Understanding Your Pathology Report: Colon Cancer

What is a pathology report?
A pathologist is a doctor who specializes in diagnosing diseases by examining tissue from the body. You will probably never meet the pathologist, but samples of your colon tissue, removed during surgery or biopsy, will be sent to them for review. The pathologist prepares a report of their findings. This is called the pathology report. This report contains important information about the tumor and helps to guide treatment decisions. You should request a copy of this report and keep it in your personal files.

What will you find on a pathology report?
The actual content of a report may vary based on where it is completed. The report is broken down into a few sections and may include:

- Demographic information about the patient: name, birthdate, medical record number, presumed diagnosis (if known), name of physician.
- Description of the procedure and how/from where the specimen was obtained.
- Gross description: what the specimen looks like to the naked eye. This can include weight, color and size of the tissue.
- Microscopic description: what was seen under the microscope.
- Tumor cell type: what type of cells make up the cancer? Adenocarcinoma is the most common type of colon cancer.
- Histologic grade: describes how different the cells look compared to normal cells.
- Lymphovascular Invasion: if the cancer cells have gotten into the lymph or blood systems.
- T-stage: describes the tumor size and how far the tumor invades into the wall of the colon.
- Lymph nodes: this indicates how many lymph nodes were tested and how many have cancer cells in them.
- Margins: the pathologist looks at the edges of the sample to be sure there is no cancer cells near the edge or extending beyond.
- Diagnosis: based on all information above, the pathologist gives a diagnosis.

To help you better understand your report, let's go through these sections individually.

The Gross Description
This is generally not that important to the patient. It is a description of the sample the pathologist received and what they see with the naked eye. In a biopsy, the specimen is likely a small, nondescript piece of tissue, in which case the pathologist may describe the color, shape, feeling and size of the tissue. After a cancer surgery, multiple organs or tissues may be submitted and described in the report. This might include size, color and weight. For example, a colon specimen from a colectomy may be described as:

"Specimen #1 is labeled "colon" and consists of a segment of bowel measuring 13cm in length after fixation. The specimen is surrounded by a moderate amount of pericolonic fat. 3cm from one resection margin is an ulcerated round tumor measuring 3.2cm in diameter. The rest of the mucosa is grossly unremarkable."

This tells us the specimen was a 13cm long piece of colon, with a tumor located 3cm from one end. This isn't very helpful in determining stage or treatment, so let's move on to the next section.

Microscopic Description
This is the meat of the report, but we need to know more about the colon in order to understand this part of the report. The colon,
or large intestine, is a tube that is about 5 to 6 feet in length; the first 5 feet make up the colon, which then connects to about 6 inches of rectum, and finally ends with the anus. The colon is made up of several sections. Your report may specify which section the tumor was located in. These sections are called the cecum, ascending, transverse, descending and sigmoid colons, rectum and anus (see diagram). The splenic and hepatic flexures are areas where the colon bends (or flexes) that are named for the organs they are located near.

The colon, which is shaped like a tube, is made up of several layers, starting with the innermost layer, the mucosa (which is made up of epithelium), and then the lamina propria and muscularis mucosa. This is surrounded by the submucosa, which is surrounded by two layers of muscle (or muscularis), and finally, the serosa layer, which is the outside layer of the tube. The outside of the colon is covered with a layer of fat, also called adipose tissue, which contains lymph nodes and blood vessels which feed the colon tissue.

### Tumor Cell Type

The type of colon tumor describes the cells from which the tumor arises. Adenocarcinoma is the most common type, accounting for 95-98% of colon cancers. An adenocarcinoma arises from the glandular cells that line the inside of the colon. Two subtypes of adenocarcinoma are signet ring and mucinous, which are both named for the way the cells look under the microscope. The other 2-5% of cancers found in the colon are lymphomas, gastrointestinal stromal tumors (GIST), and carcinoid tumors, which are not discussed in this article.

