UNIVERSITY OF CANTERBURY TE WHARE WĀNANGA O WAITAHA

MEDICAL PHYSICS

COURSE OUTLINE / STUDY GUIDE / CORE NOTES

MDPH401

ANATOMY, PHYSIOLOGY AND PATHOLOGY

2020

DEPARTMENT OF PHYSICS AND ASTRONOMY

ANATOMY, PHYSIOLOGY AND PATHOLOGY

GENERAL AIM

- To investigate and study the structure and functions of the body systems
- To develop an understanding of the processes affecting cells with emphasis on neoplasia

LEARNING OUTCOMES

On completion of this course, the student should be able to:

- Apply standard medical terminology in the study of the structural and functional organisation of the human body
- Relate the basic anatomical features and physiological processes in cellular biology
- Describe the anatomical features and physiological processes in the body systems
- Describe the basic principles and concepts of growth disorders with emphasis on cellular injury and neoplasia

A ORGANISATIONAL COMPONENT

1. Syllabus themes

1.1. Introduction
1.2. Structural and functional organisation
1.3. Cellular biology
1.4. Tissues
1.5. Cellular pathology: adaptations and injury
1.6. Neoplasia
1.7. Integumentary system
1.8. Skeletal system
1.9. Muscular system
1.10. Nervous system
1.11. Cardiovascular system
1.12. Respiratory system
1.13. Digestive system
1.14. Urinary system
1.15. Reproductive system

2. Required texts

Principles of Anatomy & Physiology (14th Ed.) by Gerard J. Tortora and Bryan Derrickson – John Wiley & Sons Inc. If you can get hold of an earlier edition of this book from a student of last year it will do just as well. The new edition is available at the campus bookstore.

Core notes on pathology are included here.

3. Assessment

Test 1	15%	}	
Test 2	15%	}	100%
Exam	70%	}	

Test dates

Test 1	Rutherford 141	Monday 23th March	(1 hour)
Test 2	Rutherford 141	Monday 23rd April	(1 hour)
Exam	Location and time TBC	11th – 23rd June	(3 hours – entire syllabus)

4. Course lecturer

Warwick Shillito
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Warwick.shillito@canterbury.ac.nz

5. Venue

Tuesdays:	Erskine 340	4 - 5 pm
Wednesdays:	Erskine 111	2 - 3 pm
Wednesdays:	West 701	3 - 4 pm

6. Syllabus year planner

WK	DATE	SYLLABUS THEME	STUDY UNIT THEME
1	Mon 17.02.20	Introduction	Terminology / Levels / Homeostasis
	Thurs 20.02.20	Functional organisation	Planes / Regions / Cavities / Position
	Thurs 20.02.20	Cellular biology	Cell structure / Functions / DNA structure / Replication / Mitosis
2	Mon 24.02.20	Cellular biology	Cell structure / Functions / DNA structure / Replication / Mitosis
	Thurs 27.02.20	Tissues	Tissue types / Membranes
	Thurs 27.02.20	Tissues	Tissue types / Membranes
3	Mon 2.03.20	Neoplasia	Inflammation
	Thurs 5.03.20	Neoplasia	Cellular changes
	Thurs 5.03.20	Neoplasia	Cellular changes
4	Mon 9.03.20	Neoplasia	Carcinogens
	Thurs 12.03.20	Neoplasia	Classifications
	Thurs 12.03.20	Neoplasia	Warning signs
5	Mon 16.03.20	Integumentary system	Skin structure
	Thurs 19.03.20	Skeletal system	Long bone / Microscopic structure
	Thurs 20.03.20	Skeletal system	Synovial joint / Skeletal bones
6	Mon 23.03.20	**Test 1: All the work from 17th Feb to 16th March (Introduction to Integumentary System)**	
	Thurs 26.03.20	Muscular system	Macro & microscopic structure of skeletal muscle
	Thurs 26.03.20	Muscular system	Impulse transmission at NMJ
7	Mon 30.03.20	Muscular system	Identification of main muscles / Muscle groups
	Thurs 2.04.20	Nervous system	Organisation of the CNS
	Thurs 2.04.20	Nervous system	Structure of a neuron / Impulse conduction
Mid Semester Break 6th April – 26th April 2018			
8	Mon 27.04.20	ANZAC Day	
	Thurs 30.04.20	Nervous system	Transmission at synapses / Spinal cord / Meningeal Coverings
	Thurs 30.04.20	Nervous system	Brain stem / Cerebellum / Diencephalon
9	Mon 4.05.20	Nervous system	Cerebrum / Functional areas
	Thurs 7.05.20	Nervous system	Ventricles / Cerebrospinal fluid
	Thurs 7.05.20	Cardiovascular system	Thorax / Pericardium / Heart
10	Mon 11.05.20	Cardiovascular system	Main systemic arteries & veins
	Thurs 14.05.20	Respiratory system	Upper & lower respiratory tract
	Thurs 14.05.20	Respiratory system	Upper & lower respiratory tract
11	Mon 18.05.20	**Test 2: All the work from 19th March to 7th April (Skeletal System to Nervous System)**	

	Thurs 21.05.20	Digestive system	Peritoneum / Bowel
	Thurs 21.05.20	Digestive system	Digestive glands / Pancreas / Gallbladder
12	Mon 25.05.19	Urinary system	Kidneys / Ureters / Bladder / Urethra
	Thurs 28.05.19	Reproductive system	Male reproductive system
	Thurs 28.05.19	Reproductive system	Female reproductive system
Semester 1 Study Period 2nd – 5th June			
Semester 1 Examination Period 8th - 20th June			

B STUDY COMPONENT

Syllabus theme: 1. Introduction

Study unit: 1.1 Anatomy, physiology and pathology
Differentiation and integration

1.2 Medical terminology

Study unit themes: 1.1.1 Discipline differentiation and integration
1.1.2 Levels of structural & functional organisation

1.2.1 Word roots, prefixes and suffixes
1.2.2 Anatomical directional terminology
1.2.3 Anatomical terms to describe joint movement

