then further testing will be necessary, and often surgery as well.

Peritoneal cancer occurs extremely rarely: about 1 in 2,000 women. Ovarian cancer is much more common, about 1 in 70 women. After removal of the ovaries from most women, peritoneal cancer is incredibly rare, unless there is a mutation in the BrCa gene. The BrCa gene makes a protein that protects women from cancers. About 1 in 500 women, or .2% have a mutated copy of the gene, but this mutated gene is responsible for about 7% of breast and 10% of ovarian cancers. In these families *many* women will have breast cancers, *bilateral* breast cancer, breast cancer *at a young age*, or *ovarian cancer*, and most rarely, peritoneal cancer. If a woman's family tree has many members with these features, or if genetic testing has already indicated one of the members has a mutation of the BrCa gene, then she should see a geneticist or Gynecologic oncologist about testing for BrCa mutation in herself. Also a Ca-125 test and diagnostic ultrasound may be appropriate for her, even in the absence of symptoms or abnormal results from a screening test. Elevated Ca-125 levels in women with a BrCa positive mutation indicate the need for investigation. It should be stressed here that Ca-125 does not prevent malignancy, but if it is elevated, it can help to diagnose cancer earlier.

For post-menopausal women, the Ca-125 blood test is a good diagnostic tool, because their ovaries and uterine lining are normally inactive and not secreting any Ca125-like proteins. Research confirms that for older women, this test is a reliable way to find problems in the gynecologic organs. Occasionally the problem may actually be found in the heart, pancreas, thyroid or lungs, or turn out to be benign gynecologic changes. An elevated Ca-125 count in a postmenopausal woman indicates the need for further testing, probably including surgery. But even in the post-menopausal woman, and certainly in the hysterectomized/oophorectomized woman, Ca 125 is not useful as a screening test.

In my practice, I see many younger women with elevated Ca-125 levels, between 35 and 100 (normal is under 35). When this happens, the next step is an ultrasound test, which usually reveals that the pelvic anatomy is normal. So then we discuss endometriosis or the other non-cancer causes of elevated Ca-125, but the women are still somewhat scared. At this point, we can use further scheduled Ca-125 testing on days 12 and 26 of the menstrual cycle to confirm fluctuations with the cycle and that the problem is benign endometriosis or adenomyosis. A Ca-125 level on day 26 that is nearly twice the level observed on day 12 is very reassuring for a diagnosis of endometriosis or adenomyosis, because the level should fluctuate over the month if it is caused by monthly fluctuation of cycling tissues. Surgery is not necessary in the absence of bothersome symptoms or abnormal ultrasound findings. A Ca-125 over 100 can still be endometriosis, but detailed investigation is needed—and this may need to include laparoscopic biopsies, or possibly more surgery.

Ultrasound: a valuable, non-surgical diagnostic tool

Trans-vaginal ultrasound is highly reliable in measuring the size and shape of the uterus and ovaries. Unlike the Ca-125, the error rate for diagnosing cancer is low for vaginal ultrasound. The "pictures" we get from ultrasound can be put into four categories: benign and okay to ignore, benign and must be removed, *probably* benign but must be removed to be sure, and cancerous.

Benign: Ultrasound can tell the difference between the characteristic features of cancer and those of benign "functional" cysts, which normally come and go on ovaries. Remember that ovulation is the function of making cysts with eggs every month. "Simple" cysts look like a water balloon containing pure fluid with no internal walls or any solid areas on the

outer walls. If smaller than 2 inches, "simple" cysts need no further follow up because their risk of malignancy is under .3%, even if they do not disappear over time.
Benign but must remove: Larger "simple" cysts may be observed for a while to see if they go away, but may need removal because they may twist. Dermoid cysts fall into this category as they have a 1% chance of malignancy, but must be removed. Endometriosis cysts should also be removed.
Probably benign, but must remove to be sure it is not cancer: "Complex" cysts have solid areas in the walls, on the inner linings or contain multiple cysts and can be malignant between 8-30% of the time. They should be removed surgically, usually by laparoscopy, without spillage into the peritoneal cavity, for microscopic study to confirm that they are not cancerous.
Ovarian Cancer: In cases of ovarian cancer, ultrasound usually reveals complex cysts on one or both ovaries, multiple solid masses, nodule on the bowel or excess pelvic and/or abdominal fluid.

If the ultrasound reveals complex cysts, or if there is any other suspicion that ovarian cancer may be present, it is time to see a cancer doctor who specializes in women's reproductive systems: a gynecologic oncologist. These specialists can determine the extent of the spread of the cancer, and remove all the possible sites of spread — all in the same anesthesia and operation. One research project showed that many of the steps in surgical management of cancer were omitted when a general gynecologist did the initial surgery because they are not trained to perform the cancer staging. On the other hand, a gynecological oncologist actually may tell you "It definitely ain't cancer and you don't need any surgery!" You can trust that. That's our niche.

More about OVARIAN CANCER

Risk Factors:	Low # children. Never used oral contraceptives, some families with extensive cancer rates or BrCa1 or 2 positivity, urban, extensive use of fertility drugs without conception.
Screening:	None, but do have yearly pelvic exam. Report any vague symptoms in abdomen or pelvis. Can test with vaginal ultrasound, Ca125 if concern.
Symptoms:	Vague change in gastro intestinal tract function or urinary function, pelvic or abdominal pressure or pain, abdominal swelling or mass.
Treatment:	Surgical removal of all visible cancer, removal of uterus, tubes, ovaries, lymph nodes, appendix and omentum (fat pad in abdomen), followed by chemotherapy.
Survival:	40% overall. 88% if early. 15-45% if advanced.
Risk Reduction:	Oral contraceptives for 5 years reduces risk by 25% and for 10 years reduces risk by 50%, tubal ligation reduces risk by 50%, large number of children. Remove ovaries.

To find a gyn oncologist near you, call the Society of Gynecologic Oncologists at 1-800-444-4441, or go to SGO.org and find one.