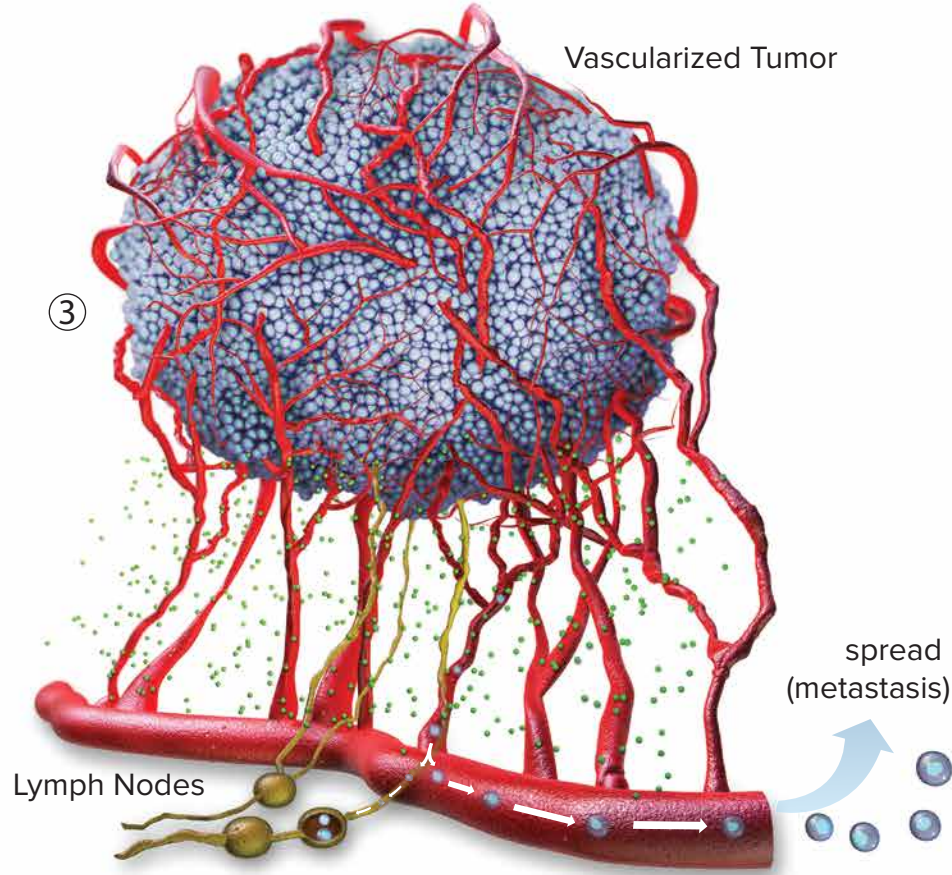
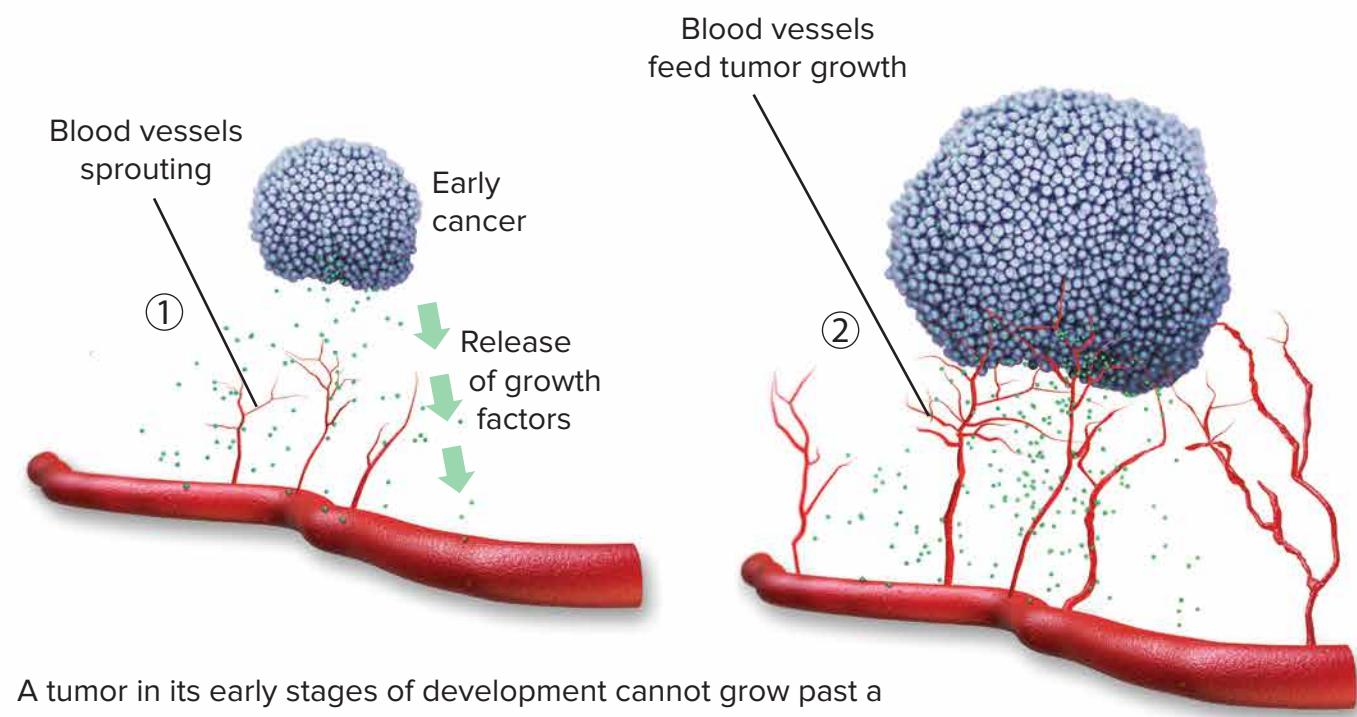


