Chemotherapy and Radiotherapy

5th year lecture

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Learning objectives:

By the end of this lecture, the student will be able to:

1. Define chemotherapy and radiotherapy and their roles in gynecologic cancers.
2. Identify main indications and types of both therapies.
3. List common drug classes and regimens used.
4. Recognize main side effects and patient-care principles.

Introduction

Gynaecologic cancers, including cervical, ovarian, endometrial, vulvar, and vaginal malignancies, are managed using a combination of surgery, radiotherapy, and chemotherapy. Radiotherapy is mainly used as a local treatment, while chemotherapy is a systemic therapy. Both modalities play a major role in improving survival, reducing recurrence, and achieving tumor control, either alone or as part of multimodal treatment.

Chemotherapy

Indications of Chemotherapy in Gynaecological Cancers

1. **Neoadjuvant Chemotherapy** (Before Surgery): Used to shrink the tumor and make it operable or to allow fertility-sparing surgery.

Advanced ovarian cancer (to improve operability)

Locally advanced cervical cancer (large bulky tumors)

Selected cases of endometrial cancer (non-surgical candidates)

Sarcomas when tumor size is large or borderline resectable

2. **Adjuvant Chemotherapy** (After Surgery): Used to eliminate micro metastasis and reduce recurrence.

Ovarian cancer (Stage IC and above)

High-risk or advanced endometrial cancer

High-risk cervical cancer (after surgery, if lymph nodes are positive)

Uterine sarcomas (e.g., leiomyosarcoma, carcinosarcoma)

3. **Primary / First-Line Chemotherapy**: When chemotherapy is the main treatment

Advanced, metastatic, or recurrent ovarian cancer

Metastatic cervical cancer

High-grade uterine sarcomas

Gestational Trophoblastic Neoplasia (GTN) → very chemosensitive

4. **Concurrent Chemoradiation**: Chemotherapy used as a radiosensitizer

Locally advanced cervical cancer (standard: weekly Cisplatin + radiotherapy)

Selected high-risk endometrial cancer cases after surgery

5. **Palliative Chemotherapy**: Used for symptom control and to prolong survival in incurable or recurrent disease

Recurrent ovarian cancer

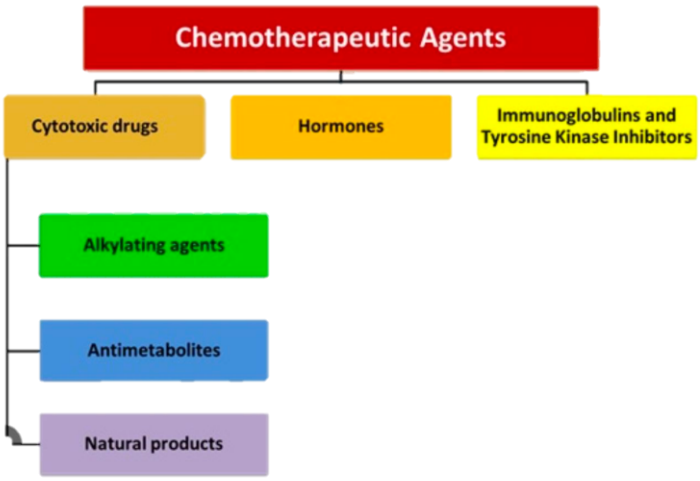
Recurrent or metastatic cervical cancer

Recurrent endometrial cancer not responding to hormone therapy

6. **Chemotherapy for Highly Chemo-Sensitive Tumors**

Gestational Trophoblastic Neoplasia (GTN) → MTX or Actinomycin-D (**curative** even in metastatic disease)

Some ovarian germ cell tumors → BEP regimen (Bleomycin, Etoposide, Cisplatin)



Main Classes Used in GYN Oncology

- Alkylating agents (e.g., cyclophosphamide)
- Antimetabolites (e.g., methotrexate)
- Plant alkaloids (e.g., paclitaxel)
- Antitumor antibiotics (e.g., doxorubicin)
- Platinum compounds (e.g., cisplatin, carboplatin — cornerstone for ovarian cancer)

Most Common Chemotherapy Regimens in Gynaecology

Cancer	Common Regimen
Ovarian	Paclitaxel + Carboplatin
Endometrial	Carboplatin + Paclitaxel
Cervical	Cisplatin , Carboplatin + Paclitaxel
GTN	MTX, Act-D, or EMA-CO
Germ Cell Tumors	Bleomycin, Cisplatin, Etoposide

Mechanism of Action

- Blocks DNA synthesis or mitosis
- Targets rapidly dividing cells

Side Effects of Chemotherapy

- Bone marrow suppression (neutropenia, anaemia, thrombocytopenia)
- GI toxicity (nausea, vomiting)
- Hair loss
- Organ-specific toxicities (e.g., nephrotoxicity with cisplatin)

Directing Care of the Patient

- Prior to drug infusion, a complete medical history and comprehensive physical examination are mandatory
- Perform blood tests: CBC, Comprehensive metabolic panel, and tumor markers as needed.
- BSA calculates chemotherapy doses; weight is checked before each cycle.
- Most chemotherapeutic agents are administered IV, preferably via central line.
- Hypersensitivity or allergic reactions may occur despite prior history review.