Learning objectives

After you have studied this section, you should be able to meet at least the following objectives:-

1.1.1 Discipline differentiation and integration

- Define anatomy, physiology and pathology

1.1.2 Levels of structural & functional organisation

- Outline the different levels of structural and functional organisation that can be found in the human body
- Describe briefly the components of a homeostatic feedback system with an example of negative and positive feedback

1.2.1 Word roots, prefixes and suffixes

- Outline, by making use of appropriate examples, how prefixes and suffixes can be used in medical terminology

1.2.2 Anatomical directional terminology

- Outline, by making use of appropriate examples, the different terms that can be used to indicate direction in anatomy

1.2.3 Anatomical terms to describe joint movement

- Outline, by making use of use of appropriate examples, the different terms that can be used to indicate different joint movement

Syllabus theme: 2. Structural and functional organisation

Study unit: 2.1 Basic anatomical terminology

Study unit themes: 2.1.1 Anatomical planes, regions and cavities

Learning objectives

After you have studied this section, you should be able to meet at least the following objectives:-

2.1.1 Anatomical planes, regions and cavities

- Define the anatomical position
- List the body planes and outline how each divides the body
- List the principal body cavities and their associate linings
- Name the nine regions of the abdomen and the planes which form them
- List two organs found in each of the nine regions

Syllabus theme: 3. Cellular biology

Study unit: 3.1 Anatomical and physiological processes

Study unit themes: 3.1.1 Cell structure, organelles and functions
3.1.2 DNA structure and replication
3.1.3 Mitosis

Learning objectives

After you have studied this section, you should be able to meet at least the following objectives:-

3.1.1 Cell structure, organelles and functions

- Outline the structure of a typical cell
- List the organelles found in a cell and state the function/s of each

3.1.2 DNA structure and replication

- Outline the structure, function and replication of DNA

3.1.3 Mitosis

- Describe briefly the phases of the cell cycle and the function of mitosis

Syllabus theme: 4. Human tissue organisation

Study unit: 4.1 Tissues

Study unit themes: 4.1.1 Tissue types and characteristics

Learning objectives

After you have studied this section, you should be able to meet at least the following objectives:-

4.1.1 Tissue types and characteristics

- List the four major types of tissues
- Outline the general features of epithelial tissue
- Outline the general features of connective tissue
- List the different types of connective tissue
- Differentiate between the three muscle tissue types

Syllabus theme: 5. Cellular pathology

Study unit:
5.1 Cellular adaptations
5.2 Cellular injury
5.3 Cellular regeneration
5.4 Inflammation and healing

Study unit themes:
5.1.1 Atrophy
5.1.2 Hypertrophy
5.1.3 Hyperplasia
5.1.4 Metaplasia
5.1.5 Dysplasia
5.1.6 Carcinoma in situ

5.2.1 Reversible cellular injury
5.2.2 Irreversible cellular injury

5.3.1 Cellular regeneration

5.4.1 Inflammation

Learning objectives

After you have studied this section, you should be able to meet at least the following objectives:-

5.1 Cellular adaptations

- Define/outline atrophy, hypertrophy, hyperplasia, metaplasia and dysplasia
- Describe briefly carcinoma in situ

5.2 Cellular injury

- Describe reversible cellular injury
- Describe water disturbance (cloudy swelling) as a type of reversible cellular injury
- Describe the appearance of the cell in irreversible cellular injury
- Define necrosis
- List the different forms of necrosis
- List the complications of necrosis

5.3 Cellular regeneration

- Define cellular regeneration and outline the three types of cellular regeneration

5.4 Describe the inflammation process

Syllabus theme: 6. Neoplasia

Study unit:
6.1 Characteristics of benign and malignant neoplasms
6.2 Spreading of neoplasms
6.3 Carcinogenesis and causes of cancer
6.4 Diagnosis of cancer

Study unit themes:
6.1.1 Cell proliferation
6.1.2 Cell differentiation
6.1.3 Benign and malignant neoplasms
6.1.4 Characteristics of cancer cells
6.1.5 Classification of neoplasms

6.2.1 Invasion
6.2.2 Seeding of cancer cells
6.2.3 Metastasis

6.3.1 Carcinogenesis and oncogenesis

6.4.1 Diagnosis of cancer

Learning objectives

After you have studied this section, you should be able to meet at least the following objectives:-

6.1 Characteristics of benign and malignant neoplasms

- Differentiate between cell proliferation and cell differentiation
- Outline the behavioural characteristics of cancer cells
- Define benign, malignant and tumour
- Differentiate between benign and malignant tumours by making use of their clinical features
- Describe the TNM classification system for neoplastic growths

6.2 Spreading of neoplasms

- List the different ways of cancer spreading
- Describe briefly the spreading of cancer via the lymphatic system
- Outline haematogenous spreading of cancer

6.3 Carcinogenesis and causes of cancer

- Define carcinogenesis and oncogenesis

6.4 Diagnosis of cancer

- List five diagnostic procedures that can be used in the diagnosis of cancer
- Define tumour markers and list two markers that can be used in diagnosing cancer

Syllabus theme: 7. Integumentary system

Study unit: 7.1 Layers of the skin

Study unit themes: 7.1.1 Skin structure

Learning objectives

After you have studied this section, you should be able to meet at least the following objectives:-

7.1.1 Skin structure

- Briefly describe the structures found in the **epidermal layer** of the skin
- Briefly describe the structures found in the **dermal layer** of the skin
- Briefly describe the thermoregulation as a homeostatic mechanism of the skin

Case Study – hypothermia

Case Study – skin cancers

Case study – wound healing

Syllabus theme: 8. Skeletal system

Study unit: 8.1 Bony skeleton
8.2 Joints

Study unit themes: 8.1.1 Bone tissue
8.1.2 Individual bones
8.2.1 Joint classification
8.2.2 Structure of a synovial joint

Learning objectives

After you have studied this section, you should be able to meet at least the following objectives:-