If a polyp was removed, this section will describe the type of polyp. A colon polyp is a benign growth that, over time, can turn into cancer. For that reason, they are removed during a colonoscopy and may be sent to the pathologist to determine what type of polyp it is. There are several types of polyps that can be found in the colon:

- **Tubular adenoma** (also called adenomatous polyp): this accounts for 70% of the polyps found in the colon and can progress into cancer, but this happens over many years. If they are found early, they can be removed during colonoscopy.
- **Villous adenoma**: this accounts for 15% of the polyps found in the colon. This type of polyp has the highest risk of turning into cancer. In some cases these can be removed during colonoscopy, but in other cases surgery is required.
- **Hyperplastic polyps and Inflammatory (or pseudopolyps)**: these two types of polyps are not likely to turn into a cancer.

In addition, colon polyps come in two forms, called pedunculated and sessile. Pedunculated polyps grow on a stalk and look like a small mushroom, which can usually be easily removed during a colonoscopy. The sessile type of polyp is flat and grows on the wall of the colon. These are much more difficult to remove and may require surgery to remove the entire polyp.

### Histologic Grade

As normal cells develop, they “differentiate” to become a specific type of cell. Histologic grade describes how closely the tumor cells resemble normal cells. The more a tumor cell looks like a normal cell, the more well-differentiated it is. On the other hand, the more cells do not look like normal cells (higher grade), the more aggressive they are. They can grow and spread faster.
Histologic tumor grade is broken down as follows:

**Tumor Grade (G)**
- **GX:** The tumor grade cannot be identified.
- **G1:** Well differentiated. Cells appear the most normal.
- **G2:** Moderately differentiated. Cells appear somewhat like normal cells.
- **G3:** Poorly differentiated. Cells look less like normal cells.
- **G4:** Undifferentiated. Cells appear the most abnormal and barely look like normal cells.

**Lymphovascular Invasion**
When the pathologist examines the tumor and surrounding tissue available to them, they look at the tiny blood vessels and lymphatic drainage to see if any tumor cells have invaded them. This is different from the lymph nodes and would be reported as whether or not lymphovascular invasion is seen. The presence of this may be a sign of a more aggressive or advanced tumor.

**T Stage/Depth of Invasion**
A tumor that has not invaded the surrounding tissues is sometimes called "in situ", while tumors that have penetrated surrounding tissues are called invasive. T stage is classified as Tx (tumor cannot be measured), T0 (no evidence of tumor), T1s (cancer cells are found only in superficial tissue, often called cancer in-situ or pre cancer), T1, T2, T3, T4 describe the tumor based on size and if it has spread to surrounding tissues and structures. Some examples include:

- "The biopsy shows involvement of the mucosal lamina propria by neoplastic glands. The submucosa is not involved." *This tumor invades only the innermost layer of the colon.*
- "The tumor invades through the muscularis propria but not into the pericolonic adipose tissue. The serosal surface is not involved." *This tumor invades the muscle layer, but does not invade the serosa (the outer layer of the colon) or the surrounding fat.*
- "The tumor is invasive through the muscularis propria into the pericolonic fat." *This tumor has penetrated through the colon wall and into the surrounding fat.*

**Lymph Nodes**
The lymph system is essentially the "housekeeping system" of the body. It is a network of vessels (tubes) which connect lymph nodes. These nodes can vary in size, but are normally up to about 2 centimeters in width. They contain cells that clear bacteria and other foreign debris from the body. Lymph is a watery liquid that flows between cells in the body, picking up foreign debris and taking it into the lymph node for filtering and ultimately, elimination by the liver.

Cancer cells use the lymph system as a first step to traveling to other areas of the body. During a colon cancer surgery, numerous lymph nodes are removed and checked for the presence of cancer cells. This will be reported as the number of lymph nodes that contained cancer cells and how many were examined. For example, the report might state "fifteen benign lymph nodes (0/15)" or "tumor seen in sixteen of twenty lymph nodes (16/20)."

In a colon cancer surgery, the more lymph nodes removed the more certain you can be that no lymph nodes are involved. It is not uncommon to have as many as 30 lymph nodes removed during a colon cancer surgery. This is different from many other types of cancer, where far fewer nodes are removed.

**Margins**
This is the area at the edge of the specimen that was submitted. When performing a cancer surgery, the surgeon attempts to remove the entire tumor and some normal tissue surrounding it. This area of "normal tissue" is important because any stray cancer cells may be included in this. If the edge (or margin) contains tumor, there may have been cancer cells left behind. The goal of surgery is to achieve a "clear margin", that is, clear of any cancer cells.

