



First Year MBBS - Batch 51 Foundation Module Small Group Discussion Cellular Control Mechanism, Cell Cycle & Apoptosis

DR. NAYAB ZONISH NAWAZ PGT Physiology

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Motto

Vision; The Dream/Tomorrow



- To impart evidence based research oriented medical education
- To provide best possible patient care
- To inculcate the values of mutual respect and ethical practice of medicine





Professor Umar Model of Integrated Lecture





Bloom's Taxonomy : Domains Of Learning

Sr. #	Domain of learning	Abbreviat ion	Levels of the domain	Meaning
1	cognition	С	C1	Recall / Remembering
2			C2	Understanding
3			C3	Applying / Problem solving
4	Psychomotor	Ρ	P1	Imitation / copying
5			P2	Manipulation / Follows instructions
6			Р3	Precision / Can perform accurately
7	Attitude	A	A1	Receiving / Learning
8			A2	Respond / Starts responding to the learned attitude
9			A3	Valuing / starts behaving according to the learned attitude



Diagrammatic Representation Of Blooms Taxonomy





Learning Objectives

Sr. #	Learning Objective	Domain of Learning
1	To understand control of cell growth and cell reproduction	C2
2	To explain replication of chromosomes and cell cycle	C1
3	To understand programmed cell death / apoptosis	C2



Horizontal Integration





DNA, genes, & chromosomes





Control of cell growth

Growth of the cells is controlled by three ways:

- **1. Growth factors** from other parts of the body e.g. pancreatic growth
- 2. Availability of **space** for growth e.g. cell growth in tissue culture
- **3. Negative feedback** effect e.g. own secretions in tissue culture



Cell Reproduction

Reproduction and growth of different types of cells:

- 1. Do not reproduce for many years e.g. smooth muscle cells
- 2. Reproduce only during fetal life e.g. neurons

3. Reproduce all the time e.g. blood-forming cells



Cell Reproduction

 Regeneration of the organs occurred by rapid division of the cells until appropriate numbers again available e.g. liver transplantation



Replication of Chromosomes

- Number of chromosomes in human cell is 46
- Number of pairs is 23
- Genes also exist in pairs
- Replication occurs after few minutes of replication of DNA.





Histones

- Electro positively charged small molecules that lead to the formation of large number of proteins present in chromosomes.
- Organized in vast numbers of small, bobbin like cores.





Functions of Histones

- Regulates DNA activity.
- Decondense by regulatory proteins.





Cell Cycle

'Cell cycle is the period of time between the birth of a cell and its own division to produce two daughter cells'

The Rawalpindi Medical University





Reference: Silverthorn Physiology 6th Edition A-22 appendix C







Cell Division

The process by which cells divide into two daughter cells with the

same genetic material are:

- Mitosis
- Meiosis
- 1. Meiosis I
- 2. Meiosis II
- Karyokinesis
- Cytokinesis





Interphase





Mitosis

'A type of cell division in which parent cell divides into two daughter cells and each of two daughter cells receive a chromosomal karyotype identical to parent cells'





Core knowledge

Reference : Guyton and Hall Textbook of Medical physiology page no.41 23



Phases of Mitosis

Prophase

- Metaphase
- > Anaphase
- > Telophase

MITOSIS STAGES







Prophase

- Chromosomes becomes visible
- Centriolar migration
- Assembling of microtubules
- Formation of asters





Prometaphase - Metaphase





Metaphase

- Equatorial plate and chromosomal alignment
- Centromeres lie in single transverse plane
- Chromosomes acquire two groups of kinetochore microtubules which exert pull on chromosomes





Anaphase

- Separation of sister chromatids due to split in centromeres
- Chromosomes clustered at spindle poles
- Formation of cleavage furrow starts





Telophase

- Cleavage furrow gradually deepens.
- Bundles of spindle microtubules still connecting daughter cells.
- Formation of nuclear envelope and reappearance of nucleoli occurs.
- Uncoiling of chromosomes.





Meiosis

Special type of cell division in germ cells

> Two successive cell divisions

- 1. Meiosis I
- 2. Meiosis II
- ➢ Four daughter cells

Haploid chromosomes + genetic variation



Phases of Meiosis I



The chromosomes condense, and the nuclear envelope breaks down. Crossing-over occurs. Pairs of homologous chromosomes move to the equator of the cell. Homologous chromosomes move to the opposite poles of the cell.

Chromosomes gather at the poles of the cells. The cytoplasm divides. Core knowledge



- Prophase I
 - Laptotene
 - > Zygotene
 - Pachytene
 - > Diplotene
 - Diakinesis



> Laptotene:

- -Leptonema (Thin threads)
- Chromosomes visible as long, thin threads with beading pattern.
- -Short duration



• Pachytene:

Pachynema (Thick threads)

- > Chromosomes thicker & shorter due to coiling
- Closely apposed so homologous chromosome appear as one chromosome
- > Crossing over between homologous chromosomes
- ➤ Chiasmata formation → site where chromosomes remain attached & exchange of chromosomal segments occur.



• Diplotene:

Diplonema(two threads)

> Chromosomes begins to separate along their length.

