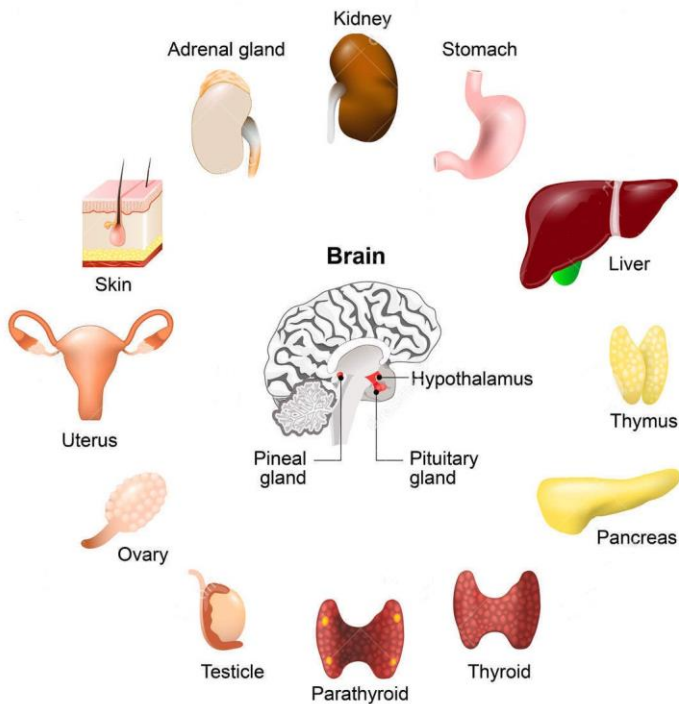


ENDOCRINE SYSTEM



STUDY GUIDE

SECOND YEAR MBBS

18th Aug- 13th Sep 2025

DURATION: 4 WEEKS

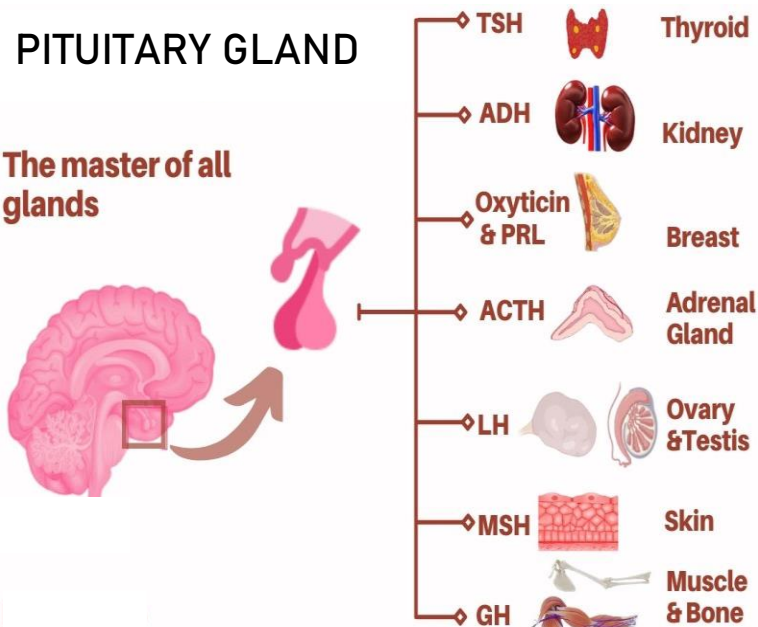
Insulin



ENDOCRINE MODULE-I

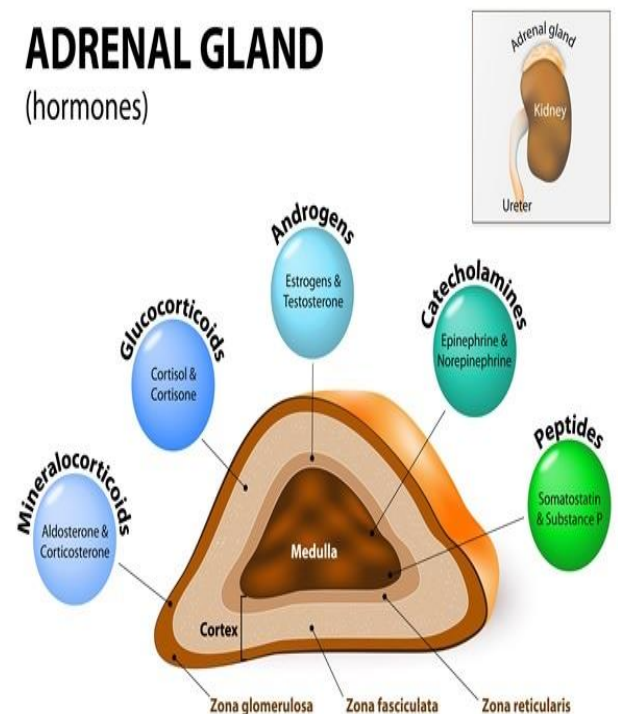
PITUITARY GLAND

The master of all glands



ADRENAL GLAND

(hormones)



LIAQUAT NATIONAL HOSPITAL AND MEDICAL COLLEGE

Institute for Postgraduate Medical Studies & Health Science



STUDY GUIDE FOR ENDOCRINE MODULE

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Module name: Endocrine

Year: Two

Duration: 4 weeks (Aug 18th to Sep 13th, 2025)

Timetable hours: Lectures, Case-Based Learning (CBL), Self-Directed Learning, Flipped Classroom, Practical, Skills, Demonstrations

MODULE INTEGRATED COMMITTEE

MODULE COORDINATOR:	Professor Faiza Waseem (Biochemistry)
CO-COORDINATORS:	Dr. Lubna Faisal (Anatomy)

DEPARTMENTS' & RESOURCE PERSONS' FACILITATING LEARNING

BASIC HEALTH SCIENCES	CLINICAL AND ANCILLARY DEPARTMENTS
ANATOMY Professor Zia-ul-Islam	RESEARCH & SKILLS DEVELOPMENT CENTER Dr. Kahkashan Tahir
BIOCHEMISTRY Professor Faiza Waseem	
PATHOLOGY Professor Naveen Faridi	
PHYSIOLOGY Professor Syed Hafeez ul Hassan	
DEPARTMENT OF HEALTH PROFESSIONS EDUCATION <ul style="list-style-type: none"> • Professor Nighat Huda • Dr. Yusra Nasir • Professor Sobia Ali • Dr. Syed Asad Sibtain • Dr. Afifa Tabassum • Dr. Asra Zia 	
LNH&MC MANAGEMENT <ul style="list-style-type: none"> • Professor KU Makki, Principal LNH&MC • Dr. Shaheena Akbani, Director A.A&R.T LNH&MC 	
STUDY GUIDE COMPILED BY: Department of Health Professions Education	

INTRODUCTION

WHAT IS A STUDY GUIDE?

It is an aid to:

- Inform students how student learning program module has been organized
- Help student's organize and manage their studies throughout the module
- Guide students on assessment methods, rules and regulations

THE STUDY GUIDE:

- Communicate information on organization and management of the module, this will help the student to contact the right person in case of any difficulty.
- Define the objectives which are expected to be achieved at the end of the module.
- Identify the learning strategies such as lectures, small group teachings, clinical skills, demonstration, tutorial and case based learning that will be implemented to achieve the module objectives.
- Provide a list of learning resources such as books, computer assisted learning programs, web-links and journals for students to consult in order to maximize their learning.
- Highlight information on the contribution of continuous and examinations on the Students overall performance.
- Include information on the assessment methods that will be held to determine every student's Achievement of objectives.
- focuses on information pertaining to examination policy, rules and regulations.

CURRICULUM FRAMEWORK

Students will experience integrated curriculum in module at LNMC in accordance with the JSMU guidelines and most recent developments that have an impact on individual health.

INTEGRATED CURRICULUM

Comprise of system-based modules such as Head and Neck & Special Senses, Neurosciences and Endocrinology which links basic science knowledge to clinical problems. Integrated teaching means that subjects are presented as a meaningful whole. Students will be able to have better understanding of basic sciences when they repeatedly learn in relation to clinical examples.