# Tumor Angiogenesis in Colorectal Cancer

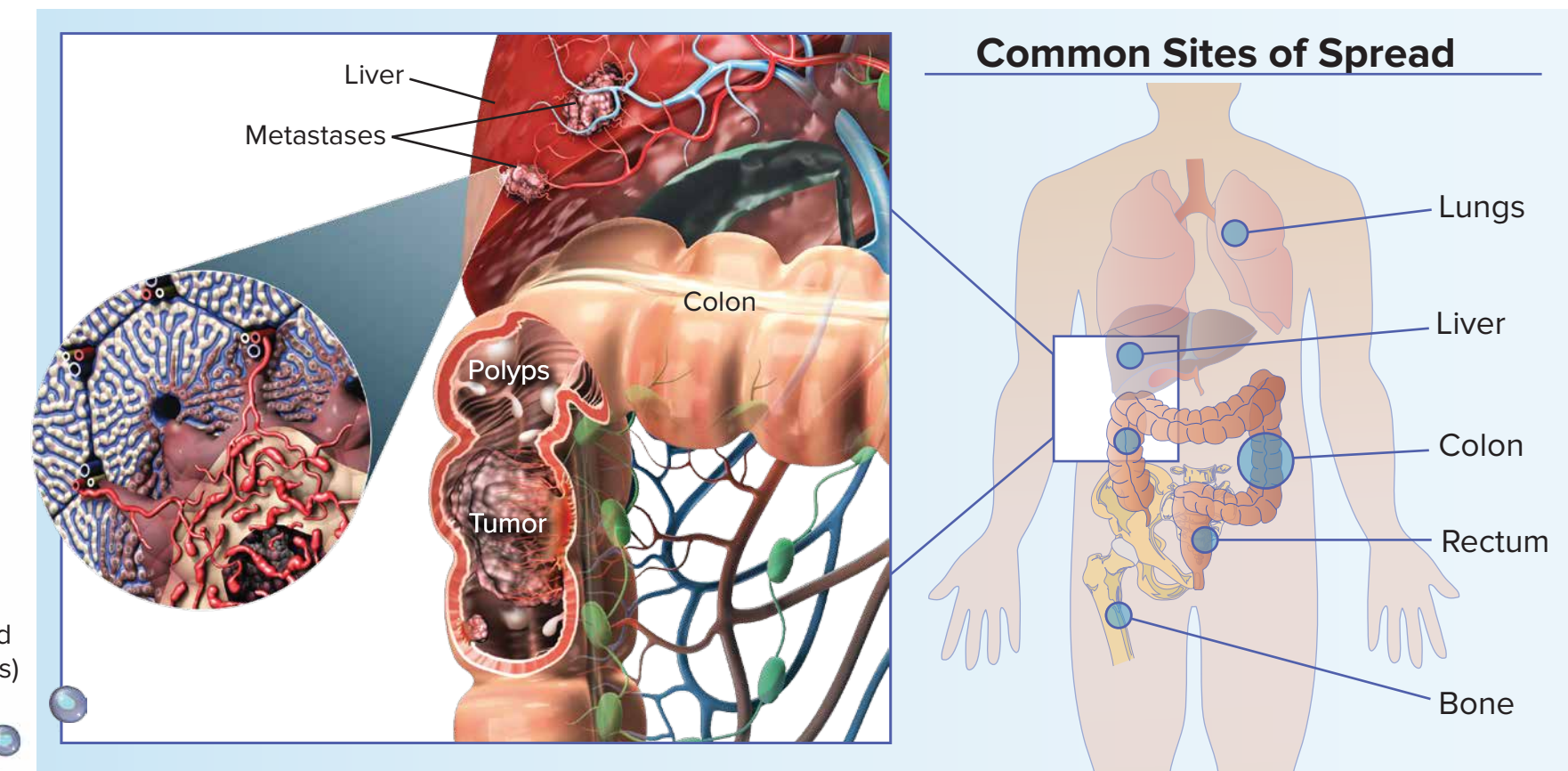
Metastatic colorectal cancer (mCRC) is the third leading cause of cancer-related deaths in the United States. Treatment algorithms must be updated to accommodate all targeted and antiangiogenic agents as potential therapy for patients with mCRC.

