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CHAPTER

2 Chemotherapy in Gynecological Oncology

1. The doubling time for germ cell tumor:

a. 20–40 days
b. 60–80 days
c. 100–120 days
d. 130–150 days

2. 1 cm malignant mass would have undergone:

a. 10 tumor doubling time
b. 20 tumor doubling time
c. 30 tumor doubling time
d. 40 tumor doubling time

3. The cell generation time means:

a. M phase to M phase
b. M phase to G1 phase
c. M phase to S phase
d. M phase to G2 phase

4. New deoxyribonucleic acid (DNA) replication occurs in:

a. G1 phase
b. S phase
c. G2 phase
d. M phase

5. Phase of cell division is:

a. G1 phase
b. S phase
c. G2 phase
d. M phase

6. Sanctuary sites in cancer biology means all, *except*:

a. Tumor is inaccessible to chemotherapeutic drugs
b. Drug concentration becomes less overactive for cell kill
c. Cerebrospinal fluid
d. Sites of cancer stem cells

7. Sanctuary sites in cancer biology means all, *except*:

a. Areas of tumor necrosis
b. Tumor cells with maximum growth fractions
c. Tumor cells with minimum growth fractions
d. Cerebrospinal fluid

8. Cockcroft–Gault equation for calculating carboplatin dose using estimated creatinine clearance or glomerular filtration rate (GFR) is based upon patient's, *except*:

a. Weight
b. Age
c. Height
d. Creatinine

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9. Recommended GFR in Calvert formula should not exceed:

a. 125 mL/min
b. 150 mL/min
c. 140 mL/min
d. 100 mL/min

10. Neutropenia can occur when absolute neutriphil count decreases below:

a. 500 per mm^3
b. 1,000 per mm^3
c. 1,500 per mm^3
d. None of the above

11. True about cisplatin and carboplatin are all, *except*:

a. Cell cycle nonspecific bifunctional alkylating agents
b. Radiomimetic agents
c. Disrupts the DNA cross-linkages
d. G2 cell cycle arrest
e. S-phase cell cycle arrest

12. Antitumor antibiotics include all, *except*:

a. Actinomycin D
b. Bleomycin
c. Doxorubicin
d. Dacarbazine

13. Antitumor antibiotics developed from fungi are all, *except*:

a. Actinomycin D
b. Bleomycin
c. Mitomycin C
d. Dacarbazine

14. Mechanism of action of cell-cycle nonspecific antitumor antibiotics include all, *except*:

a. Intercalation into DNA base pairs
b. Formation of free radicals
c. Alteration of tumor cell membranes
d. Chelation of metal ions
e. Damages DNA intercross-linkages

15. Paclitaxel acts by:

a. Intercalation into DNA base pairs
b. Polymerization and stabilization of intracellular microtubules
c. Damages DNA intercross-linkages
d. All of the above

16. Common side-effects of bevacizumab include all, *except*:

a. Hypertension
b. Thromboembolism
c. Impaired wound healing
d. Risk of bowel perforation
e. Neuropathy

17. Risk of teratogenic effects of chemotherapeutic agents are highest in:

a. First trimester
b. Second trimester
c. Third trimester
d. Same in all trimester

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18. Antimetabolites include all, *except*:

a. Methotrexate
b. Gemcitabine
c. 5-Fluorouracil
d. Paclitaxel

19. Hypersensitivity reactions of Paclitaxel is due to:

a. Cremophor
b. Acrolein
c. Adjuvant contents
d. None of the above

20. Chemotherapeutic agents made from plant alkaloids include all, *except*:

a. Vincristine
b. Etoposide
c. Docetaxel
d. Gemcitabine

21. Mechanism of action of paclitaxel:

a. Disrupts the microtubular functions in a cell
b. Inhibits the DNA
c. Inhibits the ribonucleic acid (RNA)
d. None of the above

