Update on Cancer in the United States and Special Ophthalmic Considerations for Cancer Patients (Stella K. Kim, MD)

Overview of cancer statistics/trends in US

What’s new in cancer treatment modalities.

Update on common cancers

Ocular toxicities from cancer treatment
Update on Cancer in the United States and Special Ophthalmic Considerations for Cancer Patients (Stella K. Kim, MD)

**Cancer Facts & Figures 2008**

**2008 Estimated US Cancer Deaths**

<table>
<thead>
<tr>
<th>Tumor Type</th>
<th>Men 254,120</th>
<th>Women 271,530</th>
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<tbody>
<tr>
<td>Lung &amp; bronchus</td>
<td>31%</td>
<td>26%</td>
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<tr>
<td>Prostate</td>
<td>10%</td>
<td>15%</td>
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<tr>
<td>Colon &amp; rectum</td>
<td>8%</td>
<td>9%</td>
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<tr>
<td>Pancreas</td>
<td>6%</td>
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<tr>
<td>Liver &amp; intrahepatic bile duct</td>
<td>4%</td>
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<td>Leukemia</td>
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<tr>
<td>Esophagus</td>
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<td>3%</td>
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<tr>
<td>Urinary bladder</td>
<td>3%</td>
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<tr>
<td>Non-Hodgkin lymphoma</td>
<td>3%</td>
<td>2%</td>
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<tr>
<td>Kidney &amp; renal pelvis</td>
<td>3%</td>
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<tr>
<td>All other sites</td>
<td>24%</td>
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**US Mortality, 2005**

<table>
<thead>
<tr>
<th>Rank</th>
<th>Cause of Death</th>
<th>No. of deaths</th>
<th>% of all deaths</th>
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<tbody>
<tr>
<td>1</td>
<td>Heart Diseases</td>
<td>652,001</td>
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<tr>
<td>2</td>
<td>Cancer</td>
<td>597,312</td>
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<tr>
<td>3</td>
<td>Cerebrovascular diseases</td>
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<td>5</td>
<td>Accidents (unintentional injuries)</td>
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<td>Diabetes mellitus</td>
<td>75,119</td>
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<td>7</td>
<td>Alzheimer disease</td>
<td>71,599</td>
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<tr>
<td>8</td>
<td>Influenza &amp; pneumonia</td>
<td>63,001</td>
<td>2.6</td>
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<tr>
<td>9</td>
<td>Nephritis*</td>
<td>43,901</td>
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<td>10</td>
<td>Septicemia</td>
<td>34,136</td>
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</table>

*Includes nephrotic syndrome and nephrosis.
Update on Cancer in the United States and Special Ophthalmic Considerations for Cancer Patients (Stella K. Kim, MD)
Cancer Incidence Rates* by Sex, US, 1975-2004

Rate Per 100,000

Men

Both sexes

Women


Cancer Incidence Rates* Among Men, US, 1975-2004

Rate Per 100,000

Prostate

Lung & bronchus

Cancer and rectum

Urinary bladder

Non-Hodgkin lymphoma

Melanoma of the skin


Cancer Incidence Rates* Among Women, US, 1975-2004

Rate Per 100,000

Breast

Cancer and rectum

Lung & bronchus

Ovarian cancer

Uterine corpus


*Age-adjusted to the 2000 US standard population and adjusted for delays in reporting.

Source: Surveillance, Epidemiology, and End Results Program Delay-adjusted incidence database:
### Lifetime Probability of Developing Cancer, Men, 2002-2004*

<table>
<thead>
<tr>
<th>Site</th>
<th>Risk</th>
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<tr>
<td>All sites†</td>
<td>1 in 2</td>
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<tr>
<td>Prostate</td>
<td>1 in 6</td>
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<tr>
<td>Lung and bronchus</td>
<td>1 in 13</td>
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<tr>
<td>Colon and rectum</td>
<td>1 in 18</td>
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<tr>
<td>Urinary bladder‡</td>
<td>1 in 27</td>
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<tr>
<td>Melanoma</td>
<td>1 in 41</td>
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<tr>
<td>Non-Hodgkin lymphoma</td>
<td>1 in 46</td>
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<tr>
<td>Kidney</td>
<td>1 in 59</td>
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<tr>
<td>Leukemia</td>
<td>1 in 67</td>
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<tr>
<td>Oral Cavity</td>
<td>1 in 71</td>
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<tr>
<td>Stomach</td>
<td>1 in 88</td>
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</table>

