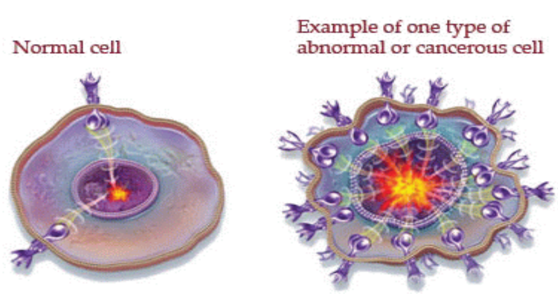
EDUCATION UPDATE

FUNDAMENTALS OF ONCOLOGY

February 5,2026



Allegheny Health Network Cancer Institute

Allegheny Health Network
<u>Fundamentals of Oncology Course</u>

The Fundamentals of Oncology Course is a 4-day introductory course intended for novice clinicians who practice in hematological-medical units, skilled nursing facilities, home care, hospice, radiation oncology and/or cellular transplant. This course may also be applicable to experienced oncology clinicians who require a basic review of oncology diseases and emergencies as well as complications surrounding these processes.

This course is designed to provide the oncology clinicians with basic oncology information and skills that would be applicable to any oncology patient population. The course NCPD can also be applied to the ILNA blueprint for ONCC certifications. Codes have been noted under each lecture. Please keep the course flyer for your ONCC renewal application process.

<u>Course Faculty:</u> This course uses a multidisciplinary approach from the knowledge and expertise of physicians, nurses, clinical nurse specialists, nurse practitioners, managers, genetic counselors, and social workers to provide a comprehensive overview of oncology.

Criteria for earning contact hours

<u>Attendance</u>: Participants are eligible for Nursing Continued Professional Development (NCPD) credits based on the sections they attend. Credits are only offered on the scheduled course dates attended.

<u>Course Materials:</u> Course materials will be distributed at the beginning of each course with additional handouts as necessary throughout the course. Materials include the course schedule, objectives, evaluation form, and content outlines. Post assessment will be provided at the end of each day, with a review conducted at beginning of next class day. Expectation is a passing score of 85%

<u>Course Evaluation</u>: Participants are requested to complete an evaluation for each speaker/lecture. The evaluations will be collected at the conclusion of each day. Feedback will be utilized for subsequent course evaluations.

Activity approval

West Penn Hospital is approved as a provider of nursing continuing professional development by Pennsylvania State Nurses Association, an accredited approver by the American Nurses Credentialing Center's Commission on Accreditation.

Allegheny General Hospital is accredited by the Accreditation Council for Continuing Medical Education to provide continuing education for physicians. Allegheny General Hospital designates this live activity for a maximum of 1.0 AMA PRA category 1 Credit(s)™. Physicians should claim only the credit commensurate with the extent of their participation in this activity

<u>Disclosure Statements</u>

- The planners and presenters have no conflicts of interest to disclose for this activity <u>except</u>:
  - Shelbie O'Hara- Content Creator, Item writer-Oncology Nursing Society
  - Justin Engleka- Highmark Health, Pittsburgh Mobile Footcare
  - Katherine Chorik- Beautox Aesthetics
  - Cyrus Khan- Speakers Bureau – Roche; Beigene; AstraZeneca; AbbVie; BMS; Lily; Pfizer; Kite; ADC Therapeutics
- Any relevant conflicts have been mitigated
- There is no commercial support or sponsors for this educational activity.

Expiration date of enduring material (if applicable) After completion of the live course, enduring materials will be available until December 31, 2026.

Fundamentals of Oncology – Day 1

Thursday February 5, 2026

7:30 a.m. Registration and welcome
Mary E. Kern, MSN, RN, OCN, CHSE

8:00 a.m. Cancer Process, Treatment Modalities, Principles
Marissa Venanzi, PA-C

9:45 a.m. Break

10:00 a.m. Genetics
Kyla Morphy, MS CGC

11:00 a.m. Nutritional Issues
Christy Bender, MS, RD, CSO, LDN

11:45 p.m. Lunch

12:30 p.m. Basics of Radiation/Radiobiology
Abigail Dare, MS

1:15 p.m. Radiation oncology team
Shelbie O'Hara, BSN, RN
Jennifer Carmichael, RT (R)(T)

2:00 p.m. Wrap-up and Evaluations

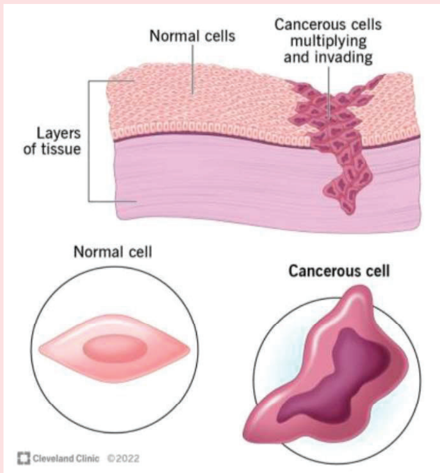
Learning Outcomes

Upon conclusion of this conference, participants will be able to:

- Explore the genetic basis of inherited cancer syndromes

- Describe the genetic counseling process: referrals, genetic counseling, and genetic counseling
- Explain tumor nomenclature, molecular biology concepts, diagnosis, and treatment principles
- Distinguish the phases and components of clinical research trials
- Recognize Diversity, Equity, and Inclusion (DEI) and how it relates in oncology
- Discuss management of various vascular access devices available for use in patients with cancer
- Summarize care of medical, surgical, hematological, and radiation oncology patients including the common side effects, complications, and management related to treatment modalities
- Examine basic pathophysiology, assessment, diagnosis and treatment interventions of solid tumor, hematologic malignancies, and benign heme disorders
- Review rationale for the use of various blood products and components
- Identify the basic process of autologous, allogenic, haplo, and cord blood transplantation
- Recall radiation terminology and safety principles
- Explain the different radiation treatment modalities: External Beam Therapy, Brachytherapy
- Give examples of radiation disciplines coordinating patient care and treatment
- State principles of radiation treatment planning and process
- Differentiate the various oncologic emergencies and complications that may arise in the immunocompromised oncology patient
- Summarize nutritional issues impacting patients with cancer
- Examine survivorship issues associated with cancer diagnosis and various treatment modalities
- Assess fertility and sexuality issues related to cancer diagnosis and treatment modalities
- Differentiate between hospice and palliative care programs
- Distinguish the treatment modalities for acute , chronic, and oncologic pain
- Integrate coping strategies for clinicians when caring for patients with cancer
- Recommend oncology rehab strategies contributing to survivorship outcomes and quality of life
- Recognize various psycho-social issues pertinent to patients with cancer throughout the continuum of care
- Relate knowledge from course to clinical practice

Pathophysiology of Cancer



Marissa Venanzi, PA-C
Medical Oncology/Hematology Oncology- AGH
Marissa.Venanzi@ahn.org

1

Learning Outcomes

Upon completion of this session, the learner will be able to:

1. Define cancer.
2. Recall basic cancer terminology and tumor nomenclature.
3. List cancer statistics related to incidence, cases, and deaths.
3. Explain theories of causation, grading, and staging of cancer.
4. Describe the carcinogenesis process.
5. Summarize the clinical workup for patients with cancer.
6. Discuss various treatment modalities available for cancer.

2

STATISTICS

- Estimated 2 million new diagnoses in 2024 (Men and Women)

Does not include:

- carcinoma in-situ = non-invasive (except urinary)
- basal and squamous cell of skin
- another estimated 3 million

- Estimated 611,720 deaths (Men and Women)
- 1680 deaths/day
- Second leading cause of death in the US
- The 5-year survival rate for all cancers has increased from 49% to 69%.
- Cancers with highest survival rate: thyroid (99%), prostate (97%), testis (95%), and melanoma (94%)
- Cancer with lowest survival rate: late pancreas (13%), liver and esophagus (22%), and lung (25%).

3

American Cancer Society Facts and Figures 2024

- The death rate from cancer in the US has declined steadily over the past 25 years
- As of 2016, the cancer death rate for men and women combined had fallen 27% from its peak in 1991
- This decline translates to about 1.5% per year and more than 2.6 million deaths avoided between 1991 and 2016.

https://www.cancer.org/content/dam/cancer-org/research/cancer-facts-and-statistics/annual-cancer-facts-and-figures/2024/2024-cancer-facts-and-figures-acs.pdf

4

STATS

Estimated New Cases

Male			Female		
Prostate	299,010	29%	Breast	310,720	32%
Lung & bronchus	116,310	11%	Lung & bronchus	118,270	12%
Colon & rectum	81,540	8%	Colon & rectum	71,270	7%
Urinary bladder	63,070	6%	Uterine corpus	67,880	7%
Melanoma of the skin	59,170	6%	Melanoma of the skin	41,470	4%
Kidney & renal pelvis	52,380	5%	Non-Hodgkin lymphoma	36,030	4%
Non-Hodgkin lymphoma	44,590	4%	Pancreas	31,910	3%
Oral cavity & pharynx	41,510	4%	Thyroid	31,520	3%
Leukemia	36,450	4%	Kidney & renal pelvis	29,230	3%
Pancreas	34,530	3%	Leukemia	26,320	3%
All sites	**1,029,080**		**All sites**	**972,060**	

Estimated Deaths

Male			Female		
Lung & bronchus	65,790	20%	Lung & bronchus	59,280	21%
Prostate	35,250	11%	Breast	42,250	15%
Colon & rectum	28,700	9%	Pancreas	24,480	8%
Pancreas	27,270	8%	Colon & rectum	24,310	8%
Liver & intrahepatic bile duct	19,120	6%	Uterine corpus	13,250	5%
Leukemia	13,640	4%	Ovary	12,740	4%
Esophagus	12,880	4%	Liver & intrahepatic bile duct	10,720	4%
Urinary bladder	12,290	4%	Leukemia	10,030	3%
Non-Hodgkin lymphoma	11,780	4%	Non-Hodgkin lymphoma	8,360	3%
Brain & other nervous system	10,690	3%	Brain & other nervous system	8,070	3%
All sites	**322,800**		**All sites**	**288,920**	

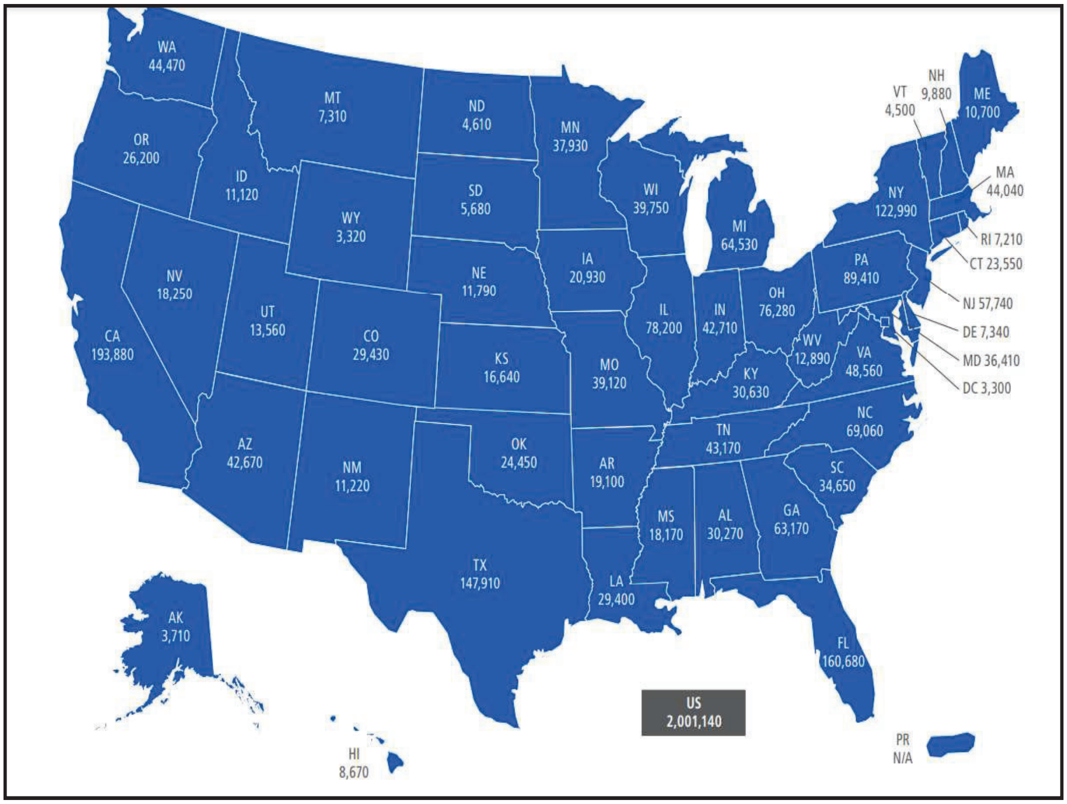
Estimates are rounded to the nearest 10, and cases exclude basal cell and squamous cell skin cancers and in situ carcinoma except urinary bladder. Estimates do not include Puerto Rico or other US territories. Ranking is based on modeled projections and may differ from the most recent observed data.

5

The effect of COVID-19 on cancer incidences in the U.S

- Although new cancer diagnoses largely returned to pre-pandemic levels by 2021, the recovery does not account for the potential missed diagnoses due to delays in screening and other medical care in early 2020.
- Additionally, patients who were already diagnosed experienced treatment delays and/or modifications.
- The consequences of this interruption in care will become evident in our cancer statistics over the next several years.

6



7

Table 6. Probability (%) of Developing Invasive Cancer During Selected Age Intervals by Sex, US, 2017-2019*

Site	Sex	0-49	50-64	65-84	85+	Birth to death
All sites†	Male	3.5 (1 in 29)	11.8 (1 in 8)	31.9 (1 in 3)	19.1 (1 in 5)	41.6 (1 in 2)
	Female	5.9 (1 in 17)	10.8 (1 in 9)	24.3 (1 in 4)	14.4 (1 in 7)	39.6 (1 in 3)
Breast	Female	2.1 (1 in 48)	4.0 (1 in 25)	7.2 (1 in 14)	2.6 (1 in 38)	13.0 (1 in 8)
Colon & rectum	Male	0.4 (1 in 239)	1.2 (1 in 83)	2.7 (1 in 37)	1.8 (1 in 57)	4.3 (1 in 23)
	Female	0.4 (1 in 265)	0.9 (1 in 117)	2.2 (1 in 46)	1.7 (1 in 60)	3.9 (1 in 25)
Kidney & renal pelvis	Male	0.3 (1 in 384)	0.7 (1 in 142)	1.5 (1 in 67)	0.6 (1 in 178)	2.3 (1 in 43)
	Female	0.2 (1 in 603)	0.3 (1 in 287)	0.8 (1 in 126)	0.3 (1 in 303)	1.4 (1 in 73)
Leukemia	Male	0.3 (1 in 375)	0.3 (1 in 287)	1.2 (1 in 82)	0.9 (1 in 117)	1.9 (1 in 53)
	Female	0.2 (1 in 488)	0.2 (1 in 448)	0.7 (1 in 136)	0.5 (1 in 196)	1.3 (1 in 75)
Lung & bronchus	Male	0.1 (1 in 840)	1.2 (1 in 82)	5.1 (1 in 20)	2.7 (1 in 37)	6.3 (1 in 16)
	Female	0.1 (1 in 738)	1.1 (1 in 90)	4.3 (1 in 23)	1.9 (1 in 52)	5.9 (1 in 17)
Melanoma of the skin‡	Male	0.4 (1 in 243)	0.9 (1 in 116)	2.4 (1 in 42)	1.4 (1 in 73)	3.6 (1 in 28)
	Female	0.6 (1 in 160)	0.7 (1 in 153)	1.1 (1 in 92)	0.5 (1 in 188)	2.5 (1 in 41)
Non-Hodgkin lymphoma	Male	0.3 (1 in 395)	0.5 (1 in 196)	1.6 (1 in 63)	0.9 (1 in 105)	2.4 (1 in 42)
	Female	0.2 (1 in 528)	0.4 (1 in 264)	1.2 (1 in 86)	0.7 (1 in 153)	1.9 (1 in 52)
Prostate	Male	0.2 (1 in 449)	3.9 (1 in 26)	10.4 (1 in 10)	3.1 (1 in 32)	12.9 (1 in 8)
Thyroid	Male	0.2 (1 in 483)	0.2 (1 in 480)	0.3 (1 in 354)	0.1 (1 in 1429)	0.7 (1 in 153)
	Female	0.8 (1 in 124)	0.5 (1 in 200)	0.5 (1 in 217)	0.1 (1 in 1194)	1.7 (1 in 58)
Uterine cervix	Female	0.3 (1 in 337)	0.2 (1 in 554)	0.2 (1 in 564)	0.1 (1 in 1535)	0.7 (1 in 152)
Uterine corpus	Female	0.3 (1 in 303)	1.1 (1 in 91)	1.7 (1 in 58)	0.4 (1 in 239)	3.1 (1 in 32)

*For those who are free of cancer at the beginning of each age interval. †All sites excludes basal and squamous cell skin cancers and in situ cancers except urinary bladder. ‡Statistic is for non-Hispanic White individuals.

Source: DevCan: Probability of Developing or Dying of Cancer Software, Version 6.9.0. Statistical Research and Applications Branch, National Cancer Institute, 2023. surveillance.cancer.gov/devcan/.

Please note: The probability of developing cancer for additional sites, as well as the probability of cancer death, can be found in Supplemental Data at cancer.org/research/cancer-facts-statistics.html.

8

Survivorship Facts

- More than 18 million survivors as of January 2022
- Estimated more than 22.1 million survivors as of January 2030
  - **Acute Survivorship** starts at diagnosis and goes through to the end of initial treatment. Cancer treatment is the focus.
  - **Extended Survivorship** starts at the end of initial treatment and goes through the months after. The effects of cancer and treatment are the focus.
  - **Long-Term Survivorship** is when years have passed since cancer treatment ended. There is less of a chance that the cancer may come back. Long-term effects of cancer and treatment are the focus.

9

Survivorship Facts

- About 67% of today's cancer survivors were diagnosed five or more years ago
- About 18% of all cancer survivors were diagnosed 20 or more years ago
- Nearly 2/3 (64%) of survivors are age 65 or older
- Most cancer survivors have had common cancers:
  - 23% - breast cancer
  - 21% - prostate cancer
  - 9% - colorectal cancer
  - 8% - cervical, uterine, or ovarian cancers
  - 8% - melanoma

10

Table 7. Trends in 5-year Relative Survival Rates* (%) by Race, US, 1975-2019

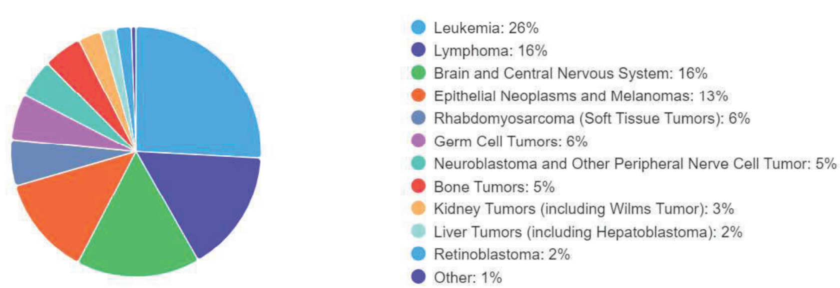
	All races & ethnicities			White			Black		
	1975-77	1995-97	2013-19	1975-77	1995-97	2013-19	1975-77	1995-97	2013-19
All sites	49	63	69	50	64	69	39	54	65
Brain & other nervous system	23	32	34	22	31	31	25	39	39
Breast (female)	75	87	91	76	89	93	62	75	83
Colon & rectum**	50	61	64	50	62	65	45	54	59
Colon**	51	61	63	51	62	64	45	54	57
Rectum	48	62	67	48	62	67	44	55	65
Esophagus	5	13	22	6	14	23	4	9	17
Hodgkin lymphoma	72	84	89	72	85	90	70	82	88
Kidney & renal pelvis	50	62	78	50	62	78	49	62	77
Larynx	66	66	62	67	68	62	58	52	55
Leukemia	34	48	67	35	50	68	33	42	61
Liver & intrahepatic bile duct	3	7	22	3	7	21	2	4	21
Lung & bronchus	12	15	25	12	15	25	11	13	23
Melanoma of the skin	82	91	94	82	91	94	57†	76†	71
Myeloma	25	32	60	24	32	59	29	32	61
Non-Hodgkin lymphoma	47	56	74	47	57	76	49	49	70
Oral cavity & pharynx	53	58	69	54	60	70	36	38	55
Ovary	36	43	51	35	43	50	42	36	42
Pancreas	3	4	13	3	4	12	2	4	11
Prostate	68	97	97	69	97	98	61	94	97
Stomach	15	22	36	14	20	36	16	22	37
Testis	83	96	95	83	96	97	73‡†	86†	91
Thyroid	92	95	99	92	96	99	90	95	97
Urinary bladder	72	80	78	73	81	79	50	63	65
Uterine cervix	69	73	67	70	74	68	65	66	57
Uterine corpus	87	84	81	88	86	84	60	62	63

*Rates are age adjusted for normal life expectancy and are based on cases diagnosed in the SEER 9 areas for 1975-1977 and 1995-1997, and in the SEER 22 areas for 2013-2019; all cases were followed through 2020. Rates for White and Black patients diagnosed during 2013-2019 are exclusive of Hispanic ethnicity. †The standard error is between 5 and 10 percentage points. ‡Survival rate is for cases diagnosed from 1978 to 1980. **Excludes appendix.

Sources: 2013-2019 survival – SEER*Explorer, National Cancer Institute, 2023. Available from https://seer.cancer.gov/explorer/. Colon & rectal cancer – SEER*Stat software (version 8.4.0.1), National Cancer Institute, 2023. Historical survival was previously calculated using SEER*Stat version 8.3.9.

11

Number of Childhood Cancer Diagnoses Per Year, Age 0-19



https://curesearch.org/number-of-diagnoses

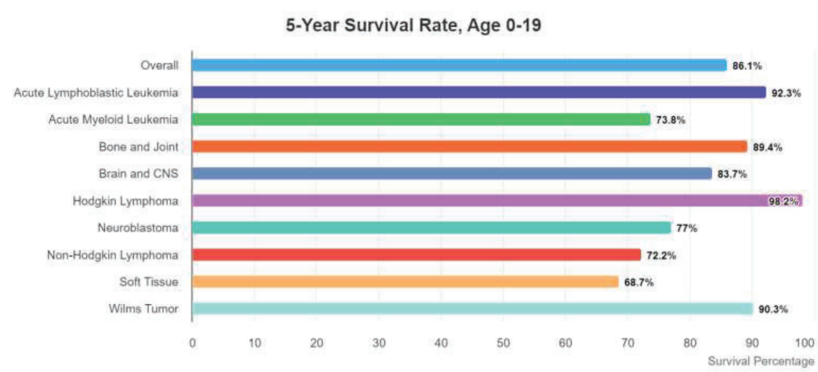
12

Types of Childhood Cancers

	Children (0-14)	Adolescents (15-19)
• **Overall adolescent incidence increasing 1% annually**		
Overall Diagnoses	9,910	5,280
Overall Deaths	1,040	550
Overall Mortality	6.3 down to 1.9%	7.2 down to 2.6 %
Overall Survival	85%	86%
Leukemia Dx **(ALL & AML)**	28%	13%
Brain Dx **(Cerebellum & Brain Stem)**	26%	21%
Lymphoma **(NHL & HD)**	12%	19%
Neuroblastoma (6%) Wilms (5%) Rhabdomyosarcoma (3%) Retinoblastoma (3%) Bone Osteosarcoma (2%) Ewing (1%)		

13

In the last 40 years, the overall survival rate for children's cancer has increased from 10% to over 85% today, but for many more rare childhood cancers, the survival rate is much lower. There are approximately 483,000 adult survivors of children's cancer in the United States.



Source: NCCR*Explorer: An interactive website for NCCR cancer statistics [Internet]. National Cancer Institute. Accessed at nccrexplorer.ccdi.cancer.gov on May 23, 2023, 09:14:31 AM.
Years: 2012-2018. By Cancer Site, Both Sexes, All Races, Ages <20.

14

What have we learned? How are we doing?

Glossary of Terminology

Neoplasm

- “new plasma”…abnormal tissue growth with rapid growth

Benign

- no metastasis – moles and fibroids

Malignant

- local invasion and destructive growth…”wicked”

Metastasis

- spread from primary via lymphatic and/or circulatory system or adjacent organs – primary mets to lung, bone, liver, brain

Malignant Tumor Nomenclature:

Certain prefixes are used to describe the type of **epithelial tissue** from which the carcinoma originate.