8.1.1 Bone tissue

- Describe the components of a typical long bone
- Outline the microscopic structure of compact bone

8.1.2 Individual bones

- Identify the individual bones of a skeleton

8.2.1 Joint classification

- Outline structural classification of joints

8.2.2 Structure of a synovial joint

- Outline the structure of a typical synovial joint

Case study – Osteoporosis

Case study – Facture

Case study – Degenerative arthritis

Case study – Inflammatory arthritis

Syllabus theme: 9. Muscular system

Study unit: 9.1 Skeletal muscles

Study unit themes: 9.1.1 Macro and microscopic structure of skeletal tissue
9.1.2 Selected muscles and muscle groups

Learning objectives

After you have studied this section, you should be able to meet at least the following objectives:-

9.1.1 Macro and microscopic structure of skeletal tissue

- Outline the basic structure, blood and nerve supply to skeletal muscle (macroscopic structure)
- Outline the basic microscopic structure of a skeletal muscle fibre
- Briefly describe the events that will take place when a nerve impulse arrives at the **neuromuscular junction**

9.1.2 Selected muscles and muscle groups

- Identify and name selected muscles/muscle groups

Case study – Muscle strain

Syllabus theme: 10. Nervous system

Study unit: 10.1 Overview of the nervous system

Study unit themes:
10.1.1 Organisation of the nervous system
10.1.2 Histology
10.1.3 Structure of a typical neuron

Learning objectives

After you have studied this section, you should be able to meet at least the following objectives:-

10.1.1 Organisation of the nervous system

- Outline the basic organisation of the nervous system

10.1.2 Histology

- List the different types of cells found in neuroglia
- Differentiate between gray and white matter

10.1.3 Structure of a typical neuron

- Differentiate between afferent (sensory) neurons and efferent (motor) neurons
- Outline the structure of a typical neuron

Syllabus theme: 10. Nervous system

Study unit: 10.2 Neurophysiology

Study unit themes: 10.2.1 Impulse conduction
10.2.2 Transmission of synapses

Learning objectives

After you have studied this section, you should be able to meet at least the following objectives:-

10.2.1 Impulse conduction

- Outline the principal steps in the conduction of a nerve impulse

10.2.2 Transmission at synapses

- Outline the events of chemical synaptic transmission

Case study – Multiple sclerosis

Syllabus theme: 10. Nervous system

Study unit:
10.3 Spinal cord
10.4 Brain stem
10.5 Cerebellum
10.6 Diencephalon

Study unit themes:
10.3.1 Structure of the spinal cord
10.3.2 Coverings (meninges)
10.4.1 Components of the brain stem
10.5.1 Basic structure of the cerebellum
10.6.1 Basic structure of the diencephalon

Learning objectives

After you have studied this section, you should be able to meet at least the following objectives:-

10.3.1 Structure of the spinal cord

- Describe briefly the structure of the spinal cord
- Describe a cross section of the spinal cord at the thoracic level

10.3.2 Coverings (meninges)

- Describe the spinal cord meninges and their associated spaces

10.4.1 Components of the brain stem

- List the components of the brain stem
- Describe the structure and relations of the brain stem

10.5.1 Basic structure of the cerebellum

- List the principal parts of the cerebellum

10.6.1 Basic structure of the Diencephalon

- List the principal parts of the diencephalon

Syllabus theme: 10. Nervous system

Study unit: 10.7 Cerebrum
10.8 Sensory and motor functional areas

Study unit themes: 10.7.1 Lobes and major sulci
10.7.2 Cerebral white matter
10.7.3 Basal ganglia
10.8.1 Sensory and motor functional areas

Learning objectives

After you have studied this section, you should be able to meet at least the following objectives:-

10.7.1 Lobes and major sulci

- List and locate the lobes and principal sulci of the cerebrum
- Describe the cerebrum indicating the principal sulci, gyri and lobes on the lateral and medial surfaces

10.7.2 Cerebral matter

- List the three main connecting white fibres of the cerebrum and indicate which areas of the cerebrum is connected by them

10.7.3 Basal ganglia

- List the basal ganglia of the brain

10.8.1 Sensory and motor functional areas

- List, locate and give the function of the main cortical cerebral functional areas

Case study – Acute complete stroke

Case study – Parkinson's disease

Case study – Spinal cord lesion

Syllabus theme: 10. Nervous system

Study unit: 10.9 Cerebrospinal fluid
10.10 Blood supply

Study unit themes: 10.9.1 Brain ventricles
10.9.2 Cranial meninges
10.9.3 Cerebrospinal fluid

Learning objectives

After you have studied this section, you should be able to meet at least the following objectives:-

10.9.1 Brain ventricles

- List briefly the brain ventricles and their associated apertures

10.9.2 Coverings (meninges)

- Describe the brain/spinal cord meninges and their associated spaces

10.9.3 Cerebrospinal fluid

- Outline the formation/circulation and absorption of CSF

Case study – Subdural haemorrhage

Case study – Hydrocephalus

Syllabus theme: 11. Cardiovascular system

Study unit: 11.1 Heart and blood vessels
11.2 Cardiac conduction

Study unit themes: 11.1.1 Thorax
11.1.2 Pericardium
11.1.3 Structure of the heart
11.1.4 Main arteries and veins
11.1.5 Blood vessels
11.2.1 Cardiac conduction and ECG

Learning objectives

After you have studied this section, you should be able to meet at least the following objectives:-

11.1.1 Thorax

- Outline the position of the heart and associated structures in the thorax (mediastinum)
- Outline the surface anatomy (surface projection) of the heart

11.1.2 Pericardium

- Outline the structure of the pericardium

11.1.3 Structure of the heart

- Describe briefly the external and internal anatomy of the heart
- Outline the arterial blood supply of the heart

11.1.4 Main systemic arteries and veins

- List the main systemic arteries and veins found in the body

11.1.5 Blood vessels

- Outline the basic structure of arteries, veins and capillaries
- Define anastomoses
- Define blood pressure and outline how blood pressure is measured
- List the anatomical areas where the pulse may be felt
- Outline the factors assisting in the venous return of blood to the heart