* For those free of cancer at beginning of age interval.
† All sites exclude basal and squamous cell skin cancers and in situ cancers except urinary bladder.
‡ Includes invasive and in situ cancer cases.

### Lifetime Probability of Developing Cancer, Women, US, 2002-2004*

<table>
<thead>
<tr>
<th>Site</th>
<th>Risk</th>
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<tr>
<td>All sites†</td>
<td>1 in 3</td>
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<tr>
<td>Breast</td>
<td>1 in 8</td>
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<tr>
<td>Lung &amp; bronchus</td>
<td>1 in 16</td>
</tr>
<tr>
<td>Colon &amp; rectum</td>
<td>1 in 19</td>
</tr>
<tr>
<td>Uterine corpus</td>
<td>1 in 41</td>
</tr>
<tr>
<td>Non-Hodgkin lymphoma</td>
<td>1 in 53</td>
</tr>
<tr>
<td>Melanoma</td>
<td>1 in 61</td>
</tr>
<tr>
<td>Ovary</td>
<td>1 in 71</td>
</tr>
<tr>
<td>Pancreas</td>
<td>1 in 76</td>
</tr>
<tr>
<td>Urinary bladder‡</td>
<td>1 in 85</td>
</tr>
<tr>
<td>Uterine cervix</td>
<td>1 in 142</td>
</tr>
</tbody>
</table>

* For those free of cancer at beginning of age interval.
† All sites exclude basal and squamous cell skin cancers and in situ cancers except urinary bladder.
‡ Includes invasive and in situ cancer cases.


<table>
<thead>
<tr>
<th></th>
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<tbody>
<tr>
<td>All sites</td>
<td>50</td>
<td>54</td>
<td>56</td>
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<tr>
<td>Breast (female)</td>
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<td>79</td>
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<td>51</td>
<td>59</td>
<td>65</td>
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<tr>
<td>Leukemia</td>
<td>35</td>
<td>42</td>
<td>50</td>
</tr>
<tr>
<td>Lung and bronchus</td>
<td>13</td>
<td>13</td>
<td>16</td>
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<tr>
<td>Melanoma</td>
<td>82</td>
<td>87</td>
<td>92</td>
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<tr>
<td>Non-Hodgkin lymphoma</td>
<td>48</td>
<td>53</td>
<td>64</td>
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<td>37</td>
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<td>45</td>
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<td>Pancreas</td>
<td>2</td>
<td>3</td>
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<tr>
<td>Prostate</td>
<td>69</td>
<td>76</td>
<td>99</td>
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<tr>
<td>Rectum</td>
<td>49</td>
<td>57</td>
<td>66</td>
</tr>
<tr>
<td>Urinary bladder</td>
<td>74</td>
<td>78</td>
<td>81</td>
</tr>
</tbody>
</table>

† Five-year relative survival rates based on follow up of patients through 2004.

Source: Surveillance, Epidemiology, and End Results Program, 1975-2004, Division of Cancer Control and Population Sciences, National Cancer Institute.
Cancer Incidence & Death Rates* in Children 0-14 Years, 1975-2004

*Age-adjusted to the 2000 Standard population.

Cancer Incidence Rates* in Children 0-14 Years by Sex, 2000-2004

*Per 100,000, age-adjusted to the 2000 US standard population.