In the anatomic classification of tumors, the tumor is identified by the tissue of origin, the anatomic site, and the behavior of the tumor

Adeno:

- Carcinomas originating from grandular epithelium (columnar)
  - Exocrine and endocrine
  - Adrenal, ovarian, pancreatic, testicular, liver, lung – solid

Squamous:

- Arise in squamous epithelial tissue
  - Lungs, kidneys, esophageal, bladder– lining of cells

Connective tissue origin

- **Osteo**: sarcoma arising in the bone
- **Chondro**: sarcoma arising from cartilage
- **Lipo**: sarcomas arising from fat
- **Rhabdo**: sarcoma arising from skeletal muscle
- **Leiomyo**: sarcomas arising from smooth muscle

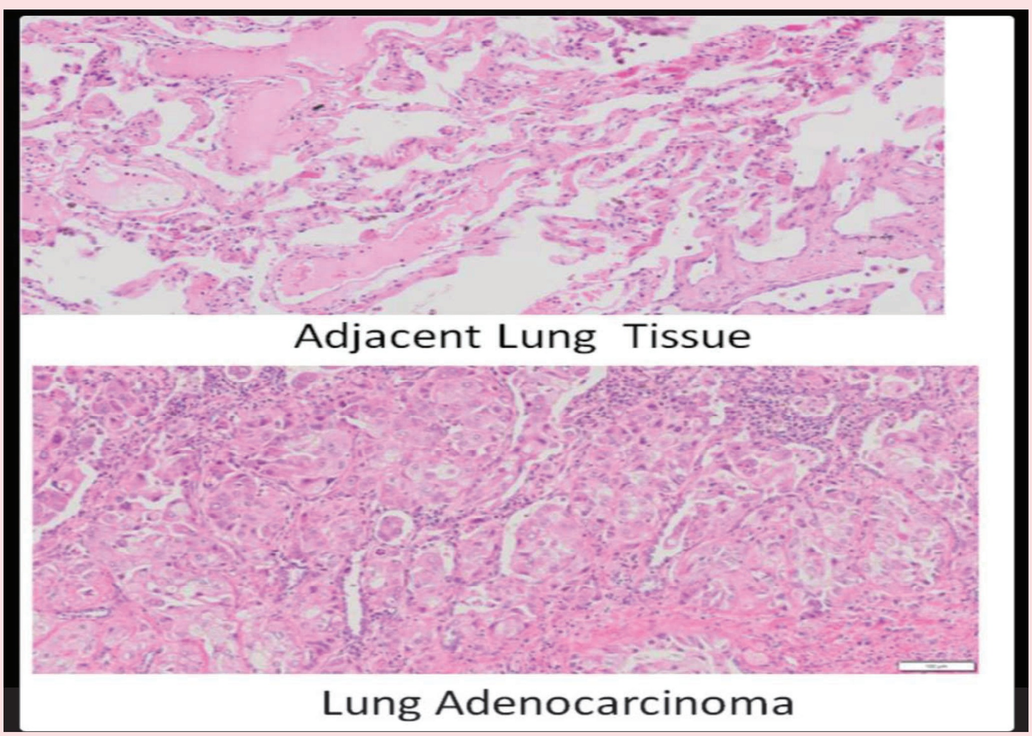
Other Tumor Types

- Blastoma (pre-cursor cells)
- Hematologic

Some Prefixes Used in Naming Cancers

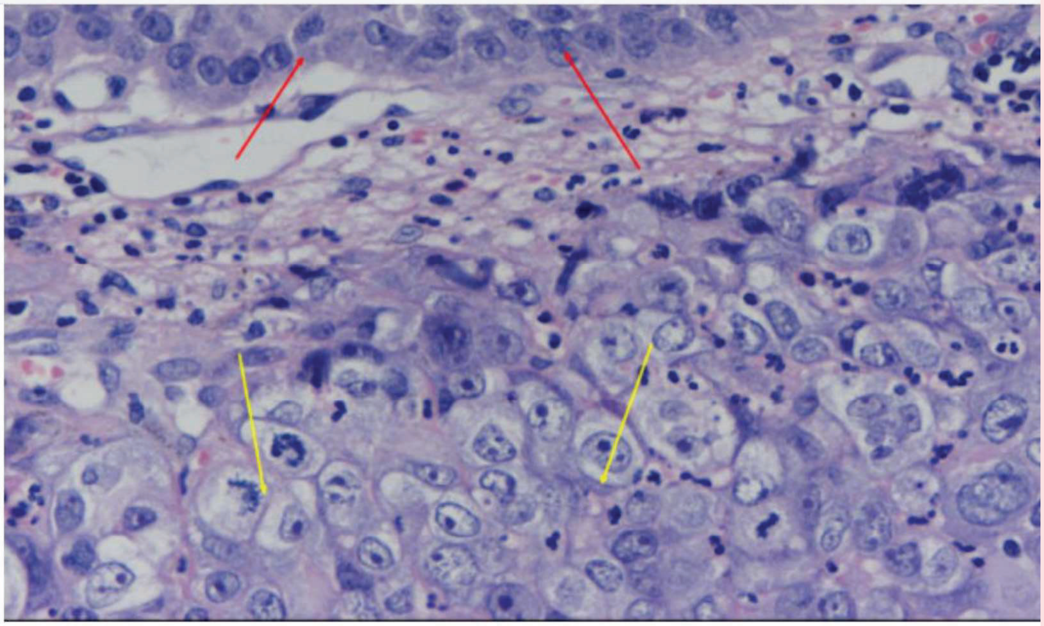
PREFIX	MEANING
adeno-	gland
chrondro-	cartilage
erythro-	red blood cell
hemangio-	blood vessels
hepato-	liver
lipo-	fat
lympho-	lymphocyte
melano-	pigment cell
myelo-	bone marrow
myo-	muscle
osteo-	bone

17



https://vitrovivo.com/product/human-lung-adenocarcinoma-ffpe-sections-2/

18



Histology: normal squamous epithelium (red arrows); carcinoma showing immature cells without keratosis which corresponds to a G3-grading (hematoxylin and eosin (HE) staining; magnification: 100×).

https://www.researchgate.net/figure/Histology-normal-squamous-epithelium-red-arrows-carcinoma-showing-immature-cells_fig3_5485242

19

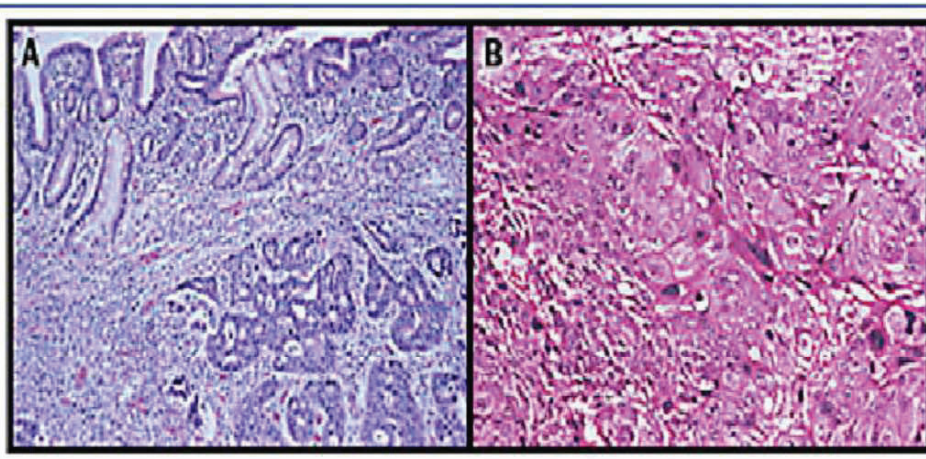


Figure 3. Histology; A, adenocarcinoma; B, squamous cell carcinoma

Figure 3. Histology; A, adenocarcinoma; B, squamous cell carcinoma

https://www.semanticscholar.org/paper/%5BEsophageal-cancer.-Introduction%5D.-Makuuchi/550dcea5f4f9a4cc3053e9aed39804822149761d/figure/1

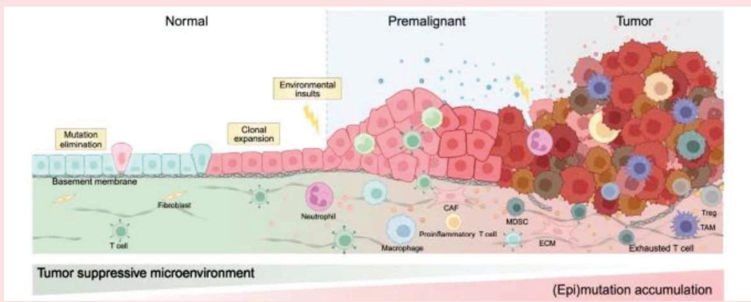
20

Carcinogenesis = Oncogenesis

- Multi-step process by which normal cells are transformed into cancer cells.
- Involves a series of complex <u>molecular and cellular events</u> that lead to an abnormal cellular division.
- It occurs in multiple states.

Terms and Definitions for pre-cancerous changes:

- **Atrophy –** degeneration of cells
- **Hypertrophy -** increase in size of cells
- **Hyperplasia -** increase in number of cells
- **Dysplasia -** disturbance in size, shape, organization of an abnormal cell
- **Metaplasia -** abnormal change in the nature of a tissue/replacement of mature cell type
- **Anaplasia** - loss of structural organization and function of cel = CANCER



21

Carcinogenesis = Oncogenesis

Stages:

1. **Initiation:** Genetic damage occurs in a normal cell, often due to exposure to carcinogens. The damage results in mutations in critical genes, mainly those regulating cell growth like oncogenes.
2. **Promotion:** Mutated cells are exposed to factors that promote their survival and proliferation such as hormones or chronic inflammation, creating an environment that encourages growth.
3. **Progression**: The genetically altered cells accumulate additional mutations, leading to more aggressive and invasive behavior. This stage involves changes that allow these cells to invade near by tissues.

Contributing Factors

- Genetic factors: inherited mutations in specific genes (BRCA 1/2)
- Environmental Exposures: Tobacco, UV radiation, asbestos.
- Lifestyle Factors: Diet, physical inactivity, alcohol consumption.

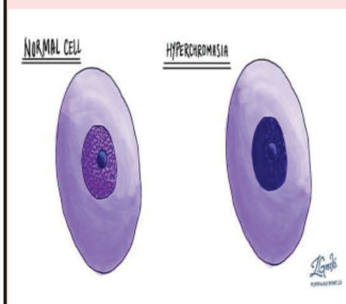
Mechanisms Involved

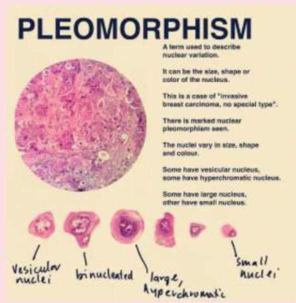
- **DNA damage and repair failures:** Mutations in DNA repair genes reduces the ability to fix errors, leading to genomic instability.
- **Cell cycle dysregulation:** Mutations in genes controlling the cell cycle (p53) resulting in unchecked cell division.
- **Evading apoptosis:** Cancer cells often acquire mechanisms to avoid programmed cell death.

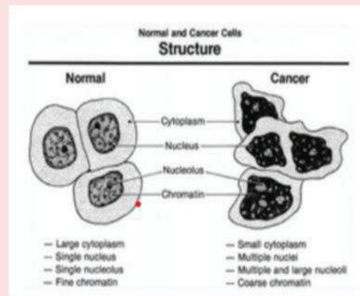
22

Cellular Alterations - Abnormal cell structure and proliferation

- Poorly identified intracellular structures and nuclei stain darker
  - Hyperchromatic -nuclear chromatin more pronounced staining
- Pleomorphism -cells vary in size and shape
- Polymorphism -nucleus enlarged and varies in shape

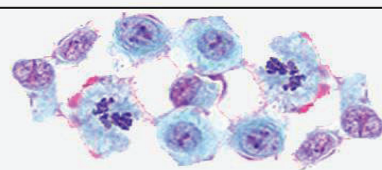
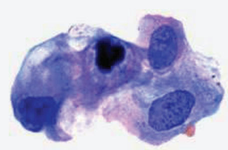
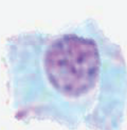
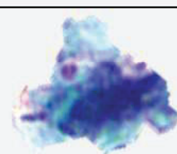




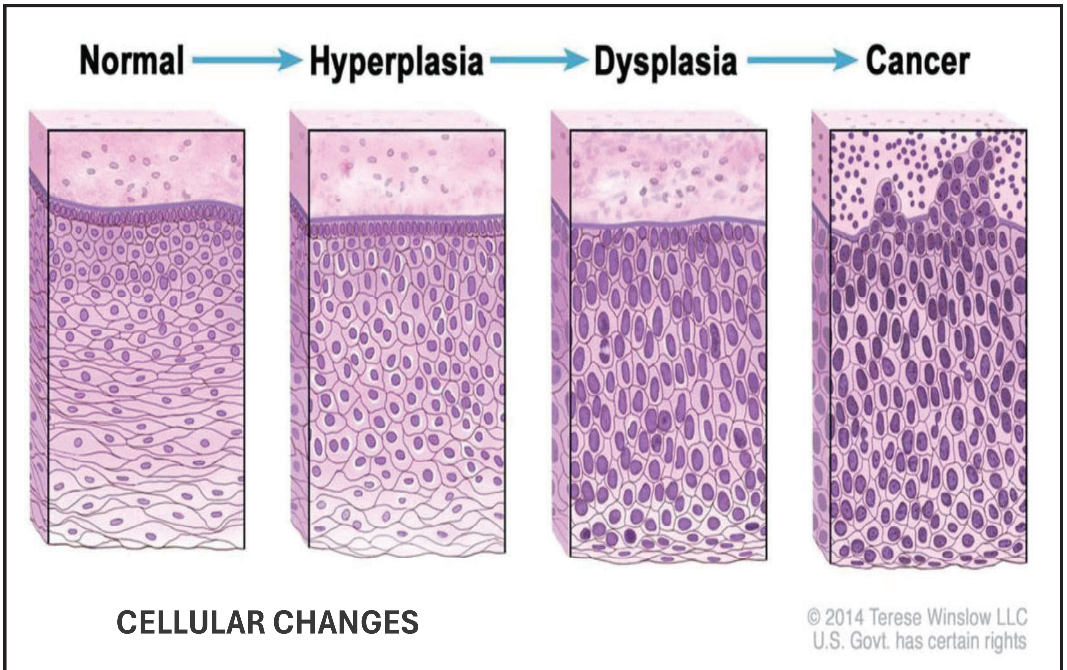


https://visuals.nci.nih.gov/details.cfm?imageid=2512
https://www.researchgate.net/figure/Normal-cell-cycle-and-uncontrolled-division-in-cells-leading-to-formation-of-tumors_fig2_269098315
https://www.google.com/search?q=pleomorphism&tbm=isch&ved=2ahUKEwjw0ZbS6rH1AhXFsHIEHTV-ChEQ2-cCegQIABAA&oq=pleomorphism&gs_lcp=CgNpbWcQAzIFCAAQgAQyBQgAEIAEMgUIABCABDIFCAAQgAQyBQgAEIAEMgUIABCABDIFCAAQgAQyBQgAEIAEMgUIABCABDIFCAAQgAQ6BAgAEEM6BggAEAcQHjoICAAQgAQQsQM6BwgAELEDEENQqgpYixxg8x5oAHAAeACAAVKIAeUGkgECMTOYAQCgAQGqAQtnd3Mtd2l6LWltZ8ABAQ&sclient=img&ei=srvhYfCwE8XhytMPtfypiAE&bih=577&biw=1263&hl=en#imgrc=QEE0bdbCcH7TkM&imgdii=AgzAI6TaGet-HM
https://www.google.com/search?q=Hyperchromatic+&tbm=isch&ved=2ahUKEwjG0o7G77H1AhWyrXIEHYSACTYQ2-cCegQIABAA&oq=Hyperchromatic+&gs_lcp=CgNpbWcQAzIFCAAQgAQyBQgAEIAEMgUIABCABDIFCAAQgAQyBQgAEIAEMgUIABCABDIFCAAQgAQyBQgAEIAEMgQIABAYMgQIABAYOgQIABBDUKEKWO5wYPp1aABwAHgAgAFAiAGAAZIBATKYAQCgAQGqAQtnd3Mtd2l6LWltZ8ABAQ&sclient=img&ei=18DhYYaLDLLbytMPhIGmsAM&bih=577&biw=1263&hl=en#imgrc=4-dxaVgTMML7XM

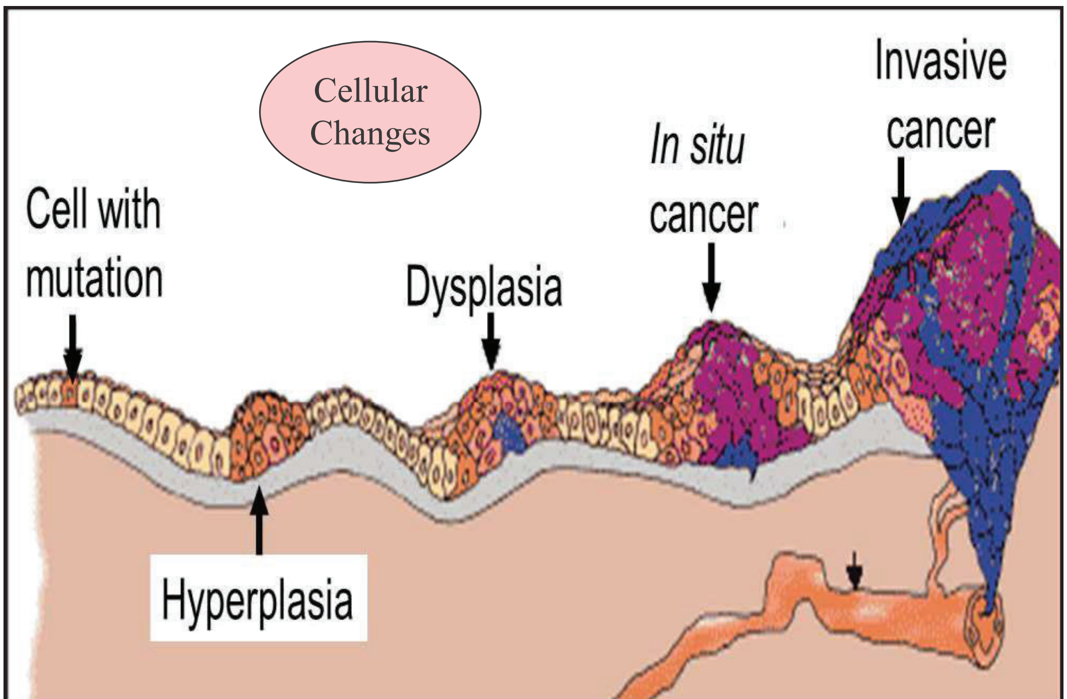
23

Normal	Cancer	
		Large, variably shaped nuclei
		Many dividing cells; Disorganized arrangement
		Variation in size and shape
		Loss of normal features

24

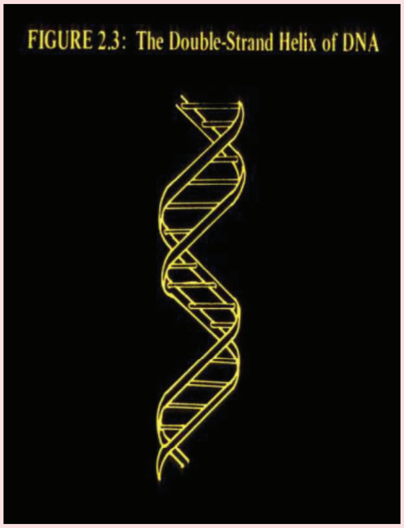


https://www.google.com/search?q=picture+carcinogenesis&espv=2&biw=1366&bih=658&site=webhp&source=lnms&tbm=isch&sa=X&ved=0ahUKEwiMpZmDnfTRAhUE4SYKHW-eC3UQ_AUIBigB&dpr=1#tbm=isch&q=picture+hyperplasia+cancer+cell&imgrc=kAceZ85XHLRdgM:

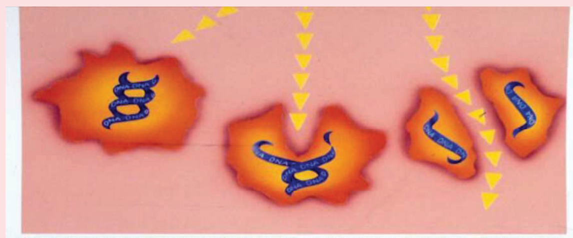


https://www.google.com/search?q=picture+carcinogenesis&espv=2&biw=1366&bih=658&site=webhp&source=lnms&tbm=isch&sa=X&ved=0ahUKEwiMpZmDnfTRAhUE4SYKHW-eC3UQ_AUIBigB&dpr=1#tbm=isch&q=picture+hyperplasia+cancer+cell&imgrc=IQ8gpmZPgizkyM:

All Cancer is “Genetic”



- Inherited or acquired mutations (5-15%)
  - Chromosomes = a book
  - Genes = individual chapter in the book
  - DNA = recipe



Chemotherapy agents destroy cancer cells by several different methods, including the destruction of cellular DNA.

Genetic Alterations

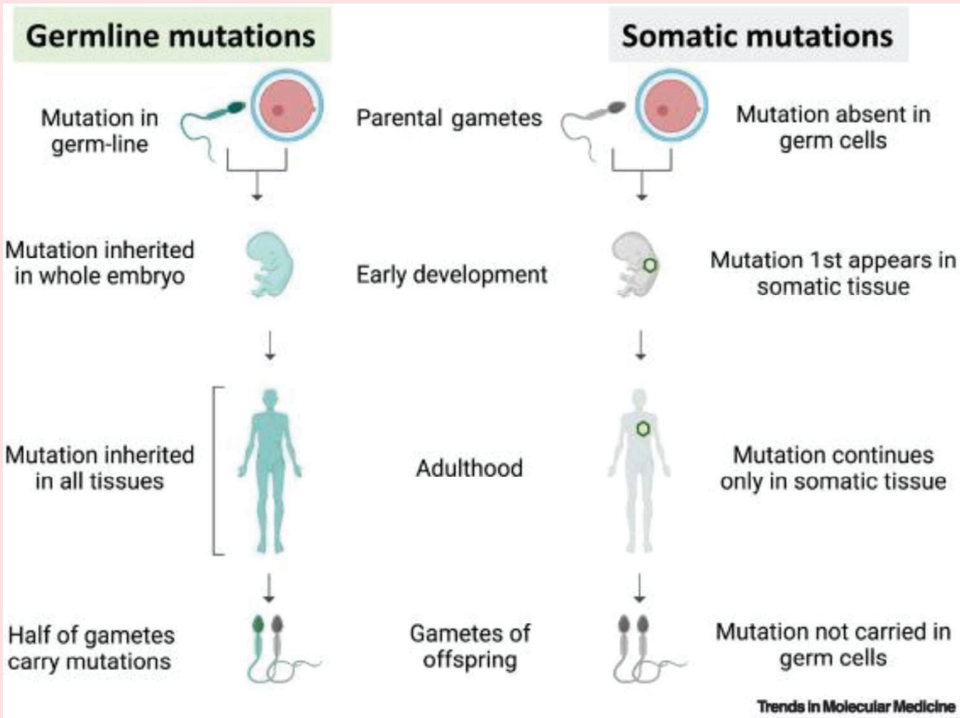
Germline inherited mutations

Germline mutations affect every cell in an organism and are passed on to offspring

- BRCA1 and BRCA2
- Lynch syndrome (MLH1, MSH2, MSH6, PMS2, or EPCAM)
- PALB2
- ATM
- CHEK2
- PTEN (Cowden syndrome)
- TP53 (Li-Fraumeni syndrome)
- STK11 (Peutz-Jeghers syndrome)
- CDH1 (Hereditary diffuse gastric cancer syndrome)
- BARD1
- BRIP1
- RAD51C
- RAD51D
- NBN
- NF1

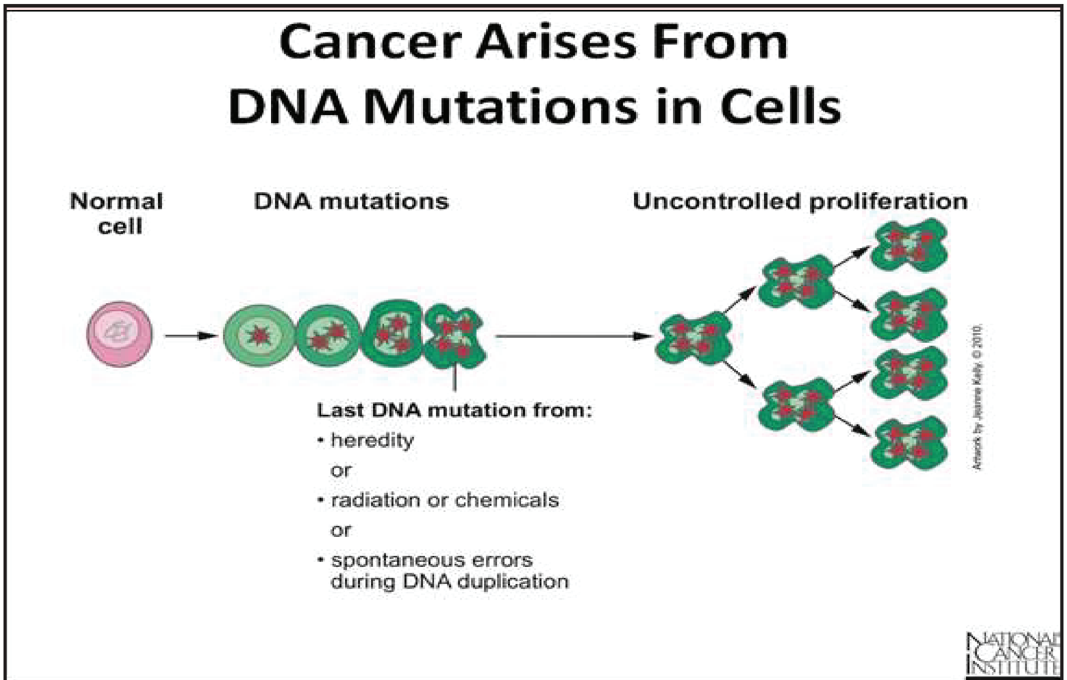
Somatic mutations

Genetic alterations that occur in the DNA of somatic cells, thus the **mutation** is not passed on to offspring. Instead the accumulate in the cells due to various internal or external factors.



Germline Hereditary Genetic Alterations

Type of cancer	List of gene mutations
Breast cancer	ATM, BARD1, BRCA1, BRCA2, CDH1, CHEK2, NBN, NF1 PALB2, PTEN, STK11, TP53
Ovarian/fallopian tube cancer	BRCA1, BRCA2, BRIP1, RAD51C, RAD51D, EPCAM, MLH1, MSH2, MSH6, PMS2, STK11
Pancreatic cancer	BRCA1, BRCA2, EPCAM, MLH1, MSH2, MSH6, PMS2, TP53, STK11 (ATM and PALB2 require further study)
Prostate cancer	BRCA1, BRCA2, CHEK2, (ATM and NBNrequire further study)
Melanoma	BRCA1, BRCA2, PTEN
Uterine cancer	EPCAM, MLH1, MSH2, MSH6, PMS2, PTEN, STK11
Colon cancer	CHEK2, EPCAM, MLH1, MSH2, MSH6, PMS2, PTEN, STK11, TP53
Gastric cancer	CDH1, STK11



https://www.google.com/search?q=gene+mutation+drivers&rlz=1C1GGRV_enUS751US751&source=lnms&tbm=isch&sa=X&ved=0ahUKEwiumPeI6vXVAhVIxoMKHa1fAPgQ_AUICigB&biw=1366&bih=634#imgrc=4H7FlUHMVCMxBM:

31

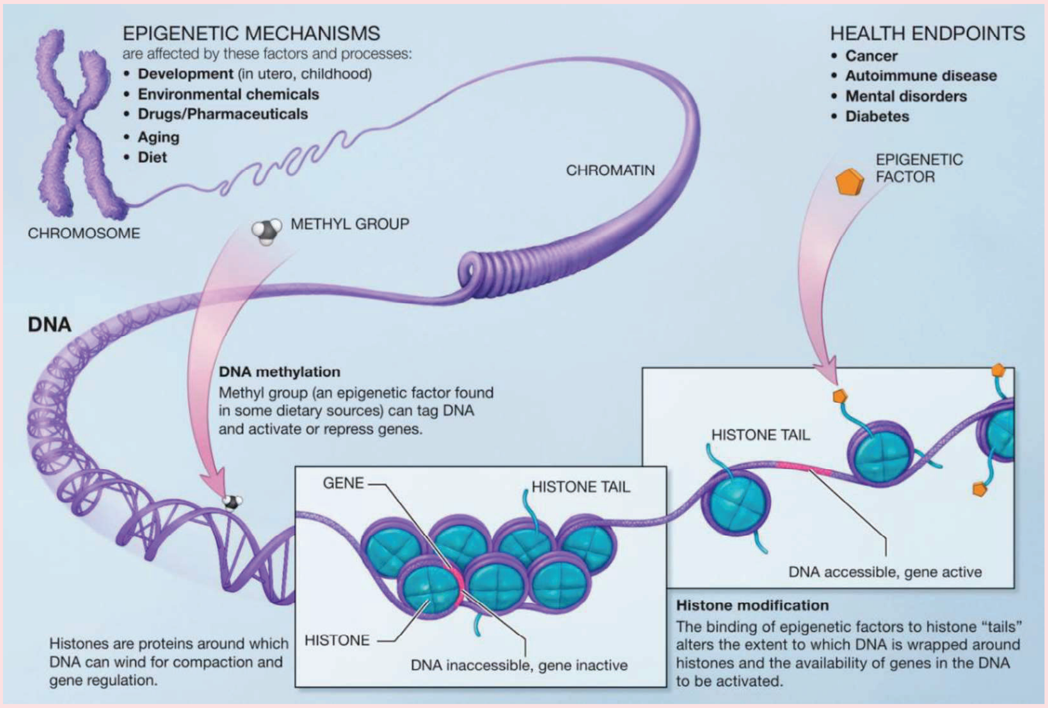
Epigenetic Alterations

- Changes in gene expression or cellular function that occur without altering the DNA sequence itself.
- These changes are mediated by chemical modifications to the DNA, RNA, or histone proteins that regulate gene activity.

