Understanding Pediatric Radiation Therapy

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Introduction to Radiation Oncology

- Radiation therapy, or radiotherapy, is the use of various forms of radiation to safely and effectively treat cancer and other diseases.
- Radiation therapy has been an effective tool for treating cancer for more than 100 years.
- About two-thirds of all cancer patients will receive radiation therapy as part of their treatment.
- Radiation oncologists are doctors trained to use radiation to treat cancer.

Patient being treated with modern radiation therapy equipment.

Brief History of Radiation Therapy

- The first patient was treated with radiation therapy in 1896, just two months after the discovery of the X-ray.
- Rapid technology advances began in the early 1950s, with the invention of the linear accelerator.
- Planning and treatment delivery advances have enabled radiation therapy to be more effective and precise, while decreasing the severity of side effects.

The linear accelerator is still used today to deliver external beam radiation therapy.

How Does Radiation Therapy Work?

- Radiation therapy works by damaging the DNA within cancer cells, destroying their ability to reproduce and causing the cells to die.
- When the damaged cancer cells are destroyed by radiation, the body naturally eliminates them.
- Normal cells can be affected by radiation, but they can repair themselves in a way cancer cells cannot.

When is radiation used?

Tumor boards meet to discuss comprehensive patient treatment plans

- The best treatment plan for each patient is frequently determined by a team of doctors, including a radiation oncologist, a medical oncologist and a surgeon.
- Sometimes radiation therapy is the only treatment a patient needs.
- Other times, it is combined with other treatments, such as surgery and chemotherapy.

Is Radiation Therapy Safe?

- New advances in technology and treatment delivery continue to make radiation safe and effective.

- A team of medical professionals develop and review the treatment plan for each patient to minimize side effects and assure that the area where the cancer is located is receiving the dose of radiation needed.

- The treatment plan and equipment are constantly reviewed to ensure the proper treatment is being given.

Why Use Radiation Therapy?

- To cure cancer:
  - Destroy tumors that have not spread to other body parts.
  - Reduce the risk that cancer will return after surgery or chemotherapy.
  - Shrink the cancer before surgery.
- For palliation (to reduce symptoms):
  - Shrink tumors affecting quality of life, like a lung tumor that is causing shortness of breath.
  - Alleviate pain or neurologic symptoms by reducing the size of a tumor.

Meet the Radiation Oncology Team

A team of highly trained medical professionals work together to make sure you receive the best possible care while you are undergoing radiation therapy.

- **Radiation Oncologist**
  - Oversees the radiation therapy treatments, including working with other members of the radiation therapy team to develop the treatment plan and ensure that each treatment is given safely and accurately.

- **Medical Radiation Physicist**
  - Ensures that complex treatment plans are properly tailored for each patient and directs quality control programs for equipment and procedures.

Meet the Radiation Oncology Team, cont.

- **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 radiation oncologist's prescription and supervision.
- **Radiation Oncology Nurse**
  - Cares for the patient and family by providing education, emotional support and tips for managing side effects.
- **Additional Members of the Team**
  - Social workers, nutritionists, dentists, physical therapists and patient navigators may also assist in a patient's care during their treatment.

What to Expect

- Referral
- Consultation
- Simulation
- Treatment Planning
- Treatment Process

Referral

- A cancer is diagnosed.
- The diagnosing or referring physician reviews potential treatment options with patient.
- Treatment options may include radiation therapy, surgery, chemotherapy or a combination.

It is important for a patients to ask their referring physician about all possible treatment options available to them

Consultation

- Radiation oncologist discusses the radiation therapy treatmer options with patient.
- A treatment plan is developed.
- Care is coordinated with other members of patient's oncology team.

The radiation oncologist will discuss with the patient which type of radiation therapy treatment is best for their type of cancer

Simulation

A CT scan of the area of the body to be treated with radiation. The CT images are reconstructed and used to design the best and most precise treatment plan.

- Patient is set up in treatment position on a dedicated CT scanner.
  - Immobilization devices may be created to assure patient comfort and daily reproducibility.
  - Reference marks or “tattoos” may be placed on patient.

- CT simulation images are often fused with other scans such at MRI or PET scans to create a treatment plan.

Treatment Planning

- The radiation oncologist works with the medical physicist and dosimetrist to create an individualized treatment plan for the patient.

- The treatment is mapped out in detail including the type of machine to be used, the amount of radiation that is needed and the number of treatments that will be given.

Radiation oncologist and dosimetrist creating a treatment plan

Treatment Process

- Each day the patient will check in at the cancer center for treatment.
- They will then be verified as the correct patient and be set up for their treatment.
- The radiation oncologist will monitor the treatments and the patient will meeting with them weekly to discuss their treatment.

During their check in at the cancer center, a patient's identity will be verified.

How is Radiation Therapy Delivered?

The type of treatment used will depend on the location, size and type of cancer.

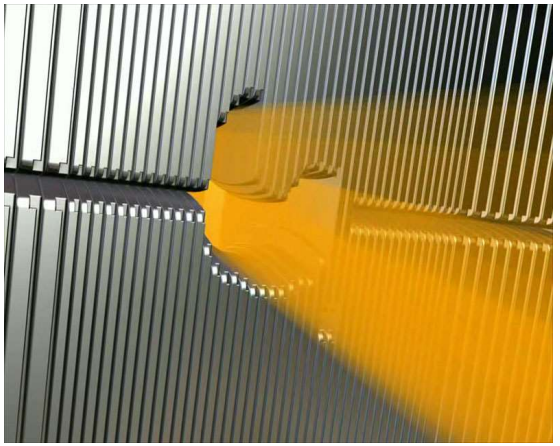
- Radiation therapy can be delivered either externally or internally.
  - *External beam* radiation therapy typically delivers radiation using a linear accelerator.
  - Internal radiation therapy, called *brachytherapy*, involves placing radioactive sources into or near the tumor.

Types of External Radiation Therapy

The type of equipment used will depend on the location, size and type of cancer.

