Neoplasia II: Tumor Characteristics
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Neoplasia Outline

- Tumor nomenclature
- Tumor characteristics
- Epidemiology
- Cancer pathogenesis
Neoplasia Outline

- Tumor nomenclature
- Tumor characteristics
  - Differentiation and anaplasia
  - Rate of growth
  - Local invasion
  - Metastasis
Neoplasia Outline

• Tumor nomenclature

• Tumor characteristics
  • Differentiation and anaplasia
Differentiation and Anaplasia

- Differentiation = how much the tumor cells resemble their cells of origin
  - Well-differentiated: closely resembles
  - Moderately-differentiated: sort of resembles
  - Poorly-differentiated: doesn’t resemble
- Benign tumors are usually well-differentiated
- Malignant tumors can show any level of differentiation
Thyroid adenoma (well-differentiated)
Squamous cell carcinoma, well-differentiated
Squamous cell carcinoma, moderately-differentiated
Squamous cell carcinoma, poorly-differentiated
Anaplasia: a state of complete un-differentiation

- Literally, “to form (-plasia) backwards (ana-)”
- Misnomer! Cells don’t de-differentiate.
- Just means cells are very poorly-differentiated
- Almost always indicates malignancy
Anaplastic cells show:

- Pleomorphism
- Hyperchromatic, large nuclei
- Bizarre nuclear shapes, distinct nucleoli
- Lots of mitoses, and atypical mitoses
- Architectural anarchy
Anaplastic carcinoma
Abnormal mitoses
Dysplasia = disorderly (dys-) growth (-plasia)

- “Dysplasia” is used to describe disorderly changes in non-neoplastic epithelial cells
- Graded as mild, moderate or severe
  - Mild-moderate: usually reversible
  - Severe: usually progresses to carcinoma in situ (CIS)
- Next step after CIS: invasive carcinoma
Dysplastic cells show:

- Pleomorphism
- Hyperchromatic, large nuclei
- Lots of mitoses
- Architectural anarchy
Q. Wait a minute, “dysplasia” sounds suspiciously similar to “differentiation” – what’s the difference?
Q. Wait a minute, “dysplasia” sounds suspiciously similar to “differentiation” – what’s the difference?

A. Both terms describe whether cells look normal or not!

   But:

   • “Differentiation” is only used with neoplastic cells, and “Dysplasia” is only used with non-neoplastic cells!
   • “Dysplasia” is only used with epithelial cells, but “Differentiation” can apply to any cell type.
Non-neoplastic epithelial cells

- mild dysplasia
- moderate dysplasia
- severe dysplasia

Neoplastic cells

- well-differentiated
- moderately-differentiated
- poorly-differentiated
- anaplastic

carcinoma in situ
Dysplasia
Normal glands
Mild dysplasia
Moderate dysplasia
Severe dysplasia
Dysplastic epithelium  Normal epithelium
Invasive squamous cell carcinoma
Neoplasia Outline

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  - Rate of growth
Generalizations about Growth

- Malignant tumors grow faster than benign ones.
- Poorly-differentiated tumors grow faster than well-differentiated ones.
- Growth is dependent on:
  - Blood supply
  - Hormonal factors
  - Emergence of aggressive sub-clones
Growth Fraction

• GF = % of tumor cells that are dividing

• Age of tumor matters
  • Early on (subclinical), GF high.
  • Later (clinically detectable), GF low.

• Type of tumor matters
  • Leukemias, lymphomas, small-cell lung cancer: high GF
  • Breast, colon cancer: low GF

• Important for treatment
  • High GF tumor: treat with chemotherapy/radiation
  • Low GF tumor: treat by debulking
Normal cell → Single tumor cell

30 doublings

1 gm → \(10^9\) cells
Smallest clinically detectable mass

10 doublings

Microscopic metastases

1 kg → \(10^{12}\) cells
Maximum mass compatible with life

Metastases
Tumor cells undergoing apoptosis
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Local Invasion

Benign tumors
• Stay where they are.
• Can’t invade or metastasize.
• Usually encapsulated.

Malignant tumors
• Infiltrate, invade, destroy surrounding tissue.
• Then metastasize to other parts of body.
• Not encapsulated.
Malignant tumor invading kidney
Malignant tumor invading kidney
Malignant tumor invading kidney
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Carcinoma in situ
Invasive carcinoma
Invasive carcinoma
Metastasizing carcinoma
Liver with multiple metastases
Metastasis

- Metastasis = development of secondary tumor implants in distant tissues
- Half of all patients with malignancies have mets at the time of diagnosis!!
- Metastasis depends on:
  - Type of tumor
  - Size of tumor
  - Degree of differentiation of tumor
Three Ways Tumors Metastasize

- Seeding
- Lymphatic spread
- Hematogenous spread
Three Ways Tumors Metastasize

• **Seeding**
  • Tumor invades body cavity
  • Bits break off and implant on peritoneal surfaces
  • Ovarian cancer can spread easily this way
Liver seeded with metastatic ovarian carcinoma
Three Ways Tumors Metastasize

- Seeding
- Lymphatic spread
  - Tumor spreads to local lymph nodes
  - Sentinel lymph node first
  - Moves through thoracic duct
  - Empties into subclavian vein
  - Carcinomas like to spread this way
Tumor in lymphatic
Tumor in lymph node
Three Ways Tumors Metastasize

- Seeding
- Lymphatic spread
- Hematogenous spread
  - Veins are easier to invade than arteries
  - Liver and lungs are the most common metastatic destinations
  - Sarcomas like to spread this way (but so do carcinomas)
Sarcoma metastatic to lung
Sarcoma metastatic to lung