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FEATURE STORY

About Cancer: Pathology & Staging

How much, what it looks like, and where it is guide diagnosis and treatment

Diagnosing cancer involves much more than determining whether a lump is malignant or benign. In order for your doctor to decide what course of treatment to recommend, it is necessary to know how much cancer is present, whether cancer has spread to other areas of your body, the specific type of cells comprising the tumor, and how severely abnormal the cancer cells have become.

The Pathologist

Since many different types of treatments are available for many different types of cancers, it's important to make the right diagnosis so that the correct treatment can be delivered. The role of the pathologist is to make the diagnosis.

A pathologist is a doctor who specializes in conducting laboratory tests to diagnose diseases. For example, pathologists examine tissue and fluid samples taken from the body to determine whether cancer is present. If cancer is present, the pathologist identifies important attributes of the cancer, including the type of cancer cells, the grade of the cancer, the size of the tumor that has been removed, the extent of invasiveness, and if and how much the cancer has spread. This information, compiled in the pathology report, allows you and your medical team to determine the best treatment.

The pathologist first looks at the tissue with the naked eye in a "gross examination." Its appearance and characteristics, such as size, weight, color, and texture, are recorded.

If an entire tumor or lesion has been surgically removed, it is microscopically measured, as is the distance from the edge of the mass to the specimen's edge or "margin." A positive margin means cancer cells continue to the edge of the tissue and suggests the tumor has not been completely removed, whereas a negative margin means the cancer cells do not extend to the specimen's edge. If the margin is close, it may be difficult to determine if the entire tumor has been removed. A positive or close margin typically means more surgery may be needed.

View Image: FISH and IHC

The pathologist cuts the specimen into thin slices, and portions of the tissue are chosen for further testing. The pathologist examines the tissue under a conventional light microscope. There are many sensitive techniques, including immunohistochemistry (IHC) and fluorescent in situ hybridization (FISH), that pathologists can use in the microscopic examination of tissue samples to identify genes and proteins involved in the abnormal growth of tumor cells. Many of these attributes of a tumor can be important factors in choosing the right treatment.

IHC is a widely used staining technique that helps to characterize the cells comprising the cancer by identifying specific protein and carbohydrate molecules within the nucleus, cytoplasm, or on the surface of the cancer cell. With hundreds of different types of tumors, each with its own typical biology, specialized immunohistochemical tumor marker tests are often used. The challenge in interpreting these results is that many tumor markers are applicable to more than one type of cancer. For this reason, pathologists may need to consider several tests in order to reach a diagnosis.

FISH uses fluorescent molecules to “paint” genes. These molecules, called probes, are portions of single-stranded DNA that are chosen to correspond with selected genes within DNA that the pathologist wants to examine. The probes bind to a specific gene or segment of DNA, making it possible to determine how many copies of that gene exist in each cell.

If a pathologist is having difficulty making a diagnosis, you should talk to your doctor about whether you should get a second opinion (see “Seeking a Second Opinion”). For instance, if your cancer is very rare, or if your doctor thinks the pathologist’s diagnosis does not seem consistent with your symptoms and other test results, a second opinion might be appropriate.

Grading Systems

Tumor grade, also called histologic grade, is the system used to describe how abnormal the cancerous tissue appears when viewed under the microscope. Features that the pathologist will consider depend on the type of cancer, but usually include the size and shape of the cell’s nucleus, the proportion of cancer cells that are dividing, and the patterns that cells form as they join together. If many of the cells are dividing, that can be a sign the cancer is more aggressive. Cancer cells that look more like normal cells usually grow and multiply slowly, and are described as being low grade, well differentiated, or grade 1. Conversely, cancers that do not resemble normal tissues are called high grade, poorly differentiated, or grade 3 or 4. The attributes are combined into an overall tumor grade that usually ranges from 1 to 3 or 4.

Grading systems vary for different kinds of cancer. For example, pathologists use a system for prostate cancer that ranges from 2 to 10. Generally, though, whatever the system used, lower numbers signify the least aggressive cancers,

while tumors assigned higher numbers have a higher risk of rapid growth and spread. Tumor grade is an important indicator of prognosis in some cancers, such as breast cancer, prostate cancer, lymphoma, brain tumors, and soft-tissue sarcoma.

View Illustration: How Big Is My Tumor

Staging Systems

Most staging systems apply to specific kinds of cancer, and over time, these systems have been refined to take into consideration a new medical understanding of cancer. Nonetheless, there are similarities in the way many cancers are staged, and staging for most cancers is based on the following:

- Location of the primary tumor
- Size of the tumor
- How many tumors are present
- Whether cancer has spread to nearby organs and tissues
- Whether cancer has spread to the lymph nodes
- Whether the cancer has spread to distant parts of the body

View Chart: Typical TNM Tumor Staging System

For a few kinds of cancer, such as bone and soft-tissue sarcoma, the stage also considers the cancer's grade, or how much the cancer cells differ in appearance from normal cells.

In addition to the pathology report, information used for staging is gathered from physical examinations and imaging tests, such as X-rays, CT (computed tomography) scans, and MRI (magnetic resonance imaging) scans.

TNM staging is one of the most commonly used systems, and is based on three characteristics of the cancer. The T refers to the primary tumor (the place where the cancer began); the N refers to the level, if any, of lymph node involvement; and the M refers to the presence or absence of metastasis (cancer that has spread to distant organs). These letters and numbers don't mean the same thing for every type of cancer. For example, some cancers may not have N3 as a category, and in other cancers, the classifications may have subcategories, such as T3a or T3b. Some cancers that do not use TNM designations are brain and spinal cord tumors, and cancers of the blood or bone marrow.

View Chart: Overall Stage Groupings

Once these attributes have been determined, an overall stage of 0, 1, 2, 3, or 4 (also written as Roman numerals) is assigned, and it never changes. Even if the

cancer spreads or comes back after initially successful treatment, it is usually referred to as having the same stage as when it was first diagnosed. The exception to this is that on rare occasions, cancer that has been in remission may be restaged if further treatment is planned. A restaged cancer often is indicated by inclusion of the letter “R.”

Stage and grade are not the only factors that influence your prognosis. The type of cancer, the treatment you receive, and your general health are also important. But understanding the information signified by your cancer’s stage and grade can help you and your health care team choose the best course of action for your individual situation.