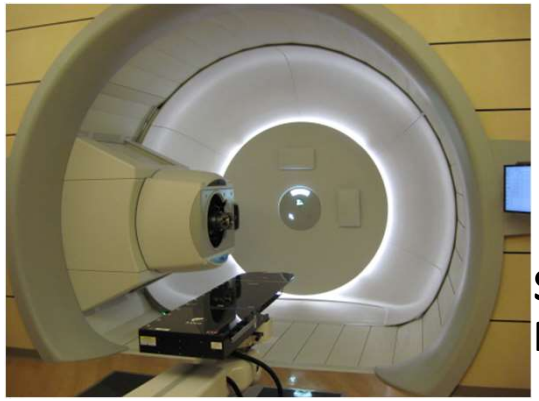
- **Three-dimensional conformal radiation therapy (3D-CRT)**
  - A technique where beams of radiation used in treatment are shaped to match the tumor and are delivered accurately from several directions.

- **Intensity modulated radiation therapy (IMRT)**
  - A form of 3-D CRT in which the physician designates specific doses of radiation that the tumor and normal surrounding tissues receive.



A multileaf collimator is used to shape the radiation beam to match the tumor, sparing surrounding healthy tissue

Types of External Beam Radiation Therapy



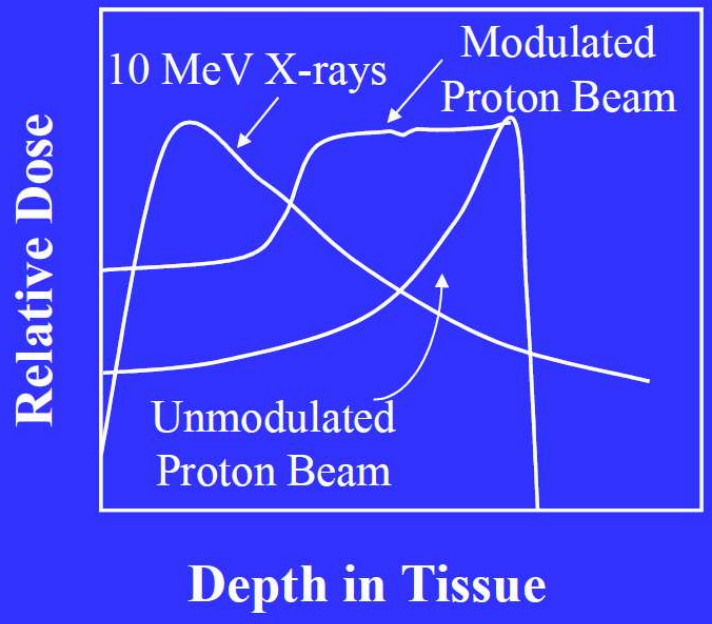
- **Proton Beam Therapy**
  - A type of radiation therapy that uses high-energy beams (protons) rather than X-rays to treat certain types of cancer.
  - Most commonly used in the treatment of pediatric, CNS and intraocular cancers.

Stereotactic Body Radiotherapy or Stereotactic Radiosurgery

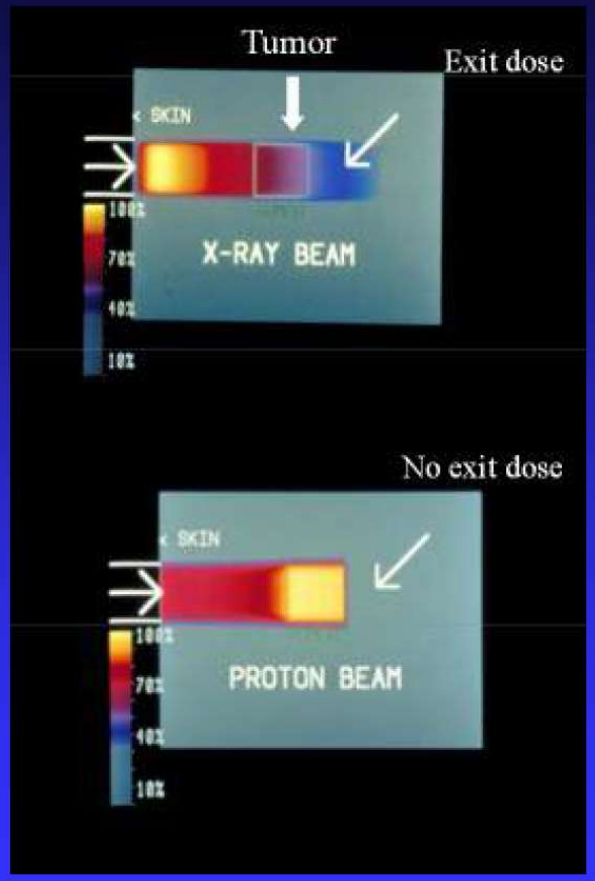
- A specialized form of radiation therapy that focuses high-power energy on a small area of the body. Despite its name, radiosurgery is a treatment, not a surgical procedure.
- Radiosurgery generally implies a single high dose or just a few high dose treatments.

Why protons are advantageous in radiotherapy

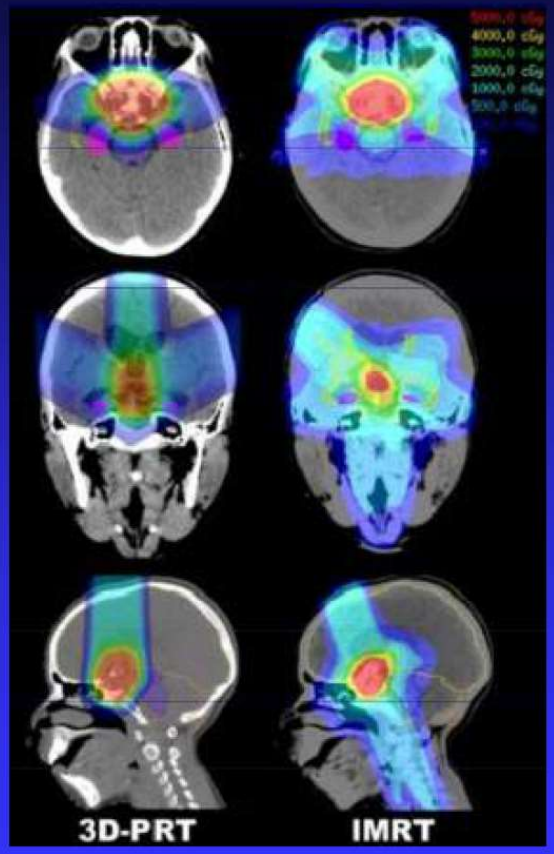
- Relatively low entrance dose
- Maximum dose at depth depending on the energy protons (Bragg peak !)
  ➔ Tumour location
- Energy modulation for broadening maximum
  ➔ Spread out Bragg peak (SOBP)
- Rapid distal fall-off
  ➔ Sparing distal normal tissues



