Circulating Tumor DNA Testing—Liquid Biopsy of a Cancer

DNA Variations Detectable in Blood
A biopsy sample of tissue often is tested for specific genetic variations (also referred to as mutations) that may have a targeted inhibitor that represents a clear optimal treatment for that cancer. However, it may not be possible to get enough tissue from the tumor to do these studies. DNA from our cells, including cancer cells, breaks down as part of its normal life cycle. This causes it to be shed into the bloodstream, where it is known as circulating tumor DNA (ctDNA). It is now possible to look for a wide range of cancer-associated variations in the ctDNA in a patient’s blood sample.

Advantages and Disadvantages of ctDNA Testing
Testing of ctDNA offers several advantages over attempts at repeated tissue biopsies. First, many patients often have very limited tissue available after a biopsy, which may not be enough for all the genetic testing that could shape treatment. Furthermore, tumors may be difficult or dangerous to reach by a repeated biopsy. As an alternative, looking in the blood for ctDNA can identify important molecular markers that could be missed if another tissue biopsy is difficult to pursue. Also, a blood draw can be done in any clinic that performs basic laboratory tests without the need for a more invasive procedure. Finally, while a tissue biopsy allows testing for cancer-association variations from only 1 sampled location, shed ctDNA comes from cancer cells anywhere in the body, casting a wider net for potentially important variations.

However, ctDNA testing is not ideal for every situation. One challenge is that it can be difficult to detect tiny amounts of DNA variation in the blood, especially when patients have a small volume of cancer. Although ctDNA detection of a variation is a reliable guide to direct treatment recommendations, a negative test may occur because the amount of ctDNA is too low, even if an important variation is present. For this reason, oncologists often recommend pursuing a tissue biopsy, which may identify a variation after a false-negative ctDNA test result. Finally, another challenge is that ctDNA testing typically costs several thousand dollars, and insurance coverage is variable.

Emerging Roles for ctDNA Testing
Along with its role in testing for variations at the time of initial cancer diagnosis, blood-based ctDNA testing opens the door to other potential uses. These could include screening and early detection of a primary cancer or recurrence, assessment of the effectiveness of cancer treatment, and identification of treatment-resistant genetic variations. Testing of ctDNA requires additional study and an acceptable cost before these applications become commonplace.

FOR MORE INFORMATION
• My Cancer Genome
https://www.mycancergenome.org/content/page/circulating-dna/
• US National Library of Medicine Genetics Home Reference
https://ghr.nlm.nih.gov/primer/testing/circulatingtumordna

Authors: Kyriillus S. Shohdy, MD, MSc; Howard (Jack) West, MD
Published Online: March 26, 2020. doi:10.1001/jamaoncol.2020.0346
Correction: This article was corrected on May 14, 2020, to fix a misspelling in author Kyriillus S. Shohdy’s first name in the byline.
Author Affiliations: Division of Hematology and Medical Oncology, Weill Department of Medicine, Weill Cornell Medical College, New York, New York (Shohdy), Department of Medical Oncology and Therapeutics Research, City of Hope Comprehensive Cancer Center, Duarte, California (West).
Conflict of Interest Disclosures: Dr Shohdy reported receiving grants from the Conquer Cancer Foundation of the American Society of Clinical Oncology. No other disclosures were reported.

Section Editor: Howard (Jack) West, MD.
The JAMA Oncology Patient Page is a public service of JAMA Oncology. The information and recommendations appearing on this page are appropriate in most instances, but they are not a substitute for medical diagnosis. For specific information concerning your personal medical condition, JAMA Oncology suggests that you consult your physician. This page may be photocopied noncommercially by physicians and other health care professionals to share with patients. To purchase bulk reprints, email reprints@jamanetwork.com.