11.2.1 Cardiac conduction and ECG

- Outline the structural and functional features of heart conduction
- Outline the functional components of an ECG (electrocardiogram)

Case study – Angina pectoris

Case study – Acute myocardial infarction

Case study – Hypertension

Case study – ECG after acute myocardial infarction

Syllabus theme: 12. Respiratory system

Study unit: 12.1 Upper and lower respiratory tract
12.2 Ventilation

Study unit themes: 12.1.1 Upper and lower tract

Learning objectives

After you have studied this section, you should be able to meet at least the following objectives:-

12.1.1 Upper and lower tract

- Outline the structure of the upper and lower respiratory tract
- Describe briefly the structure of the lungs

Case study – Pneumonia

Case study – Pneumothorax

Case study – Emphysema

Syllabus theme: 13. Digestive system

Study unit:
13.1 Abdominal cavity
13.2 Peritoneum
13.3 Bowel
13.4 Digestive glands

Study unit themes:
13.1.1 General organisation
13.2.1 Structure and function of peritoneum
13.3.1 Structure and components of the bowel
13.4.1 Digestive glands

Learning objectives

After you have studied this section, you should be able to meet at least the following objectives:-

13.1.1 General organisation of the abdominal cavity

- Identify the content of the abdominal cavity and their relationship to each other

13.2.1 Structure and function of peritoneum

- Define peritoneum and outline its structure and function

13.3.1 Structure and components of the bowel

- Outline the basic structure of the:-
  - Mouth
  - Pharynx
  - Oesophagus
  - Stomach
  - Small intestine
  - Large intestine

13.4.1 Digestive glands

- Outline the structure of the:-
  - Liver and peritoneal folds
  - Gall bladder and ducts
  - Pancreas

Case study – Peptic ulcer

Case study – Crohn's disease

Case study – Liver cirrhosis

Syllabus theme: 14. Urinary system

Study unit: 14.1. Urinary system

Study unit themes:
14.1.1 Kidneys
14.1.2 Ureters
14.1.3 Bladder
14.1.4 Urethra

Learning objectives

After you have studied this section, you should be able to meet at least the following objectives:-

14.1.1 Kidneys

- Outline the external and internal structure of a kidney
- Describe the location and relations of the kidney

14.1.2-4 Ureters/bladder/urethra

- Outline the basic structure and location of the ureters, bladder and urethra

Case study – Kidney infection

Case study – Kidney stones

Syllabus theme: 15. Reproductive system

Study unit: 15.1 Male reproductive system
15.2 Female reproductive system

Study unit themes: 15.1.1 Components of the male reproductive system
15.2.1 Components of the female reproductive system

Learning objectives

After you have studied this section, you should be able to meet at least the following objectives:-

15.1.1 Components of the male reproductive system

- Outline the basic structure of the male reproductive system

15.2.1 Components of the female reproductive system

- Outline the basic structure of the female reproductive system and female breast

Case study – Benign prostatic hyperplasia

Case study – Cervical cancer

Case study – Childbirth

Case study – Breast cancer

PATHOLOGY CORE NOTES

INTRODUCTION

PATHOLOGICAL TERMINOLOGY

- Pathology – scientific study of a disease or disease process. This process will include the causes and mechanisms (pathophysiology) by which disease is produced.
- Disease – condition in which some abnormality occurs in either the structure or function, or both structure and function of body tissue.
- Symptoms – abnormalities experienced by the patient himself (complaints), e.g. pain, coldness
- Signs – physical abnormalities found on examination (manifestations) by the doctor, e.g. arrhythmia, skin colour
- Diagnosis – recognising a specific disease by making use of the symptoms, signs and diagnostic tests
- Prognosis – the possible outcome and duration of the disease

CELLULAR PATHOLOGY

CELLULAR ADAPTATIONS

- Adaptations that cells can undergo when placed under stress could include cellular atrophy, hypertrophy, hyperplasia, metaplasia, dysplasia and carcinoma in situ.
- All human beings (living cells) are exposed on a continuous basis to internal and external environmental stimuli, e.g. toxins, heat etc.
- These stimuli include anything within or on the outside of the body that could disturb the normal internal milieu of the body (cells).
- The internal milieu (environment) of the body is kept in a state of equilibrium by the body's own regulatory processes.
- Any changed condition (disturbance of the internal milieu) will be changed back to normal (state of equilibrium) by making use of the body's feedback system.
- Normally we are not aware of any changes taking place in our bodies until the disturbance is to such an extent (pathological stimuli) that it causes certain symptoms and signs.
- These changes could lead to cellular disturbances or damage that is usually reversible back to its normal state.
- However, from time to time these disturbances could be so severe that they are irreversible.
- The process where the body's equilibrium is maintained, thus, where the internal environment is undisturbed, is known as homeostasis.
- The cellular changes, due to the external or internal stimuli, will lead either to structural or functional changes.

- The natural response of cells towards these stimuli will be to undergo cellular adaptations to bridge the period of exposure until the stimuli is removed. The cells could then return to its normal state (reversible changes) provided that changes or damage didn't cause permanent damage (irreversible changes).
- Cellular growth adaptations will include changes in cellular size, number, type and metabolism.
- Irreversible changes usually leads to permanent cellular damage or cell death.
- In growth adaptations there could be:-
  - ❖ Increased cellular activity (increase in size and/or number) due to increased functional demand or,
  - ❖ Decreased cellular activity (reduction in size and/or number) due to decreased functional demand or,
  - ❖ Alteration of cellular structure (cell differentiation) due to changes in cellular environment.
- Metabolic adaptations takes place on a biochemical level where the metabolism of the cell changes according to demand.

Atrophy is the reduction in size of the individual functioning cells, tissues or organs.

