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Editorial



# What Is "Cancer"? Is There A Need for New Terminologies?

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## Editorial

Cancer was known and surgically treated by ancient Mesopotamians and Egyptians, but the name "cancer" was not used in their writings.

The word cancer is credited to the Greek physician Hippocrates (460-370 BC), who is considered the "Father of Medicine." Hippocrates used the terms *carcinos* and *carcinom*a to describe non-ulcer forming and ulcer-forming tumors. In Greek, these words refer to a crab, most likely applied to the disease because the finger-like spreading projections from a cancer called to mind the shape of a crab.

In the 1860s, German surgeon, Karl Thiersch, showed that cancers metastasize through the spread of malignant cells and not through some unidentified fluid.

In recent years, partly due to aging populations and partly due to worsening environmental factors, the frequency of cancer has increased significantly. Fortunately, thanks to the modern technological revolution, the end of the twentieth and the first years of the twenty-first centuries witnessed a progress of epical proportions in the molecular biology, immunology and genetics of cancer. This progress was reflected as remarkable advances in diagnosis and treatment of cancer. Yet the definition of "cancer" remained the same for centuries.

The diagnosis of "cancer" is a very traumatic and is usually associated with huge psychological, social and economic burdens to most patients and their families. It is obvious that a "modern" definition of "cancer" may not improve research and management of this rather complex disease only, but will also reduce the burden of cancer diagnosis and improve the patient-provider communications and clarify the diagnostic and therapeutic decisions.

So, what is the present definition of "cancer"? This seems to be an absurd question from a person who has spent more than half a century diagnosing and researching cancer, like myself. (http://www.cancer.gov/) The National Cancer Institute (NCI) defines cancer as follows "cancerous tumors are malignant, which means they can spread into, or invade, nearby tissues. In addition, as these tumors grow, some cancer cells can break off and travel to distant places in the body through the blood or the lymph system and form new tumors far from the original tumor". Similarly, The World Health Organization (WHO) states: "a malignant tumor of potentially unlimited growth that expands locally by invasion and systemically by metastasis". Do all lesions we call "cancer" satisfy these definitions of invasion and metastasis?

Atypical epithelial proliferations called "carcinoma in-situ" may not qualify for the name "cancer"; the lowest-grade ductal carcinoma in situ lesions behave more like atypia, with risks for invasive cancer at 10 years in patients with low-grade lesions similar to risks in patients diagnosed with atypia.[1] The so-called lobular carcinoma in situ is generally considered a marker of higher risk of developing mammary carcinoma rather than a non-invasive malignancy itself.

The low grade non-invasive papillary urothelial "carcinoma" rarely if ever invades the lamina propria and may never metastasize; still we call it "cancer". In certain organs, e.g. gastrointestinal tract, the term carcinoma-in situ was abandoned in favor of "high grade dysplasia" without obvious effect on the rigorous management and/or follow up as needed.[2] HPV associated squamous lesion that used to be called carcinoma in-situ of the cervix is now named "grade III cervical intraepithelial neoplasia.[3] Yet, a morphologically and etiologically similar lesion in the oral cavity or oropharynx is still called "carcinoma in situ"!

Adenocarcinoma of the prostate is probably the tumor with the greatest risk for over diagnosis and overtreatment. With repeated prostate-specific antigen (PSA) testing and 10–12-core biopsy of the prostate, often done repeatedly, small, low-grade tumors are frequently detected. The 99% and 97% disease-specific survivals at 5 years and 10 years of follow-up, respectively, for men diagnosed with such small low-grade "cancers" who are simply monitored and only given treatment if they have evidence of a grade or volume increase. As a matter of fact, Gleason score 6 prostatic "carcinoma", the most commonly diagnosed prostatic cancer is locally invasive and is not known to metastasize[4] thus may not satisfy the definition of "cancer"! . Yet most patients are treated aggressively resulting in considerable mortality and morbidity.

On March 8-9, 2012, the National Cancer Institute convened a meeting to assess the problem of cancer over diagnosis, which occurs when tumors that would otherwise not become symptomatic are identified and treated. The meeting issued, among others, an important recommendation to "Embrace the development of new terminology to replace the word cancer when appropriate, when data or companion diagnostics support the classification of low-risk lesions as indolent lesions …".[5]

I call on my fellow pathologists to take these recommendations seriously and revise some of the present terminologies in favor of unified, reproducible clinico-pathologic and molecular entities to

enhance patient-oncologist communications and to open new avenues for research in "cancer" prevention, detection and management.

## Conflicts of Interest

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