EXAMINATION

Part I Exam changes to Radiobiology as at October 2006.

Radiobiology - Short Answer Questions only (no multiple choice questions)
Physics *- No change*
Anatomy *- From 2 hours to 3 hours. This will include additional images and questions.*

Previous Clinical Radiobiology Examination Papers 1999 - 2009

May 2009

INSTRUCTIONS

- There are a total of SIX questions.
- Write your answers in the book provided.
- All questions are of equal value. Sections within questions are not necessarily of equal value.
- All questions are to be attempted.
- You may use diagrams, tables or lists in your answers.
- Answers should be given from a clinical radiobiology viewpoint.
- Hand **all** papers to invigilator, no papers are allowed to be taken from the exam room. THIS INCLUDES EXAM PAPERS.

Question 1

a) Describe the different types of radiation induced cell death, including the microscopic appearances and molecular mechanisms. (5 marks)

b) Describe the characteristics of stochastic and deterministic effects of ionising radiation. Give an example for each effect. (3 marks)

c) Define DNA polymorphism. (2 marks)

Question 2

a) Explain the rationale for the use of hyperthermia in the treatment of cancer. (3 marks)

b) Define the phenomenon of accelerated repopulation during radiation therapy and list the clinical strategies to overcome this. (4 marks)

c) Draw a labelled diagram showing tumour control probability (TCP) and the normal tissue complication probability (NTCP) curves as a function of total radiation dose. On the same diagram, draw the TCP and NTCP curves for treatment with concurrent chemo-radiotherapy. (3 marks)

Question 3

a) Describe the pathogenesis of radiation induced normal tissue injury. (4 marks)

b) Describe the volume effect and its significance for radiation damage according to the different types of arrangement of functional subunit of normal tissues. (4 marks)

c) Describe the effects of radiation on the human liver. (2 marks)

Question 4

a) Patients with ataxia telangiectasia have a defect in the functioning of the protein ATM.

i) Describe the normal function of the protein ATM in DNA double strand break repair. (1.5 marks)

ii) Describe the clinical effect of mutations in the ATM gene. (1.5 marks)

b) Name the two predominant pathways for DNA double strand break repair. Write brief notes on each pathway for:

i) Accuracy of repair (1 mark)

ii) Portion of the cell cycle where it can occur (1 mark)

iii) Relative proportion of repair by each pathway in

a) Stem / germ cells (1 mark)

b) Somatic cells (1 mark)

c) Describe the effect of delivering two fractions of radiation therapy with less than four hours between fractions on DNA double strand break repair. Describe the consequences of this on early and late reacting tissues. (3 marks)

Question 5

a) Write short notes on in situ hybridisation. (2 marks)

b) Define the gonadal dose and genetically significant dose (GSD). (3 marks)

c) Define the formula to calculate cell loss factor in solid tumour. (1 mark)

d) List the mechanism of cell loss in solid tumours. (3 marks)

e) How would the dimension of a solid tumour mass change with a cell loss factor of 100%? (1 mark)

Question 6

a) Explain the mechanisms of the radiosensitization effect of oxygen. (3 marks)

b) Define oxygen enhancement ratio (OER) and give a value for low LET radiation. (2 marks)

c) Describe the function of a tumour suppressor gene and the cellular effect of loss of heterozygosity in the gene. (3 marks)

d) Describe a "telomere" and its function. (2 marks)

September 2008

INSTRUCTIONS

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Question 1

a) Define the term 'intron'. (2 marks)

b) Draw a diagram indicating the main features of a eukaryotic gene. (3 marks)

c) Describe, with the aid of a diagram, the sequence of molecular events involving transcription and translation of a eukaryotic gene. Include the subcellular compartments where the different events take place. (5 marks)

Question 2

a) Describe the radiation effects on:

i) the heart. (3 marks)

ii) the salivary glands. (3 marks)

b) Discuss the principle of the SOMA system in evaluating the late effects of radiation therapy. Give an example of the SOMA system for an organ. (4 marks)

Question 3

a) For a tumour that requires 18 days to double its diameter, calculate the approximate cell cycle time of the cells (assume no cell loss and that all cells are actively dividing). (2 marks)

b) i) Draw a labelled graph of the typical relationship between radiation dose and tumour control probability (TCP) expected from a radical course of radiotherapy and describe the events underlying each section of the curve. (4 marks)

ii) Briefly describe how this relationship changes for:

1) a larger population of patients with similar tumours receiving the same treatment. (2 marks)

2) radiotherapy being delivered as adjuvant treatment. (2 marks)

Question 4

a) Describe the dose rate effect and the inverse dose rate effect. (3

marks)

b) Describe the rationale and scheduling for concomitant boost in the definitive radiation therapy of oropharyngeal squamous cell cancer. (3 marks)

c) Describe the radiation effects in the developing embryo and foetus. (4 marks)

Question 5

a) Hot spots in radiotherapy plans have been described as creating "double trouble" by providing a higher total dose and delivering it at a higher dose per fraction. Describe how these two events act independently to increase the risk of treatment toxicity. (4 marks)

b) Define the terms "TD 5/5" and "TD 50/5". (2 marks)

c) Explain why doses close to the TD 5/5 are frequently delivered to connective tissues while the maximum dose delivered to the spinal cord is almost always more than 10Gy below the TD 5/5 for this structure. (4 marks)

Question 6

a) Define the term "α/β ratio" as it applies to the linear quadratic model. (2 marks)

b) On the same diagram, draw the radiation survival curves (for low LET radiation) for a cell line with: (3 marks)

i) a high α/β ratio.

ii) a low α/β ratio.

c) Explain the difference in survival when a cancer cell line is irradiated with a single dose of 8 Gy compared with 2 fractions of 4 Gy with a 2 hour interval. (3 marks)

d) Briefly describe the radiosensitizing mechanism of: (2 marks)

i) cisplatin.

ii) 5-fluorouracil.

May 2008

INSTRUCTIONS

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- All questions are to be attempted.
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Question 1

a) One of the most serious complications of the treatment of cancer is radiation damage to the spinal cord. Discuss the pathogenesis of radiation myelitis. (4 marks)

b) Define the TD5/5 and TD 50/5 tolerance doses and end points for human spinal cord. (2 marks)

c) Define deterministic and stochastic effects. Give one example of each. (4 marks)

Question 2

a) Describe the function of p53 protein cells after a dose of ionising radiation. (4 marks)

b) Describe the morphological features of apoptosis. (2 marks)

c) Describe the two main pathways that can lead to apoptosis. (4 marks)

Question 3

a) Describe the prodromal syndrome after total body irradiation. (4 marks)

b) Write short notes on cDNA libraries. (3 marks)

c) Name and briefly discuss techniques to study gene expression at the protein level. (3 marks)

Question 4

a) A patient received 17 Gy in 2 equal fractions over one week to the midplane of the chest for lung cancer. Using the linear quadratic equation, calculate the equivalent total dose at 2Gy per fraction received by the spinal cord. Assume i) that the spinal cord received the same total dose as the midplane and ii) that the anterior-posterior separation was the same throughout the treatment volume. Show the steps in your calculation. (2 marks)

b) i) Define accelerated treatment schedules.

ii) List the advantages and disadvantages of accelerated treatment schedules from a radiobiological point of view. (4 marks)

c) Draw a labelled diagram of the survival curves of cells from early and late reacting tissues treated with: (4 marks)

i) single doses of sparsely ionising radiation and

ii) fractionated sparsely ionising radiation.

Question 5

a) Define and explain the phenomena of (4 marks)

i) "potentially lethal damage repair" and

ii) "sublethal damage repair" in cells after irradiation.

b) List the mechanisms by which a drug can sensitize tumour cells to radiation. (3 marks)

c) Define the terms "volume doubling time" and "potential volume doubling time" in tumours. Explain the factors that influence the difference in volume doubling time and potential volume doubling time in tumours. (3 marks)

Question 6

a) Discuss the factors that influence radiation response in cancers and normal tissues. (7 marks)

b) Discuss the role of normal tissue vasculature in the radiation response. (3 marks)

October 2007

INSTRUCTIONS

- There are a total of SIX questions.
- Write your answers in the book provided.
- All questions are of equal value. Sections within questions are not necessarily of equal value.
- All questions are to be attempted.
- You may use diagrams, tables or lists in your answers.
- Answers should be given from a clinical radiobiology viewpoint.
- Hand all papers to invigilator, no papers are allowed to be taken from the exam room. THIS INCLUDES EXAM PAPERS.