Case-based discussions, computer-based assignments, early exposure to clinics, wards, and skills acquisition in skills lab a characteristics of integrated teaching program.

LEARNING METHODOLOGIES

The following teaching / learning methods are used to promote better understanding:

- Interactive Lectures
- Small Group Discussion
- Case- Based Learning
- Practical
- Skills session
- Flipped Classroom
- Self-Study

INTERACTIVELECTURES

In large group, the lecturer introduces a topic or common clinical conditions and explains the underlying phenomena through questions, pictures, videos of patients' interviews, exercises, etc. Students are actively involved in the learning process.

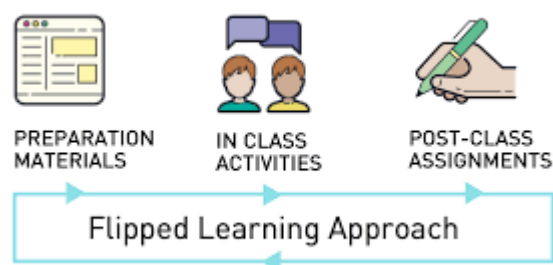
SMALL GROUP DISCUSSION: This format helps students to clarify concepts acquire skills or attitudes. Sessions are structured with the help of specific exercises such as patient case, interviews or discussion topics. Students exchange opinions and apply knowledge gained from lectures, tutorials and self-study. The facilitator role is to ask probing questions, summarize, or rephrase to help clarify concepts.

CASE-BASEDLEARNING: A small group discussion form at where learning is focused around a series of questions based on a clinical scenario. Students' discuss and answer the questions applying relevant knowledge gained in clinical and basic health sciences during the module.

PRACTICAL: Basic science practical's related to anatomy, biochemistry, pathology, pharmacology and physiology rescheduled for student learning.

SKILLS SESSION: Skills relevant to respective module are observed and practiced where applicable in skills laboratory or Department of Physiotherapy.

FLIPPED CLASSROOM: A flipped classroom is a **type of blended learning** where students are introduced to content at home and practice working through it at Classroom. This is the reverse of the more common Practice of introducing new content classrooms, then



assigning homework and projects to completed by the

Students in dependently at home.

The concept behind the flipped classroom is to rethink when students have access to the resources they need most. If the problem is that students need help doing the work rather than being introduced to the new thinking behind the work, then the solution the flipped classroom takes is to reverse that pattern.

SELF DIRECTED LEARNING: Students' assume responsibilities of their own learning through individual study, sharing and discussing with peers, seeking information from Learning Resource Center, teachers and resource persons within and outside the college. Students can utilize the time within the college scheduled hours of self-directed learning.

**Apart from attending daily scheduled sessions,
Students too should engage in self-study to ensure
that all the objectives are covered.**



MODULE: ENDOCRINE-1**INTRODUCTION**

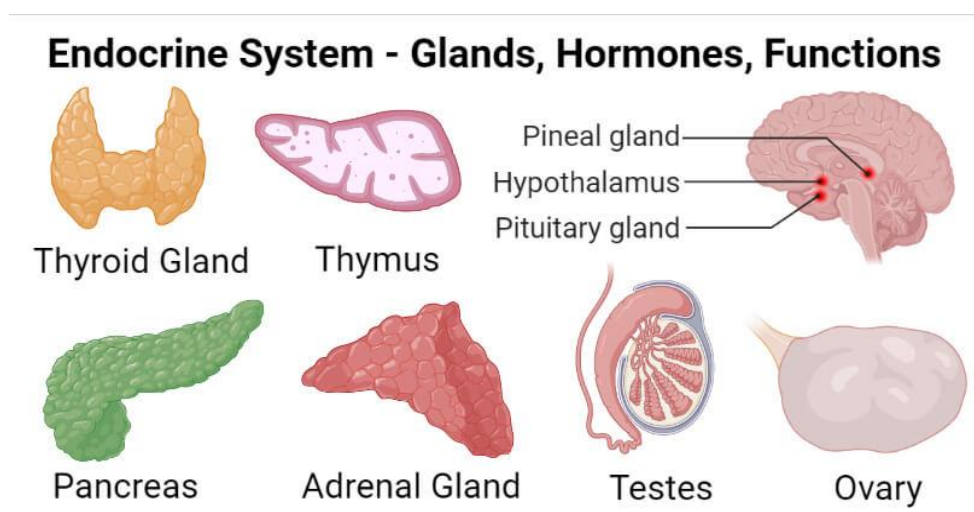
The Endocrine system relays information and maintains a constant internal environment of the body called homeostasis. It acts through chemical messengers called hormones that influence growth, development, and metabolic activities. The action of the endocrine system is measured in minutes, hours, or weeks and is more generalized than the action of the nervous system.