> Chromosomes begin to uncoil except

Chiasmata



Diakinesis

- Chromosomes, still as bivalents, become even shorter and thicker.
- ➢Nucleoli disappear
- Formation of spindle and asters
- The nuclear membrane disappears and bivalent chromosomes move towards equatorial plate (prometaphase)


Phases of Prophase I



Metaphase I

- Bodies attach to the spindle microtubules are bivalents, not single chromosomes
- Homologous pairs lie parallel to the equatorial plate, with one on either side.

C Meiosis I





Anaphase I

- Homologous pair completely separates from each other & move to opposite poles of spindles
- No division of centromeres occurs & whole chromosome move to opposite poles
- > Positioning of bivalent pairs is random.





Telophase I

- Assortment of maternal and paternal chromosomes in each Telophase nucleus is also random.
- Nuclei reconstructed & Cytokinesis divide parent cell

into two daughter cells





Meiosis II

- Meiosis II is more like mitosis commences after a short interval
- No DNA synthesis occurs.
- Unlike mitosis, the separating chromatids are genetically different.
- Cytoplasmic division also occurs



Phases of Meiosis II





A new spindle forms around the chromosomes.













Centromeres divide. Chromatids move to the opposite poles of the cells.



Telophase II & cytokinesis



A nuclear envelope forms around each set of chromosomes. The cytoplasm divides.



Core knowledge



Prophase II

- Disappearance of the nucleoli and the nuclear envelope
- Shortening and thickening of the chromatids
- Centrioles move to the polar regions and arrange spindle fibers for the second meiotic division





Metaphase II

 Two kinetochore attach to spindle fibers from the centrioles at each pole.



Anaphase II

 Centromeres are cleaved
Sister chromatids pulled apart

• The sister chromatids are now called sister chromosomes Separation of daughter chromosomes (with two sister chromatids)







Telophase II

- Uncoiling and lengthening of the chromosomes
- Spindle disappear
- Nuclear envelopes reform and cell wall formation
- Four daughter cells formed, each with a haploid set of chromosomes.





Karyokinesis vs. Cytokinesis

Karyokinesis:

Division of cell nucleus.

Cytokinesis:

Division of a cell bringing about separation into two daughter cells

Core knowledge



Difference Between Cytokinesis and karyokinesis



Cytokinesis





karyokinesis

Core knowledge



Apoptosis

- The process of programmed cell death.
- The death of cells which occurs as a normal and controlled part of an organism's growth or development.



Mechanism of Apoptosis

- Initiated by activation of family of proteases, called caspases.
- Caspases are formed and stored in proactive form known as procaspases.
- Once activated , cleave and activate other procaspases, triggering a cascade that breaks down protein within a cell.



Steps of Apoptosis

Major steps:

- Cell shrinks
- Cell fragments
- Cytoskeleton collapses
- Nuclear envelope disassembles
- Cells release apoptotic bodies
- Macrophages phagocytose apoptotic bodies

Core knowledge







Vertical Integration





Apoptosis in Relation to Breast tissue

 Apoptosis is involved in the remodelling of breast tissue during pregnancy and lactation.

 The balance of cell survival and death is critical for the functional changes in the breast during these periods.

> Vertical integration (Surgery)



Breast Cancer

- Dysregulation of apoptosis is a hallmark of cancer.
- In breast cancer, a disruption in the balance between cell survival and apoptosis.

Vertical integration (Surgery)



Bioethics





CULTURAL PRIZE PUBLIC MORALITY



Example

- A 45 years lady has been diagnosed with advanced breast cancer. The oncologist proposes an aggressive treatment plan that involves a combination of chemotherapy and radiation therapy.
- The treatment aims to induce apoptosis, and preventing the further spread of the disease.

Bioethics



Bioethical considerations

Includes:

- 1. Impact on healthy cells
- 2. Quality of life
- 3. Balance between potential benefits and risks.



Ethical Issue

- Apoptosis is not entirely selective because normal cells may also undergo apoptosis e.g. hair loss, nausea, and weakened immune function.
- Ensuring informed consent
- Affecting her ability to work
- Expensive treatments

Bioethics



Consideration

- How much collateral damage to healthy cells is ethically acceptable?
- Are there alternative treatments that could minimize the impact on normal cells?
- How much emphasis should be placed on extending life versus maintaining a certain quality of life?
- How much information is ethically necessary?

Bioethics



Autonomy

- The patients are able to make **independent decisions**.
- Patients should have all the needed information that is required to make a decision about their medical care and are educated.
- Doctors do not influence the patient's choice.
- The **right to refuse treatment**, the right to participate in research or refuse it.
- To exercise this right would require Informed Consent.

THE PILLAR OF AUTONOMY



Family Medicine





Example

- A 30 years lady scheduled an appointment with her family physician for the guidance on a hereditary condition that has affected multiple family members.
- Several members in the family have already been diagnosed with a genetic disorder that leads to the formation of tumors.
- She is concerned about the risk of passing the condition to future generations.