Key types of epigenetic modifications:

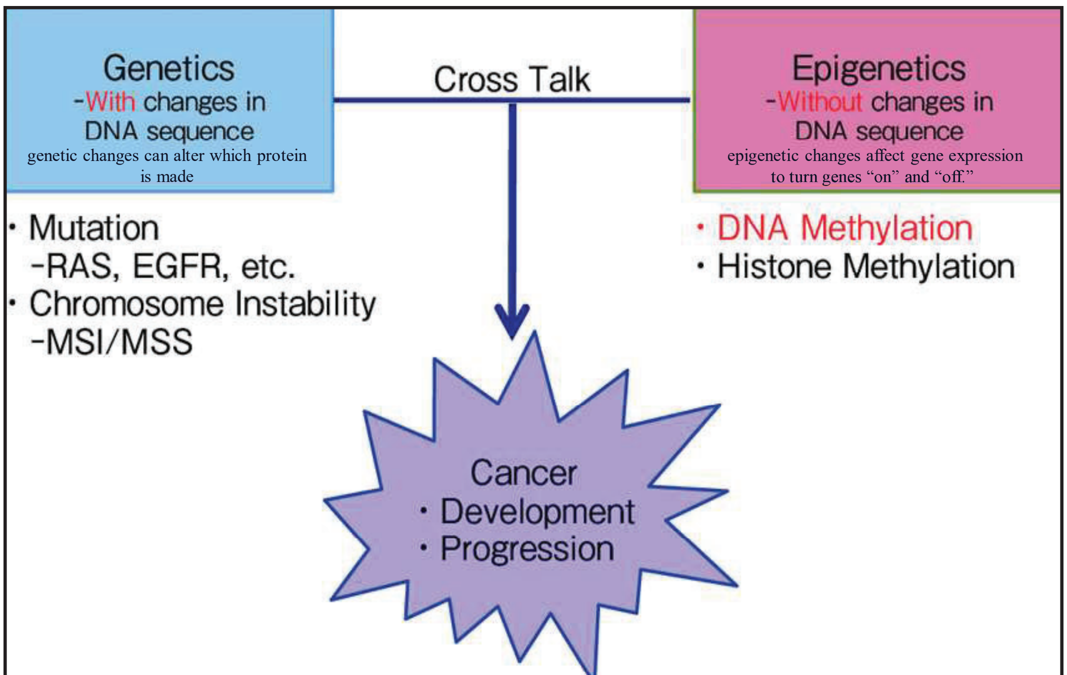
1. DNA Methylation: process that adds methyl groups to DNA, which can alter gene expression and influence cell differentiation. Hypomethylation can lead to genomic instability and activation of oncogenes.
2. Histone Modification: changes to histone proteins that affect transcription, chromosome packaging, and DNA damage repair > Histone acetylation, loosens chromatin, making genes more accessible for transcription. Histone methylation, activate or repress genes = aberrant gene expression.
3. Non-Coding DNA: Regulate gene expression by interacting with mRNA or Chromatin. Altered non-coding RNA (ncRNA) expression is linked to cancer expression and other diseases.
4. Chromatin remodeling: ATP (adenosine triphosphate) dependent complexes reorganize chromatin structure to regulate DNA. Alterations in chromatin remodelers can disrupt gene regulation and contribute to cancer.

32



https://en.wikipedia.org/wiki/Epigenetics#/media/File:Epigenetic_mechanisms.png

33

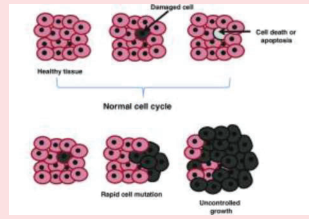


https://www.google.com/search?q=genetic+changes+in+cancer&source=lnms&tbm=isch&sa=X&ved=2ahUKEwjz4rGa4pLuAhWQ1VkKHfk1BbQQ_AUoAXoECA8QAw&biw=1280&bih=578#imgrc=ZC5OlD2AmWCPWM

34

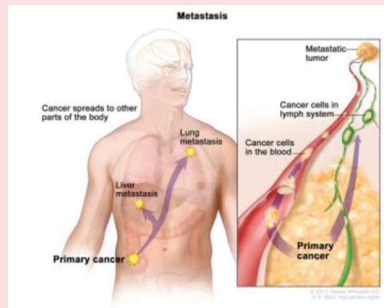
Uncontrolled growth (no apoptosis)

- Not density dependent with no contact inhibition



Ability to spread (metastasis)

- Adhesion between cancer cells is poor and easily dislodge
- Divide in suspension or when traveling
- ***Bone-liver-brain-lungs



https://visuals.nci.nih.gov/details.cfm?imageid=2512
https://www.researchgate.net/figure/Normal-cell-cycle-and-uncontrolled-division-in-cells-leading-to-formation-of-tumors_fig2_269098315
https://www.google.com/search?q=metastatci+disease&tbm=isch&ved=2ahUKEwjF77-t87H1AhW0snIEHWtJBfsQ2-cCegQIABAA&oq=metastatci+disease&gs_lcp=CgNpbWcQAzoECAAQQzoKCAAQsQMQgwEQQzoLCAAQgAQQsQMQgwE6BQgAEIAEOggIABCABBCxAzoICAAQsQMQgwE6BggAEAoQGFAAWLYbYMQcaABwAHgAgAFPiAGiCZIBAjE4mAEAoAEBqgELZ3dzLXdpei1pbWfAAQE&sclient=img&ei=1cThYYWxE7TlvtMP65KV2A8&bih=577&biw=1280&hl=en#imgrc=odJpDc12PbO5HM

Ability to invade normal tissue

- Cancer cells secrete cell-dissolving enzymes which allows them to invade the blood and lymphatic systems

Immortality

- Normal cells die after about 50 doublings cancer cells continue to reproduce

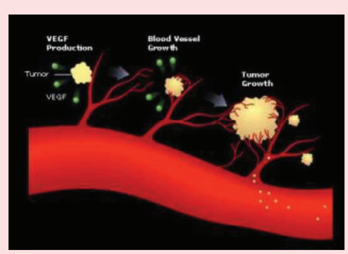
Accelerated use of nutrients

- Use body's nutrients more rapidly than normal cells

Angiogenesis

- Cancer cells secrete angiogenesis factors, which promote building of new capillaries then in turn supply tumor cells

https://medivizor.com/blog/2015/01/22/eat-to-beat-cancer-using-angiogenesis/



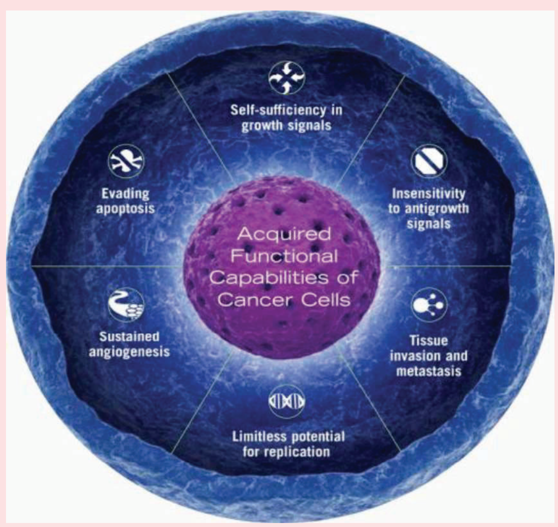
Cell Signaling Alterations:

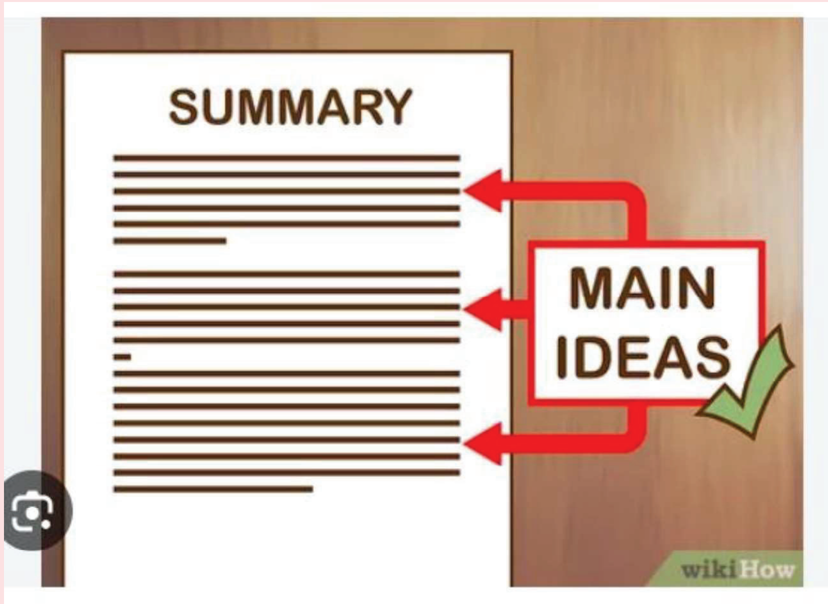
- Communication between cells is critical for survival
- Exchanges most often in form of extracellular signaling molecules or chemical signals produced and secreted by neighboring cells (paracrine) or cells in more remote tissues (endocrine)
- Relay vital information to govern specific changes
  - (growth, proliferation, metabolic)
- Initiation of these systems usually begins with binding of a signaling molecule (ligand) to specific cellular receptors
- In turn this activates other intracellular signaling molecules in a cascading chain resulting in a response

- In tumor cells several signaling pathways involved in proliferation survival, and migration become aberrant or overactive
- This is due to mutations or increased expression of certain proteins in the signaling systems
- Leads to rapid uncontrolled proliferation and enhanced survivability

Large group of diseases characterized by:

1. Sustained Proliferation
2. Evades Growth Suppressors
3. Resists Cellular Death
4. Enables Replicative Immortality
5. Induces Angiogenesis
6. Activates Invasion and Mets
7. Evades Immune Destruction
8. Reprograms Energy Metabolism





https://www.google.com/search?safe=active&sca_esv=12b499cd2f045e88&sca_upv=1&q=summarized&udm=2&fbs=AEQNm0AVbySjNxIXoj6bNaq7uSpw-2eW7KIQ8H4T_tEPJYsPzOi5GKsV0RKGmy84LfyUxrl-4_0AusV0IdjeUAdX2KBg7BmnGLOak5d-z-_u-BD5mANqasZxTMen5uZGRcW3Asxblx5Q1OYqkbmwkXLBzqCwgdzwtvZKVFrUj4v_fdTR68ZFGhx48b8eVoqoZU1-F3aJ5DD9pJyvzF_j7l0x84J8mAwSfQ&sa=X&ved=2ahUKEwiSx6uZkf-HAxWahIkEHU6_DlkQtKgLegQIExAB&biw=1280&bih=631&dpr=1.5#vhid=DBg1MbGUeE3x8M&vssid=mosaic

Carcinogenesis

Initiation

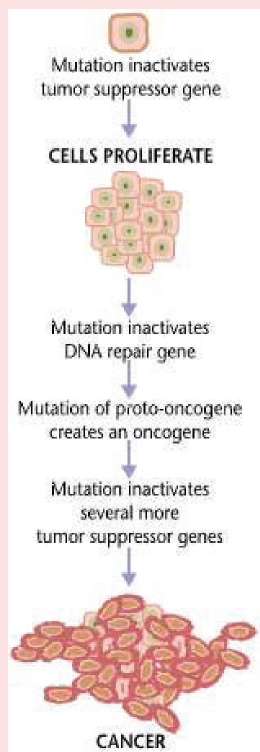
- Genetic mutation occurs in the DNA of a normal cell, often caused by exposure to carcinogens. The mutations are permanent.

Promotion

- Mutated cells are stimulated to divide and proliferate due to external or internal factors, such as hormones, chronic inflammation, or growth signals.
- This stage involves reversible changes, meaning intervention at this point can potentially prevent cancer from developing.

Progression

- Further epigenetic and genetic changes occur, resulting in more aggressive and malignant cell behavior.
- Tumor cells gain the ability to invade nearby tissues.



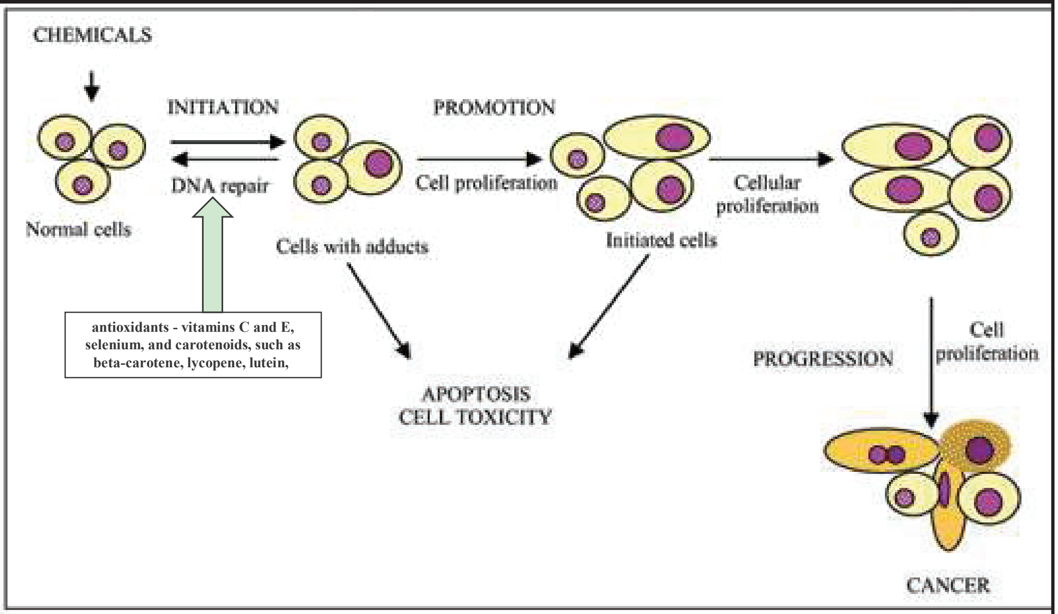
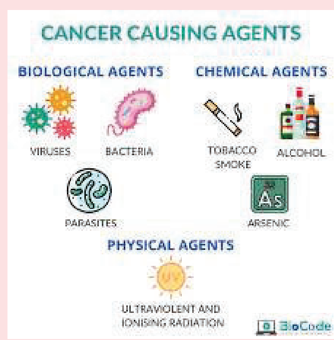


Fig. 2 – Chemical carcinogenesis stages and the occurrences involved in each one.

https://www.google.com/search?q=picture+carcinogenesis&espv=2&biw=1366&bih=658&site=webhp&source=lnms&tbm=isch&sa=X&ved=0ahUKEwiMpZmDnfTRAhUE4SYKHW-eC3UQ_AUIBigB#imgrc=4lN0ooFwseinaM:

Mechanisms of Carcinogenesis



1. **Genetic mutations:**
   - Oncogenes activation (proto-oncogenes)
   - Tumor suppressor gene activation
   - DNA repair gene defects
2. **Epigenetic alterations**
3. **Genomic instability:** Chromosomal abnormalities (deletions, amplifications).
4. **Inflammation and oxidative stress:** Chronic inflammation produces reactive oxygen species (ROS), which damages DNA and promotes tumor progression.
5. **Immune evasion:** Cancer cells develop mechanisms to avoid detection and destruction by the immune system, such as expressing immune checkpoint proteins (e.g. PD-L1).
6. **Viruses:** Infect DNA and RNA, which results in oncogene formation and interferes with cell cycle regulation and apoptosis (e.g. CMV, Epstein-Barr, HepB & C, HIV, H.Pylori, HPV).

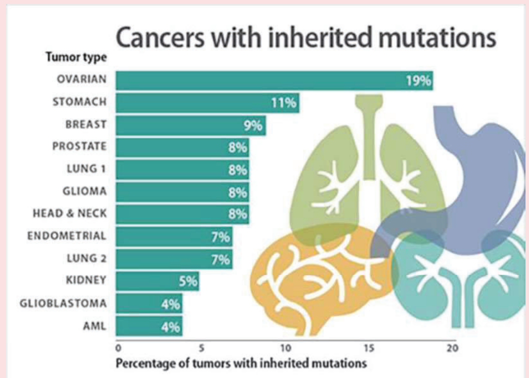
Additional Causation of Carcinogenesis

- Exposure to chemical carcinogens-chemical substances that alter DNA:

(e.g. tobacco smoke; arsenic; alcoholic beverages; nickel compounds; benzopyrene; coal and tar pitch; mustard gas; smoked, salted and pickled foods; vinyl chloride; benzene; antineoplastic agents)

- Genetics (germline), whereby inherited cancers occur via carcinogenic mutations in germ cells:

  Colon adenomatous polyposis (FAP), breast, renal cell, Wilms, BRCA 1 & 2, Lynch Syndrome.



43

Theories of Causation of Carcinogenesis

Proto-oncogene (normal gene)

- Genetic portion of DNA that regulates normal cell growth and repair
  - Some **proto-oncogenes** provide signals that lead to cell division
  - Other **proto-oncogenes** regulate programmed cell death (apoptosis)
  - Encode for protein products that stimulate cell growth and division
  - When altered, they become oncogenes and drive cancer growth

- Genes that code for proteins responsible for proliferation
- When altered by mutation, it becomes oncogene and permits cells to proliferate beyond body needs - it increases protein expression, hyperactivity (i.e., gain-of-function), and/or loss of regulation.

<u>Results</u>

- Protein begins to be formed in cells in which they normally do not form
- Protein is made in appropriate cells but in excessive amounts
- Protein is formed in a form that normal mechanisms can not regulate

44

Theories of Causation of Carcinogenesis

Proto-oncogene (normal gene)

Examples

- *ERBB2 (HER2)*: breast cancer amplification
- *KRAS*: tumors of the esophagus, colon, pancreas, point mutation
- *Beta-Catenin:* pancreatic cancer
- *Cyclin E:* liver tumors
- *BRAF*: melanomas
- *BCR-ABL*: chronic myeloid leukemia

Target	Disease	Agent	Regimen
HER-2	Breast[a]	Trastuzumab	Combination
BCR/ABL	Chronic myeloid leukemia[a]	Imatinib	Monotherapy
C-KIT	Gastrointestinal stromal tumor[a]	Imatinib	Monotherapy
EGFR	NSCLC[a]	Gefitinib, erlotinib	Monotherapy
EGFR	Head and neck, colorectum[a]	Cetuximab	Combination
EGFR	Pancreas[a]	Erlotinib	Combination
VEGF	Breast, colorectum[a], kidney	Bevacizumab	Combination
VEGFR, B-Raf	Kidney[a]	Sorafenib	Monotherapy

Theories of Causation of Carcinogenesis

Tumor Suppressor Genes (normal gene)

- Tumor suppressor genes are normal genes that slow down cell division, repair DNA mistakes, or tell cells when to die (apoptosis/programmed cell death)
  - Mutation permits cells to proliferate beyond body needs, inhibits apoptosis, disrupts DN repair, induces immortality, replicates mutated genes = cancer
  - P53 = most commonly mutated tumor suppressor gene (TSG)
    - INK4 and PTEN (lung, prostate, melanoma)
    - APC and MADR2 (colon)

https://www.youtube.com/watch?v=l4Ul9LaYg_w

Theories of Causation of Carcinogenesis

Oncogenes (abnormal)

- Abnormal mutated genes responsible for transformation of normal cell to a cancerous cell
- May arise from mutations in proto-oncogenes, tumor suppressor genes, or other genes
- Alters signal transduction from cell membrane to nucleus
- Driver variants activated during carcinogenesis - send massages to grow and divide

Examples

- Abl gene in chronic myeloid leukemia (the Philadelphia chromosome)
- Src family
- Syk-ZAP-70 family
- BTK family of tyrosine kinases
- Cytoplasmic serine/threonine kinases –Raf kinase and cyclin-dependent kinases
- See attached Table http://www.ganfyd.org/index.php?title=Oncogenes/table

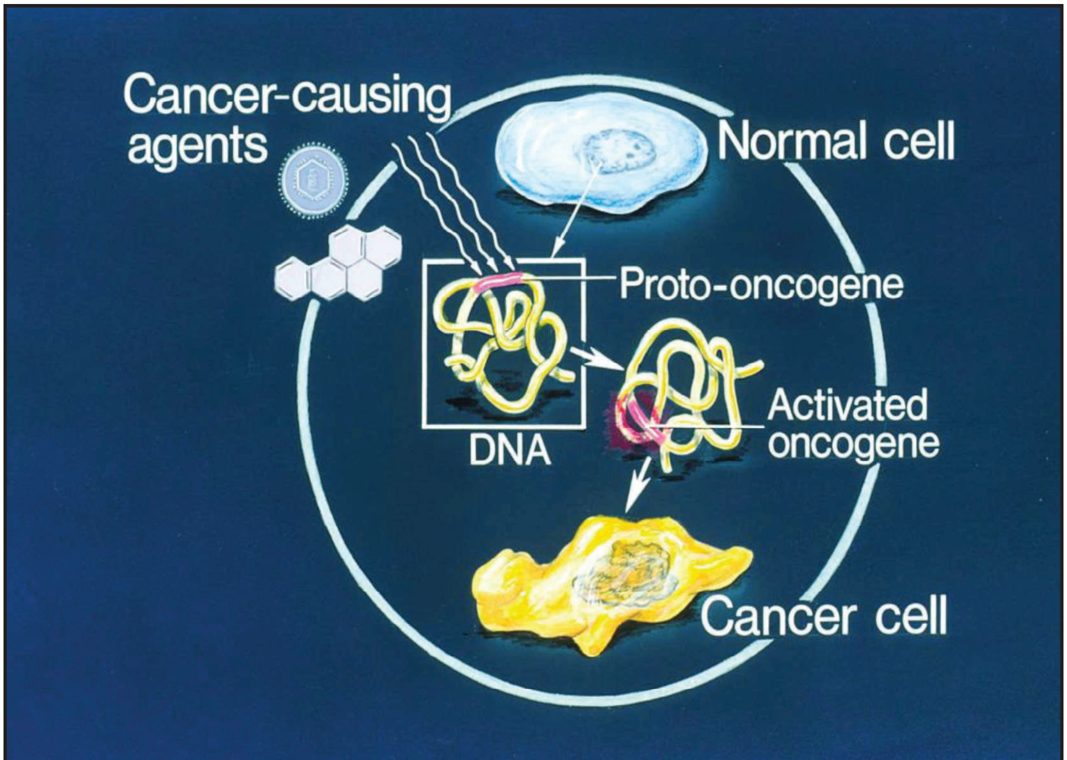
https://www.youtube.com/watch?v=2wIVwZksIt4

An important difference between oncogenes and tumor suppressor genes:

oncogenes result from the activation (turning on) of proto-oncogenes,

but

Tumor suppressor genes cause cancer when they are inactivated (turned off). Most tumor suppressor gene mutations are acquired, not inherited.



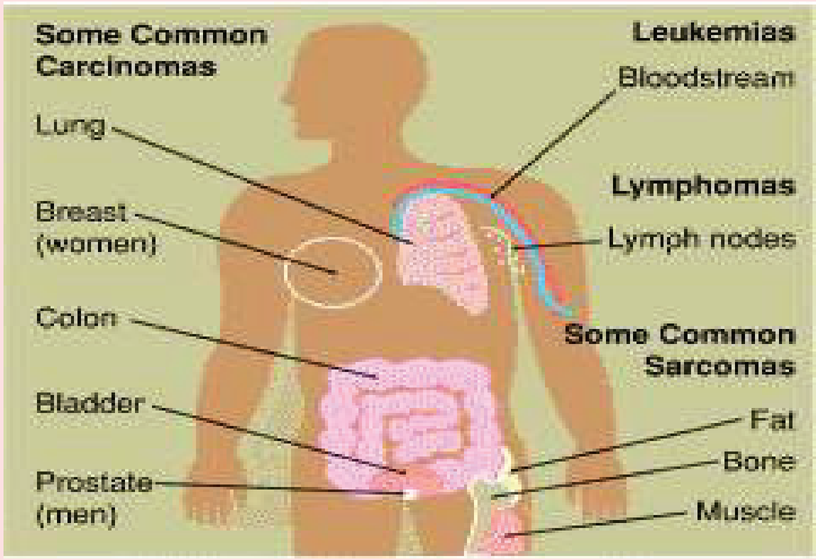
https://upload.wikimedia.org/wikipedia/commons/d/de/Oncogenes_illustration.jpg

49

Cancer cells follow no rules and have the ability to stimulate the growth of a new blood supply

50

Cancer



51

Malignancies

Solid Tumors

- Brain
- Spinal Cord
- Head and Neck
- Bone and Soft Tissues
- Lung
- Esophageal
- Gastric
- Pancreatic
- Gall Bladder
- Hepatocellular
- Colon
- Kidney
- Bladder
- Prostate
- Cervical
- Endometrial
- Ovarian
- Testicular
- Breast
- Skin

Hematological

- Acute Myelogenous Leukemia (AML)
- Acute Lymphocytic Leukemia (ALL)
- Chronic Myelogenous Leukemia (CML)
- Chronic Lymphocytic Leukemia (CLL)
- Myelodysplastic Syndrome (MDS)
- Non-Hodgkin Lymphoma (NHL)
- Hodgkin Lymphoma (HL)
- Multiple Myeloma
- Aplastic Anemia

52

STAGING –
American Joint Committee on Cancer (AJCC)

- Done to:
  - determine extent of disease
  - plan of treatment
  - estimate prognosis
  - data collection
- Data collected by tumor registry

- Stage by:
  - Diagnostic testing
  - Biopsies (need tissue)
  - Blood test
  - Radiographs
  - CT Scans
  - PET scans
    - Evaluate isotope uptake and decay
    - How body uses radioactive decay to pick up energy
    - Tumor cells use glucose inefficiently
  - MRI
  - Nuclear medicine
  - Tumor/biomarkers markers
  - Bone marrows
  - Flow cytometry
  - Molecular testing
  - Cytogenetics

TNM Staging

T= Tumor T0-T4

-size and depth

N = Node No-N3

-size, number, location

M = Metastasis

FIGO Staging

International Federation of Gynecology and Obstetrics

- Ovarian
- Endometrial/uterine
- Cervical
- Staging I-IV

Heme Staging

- Ann Arbor- Hodgkin Lymphoma
- RAI – CLL
- ISS – Multiple Myeloma

Brain Tumors

Grade I - slow growing and unlikely to spread - often be cured with surgery

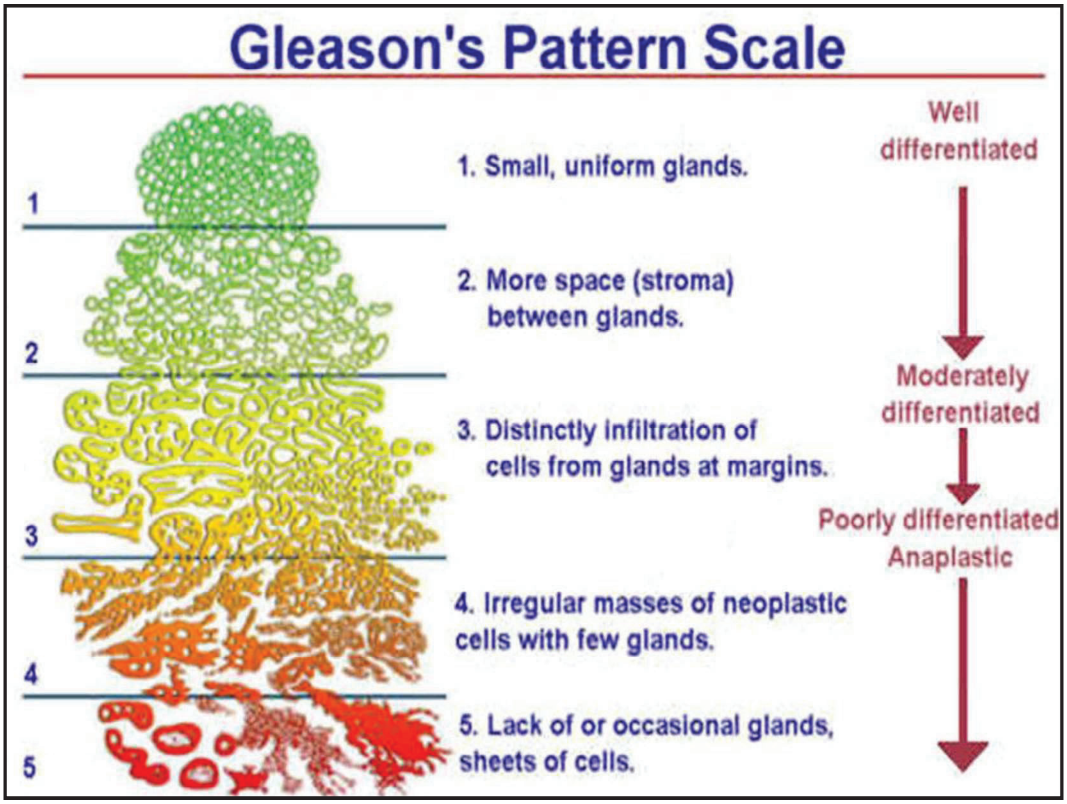
Grade II - less likely to grow and spread but are more likely to come back after treatment

Grade III - more likely to have rapidly dividing cells but no dead cells and grow quickly

Grade IV - cells in the tumor are actively dividing, the tumor has both abnormal blood vessel growth and areas of dead tissue - grow and spread quickly

Small – Cell Lung Cancer

- Limited
- Extensive



55

Differentiation = Maturation

&

Proliferation = Division

56

Grading and Differentiation (need tissue diagnosis)

Grade 1 = Well-Differentiated

(confined to organ of origin = 70-90% survival)

Grade 2 = Moderately differentiated

(local spread with close nodal involvement = 45-55% survival)

Grade 3 = Poorly-differentiated

(tumor fixed with extensive nodal involvement = 25% survival)

Grade 4 = Undifferentiated

(mets to other organs/tissues - <5% survival)

57

Molecular Markers

- Provide information about cancer (proteins, genes, DNA mutations)
- Proteins that are made by both healthy cells and cancer cells in the body
  - Proteins produced by the body in response to cancer growth or by cancer tissue itself
- A substance found in your blood, urine, or body tissue
- A biological molecule secreted by a tumor found in blood, other body fluids, or tissues that is a sign of a normal or abnormal process, or of a condition or disease
- Released by cancer cells or other cells in the body in response to cancer
- Refer to mutations, changes, or patterns in a tumor's **DNA**
- Represent abnormalities in genetic or epigenetic pathways controlling cellular proliferation, differentiation, or cell death
- Gain or loss of function alterations in key signaling pathways
- Unique to the cancer type
- Used for diagnosis, prognosis, and predicting response to a treatment
  - chromosomal translocation and rearrangements
  - gene amplification
  - point mutations
  - epigenetic alterations
  - single nucleoside polymorphisms

58

Tumor = Bio = Molecular Markers

Diagnostic:
- Screening markers
- Aid in identifying cancer in an individual
- May have false positives

Prognostic:
- Estimate risk of death or cancer recurrence following surgical removal of cancer without adjuvant therapy

Predictive:
- Forecast how patients will respond to a given therapy

Monitoring:
- Help to detect the recurrence or remission of cancer after treatment has been completed

Examples of Markers

Carcinoembryonic antigen (CEA)= colon and breast
Alphafetoprotein (AFP) = liver and testicular
Prostate-specific antigen (PSA) = prostate
Human chorionic gonatropin = germ cell tumors
CA-125 = ovarian
CA-19-9 = gastric, colorectal, pancreatic
CA-15-3 or 27-29 = breast
HER-2 = breast
CA-72-4 = gastric
Proto-oncogenes, tumor suppressor genes, oncogenes

Genomic Fusions

Merging of genetic material from two distinct genes, either within the same organism or different ones. They can provide insights into gene evolution and disease mechanisms like in cancer.