Question 1

a) List and define the different types of fractionation schedule used in clinical practice. (4 marks)

b) What are the potential advantages and disadvantages of the different types of schedule from a radiobiological point of view? (6 marks)

Question 2

a) Define the Relative Biological Effectiveness (RBE) of ionising radiation with regard to its Linear Energy Transfer (LET). (1 mark)

b) Draw a labelled diagram comparing Cell Survival versus Radiation Dose for each of the following:

i. Cells in the different phases of the cell cycle irradiated with low LET radiation. (2 marks)

ii. Cells with either high or low α/β ratio irradiated with low LET radiation. (2 marks)

iii. Cells treated with either high or low LET radiation (2 marks)

c) Discuss the relative effect on expected cell kill when treating a tumour with low α/β ratio with high and low LET radiation. (3 marks)

Question 3

a) Draw a labelled diagram showing the main phases and the relative duration of each phase in the cell cycle. (1 mark)

b) Define the key DNA events in the cell cycle. (3 marks)

c) Name and describe the function of the major protein families that regulate cell cycle progression. (6 marks)

Question 4

a) Define the oxygen enhancement ratio (OER). (1 mark)

b) Discuss the mechanism of the oxygen effect during radiation therapy. (4 marks)

c) Discuss the characteristics of the oxygen effect during radiation therapy. (5 marks)

Question 5

Write short notes on:

a) Western Blotting. (3 marks)

b) The generation of monoclonal antibodies for clinical use. (3 marks)

c) The steps and physical conditions of the polymerase chain reaction (PCR). (4 marks)

Question 6

a) Define flexure dose. (2 marks)

b) Write short notes on the Comet assay. (3 marks)

c) Write short notes on the mechanism of actions of radiation therapy in benign and non-neoplastic conditions. (5 marks)

May 2007

INSTRUCTIONS

- There are a total of SIX questions.
- Write your answers in the book provided.
- All questions are of equal value.
- All questions are to be attempted.
- You may use diagrams, tables or lists in your answers.
- Answers should be given from a clinical radiobiology viewpoint.

Question 1

a) List the different types of radiation-induced DNA damage (3 marks)

b) List the morphological hallmarks of apoptosis (2 marks)

c) Describe the pathways involved in apoptosis (5 marks)

Question 2

a) Define stochastic and deterministic effects of ionising radiation, giving an example of each effect (3 marks)

b) Define and describe consequential late effects in normal tissues after radiation therapy (4 marks)

c) List the treatment factors that can affect the development of a consequential late effect. (3 marks)

Question 3

Regarding acute radiation pneumonitis arising from chemo-radiotherapy treatment:

a) Describe the clinical features of radiation pneumonitis. (2 marks)

b) Describe the pathophysiology of radiation pneumonitis. (4 marks)

c) Which drugs are particularly implicated? (2 marks)

d) List endogenous mediators thought to be involved. (2 marks)

Question 4

With regard to repopulation

a) Define repopulation. (2 marks)

b) What is the evidence for the existence of repopulation in the clinic? (4 marks)

c) Briefly discuss the approaches that have been used for overcoming repopulation in the clinic. (4 marks)

Question 5

Write short notes on:

a) fluorescence *in situ* hybridisation. (3 marks)

b) knockout mice (4 marks)

c) ATM kinase (3 marks)

Question 6

Write notes on:

a) ionising radiation effects on lymphocytes (4 marks)

b) ionising radiation effects on the ovary. (4 marks)

c) Knudson's 'two-hit' hypothesis (2 marks)

October 2006

INSTRUCTIONS

- There are a total of SIX questions. Each of these six questions is worth 10 marks.
- Write your answers in the book provided. You may request additional answer books from the invigilator.
- All questions are to be attempted.
- Answers should be given from a clinical radiobiology viewpoint.
- Hand **all** papers to invigilator, no papers are allowed to be taken from the exam room. THIS INCLUDES EXAM PAPERS