Cancer Death Rates* in Children 0-14 Years by Sex, US, 2000-2004

*Per 100,000, age-adjusted to the 2000 US standard population.
Tobacco Use in the US, 1900-2004

Per capita cigarette consumption

Male lung cancer death rate

Female lung cancer death rate

Year

0

500

1000

1500

2000

2500

3000

3500

4000

4500

5000

1900

1905

1910

1915

1920

1925

1930

1935

1940

1945

1950

1955

1960

1965

1970

1975

1980

1985

1990

1995

2000

Per capita cigarette consumption

Male lung cancer death rate

Female lung cancer death rate

Year

0

10

20

30

40

50

100

110

120

130

140

150

160

170

180

190

200

210

220

230

240

250

260

270

280

290

300

310

320

1965

1974

1979

1983

1985

1990

1992

1994

1995

1997

1998

1999

2000

2001

2002

2003

2004

2005

2006

Year

Prevalence (%)

Men

Women

Trends in Cigarette Smoking Prevalence* (%), by Sex, Adults 18 and Older, US, 1965-2006

*Redesign of survey in 1997 may affect trends.


*Overweight is defined as at or above the 95th percentile for body mass index by age and sex based on reference data.

Trends in Overweight* Prevalence (%), Adults 18 and Older, US, 1992-2006

Less than 50% 50 to 55% More than 55% State did not participate in survey


Screening Guidelines for the Early Detection of Breast Cancer, American Cancer Society

• Yearly mammograms are recommended starting at age 40.
• A clinical breast exam should be part of a periodic health exam, about every 3 years for women in their 20s and 30s, and every year for women 40 and older.
• Women should know how their breasts normally feel and report any breast changes promptly to their health care providers. Breast self-exam is an option for women starting in their 20s.
• Screening MRI is recommended for women with an approximately 20%-25% or greater lifetime risk of breast cancer, including women with a strong family history of breast or ovarian cancer and women who were treated for Hodgkin disease.

Screening Guidelines for the Early Detection of Cervical Cancer, American Cancer Society

• Screening should begin approximately three years after a woman begins having vaginal intercourse, but no later than 21 years of age.
• Screening should be done every year with regular Pap tests or every two years using liquid-based tests.
• At or after age 30, women who have had three normal test results in a row may get screened every 2-3 years. However, doctors may suggest a woman get screened more frequently if she has certain risk factors, such as HIV infection or a weakened immune system.
• Women 70 and older who have had three or more consecutive Pap tests in the last ten years may choose to stop cervical cancer screening.
• Screening after a total hysterectomy (with removal of the cervix) is not necessary unless the surgery was done as a treatment for cervical cancer.
Screening Guidelines for the Early Detection of Colorectal Cancer and Adenomas, American Cancer Society 2008

Beginning at age 50, men and women should follow one of the following examination schedules:

- A flexible sigmoidoscopy (FSIG) every five years
- A colonoscopy every ten years
- A double-contrast barium enema every five years
- A Computerized Tomographic (CT) colonography every five years
- A guaiac-based fecal occult blood test (FOBT) or a fecal immunochemical test (FIT) every year
- A stool DNA test (interval uncertain)

Tests that detect adenomatous polyps and cancer
Tests that primarily detect cancer

People who are at moderate or high risk for colorectal cancer should talk with a doctor about a different testing schedule.

Screening Guidelines for the Early Detection of Prostate Cancer, American Cancer Society

The prostate-specific antigen (PSA) test and the digital rectal examination (DRE) should be offered annually, beginning at age 50, to men who have a life expectancy of at least 10 years.

Men at high risk (African-American men and men with a strong family history of one or more first-degree relatives diagnosed with prostate cancer at an early age) should begin testing at age 45.

For men at average risk and high risk, information should be provided about what is known and what is uncertain about the benefits and limitations of early detection and treatment of prostate cancer so that they can make an informed decision about testing.

Recent* Prostate-Specific Antigen (PSA) Test Prevalence (%), by Educational Attainment and Health Insurance Status, Men 50 Years and Older, US, 2001-2006

* A prostate-specific antigen (PSA) test within the past year. Note: Data from participating states and the District of Columbia were aggregated to represent the United States.

