

# Mastering the Intricate Maze of Metastasis

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Cancer metastasis is the process by which malignant cells move from the primary tumor and establish new distant sites of cancer throughout the body. This ability of cancer cells to move beyond the primary tumor is one of the hallmarks of malignant disease. Metastasis is a complex and intricate process that is responsible for treatment failure and the eventual death of most patients with cancer. The discovery of metastasis as an active process rather than a random act of nature has increased our understanding of this dynamic process and has inspired researchers to explore the sequence of events leading to metastasis.

The term “metastasis” first was used by French physician Joseph Claude Recamier in 1829. Prior to Recamier’s work on metastasis, physicians recognized that tumors could extend beyond their borders by direct extension and invading lymph nodes. However, they believed that distant metastasis was caused by independent tumor growth, unrelated to the primary cancer. Recamier was the first physician to provide anatomic confirmation that metastasis was caused by cancer cells breaking away from the primary tumor and entering the blood or lymphatic circulation to travel to distant sites in the body (Liotta, 1992). Since this discovery, a clearer understanding of the genetic and molecular steps involved in the metastasis process has been sought in hopes of developing new diagnostic and therapeutic strategies for metastasis.

This article provides an in-depth review of the concepts of metastasis, such as angiogenesis, cell migration, attachment, invasion, and the role of growth factors. The goals of this article are to provide nurses with a clear description of the concepts involved in the metastatic process and describe clinically relevant examples of these concepts.

## Incidence

The incidence of metastatic disease is quite staggering. Approximately 50%–60% of patients with solid tumors have metastatic disease at the time of diagnosis (see Table 1). Thirty percent of patients with cancer will have clinically detectable metastasis at the time of diagnosis, whereas 20%–30% will have micrometastases or clinically undetectable metastatic disease (Liotta & Kohn, 1990). If a primary tumor is detected early and removed before metastasis occurs, then

the cancer will be eradicated. However, if metastases or even micrometastases already are present at the time of diagnosis, the prognosis is guarded and may become fatal.

Cancers of unknown primary origin represent the subgroup of patients with cancer who present with metastatic disease yielding a poor prognosis. These cancers comprise 2%–6% of all cancers (Greco & Hainsworth, 2001). The broad types of unknown primary cancers include (a) poorly differentiated neoplasm, (b) well-differentiated and moderately well-differentiated adenocarcinoma, (c) squamous cell carcinoma, and (d) poorly differentiated carcinoma. Each type differs in clinical presentation, recommended diagnostic workup, treatment, and prognosis.

One of the greatest challenges when treating patients with an unknown primary is determining the primary site. The primary site of the cancer is only detectable in 15%–20% of patients during their lifetime. Despite these odds, attempts are made to locate the primary site, but exhaustive evaluations are not recommended. Ironically, the primary site eventually is determined at autopsy in 70%–80% of patients.

Adenocarcinoma accounts for 60% of all cancers of unknown primary origin. Most present with widespread metastatic disease and have a poor performance status at the time of presentation (Greco & Hainsworth, 2001; Hillen, 2000). Typically, patients with adenocarcinoma are elderly and have metastatic tumors at multiple sites, including the lymph nodes, liver, lung, and bone. Clinical symptoms usually correlate with the sites of metastasis. Overall, the prognosis of these patients is poor, with a median survival of only three to four months. This reflects the fact that many patients with unknown primaries eventually will be diagnosed with lung or gastrointestinal cancers.



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