Comparison dose distribution protons versus x-rays



Homogeneous phantom

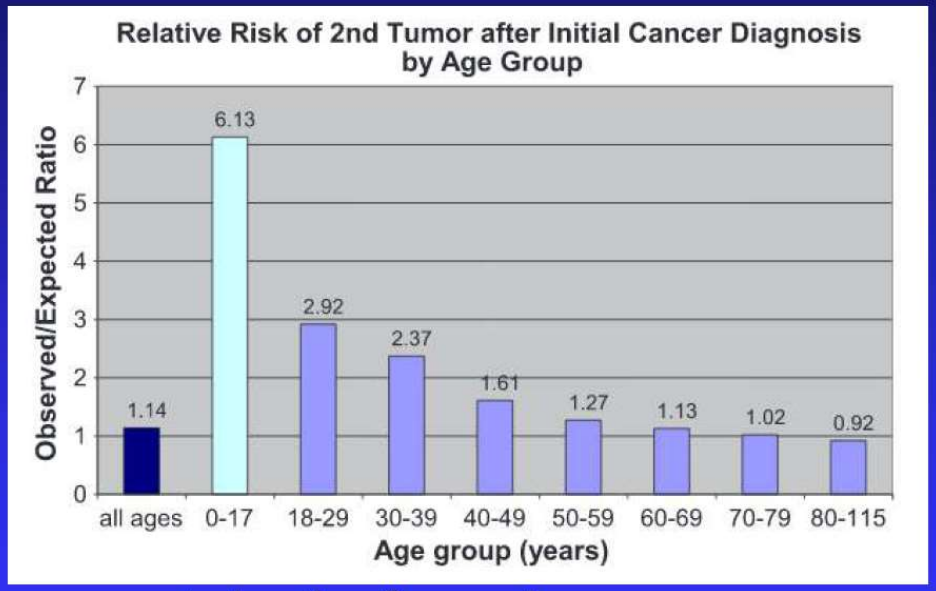


paediatric craniopharyngioma

(A.K. Lee, MD Anderson Hospital)

Secondary neoplasms by age group at diagnosis

- **Relative risk of secondary tumor after initial cancer diagnosis in patients treated with photon RT by age group according to the SEER (Surveillance, Epidem and End Results program) US cancer registries (Curtis NIH 2006)**

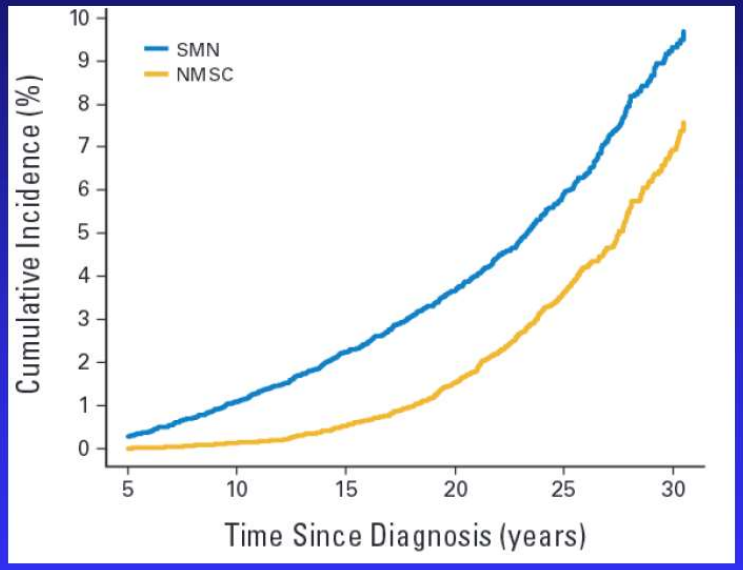


➔ **Observed versus expected ratio of secondary cancers versus age of diagnosis**

➔ **Issue of secondary cancer especially important for paediatric patients !!**

Secondary neoplasms after radiotherapy x-rays in childhood

- Secondary neoplasm incidence data of the childhood Cancer Survivor Study (CCSS) cohort (age at treatment younger than 21 years) treated with photon RT between 1970 and 1986 (Meadows J Clin Onc 2009)



- Data secondary neoplasms (SMN) and non-melanoma skin cancer (NMSC)
  ➔Breast ca, thyroid ca, CNS, sarcoma, leukemia, lymphoma e.a.
- 60-80 % developed in radiation field, 20 % completely out of field (>5 cm)

Risk of secondary malignant neoplasms in pediatric patient treatments of central spine and cranium : comparison of 6 MV IMRT and proton therapy conclusions (Athar et al Rad & Onc 2011)

- After averaging over relevant organs risks of secondary cancer from out-of-field doses risks related to IMRT are less than for PPT proton therapy.
- However within the radiation fields the integral dose to the patient is 2-3 times less in PPT proton therapy compared to IMRT, compensating for the difference in the out-of-field organs risk.
- Without any doubt pencil beam scanning proton (PBS) beams are the best choice from viewpoint of secondary cancer risk
- Furthermore the difference in risk estimation between PPT proton therapy and IMRT is determined by the choice of the biological factors DDREF for photon therapy and w_R for proton induced neutrons (LAR values for PPT can be 10 times higher) !

➔ For a more reliable determination of LAR values of proton therapy and comparison between protons and IMRT a thorough study of w_R for relevant biological endpoints is indicated as well as the availability of epidemiological data.

Internal Radiation Therapy

- Radioactive material is placed into tumor or surrounding tissue.
  - Also called brachytherapy.
  - Radiation sources are placed close to the tumor so large doses can damage the cancer cells.
  - Allows minimal radiation exposure to normal tissue.
  - Radioactive sources used are thin wires, ribbons, capsules or seeds.
  - These can be either permanently or temporarily placed in the body

Radioactive seeds for a permanent prostate implant, an example of low-dose-rate brachytherapy.