22. Which is not an epidermal growth factor receptor (EGFR)?

a. Trastuzumab
b. Pertuzumab
c. Bevacizumab
d. None of the above

23. Which is not an EGFR?

a. Gefitinib
b. Erlotinib
c. Lapatinib
d. Pazopanib

24. Antibody (Ab) against CA125 include:

a. Oregovomab
b. Abagovomab
c. Both a and b
d. None of the above

25. Dual EGFR and human EGFR-related receptor 2 (HER2) kinase Inhibitor:

a. Lapatinib
b. Cetuximab
c. Trastuzumab
d. Gefitinib

26. Bevacizumab targets:

a. Tyrosine kinases
b. Epidermal growth factor receptors
c. Poly (ADP-ribose) polymerase (PARP)
d. Angiogenesis

27. Which is not a PARP inhibitor?

a. Niraparib
b. Gefitinib
c. Olaparib
d. Rucaparib

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28. Bevacizumab is a:

a. VGEF-A Ab
b. VGEF-1 Ab
c. VGEF-2 Ab
d. VGEF-3 Ab

29. Side-effects of bevacizumab include all, *except*:

a. Hypertension
b. Thromboembolism
c. Impaired wound healing
d. Palmar-plantar erythrodysesthesia

30. Trastuzumab is a monoclonal antibody that blocks:

a. HER-2/neu receptor
b. EGFR
c. EGFR tyrosinase kinase
d. Dual EGFR/HER-2 neu kinase inhibitor

31. Palmar-plantar erythrodysesthesia is a side-effect of:

a. Liposomal doxorubicin
b. Docetaxel
c. Doxorubicin
d. Dactinomycin

32. Tyrosine kinase inhibitors include all, *except*:

a. Pazopanib
b. Cediranib
c. Sunitinib
d. Topotecan

33. Topoisomerase inhibitors chemotherapeutic agent:

a. Topotecan
b. Melphalan
c. Ifosfamide
d. Cisplatin

34. Carboplatin include all, *except*:

a. Conformational change in DNA
b. Bifunctional alkylating like agent
c. Highly neurotoxic
d. More hematopoietic toxicity

35. Antitumor antibiotics include all, *except*:

a. Dactinomycin
b. Doxorubicin
c. Liposomal doxorubicin
d. Docetaxel

36. Second malignancies are associated with all, *except*:

a. Melphalan
b. Etoposide
c. Procarbazine
d. Paclitaxel

37. Chemotherapeutic agents with highest gonadal toxicity:

a. Vinca alkaloids
b. Antimetabolites
c. Alkylating agents
d. Antitumor antibiotics

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38. Cardiac toxicity is usually seen with all, *except*:

a. Doxorubicin
b. Busulfan
c. Trastuzumab
d. Cyclophosphamide

39. True about neurotoxicity of cisplatin include all, *except*:

a. Progressive peripheral neuropathy
b. Delayed peripheral neuropathy
c. Sensory neuropathy
d. Motor neuropathy

40. Endocardial fibrosis is a side effect of:

a. Busulfan
b. Mitomycin C
c. Methotrexate
d. All of the above

41. Myocardial fibrosis is a side effect of:

a. Busulfan
b. Mitomycin C
c. Methotrexate
d. All the above

42. Hepatic fibrosis is a side effect of:

a. Busulfan
b. Mitomycin
c. Methotrexate
d. All the above

43. Severe cardiomyopathy can be a side effect of:

a. Doxorubicin
b. Docetaxel
c. Bevacizumab
d. Trastuzumab

44. Nephrotoxic side effect of cisplatin is by:

a. Damage of renal tubular cells
b. Oliguric renal failure
c. Interstitial nephritis
d. All the above

45. Nephrotoxic side effect of methotrexate is by:

a. Damage of renal tubular cells
b. Oliguric renal failure
c. Interstitial nephritis
d. All of the above

46. Neuropathy of vincristine first affects:

a. Loss of deep tendon reflex and distal paresthesia
b. Postural hypotension
c. Urinary retention
d. Facial palsy

47. Neuropathy is a side effect of:

a. Vinca alkaloids
b. Cisplatin
c. Paclitaxel
d. All of the above

48. Skin necrosis by extravasation is a side effect of:

a. Vincristine
b. Actinomycin D
c. Doxorubicin
d. All of the above

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49. Interstitial pneumonitis is a side effect of:

a. Bleomycin
b. Gemcitabine
c. Nitrosoureas
d. All of the above

50. Radiation recall dermatological reactions is seen with:

a. Bleomycin
b. Actinomycin D
c. Methotrexate
d. Doxorubicin

51. Drugs causing severe alopecia include all, *except*:

a. Carboplatin
b. Paclitaxel
c. Docetaxel
d. Cyclophosphamide

52. As per RECIST criteria: 30% reduction in the sum of diameters of all target measurable lesions:

a. Complete response
b. Partial response
c. Progressive disease
d. Stable disease