Implications:

1. **Cancer biology:** Fusion genes like BCR-ABL, ETV6-RUNX1, and TMPRSS2-EGR are critical drivers of various cancers.
2. **Evolutionary insight:** Helping understand the development of new gene functions.
3. **Biotechnology and therapeutics:** Fusion proteins like monoclonal antibodies are engineered for drug development.
4. **Diagnostics:** Detection of specific fusion genes aids in the diagnostics of cancer.

Molecular and Cytogenetic Testing

Molecular

- Studies specific genes and DNA sequences in sample of tissue, blood, or other body fluid
- Helps identify genes, proteins, or other molecules that may be sign disease
- Provides insight into small structural genomic variations that cause disease

Cytogenetic

- Analysis of number and structure of chromosomes
- Looks for abnormalities like aneuploidy and structural abnormalities

Types of Molecular Testing

- **Polymerase Chain Reaction (PCR)**
  - Analyzes DNA and RNA unique genetic codes and sequencing for 'red flags'
  - Technique used in molecular biology to **amplify** a single copy or a few copies of a selected segment of DNA genome across several orders of magnitude, generating thousands to millions of copies of a particular DNA sequence
  - 60% sensitivity – likelihood the test correctly identifies the disease as positive
  - 98% specificity – likelihood the test correctly identifies the disease as negative
    - Inversely related
      - A test with 95% sensitivity will correctly identify 95% of people with disease but incorrectly identifies 5% as negative
      - A test with 95% specificity will correctly identify 95% of people without the disease but incorrectly identifies 5% as positive

Advantages	Disadvantages
• More reliable and accurate • Amplification from a single copy of material • More sensitive and gold standard for detecting for measurable residual disease (MRD)	• Lengthy turnaround time (3-7 days) • Higher false positive rate • Only detects what's ordered for the test

https://www.google.com/search?q=PCR+you+tube+made+simple&safe=active&sca_esv=602485622&sxsrf=ACQVn09o7WIVgWZdGgHauH4NXzu49QP7mw%3A1706569440597&ei=4C64ZYT0I6us5NoPi9udiAM&ved=0ahUKEwiE5KnK2oOEAxUrFlkFHYttBzEQ4dUDCBA&uact=5&oq=PCR+you+tube+made+simple&gs_lp=Egxnd3Mtd2l6LXNlcnAaAhgDIhhQQ1IgeW91IHR1YmUgbWFkZSBzaW1wbGUyChAhGAoYoAEYiwMyChAhGAoYoAEYiwMyCBAhGKsCGIsDMggQIRirAhiLA0i8M1C5BVjyMXAGeACQAQCYAccBoAHZF6oBBDAuMjC4AQPIAQD4AQHCAg4QABiABBiKBRiGAxiwA8ICBBAjGCfCAgsQABiABBiKBRiRAsICCBAAGBYYHhgKwgIKEAAYFhgeGA8YCsICCxAAGIAEGIoFGIYDwgIGEAAYFhgewgIIEAAYCBgeGA3CAggQABiABBiiBMICBRAhGKsCwgIHECEYChigAeIDBBgBIEGIBgGQBgE&sclient=gws-wiz-serp#fpstate=ive&vld=cid:277d963e,vid:3XPAp6dgl14,st:0

63

Types of Molecular Testing

- **Fluorescence In Situ Hybridization (FISH)**
  - Molecular cytogenetic technique that uses fluorescent probes that bind to only those parts of the chromosome with a high degree of sequence complementarity (specific nucleotide sequences)
  - Fluorescent probes identify specific DNA or RNA sequences or chromosomes in cells and tissues
  - Maps genetic materials in cells specific to portion of genes

Advantages	Disadvantages
• Detects gene fusions • Highly sensitive and specific • Detects genomic abnormalities in non-viable and non-dividing tissues	• Less sensitive detecting for measurable residual disease (MRD) • Targeted test with only limited number of probes used at once • Only specific locus or gene tested • Cannot see which gene is fused

https://www.youtube.com/watch?v=KXn533DTrsM

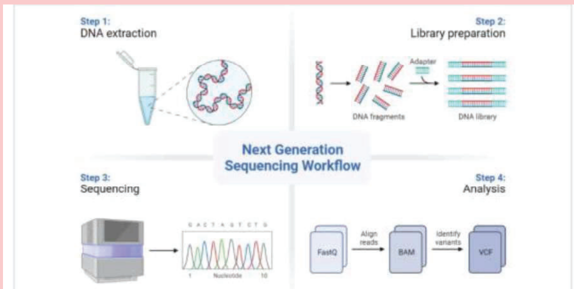
https://www.google.com/search?q=youe+tube+FISH+cytogenetics#fpstate=ive&vld=cid:96a1cb57,vid:qcSxdTKpMzg,st:0

64

Types of Molecular Testing

- **Next generation sequencing**
  - High-throughput sequencing results in 1 day
  - Can sequence hundreds and thousands of genes or whole genome in 1 assay
  - Technology that determines the order of nucleotides in DNA or RNA by sequencing millions of small fragments simultaneously

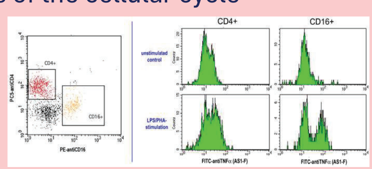
Advantages	Disadvantages
• Sequences more fragments at once • Can detect rare variants and transcripts • More sensitive and specific detection MRD	• More complex • Cost • Data storage



https://microbenotes.com/next-generation-sequencing-ngs/

Types of Molecular Testing

- **Flow Cytometry**
  - Laser-based cell surface antigens
  - Analyzes characteristics of cells or particles
  - Detects, identifies, and counts specific cells
  - Measures DNA in cells
  - Identifies portions of the cell in different parts of the cellular cycle
  - Clusters of Differentiation (CDs)



Advantages	Disadvantages
• High throughput analyzing millions of cells at once • Simultaneously measures multiple markers • Qualitative and quantitative analysis • Superior to immunohistochemistry (IHC) for detecting antigens in low amounts	• Cost and time • May cause cell damage due to high pressures

https://www.youtube.com/watch?v=B2zreF2dnWk

Types of Molecular Testing

- **Immunohistochemistry (IHC)**
  - Sees overexpression of cellular proteins and gene fusions (ie. PD-L) but can only see 1 cell at a time
  - Uses antibodies to detect antigens in a tissue sample
  - Diagnostic technique that involves analyzing a patients biopsy tissue sample
  - Pathology uses modified antibodies to stain specific proteins in the tissues to identify certain types and subtypes of a disease
  - Also used to identify protein markers (identifies surface markers)

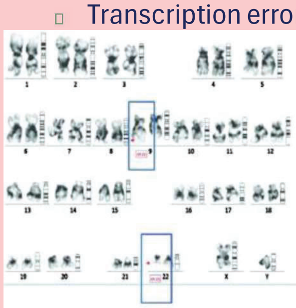
Advantages	Disadvantages
• Cornerstone for diagnostic pathology • Can use fresh or frozen tissue samples • inexpensive	• IHC stains not standardized worldwide • Lacks high resolution imaging • Difficult to quantify results

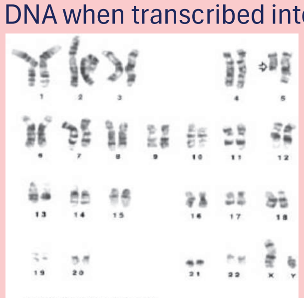
https://www.youtube.com/watch?v=B2zreF2dnWk

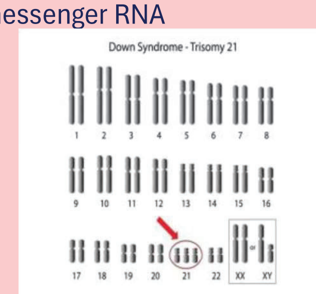
Types of Molecular Testing

A series of cellular and/or genetic alterations or translocations, chromosomal abnormalities

- Translocations (ie: **t**9;22 – **t**15;17)
- Deletions (ie: **q**5 with MDS)
- Inversions (ie: **i**16 with leukemia)
- Amplifications (more copies of DNA sequence)
- Aneuploidy (abnormal number chromosomes)
- Transcription errors of DNA when transcribed into messenger RNA







https://www.google.com/search?q=chromosomal+translocation+9.+22&tbm=isch&ved=2ahUKEwiS7ZjQ8bH1AhVQrHIEHTiKAO8Q2-cCegQIABAA&oq=chromosomal+translocation+9.+22&gs_lcp=CgNpbWcQAzoECAAQQzoFCAAQgAQ6BAgAEB46BggAEAUQHlAAWJ8SYMITaABwAHgAgAFAiAGZA5IBATeYAQCgAQGqAQtnd3Mtd2l6LWltZ8ABAQ&sclient=img&ei=BcPhYdLWDNDYytMPuJSC-A4&bih=577&biw=1280&hl=en#imgrc=LXpL4uZoI92iLM
https://www.google.com/search?q=chromosomal+deletion+5+mds&tbm=isch&ved=2ahUKEwiGgL6L8rH1AhWunnIEHU89CRIQ2-cCegQIABAA&oq=chromosomal+deletion+5+mds&gs_lcp=CgNpbWcQA1CZBVjBCmCGDWgAcAB4AIABfIgB5gKSAQM0LjGYAQCgAQGqAQtnd3Mtd2l6LWltZ8ABAQ&sclient=img&ei=gcPhYca7Ia69ytMPz_qkkAE&bih=577&biw=1280&hl=en#imgrc=_XAdsZUw8yCH0M
https://www.google.com/search?q=Aneuploidy+&tbm=isch&ved=2ahUKEwiHiaSF87H1AhXqhXIEHZJ3BaEQ2-cCegQIABAA&oq=Aneuploidy+&gs_lcp=CgNpbWcQAzIFCAAQgAQyBQgAEIAEMgUIABCABDIFCAAQgAQyBQgAEIAEMgUIABCABDIFCAAQgAQyBQgAEIAEMgUIABCABDIFCAAQgARQAFgAYIcGaABwAHgAgAE-iAE-kgEBMZgBAKABAaoBC2d3cy13aXotaW1nwAEB&sclient=img&ei=gMThYYfJO-qLytMPku-ViAo&bih=577&biw=1280&hl=en#imgrc=6-jhUTQCYNxfZM

https://www.google.com/search?q=what+have+you+learned&safe=active&sca_esv=77e9856747e8aa3f&sca_upv=1&udm=2&biw=1280&bih=631&ei=Jz7CZruaHeawptQP7MPj-Qs&ved=0ahUKEwj7yZfH1v-HAxVmmIkEHezhOL8Q4dUDCBA&uact=5&oq=what+have+you+learned&gs_lp=Egxnd3Mtd2l6LXNlcnAiFXdoYXQgaGF2ZSB5b3UgbGVhcm5lZDIFEAAYgAQyBRAAGIAEMgUQABiABDIFEAAYgAQyBRAAGIAEMgUQABiABDIFEAAYgAQyBRAAGIAEMgUQABiABDIFEAAYgARIohJQAFiNEXAAeACQAQCYAZsBoAGxEKoBBDEzLji4AQPIAQD4AQGYAhWgApMRwgIIEAAYgAQYsQPCAgoQABiABBhDGIoFwgIQEAAYgAQYsQMYQxiDARiKBcICDhAAGIAEGLEDGIMBGIoFwgIEEAAYA5gDAJIHBDcuMTSgB9B4&sclient=gws-wiz-serp#vhid=vm7yCBb-yoiREM&vssid=mosaic

69

Precision Medicine/Genomics/Pharmacogenomics

- Cellular Testing
  - pathology
- Tumor Markers/Biomarkers
  - molecule secreted by a tumor
- Cell Signaling
  - leads to changes in gene expression
- Molecular Testing
  - looks for biomarkers
- Genomics
  - mapping of genomes
- Pharmacogenomics
  - drug-gene testing

- Genomics = DNA sequencing
- Pharmacogenomics = the study of how genes affect individual responses to specific pharmacologic treatments
  - How genes metabolize different drugs

70

Precision Medicine/Genomics/Pharmacogenomics

Targeted

Cellular Molecular Therapy (extra- and intra-cellular)

- Tyrosine kinase inhibitors (TKIs)
- Multi-kinase inhibitors (MKIs)
- Proteasome inhibitors
- Protein kinase inhibitors
- PARP inhibitors
- mTOR inhibitors
- Hedgehog
- Epidermal growth factor receptor (EGFR)
- Vascular endothelial growth factor (VEGF)/Antiangiogenesis

Immunotherapy

- Cytokines
- Immumodulators
- Monoclonal Antibodies (MABs)
- Bispecific Antibodies
- Radio-Immunotherapy
- Immunotherapy
  - Checkpoint inhibitors
    - CTLA-4
    - PD-1 and PD-L1
- Chimeric Antigen Receptor-T (CAR-T)
- Oncolytic Viral Therapies

71

Precision Medicine/Genomics/Pharmacogenomics
Targeted Therapy Cellular Pathways

- Molecularly targeted anticancer therapy agents with selectively targeted molecular pathways
- Direct cellular functions including cell signaling, growth, and division
- When introduced into pathways, the enhanced activity is inhibited – leading to decreased cell proliferation

- Anaplastic lymphoma kinase (ALK) – (3-5% NSCLCA)
- *BCR-ABL - (CML)*
- *BCRA 1/2 - (breast)*
- BRAF V600E inhibitors - (met melanoma)
- BCL- 2 inhibitors – (leukemia and lymphoma)
- B-cell receptor pathway inhibitors (BTK) and P13K – (B-cell malignancies)
- CDK inhibitors (cyclin dependent) – (different cancers)
- Epidermal Growth Factor Receptors (EGFR) – (breast)
- Fibroblast Growth Factor Receptors (FGFR) – (bladder, colon, GI)
- Fm-like tyrosine kinase 3 (FLT3) inhibitors – (leukemia)
- Hedgehog pathway inhibitors – (different types of cancers)
- IDH1 and IDH 2 – (leukemia)
- Janus kinase-2 (JAK2) inhibitors – (polycythemia vera, myelofibrosis, essential thrombocytosis)
- KIT – (GI, leukemia)
- KRAS - (colon, GI, lung)
- Mammalian target of rapamycin (mTOR) – (renal)
- Mediators of apoptosis Bcl-2 (many cancers)
- MEK/MAPK inhibitors (met melanoma)
- Poly (ADP-ribose)polymerase (PARP) inhibitors – (ovarian)
- Proteasome inhibitors – (myeloma)
- ROS1 inhibitors – (Lung)
- Vascular endothelial growth factor (VEGF) – (colon/rectal)

72

TREATMENT MODALITIES

PRINCIPLES OF CANCER TREATMENT

CURE

CONTROL

PALLIATION

GOALS
CURE-CONTROL-PALLIATIVE

Adjuvant Therapy

- Prophylactic treatment
- Chemotherapy after surgery....surgery is primary treatment
- There are no margins or known mets, but treat in case microscopic areas are not seen

Neo-Adjuvant Therapy

- Administer chemotherapy prior to surgery (shrink tumor bulk and load)

MEASURE TUMOR RESPONSE

Complete Response

(complete disappearance for at least one month)

Partial Response

(reduction in measurable tumor mass >50% for one month without new tumor growth)

Stable Disease

(unchanged without tumor growth or reduction)

Progressive Disease

(advancing disease in presence of therapy)

Factors Affecting Response

1. **Tumor burden**
   - inverse relationship between # tumor cells and chemotherapy response
   - LDH factor (140 units per liter (U/L) to 280 U/L)
   - What is the biological function of LDH in cancer?
     - It has been shown that that Lactate dehydrogenase-A (LDH-A) is one of the main isoforms of LDH expressed in breast tissue, prostate, colon cancer and it is a marker of altered intracellular anaerobic metabolism, which allows cancer cells to proliferate in hypoxic microenvironment
2. **Hormone receptor status**
3. **Drug resistance (intrinsic or acquired)**
4. **Rate of tumor growth**
   - Smaller tumors have higher growth fraction
   - Tumor grows larger and growth rate decreases

Summary/Key Points

- Statistics
- Cellular alterations
- Genetic alterations
- Epigenetic alterations
- Carcinogenesis
- Proto-oncogenes
- Tumor suppressor genes
- Oncogenes
- Staging
- Molecular biology and precision medicine
- Treatment modalities and response

77

References

Abbas, A. K., Lichtman, A. H., & Pillai, S. (2018). *Cellular and molecular immunology* (9th ed.). Philadelphia, PA: Elsevier Saunders.

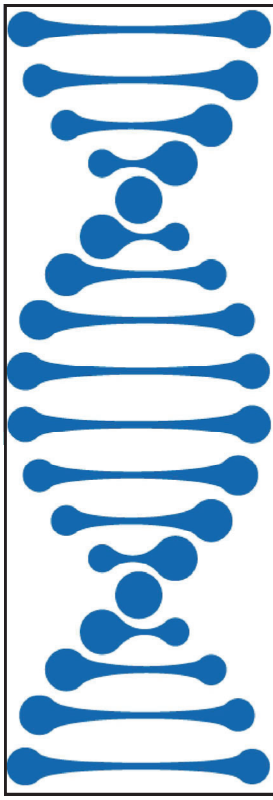
American Cancer Society. (2022). *Cancer facts and figures 2023. https://www.cancer.org/content/dam/cancer-org/research/cancer-facts-and-statistics/annual-cancer-facts-and-figures/2023/2023-cancer-facts-and-figures.pdf*

Devita, V. T., Lawrence, T. S., & Rosenberg, S. A. (2015). *Primer of the molecular biology of cancer* (2nd ed.). Philadelphia, PA: Wolters Kluwer.

Yarbro, C. H., Frogge, M. H., & Goodman, M. (Eds.). (2018). *Cancer nursing: Principles and practice (8th ed.)*. Boston: Jones and Bartlett Publishing.

Note- references also on individual slides for pictures and You Tube references

78



Hereditary Cancer

Kyla Morphy, MGC, LCGC
Cancer Genetics Program
Allegheny Health Network

1

Cancer is a common disease

1 in 2 men
1 in 3 women

Figure 3. Leading Sites of New Cancer Cases and Deaths – 2017 Estimates

Estimated New Cases

Male			Female		
Prostate	161,360	19%	Breast	252,710	30%
Lung & bronchus	116,990	14%	Lung & bronchus	105,510	12%
Colon & rectum	71,420	9%	Colon & rectum	64,010	8%
Urinary bladder	60,490	7%	Uterine corpus	61,380	7%
Melanoma of the skin	52,170	6%	Thyroid	42,470	5%
Kidney & renal pelvis	40,610	5%	Melanoma of the skin	34,940	4%
Non-Hodgkin lymphoma	40,080	5%	Non-Hodgkin lymphoma	32,160	4%
Leukemia	36,290	4%	Leukemia	25,840	3%
Oral cavity & pharynx	35,720	4%	Pancreas	25,700	3%
Liver & intrahepatic bile duct	29,200	3%	Kidney & renal pelvis	23,380	3%
All sites	836,150	100%	All sites	852,630	100%

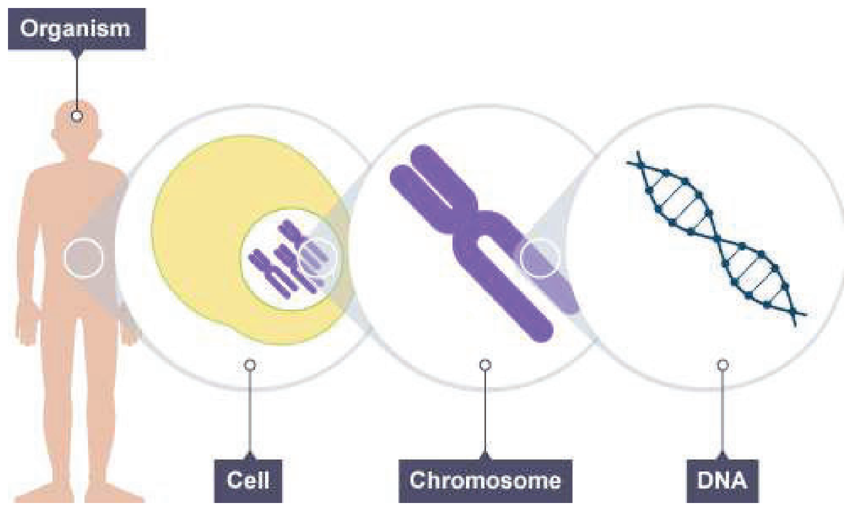
Estimated Deaths

Male			Female		
Lung & bronchus	84,590	27%	Lung & bronchus	71,280	25%
Colon & rectum	27,150	9%	Breast	40,610	14%
Prostate	26,730	8%	Colon & rectum	23,110	8%
Pancreas	22,300	7%	Pancreas	20,790	7%
Liver & intrahepatic bile duct	19,610	6%	Ovary	14,080	5%
Leukemia	14,300	4%	Uterine corpus	10,920	4%
Esophagus	12,720	4%	Leukemia	10,200	4%
Urinary bladder	12,240	4%	Liver & intrahepatic bile duct	9,310	3%
Non-Hodgkin lymphoma	11,450	4%	Non-Hodgkin lymphoma	8,690	3%
Brain & other nervous system	9,620	3%	Brain & other nervous system	7,080	3%
All sites	318,420	100%	All sites	282,500	100%

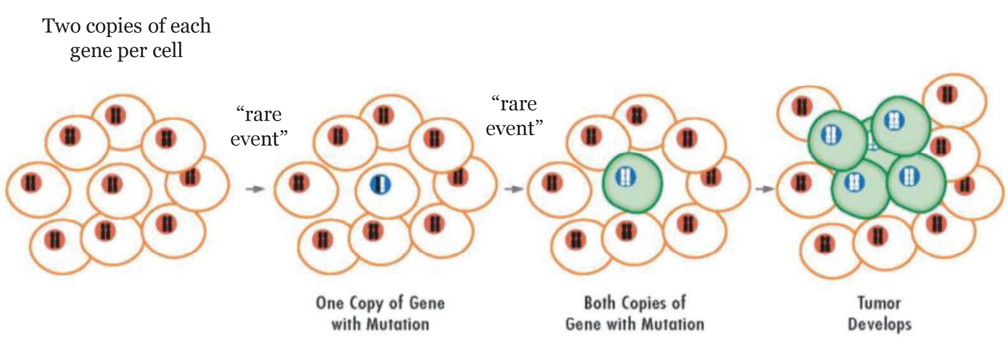
Estimates are rounded to the nearest 10, and cases exclude basal cell and squamous cell skin cancers and in situ carcinoma except urinary bladder.

