American Association for Cancer Research/ONS
Bench to Bedside: The Role of Inflammation in Cancer
(and the Tumor Microenvironment)

Objectives
• Discuss differences between acute and chronic inflammation
• Evaluate evidence for associations between chronic inflammation and cancer
• Analyze the tumor microenvironment
• Discuss contributors to chronic inflammation and their sequelae in patients undergoing treatment for cancer
• Discuss implications for practice

Acute vs Chronic Inflammation

<table>
<thead>
<tr>
<th></th>
<th>Acute</th>
<th>Chronic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trigger</td>
<td>Foreign microorganism, trauma / tissue injury, allergen</td>
<td>Perpetuated acute inflammatory response, genetic &amp; epigenetic (environment, lifestyle) factors</td>
</tr>
<tr>
<td>Onset</td>
<td>Immediate</td>
<td>Insidious</td>
</tr>
<tr>
<td>Duration</td>
<td>Days → Weeks</td>
<td>Months → Years</td>
</tr>
<tr>
<td>Mediator response</td>
<td>Normal cytokine signaling response</td>
<td>Constitutive overexpression of proinflammatory cytokines, chemokines, prostaglandins</td>
</tr>
<tr>
<td>Cellular response</td>
<td>Innate immune response (e.g. neutrophils, macrophages)</td>
<td>Adaptive immune response (e.g. lymphocytes, B-cell → plasma cells, fibroblasts)</td>
</tr>
<tr>
<td>Outcome</td>
<td>With healthy immune system, completely resolves</td>
<td>Can lead to chronic conditions: cancer, cardiovascular disease, type 2 diabetes, others</td>
</tr>
</tbody>
</table>

Sterile Inflammation
• Inflammatory response not caused by microbial invasion
• Same response
  – Elicitation of neutrophils & macrophages
  – Inflammatory cytokine/chemokine response (TNF-α, IL-6) → recruitment of more leukocytes
Chronic Inflammation
- Structural damage to immune cells
- Functional impairments
  - Loss of the ability to detect and eliminate foreign microorganisms
  - Interference with mechanisms that normally detect and arrest aberrant cell growth

Inflammation and Cancer
- Perpetual inflammatory cycle within the tumor microenvironment
  - Chronic inflammation triggers nuclear transcription factors within the tumor cells
  - Inflammatory mediators (cytokines, chemokines, prostaglandins) secreted from tumor cells → leukocyte recruitment
  - Cancer-related inflammation promotes tumor progression

Inflammatory Breast Cancer
- IBC (1-5% of breast cancers)
- Usually invasive ductal carcinoma → blocks lymph vessels
- Named “inflammatory” due to phenotype of red, swollen breast tissue
  - Note: this is analogous to acute Inflammation!
- Not currently on the list of chronic inflammatory-linked cancers, but it may be…..

Contributions to Chronic Inflammation
- Infectious agents
- Cigarette smoking
- Exposure to asbestos and silica
- Nutritional imbalances: high fat, high sugar, processed foods diet
- Stress

Viruses & Cancer

| Virus                                      | Cancer                                                               |
|--------------------------------------------|                                                                     |
| Human Papilloma Viruses (HPVs)             | Cervical, anal, vaginal, vulvar, penile, and oropharyngeal cancers  |
| Hepatitis B Virus                          | Liver cancer                                                       |
| Human T-cell leukemia virus 1 (HTLV-1)     | Adult T-cell leukemia                                              |
| Human T-cell leukemia virus 2 (HTLV-2)     | Hairy-cell leukemia                                                |
Inflammation and Cancer

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Hepatitis B Virus
Liver cancer

Human T-cell leukemia virus 1 (HTLV-1)
Adult T-cell leukemia

Human T-cell leukemia virus 2 (HTLV-2)
Hairy cell leukemia

Epstein-Barr Virus
Burkitt’s lymphoma (African children), lymphoma (people with AIDS), Hodgkin’s disease (~1/2 of all cases)

Human Herpes Virus
Kaposi Sarcoma (people with AIDS)

Research

• Specific cancers linked to chronic inflammation
• Molecular studies
• Microbiome
• Immunotherapy
• Precision science
• Glycemic studies
• Symptoms studies

Immune Therapy

• Inducing the immune system to recognize and arrest aberrant (cancerous) cell formation
• Various types
  – Monoclonal antibodies
    • Alemtuzumab binds to CD52 antigens on chronic lymphocytic leukemia cells → immune response destroys leukemia cell
    • Trastuzumab [herceptin] targets HER2 proteins on breast & stomach cancer cells
  – Vaccines (Gardasil for HPV)
  – Immune checkpoint inhibitors

Precision Medicine and Moonshot Initiatives

• Precision Medicine Initiative (2015)
  – Personalized Medicine
  – Genomics
  – Patients as active partners in research → access to study outcomes they participate in
  – Centralized resources
  – Pooled information / data science
  – Generalized consent forms
• Moonshot Initiative (2016)
  – $1 billion to eliminate cancer “as we know it”
  – Accelerated research efforts
  – Impact on cancer associated inflammation

Nurse Scientist Research Studies

• Glycemic studies
  – Malglycemia → inflammation → impaired immune response
• Hematopoietic cell transplantation recipients
  – Increased risk for infections
  – Increased risk for mortality (independent of infections and malignancy)

Symptom Science Research

• Inflammatory components?
• Exemplar studies
  – Christine Miaskowski
  – Ruth McCorkle
  – Donna Berry
  – Barbara Given
  – Janet Carpenter
  – Susan Beck

Oncology Nursing Input

• Promote anti-inflammatory nutrients
  – Mediterranean diet (fish oil, fresh fruits & vegetables, lean proteins, whole grains, walnuts)
• Promote physical activity
• Encourage and guide patients in smoking cessation
• Stress control!
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Oncology Nursing Input
• Promote anti-inflammatory nutrients
  – Mediterranean diet (fish oil, fresh fruits & vegetable, lean proteins, whole grains, walnuts)
  – Curcumin (potent anti-inflammatory ingredient in tumeric)
• Promote physical activity
• Encourage and guide patients in smoking cessation