This M.B.B.S second year module will help you develop knowledge and understanding of the:

- Basic concepts of molecular endocrinology that underpin hormone actions, how dysfunction relates to primary pathogenesis, and how this knowledge informs improvement in diagnosis and the potential for novel therapies
- Hypothalamic - pituitary axes and their role in health and disease, including the reproductive, adrenal, and thyroid axes
- Neuro-endocrine control of food intake, energy expenditure and obesity
- Theories of the etiology and pathogenesis of type 2 diabetes mellitus

Similarly, this module of endocrine system will enable you to recognize the clinical presentations of common endocrine logical and metabolic disorders and relate clinical manifestations to basic sciences. This Endocrine module will be revisited in the following years.

The study guide will help you prioritize the important topics for learning in relation to the module objectives through lectures, demonstrations, tutorials, practical and skills lab sessions.



COURSE TOPICS, OBJECTIVES AND TEACHING STRATEGIES

At the end of the module the students will be able to:

ANATOMY

TOPICS & OBJECTIVES	LEARNING STRATEGIES
1. Anatomical overview of all endocrine glands in body	Interactive Lecture
• Classify the glands	
• Define endocrine glands	
• Describe the location of all endocrine glands in the body	
• Discuss the functions of all endocrine organs in the body	
2. Gross anatomy and development of the Pituitary gland	Interactive Lecture/ Tutorial
• Describe the location, relations and external features, and division/components of pituitary gland	
• Describe the neurovascular supply of pituitary gland	
• Discuss the hypophyseal portal system	
• Explain the development of pituitary gland	
• Discuss the related clinical conditions & congenital anomalies of the pituitary gland	Interactive Lecture/ Practical
3. Microscopic anatomy of the Pituitary gland	
• Enumerate different parts of adenohypophysis and neurohypophysis	
• Discuss the histological features of adenohypophysis and neurohypophysis	
• Explain the different cell types and functions of both parts of pituitary gland	Interactive Lecture/ Practical
4. Review of gross and microscopic anatomy of the Thyroid and Parathyroid glands	
• Describe the location, relations & neurovascular supply of thyroid gland.	
• Describe the cellular architecture found in the thyroid gland	
• Correlate microscopic structures with clinical conditions of the thyroid gland	
• Describe the gross and microscopic anatomy of the parathyroid gland.	Interactive Lecture
5. Developmental and microscopic anatomy of the Pancreas	
• Describe the histological structure and components of exocrine and endocrine pancreas	Interactive Lecture
6. Gross and microscopic anatomy of the Adrenal Gland	
• Describe the gross anatomical features and location of the adrenal gland along with its neurovascular supply	
• Describe the cells found in cortex and medulla	
• Correlate the gross and microscopic structure of the adrenal gland with common clinical conditions	Interactive Lecture
7. Development and anomalies of the Adrenal Gland	
• Explain the embryological origin and development of the cortex and medulla of adrenal gland	
• Discuss the developmental anomalies of the adrenal gland	Interactive Lecture / Practical
8. Histology of Pituitary gland	
• Identify the slide of Pituitary gland	
• Describe the microscopic features of pituitary gland	Interactive Lecture / Practical
9. Histology of Thyroid and Parathyroid gland	
• Identify the slide of Thyroid and Parathyroid gland	
• Discuss the microscopic features of Thyroid and Parathyroid gland	Interactive Lecture / Practical
10. Histology of Pancreas	