53. RECIST stands for:

a. Response Evaluation Criteria in Solid Tumors
b. Response Estimation and Control in Solid Tumors
c. Recount Evaluation Criteria in Solid Tumors
d. Response Endorsement and Control in Solid Tumors

54. Delayed bone marrow suppression is seen with:

a. Carboplatin
b. Paclitaxel
c. Cisplatin
d. Mitomycin C

55. Drug interactions causing maximum clinical benefit:

a. Additive effect
b. Synergistic effect
c. Antagonistic effect
d. Multiplication effect

56. In dose dense chemotherapy:

a. Increasing frequency of chemotherapy
b. Increasing dose of chemotherapy
c. Increasing both dose and frequency of chemotherapy
d. None of the above

57. Drugs acting in the mitotic phase (M) of the cell cycle include all, *except*:

a. Paclitaxel
b. Vincristine
c. Vinblastine
d. Doxorubicin

58. Doxorubicin acts upon which phase of the cell cycle?

a. Mitotic (M) phase
b. Postmitotic (G1) phase
c. Early synthetic phase
d. Late synthetic phase

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59. Drugs acting in the postmitotic phase of the cell cycle:

a. Actinomycin D
b. Methotrexate
c. 5-Fluorouracil
d. Hydroxyurea

60. Drugs acting in the early synthetic phase of the cell cycle include all, *except*:

a. Methotrexate
b. 5-Fluorouracil
c. Hydroxyurea
d. Actinomycin D

61. Drugs acting in the postsynthetic phase of the cell cycle include all, *except*:

a. Carboplatin
b. Cisplatin
c. Etoposide
d. Paclitaxel

62. Tumors grow in a sigmoidal growth pattern is known by:

a. Gompertzian growth theory
b. Skipper's cell kill theory
c. Goldie–Coldman theory
d. Norton–Simon theory

63. Chemotherapeutic agents work by first order kinetics is given by:

a. Gompertzian growth theory
b. Skipper's cell kill theory
c. Goldie–Coldman theory
d. Norton–Simon theory

64. Sequential use of chemotherapeutic drugs to produce maximal effects and minimizing resistance is given by:

a. Norton–Simon theory
b. Goldie–Coldman theory
c. Skipper's cell kill theory
d. Gompertzian growth theory

65. Increase treatment efficacy of chemotherapeutic drugs with the use of optimal dose levels:

a. Norton–Simon theory
b. Goldie–Coldman theory
c. Skipper's cell kill theory
d. Gompertzian growth theory

66. Current use of bevacizumab in ovarian cancer includes:

a. Combination therapy
b. Maintenance therapy
c. Platinum resistant ovarian cancer
d. All of the above

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ANSWERS KEY						
1. a	2. c	3. a	4. b	5. d	6. d	7. c.
8. c	9. a	10. a	11. e	12. d	13. d	14. e
15. b	16. e	17. a	18. d	19. a	20. d	21. a
22. d	23. d	24. c	25. a	26. d	27. b	28. a
29. d	30. a	31. a	32. d	33. a	34. c	35. d
36. d	37. c	38. d	39. d	40. a	41. b	42. c
43. a	44. a	45. b	46. a	47. d	48. d	49. d
50. d	51. a	52. a	53. a	54. c	55. b	56. a
57. d	58. d	59. a	60. d	61. d	62. a	63. b
64. b	65. a	66. d				