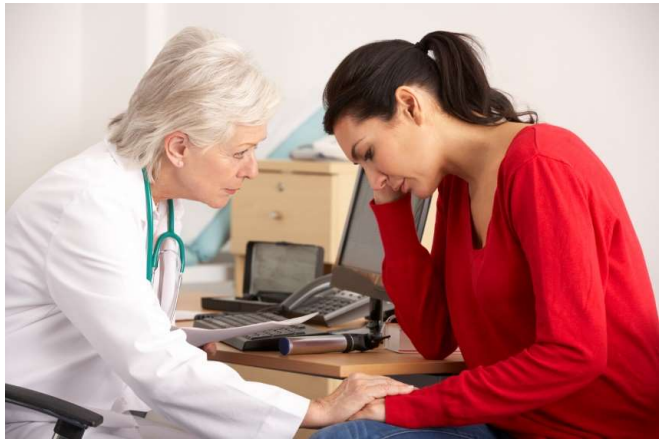
Permanent vs. Temporary Implants

- Permanent implants release small amounts of radiation over a period of several months
  - Examples include low-dose-rate prostate implants (“seeds”),
  - Patients receiving permanent implants may be minimally radioactive and should temporarily avoid close contact with children or pregnant women.

- Temporary implants are left in the body for several hours to several days
  - Patient may require hospitalization during the implant depending on the treatment site ,
  - Examples include low-dose-rate gynecologic implants and high-dose-rate prostate or breast implants,

Side Effects of Radiation Therapy

- Most side effects begin during the second or third week of treatment. Doctors and nurses may prescribe medications to help with these side effects.
- Side effects, like skin redness, are generally limited to the area receiving radiation.
- Fatigue is a common side effect for all cancer patients.
- Side effects may last for several weeks after the final day of treatment.



Side effects vary based on a patient's medical profile or diagnosis

Who is the Cancer Care Team?

All those involved with a patient during and after their care is part of the Cancer Care Team. This includes:

- The Treatment Team including
  - Physicians
  - Nurses
  - Radiation therapists
  - Physicists
  - Dosimetrists
  - Social workers
  - Receptionists
- Family and Friends

The Cancer Care Team, cont.

It is important for the Cancer Care Team to have an open dialogue throughout the treatment process.

- Always ask questions if you have them - there are no dumb questions.
- Always share your concerns – whether you are the patient or the caregiver, discuss your concerns with the medical team during the treatment consultations.
- Do your research – there are many good resources out there to help patients before, during and after their treatment.

Basics of Pediatric Oncology

Objectives

- Review epidemiology of pediatric oncology
- Discuss unique aspects of pediatric oncology treatment
- Discuss general chemotherapy principles in pediatric oncology
- BRIEF review of the most common pediatric malignancies

Pediatric Malignancy Epidemiology

- Rare - 2% of all cancer
- Most often occur before 15 years of age
- Accounts for 10% of childhood deaths
  - most common cause of death from disease
  - second to accidents
- Leukemia, Lymphoma and CNS Tumors are the most common

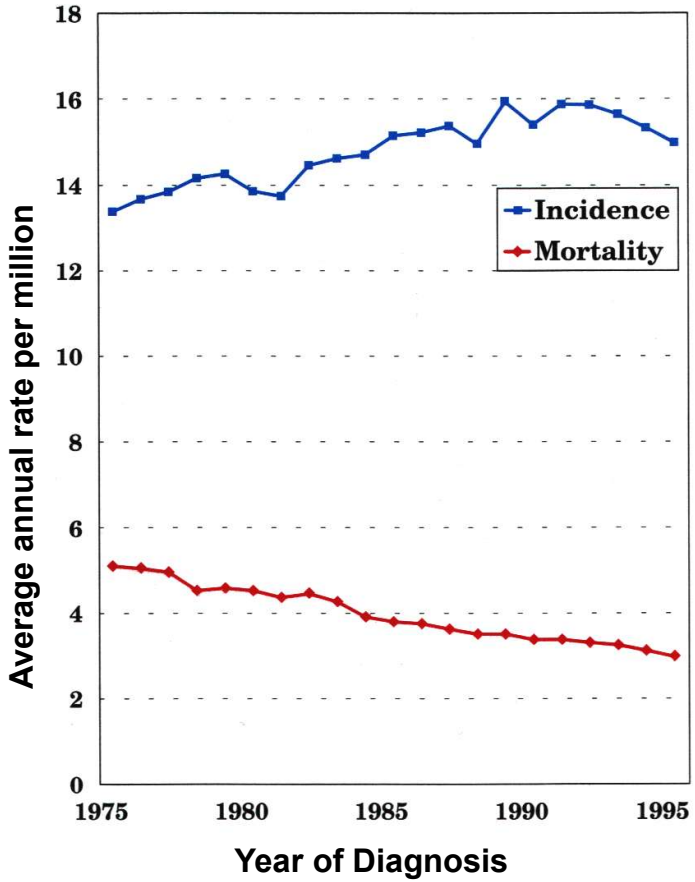
Cancer Treatment in Europe

- >90% of children diagnosed with cancer are seen and treated at a COG affiliated institute
- Overall Survival is > 65% (> 70% ?) in Europe

Predisposing Factors

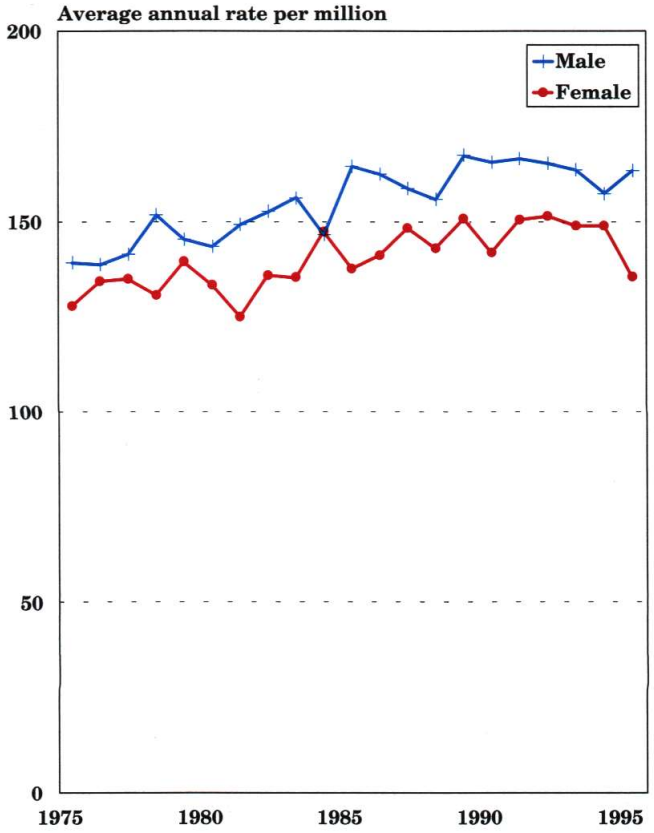
- Genetic
  - Syndromes (trisomy 21), bone marrow failure
- Hereditary
  - Wilms Tumor, Retinoblastoma
- Environmental
  - Radiation, toxins