2

All cancer is genetic…

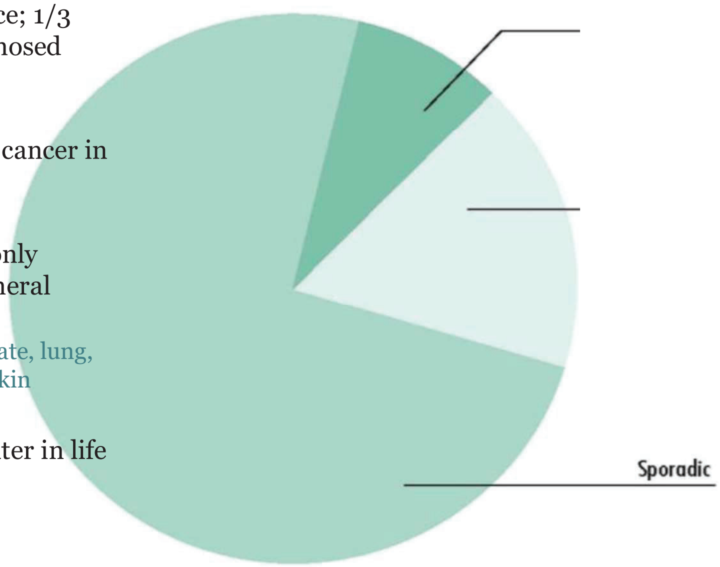


All cancer is genetic…

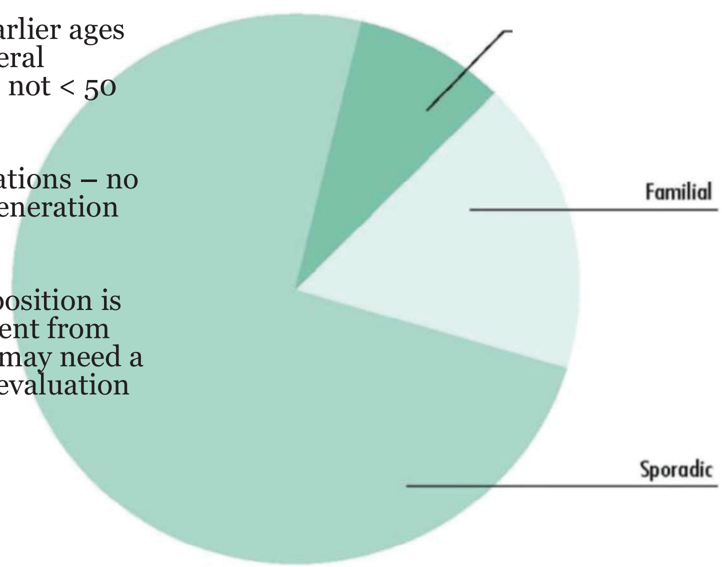


…but not all cancer is hereditary

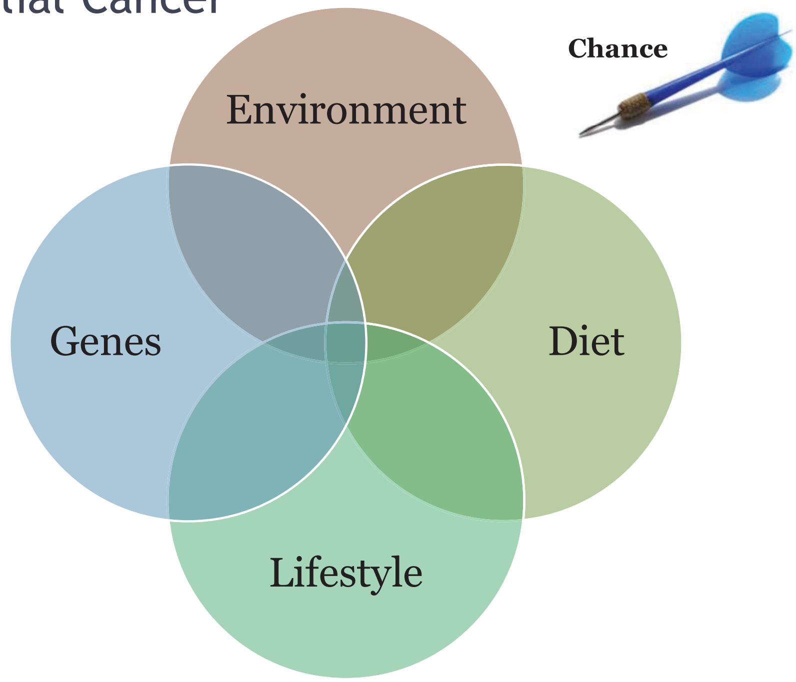
- Occurs by chance; 1/3 people are diagnosed with cancer
- Isolated case of cancer in an individual
- Cancers commonly found in the general population
  - Ex: breast, prostate, lung, bladder, colon, skin
- Onset usually later in life



- Clustering of cancers in the family (same type or related types)
- Diagnosed at earlier ages than in the general population, but not < 50 years
- Can skip generations – no generation to generation pattern
- Genetic predisposition is not clearly evident from family history; may need a more in-depth evaluation
- Multifactorial

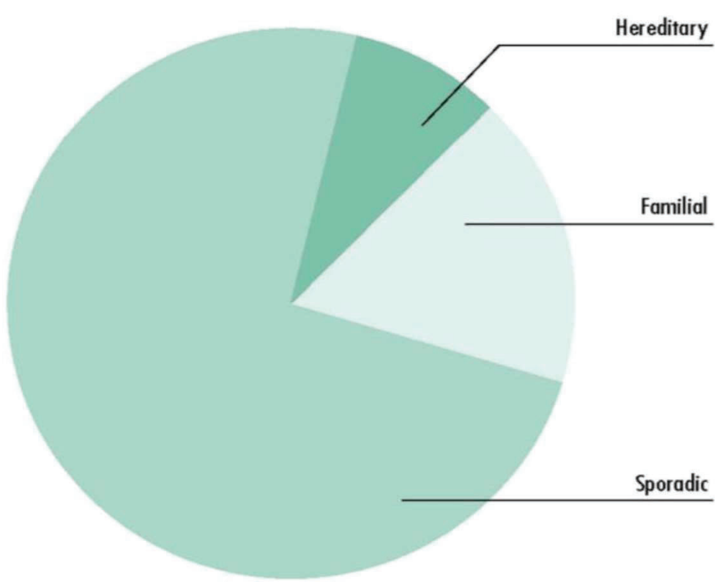


Familial Cancer



7

Hereditary cancer only makes up a small proportion of causes of cancer

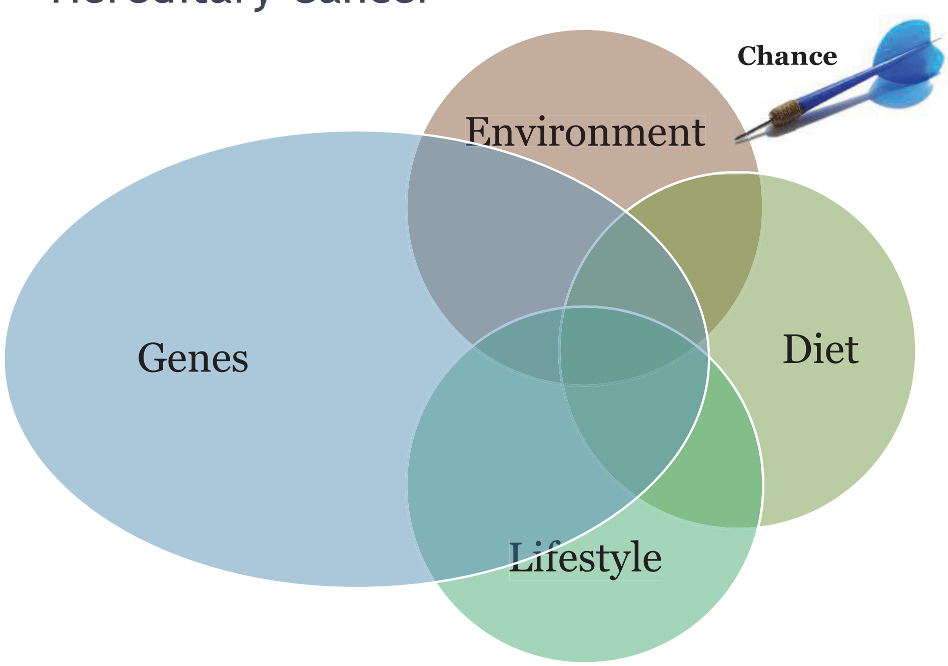


8

Hereditary (5-10%)

- 2 or more closely related individuals with cancer diagnosed before age 50
- Individuals with multiple primary tumors
- Several affected generations in the same bloodline
- Unusual/rare tumors
- Ethnicity

Hereditary Cancer



How do we assess for hereditary cancer?

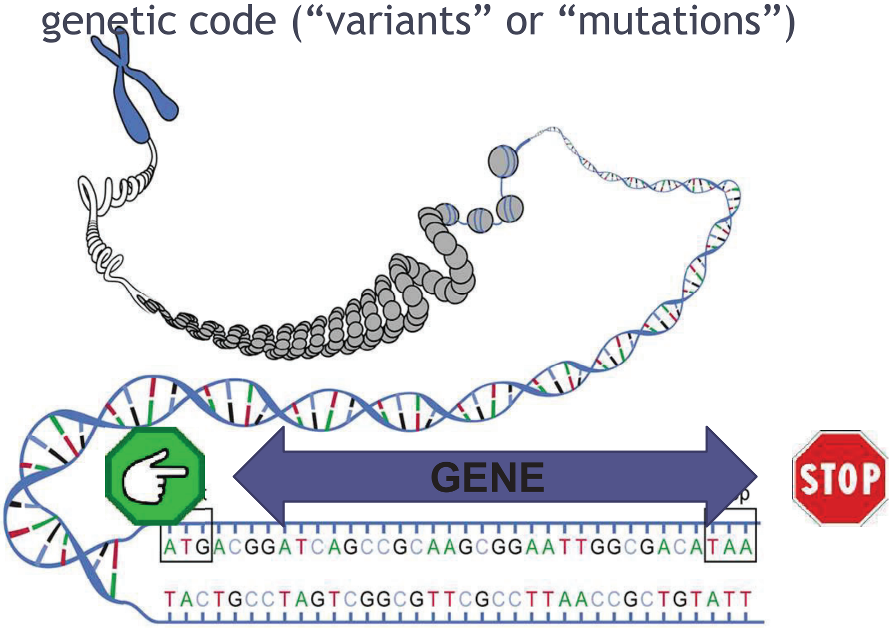
- Personal history
  - A common cancer diagnosed younger than usual
  - Diagnosed with multiple cancers that are the same or related *
  - A rarer cancer with a higher chance of being genetic*
  - Molecular tests on the tumor (tumor genomic profiling, pathological features, IHC screening tests)*
- Family history
  - Does this cancer run in the family within the same blood line?
  - Are family members also being diagnosed at a younger age?
  - Note: Not all families discuss health information – it's normal to not know all or any of this information

*stay tuned for more in this talk

What is genetic testing?

- Analysis of an individual's genetic makeup
- Most commonly completed on blood or saliva
- Identifies differences (variants) in genetic material
- Medical genetic testing can confirm or rule out a suspected genetic condition or help determine a person's chance of developing or passing on a genetic disorder

Genetic testing looks for differences in the genetic code ("variants" or "mutations")



http://www.genome.gov/Images/EdKit/bio2b_large.gif

13

Variant Classification

- Pathogenic
- Likely Pathogenic
- Uncertain Significance (VUS)
- Likely Benign
- Benign

14

Variants of Uncertain Significance

UNCERTAINTY

May or **may not** be causing cancer in the patient/family

Ongoing reassessment; days/months/years

NO action- personal/family history must drive management

15

Which types of genes cause cancer?

Tumor Suppressor Genes	Proto-oncogenes	DNA Repair Genes
• "Brakes in a car"	• "Gas pedal"	• Help to correct any mistakes in a cell's DNA made during cell division
• Keep cells from multiplying too quickly	• Signals to a cell to multiply	• Accumulation of mistakes in DNA can cause cells to growth irregularly
• Mutations cause "loss of function"	• Mutations cause "gain of function"	
• Example: BRCA1/2 (Hereditary Breast and Ovarian Cancer syndrome)	• Example: RET gene (Multiple Endocrine Neoplasia Type 2)	• Ex: mismatch repair genes (Lynch syndrome)

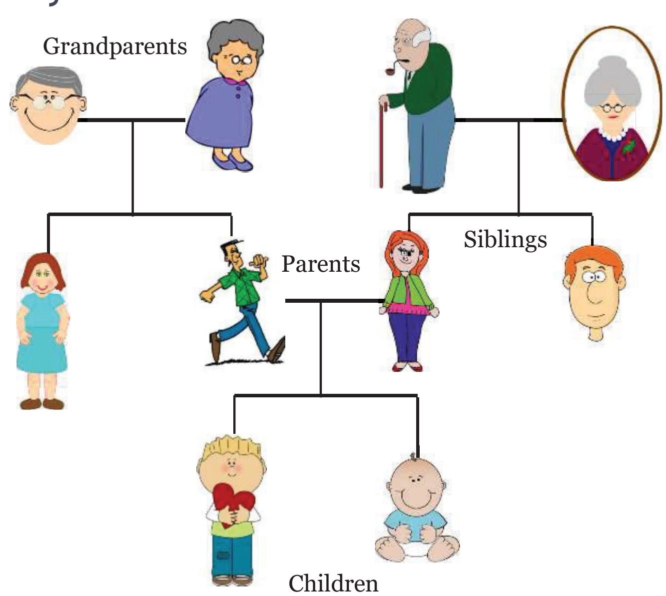
16

“Rules” of Cancer Genetics

- A family tree helps to assess for patterns and risk as genes travel in families in specific ways
- Closer relatives have a greater impact on risk than more distant relatives
  - Related to percentage of shared DNA

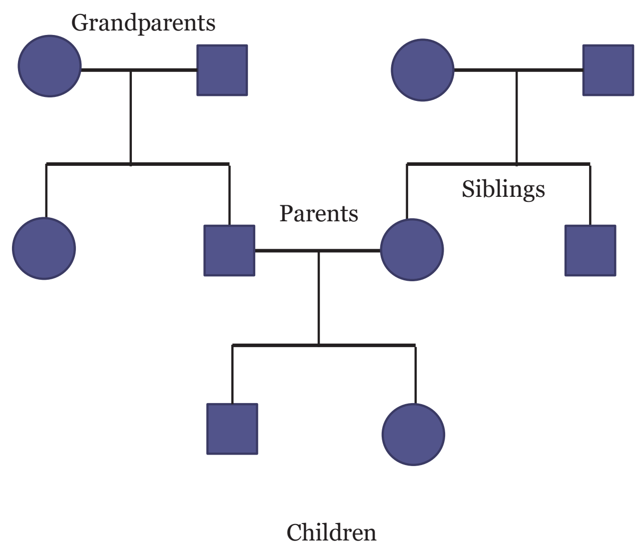
17

A family tree describes how relatives are genetically connected



18

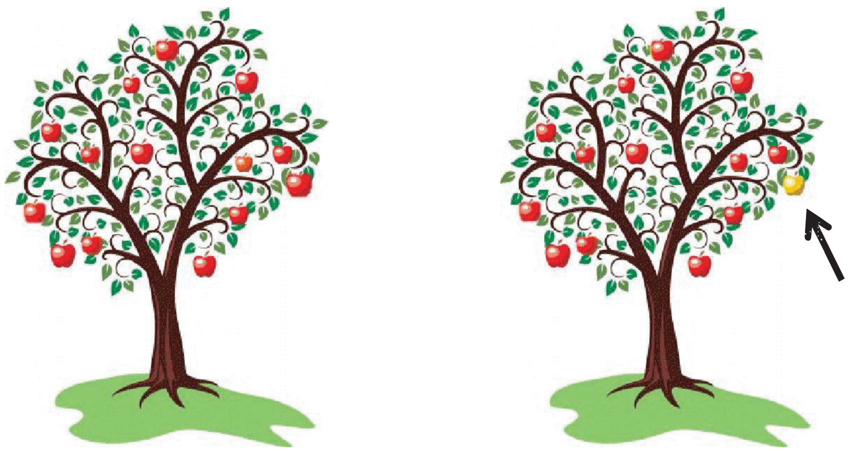
A family tree describes how relatives are genetically connected



"Rules" of Cancer Genetics

- A family tree helps to assess for patterns and risk as genes travel in families in specific ways
- Closer relatives have a greater impact on risk than more distant relatives
- It is more informative to test the person with cancer

It is more informative (but not required) to test the person with cancer



Courtesy of Kallie Weinan, MS, CGC

21

"Rules" of Cancer Genetics

- A family tree helps to assess for patterns and risk as genes travel in families in specific ways
- Closer relatives have a greater impact on risk than more distant relatives
- It is more informative to test the person with cancer
- Genetic testing isn't a crystal ball

22

Myths of Genetic Testing

- **True or false**: Breast cancer genes are only passed down through your mothers side

23

Myths of Genetic Testing

- **True or false**: Men do not need to worry about testing for genes linked with breast and ovarian cancer because they can't (or very rarely) develop these cancers

24

Myths of Genetic Testing

- **True or false**: Your mother was diagnosed with breast cancer. She had genetic testing and was *negative*, therefore you do not need to be tested.

25

Myths of Genetic Testing

- **True or false**: Testing *positive* for a hereditary cancer gene means you are certain to get cancer

26

Myths of Genetic Testing

- **True or false**: Testing *negative* for a hereditary cancer gene means you are protected from getting cancer

27

Myths of Genetic Testing

- **True or false**: Because it is best to detect cancer as early as possible, it is best to test family members very early – even in childhood

28

Myths of Genetic Testing

- **True or false**: It is risky to undergo genetic testing for cancer because of the possibility of genetic discrimination

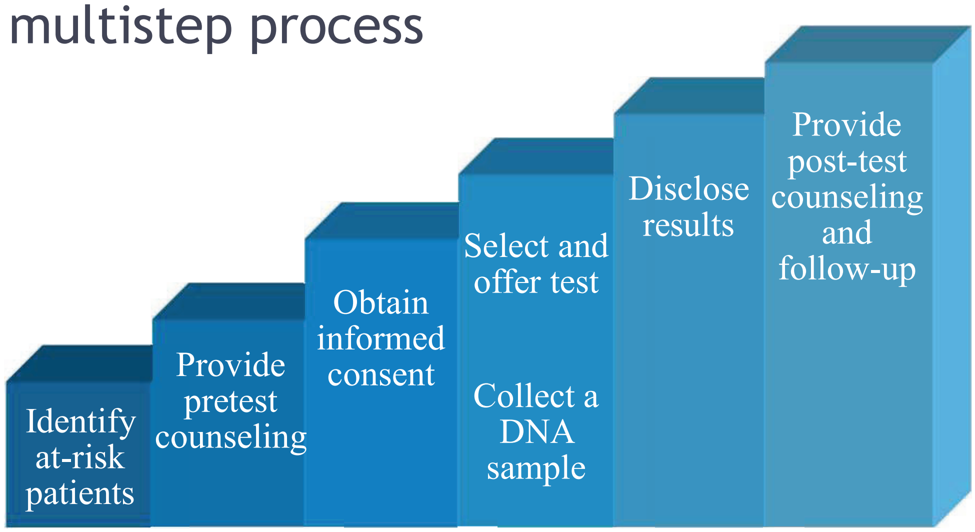
It is partially true and false…

- As a medical test, cancer genetic testing is part of a medical record
- It is protected by HIPAA ; may be viewable by other members of your healthcare team
- **Genetic Information Nondiscrimination Act** (GINA)
  - Bill signed into law in 2008
  - Prohibit discrimination against individuals seeking health insurance and employment on the basis of genetic information (i.e. a genetic mutation is not a pre-existing condition)
  - Does not pertain to life insurance or long term disability insurance policies

Myths of Genetic Testing

- **True or false**: DNA tests advertised online and on television (i.e. 23 and Me) would tell me if I had a hereditary cancer gene

Genetic counseling and testing is a multistep process



Why do patients chose to test?

- Treatment decisions
  - Surgical planning
  - Chemotherapy selection
- Information for the future
  - Personalized cancer screenings
  - Risk reducing surgery
- Family members
  - Empowerment
  - If higher risk, changes in medical care considered
  - Relief
  - If not at high risk, then no unnecessary additional screening
- "Why did this happen?"

33

Why do patients chose not to test?

- Self
  - Overwhelmed with treatment or other appointments
  - Not interested in changes to medical management or changes in medical management would not apply
  - Anxiety and fear
  - Stigmatization
  - Discrimination and privacy
  - Cost (though this is becoming much less of an issue)
- Family members
  - Guilt or shame
  - "Protecting" others
  - Changes in family dynamics

34

Does insurance cover genetic testing?

Usually, yes!

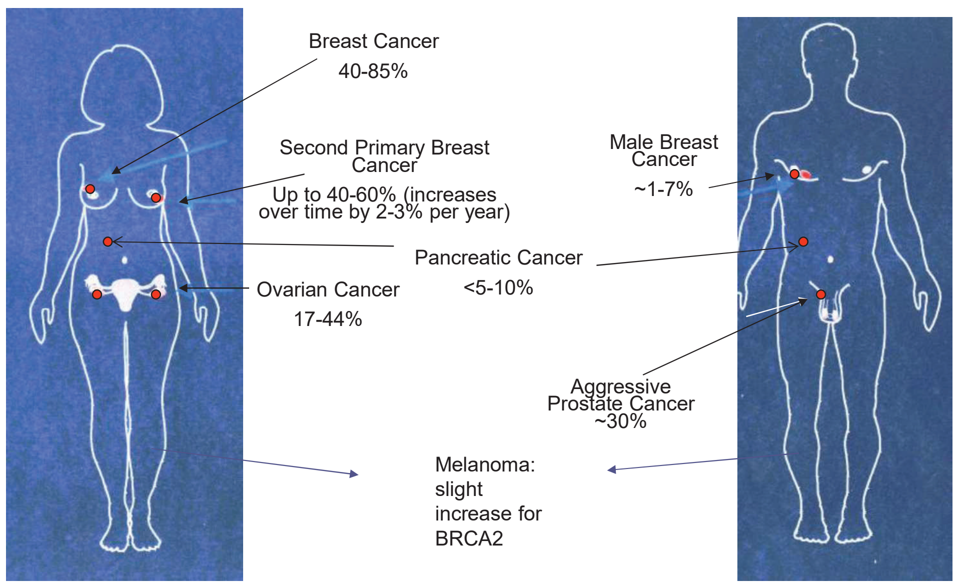
- Determined based on assessment of the patient and/or family (i.e. high risk criteria)
- A copay/deductible may apply
- BRCA1/2 testing 100% covered under the ACA/Obamacare
- A genetic counselor is familiar with what is in-network and what insurances will likely cover based on personal history and family history
- Testing can range from $250 – several thousands of dollars if not covered by insurance

Questions?

Syndromes to know

- Hereditary Breast and Ovarian Cancer (BRCA)
- Other hereditary breast cancer genes
- Lynch syndrome
- Familial Adenomatous Polyposis
- Li Fraumeni syndrome

Hereditary Breast and Ovarian Cancer syndrome (BRCA1 and BRCA2)



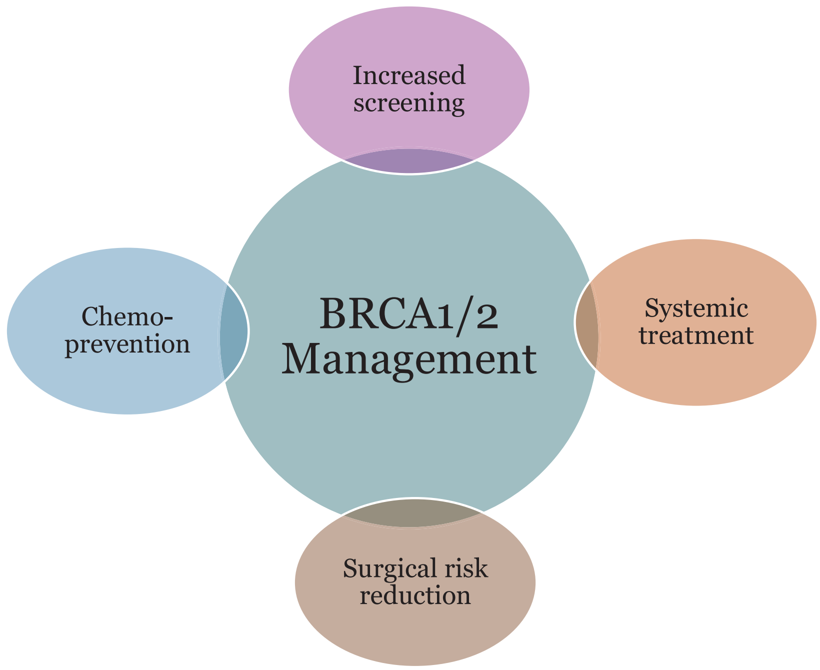
37

Hereditary Breast and Ovarian Cancer syndrome (BRCA1 and BRCA2)

- Most common cause of hereditary breast cancer
- 1 in 400 have a BRCA mutation
  - Ashkenazi Jewish: 1 in 40

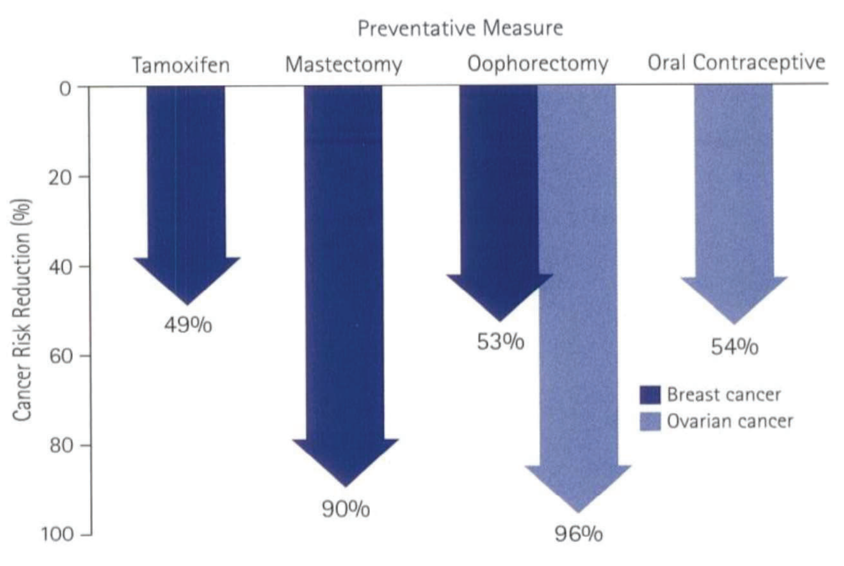
- Refer:
  - All women with ovarian cancer
  - All men with breast cancer
  - All men and women with pancreatic cancer
  - Women with 2-3 cases of breast cancer in the family
  - Women with young breast cancer (dx<50)
  - Women with metastatic or high risk breast cancer if results will impact systemic treatment (Ex: PARP inhibitor use)
  - Women with triple negative breast cancer
  - Men with metastatic prostate cancer

38



39

Risk reduction in BRCA1/2 carriers



Myriad Genetic Laboratories 2004

40

BRCA1/2 Increased Screening

- Breast screening options in women:
  - Clinical breast examination every 6-12 months starting at 25y
  - Annual breast MRI starting at 25y
  - Annual mammogram starting at age 30y

- Both men and women:
  - Annual pancreatic surveillance starting at 50 or 10 years before earliest age of diagnosis in the family (especially in those with FHx of pancreatic cancer)
  - Regular skin exams

- Males:
  - Annual prostate screening starting at 40
  - Monthly SBE and annual CBE at 35y

BRCA1/2 are not the only genes associated with breast cancer

High Lifetime Risk (>50%)	**Moderate Lifetime Risk (20-50%)**	**Newer genes (possible elevated risk)**
BRCA1/ BRCA2 STK11 PTEN TP53 CDH1 PALB2	ATM CHEK2 BARD1 NF1	MUTYH BRIP1 RAD51C RAD51D Mismatch repair genes
Increased and early surveillance Option for bilateral mastectomy Risks for other cancer	Increased and early surveillance Risks for other cancers	No current guidelines Risks for other cancers

Lynch syndrome

- Also known as Hereditary Non-Polyposis Colorectal Cancer (HNPCC) syndrome
- Characterized by an strongly increased risk of colorectal and uterine cancer
- Also associated with other cancers of the gastrointestinal system, urinary tract, ovaries, brain (glioblastoma), and skin (sebaceous glands)
- Hallmark of Lynch syndrome is **mismatch repair deficiency (dMMR)** and **microsatellite instability**
- 5 genes (MLH1, MSH2, MSH6, PMS2, EPCAM)

Lynch syndrome cancer risks

Site	Average Risk	Lynch syndrome*
Colon	4-5%	10-60%
Endometrium	3%	15-55%
Ovary	1-2%	1-35%
Upper GI	<1% respectively for stomach and small bowel	Up to 5-10% for stomach and small bowel respectively
Urinary tract	2-3%	Up to 30% for renal pelvic/ureter Up to 13% for bladder
Prostate	11-12%	Slightly increased to double (12-24%)
Pancreas Hepatobiliary Sebaceous Brain/CNS	<1-2% each	Increased, but <5-10% each

*Varies by gene significantly

Lynch syndrome

Cancer site	Intervention	Onset (years)*	Interval*
Colon	Colonoscopy	20-35*	every 1-3 years*
Endometrium/ovaries*	Consider hysterectomy (TAH) and bilateral salpingo-oophorectomy (BSO)	Can be considered upon completion of childbearing for higher risk genes. For lower risk genes, may not have specific recommendation for BSO	
	Evaluation of AUB Possible surveillance for those who do not get surgery	Ongoing	
Upper GI	Upper endoscopy	30-40	Every 2-4 years
Urinary tract	Consider urinalysis	30-35	Annually
Other	• Regular PSA screening for men • Regular pancreatic surveillance for those with a FHx • Regular skin exams to look for sebaceous tumors • Report abnormal neurological findings		