1. Write short notes on:
   a. Translation of genetic information. *[3 marks]*
   b. Wild type & mutant phenotypes. *[4 marks]*
   c. Genetic mutation. *[3 marks]*
2. a. Discuss the risk of therapeutic radiation during different stages of pregnancy. *[4 marks]*
   b. Discuss the risk of radiation induced malignancy in this situation. *[3 marks]*
   c. Discuss different strategies to minimise the risk to the fetus of delivering therapeutic irradiation to the mother during pregnancy. *[3 marks]*
3. Unrepaired DNA damage can have severe consequences in mammalian cells.
   a. List the external agents and intrinsic biological processes that can cause damage to DNA. *[3 marks]*
   b. List the types of damage induced in DNA by ionising radiation. *[2 marks]*
   c. Describe the repair pathways that deal with DNA damage induced by ionising radiation. *[5 marks]*
4. a. Draw a labelled diagram of the typical relationship between radiation dose and the tumour control probability (TCP) curve expected from a radical course of radiotherapy and describe the events underlying each section of the curve. *[4 marks]*
   b. List the factors that influence tumour control probability. *[2 marks]*
   c. Briefly describe how this relationship changes for:
      i. A larger population of patients with similar tumours receiving the same treatment. *[2 marks]*
      ii. Radiotherapy being delivered as adjuvant therapy. *[2 marks]*
5. Write short notes on:
   a. Epidermal growth factor. *[4 marks]*

b. Osteoradionecrosis. *[3 marks]*
c. Late radiation effects on the kidney. *[3 marks]*

6. a. How do early and late radiation reactions differ with respect to latency, rates of evolution once established, fractionation sensitivity and the effects of overall treatment time? *[5 marks]*
b. List and define three radiation reaction scoring systems in common clinical use. Give an example from one scoring system of an early and a late reaction. *[3 marks]*
c. How are dose-response data for these radiation reactions plotted on graphs? *[2 marks]*

Part One
One three hour written paper, with six equally weighted questions. The last of these questions is a multiple-choice format.

Exam Technique
Candidates are strongly advised to study multiple previous examination essay topics and extensively practice both technique and content. Essay answers are not required to be exhaustive or incredibly factually detailed. Often, a well set out 2-page answer with a comprehensively and accurately labelled graphic will be marked higher than a 3-4 page rambling text. The critical factors for demonstrating good knowledge of a subject relate to clear and accurate initial definitions, thorough and logical organisation of the coverage of the subject and appropriate perspective on the subject.

All questions should be answered with some clinical emphasis, unless they are purely laboratory-related questions. Extensive description of clinical findings and symptomatology is *not* required. Answers should be aimed at a general high level biological type audience. Recurring difficulties of candidates reflect nonadherence to definite instructions, eg. when a question specifically asks for a list, the candidate will commonly enter into a discursive discussion of that or a related subject. eg. a question may call for a discussion of the *clinical aspects* of fractionation and candidates will commonly spend the entire question discussing the 5R's and theory of fractionation.

Part Two
In the Radiotherapy papers, candidates will be expected to provide relevant radiobiological content in their answers, where appropriate. No specific Radiobiology exam questions will be set. Brief radiobiological comment may also be expected in the oral exam. Familiarity with basic BED calculations and their application will be expected.

Multiple Choice Question
1 PLD (Potentially Lethal Damage) and SLD (Sub Lethal Damage) are:
(A) both measured by the size of the "shoulder" of the survival curve.
(B) operational concepts derived to describe observed post irradiation cell survival.
(C) are additive in total amount.
(D) are both predominantly mediated through DNA polymerase.

True/False question
Radiation induced apoptosis;
(A) is not seen in any mammalian acute renewal cellular systems.
(B) is readily identifiable in-vitro and in-vivo with the Comet assay.
(C) May occur in human bone marrow and intestinal crypts at low radiation doses.
(D) Is thought to be maximal approximately 3-5 days following radiation exposure.
(E) Cannot be assayed in any in-vivo mammalian systems.

May 2006

Time Allowed: 3 hours
Instructions for this examination:

- There are a total of SIX questions.
- Question six is of multiple choice and true/false format
- All questions are of equal value.
- All questions are to be attempted.
- You may use diagrams, tables or lists in your answers.
- Answers should be given from a clinical radiobiology viewpoint.