Trends in age-adjusted SEER incidence and U.S. mortality rates for all childhood cancers age < 20, all races, both sexes, 1975-95



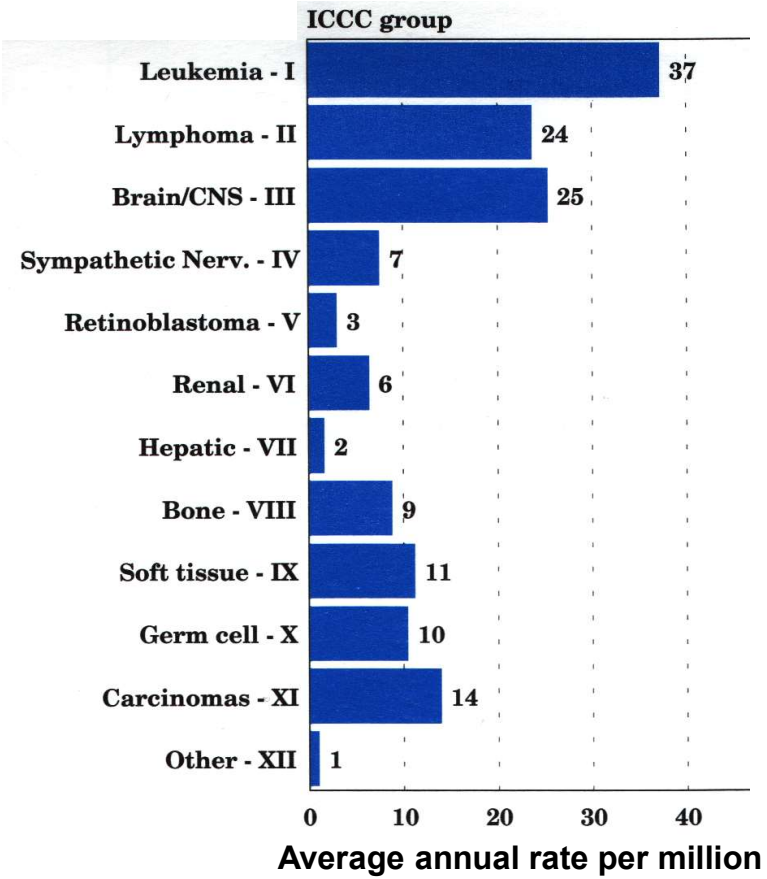
SEER, NCI 1995

Trends in age-adjusted incidence rates for all childhood cancers by sex, age <20 all races combined



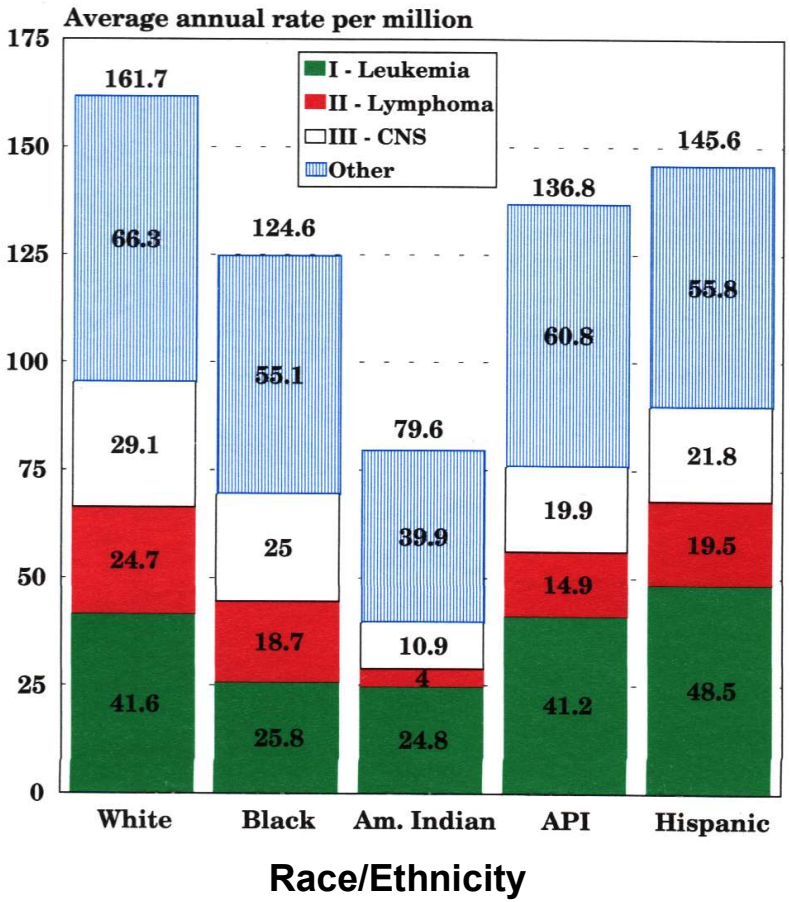
SEER, NCI 1995

Age-adjusted incidence rates for childhood cancer by ICCC groups, age <20 all races, both sexes, SEER, 1975-1995