*Varies by gene significantly

45

Lynch syndrome

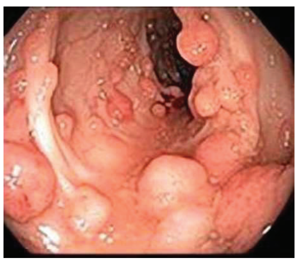
- IHC test for mismatch repair deficiency
  - May also be called "microsatellite instability"
  - Screening test for Lynch syndrome
  - Completed on all colon cancers and most uterine cancers at AHN
  - Look for it on pathology reports
  - Can have false positives and false negatives

- Refer:
  - All women with ovarian cancer
  - Colon cancer under age 50
    - New guidelines state to consider for CRC of all ages, although insurance coverage unclear
  - Uterine cancer under age 50
  - A single individual with multiple Lynch-related cancers
  - Tumors with abnormal IHC screening test
  - Families with multiple relatives with colon and/or uterine cancer (or other Lynch cancers listed)

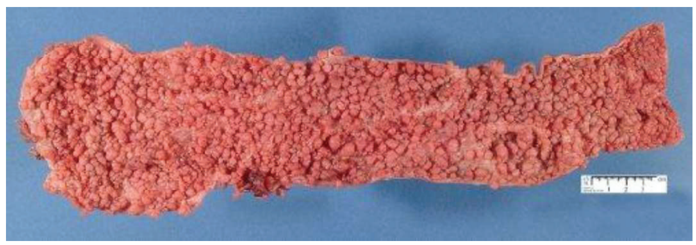
46

Familial Adenomatous Polyposis

- Characterized by the development of 10s-100s of colon polyps
  - Polyps may begin as early as the teenage years
- Very high risk of cancer of the large intestine (colon) and rectum
- Increased risk of polyps and cancer in other areas of the body
  - Small intestine, stomach, thyroid, pancreas, desmoids



http://www.cancer.gov/images/cdr/live/CDR772851-750.jpg



http://www.humpath.com/local/cache-vignettes/L500xH170/fap_002-26ec2.jpg

Surveillance: FAP

Site	Procedure	Age to Begin	Interval
Colon and rectum (FAP)	Colonoscopy	10-15	Annually
Colon and rectum (AFAP)	Colonoscopy	Late teens or early 20s	1-2 years
Stomach/ duodenum	EGD	20-25 or earlier based on findings	Based on findings
COLECTOMY is required when polyp burden becomes unmanageable			

Gastroenterology 2000;119:837-53
Gastroenterology 2001;121:198-213
Gastroenterology 2003;124:544-60
Gastroenterology 2004;127:9-16

Familial Adenomatous Polyposis

- Refer:
  - Individual with at least 10-20 adenomatous colon polyps cumulatively
    - *Consider* individuals who have had 10 polyps, especially if younger
  - Individuals with a family history of severe polyposis
  - Individuals with a family history of early onset colon or rectal cancer (dx < 50)

- No family history of polyps?
  - 20-25% are de novo (first in their family to have the condition)
  - Autosomal recessive polyposis due to the MUTYH gene
    - Caused when both parents are carriers of a MUTYH mutation
    - Estimated 2 in 100 carrier frequency

Li Fraumeni syndrome

- TP53 gene
  - *"Guardian of the genome"*

- Associated with:
  - Breast (very early onset breast cancer)
  - Bone (sarcomas of bone and soft tissue)
  - Brain (tumors, choroid plexus carcinoma)
  - Blood (acute leukemia)
  - Adrenocortical carcinoma
- Potential associations with other cancers
- Men 73%, Women nearly 100% risk of cancer
- Childhood and young adult onset
- 20% de novo

Tumor Genomic Profiling (TGP)

- Aka “Genomic” testing
- Testing a tumor for genetic mutations that are driving the growth of the cancer
- Aids in chemotherapy selection or clinical trials
- Examples: AHN Pan Cancer Panel, Tempus xT, Foundation One, Caris, Mammaprint, OncotypeDx
- Most mutations found on a genomic report are not hereditary
  - But some could be hereditary because they are actually from the germline
  - BRCA1 and BRCA2 → **refer!**
  - TP53 or APC → Commonly mutated somatically in certain cancers, less likely hereditary but can be in rare cases
  - Other mutations: Ask your friendly genetic counselor ☺

51

Who is a good candidate for cancer genetic counseling?

- Cancers that have a **higher chance of being hereditary**
  - Ovarian, fallopian tube, peritoneal (25%)
  - Metastatic prostate cancer (12%)
  - Pancreatic (10%)
  - Male breast cancer (10%)
  - Rarer tumors: Adrenal cancer, medullary-type thyroid cancer, pheochromocytomas, paragangliomas, hemangioblastomas

- Common cancers that are **diagnosed at a younger age than usual**
  - Breast cancer (< age 50)
  - GI (colon, rectal, stomach) cancer (< age 50)
  - Uterine cancer (< age 50)
  - Kidney cancer (< age 45)

- Families with **multiple people having the same types of cancer**

52

Cancers that are not usually hereditary*

- Environmental or have known non-genetic risk factors:
  - Lung, Mesothelioma
  - Esophageal
  - Skin cancer
  - Bladder
  - Cervical
  - "Head and Neck"
  - Anal

There are exceptions… when in doubt, give us a call or refer

- Sporadic
  - Primary brain/brain tumors (some exceptions)
  - Lymphoma/multiple myeloma
  - Primary bone
  - Primary liver
  - Testicular
  - Thyroid (especially papillary)

Contact us!

Don't hesitate to reach out to us with any questions

- Kyla Morphy, MS, LCGC
- Jacqueline (Jackie) Hoover, MS, LCGC
- Amy Kunz, MS, LCGC
- Anna (Chloe) Phillips, MS, LCGC
- Jaclyn Amurgis, MS, LCGC
- Claire Plack, MS, LCGC
- Stephanie Betts, MS, LCGC

Phone: 412-359-8064

We see patients at AGH, West Penn, Wexford, Forbes, Jefferson, Beaver, Butler, St. Vincent

We also do telemedicine visits

Nutritional Assessment of the Oncology Patient

Christy Bender, MS, RD, CSO, LDN
christy.bender2@ahn.org

Objectives

- Discuss nutrition recommendations throughout the cancer continuum
- Identify risk factors for malnutrition
- Discuss importance of early nutrition intervention in preventing and treating malnutrition
- Review nutritional side effects of cancer therapy and symptom management

Nutrition Across the Cancer Continuum

Prevention →

Treatment →

Posttreatment →

Survivorship

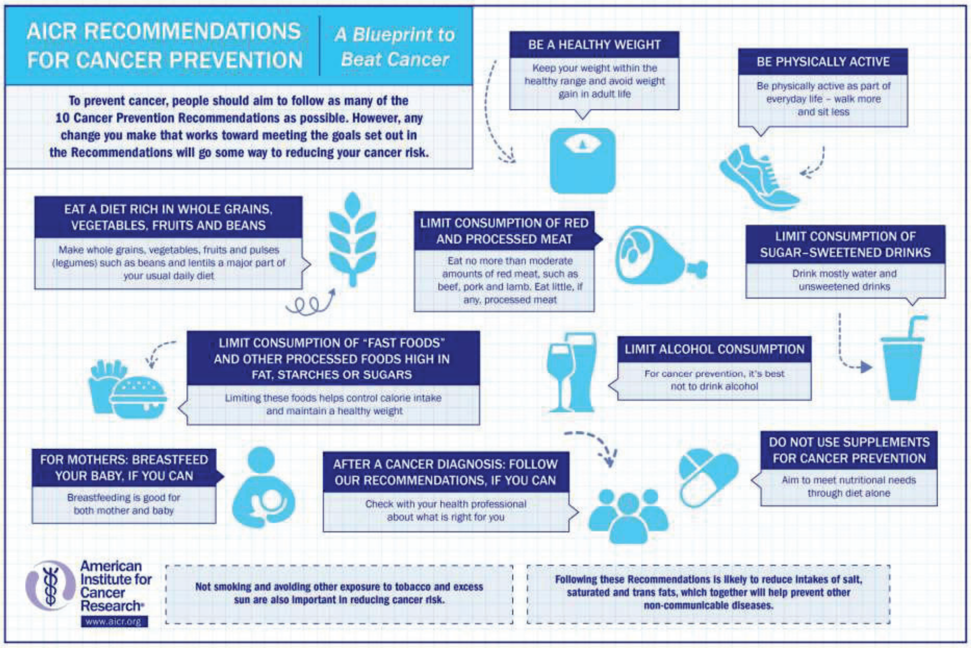
Allegheny Health Network

3

Photo from: https://www.hanscom.af.mil/News/Article-Display/Article/846787/february-is-national-cancer-prevention-month/

Allegheny Health Network

4



Allegheny Health Network

Diet Recommendations

- New American Plate
- Plant based diet

The New American Plate

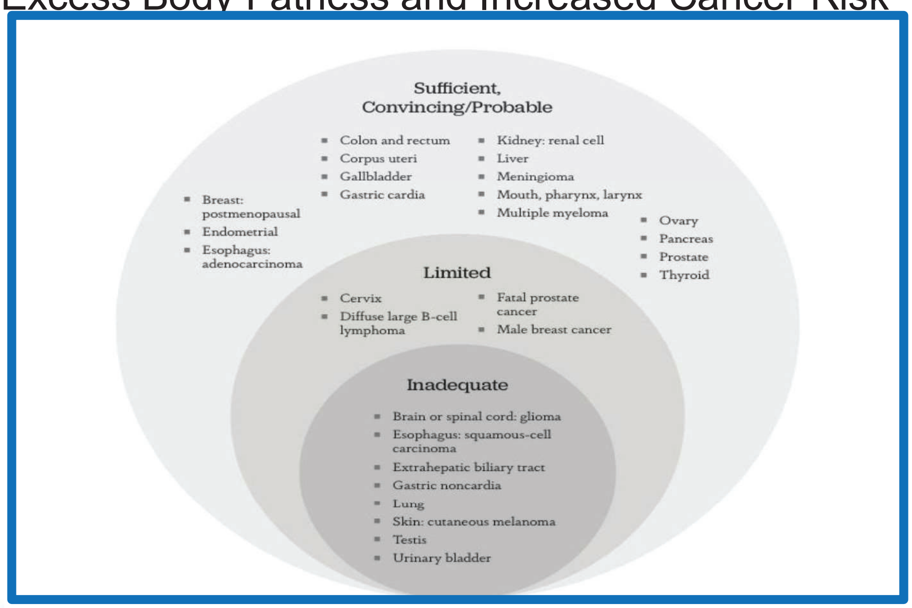
Allegheny Health Network

Weight, Physical Activity and Cancer

- Intentional weight loss may decrease cancer risk, especially for breast and endometrial cancer
- No current studies that illustrate if fasting/calorie restriction reduces cancer risk
- Increased physical activity is associated with decreased cancer risk
  - Recommendation is 150 minutes of moderate activity or 75 minutes of vigorous activity each week
  - Cancer survivors, once recovered from treatment, should get at least 150 minutes of moderate physical activity weekly in addition to strength training two days per week

Allegheny Health Network

Excess Body Fatness and Increased Cancer Risk



Allegheny Health Network

Nutrition During Treatment

Photo from: ihadcancer.com

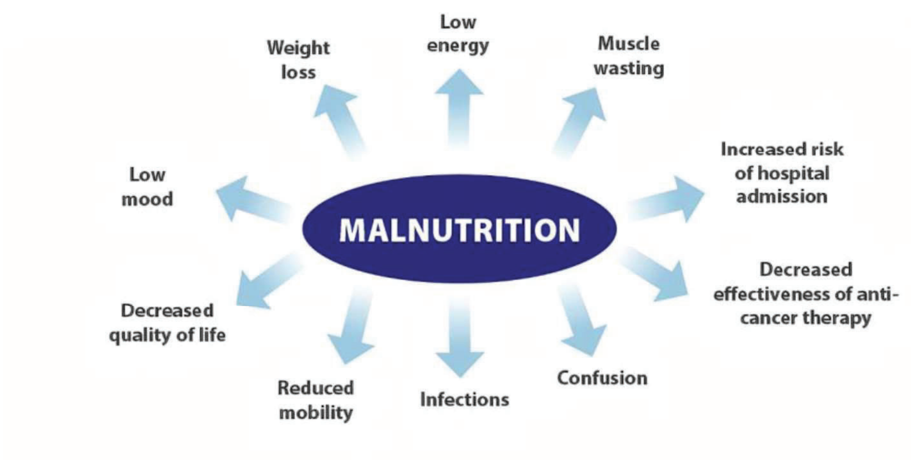
Allegheny Health Network

Importance of Nutrition

- As many as 40% of patients experience weight loss and anorexia prior to cancer diagnosis
- 40%-80% of patients will experience malnutrition at some point in their treatment
- Weight loss of as little as 6% of body weight correlates to a decreased response to treatment, decreased quality of life and decreased survival

Allegheny Health Network

Sequelae of Malnutrition



Allegheny Health Network

Stages of Cancer Cachexia

- Weight loss
- Anorexia
- Progression depends on cancer type and stage and on factors such as systemic inflammation, low food intake, and lack of response to anticancer therapy

- Weight loss of ≥5% over 6 months
- BMI <20 with >2% weight loss
- Sarcopenia and >2% weight loss
- Reduced food intake
- Presence of systemic inflammation

- Active catabolism
- Management of weight loss not possible
- Very advanced or rapidly progressive cancer unresponsive to anticancer therapy

Allegheny Health Network

Early Intervention is Key

Allegheny
Health Network

Goals of Nutrition Therapy

- Preventing/reversing nutrient deficiencies
- Preserving lean body mass
- Increasing tolerance of treatments
- Minimizing nutrition-related side effects
- Maintaining strength and energy
- Protecting immune function
- Maximizing quality of life

Allegheny
Health Network

Risk Factors for Malnutrition

- Weight loss
  - 5% loss of usual body weight in 1 month
  - 10% loss of usual body weight in 6 months
- BMI < 18.5
- Chronic illness
- Inadequate nutrient intake >7 days
- Increased metabolic requirements

Allegheny
Health Network

15

Malnutrition Screening Tool (MST)

Have you lost weight recently without trying?	
If NO	0
If unsure	2
If YES, how much weight have you lost?	
1 – 5 kg (2 – 11 lb)	1
6 – 10 kg (1 – 1½ st)	2
11 – 15 kg (1¾ - 2⅓ st)	3
> 15 kg (> 2⅓ st)	4
Unsure	2
Have you been eating poorly because of a decreased appetite?	
If NO	0
If YES	1
Total	

If the score is 2 or more please refer to the dietitian.
(Ref: Ferguson M et al, Nutrition 15: 458-464, 1999)

Allegheny
Health Network

16

Screening for Malnutrition

- Malnutrition Screening Tool (MST)
- Validated tool to assess for malnutrition risk in the outpatient oncology setting
- Flowsheet in EPIC – AHN AMB Malnutrition Screening Tool

	5/24/2023	6/19/2023	7/17/2023	7/19/2023	7/24/2023	8/7/2023	8/8/2023	8/14/2023
AHN AMB MALNUTRITION SCREENING TOOL								
Have you lost weight recently without trying?								
Have you recently lost weight without trying?	1	0	1 2	1	0	1 2	0 0	0
Weight Loss Score								
Have you been eating poorly because of decreased appetite?	1	1	1 1	1		1 1	0 0	0
MST Total Score	2	1	2 3	2	0	2 3	0 0	0

Allegheny Health Network

Malnutrition Diagnosis

- Indicators of malnutrition
  - Decreased energy intake
  - Weight loss
  - Muscle loss
  - Loss of subcutaneous body fat
  - Fluid accumulation
  - Reduced grip strength
- Two of the six criteria = diagnosis of malnutrition
- Lab values are not used to identify/diagnose malnutrition

Allegheny Health Network

Side Effects of Treatment

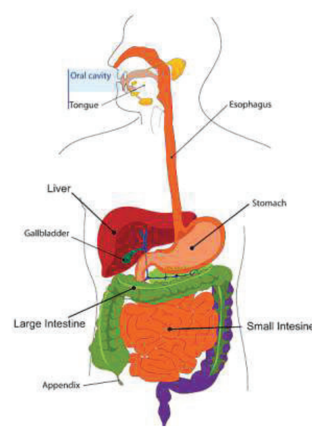
- Surgery
- Radiation
- Chemotherapy
- Immunotherapy

Allegheny Health Network

19

Nutrition Related Side Effects: Surgery

- Head/Neck, Esophageal, GI, Gynecological Cancers
  - Difficulty swallowing
  - Acid reflux
  - Early satiety
  - Fat intolerance, lactose intolerance
  - Malabsorption
  - Bowel issues
  - Dehydration
  - Decreased appetite



Allegheny Health Network

20

Nutrition Related Side Effects: Radiation Therapy

- Fatigue
- Side effects depend on site receiving radiation
  - Head/Neck
    - Mucositis
    - Change in food taste
    - Difficulty swallowing, trismus
  - Abdomen (GI)
    - Nausea, vomiting
    - Diarrhea (malabsorption, enteritis, stricture, fistula)

Allegheny Health Network

Nutrition Related Side Effects: Chemotherapy

- Common Side Effects
  - Anorexia
  - Nausea
  - Vomiting
  - Diarrhea
  - Constipation
  - Changes in taste and smell
  - Mucositis

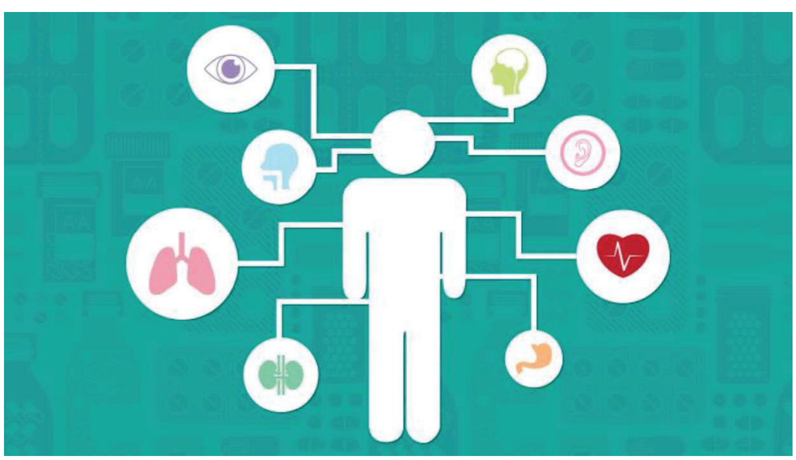
Allegheny Health Network

Nutrition Related Side Effects: Immunotherapy

- Fatigue
  - Increased with dual immunotherapy
- Flu-like symptoms
  - Nausea, vomiting
- Diarrhea
  - Immune-mediated

Allegheny Health Network

Management of Nutrition Impact Symptoms



Allegheny Health Network

Poor Appetite

- Eat most when feeling best
- Small frequent meals and snacks
  - Eat on a schedule
  - Two-three bites every hour
- Increase protein and calories
  - Maximize intake with nutrient dense foods including healthy fats, good protein sources with all snacks and meals
- Drink beverages between meals
- Liquids may be better tolerated
  - Oral nutritional supplements, shakes, smoothies
- Physical activity

Allegheny Health Network

Nausea/Vomiting

- Soft, bland, room temperature or cold foods
- Small, frequent meals
- Try not to skip meals to avoid having an empty stomach
  - Something small is better than nothing
- Avoid gastric irritants
  - Greasy, fried, spicy, and overly sweet foods and foods with strong odors
- Drink liquids between meals and throughout day
  - Clear Liquids
- Rest sitting up after meals
- Natural remedies

Allegheny Health Network

Diarrhea

- Fluid and electrolyte replacement
- Smaller more frequent meals; bland diet
- Avoid caffeine, alcohol, greasy, fried, spicy and very sweet foods (high sugar)
- May need to limit or avoid dairy
- Limit gas forming foods and fluids
- Fiber (soluble)
- Avoid temperature extremes

Allegheny Health Network

Constipation

- Increased fluid intake
  - Warm versus cold beverages
- Fiber intake*
- Physical activity
- Bowel regimen

Allegheny Health Network

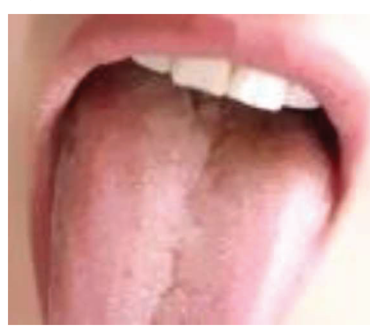
Changes in Taste and Smell

- For smell changes: Avoid strong odors; cold or room temperature foods
- Use plastic or wooden utensils especially if experiencing metallic taste
- Make foods sweeter or use spices, seasoning and marinades
- Tart foods and drinks*
- Experiment with foods, include variety
- Try Ethnic foods
- Good oral hygiene
- Small, frequent meals

Allegheny Health Network

Dry Mouth

- Increased fluid intake
  - Sip water throughout the day
- Stimulation of saliva
  - Gum, hard candy, popsicles, ice
  - Very tart/very sweet foods and beverages
- Eat easy to swallow foods
- Moisten/lubricate foods
- Rinse mouth every 1-2 hours



Allegheny Health Network

Mucositis

- Try soft foods and smaller pieces/bites of food
- Choose foods that are easy to swallow
- Avoid irritants – spicy and acidic foods, salty foods, raw vegetables, alcohol, sharp and crunchy foods
- Moisten/lubricate foods; puree or liquefy foods
- Drink liquids through a straw
- Temperature of foods – cold or room temperature better tolerated
- Increase calorie and protein intake for healing
- Oral mouth rinse, ice chips

Allegheny Health Network

31

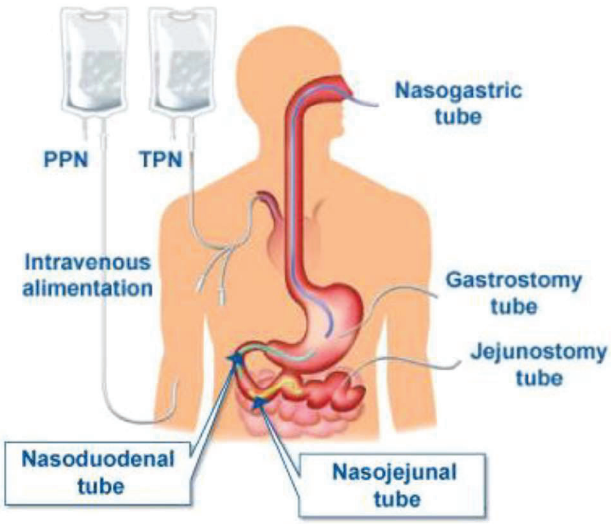
Food Safety

- "Neutropenic diet" is outdated – studies have shown no benefit
- Basic food safety guidelines should always be followed
- Especially important to follow, though, when neutrophils are low

Allegheny Health Network

32

Nutrition Support



Allegheny Health Network

Enteral Nutrition

- Benefits
  - Maintain normal gut function/gut microbiome
  - More effective metabolism and utilization of nutrients
- Indications
  - Inadequate oral intake
  - Functional GI tract
- Contraindications
  - Non-functioning GI tract due to ileus, GI bleed, fistula, intractable nausea/vomiting, severe malabsorption
  - Bowel obstruction or indication for bowel rest
  - Hemodynamically unstable

Allegheny Health Network

Parenteral Nutrition

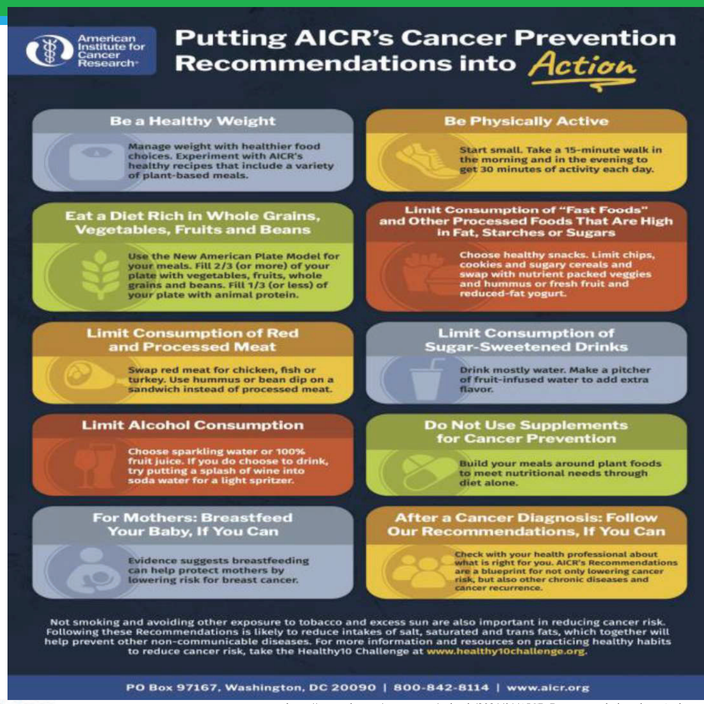
- Indications
  - Non-Functioning GI tract
  - Bowel Rest
  - Inability to initiate enteral nutrition
  - Severe malnutrition
- Contraindications
  - Treatment <7 days
  - Functioning GI tract
  - Inability to obtain venous access
  - Risk for infection

Allegheny Health Network

Survivorship

- Continue to manage long-term side effects from treatment
- Nutrient deficiencies
- Weight management
- Recommending plant-based diet for prevention of recurrence.
- Promotion of wellness

Allegheny Health Network



https://www.aicr.org/wp-content/uploads/2021/01/AICR-Recommendations-into-Action.png

Allegheny Health Network

37

Plant-based Diet Options

- Flexitarian diet
  - Plant-focused; may include eggs, dairy, fish, poultry, red meat
- Mediterranean diet
  - Focus on whole grains, fruits, vegetables, and beans with fat from olives and olive oil and nuts
- Pescatarian diet
  - Vegetarian + fish and seafood
- Lacto-ovo vegetarian diet
  - Includes moderate amounts of dairy and/or eggs
- Vegan diet
  - Plant foods only; avoids all animal sources

Allegheny Health Network

38

A Word about the new Dietary Guidelines for Americans, 2025-2030

Supported by Evidence

- Encouraging nutrient-dense foods (fruits, vegetables, whole grains)
- Recommendations to limit highly processed foods and added sugars
- Maintaining a limit of no more than 10% of total calories from saturated fat while prioritizing healthier fates
- Increased attention to fiber and microbiome health.

Not supported by AICR

- Emphasis on sources of saturated fat- increases risk of cardiovascular disease, red meat increased cancer risk
- Recommendation for alcohol.

Allegheny Health Network

Summary

- Nutrition across the cancer continuum
- Risk for malnutrition
- Early nutritional assessment and intervention
- Interdisciplinary intervention
- Ongoing nutrition related symptom management

Allegheny Health Network

Resources

- American Institute for Cancer Research. Available at: https://www.aicr.org/learn-more-about-cancer/infographics/10-recommendations-for-cancer-prevention.html. Accessed 07/29/2019.
- "Cancer Treatment Centers & Hospitals | Integrative Cancer Care - CTCA." CancerCenter.com, Jan. 2018, www.cancercenter.com/.
- Elliot, Laura; Levin, Rhone, and McIver, Jennifer. *The Complete Resource Kit for Oncology Nutrition*. Oncology Nutrition Dietetic Practice Group, 2013.
- Hébuterne, Xavier, and Etienne Lemarié. "Prevalence of Malnutrition and Current Use of Nutrition Support in Patients With Cancer." *Journal of Enteral and Parenteral Nutrition* 38.2 (2014): 196-204. 23 Jan. 2014. Web. 3 Jan. 2017
- Malnutrition Toolkit." *ASPEN | Malnutrition Toolkit*. Web. 5 Jan. 2017.
- *Eating Hints Before, During, and After Cancer Treatment.* National Cancer Institute, 2018.
- Voss, Ann Coble and Williams, Valaree. *Oncology Nutrition for Clinical Practice, Second Edition*. Oncology Nutrition Dietetic Practice Group, 2021.
- World Cancer Research Fund/American Institute for Cancer Research. *Diet, Nutrition, Physical Activity and Cancer: a Global Perspective*. Continuous Project Update Report 2018.