Overview of cancer trends in US

GOOD NEWS

DECLINING TRENDS: Deaths from 4 most common cancers (lung, prostate, breast, colorectal) and all cancers combined.
Rate of cancer incidence – relatively stable since mid 1990s.
Screening for breast and cervical cancer remains high. Colorectal screening, while still low, is increasing
Better sun-screening

BAD NEWS

Certain cancers incidence rising
• Non-Hodgkins lymphoma, cancer of the lung, leukemia, myeloma, cutaneous melanoma, thyroid, kidney, liver and esophagus, and in women (lung, bladder, and brain) and in men (prostate and testis)
• Childhood cancer
Death rate in women for lung cancer, in men for esophagus and thyroid cancer rising
Cancer treatment spending rising
Overview of common cancers

-Solid organ cancer
  - Prostate
  - Breast
  - Lung
  - GI/Colon

-Liquid cancer
  - Leukemias (AML, ALL, CML, CLL)
  - Lymphoid (Large Bcell, Mantle, Follicular, T cell, low grade etc)
Cancer Treatment Armamentarium

- Surgery
- Radiation
  - External beam, implant (brachytherapy), charged particles (proton, carbon)
- Chemotherapy
  - neoadjuvant – before surgery
  - adjuvant – after surgery
  - chemoradiation
- Stem Cell Transplantation (Autologous or Allogeneic)

What's Hot??

- Surgery
  - New Approach (ex. sentinel node biopsy)
  - New Technology (robotics)
- Radiation
  - Conformal treatment; Gating
  - Charged particle (proton, carbon ions)
  - Hypo or hyper fractionation
- Chemotherapy
  - Biologics and small molecule treatments
  - Bioimmunotherapy
- Stem Cell Transplantation
  - Graft vs. Tumor effect

Ocular considerations for cancer patients

- Uniques features of the primary cancer to the eye and orbit.
- Direct toxicities of treatment
- Late effects of treatment
- Surgical consideration for cancer patients
### Overview of common cancers

- **Solid organ cancer**
  - Breast
  - Prostate
  - Lung
  - GI/Colon

- **Liquid cancer**
  - Leukemias (AML, ALL, CML, CLL)
  - Lymphoid (Large Bcell, Mantle, Follicular, T cell, low grade etc)

### Breast CA

- 1/8 chance of developing invasive breast ca (life time risk)
- 2.5 million breast cancer survivors in US
- Death rate declining since 1990. Early detection.

### Breast Cancer: Treatment

- Surgery
- Chemotherapy (many combination, including Taxotere
- Radiation: External beam, hypofractionation, intracavitary brachytherapy.
- Hormone: Tamoxifen (antiestrogen), Aromatase inhibitors (Femara, Arimidex, Aromasin), progesterone-like drug (Megace).
- Targeted therapy: HER2/neu (Trastuzumab(Herceptin); Avastin
Ocular considerations: Breast Cancer

- Direct metastatic lesions in the choroid – common
- Taxotere (Epiphora).
- Orbit: Scirrhouss met (Enophthalmos)

Epiphora and Taxotere
Punctal/Canaliculforce stenosis

Q-weekly patients with epiphora all had moderate (50%) to severe (50%) punctal/canaliculforce stenosis; Annal Oncal 2002

Start of epiphora at 4-16 weeks (mean 7 weeks) for q-weekly patients, dose dependant; Annal Oncal 2002

Epiphora and Taxotere
Evaluation/ Management

Complete examination
Shirmer’s test
Probe/irrigation- assessment of canaliculforce stenosis
Medical management: Trial of topical steroid QID, 1gtt/week taper over 1 month.
Epiphora and Taxotere Evaluation/Management

Surgery (silicone intubation; Jones tube placement, dacryocystorhinostomy, DCR) can be performed safely and effectively during q-wkly administration.

Mean interval between start of Taxotere treatment to surgery 14 - 44 weeks (17wks for silicone tube; 30 wks for DCR).

Arch Ophthalmol 2001

Botulinum Toxin for Palliative Treatment of Epiphora in a Patient with Canicular Obstruction

Single Injection (0.1ml)
Lasting 5 months.