- The wasting or decrease in size of the organ/tissue is due to a failure or decrease in functional demand.
- Atrophy is reversible and the cell/organ is restored to its normal size if the stimulus is removed.
- A typical example can be seen where a fractured limb is placed in a cast. The muscles will waste away due to the inability to use them (disuse atrophy).

Hypertrophy is an increase in the size of individual functioning cells, tissues or organs.

- Hypertrophy leads to the excessive enlargement or overgrowth of tissue without cell division and is the result of an increase in functional demand or workload.
- Hypertrophy occurs in tissues where no mitotic cellular division can take place, e.g. muscles.
- A typical example can be found in a patient that underwent a nephrectomy (removal of kidney). In this case the remaining kidney will enlarge to cope with the increased workload (compensatory hypertrophy).

Hyperplasia is an abnormal increase in the number of normal functional cells in an organ or tissue.

- Here we have an increase in cellular division and it occurs in tissue where cells are capable of dividing mitotically, e.g. skin tissue.
- This also is a reversible condition if the stimulus is removed.
- A typical example can be seen in breast and uterus enlargement during pregnancy due to oestrogen (stimulus) stimulation (hormonal physiological hyperplasia).

Metaplasia is the change of one cell type to another cell type.

- This cellular change/adaptation usually occurs due to chronic irritation on target cells or tissue.
- The newly formed adapted cells are usually better equipped to survive and they all have the same appearance. They can change back to normal by removing the stimulus.
- The change from one cell type to another cell type however, never oversteps its primary cell groups. In other words, one type of epithelial cell may change to another type of epithelial cell but not to connective tissue.
- A typical example is the change of columnar epithelial cells to stratified epithelial cells in the airways of smokers.

Dysplasia is the disordered change in the size, shape, and appearance of cells or tissues due to chronic irritation or inflammation.

- It may either revert to normal if the stress factor (stimulus) is removed or it may progress to neoplasia.
- This cellular change is often associated with/seen as a precursor of cancer.
- Dysplastic changes are often seen in the squamous epithelium of the uterine cervix and may develop into cancer of the cervix if the causing irritant is not removed.

Carcinoma-in-situ indicates a localized carcinomatous growth, which does not show any evidence of invasion of surrounding tissue or distant spread.

- It is reversible if the irritant is removed.
- Is seen as an extension of dysplasia.
- Is typically found in the early stages of cervix carcinoma and detected by investigating cells taken from the cervix (Pap smear).

CELLULAR INJURY

REVERSIBLE CELLULAR INJURIES

- Any foreign internal or external factor could injure a cell.
- The injury could affect any part of the cell, e.g.
  - ❖ Cell membrane affecting the permeability or receptor complex.
  - ❖ It could affect the nucleus which could lead to chromosomal distortion.
  - ❖ Organelles.
- External or internal factors could include physical agents (heat, radiation), chemical agents (formalin), toxins (aflatoxin), viruses, nutritional, and genetic abnormalities.
- Sub-lethal cell damage is reversible if harmful agent is removed. If not, the cell will sustain lethal damage which is irreversible and leads to cell death which is known as cell **necrosis**.
- Injury to a cell could cause deterioration of the cell. The cell then can change from a higher to a lower functional unit to cope with the new environment. This phenomenon is known as cellular **degeneration**.
- Disturbances that could lead to cellular degeneration include:-
  - ❖ Water overload (cloudy swelling)
  - ❖ Fatty change
  - ❖ Protein disturbances (amyloid)
  - ❖ Calcifications
  - ❖ Pigmentations
- These disturbances are classified as sub-lethal types and are reversible.

IRREVERSIBLE CELLULAR INJURIES

- Damage to cells in this group is lethal and it leads to cellular death (necrosis).
- A cell is assumed to be dead if it shows the following features:-
  - ❖ Nuclear changes
    - ✓ Swelling and condensation of chromatin
    - ✓ Fragmentation of nucleus
    - ✓ Rupturing of nuclear membrane
    - ✓ Fading and dissolving of the nucleus
  - ❖ Cellular changes
    - ✓ Breakdown of plasma (cell) membrane
    - ✓ Releasing of K^+ by the dead cells
    - ✓ Releasing of enzymes
    - ✓ Releasing of proteins

NECROSIS AND CELLULAR DEATH

- **Necrosis** can be defined as the death of tissue cells within a localized area and the release of cellular proteolytic enzymes.

- **Cell death** can be defined as cellular damage to such an extent so that the sustained injury becomes irreversible.

- Different forms of necrosis can be identified and include:-

  - ❖ General forms, which could either be single cell necrosis or multiple cells (tissues) necrosis. In multiple cell necrosis the structure of the tissue could either be reserved or destroyed. The tissue can undergo a process that is known as **liquefaction** whereby the solid material becomes liquefied.

  - ❖ Special forms of necrosis include gangrene, fat and caseous necrosis.

- Dead necrotic tissue is experienced by the body as foreign material. The normal reaction of the body towards this will be to get rid of the foreign material or to isolate it in a sterile state. A typical example of how the body rids itself of foreign (dead) material can be seen in dry gangrene whereby the dead necrotic tissue detaches itself from the body (diabetes mellitus). Sterile isolation is usually accompanied by calcification whereby the foreign material is calcified in a sterile tumour.

- Dead necrotic tissue in the body could lead to acute or chronic inflammation, immunological reactions (foreign material), wet gangrene, abscess formation with fistula etc. These secondary complications could have a damaging effect on the normal healing process.

CELLULAR REGENERATION

- Can be defined as the ability of the body to replace the injured or dead tissue with cells of the same parenchymal (specific cells of an organ) type.

- Body cells can be classified in three basic groups according to their ability to regenerate:-

  - ❖ Cells that divide and replicate on a continuous basis throughout life, e.g. skin epithelium.

  - ❖ Cells that cease to divide on reaching maturity, but start to regenerate if an appropriate stimulus is received, e.g. liver cells after a liver lobectomy (removal of a liver lobe).

  - ❖ Cells that don't have the ability to divide. They include nerve cells, skeletal and cardiac muscle cells. Dead cells are replaced by scar tissue.