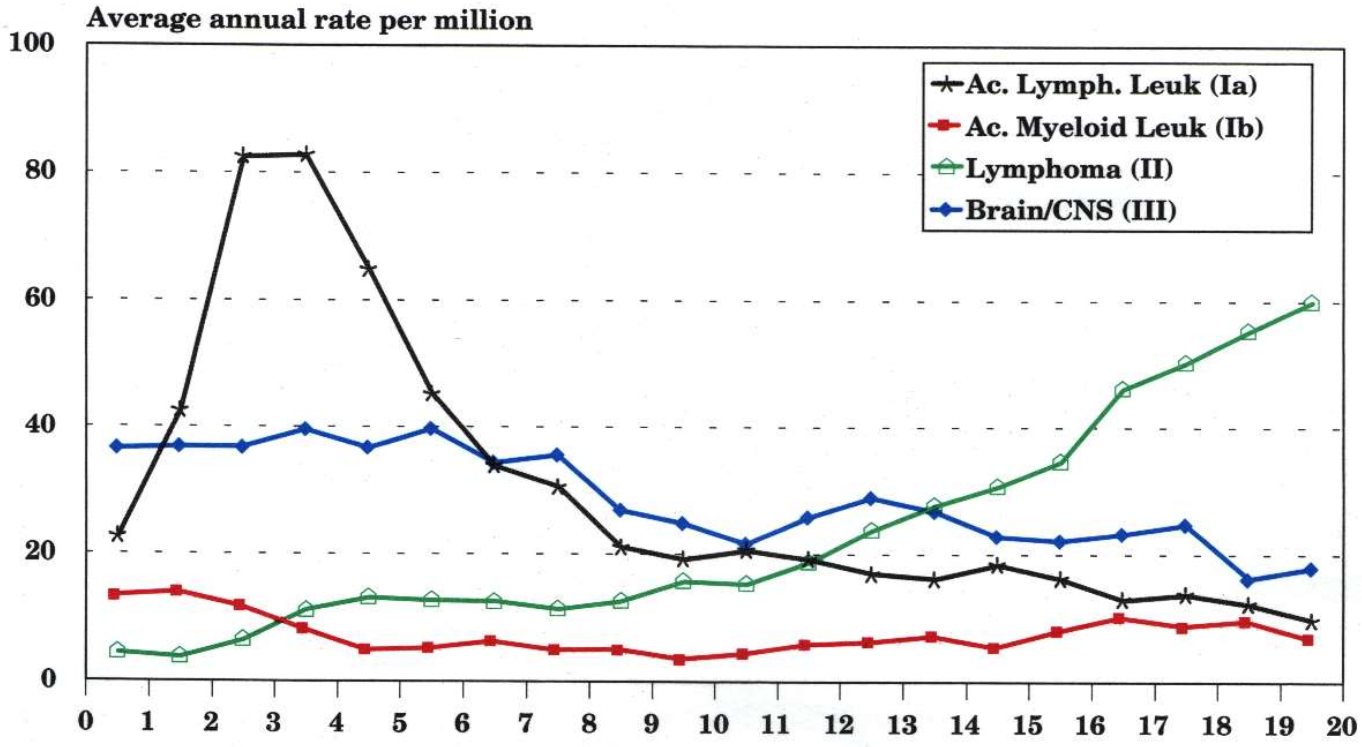
SEER, NCI 1995

Age-adjusted incidence rates for childhood cancer by ICCC groups, and race/ethnicity,age <20, both sexes, SEER 1975-1995



SEER, NCI 1995

Age Specific Incidence rates for childhood cancer by ICCC group, all races, both sexes



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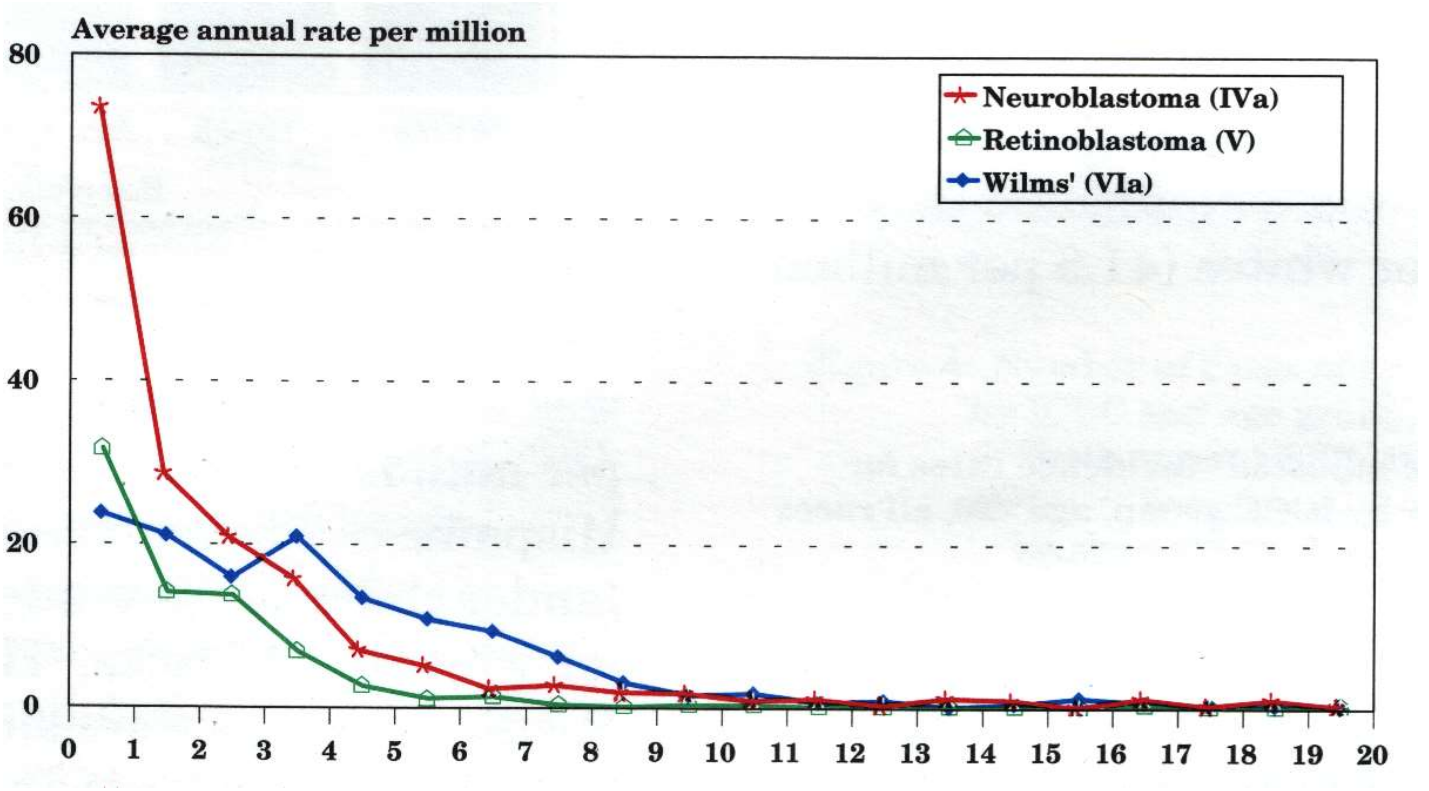