Had decrease in Schirmer's (15 to 8mm)

Injection of 5 U of botulinum toxin

Enophthalmos
Biopsy: Scirrhus Met From Breast CA
 Locally treated with XRT
 Systemically with chemo

Prostate CA: Most common for men
- Risk factors:
  - Age (2/3 over 65)
  - Race (African Americans)
  - Nationality (North America; Northwestern Europe)
  - Family history (tends to be positive)
  - Diet (uncertain – higher for more meat/less fruit diet)
  - Unclear risks
  - Obesity (higher mortality; higher stage of disease)
  - Infection/inflammation?
  - Beta-carotene?
  - Prevention (?)
  - Diet (? Vitamin E or Selenium – study ongoing)

Prostate Cancer: Treatment
- Surgery
  - Radical Prostatectomy
  - Approach: Retropubic, Perineal
  - Laparoscopic Radical Prostatectomy
  - Robotic-assisted Laparoscopic Radical Prostatectomy (limited availability)
- Radiation Therapy
  - Radioactive Implant
  - IMRT (intensity modulated radiotherapy)
  - Proton therapy
  - Adjuvant hormone therapy (Lupron monthly injections)
  - Chemotherapy
Ocular considerations: Prostate Cancer
- Taxotere: Epiphora common:
  Punctal/Canalicular stenosis (more commonly seen in breast ca patients on Taxotere)
- Direct metastatic lesions in the choroid – exceedingly rare
  - Bone Mets are common (less for parenchymal mets)

Lung CA: Leading cause of death (men/women)
- Non-small cell (NSCLC): 85-90% of lung ca
  - Squamous cell (25-30%) – mostly smoking related
  - Adenocarcinoma (40%)
  - Large-cell (undifferentiated) carcinoma (10-15%) Most aggressive
- Small cell lung CA (SCLC)
- Mixed small cell/large cell (both features present)

NSCLC: Treatment
- Surgery
  - Pneumectomy
  - Lobectomy
  - Segmentectomy (wedge)
  - Video-assisted thoracic surgery (VATS) – early stage
- Radiation
  - Gated 4-D conformal therapy.
- Chemotherapy/Targeted therapies
  - Avastin (anti-vegf)
  - Epidermal growth factor receptor (EGFR inhibitors)
Iressa
• NSCLC, H/N, others
• Mechanism:
  - Epidermal growth factor receptor-tyrosine kinase inhibitor
• Oral agent, continuous treatment

Iressa – Severe MGD
72 yow with stage IV NSCL with severe burning and itching. No previous ocular hx.
On Iressa for 1 month

Tarceva
• NSCLC, and others
• Mechanism:
  - Epidermal growth factor receptor-tyrosine kinase inhibitor
• Oral agent, continuous treatment
Erbitux

• Met Colon Ca, H/N, NSCLC
• Mechanism:
  - Epidermal growth factor receptor-tyrosine kinase inhibitor
• Injection

Colon and Rectal CA

- 95% are adenocarcinomas
- 3rd most common for men and women
- Screening has helped to remove polyps and detect early disease.

Update on Ocular Complications of Systemic Cancer Chemotherapy

<table>
<thead>
<tr>
<th>Side Effect</th>
<th>5-FU</th>
<th>Capecitabine</th>
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<th>Vincristine</th>
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[Table: Side Effects and Treatment]
## Update on Ocular Complications of Systemic Cancer Chemotherapy

<table>
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<th>Agent</th>
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<td>Breast cancer</td>
<td>Anthracyclines</td>
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<td>Stem Cells</td>
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## Ocular Considerations

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<th>Agent</th>
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<tbody>
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<td>Breast cancer</td>
<td>Anthracyclines</td>
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<td></td>
<td>Radiation Therapy</td>
</tr>
<tr>
<td></td>
<td>Stem Cells</td>
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</table>

## Additional Considerations

- Anthracyclines: Include doxorubicin and epirubicin. These agents are used in the treatment of many types of cancer, including breast cancer, lymphoma, and leukemia. They work by blocking the ability of cancer cells to grow and multiply. However, they also affect healthy cells, which can cause serious side effects.