1. This question relates to oxygen and radiation:
   a. Discuss the oxygen effect during radiation therapy *[4 marks]*
   b. Define the oxygen enhancement ratio (OER) and discuss its relationship to dose rate and the cell cycle *[4 marks]*
   c. Discuss the mechanism of the oxygen effect *[2 marks]*
2. Write short notes on the pathogenesis and sequelae of ionising radiation effects on the:
   a. thyroid gland *[3 marks]*
   b. heart *[3 marks]*
   c. retina *[4 marks]*
3. Repopulation of cancer cells after exposure to multiple doses of photons has been of considerable interest in radiotherapy.
   a. In what cancer types has repopulation been observed? *[2 marks]*
   b. What is the **radiobiological basis** for the altered fractionation schemes that are being used to overcome repopulation? *[5 marks]*
   c. What altered fractionation schemes have been used **in clinical practice** to overcome repopulation? *[3 marks]*
4. Write short notes on the following laboratory techniques, including what they are and what they can be used for:
   a. Northern blot analysis *[4 marks]*
   b. Western blot analysis *[4 marks]*
   c. *In situ* hybridisation *[2 marks]*
5. Regarding the cell cycle:
   a. Define the cell cycle and describe the cell cycle phases. *[3 marks]*
   b. Define the key events in the cell cycle which involve DNA. *[2 marks]*
   c. List key molecules which drive the cell cycle *[2 marks]*
   d. Define cell cycle checkpoints. What checkpoints occur in the cell cycle after ionising radiation exposure? *[3 marks]*
6. This question is of multiple choice format and is to be answered on the separate QUESTION 6 DOCUMENT provided, according to the instructions on the document itself.

August 2005

Time Allowed: 3 hours
Instructions for this examination:
ALL questions are to be attempted. ALL questions are of equal value.
NB – in each examination, there are six questions, the sixth being of multiple choice format. It is a separate document and the College does not release the Multiple Choice Questions.
As points are not deducted for incorrect answers, candidates should respond to all MCQ questions.

1. Combination radiation therapy and cytotoxic chemotherapy provides better local control and therapeutic ratio than radiation therapy alone for a number of malignancies. Discuss the biological mechanisms of interaction of the two modalities to provide better local control.

2. a. What factors determine local tumour control after a course of ionising radiation?
   b. With the help of diagrams or graphs, describe dose-response relationships in tumours and normal tissues.
3. Cell loss is an important kinetic factor which contributes to the dynamic state of tumour growth.
   a. Describe the mechanisms by which cell loss occurs.
   b. How is cell loss measured in normal and neoplastic tissues?
   c. What is the relevance of cell loss in tumour growth pre-irradiation and post-irradiation?

4. How do early and late radiation reactions differ with respect to latency, fractionation sensitivity and overall treatment time?
   a. Give an example of a defined scoring system for either early or late reactions.
   b. What factors might contribute to severe acute or late radiation reactions seen in the clinic?
5. In radiobiological terms, write short notes on THREE of the following:
   a. The polymerase chain reaction
   b. The radiobiological basis of radiation therapy in the management of benign neoplasms and non-neoplastic diseases.
   c. Radiation effects on the ovary
   d. Shrinking field technique

February 2005

1. In the treatment of soft tissue sarcoma, external beam radiation therapy (EBRT) and brachytherapy implants are used in both preoperative and postoperative settings. Discuss the relative radiobiological advantages and disadvantages of each strategy. Is there an ideal length of time between pre- and post-operative EBRT and surgery? If so, what are the possible radiobiological rationales guiding the timing of the two therapies?
2. Long waiting times for radiotherapy and interruptions in treatment have potentially adverse effects on treatment outcomes. Discuss the radiobiology of the tumour types likely to be most and least affected by such delays and the likely size of the effects. What radiobiological-based strategies might be employed to minimise the effects of treatment delays and interruptions?
3. (a) Describe the cellular and molecular defects in patients with Ataxia-Telangiectasia (A-T) that are responsible for their increased radiosensitivity and risk of malignancy.
   (b) Suppose you just cloned the A-T gene, ATM. Draw a table of the molecular assays you might consider using to characterise the gene, what the assay is capable of showing (or reason for the assay) and some findings you might see in A-T cells.
4. List the sources of ionising radiations to which human beings are and have been exposed. Draw a simple graph of the time course for the development of leukaemias and solid tumours in Hiroshima survivors. Discuss the radiobiologic basis of radiation carcinogenesis.
5. In radiobiological terms, write short notes on the following:
   a. The bystander effect
   b. Tumour clonogens
   c. The *Ras* gene
   d. Ionising radiation effects on the thyroid gland

August 2004

1. Discuss how useful or otherwise the linear quadratic concept of radiation cell kill is in daily clinical practice.
2. Total body irradiation is often used as part of bone marrow transplantation. Discuss the potential late effects of total body irradiation, including the cell population(s) involved and the mechanisms thought to be responsible for the effects.
3. What are the subcellular target(s) for the ionising radiation response? Classify and discuss the factors which can influence radiation response, including a brief mention of where modulators of radiation response have shown some clinical promise.