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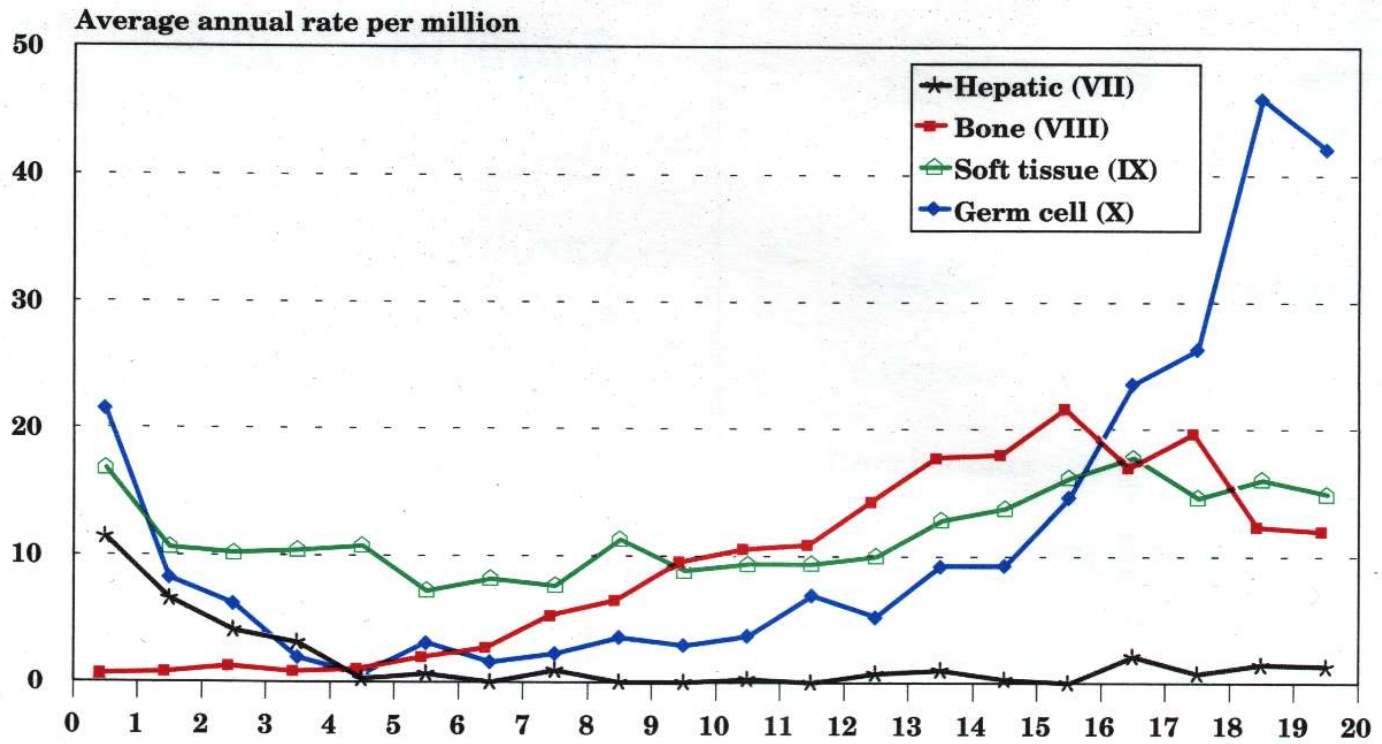

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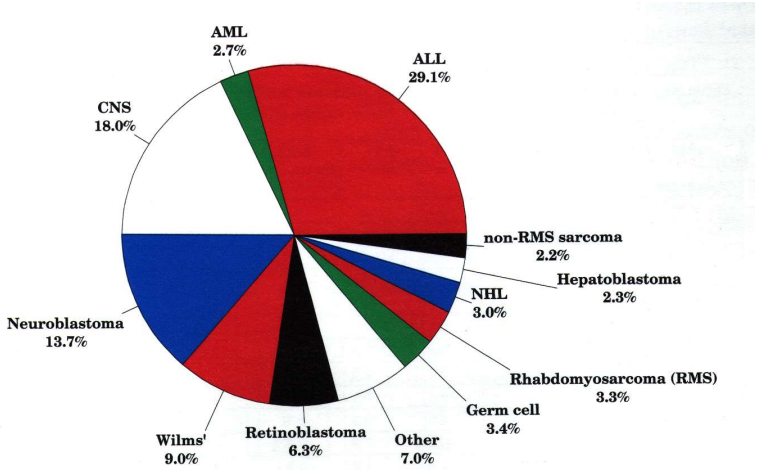
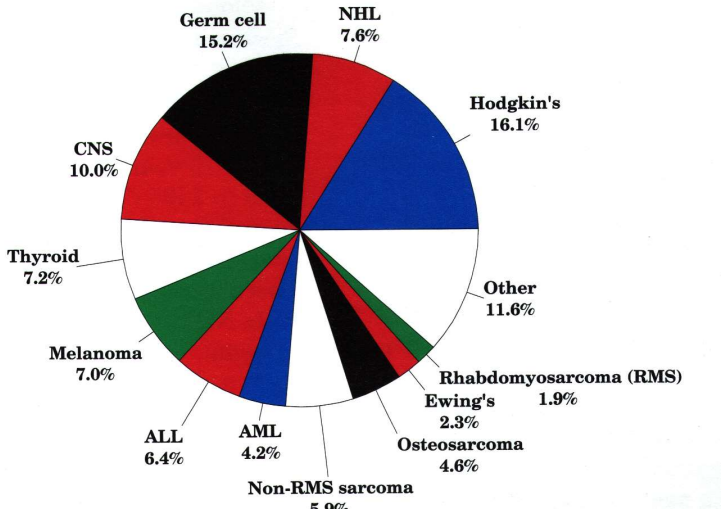