Allegheny Health Network

RDN Contact Information

- Rachel Harken, MS, RDN, CSO, LDN
  - AGH (Clinical Dietitian Lead)
  - Rachel.harken@ahn.org
- Christy Bender, MS, RDN, LDN
  - Jefferson (Peters and Bethel Park remotely)
  - Christy.bender2@ahn.org
- Marie Diulus, RDN, LDN
  - West Penn (Robinson remotely)
  - Marie.Diulus@AHN.org
- Amanda El-Rawas, MS, RDN, CSO, LDN
  - Forbes, Hempfield
  - Amanda.el-rawas@ahn.org

Allegheny Health Network

RDN Contact Information

- Amanda Capor MS, RDN, COS, LDN
  - Beaver, Wexford (New Castle remotely)
  - Amanda.Capor@ahn.org
- Janese Stamp, MS, RDN, LDN
  - St. Vincent; Janese.stamp2@ahn.org
- Maryellen Smith, MS, RDN, LDN
  - Butler (Allegheny Valley and Grove City remotely)
  - Maryellen.smith2@ahn.org

Allegheny Health Network

Casual RDN Information

- Julie Rinker, MS, RDN, LDN
  - Casual; Julie.rinker@ahn.org
- Randi Cianciotti, MS, RDN, LDN
  - Casual; Randi.cianciotti@ahn.org
- Karen Schnaekel, RDN, CSO, LDN
  - Casual; karen.schnaekel@ahn.org

Allegheny Health Network

Fundamentals of Oncology: Radiation Oncology Basics

Abigail Dare *(abigail.dare@ahn.org)*
Medical Physicist
Allegheny Health Network

KEY OBJECTIVES

- Learn how radiation works for the treatment of cancer and DNA damage
- Examine common signage and equipment to look for throughout hospitals that allude to the potential presence of radiation
- Become familiar with different types of machines and treatments involving radiation
- Learn the principles of practicing radiation safety

OUTLINE

- Physics Concepts
- Radiobiology
- Radiation Units
- Radiation Safety
- Treatment Modalities
  - Machine-Produced
  - Radioactive Materials

Dreamstime.com

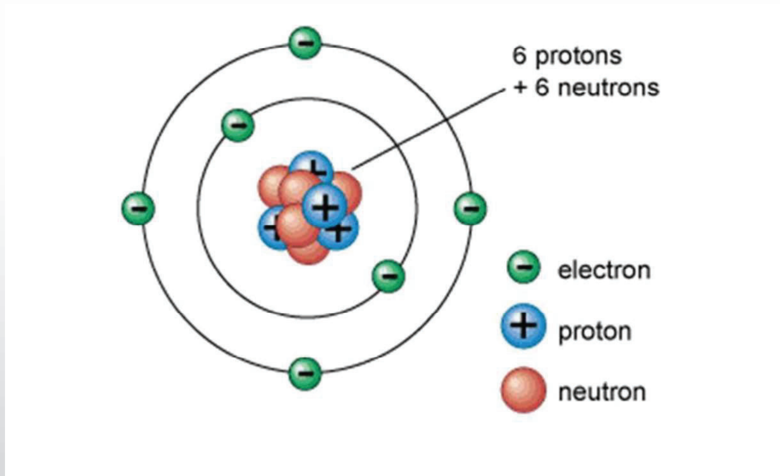
3

PHYSICS CONCEPTS

4

THE ATOM

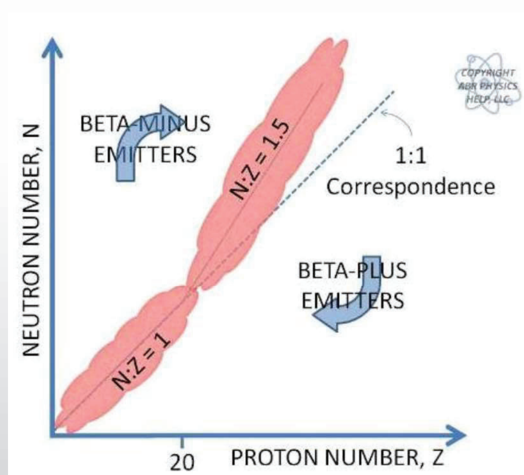
- Nucleus
  - Protons (+)
  - Neutrons (0)
- Electrons (-)



Aspenservesyou.com

LINE OF STABILITY

- Stable elements – equal neutrons and protons
- Neutrons increase as protons increase
- Neutrons – glue
- Protons – repel (stronger with more)
- Decay to return to stability



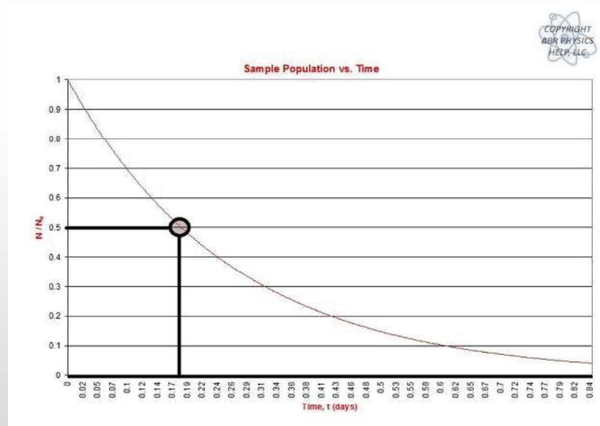
Abrphysicshelp.com

RADIOACTIVE DECAY

- Activity - disintegrations per time
- Governed by half life of material
    - Half the number of atoms will remain

Radioisotope	Nuclide notation	Radioactive emission	Half-life
Tritium-3	$^{3}_{1}H$	β	12.33 years
Carbon-14	$^{14}_{6}C$	β	5730 years
Sodium-24	$^{24}_{11}Na$	β, γ	15 hours
Cobalt-60	$^{60}_{27}Co$	β, γ	5.27 years
Technetium-99m	$^{99m}_{43}Tc$	γ	6.01 hours
Iodine-123	$^{123}_{53}I$	γ	13.2 hours

aplustopper.com

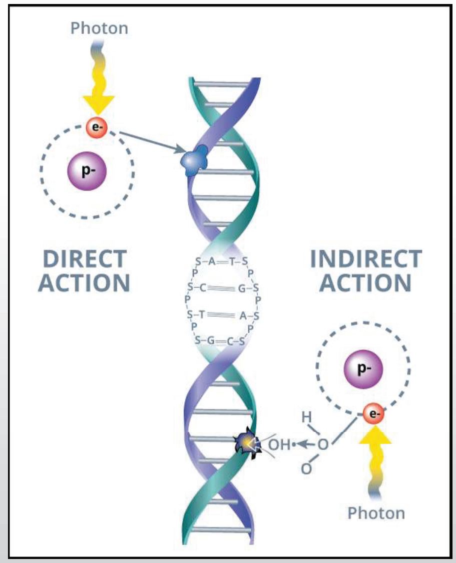


Abrphysicshelp.com

RADIATION BIOLOGY

DNA DAMAGE

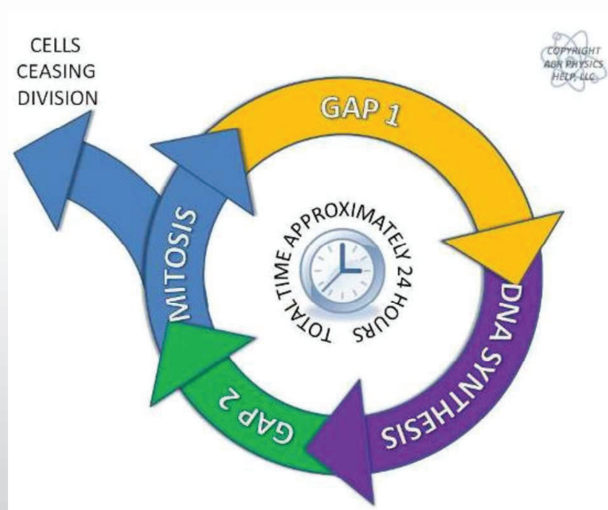
- Direct Action
  - Radiation directly damages DNA
- Indirect Action
  - Radiation releases free radical that damages DNA
  - Free radical – hydroxyl from ionization of water molecules



Dentalcare.com

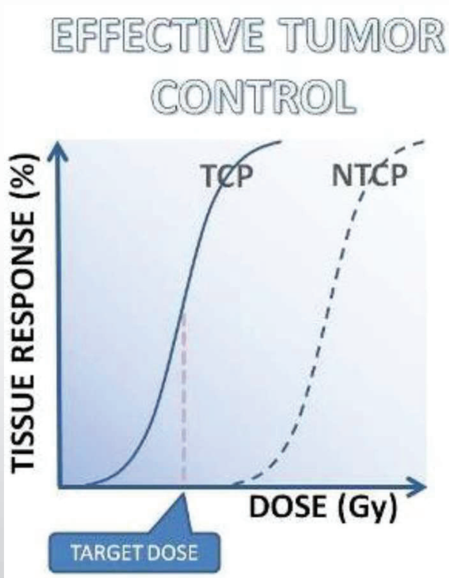
CELL CYCLE & RADIOSENSITIVITY

- Radioresistant
  - Synthesis phase – 2 copies of DNA to use as template for repair
- Radiosensitive
  - Mitosis – chromosomal breaks lead to cell not successfully dividing



Abrphysicshelp.com

THERAPEUTIC RATIO



Abrphysicshelp.com

- Goal of radiotherapy:
  - Effectively treat tumor while limiting dose to normal tissue
- TCP: Tumor Control Probability
- NTCP: Normal Tissue Complication Probability

RADIATION UNITS

RADIATION QUANTITY UNITS

- Activity
  - Becquerels (Bq): 1 disintegration/second
  - Curies (Ci): 3.7×10^{10} Bq (activity of 1g of Ra-226)
- Exposure
  - Roentgens (R): charge per mass (2.58×10^{-4} C/kg)
- Dose
  - Gray (Gy): energy absorbed per mass (J/kG)
  - rad: 1 Gy = 100 rad
- Dose Equivalent
  - Sievert (Sv): dose estimate: biological effect (J/kG)
  - rem: 1 Sv = 100 rem

Radioactive Material (ex. Nuclear Medicine)

Measured Quantity

Radiation Therapy Prescriptions

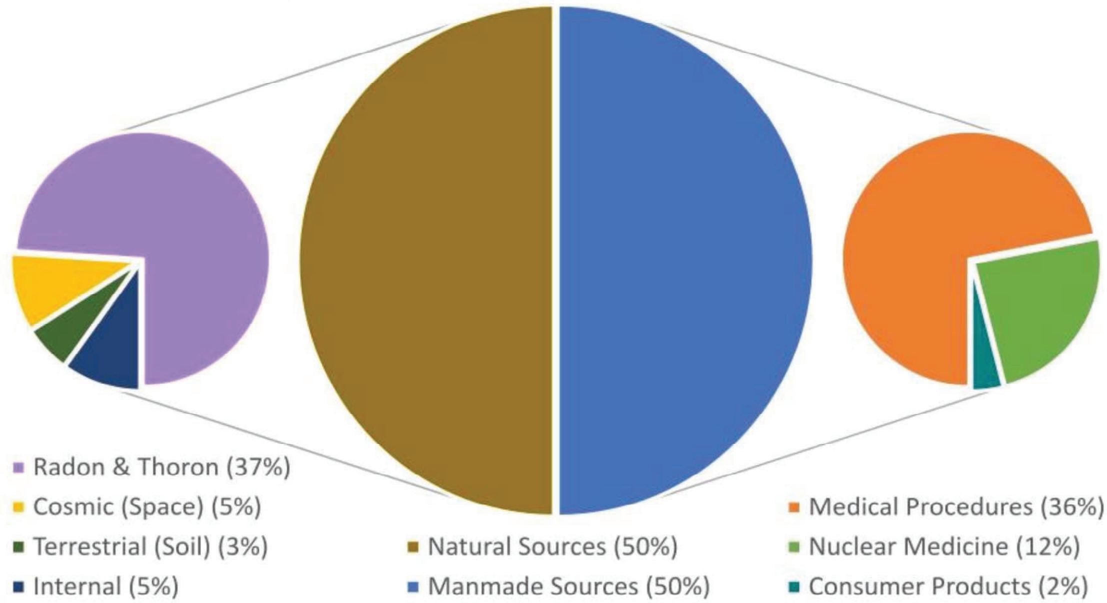
Radiation Safety Quantities

RADIATION SAFETY

Sources of Radiation Exposure in the United States

15

Source Data from: NCRP Report No. 160, Ionizing Radiation Exposure of the Population of the United States.

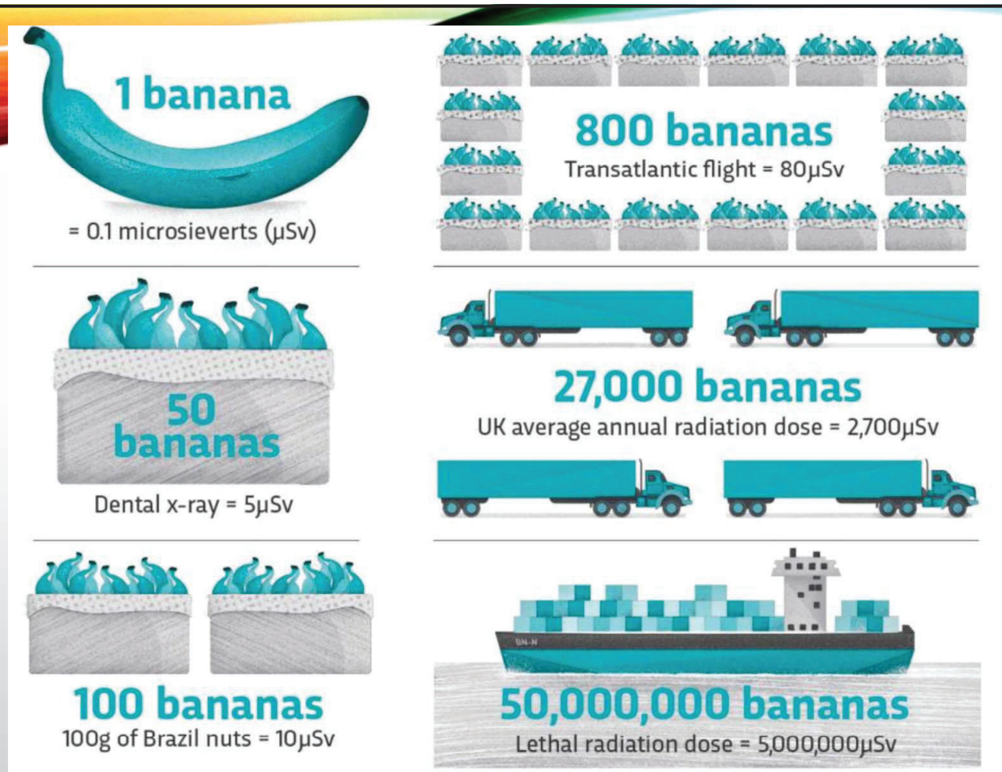


Total Annual Exposure ≈ 6 mSv

Abrphysicshelp.com

15

16



Sciencefocus.com

16

17

DOSE COMPARISON

Procedure	Dose
X-Ray	0.1 cGy
CT Scan	1 cGy
Single Treatment Fraction	200 cGy
Whole Breast RT	6000 cGy
Total Prostate RT	8000 cGy
Prostate Brachytherapy	14500 cGy

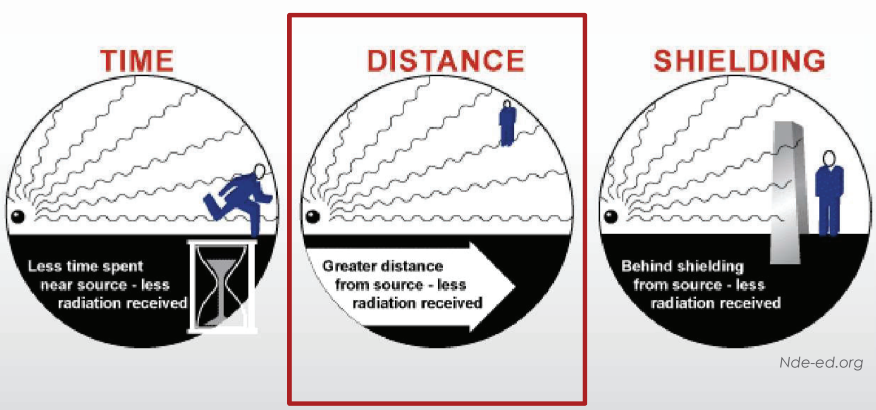
arcphysics.net

1Gy = 100cGy

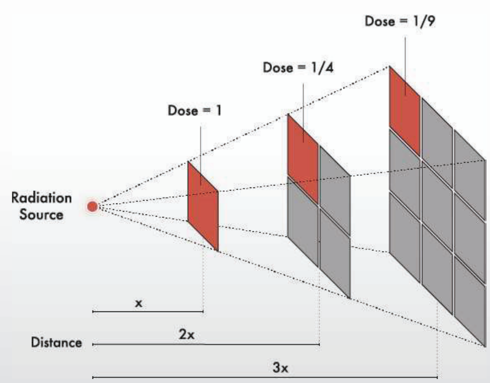
17

18

TIME, DISTANCE, AND SHIELDING



Nde-ed.org



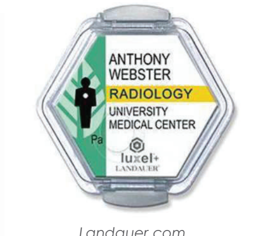
Sites,duke.edu

18

19

KEEP AN EYE OUT

Tequipment.com



Landauer.com

Radiation Monitoring

Rpdinc.com

Daltoninternational.com

Common Signage

Signal-tech.com

Mysafetysign.com

19

20

TREATMENT MODALITIES

20

21

MACHINES VS RADIOACTIVE MATERIAL

- Machine-produced radiation (x-rays)
  - No radiation produced when machine is off
  - Examples: Radiographs, CT scans, linear accelerators
- Radioactive material (gamma [γ] rays)
  - Radiation is ALWAYS ON from decaying RAM
  - Examples: Gamma Knife, brachytherapy, nuclear medicine

Medphys.royalsurrey.nhs.uk

21

22

CT SCANS

- 99% of patients start here
- Differences between radiation oncology and radiology CTs
  - Flat couchtop
  - Big bore – immobilization devices

Targetingcancer.com.au

Siemens-healthineers.com

22

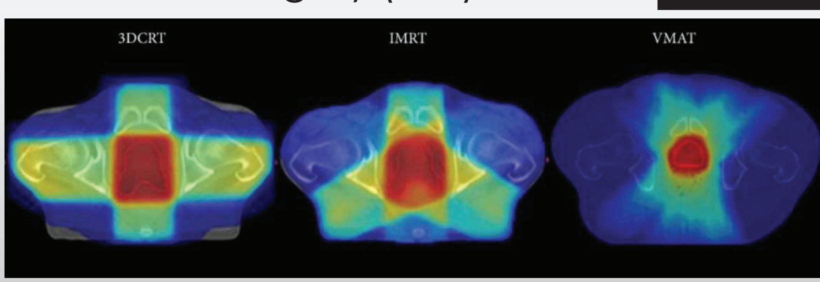
LINEAR ACCELERATOR

Elekta.com

Oncologysystems.com

LINAC TREATMENTS

- 2D/3D
- Intensity Modulated Radiotherapy (IMRT)/ Rotational IMRT (VMAT)
- Stereotactic Body Radiotherapy (SBRT)
- Stereotactic Radiosurgery (SRS)

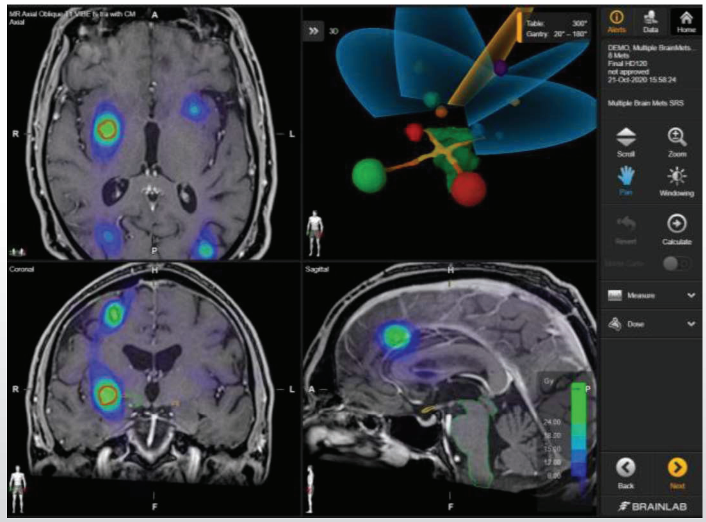


Hindawi.com

SRS/SBRT

- Short treatment course
- High dose/fraction

Mayoclinic.org



Twitter.com/brainlab

GAMMA KNIFE

- ~200 Co-60 sources converging at one point
- Frames or masks for positioning

Elekta.com

Elekta.com

27

GAMMAPOD

- Similar to Gamma Knife - Co-60
- Breast SBRT

Xcision.com

Xcision.com

27

28

BRACHYTHERAPY

- High Dose Rate (HDR)
  - Ir-192
- Low Dose Rate (LDR)
  - Pd-103
  - I-125

Blueridgeradonc.com

Elekta.com

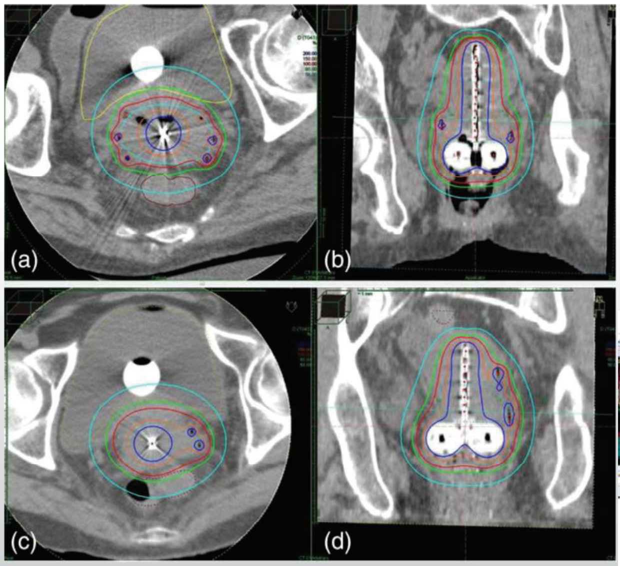
Bimedis.com

Indiamart.com

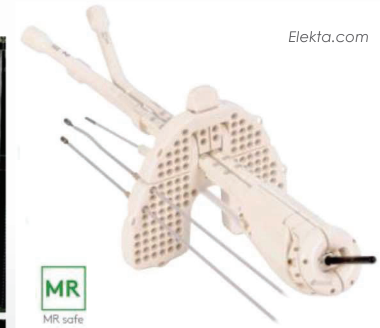
28

GYN HDR BRACHYTHERAPY

- Cervical/ Endometrial Cancer
- Interstitial needles
- Normal tissue considerations
    - Bladder
    - Rectum
    - Bowel



Bmccancer.biomedcentral.com



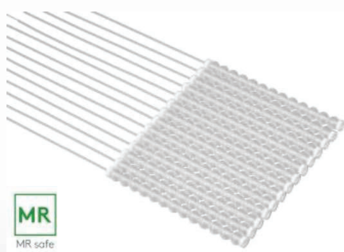
Elekta.com

Elekta.com

MISCELLANEOUS HDR

<u>Skin</u>

Brachyjournal.com



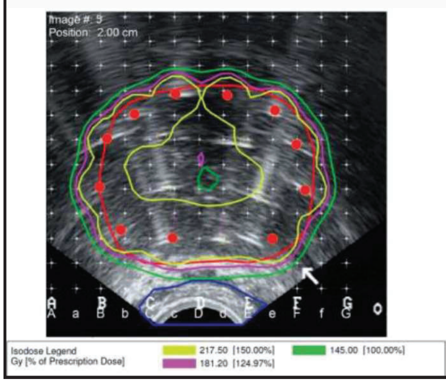
Elekta.com

<u>Esophagus</u>

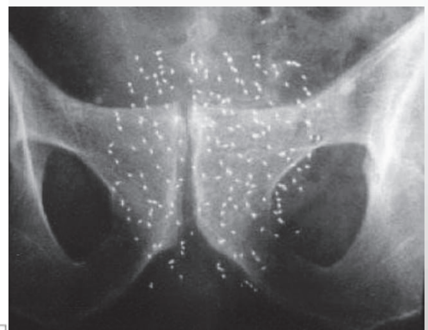
Elekta.com

LDR PROSTATE

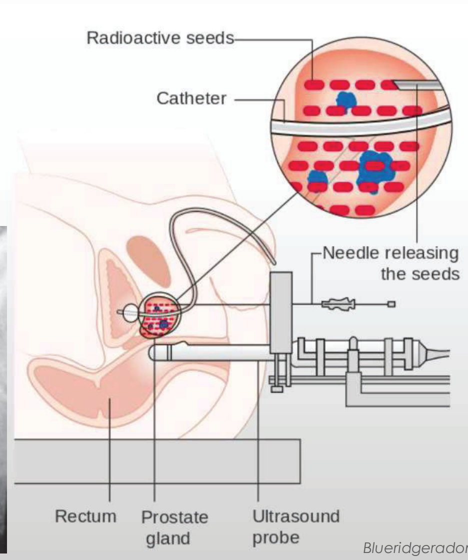
- Prostate Seed Implants
  - Pd-103 (boost following EBRT)
    - Rx = 10000 cGy (100 Gy)
  - I-125 (monotherapy)
    - Rx = 14500 cGy (145 Gy)



Researchgate.net



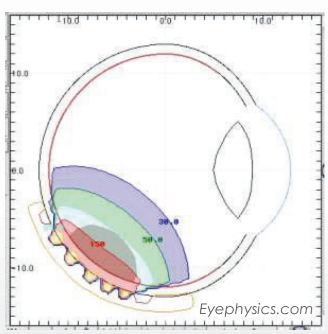
Emedicine.Medscape.com



Blueridgeradonc.com

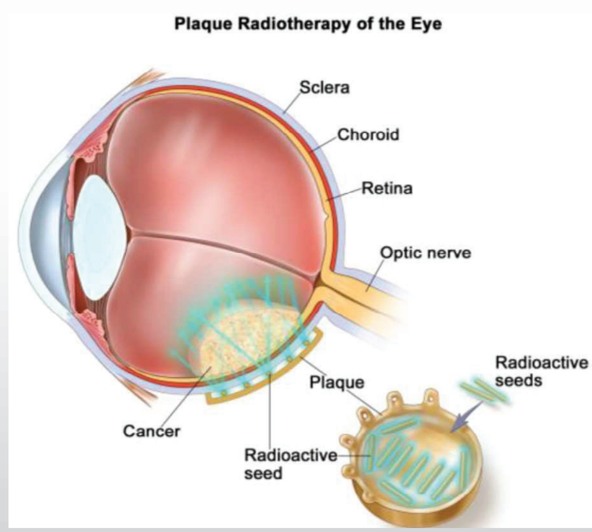
LDR EYE PLAQUE

- Ocular melanoma
  - Rx = 85 Gy
- Plaque designs
  - Notched
  - Slotted



Eyephysics.com

Isoaid.com



Cancer.gov

KEY TAKEAWAYS

- Therapeutic ratio – kill cancerous cells & spare normal tissue
  - Radiation damages DNA leading to cell death
- Some radiation is always on – pay attention to signage
  - Therapy can be delivered from outside or inside
- Radiation Safety - Time, Distance, Shielding

The Radiation Oncology Team: Consult to Treatment

Jennifer Carmichael RT(R)T

Shelbie O'Hara BSN RN

Allegheny Health Network

Objectives

- Introduction to Rad/Onc, our sites and staff
- Description of Radiation therapy and how it works
- Review patient's journey from diagnosis through follow up
- Overview of our treatment delivery process
- Brief description of Radiation Therapy Treatment modalities
- Discussion and questions

Allegheny Health Network

THE RADIATION ONCOLOGY TEAM

Radiation Oncologist -
- The doctor who oversees the radiation therapy treatments and enters all the orders for the staff to follow. Discusses with the patient their need for treatment. Enters treatment orders based on NCCN (National Comprehensive Cancer Network) and ASTRO (American Society for Radiation Oncology)

Medical Radiation Physicist -
- Ensures the safe and effective use of radioactive equipment used to treat patients with radiation

Dosimetrist -
- Works with the radiation oncologist and medical physicist to calculate the proper dose of radiation given to the tumor.

