What do Medical Tests Detect?

Medical tests are frequently used to identify medical conditions. The tests can indicate the presence of a condition before the patient has symptoms. There are many different kinds of medical tests.

The technical term for the things that are measured is a combination of the words 'biological' and 'marker' - biomarker. The term biomarker "refers to a broad subcategory of medical signs – that is, objective indications of medical state observed from outside the patient – which can be measured accurately and reproducibly." They include simple things like taking a person’s pulse, listening to their heartbeat, or taking a blood pressure reading. Some detection and diagnosis tests, like the ones just mentioned, are not invasive. Others involve the examination of samples of blood or tissue from the patient.

The following sections contain information about some of the biomarkers used in medical tests, with an emphasis on those used in cancer detection and diagnosis.

- **Types of Biomarkers**
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A biomarker is something that can be found in the blood, tissues, or bodily fluids that can indicate a medical state, such as a disease, infection, or other abnormal condition. Biomarkers have a variety of uses, including monitoring a patient’s response to treatment and the progression of disease. In cancer, biomarkers are frequently substances secreted by tumors or chemicals produced in responses to the presence of cancer in the body. The earliest examples of biomarkers for disease include indicators of cancer, such as Bence Jones proteins from multiple myeloma patients, and carcinoembryotic antigen (CEA) in colon cancer patients.

Biomarkers can be identified in a variety of ways. They may be found in excretions and secretions, such as stool, urine, and sputum, which allow for noninvasive isolation. Biomarkers can also be identified in the blood through minimally invasive tests, such as blood draws. (The Bence Jones proteins mentioned above are found in urine, and CEA is found in blood.) Some biomarkers are found in tissues/organs, and therefore require a biopsy or imaging for evaluation.
Biomarkers can be discovered in a variety of ways. Advances in technologies used to sequence DNA and identify very small amounts of protein have provided great insight into many molecules that have the potential to serve as markers of disease, including cancer.

One of the best-known biomarkers is cholesterol, a widely used biomarker for monitoring cardiovascular health. Low-density lipoprotein cholesterol (LDL-C) is measured in the blood. It is commonly used to assess the risk of coronary artery disease.

**Types of Biomarkers**

In theory, there are many different biological molecules that could serve as indicators of disease. Any molecule found in the body that is altered in some way by disease has the potential to serve as a biomarker. The changes can be changes in the structure of the marker (qualitative changes) or amount of the marker (quantitative changes).

**Deoxyribonucleic acid (DNA)**, the carrier of our genetic code, is widely used as a biomarker. Mutations found in proto-oncogenes, which lead to oncogene formation, are commonly used to evaluate cancer. **Tumor-suppressors**, genes that aid in cancer prevention, can also be monitored as biomarkers. Other abnormal genetic changes, such as the number of copies of a particular gene and the fusion of genes that are not normally found together (via translocations) are also used as biomarkers. The source of DNA can be tissue, serum, sputum, saliva, cerebrospinal fluid, or circulating tumor cells (CTCs).

**Ribonucleic acid (RNA)** is very similar to DNA, and changes in RNA may also indicate disease. Small, non-coding RNA molecules, known as microRNAs (miRNAs) are the basis of a growing field of cancer and biomarker research. miRNAs have been identified as markers for many different types of cancer, including colorectal, breast, leukemia, liver, lung, and pancreatic cancer.

**Proteins** are arguably the most important type of biomarker to date. They are responsible for controlling most cellular processes. Proteins may be a more reliable indicator of some conditions because they are created and destroyed rapidly, unlike DNA and some RNA molecules. Proteins can give a real-time indication of the body’s condition.

**Viruses** can also serve as biomarkers. Viral infections contribute to about 15-20% of all cancers. For example, Epstein-Barr virus (EBV) has been linked to carcinoma and lymphoma. Human papillomavirus (HPV) has also been shown to be the major cause of cervical cancer and also causes a growing percentage of head and neck cancers. In April of 2014, the FDA approved a HPV DNA test as a primary cervical cancer screening method.