• Identify the slide of Pancreas	Interactive Lecture / Practical
• Explain the microscopic features of Pancreas	
11. Histology of Adrenal gland	
• Identify the slide of Adrenal gland	
• Describe the microscopic features of Adrenal gland	

BIOCHEMISTRY

TOPICS & OBJECTIVES	LEARNING STRATEGIES
1.Introduction to Hormones	Interactive Lecture/ Tutorial
• Classify hormones according to the mechanism of action, and give examples	
• Classify hormone receptors with examples	
• Describe the role of second messenger system	
• Summarize the hormones of the body with their functions	
2. Hypothalamic Hormones	Interactive Lecture / Tutorial
• List the hypothalamic hormones	
• Explain the chemical structure and biochemical functions of Hypothalamic hormones	
• List the stimulatory and inhibitory hypothalamic hormones	
• Discuss the hypothalamic control of pituitary hormones	
• Describe the feedback mechanism of hypothalamic hormones	
• Describe the mechanism of circadian rhythm	
3. Anterior Pituitary Hormones (Growth Hormone)	
• List the anterior pituitary hormones	
• Explain the chemical nature of growth hormone	
• Explain the mechanism of action of growth hormone	
• Discuss the synthesis and metabolic effects of growth hormone	
• Discuss clinical complications and diseases associated with growth hormone	
4. Anterior Pituitary Hormones (ACTH, LH, FSH, TSH and PRL)	Interactive Lecture/ Tutorial / SDL
• Explain the chemical structure of anterior pituitary hormones	
• Describe the mechanism of action and biochemical functions of anterior pituitary hormones	
• Discuss the hypothalamic control of pituitary hormones	
• Discuss the regulation of anterior pituitary hormone	
• Describe the clinical diseases associated with anterior pituitary hormones	
5. Posterior Pituitary Hormones	
• List the posterior pituitary hormones	
• Explain the synthesis of Posterior Pituitary Hormones	
• Explain the chemical structure of posterior pituitary hormones	
• Describe the mechanism of action, biochemical functions of posterior pituitary hormone	
• Discuss the hypothalamic pituitary axis of posterior pituitary hormones	
• Discuss the regulation of posterior pituitary hormone	
• Describe the clinical diseases associated with posterior pituitary hormones	
6. Thyroid Hormones	
• List the Thyroid hormones	

<ul style="list-style-type: none"> • Discuss the cells type and production of thyroid hormones • Explain the synthesis and chemical structure of Thyroid hormones • Describe the mechanism of action and metabolic functions of Thyroid hormones • Discuss the hypothalamic pituitary axis of Thyroid hormones • Discuss the regulation of Thyroid hormones and feedback mechanism • Describe the clinical diseases and complication associated with Thyroid hormones 	
7. Parathormone: Serum Calcium Regulation	
<ul style="list-style-type: none"> • List the hormones regulating serum calcium (Parathormone, Calcitriol and calcitonin) • Explain the synthesis chemical structure of Parathormone • Describe the mechanism of action, metabolic functions (on GIT, Skeleton & Kidneys), and regulation of Parathormone • Describe the role of 1,25-dihydroxy vitamin D in calcium homeostasis • Describe the role of Calcitonin in calcium regulation • Describe the clinical diseases and complication associated with Parathormone 	Interactive Lecture
8. Pancreatic Hormones	
<ul style="list-style-type: none"> • List the pancreatic hormones (Insulin, glucagon and somatostatin) • Explain the synthesis and chemical structure of pancreatic hormones • Describe the mechanism of action, metabolic functions, and regulation of pancreatic hormones • Describe the clinical diseases associated with pancreatic hormones • Discuss the clinical importance of pancreatic hormones 	
9. Blood Glucose Regulation	
<ul style="list-style-type: none"> • Explain the regulation of blood glucose • Discuss the tissues which regulate fuel metabolism in blood glucose level • Describe the mechanism of metabolic regulation of blood glucose • Discuss the biochemical complications of hypoglycemia and hyperglycemia 	
10. Blood Glucose: Diabetes Mellitus (DM) and its complications	
<ul style="list-style-type: none"> • Classify diabetes mellitus • Differentiate between Type I and Type II diabetes mellitus • Describe the biochemical causes of development of diabetes mellitus • Discuss the factors responsible for metabolic changes in DM • Discuss the clinical significance of diabetes mellitus and its complications • Discuss the diagnostic investigations for diabetes mellitus 	Interactive Lecture/ Practical
11. Adrenal hormones: Glucocorticoids	
<ul style="list-style-type: none"> • List the adrenal cortex hormones • Explain the synthesis chemical structure of glucocorticoids • Describe the mechanism of action and metabolic functions of glucocorticoids • Discuss the regulation of glucocorticoids • Describe the clinical diseases and complications associated with glucocorticoids 	Interactive Lecture/Cas e- Based Learning / Tutorial
12. Adrenal hormones: Mineralocorticoids	
<ul style="list-style-type: none"> • Explain the synthesis chemical structure of mineralocorticoids • Describe the mechanism of action, metabolic functions, and regulation of mineralocorticoids • Describe the clinical diseases and complication associated with mineralocorticoids 	Interactive Lecture
13. Adrenal hormones: Adrenal medullary hormones	
<ul style="list-style-type: none"> • List the adrenal medullary hormones 	