Radiation therapist -
- Administers the daily radiation under the doctor's prescription and supervision

Radiation oncology nurse -
- Cares for the patient and family by providing education, emotional support and tips for managing side effects

Radiation oncology clerical staff (Billers, front desk, PACs) -
- Greets and registers patients on arrival. Assists with financial part of patients treatment. Works on authorizations and scheduling of important scans and appointments.

Allegheny Health Network

3

Allegheny Health Network Division of Radiation Oncology

Free Standing	Hospital Based	Contracted
Wexford Health + Wellness Pavilion	Allegheny General Hospital	Armstrong County Memorial Hospital
Peters Township Health + Wellness Pavilion	West Penn Hospital	Clarion Hospital
Beaver Cancer Center	Allegheny Valley Hospital	Tony Teramana Cancer Center (Trinity Hospital System)
Saint Vincent Cancer Center	Jefferson Regional Medical Center	
Forbes Regional Hospital		

Allegheny Health Network

4

FACTORS DETERMINING TREATMENT

Radiation treatment used is dependent on:

1. Type of Cancer
2. Tumor size
3. Tumor location
4. Proximity of tumor to normal tissue which is sensitive to radiation therapy
5. General overall health of patient, medical history and age
6. Other types of treatment patient may be receiving

Allegheny Health Network

RADIATION THERAPY ROLES

Definitive: primary treatment modality, no other treatment modalities such as chemo or surgery will be needed. More commonly seen with a true laryngeal cancer patient.

Neoadjuvant: administered prior to definitive treatment to shrink tumor and allow for higher rate of cure/palliation of cancer. More commonly seen in anal and esophageal patients.

Adjuvant: administered AFTER definitive treatment. Most common with breast patients.

Allegheny Health Network

PURPOSE OF RADIATION THERAPY

Curative: destroy tumors that have not spread to other parts of the body and/or reduce risk that cancer will return after surgery or chemotherapy.

Palliative: shrink tumors affecting quality of life and alleviate pain by reducing tumor size. For example: metastatic bone pain and cord compressions

Prophylactic: Performed for small cell lung cancer patients to decrease risk of brain mets.

Allegheny Health Network

THE PATIENT'S JOURNEY

- **Diagnosis – referring MD**
- **Referral – medical or surgical oncology, other ancillary offices**
- **Consult – RN and MD**
- **Testing – normally ordered prior, some needed to assist with radiation planning**
- **CT Simulation and Nurse Teach – RT and RN**
- **Radiation planning – Dosimetry and MD**
- **Physics 2nd check - Physicist**
- **Dry Run - RT**
- **Radiation therapy w/On Treatment Visits (OTV) – RT, RN, MD**
- **Follow up – initial and long term – RN and MD as well as referring physicians**

Allegheny Health Network

Patient Consultation:

Initial visit with Patient

- Nursing
  - Gathers and reviews patient information
  - Confirms and discusses with patient recent findings and assesses patient understanding
  - Presents patient to MD's (attending/resident)
- MD at time of consult
  - Discusses diagnosis and how RT plays a role in treatment
  - Discusses treatment options
  - Completes physical exam
  - Develops plan of care

Allegheny Health Network

Plan of care determined

Assesses ability to learn

- Patient/family receptiveness
- Level of knowledge
- What do they already know (assess what they have investigated, what are their perceptions/past experiences they may have)

Assesses any cultural, ethnic, socioeconomic, gender or age variabilities

- Elderly patients
- Patients bringing parents, parents bringing adult children
- International patients

Educates patients and families

- Starts at consult
- Continues throughout Radiation Course

Allegheny Health Network

Other Considerations at time Consultation

To Get Started:

– Scheduling a simulation
  - Allow 3-5 business days for Authorization
  - Coordination of simulation schedule and MD schedule
  - Review MD orders (IV contrast/labs/hydration)
  - Review consent was completed prior to simulation being completed
  - Determine if chemo will be given concurrently
  - Review orders for scans that may need fused with Radiation simulation

– Explanation of Simulation(Scan to plan RT)
  - Patient/family teaching (immobilization/markings)
  - What to be expected (time this takes and time to treatment)
  - What happens during the simulation
  - What after simulation completed

Allegheny Health Network

Other Considerations at time Consultation

To Get Started:

– Further work-up may be needed

– Coordination of Simulation(Scan to plan RT)

– Possible referrals to other disciplines

– Answer any further questions patients/families have

– Is additional support services needed

– Providing contact information

– Literature from Radiation Oncology

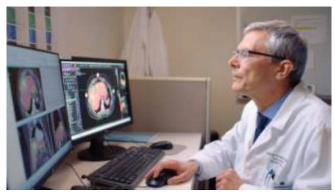
Allegheny Health Network

The Treatment Planning Process
7-10 Business Days

CT Simulation

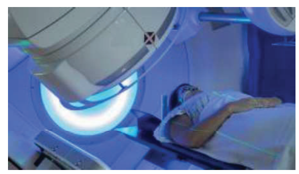
⬇

Custom Planning



⬇

Treatment Delivery



Allegheny Health Network

CT *Simulation*

What is that??

Allegheny Health Network

CT Simulation

In short….It's a CT scan that will be used for radiation planning

Allegheny Health Network

Simulation Day

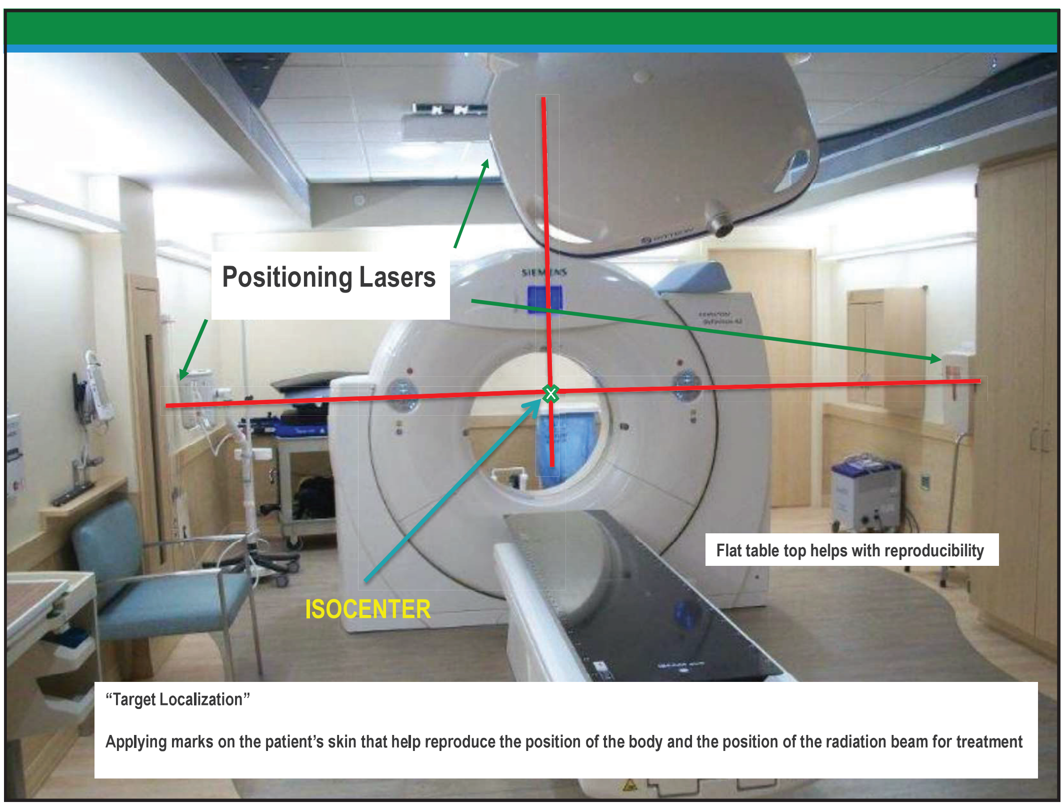
What to expect on Simulation day?

- ❖ Radiation Therapist will carry out the simulation from orders the Radiation Oncologist enters in the EMR
  - Patient is taken to CT Simulation room
  - Patient Immobilization is made
  - Patient set-up marks / tattoos
  - CT scan is performed (contrast, respiratory motion)
  - Documentation of how the patient is setup (notes, pictures)

Allegheny Health Network


CT Simulator
SIEMENS

17


Positioning Lasers
SIEMENS
Flat table top helps with reproducibility
ISOCENTER
“Target Localization”
Applying marks on the patient’s skin that help reproduce the position of the body and the position of the radiation beam for treatment

18

Radiation Therapy – Positioning Aides

19

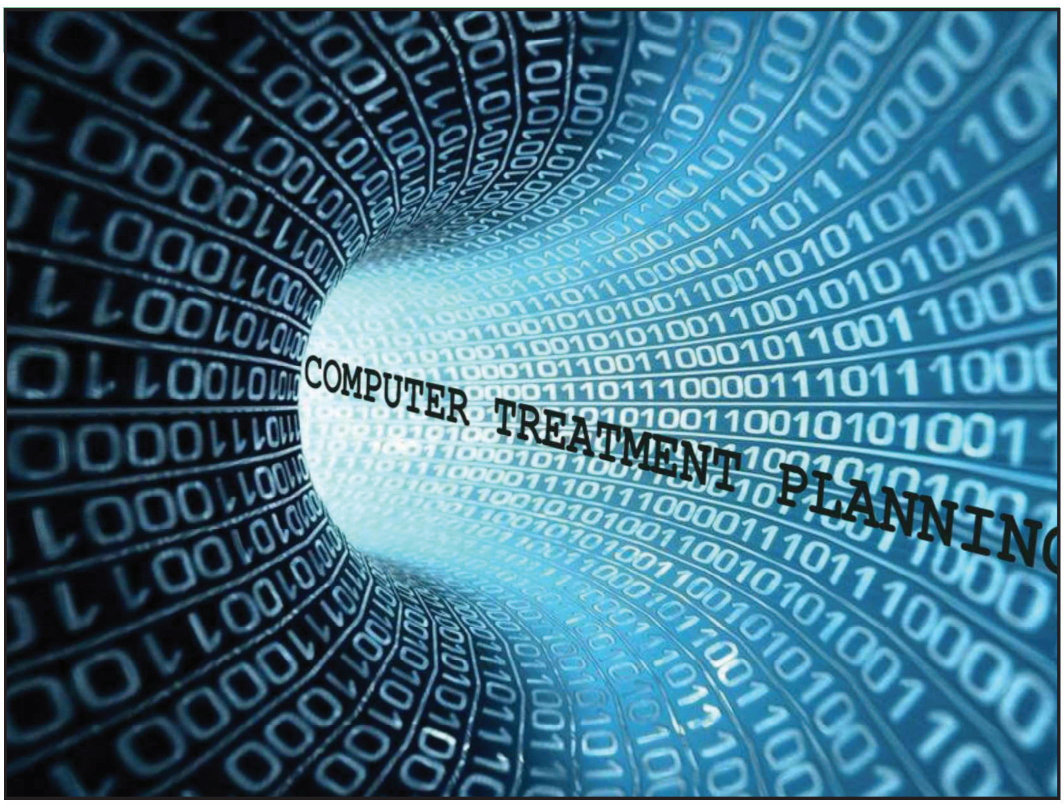
Rigid Immobilization Devices

Health Network

20

Custom Immobilization Devices

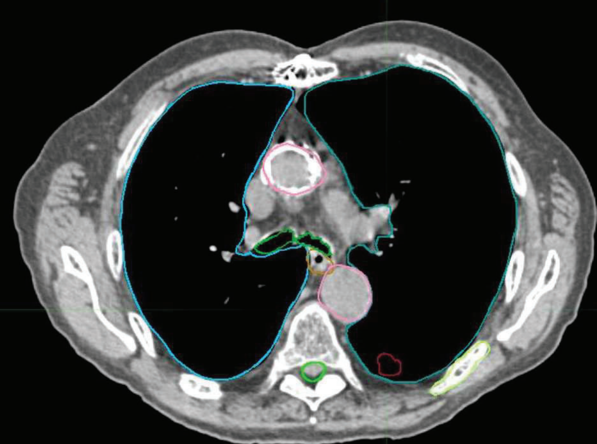
Allegheny Health Network

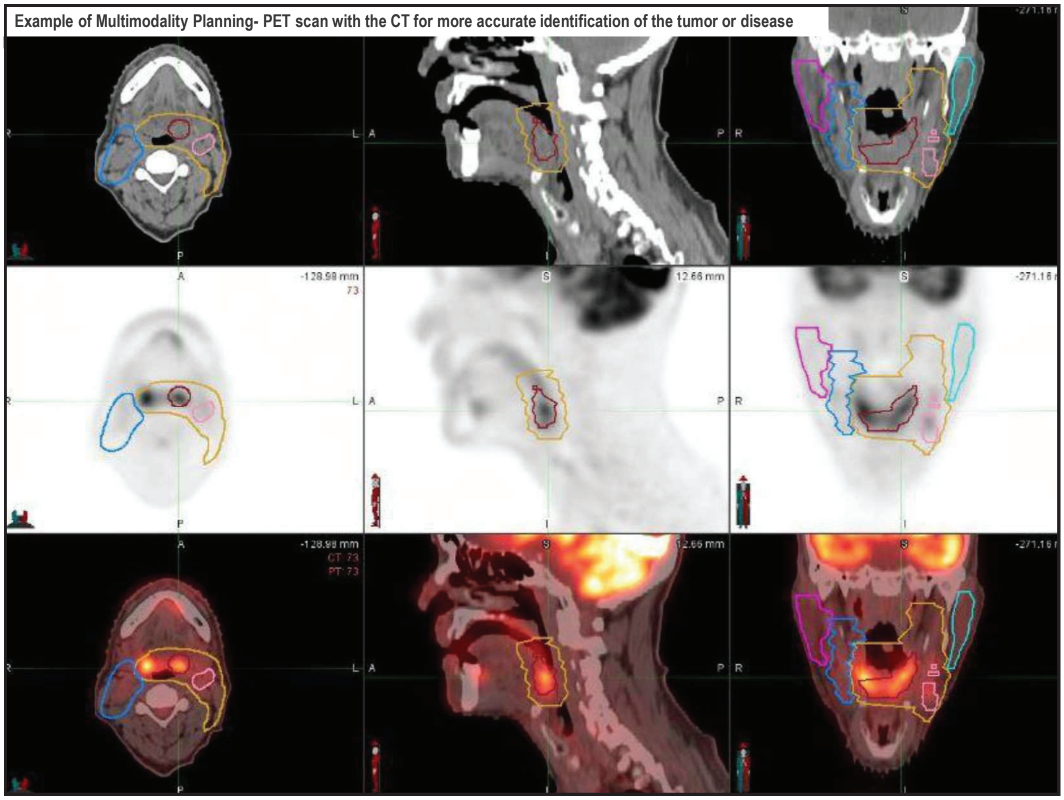


Treatment Planning – The Virtual World

- CT scan from simulation imported to a 3D virtual environment (Treatment Planning System)
  - Dosimetrist, Physics & Physician work together on a treatment plan
  - Treatment planning system-Consists of exact 3D rendering of patient anatomy and geometrical characteristics of the treatment machine
- "Multimodality" Treatment Planning
  - Diagnostic imaging (PET, MRI) fusion
  - Respiratory motion data
- Radiation Prescription defines the dose, number of treatments and objectives of the plan
  - In a perfect world: 100% dose at the tumor and nothing else
  - Reality: Maximum possible dose at tumor while balancing dose to surrounding tissue

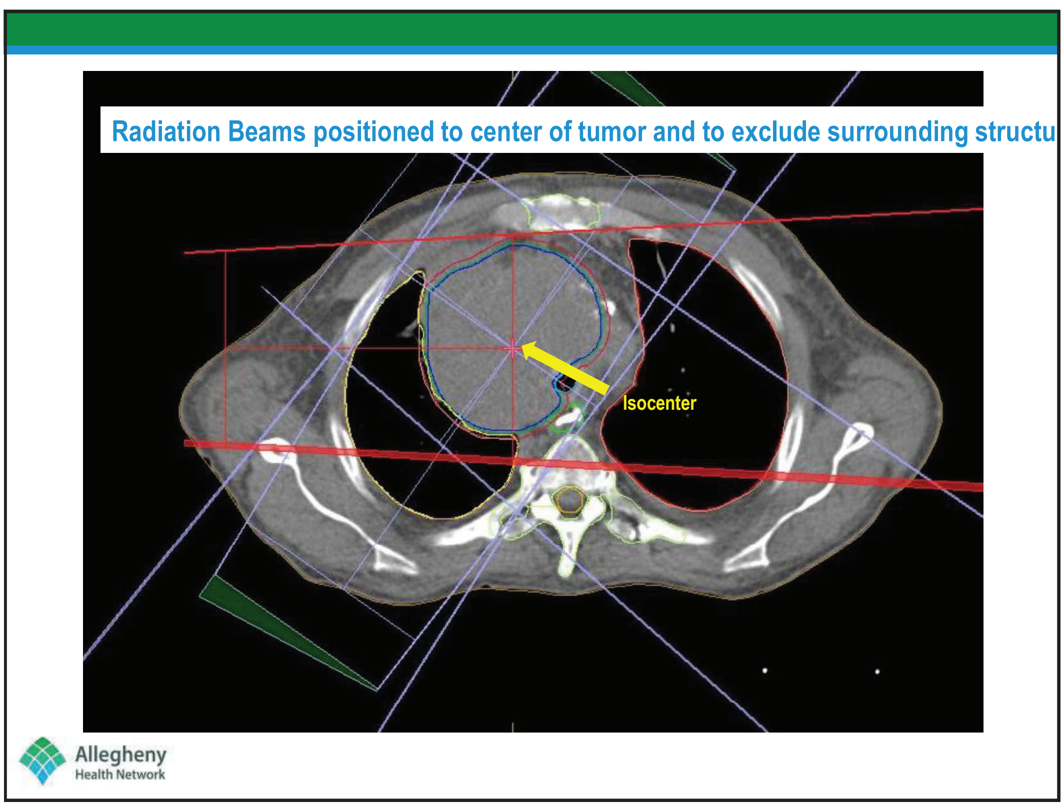
Contours -Outlines of Organs and Tumor





Example of Multimodality Planning- PET scan with the CT for more accurate identification of the tumor or disease

25



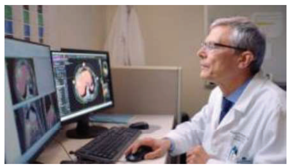
Radiation Beams positioned to center of tumor and to exclude surrounding structu
Isocenter
Allegheny
Health Network

26

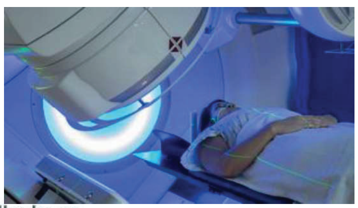
TREATMENT DELIVERY

All of the information from treatment planning is transferred to a specialized radiation oncology charting system for treatment delivery "Mosaiq"

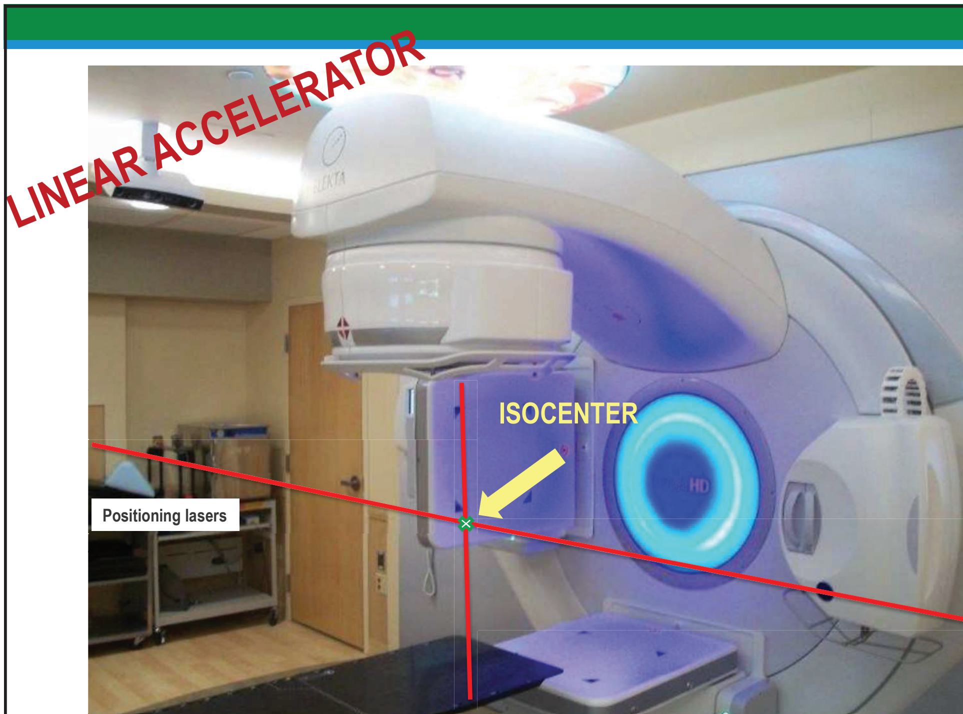
Treatment Panning System



Mosaiq EMR



Linear Accelerlator "Treatment Machine"

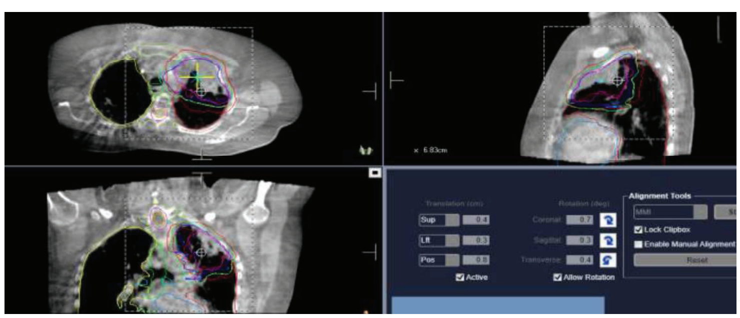


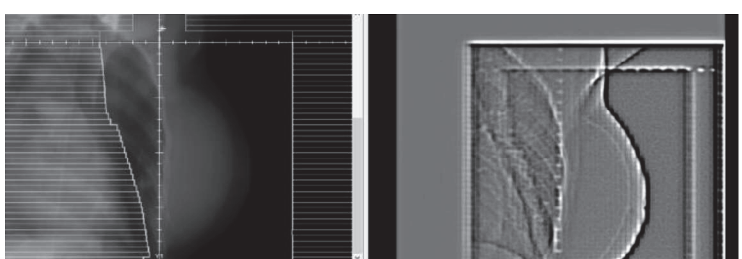
Radiation treatment

- Patient lays on treatment table
- Patient is re-positioned using the devices and marks made from the CT day
- Adjustments are made to "localize the target"
- Images are acquired to confirm accurate position of the beam for treatment
- Patient is instructed to hold still and breath normally
- Therapist are outside treatment room when radiation beam is on
- Patient can be visualized with in room cameras and an intercom system
- Overhead music can be played if patient chooses to
- Patients can not feel the radiation
- Patient can not see the radiation
- Patient set up and treatment time averages 15-20 minutes
- Patients can eat & drink normally before & after treatments unless specifically ordered otherwise by the physician

Allegheny Health Network

Verification Imaging - 3D or 2D





Allegheny Health Network

PATIENT JOURNEY (CONTINUED)

Radiation treatment – the start of radiation therapy must have 2 consecutive days to allows for dose accumulation and aid in slowing down cancer cell growth. This also allows time for the good/healthy tissues to regenerate. SBRT is an example of a treatment that this rule does not usually apply.

On Treatment Visits – both the physician and the nurse see the patient once every 5 fractions that they receive. The nurse schedules these appointments according to the physicians schedule.

Allegheny Health Network

Treatment has started (External Beam/Special Procedures)

On Treatment Visits (OTV)

- Review schedule with patient
- Reinforce education
- Patient has weekly visit with Physician & RN, more frequently if needed
- Assesses and monitor acute side effects
  - Site specific, dependent upon area that we are treating
- Reassess if needed
  - Changes made in plan of care (medications ordered)
  - Pain management
  - Change in weight
  - Change in mental status
  - Change in ADL's
- Collaboration between health team to modify plan of care as needed

Allegheny Health Network

During the weekly On Treatment Visits (OTV)

Focused Assessments

How many treatments have been completed
How are the patients managing daily treatments
Discuss expected side effects, are they displaying or reporting symptoms

Toxicity grading completed

Completed weekly using the CTCAE (Common Terminology Criteria for Adverse Side Effects), currently completed n Mosaiq (Rad Onc EMR)
With toxicity >3 or patient placed on treatment break, chart reviewed in department M&M rounds

Interventions and self-teaching

Acute side affects assessed according to system/site of treatment

Referrals to other disciplines

Pain Management, Dietary, Social Work, Financial Counselor, Oncology Rehab, etc

Allegheny Health Network

Discharge of treatment patient

Patients are given AVS to include:

- Number of treatments received
- Site that has been treated
- Acute side effects that may continue for limited time period
- Patient self-care and interventions
- Important symptoms that patient is to report
- Follow-up appointments
- Scans and testing to be completed

Allegheny Health Network

35

Follow-up

Initial follow-up with the Radiation Oncologist

- Assess for acute side effects(1-3 months post treatment)
- Discuss with patient the need to report bothersome, persistent or concerning symptoms
- Reinforce and reeducated self care
- Assess for other needed appointments, scans/labs required

Allegheny Health Network

36

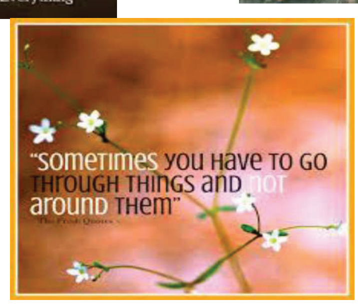
Follow-up

After initial recovery

- Assess for chronic side effects (6months to years later)
- Discuss with patient continued need to communicate any persistent symptoms or concerns
- Teach the normal course for surveillance & follow-up
- Coordination of care between providers
- Review health promotion strategies / screenings
- Offering support both psychosocial or physical
- The patient can remain in follow-up months to years post treatment

Allegheny Health Network

Questions



Allegheny Health Network

2026 Fundamentals of Oncology Day 1 Evaluation