Inflammation and Healing

General

- Inflammation is the dynamic response to local injury.
- Damaged tissue may be replaced by tissue identical in structure and function - ***restitution***.
- Restitution can only take place if
  - ✓ cell debris is cleaned
  - ✓ damaging agent is removed
  - ✓ damaged tissue can regenerate.
- If not, damaged tissue replaced by scar tissue (fibrous repair).
- If damaging agent persist → chronic inflammation.
- First response to tissue damage always acute inflammation.
- The purpose of inflammation is to
  - ✓ localise infection
  - ✓ prevent spreading of invaders
  - ✓ neutralise toxins
  - ✓ aid in repair of damaged tissue.

Clinical Signs and Symptoms

- Rubor (***redness***) → due to ↑ blood flow.
- Calor (***heat***) → due to ↑ blood flow.
- Tumour (***swelling***) → due to accumulation of exudate.
- Dolar (***pain***) → due to swelling with pressure on nerve endings and the effect of chemical mediators.
- Function laesa (***loss of function***) due to excessive swelling and pain.
- These gross signs are explained by changes at microscopic level.
- Three essential features of inflammation are
  - ✓ hyperaemia (flush, flare)
  - ✓ fluid exudation (proteins) (weal)
  - ✓ cellular exudation (emigration of leukocyte).

1.2.1

Pathogenesis of Acute Inflammation

- During the acute inflammatory process various chemical substances are released by the damaged cells or by the toxic agent (histamine, bradykinin, heparin).
- These substances have various effects on the surrounding tissues and act as mediators (vasodilatation, ↑ permeability, chemotaxis).
- Due to the release of these chemical substances, various vascular changes occur.
- Directly after injury, due to arteriolar vasoconstriction, transient ischaemia takes place. Ischaemia may last from a few seconds to a couple of minutes.

  momentarily white line
- This is followed by a progressive, later persistent vasodilatation of mainly the arterioli, and to a lesser extend also the venulae and capillaries.

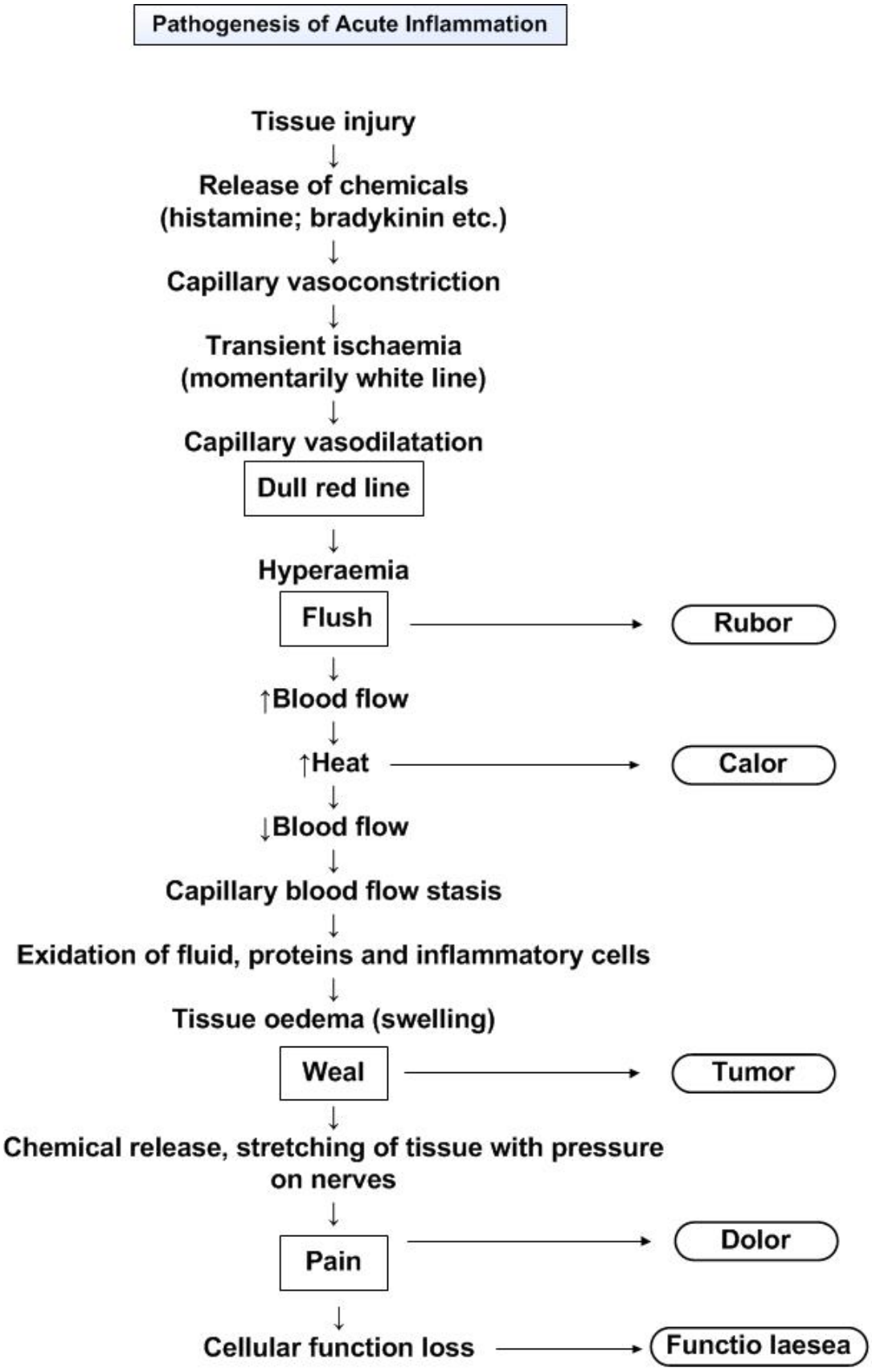
  dull red line / flush
- These vascular calibre changes are followed by blood flow changes.
  - ✓ Initially there is a rapid blood flow due to the vasodilatation.
  - ✓ With the dilatation of the arterioli, capillaries and venulae, the arteriolar pulsation is carried over to the capillaries and venulae, forming a pulsating area of the whole capillary bed (hyperaemia)

    bright, red irregular zone / flare / rubor
  - ✓ a lot of heat is generated during these processes due to ↑ blood flow

    calor
- Slowing of blood flow then takes place until stasis occur.
- At this time a loss of plasma into the neighbouring tissue takes place due to ↑ permeability of vessels → increase in the blood viscosity in blood vessel → disturbance of axial flow.