• Explain the synthesis and chemical structure of adrenal medullary hormones	Interactive Lecture/Tutorial
• Describe the mechanism of action and metabolic functions of adrenal medullary hormones	
• Discuss the regulation of adrenal medullary hormones	
• Describe the clinical diseases and complication associated with adrenal medullary hormones	
14. Pituitary hormones (Gigantism, Acromegaly, Dwarfism etc)	CBD
• Discuss the clinical importance of Pituitary hormones	
15. Thyroid & adrenal hormones (Goiter, Hypothyroidism & Hyperthyroidism, Addison's diseases , Myxedema etc.)	Tutorial/CB D/SDL
• Discuss the clinical importance of thyroid & adrenal hormones	
• Correlate the laboratory investigations with relevant clinical conditions	
16. Thyroid function tests	Practical
• Identify the chemical tests and bio-techniques to estimate the functions of the thyroid glands	
• Correlate the laboratory investigations with relevant clinical conditions	
17. Diabetes Mellitus Tests	
• Enumerate the chemical tests to detect diabetes mellitus	
• Describe the diabetes diagnostic criteria	
• Outline the method for estimation of blood glucose by glucometer	
• Describe the principle of glucometer	
• Perform blood glucose estimation by glucometer	
• Correlate the laboratory investigations with relevant clinical conditions	
18. Oral Glucose Tolerance Test (OGTT)	
• Explain the significance of OGTT and glucose challenge tests (GCT)	
• Explain the method of performance of OGTT and GCT	
• Perform OGTT and GCT	
• Interpret the results of Oral Glucose Tolerance Test & GCT	
• Estimate urine glucose with urine glucose reagent strip	
19. Pancreatic hormones Pancreatic hormones (Diabetes Mellitus)	Tutorial
• Discuss the clinical importance of pancreatic hormones	
• Interpret clinical conditions correlated with their laboratory investigations	
20. Diabetes Mellitus Tests	Tutorial
• Enumerate the biochemical tests to detect Diabetes Mellitus	

PHYSIOLOGY

TOPICS & OBJECTIVES	LEARNING STRATEGIES
1. Introduction to Endocrinology: Control and feedback of hormones	Interactive Lecture/Tutorial
• Define hormone, target cell and receptor	
• Contrast the term endocrine, paracrine and autocrine	
• Classify hormones	
• Describe the concept of second messenger	
• Explain the principles of negative and positive feedback of hormonal secretion	
2. Hypothalamus and anterior pituitary hormones	
• Name hypothalamic factors that control secretion of anterior pituitary hormones	