**Putting it all together**
All of these pieces are used to determine the stage of the cancer and what treatment is needed. By understanding the basics of
the report, you will be better able to discuss your treatment options with your healthcare team. The staging system most commonly used for colon cancers is the American Joint Committee on Cancer (AJCC) staging system. This system utilizes the extent of the primary tumor (T0-4), the absence or presence of cancer in the lymph nodes (N0-2), and the existence of metastasis (M0 or 1) to assign a TNM rating, which corresponds to a stage. The staging system is quite complex. You can see the complete TNM staging for colon cancer in OncoLink’s All About Colon Cancer Article.

### Molecular Markers to Provide Further Guidance

A molecular marker is something found in the blood, tissue or other body fluid that is a sign of a normal or abnormal process, condition or disease. There are substances in some tumors that can gauge the likelihood of recurrence (prognostic marker) or predict a response to chemotherapy (predictive marker). Two molecular markers found in colon cancers have gotten some attention in recent years; "microsatellite instability" and "18q loss of heterozygosity."

### Microsatellite Instability

Microsatellite DNA consists of nucleotide sequences, repeated over and over and linked together, which are found in all human genes. Molecular testing can identify instability, or errors, in the microsatellite DNA of tumors, such as a change in the number of repeat sequences; this is called microsatellite instability (MSI). MSI is a way to measure a deficiency of mismatch repair (MMR) in tumor DNA. A deficiency of MMR results in an increase in mutations within the colon cells, which partly contributes to the development of colon cancer.

There are two reasons to test colorectal cancers for MSI. The first is to identify those at risk for hereditary non-polyposis colon cancer (HNPCC). The second reason for MSI testing is that knowing an early-stage colorectal cancer has MSI may change the way it is treated.

HPNCC is a hereditary disorder that increases a carrier's risk for other cancers, including endometrial, ovarian, stomach, pancreas, and kidney cancers. Individuals with HNPCC should have specific cancer screenings and consider preventive steps based on their family history and personal risk. In addition, blood relatives of a person with HNPCC could also carry this genetic mutation. They may want to have genetic counseling and testing to determine how this affects their screening recommendations.

MSI testing identifies tumors as MSI-H (i.e. MSI-high), meaning they lack MMR proteins or are deficient in MMR proteins (dMMR), or MSI-stable and MSI-low, meaning they are considered MMR proficient (pMMR) or contain most or all of the MMR proteins. This information is especially helpful for those with stage II colon cancer. Studies have found MSI-H tumors are associated with a better prognosis. Approximately 22% of stage II colon tumors (but only 12% of stage III tumors) have MSI-H. Several studies have found that patients with stage II MSI-H tumors did not derive any benefit from 5-FU adjuvant therapy, and actually fared worse if they were treated with chemotherapy. This was true for stage III MSI-H tumors. MSI-stable disease, however, may benefit from 5-FU based treatment. Some experts recommend MSI testing as another tool to determine the need for treatment in stage II disease.

### Other Markers

Humans have 23 pairs of chromosomes, for a total of 46 chromosomes, found in every cell in the body. Each chromosome contains over 1000 genes. Chromosome 18q contains two genes that are linked to tumor suppression. Over a person's lifetime, he or she can develop damage to genes or chromosomes due to exposures, such as smoking and viruses. Loss of one copy of chromosome 18q is called a loss of heterozygosity (LOH). Results of studies looking at the predictive value of 18qLOH have been conflicting. One trial found a greatly improved survival when no LOH was present (96% vs. 54%), but a subsequent trial did not confirm this, therefore further study is required. In addition, the current method of testing for 18q LOH is difficult to perform. More efficient techniques would be needed to make widespread use of this test feasible.

Other molecular markers being studied include KRAS, BRAF, a tumor suppressor called guanylyl cyclase 2, p53 and ERCC-1. Studies have found some of these markers to be useful in determining cancer treatment. For instance, anti-cancer medications that target the EGFR protein, such as, Cetuximab and Panitumumab, will not be effective in people who have a KRAS or BRAF gene mutation (defect). These tests are not the standard at this time, but some practitioners are using them, so you may hear them described to you.
Resources for More Information

Oncolink: Stage II Colon Cancer: To Treat or Not To Treat?


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