1. Cancer cells release growth factors that activate endothelial cells during the switch to the angiogenic phenotype. This occurs in response to acquired gene mutations and hypoxia.
2. Growth factors bind to endothelial cell receptors, activating signal transduction pathways and causing cell proliferation.

3. Tumor blood vessels are characteristically tortuous, saccular, and leaky; blood flow is uneven and chaotic, with areas of tumor necrosis, hypoxia, and acidosis.



Angiogenesis in CRC liver metastases is initiated when a tumor co-opts sinusoidal endothelial cells lining the periphery of the lesion. The liver contributes abundant proangiogenic factors to the metastatic lesion.



## Treatments for Metastatic Colorectal Cancer

### Chemotherapy

Chemotherapy attacks the cancer cells directly, causing them to die off.

### Radiation

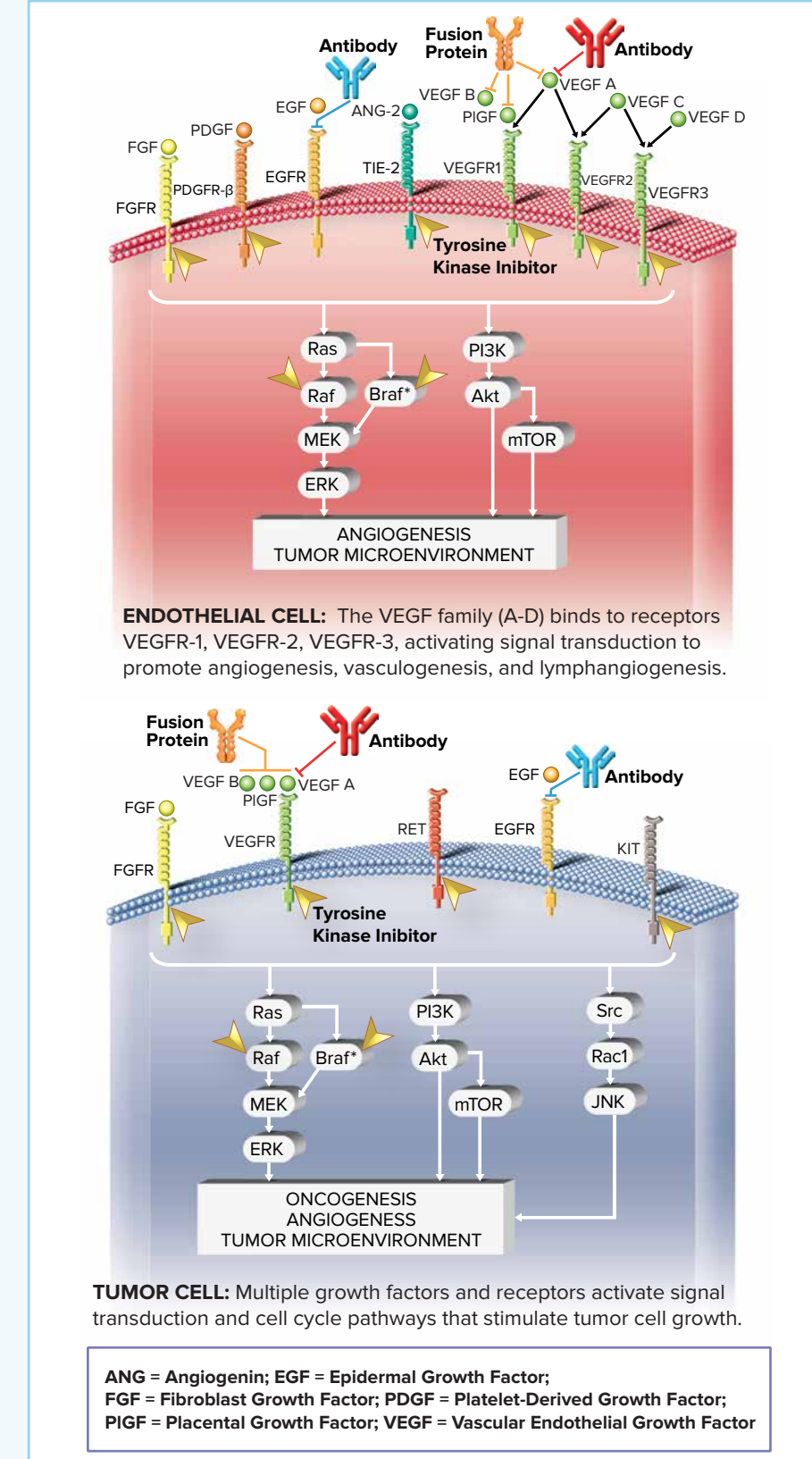
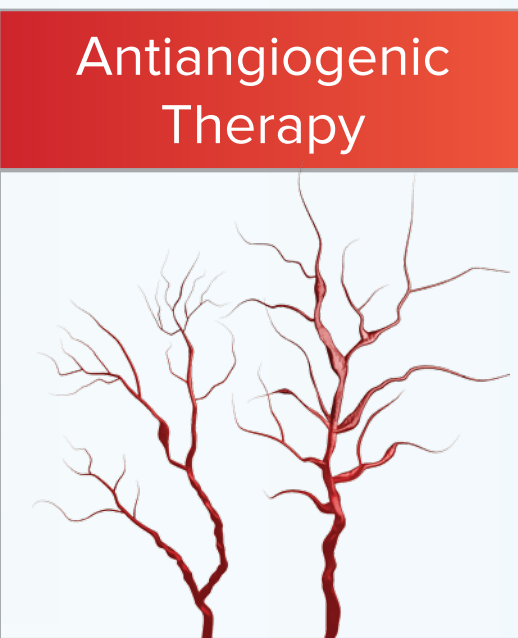
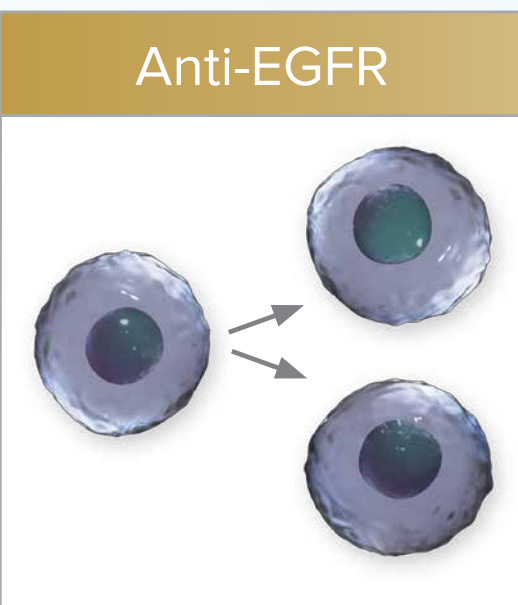
Radiation therapy kills cancer cells with high-energy rays.

### Biopsy/Genetic Test

Available EGFR inhibitors are ineffective in tumors that carry mutations of the KRAS gene. Roughly 40% of colorectal cancers have KRAS mutations.

## Targeted Therapies

Targeted cancer therapies halt the growth and spread of cancer by “targeting,” or interfering, with specific molecules that play a role in tumor progression and growth. In addition to the targeted treatments that have already gained FDA approval, numerous other agents such as monoclonal antibodies, engineered proteins, tyrosine kinase inhibitors (TKIs) and other small molecule agents with varying mechanisms of action are currently under investigation as potential therapy for patients with mCRC.



## Potential Outcomes of Targeted Therapies

- 1. Tumor Shrinkage**  
Metastatic tumors often shrink significantly with targeted treatments. Without a blood supply, the tumors cannot sustain themselves.
- 2. Stop Tumor Growth**  
Primary tumors are also affected by targeted treatments. As the vessels feeding the tumor shrink back, cells in the tumor mass are starved for oxygen and nutrients. Tumor growth is stopped and the surrounding environment becomes more stable.
- 3. Disease Progression**  
Tumors may continue to grow despite treatment. This is called “non-response” to treatment.