<ul style="list-style-type: none"> Name various cells of anterior pituitary responsible for synthesis of hormones Describe the functions and regulation of GH, FSH, LH, ACTH, TSH and prolactin Explain the hypothalamic hypophyseal portal system 	
3. Functions of Growth Hormone and associated disorders	Interactive Lecture/Tutorial
<ul style="list-style-type: none"> Describe the functions and regulation of growth hormone Describe the disorders associated with hypo and hyper secretion of GH 	
4. Hormones of Posterior Pituitary and related disorders	
<ul style="list-style-type: none"> Describe the secretion of oxytocin and ADH Explain the mechanism of action and regulation of oxytocin and ADH 	Case- Based Learning
5. Functions of Thyroid hormones	Interactive Lecture/Cas e- Based Learning
<ul style="list-style-type: none"> Explain the formation and secretion of T3 and T4 Discuss the importance of iodine metabolism and iodine pump Describe actions of thyroid hormone on development and metabolism and associated disorders Describe the role of Thyroid stimulating hormone (TSH) on thyroid hormone regulation 	
6. Functions of Parathyroid (PTH) and Calcitonin hormone (Calcium homeostasis)	
<ul style="list-style-type: none"> Describe the synthesis of parathyroid and calcitonin hormone Explain the effects of parathyroid hormone on calcium balance Describe the factors that regulate the activities of osteoclasts and osteoblasts Describe the relationship between PTH and active form of vit D Explain the regulation of calcitonin secretion List the disorders associated with calcium homeostasis (tetany, Chvostek's sign) 	
7. Hormonal secretion of the Pancreas (Insulin)	
<ul style="list-style-type: none"> Explain the synthesis of insulin Describe the insulin receptor Explain the role of insulin in maintaining blood glucose concentration Differentiate between neurogenic and nephrogenic diabetes insipidus 	
8. Hormonal secretion of the Pancreas (Glucagon, somatostatin)	
<ul style="list-style-type: none"> Describe principal actions of glucagon and its regulation Explain the functions of somatostatin on blood glucose 	
9. Adrenal cortex (Functions of Glucocorticoids)	
<ul style="list-style-type: none"> Explain the synthesis of glucocorticoid hormones Identify the actions of glucocorticoids on metabolism and target cells Discuss the mechanism for regulation of glucocorticoid secretion Describe the disorders associated with glucocorticoid hormones (Addison's disease, Cushing syndrome) 	
10. Adrenal cortex (Functions of Mineralocorticoids)	Interactive Lecture/Tutorial / SDL
<ul style="list-style-type: none"> Define Aldosterone escape, Primary Aldosteronism and Androgenital Syndrome Explain the mechanism of action of mineralocorticoids Discuss the mechanism of actions of aldosterone and its regulation 	
11. Adrenal Medulla (secretion, function and disorders)	
<ul style="list-style-type: none"> Explain the mechanism of secretion and actions of medullary hormones List the types of adrenergic receptors and their functions on target organs Enumerate consequences of over and under secretion of medullary hormones (pheochromocytoma) 	
12. Role of insulin in Diabetes Mellitus	
	Tutorial

• Discuss the role of various types of Insulin in the management of Diabetes Mellitus	
13. Consequences of Hypo and Hyperthyroidism	
• Explain the causes, sign and symptoms associated with hypo and hyperthyroidism: (Toxic goiter, Thyrotoxicosis, Graves' disease, Thyroid adenoma, Endemic colloid goiter, Idiopathic Nontoxic Colloid goiter)	

PATHOLOGY

TOPICS & OBJECTIVES	LEARNING STRATEGIES
Pituitary Adenoma	Case- Based Learning
• Discuss the histo-pathological features of Pituitary Adenoma	
Endocrine investigations	Visit to Chemical pathology Lab
• To observe and describe the procedures of sample collection, handling, and analysis as performed in a chemical pathology laboratory.	