Management of Hypersensitivity Reactions

1. Stop the chemotherapy infusion
2. Assess the patient's airway, breathing, and circulation
3. Administer intravenous normal saline if hypotensive
4. Administer oxygen if dyspnoeic or hypoxic
5. Administer intravenous antihistamine (e.g., 50 mg intravenous diphenhydramine or 25- 50 mg intravenous promethazine)
6. Administer 5 mg of nebulized salbutamol if the patient has bronchospasm
7. Administer intravenous corticosteroids (e.g., 100 mg of hydrocortisone); this may not affect the initial reaction, but may prevent rebound or prolonged allergic manifestations
8. If the patient does not promptly improve or has symptoms of persistent or severe hypotension or persistent bronchospasm or laryngeal oedema, administer adrenaline or epinephrine (O. 1- 0.25 mg intravenous); further acute resuscitation measures may be required
9. Reassure the patient that the problem is a recognized and treatable one.

Radiotherapy (RT)

Radiotherapy is the use of ionizing radiation to destroy cancer cells by causing irreversible DNA damage, leading to apoptosis or mitotic death.

Mechanism of Action

- Causes DNA double-strand breaks
- Free radical formation, especially in oxygenated tissues
- Most effective in rapidly dividing cells
- Radio sensitivity varies by cell cycle phase (most sensitive in G2/M phase)

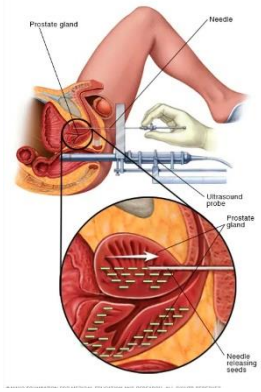
Types of Radiotherapy

1. External Beam Radiotherapy (EBRT) – delivered from outside the body using a linear accelerator
2. Brachytherapy – internal radiation placed close to the tumor (very important in cervical cancer)



Indications in Gynaecology

- Cervical cancer: definitive treatment (RT ± Cisplatin), or post-operative adjuvant therapy
- Endometrial cancer: adjuvant treatment in high-risk cases
- Vaginal and vulvar cancers: primary or adjuvant
- Ovarian cancer: rarely used; palliative cases only



Side Effects of RT

Acute: diarrhoea, cystitis, skin erythema, vaginal mucositis

Late: vaginal stenosis, ovarian failure, radiation proctitis, fistula formation

Effect of Radiation on Normal Tissue

For a given dose of radiation administered over a given time interval, risk of late effects is more with larger fraction.

1. Uterus and cervix are typically described as radio-resistant except their mucosal linings.
2. Ovary is highly sensitive, it may lead to iatrogenic ovarian failure, which is dose-dependent as well as modulated by age of the patient.

Pre-menarcheal girls exposed to 30 Gy dose may continue to have menstruation and even may carry pregnancy to term, although they experience premature ovarian failure later.

Most adult women develop premature ovarian failure after 20 Gy.

3. Vagina – the radiation tolerance varies with site, duration, and radiation dose.

Apical vagina requires higher dose for atrophic changes, shortening, and loss of elasticity, as compared to other areas.

4. Vulva can withstand some radiation, similar to skin.

Contraindication to Radiotherapy

- Severe anaemia.
- Poor general health.
- Sepsis.
- Pregnancy.
- Presence of fibroid in uterus.
- Tubo-ovarian masses.
- Utero-vaginal prolapse.
- Fistulas.
- Radio-resistant tumors.



Figure 4.10 Fletcher-Williamson type applicators used for high-dose-rate and pulsed doserate intracavitary applications. Note the tungsten shields located in the inferior-media anteriorly and posteriorly in the small (2 cm) ovoid inserts.

Summary

Chemotherapy and radiotherapy are key treatments in gynaecologic cancers targets systemic disease, while radiotherapy treats local tumours. Both improve survival but require careful monitoring due to their side effects.



Which chemotherapy regimen is considered the cornerstone for ovarian cancer?

A. Cisplatin alone

B. Paclitaxel + Carboplatin

C. MTX + Act-D

D. Bleomycin + Etoposide