  Mechanism
  - ✓ Blood flow ↓ → exudation of fluid (plasma exudate) → ↑ viscosity → stasis → change in axial stream of cellular elements → central axial stream becomes wider → endothelial plasma zone narrower → redistribution of RBC and WBC
  - ✓ Initially the larger WBC lies centrally and the smaller RBC peripherally in the axial stream → due to ↓ blood flow → Rauleaux formation of RBC → outward movement of WBC to peripheral area of blood stream and RBC centrally.
- The WBC (leukocytes) move to the vessel endothelium → margination takes place (pavementing) → leukocyte (neutrophils and polymorpus) adhere to the endothelium.
- The endothelium openings, created by the chemical mediators, enlarges and allow the leukocytes to pass through by means of pseudopodia and amaeboid movement (leukocyte migration).
- The leukocytes then migrate through the interstitium to the inflamed area under influence of the released chemical substances (mediators) by means of chemotaxis.
- The emigration of the leukocytes and the movement of protein rich fluids from intravascular to extravascular is known as cellular and fluid exudation formation.
- The infiltration of the exudation in the interstitium causes swelling weal / tumour and the stretching of the tissue and released chemicals cause pain dolor
- Phagocytosis by the leukocytes takes place with the destruction of the toxic agent.
- Grossly injured cells (tissues) will loose their function and die functio laesa

1.2.2


Pathogenesis of Acute Inflammation
Tissue injury
Release of chemicals
(histamine; bradykinin etc.)
Capillary vasoconstriction
Transient ischaemia
(momentarily white line)
Capillary vasodilatation
Dull red line
Hyperaemia
Flush
Rubor
↑Blood flow
↑Heat
Calor
↓Blood flow
Capillary blood flow stasis
Exidation of fluid, proteins and inflammatory cells
Tissue oedema (swelling)
Weal
Tumor
Chemical release, stretching of tissue with pressure
on nerves
Pain
Dolor
Cellular function loss
Functio laesea

1.2.3.1

NEOPLASIA

INTRODUCTION

NEOPLASTIC TERMINOLOGY

- Cancer – to move sideways or spread; 'crab'
- Neoplasia – 'new growth'; refers to the formation of neoplasms or tumour.
- Neoplasm – a tumour that increased in size and persisting at the expense of the surrounding tissue.
- Tumour – swelling; any kind of swelling is referred to as a tumour (infection, trauma, neoplasia). In pathology tumour is used as being synonymous with the term neoplasm.
- Neoplasms can be classified in two major divisions, the benign and malignant tumours.
- Benign tumours – not fatal/innocent growths.
- Malignant tumours – fatal growths.
- Metastasis – spreading of cancer cells to distant organs or tissues.

CELLULAR PROLIFERATION

- Proliferation refers to cellular division forming new daughter cells that grow and increase in number of similar cells.
- Differentiate between non-neoplastic proliferation (hyperplasia, metaplasia, displasia) and neoplastic proliferation. In the latter there is an **uncontrolled** cell proliferation.

CELLULAR DIFFERENTIATION

- Refers to the process whereby cells are transformed due to internal or external stimuli into different and usually more specialised types.
- Differentiation occurs in orderly steps and the higher the specialisation of a cell, the lower the ability to divide. Epithelial cells are relatively simple (less specialised) and can divide and proliferate at a high rate. Nerve cells on the other end of the scale are more specialised and have lost the ability to divide.
- Cells, under normal circumstances, will differentiate from the lower (less specialised) form to a higher (more specialised) form.
- Cells can, however, also differentiate back from higher to lower forms if they are exposed to stimuli that damage the cells (neoplasms). They lose their specialised ability (become more primitive) but gain the ability to divide faster.
- Neoplasms whose cells show a similarity to those of their tissue of origin are described as being differentiated.
- In neoplasms where the cells differ from the tissue of origin are described as being undifferentiated.
- The more differentiated a tumour, the better the prognosis. The more undifferentiated, the poorer the prognosis.

BENIGN VS MALIGNANT TUMOURS

- A localised tumour with well defined margins and who is well differentiated is usually benign.
- A tumour invading the surrounding tissue with poorly defined margins and who is undifferentiated is usually malignant.

BEHAVIOURAL CHARACTERISTICS OF CANCER CELLS

- Cancer cells probably develop from mutations that occur during differentiation. The earlier the mutation develops during the differentiation phase, the more poorly the differentiation and the higher the possibility of being malignant.
- Cancer cells behave completely different from normal body cells.
- Behavioural characteristics of cancer cells will include the following:
  - ❖ Cancer cells lack proper differentiation and function
  - ❖ They alter their appearance and shape
  - ❖ The cancer cells lose their ability to attach to one another like normal body cells.
  - ❖ The ability of cells of the same origin and structure to group together (contact inhibition) is lost.
  - ❖ They tend to be more mobile and migrate faster from one place to another.
  - ❖ They can produce specific tumour antigens and pseudo/ectopic hormones

CLASSIFICATION OF NEOPLASMS

The clinical classification of tumours (benign and malignant) can be classified according to their clinical characteristics.