Family Medicine



Role of Family Physician

- **Explain the implications** of the genetic mutation to the family
- Assess risk for each family member and providing information on preventive measures, early detection strategies, and potential interventions for those at risk.
- Provision of genetic counselling discussing the available screening methods, and the importance of regular medical check-ups.
- Collaborates with the family, specialists, and other healthcare professionals to facilitate informed decision-making regarding treatment options.

Family Medicine



Research





Suggested Research Article

TOOLS

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and Rologia

ORIGINAL ARTICLE

Minocycline can reduce testicular apoptosis related to varicocele in male rats

Majid Shokoohi, Arash Khaki, Ayda Roudi Rasht Abadi, Linda MohammadZadeh Boukani, Sepideh Hassanpour Khodaie, Hossein Kalarestaghi, Amir Afshin Khaki 🕿 ... See all authors 🖂

First published: 09 March 2022 | https://doi.org/10.1111/and.14375 | Citations: 5

Funding information

This study was granted by the Women's Reproductive Health Research Center of Tabriz University of Medical Sciences, Grant Number: 61999.

Read the full text >

Abstract

The current research aimed to assess the impacts of Minocycline on varicocele-induced regulation of apoptotic-related genes and oxidative stress in the testis of adult Wistar rats. Thirty-two rats were divided into 4 groups: sham, varicocele (Vcl), varicocele treated with Minocycline (Vcl + Mno) for 56 days and healthy rats treated with minocycline (Mno). After 8 weeks, the oxidative stress markers levels in serum were investigated, afterwards, the level of Bax and Bcl-2 expression were assessed through 'immunocytochemistry' and RT-qPCR assays. Also, the rate of apoptosis was evaluated through the TUNEL method. Johnson's score, 'the width of epithelium' and 'seminiferous tubules diameter' were ameliorated in the Vcl + Mno group in comparison with the Vcl group. Administration of Minocycline raised the 'Glutathione peroxidase' and 'Superoxide dismutase' levels in serum and declined the Malondialdehyde level in serum (p = 0.001). Furthermore, current study represented that minocycline reduced Bax and enhanced the expression of Bcl-2 gene and protein in comparison with the Vcl group (p < 0.05). In addition, Minocycline administration significantly declined the rate of apoptosis in germ cells (p < 0.05). Our study demonstrated that the administration of Minocycline could improve testicular injury in varicocele-induced rats by its antioxidant activity.

Reference: https://onlinelibrary.wiley.com/doi/abs/10.1111/and.14375



Volume 54, Issue 4 May 2022 e14375



Citation Statements beta (i)



Effects of varicocele upon the expression of apoptosis-related proteins

F.-W. Chang, G.-H. Sun, Y.-Y. Cheng, I.-C. Chen, H.-H. Chien, G.-J. Wu

Promoting

Research Culture



Crux of Suggested Research Article

- The impacts of Minocycline on varicocele induced regulation of apoptotic-related genes and oxidative stress in the testis of adult rats.
- Varicocele treated with Minocycline for 56 days and healthy rats treated with only Minocycline .
- After 8 weeks, the oxidative stress markers levels in serum were investigated and the rate of apoptosis was evaluated .
- The width of epithelium and seminiferous tubules diameter were ameliorated in the first group in Promoting comparison with the healthy group.



Research Culture

How To Access Digital Library

- Steps to Access HEC Digital Library
- 1. Go to the website of HEC National Digital Library.
- 2. On Home Page, click on the INSTITUTES.
- A page will appear showing the universities from Public and Private Sector and other Institutes which have access to HEC National Digital Library HNDL.
- 4. Select your desired Institute.
- 5. A page will appear showing the resources of the institution
- 6. Journals and Researches will appear

7. You can find a Journal by clicking on JOURNALS AND DATABASE and enter a keyword to search for your desired journal. Link:https://www.topstudyworld.com/2020/05/access-hecdigital-library.html?m=1



How to Apply for HEC Digital Library if you are not Member

 If you are not a member of HEC national digital library then you can fill the application after downloading it from

http://www.digitallibrary.edu.pk/app_form.html

- Fill the form that will appear like this
- Mail it to mailto:

Promoting Research Culture







Structured Essay Question Related To Topic

Q: A 27 years female has delivered a baby 1 week ago. After delivery Regression of uterus is function of which organelle?

Brainstorming





Brainstorming


References

1. Books:

- Guyton and Hall Textbook Of Medical Physiology fourteenth edition page no. 41-43,45
- Ganong's Review of Medical Physiology page no.5
- Silverthorn Physiology 6th Edition A22
- Google images.

2. Medical Journal articles:

Reference: Minocycline can reduce testicular apoptosis related to varicocele in male rats

Published in: First International Journal of Andrology

References



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Take-home

message



• Core knowledge:

Control of cell growth, cell cycle and apoptosis

• Horizontal Integration:

Embryology and Biochemistry

- Vertical Integration:
- Gynaecology : Example of Breast tissue (apoptosis after pregnancy and lactation)
- Research:

Minocycline can reduce testicular apoptosis related to varicocele in male rats

• Biomedical Ethics:

Example of Breast cancer (impact on quality of life, potential risks and benefits)

Autonomy

The patients are able to make independent decisions

• Family Medicine:

Genetic Counselling

Take home

message