Distribution of Cancer types, ages <5, all races, both sexes



Distribution of Cancer types, ages 15-19, all races, both sexes

SEER, NCI 1995

Age Association with Specific Malignancies

- Classically peak incidence of leukemias, CNS, Wilms and Neuroblastoma in younger age group
- Lymphomas and bone tumors in older age group

Unique Aspects of Pediatric Oncology

- Overall Prognosis is Good - 65%
- Usually otherwise healthy patients
- May have specific sensitivity to treatment
  - CNS sensitivity
  - Growth issues

Unique Aspects of Pediatric Oncology

- Long Term Survivors
  - Second Malignancies
    - **Chemotherapy and radiation therapy**
    - **Development and CNS function**
    - **Cardiac, Renal, and Pulmonary Toxicity**
    - **Reproductive Function**

Unusual Aspects of Pediatric Malignancy

- In general these are rare compared to adult malignancy
- Venous access issues usually more difficult compared to adults
- Psychosocial aspects of treatment

General Principles of Cancer Treatment

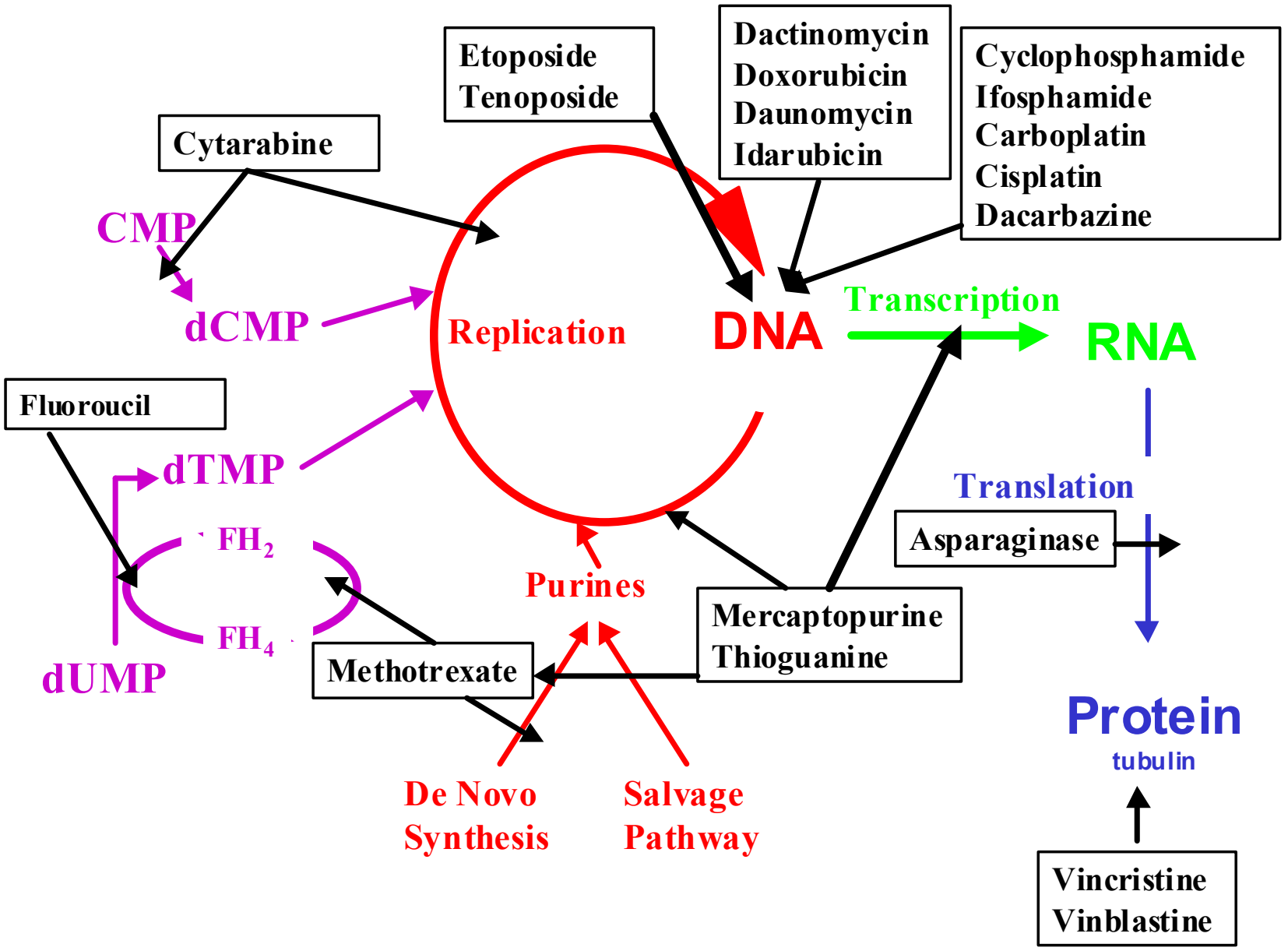
- Biopsy/Definitive Diagnosis Prior to initiation of therapy, use of immunophenotyping, cytogenetics
- Staging
- Local Therapy
  - Surgery
  - Radiation Therapy
  - Chemotherapy
    - aids in better resection in some cases

General Principles of Cancer Treatment

- Systemic Therapy
  - Chemotherapy
    - **Leukemias**
    - **For solid tumors known to have risk for recurrence/metastasis**
  - BMT

General Principles of Chemotherapy

- Addition of chemotherapy (1950s) has improved prognosis dramatically
- Chemotherapy can be used as primary therapy and as adjuvant therapy
- Combination Chemotherapy has been shown to be essential, especially in ALL
  - Single drug induces remission in 65% of ALL


Etoposide
Tenoposide
Dactinomycin
Doxorubicin
Daunomycin
Idarubicin
Cyclophosphamide
Ifosphamide
Carboplatin
Cisplatin
Dacarbazine
Cytarabine
CMP
dCMP
Replication
DNA
Transcription
RNA
Fluoroucil
dTMP
FH2
FH4
dUMP
Purines
Translation
Asparaginase
Mercaptopurine
Thioguanine
Methotrexate
Protein
tubulin
De Novo
Synthesis
Salvage
Pathway
Vincristine
Vinblastine

Combination Chemotherapy

- 4 drug induction achieves remission in 95% of ALL
- Kills non cross resistant cells

General Principles of Chemotherapy

- Duration of Therapy
- Dose intensity
- Problems
  - Toxicity
  - Drug Interaction
  - Resistance