CHARACTERISTIC	BENIGN	MALIGNANT
Metastasis	Localised	Metastasis
Growth rate	Slow	Rapid
Boundaries	Circumscribed, encapsulated, grows by expansion, no infiltration	Irregular, non-encapsulated, peripheral growth infiltrate with processes
Effect on surrounding tissue	Compresses	Destroys
Prognosis	Non fatal	Fatal

STAGING OF NEOPLASMS (TNM CLASSIFICATION)

- On discovering a malignancy in the body, the local, regional and systemic involvement should be determined.
- This process is known as staging of a neoplasm.
- This stage of the malignancy determines the treatment and prognosis of the patient.
- For this staging, the TNM classification is being used.

T = Refers to the size of the tumour
N = Lymph node involvement
M = Metastasis

T_1 = Tumours 0 – 2cm
T_2 = Tumours 2 – 5cm
T_3 = Tumours > 5cm

N_0 = No palpable lymph nodes
N_1 = Palpable but mobile lymph nodes
N_2 = Palpable but fixated lymph nodes

M_0 = No metastasis
M_1 = Metastasis present

Example

$T_1N_0M_0$ = Tumour less than 2cm in diameter, no palpable lymph nodes and without distant metastasis

WARNING SIGNS OF NEOPLASIA

- **Unusual** bleeding or discharge, e.g. from a nipple where there is no trauma or infection in the breast.
- A **newly formed** lump or tumour in the body, e.g. detecting a new lump in the breast/neck/axilla/groin or elsewhere in the body.
- A sore that does **not heal** after treatment, especially if it is a longstanding ongoing condition with ulceration.
- **Unexpected** continuous weight loss.
- Change in **size, shape, colour or sensitivity** of a wart or mole, especially if the wart/mole is in an area where chronic irritation is experienced, e.g. chafing of the wart/mole on underwear.
- **Swallow difficulty** and a change from solid to liquid food could indicate oesophageal obstruction, e.g. with oesophageal carcinoma.
- **Persistent** coughing or hoarseness with no underlying lung infection, e.g. bronchus carcinoma.
- Change in **normal** bowel habits, e.g. where normal defecation is succeeded by periods of constipation.

SPREADING OF NEOPLASMS

Invasion – cancer can spread by invading and infiltrating the surrounding tissue directly. This is done by the extension of projections from the tumour into the surrounding tissue.

Seeding of cancer cells – this method is seldom seen. It takes place where a tumour erodes the surrounding tissue until it breaks through into a body cavity. Cells break loose from the tumour and are spread with the aid of serous fluid and gravity usually to the lowest point in the cavity. On reaching this area is will start to form a new secondary tumour. The successful growth of a tumour at a site distant from its primary location is known as metastasis.

METASTASIS

The two main ways for cancer cells to disseminate is by making use of the lymphatics or blood vessels.

Lymphatic spreading

Mechanism

- After the formation of a tumour (neoplasm) it will start to increase in size and invade the surrounding tissue.
- Lymph vessels that can be found throughout the body tissue will be most vulnerable due to the fact that its walls are so thin.
- The tumour will then enter the lymph vessel.
- Cells or a small portion might detach itself (embolus) from the primary tumour and be carried away by the lymph to a nearby lymph node via afferent lymphatic vessel.
- On reaching the lymph node it establishes itself in the outer cortical area and migrate from there to the inner medulla.
- From there is will travel via the efferent lymphatic vessel to the adjacent lymph nodes.
- Groups of lymph nodes are usually infiltrated in this way, e.g. with mamma carcinoma (breast cancer) all the axillary lymph nodes could be involved.
- The cancer cells/ embolus eventually will reach the thoracic duct which in its turn drains into the subclavian veins.
- Once the cancer cells reach the venous blood stream it will be carried to the heart.
- From here it will spread via the systemic circulation to different parts of the body where the cells will establish themselves to form secondaries.
- It is especially vascular structures like the liver, brain and skeleton that are vulnerable.

Haematogenous (blood) spreading

Mechanism

- Cancer cells detach from the primary tumour and invade a blood vessel, or the tumour erodes the vessel and then cells detach from the tumour.
- They survive in the blood stream and are carried to a favourable location (liver, lungs) where they establish themselves and start to grow to form a secondary tumour.

CARCINOGENESIS AND ONCOGENESIS

- Carcinogenesis is origin, production or development of cancer by a carcinogen.
- A carcinogen is any cancer-producing substance or organism.
- Substances or organisms could include:-
    - Chemicals
    - Radiation
    - Viruses
    - Inherited
- The transformation of normal to cancer cells usually takes place on a genetic level.
- An oncogene is a gene that normally encodes for the formation of proteins that are used for/involved in cell growth or regulation.
- Where this process is disturbed in altering or destroying the specific gene by a carcinogen, a tumour (neoplasm) might develop. This process is then referred to as oncogenesis.

CAUSES OF CANCER

The following causes are the more acknowledged ones:-

- Radiation
- Viruses (hepatitis B virus in liver Ca)
- Hormones (oestrogen in breast Ca)
- Chronic irritation
- Inherited (familiar polyposis of the colon)
- Environmental
    - Chemicals (formalin)
    - Industrial (asbestos)
    - Social habits (smoking)
    - Diet (aflatoxin)
    - Sun (melanomas)
- Geography

DIAGNOSIS OF CANCER

Diagnosis procedures include:-

- X-rays; ultrasound imaging; magnetic resonance (MR); computed tomography (CT scan)
- Endoscopic examinations
- Bodily fluids (histology), e.g. sputum, serous fluid
- Specimen examination, e.g. urine, stool or blood tests
- Aspiration of bone marrow, fluid, blood
- Biopsy

TUMOUR MARKERS

- A tumour marker is a substance, released into the circulation by tumour tissue, whose detection in the serum indicates the presence of tumour and which is typical for that specific tumour.
- These tumour markers are used for the screening, diagnosis, prognosis and monitoring of treatment.

Tumour markers used in primary diagnosis:-

TYPE OF TUMOUR	MARKER
Testicular carcinoma; liver carcinoma	α – fetoprotein (AFP)
Multiple myeloma	Bence Jones proteins
Colorectal carcinoma	Carcinoembryonic antigen (CEA)