4. Repopulation of cells after exposure to multiple doses of photons has been the subject of considerable interest in radiotherapy, since it was found that the proliferation of surviving cells between successive fractions of radiation may be a determinant in tumour control. Discuss the biologic characteristics of the types of tumours in which this process has been observed. What is the radiobiological basis for the adoption of altered fractionation regimes that are presently being utilised to overcome repopulation?
5. Write short notes on THREE of the following:
   a) Northern blotting
   b) Systems for reporting normal tissue injury from radiation
   c) Fluorescent in situ hybridization
   d) Transcription and translation

February 2004

1. A single institution retrospective review of radical radiotherapy outcomes for cancer of the oesophagus reports zero toxicity.
   Discuss the implications of this statement from a RADIOBIOLOGICAL VIEWPOINT, with particular reference to tumour control.
2. How do early and late radiation reactions differ with respect to latency, rates of evolution once established, fractionation sensitivity and the effects of overall treatment time?
   List and define reaction scoring systems in common clinical use and give one example of how they rank an early and a late reaction.
   How are dose-response data for these endpoints plotted on graphs?
3. Discuss the RADIOBIOLOGICAL RATIONALE for pre-, post- and intra-operative radiation therapy.
4. How would you describe the underlying principles of CHART to an interested medical colleague?
   Can you suggest how the CHART schedule might be modified to make it more generally applicable?
5. Write short notes on three of the following:
   a. Stochastic effects of ionising radiation
   b. Tumour suppressor genes
   c. Western blotting
   d. The CDK-cyclin complex

July 2003

1 Discuss the relative RADIOBIOLOGICAL advantages and disadvantages of high dose rate and low dose rate brachytherapy.

2 For decades, tumour hypoxia has been thought important in determining overall tumour response to ionising radiation. Discuss the CLINICAL and LABORATORY evidence supporting this view, and current approaches to combat hypoxia.

3 Discuss the advantages and disadvantages of intensity modulated radiation therapy (IMRT), in terms of tumour control probability (TCP) and normal tissue complication probability (NTCP).

4 Discuss the role of cytokines in the pathogenesis of acute and late radiation effects. Illustrate your answer with reference to effects on the lung.

5 Write short notes on any three of the following:
   a) Ras oncogenes
   b) Molecular control of the G1 cell cycle checkpoint
   c) Radiation effects on the eye
   d) Hereditary effects of radiation

February 2003

1 What is the rationale for combining chemotherapy and radiotherapy? What are the side-effects of such combined therapies? 2 Define Knudson's 'two-hit' hypothesis. To which broad class of cancer-associated genes does it refer? Illustrate your answer with reference to a tumour type to which it is relevant.

3 Overall treatment time has long been recognised as a determinant of the outcome of radiotherapy. Discuss the evidence supporting this statement and describe the resulting clinical approaches/endeavours designed to address the problem.

4 A 70-year-old lady with metastatic melanoma is being treated with radiation therapy to her left thigh for multiple subcutaneous deposits of melanoma. The treatment schedule is 6 Gy per fraction, 2 fractions per week for a total of 6 fractions over a 3-week period with orthovoltage energy. Assume all relevant late reacting tissues have an alpha/beta of 2 and acute reacting tissues and tumour a value of 10. Calculate the BED (biologically effective dose). How should the patient be counselled on the potential disadvantages of this fractionation compared with standard fractionation of 36 Gy in 18 fractions over 25 days? Give an account of the radiobiology of late radiation toxicity in the skin.

5 Write short notes on any three of the following:
   a) Molecular aspects of apopotsis
   b) Cisplatin radiosensitisation
   c) The comet assay, including the biological endpoints it can measure
   d) Radiation retinopathy

August 2002

1 The reason why some human tumours are locally controlled by radiotherapy and others are not remains one of the key questions in the radiobiology of cancer treatment. Give an account of the various factors thought to be responsible for this difference in radiation response.

2 Repopulation of cells after exposure to multiple doses of photons has been the subject of considerable interest in radiotherapy since it was found that the proliferation of surviving cells between successive fractions of radiation may be a determinant in tumour control. Discuss the biologic characteristics of the types of tumour in which this process has been observed. What is the radiobiological basis for the adoption of altered fractionation regimes that are presently being utilised to overcome repopulation?