RESEARCH & SKILLS DEVELOPMENT CENTER

TOPICS & OBJECTIVES	LEARNING STRATEGIES
• Properly insert the insulin syringe.	Hand on
• Demonstrate the proper venting technique of the insulin according to the required dose	
• Perform thyroid examination	

COMMUNICATION SKILLS

TOPICS & OBJECTIVES	LEARNING STRATEGIES
Presentation Skills	Interactive Lecture
• Define the principles of effective presentations	
• Describe Mayer's Principles of Multimedia Learning relevant to PowerPoint presentations and posters	

LEARNING RESOURCES:

SUBJECT	RESOURCES
ANATOMY	A. <u>GROSS ANATOMY</u> <ol style="list-style-type: none"> 1. K.L. Moore, Clinically Oriented Anatomy 2. Neuro Anatomy by Richard Snell B. <u>HISTOLOGY</u> <ol style="list-style-type: none"> 1. B. Young J.W. Health Wheather's Functional Histology C. <u>EMBRYOLOGY</u> <ol style="list-style-type: none"> 1. Keith L. Moore. The Developing Human 2. Langman's Medical Embryology
BIOCHEMISTRY	A. <u>TEXT BOOKS</u> <ol style="list-style-type: none"> 1. Harper's Illustrated Biochemistry 2. Lehninger Principle of Biochemistry 3. Biochemistry by Devlin
PATHOLOGY / MICROBIOLOGY	A. <u>TEXT BOOKS</u> <ol style="list-style-type: none"> 1. Robbins & Cotran, Pathologic Basis of Disease, 9th edition. 2. RapidReviewPathology, 4th edition by Edward F. Goljan MD
	<ol style="list-style-type: none"> 1. http://library.med.utah.edu/WebPath/webpath.html 2. http://www.pathologyatlas.ro/
PHARMACOLOGY	A. <u>TEXT BOOKS</u> <ol style="list-style-type: none"> 1. Lippincot Illustrated Pharmacology 2. Basic and Clinical Pharmacology by Katzung
PHYSIOLOGY	A. <u>TEXT BOOKS</u> <ol style="list-style-type: none"> 1. Textbook of Medical Physiology by Guyton And Hall 2. Ganong'S Review of Medical Physiology 3. Human Physiology by Lauralee Sherwood 4. Berne & Levy Physiology 5. Best & Taylor Physiological Basis of Medical Practice B. <u>REFERENCE BOOKS</u> <ol style="list-style-type: none"> 1. Guyton & Hall Physiological Review 2. Essentials of Medical Physiology by Jaypee 3. Textbook of Medical Physiology by InduKhurana 4. Short Text book of Physiology by Mrthur 5. NMS Physiology

ASSESSMENT METHODS:

- **Best Choice Questions(BCQs)** also known as MCQs (Multiple Choice Questions)
- **Objective Structured Practical / Clinical Examination (OSPE or OSCE)**

Internal Evaluation

- Students will be assessed comprehensively through multiple methods.
- 20% marks of internal evaluation will be added to JSMU final exam. That 20% may include class tests, assignment, practical and the internal exam which will all have specific marks allocation.

Formative Assessment

Individual department may hold quiz or short answer questions to help students assess their own learning. The marks obtained are not included in the internal evaluation

For JSMU Examination Policy, please consult JSMU website!

More than 75% attendance is needed to sit for the internal and final examinations



LNH&MC EXAMINATION RULES & REGULATIONS:

- Student must report to examination hall/venue, 30minutes before the exam.
- **The Exam will start sharply at the given time.**
- No student will be allowed to enter the examination hall after 15 minutes of scheduled examination time.
- Students must sit according to their roll numbers mentioned on the seats.
- **Cell phones are strictly not allowed in examination hall.**
- If any student is found with cell phone in any mode (silent, switched off or on) he/she will not be allowed to continue his / her exam.
- No students will be allowed to sit in exam without University Admit Card, LNMC College ID Card and Lab Coat
- Student must bring the following stationary items for the exam: Pen, Pencil, Eraser, and Sharpener.
- Indiscipline in the exam hall / venue is not acceptable. Students must not possess any written material or communicate with their fellow students.

SCHEDULE

WEEKS	2 ND YEAR	MONTH
4 WEEKS	ENDOCRINE MODULE - I	18 th August 2025
		13 th September 2025

*Final dates will be announced later.