- Cytotoxic drugs: These are a broad category of chemotherapy agents that work by blocking the cell cycle and preventing cancer cells from growing and dividing. They include agents such as cyclophosphamide, cisplatin, and paclitaxel.

- Chemotherapeutic agents: These are more specifically designed to target cancer cells. They work by interfering with the DNA of cancer cells, which can cause them to stop growing and divide.

- Surgery: Surgical procedures can be used to remove cancerous tumors or to reduce their size before chemotherapy treatment. This can help to improve the effectiveness of chemotherapy.

- Radiation Therapy: Radiation therapy uses high-energy particles or waves to destroy cancer cells. It can be used to treat cancer that has spread beyond the primary site of the tumor or to reduce the size of a tumor before chemotherapy.

- Stem Cells: Stem cell transplantation can be used to treat certain types of cancer. It involves removing stem cells from a healthy patient, growing them in a laboratory, and then replacing them in the patient to help fight the cancer.

- Additional Considerations: It is important to consider the individual patient's medical history, current health status, and overall health when selecting the appropriate treatment options. This can help to minimize the risks and side effects associated with chemotherapy.

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Ocular Considerations: Leukemia, Lymphoma, Myeloma

All leukemia can cause retinal findings (Roth spots, hemorrhages, cotton wool spots, etc) depending on the blood count at the time of the presentation.

Uveitis in cancer patients workup should always include ruling out relapse of their malignancies (this includes other solid organ malignancies as well).

ALL has the highest likelihood of having CNS disease – leptomeningeal disease is common.

CML can cause unique ischemic retinopathy (similar to diabetic retinopathy)

Orbital involvement of lymphoma are relatively common; in myeloma, it presents as plasmacytomas.

For lymphoma and myeloma, patients typically undergo autologous stem cell transplantation and with its failure, have allogeneic stem cell transplantations
Ocular Side Effects

Radiation Energy (Gy)

- Optic nerve/Chiasm/Tract >50 Gy
- Retina >40 Gy
- Cornea >30 Gy
- Lid 20-30Gy
- Lacrimal Gland >30Gy
- NLD System 30Gy
- Conjunctiva >10Gy
- Cataract (2)

Conventional
3D Conformal
IMRT
Stereotactic radiosurgery
Proton
Helium
Carbon
Iodine 125
Phosphate
Strontium 89
Gold
Iridium
Palladium
Cobalt
Cesium
Phosphorous-32

External Beam
Charged particles
Brachytherapy
Gleevec (Imatinib Mesylate; STI 571)

Oral Tyrosine kinase inhibitor (family of Signal Transduction Inhibitors); (c-abl, bcr/abl, c-kit, PDGF-R)

Approved by FDA for CML and Gastrointestinal Stromal tumors (GIST). Other forms of cancer being evaluated.

A variety of adverse events: general fluid retention
Gleevec – periorbital edema (70%)

Usually mild to moderate
Reversible with discontinuation of meds

Blood and Marrow Transplantation

• Major medical scientific advancement: Nobel to Ed Thomas in 1990
• Indications: bone marrow failure, immune deficiency, metabolic, neoplastic (>80% for CA)
  - AML, ALL, MDS, CML, CLL, low grade lymphoma, myeloma, Hodgkin’s, Breast, Ovarian, Renal CA
• Types: Autologous, Syngeneic, Allogeneic

Lacrimal gland dysfunction/Sicca

(acute setting: 60-80% of acute GVHD)

PreBMT
S/Schirmer
OD=22mm
OS=27mm

PostBMT
S/Schirmer
OD=0mm
OS=0mm
Cancer Treatment Armamentarium
What’s Hot??

- Surgery
  - New Approach (ex. sentinel node biopsy)
  - New Technology (robotics)

- Radiation
  - Conformal treatment; Gating
  - Charged particle (proton, carbon ions)
  - Hypo or hyper fractionation

- Chemotherapy
  - Biologics and small molecule treatments
  - Bioimmunotherapy

- Stem Cell Transplantation
  - Graft vs. Tumor effect

Thank you for your attention

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