3 Discuss the rationale and applications of Dose-Volume-Histograms. What are their radiobiological limitations?

4 The late effects of radiotherapy observed in children treated for cancer suggest that certain tissues/organs are highly susceptible to damage. Describe the cell populations involved, and discuss the mechanisms thought to be responsible for the effects manifested.

5 Write short notes on any three of the following:
   a) Radiation effects on the kidney
   b) Radiation-induced apoptosis
   c) Fluorescent in situ hybridisation
   d) Target Cell Theory

February 2002

1 "Conventional" external beam fractionated radiotherapy generally refers to daily fractions, five days per week at approximately 2.0Gy per fraction. Discuss the underlying radiobiological factors, including tumour and tissue kinetic factors, that may have contributed to the evolution of this practice.

2 Outline the basic components of the clonogenic cell survival assay. What difficulties exist in extrapolating results from this assay to in-vivo tissue responses?

3 Define a "late effect" in radiobiological terms. Discuss the radiobiology and pathophysiology of late effects giving examples.

4 Describe the properties of high-energy neutrons. In radiobiological terms, give an account of the potential value of neutron radiotherapy for the treatment of some types of human solid tumours. Do the clinical results justify the continued employment of this form of treatment?

5 Write short notes on any three of the following:
   a) The shrinking field technique
   b) The clinical and radiobiological relevance of tumour doubling time (Td) and potential doubling time pot)
   c) Biological dosimetry
   d) Discuss the role of cytokines in the pathogenesis of acute and late radiation effects. Illustrate your answer with reference to effects on the lung.

August 2001

1 It is often stated that the technique for the combination of external beam therapy supplemented with brachytherapy is one of the most successful employed in radiotherapy. Compare and contrast the radiobiological basis for these two methods.

2 The radioresistance of a tumour is the end result of a variety of phenomena overlapping at the cellular and tissue level. In radiobiological terms, give an account of these factors including the modalities that are currently in use for overcoming the problems.

3 Describe the types of cell populations involved and the radiobiological explanation for the long term complications that might be observed following mantle irradiation in the treatment of Hodgkin's disease.

4 a) What is meant by the term "stochastic effects"? Illustrate your answer with appropriate examples.
   b) Discuss the radiobiological basis of the recommendations made by the International Commission on Radiological Protection (I.C.R.P) when setting dose limits for occupational exposure.

5 Write short notes on any three of the following:
   a) Effects of ionising radiation on the liver
   b) Radiation induced immunosuppression
   c) Predictive assays and their limitations
   d) Potentially lethal damage

February 2001

1 A new conformal technique allows significant dose escalation across a tumour volume. Unfortunately, the tumour margins may be significantly under-dosed. Explain in clinical radiobiological terms why tumour control probability outcomes may or may not be different from a conventional treatment approach in which tumour volume coverage is complete but to a conventional dose.

2 What is carcinogenesis? Describe the types of neoplasms most often induced by ionising radiation, the dose-response relationship presently employed by radiological protection authorities for risk estimates and the doses commonly involved in cancer induction. List the various groups of individuals in whom such neoplasms have been observed.

3 How do early and late radiation reactions differ with respect to latency, fractionation sensitivity and overall treatment time? Give examples of defined scoring systems for early and late reactions. How is dose-response data plotted for these endpoints?

4 What are the subcellular target(s) for the ionising radiation response? Discuss the factors which can influence radiation response, including (briefly) where measurement of factors affecting radiation response have shown some clinical promise.

5 Write short notes on any three of the following:
   a) p53 mutations in human malignancy
   b) functional sub-units and tissue response to ionising radiation
   c) hyperfractionated radiotherapy schedules
   d) Predictive assays and their limitations

August 2000

1 List methods which have been used for the treatment of cancer by hyperthermia. Discuss the biological effects of heat on cells, and compare/contrast cell killing by heat and ionising radiation.

2 A 120 kg male has had 4 separate fluoroscopic cardiac interventional procedures over the past week. The beam used wide field imaging at 120kv, averaging 30 minutes beam on time per exposure at 0.2 gray per minute. How should this man be counselled on all the relevant effects from his absorbed dose? Outline the radiobiology of acute human skin reactions (timing, cellular changes and gross skin changes).

3 Discuss the relevance of tumour hypoxia in current Radiation Oncology practice.

4 Describe the mammalian cell cycle, emphasising its main components and the molecules and processes which both regulate, and are regulated, during the cycle. What changes can ionising radiation induce in the cell cycle?

