After a Biopsy: Making the Diagnosis [1]

After a biopsy (the removal of a small amount of tissue), the tissue sample (called a specimen) must be processed and examined under a microscope before a definite diagnosis can be made.

Visual examination

The specimen is first placed in a container with a fluid that preserves it, and the container is labeled with the patient's name and other information. A pathologist (a doctor who specializes in interpreting laboratory tests and evaluating cells, tissues, and organs to diagnose disease) then examines it and describes how it looks to the naked eye, including the color, size, and other characteristics. This is called a gross or macroscopic examination. The gross description includes the label by the doctor who took the specimen, the visual characteristics of the specimen, the specimen measurements, and what was done to the specimen. If molecular tests (tests for genes that might be active, changed or missing because of the diagnosis) or other specialized tests (gene or protein tests that will help identify which treatments will work) are needed because of the suspected diagnosis, the pathologist will prepare a part of the specimen for these tests during this examination.

Making a slide

Before the tissue can be examined with a microscope, the pathologist or a technician cuts the specimen into thin slices and stains it with various dyes to show the parts of the cells. These slices are called histologic (relating to the study of the microscopic structure of tissue) sections. They are placed on a glass slide, protected with a coverslip (a thin cover that holds the specimen in place), and viewed under a microscope.

Permanent section. To create a permanent section, the technician places the specimen in a fixative for several hours; the length of time depends on the size of the specimen. Formalin is the fixative used most often. It causes the proteins in the cells to become hard and ?fixed,? meaning they won't change.

The fixed specimen is then processed in a machine that removes water from the tissue and replaces it with paraffin wax. The specimen is then embedded in a larger block of paraffin. Paraffin blocks are very durable and can be stored indefinitely. Once the paraffin block is hardened, the person making the slide cuts the specimen into extremely thin slices using a

machine called a microtome. The slices are so thin that they are placed in water to float so that they can be scooped up onto the slide.

After the slice is on the slide, the paraffin is dissolved from the tissue and water is added back. Then, dyes (typically hematoxylin and eosin) are used to stain the nucleus (the center of a cell where the genes are found) of each cell a dark blue and the cytoplasm (the contents of a cell between the nucleus and the cell membrane) pink or orange.

Frozen section. To create a frozen section, the specimen is quickly frozen after the surgeon removes it from the patient's body. The frozen specimen can then be cut into thin layers using a special cutting device called a cryostat. These slices are placed on the slide and stained using the same method used for a permanent section. Although the quality of a frozen section is often not quite as good as a permanent section, it can be processed within a few minutes to tell whether the tissue is cancerous and whether a patient may require further surgery.

Smears

If the specimen is a liquid or if small pieces of tissue are placed in a liquid, it is processed differently. The doctor smears the specimen on a microscope slide, lets it air dry, and sprays a fixative on it or places it in liquid to fix it. The fixed cells are then stained and examined under a microscope.

Microscopic evaluation

Once one or more slides are made, the pathologist evaluates the specimen under a microscope. The pathology report [2] usually includes a description of what the pathologist sees when looking at the specimen under a microscope. This description is very technical, using terms that are meaningful to other pathologists and doctors. Generally, the pathologist describes the cell types of the specimen, how they are arranged, whether they are irregular, and other characteristics.

In some cases, the pathologist may want to see more tissue before making a diagnosis. If that is the case, the pathologist will note in the report that other examinations will need to be done before a diagnosis can be made.

The diagnosis

In addition to the gross and microscopic descriptions mentioned above, a section of the pathology report describing the diagnosis is always included in the report. The diagnosis is often short. It is determined based on the combined results of the biopsy, gross examination, processing, and microscopic examination. There is a general format for diagnoses, including the organ or tissue involved, the specific site of the organ from which the biopsy was taken, the procedure used to take the biopsy, and the specific findings in the tissue. If other important results are found or other examinations are planned, they will often be included in this portion of the report. Patients can review their pathology reports with their doctors. Because technical terms are used, it helps to have a basic understanding of the following common terms.

- Atypical: Referring to cells that are not normal but are not cancerous. Atypical cells may be precancerous cells (cells could become cancerous over time) or may increase a person's risk

of developing cancer.

- Carcinoma: Cancer cells that started from epithelial cells (cells that line organs)
- Sarcoma: Cancer cells that started in cells other than epithelial cells
- Lymphoma: Cancer cells that started in the lymph system
- Leukemia: Cancer cells that started in the blood or bone marrow
- Hyperplasia: An abnormal increase of cells in a tissue or organ. Hyperplasia may increase the risk of developing some types of cancer, or it can be the body's response to various types of hormonal or infectious disease stimulation.
- Dysplasia: An increase in the numbers of abnormal or atypical cells in an organ. Dysplasia is a response to a viral infection or an intermediate state between normal cells and cancer cells.
- Neoplasia: A growth of cells no longer under normal control. The cells can be benign or malignant (cancerous).

Molecular evaluation for diagnosis

Sometimes, additional tests will be done on the specimen to help the doctor further classify the tumor. For example, to diagnose some types of leukemia, the pathologist looks for specific molecular (genetic) changes in the malignant blood cells. *BCR-ABL* is one such modified gene, found in chronic myelogenous leukemia. The findings of these additional tests will be included as part of the pathology report or listed in separate reports.

Molecular evaluation to predict response to treatment

Once the diagnosis is established, additional tests may be done to help the doctor decide on the best treatment for the patient. Tumor markersâ€” substances found at higher than normal levels in the blood, urine, or body tissues of some people with cancerâ€”can help predict a cancer's response to treatment. These may be identified through testing of a specific gene or protein. For example, tests for the HER2 protein and *HER2* gene are used to predict how a patient's breast cancer would respond to drugs like trastuzumab (Herceptin).

More Information

Biopsy?€”What to Expect [3]

Understanding Tumor Markers [4]

Facts About Personalized Cancer Medicine [5]

Additional Resources

College of American Pathologists: How to Read Your Pathology Report [6]

Links:
[1] http://www.cancer.net/navigating-cancer-care/diagnosing-cancer/reports-and-results/after-biopsy-making-diagnosis
[2] http://www.cancer.net/node/24715
[3] http://www.cancer.net/node/24406
[4] http://www.cancer.net/node/24730

[5] http://www.cancer.net/node/24522
[6] http://www.cap.org/apps/docs/reference/myBiopsy/pathology_report.html