NOTES: CHEMOTHERAPY IN GYNECOLOGICAL ONCOLOGY

- Response evaluation criteria in solid tumors:
  - The target lesions are those which are suitable for repeated radiological assessment and depends upon their size [lesions with longest diameter (LD)].
  - *Complete response (CR)*: Disappearance of all target lesions.
  - *Partial response (PR)*: At least a 30% decrease in the sum of the LD of target lesions, taking reference of the baseline sum of LD.
  - *Progressive disease (PD)*: At least a 20% increase in the sum of the LD of target lesions, taking as reference the smallest sum of LD recorded since the treatment started or the appearance of one or more new lesions.
  - *Stable disease (SD)*: Neither sufficient shrinkage to qualify for PR nor sufficient increase to qualify for PD, taking as reference the smallest sum of LD since the treatment started.
  - Limitations include the inability to measure the extent of response in sites with unmeasurable tumor (pleural, ascitic, bone and leptomeningeal disease).
- Hypothesis in chemotherapy:
  - *Skipper's hypothesis (log kill hypothesis)*: If the tumor were treated at the level of micro metastases rather than larger volume tumors, it was more

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likely that the treatment would be effective. Chemotherapeutic agents work by first-order kinetics and that they kill a constant fraction of cells rather than a constant number of cells. It also extrapolates the need for intermittent courses of chemotherapy to achieve the magnitude of cell kill necessary to produce tumor regression and cure. It also provides a rationale for multiple-drug or combination chemotherapy.

- *Goldie–Coldman hypothesis*: Spontaneous mutation to a drug-resistant phenotype occurs in rapidly growing malignant tumors at variable rate. This model predicts that alternating cycles of treatment should be superior to the sequential use of particular agents because sequential use of antineoplastic drugs would allow for the development and regrowth of a doubly resistant line.
- *Norton–Simon hypothesis*: The efficacy of treatment for tumors exhibiting sensitivity to particular chemotherapeutic agents will be enhanced if single agents, or in combination regimes, are delivered at their optimal dose levels in a so-called dose-dense manner, rather than as alternating regimes. It focuses on the rapid administration of as many active agents as possible and frequent modification of dose levels because of overlapping side effects of the chemotherapeutic agents.
- Dose-dense and dose-fractionated chemotherapy may be more active than the same treatment given every 3 week. The antiangiogenic effect of weekly metronomic chemotherapeutic agent decreases the accelerated repopulation of cancer cells between cycles and also reduces the acquisition of drug resistance.

- Hyperthermic intraperitoneal chemotherapy (HIPEC) is a highly concentrated and heated chemotherapy treatment that is delivered directly to the abdomen during surgery. This procedure is used to treat tumors in the peritoneal lining of the abdomen that results from ovarian, gastric, colon, appendix tumors, mesothelioma, and other types of cancers.
- Pressurized intraperitoneal aerosol chemotherapy (PIPAC) is a procedure where aerosolized chemotherapy is directly injected into abdomen via a high-pressure injector.
- *Metronomic therapy:* Repeated administration of chemotherapeutic drugs at low doses frequently and without any prolonged drug free period. The aim is to avoid adverse side-effects of chemotherapeutic agents which causes disruption of chemotherapy treatment. It uses biological optimised dose instead of maximum tolerated dose and preferably by oral administration. It acts by multi-targeted mechanism like anti-angiogenesis mechanism, enhancing immune mechanism and by inducing tumor dormancy. Use of metronomic therapy may lead to development of potential drug resistance. Example of metronomic therapy are use of Cyclophosphamide and Methotrexate.

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Bidhan Roy MBBS MS DNB FGO PGDHHM is serving as a Colonel and Senior Adviser in the Armed Forces Medical Services. Smiles in thousands of patients reflects his dedication, knowledge and surgical expertise. He has been a faculty at premier institutes like Army Hospital (Research & Referral) and Armed Forces Medical College. His interest encircles advanced gynecological cancer surgeries, emergency and critical care obstetrics, robotic surgeries and uterine transplant surgeries. He is a sport lover and a music enthusiast, Harmonica player, passionate mentor, loving teacher, insightful writer- columnist, sincere reviewer, devoted researcher, administrator, university examiner and guide to many postgraduate students. Above all - a ground soldier and an olive-green gentleman officer. He is currently developing MOOCs platform, cadaveric dissections, anatomical models, scientific photography and other teaching interfaces.

Kamalika P Roy MBBS DNB FICS PGDHHM PGDMLS has been actively involved in teaching both postgraduate and undergraduate students for the last ten years. She has keen interest in clinical research and loves developing innovative teaching aids. She has won several awards for her clinical and scientific endeavors. She has also published a few papers in reputed journals. Elocution and painting are her forte.

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