5 Write short notes on any three of the following:
   a) Rationale for post-operative irradiation
   b) The significance of chromosome aberrations following irradiation
   c) CHART
   d) Potentially lethal damage and its repair

February 2000

1 A 30 year old man had an orchidectomy for a seminoma of the testis and is to be treated with radiotherapy to the para-aortic and ipsilateral iliac region. Inevitably some scattered radiation will occur to the remaining testicle. Assuming that the remaining testicle receives a total dose of approximately 0.5Gy,discuss the biological consequences of such a dose. What advice would you give regarding future fertility and hazards to progeny?

2 Compare and contrast conformal photon treatment techniques and proton treatments from a RADIOBIOLOGICAL perspective.

3 A planning error resulted in the delivery of 4 Gy per fraction for a patient being treated radically for tonsillar cancer. His treatment was stopped after 14 fractions to a dose of 54 Gy. His original prescription was for 70 Gy in 35 fractions over 7 weeks. Describe the expected acute and late effects on all the sensitive tissues of relevance for the actual and intended treatment and outline the potential risks in terms of tumour cure rates arising from this error. (Assume all relevant late reacting tissues have an alpha/beta of 2 and acute reacting tissues and tumour a value of 10. Assume re-population begins at 16 days into treatment).

4 Cell loss is an important kinetic factor which contributes to the dynamic state of tumour growth. Describe the various mechanisms by which cell loss occurs, how it is measured in normal and neoplastic tissues and, in particular, the relevance of cell loss in tumour growth pre-irradiation and post-irradiation

5 Write short notes on any three of the following:
   a) Radiation effects on the parotid gland
   b) Inflammatory Modulators of Radiation Reactions
   c) Free Radicals
   d) Radiation Pneumonitis arising from Chemoradiotherapy Treatment

August 1999

1 Repopulation of cells after exposure to multiple doses of photons has been the subject of considerable interest in radiotherapy, since it was found that the proliferation of surviving cells between successive fractions of radiation may be a determinant in tumour control. Discuss the biologic characteristics of the types of tumours in which this process has been observed. What is the radiobiological basis for the adoption of altered fractionation regimes that are presently being utilised to overcome repopulation?

2 Describe the biological effects of ionising radiation on the mammalian cell, ranging from the macromolecular level and sub-cellular components to the whole cell.

3 A recent large phase 3 clinical trial has demonstrated that there is no survival advantage associated with the addition of Cis-Platinum and 5-FU in combination with surgery for localised oesophageal cancer. Other trials have demonstrated that the combination of radiotherapy and the same drugs produce measurable benefits in local control and survival. Explain why this may be so, given that radiotherapy, like surgery, is a local modality. How do Cis-Platinum and 5-FU interact with radiation?

4 What, from a RADIOBIOLOGICAL perspective, are the advantages and disadvantages of using high LET radiotherapy for cancer treatment? Discuss the situations where high LET radiation has been used in the clinical situation.

5 Write short notes on any three of the following:
   a) Genes controlling radiosensitivity
   b) Consequential late reactions
   c) Tumour growth delay assay
   d) TGF-Beta and radiation

February 1999

1 Tumour radioresistance has often been ascribed to tumours containing a high proportion of hypoxic cells. On the other hand, the process of re-oxygenation taking place during a fractionated course of radiotherapy has led some investigators to doubt the validity of this opinion. In RADIOBIOLOGICAL terms, describe the basis for both phenomena, citing any experimental or clinical evidence to support your viewpoint/s.

2 In the treatment of carcinoma of the cervix, compare and contrast the differences, particularly RADIOBIOLOGICAL between:
   a) High dose rate external beam radiotherapy only
   b) Low dose rate continuous brachytherapy only
   c) High dose rate pulsed brachytherapy (remote afterloading system)

3 "Conventional" external beam fractionated radiotherapy generally refers to daily fractions, five days per week at approximately 2.0Gy per fraction. Discuss the underlying RADIOBIOLOGICAL factors including tumour and tissue kinetic factors that may have contributed to the evolution of this practice.

4 Discuss the rationale and applications of Dose-Volume-Histograms. What are their RADIOBIOLOGICAL limitations?

5 In RADIOBIOLOGICAL TERMS write short notes on three of the following:
   a) Hypoxia and haemoglobin
   b) Radiation-induced cataracts
   c) Bone marrow syndrome
   d) Effects of X-Rays on embryo/fetus