**Bacteria** can also be used as a biomarker. Bacteria that cause chronic, low-level inflammation have been known to cause cancer. For example, *H. pylori*, a bacterium that inhabits the stomach lining has been linked to the formation of ulcers and stomach cancer.

**Exosomes** are small bubble-shaped structures (vesicles) secreted by cells. They can contain DNA, RNA, miRNA, and/or proteins specific to cancer cells. Exosomes can be found in bodily fluids, such as blood and urine. In many cancers, exosomes have been found to prepare distant sites for metastasis. There are many ongoing efforts examining the use of exosomes as a tool for the diagnosis of cancer and predicting likely cancer outcomes.

**Cancer cells** themselves can be used as biomarkers. Cancer cells circulating the bloodstream, known as circulating tumor cells (CTCs), can also be used to provide an indication of disease progression. Cancer stem cells (CSCs) have also been used to monitor disease. CSCs are thought to be a small subset of tumor cells that actively drive tumor growth and spread.

**Uses of Biomarkers**

Biomarkers have several main uses in cancer.

- **Determining what condition a patient has (diagnosis):** The goal of using biomarkers as a diagnostic tool is to identify cancer in its early stages. Diagnostic tests can be used to determine the exact nature of a cancer. They may be used to help guide treatment plans.
- **Determining the likely outcome for the patient (prognosis):** A prognostic biomarker is used to determine how aggressive the cancer likely to be.
- **Predicting disease progression:** A predictive biomarker is used to assess how well a patient will respond to a particular treatment. This type of biomarker can also be used to determine what drugs or chemotherapy agents will be most effective for a particular patient. For example, the drugs erlotinib and gefitinib used to treat lung cancer are only effective in patients with a specific mutation in a cell surface protein - called...
**Biomarker Requirements**

Despite the fact that many molecules have potential to serve as biomarkers, few have made it to the clinic and gained approval from the U.S. Food and Drug Administration (FDA). To be effective, a biomarker must be able to diagnose early stage tumors and be highly specific to the condition of interest. The molecule must also be present at high enough levels to be detectable. Ideally, the biomarker should be readily found in the blood, serum or other body fluid of affected individuals. Other features include low testing cost, and tests that are easily done.\[12\][13]

- **Specific**
- **Sensitive**
- **Predictive**
- **Robust**
- **Simple**
- **Accurate**
- **Inexpensive**

**Biomarker Limitations**

Although biomarkers have been successfully used to identify and monitor disease, there are trade-offs between sensitivity, specificity, and cost.\[14\] Sensitivity is the ability of a test to identify people who are affected by the condition. Specificity is the ability of a test to exclude those who do not have the condition.

Learn more about sensitivity and specificity

Another limitation of biomarkers is the possibility of over-diagnosis. Biomarkers may identify cancer that may never have led to symptoms during a person’s lifetime.\[14\] An example of this is prostate specific antigen (PSA), a biomarker for prostate cancer. PSA tests are not able to distinguish between slow growing (indolent) cancers and aggressive cancers that would harm the patient. Because of this limitation, the test is no longer recommended for screening of men at normal risk for prostate cancer.\[15\]

**Approved Cancer Biomarkers**

List of FDA-approved cancer biomarkers\[12\]

- **AFP (Alpha-Fetoprotein)**: elevated in non-seminomatous germ-cell tumors (NSGCTs) and liver cancer (also called hepatocellular carcinoma or HCC)
- **CA-125 (Cancer Antigen 125)**: used to monitor response to treatment and recurrence of ovarian cancer
- **HE4 (Human Epididymis Protein 4)**: used to monitor recurrence of ovarian cancer
- **TG (Thyroglobulin)**: a marker for thyroid cancer
- **PSA (Prostate-Specific Antigen)**: increased levels in men may indicate prostate cancer
- CEA (Carcinoembryonic Antigen): a marker for colon cancer
- CA 19-9 (Cancer Antigen 19-9): a marker used to measure response to treatment in pancreatic cancer
- CA 15-3/CA 27-29 (Cancer Antigen 15-3/Cancer Antigen 27-29): used to monitor breast cancer