The Endocrine System

ANATOMY

☑ Sheet ☐ Slide ☐ Handout

Number:	**4**
Subject:	Islets of Langerhans & Immunohistochemistry
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General Notes

1. Endocrine system is based mainly on histology and embryology.
2. Endocrine glands, in general, have two embryological origins:
    a. Pituitary gland have two embryological origins
        I. Oral ectoderm
        II. Neural ectoderm
    b. Thyroid gland:
        I. Endodermal branchial arches
        II. Ultimobranchial body (some cells)
    c. Parathyroid glands:
        I. Superior parathyroid gland (3^{rd} branchial arch)
        II. Inferior parathyroid gland (4^{th} branchial arch)
    d. Adrenal glands:
        I. Mesoderm (cortex)
        II. Modified sympathetic ganglion (medulla)

3. Blood supply of endocrine glands:
    a. Pituitary glands are supplied by two sources:
        I. Internal carotid artery gives **superior hypophyseal artery.** It goes to pars tuberalis and then into the primary plexus then the portal hypophyseal vein arises which makes a secondary plexus on pars distalis.
        II. Internal carotid artery gives inferior hypophyseal artery which goes to pars nervosa.
    b. Thyroid glands
        I. Superior thyroid artery which is the first branch of external carotid artery below the level of the hyoid bone.
        II. Inferior thyroid artery arises from the thyrocervical trunk which in turn is a branch of the subclavian artery (approximately 80% of the blood supply).

        Therefore, the anastomosis between external carotid artery and the subclavian artery will be through the thyroid gland.

    c. Parathyroid gland
        I. Superior thyroid artery
        II. Inferior thyroid artery (again, most of the blood supply is from this artery).

In the past the surgeons used to find the parathyroid gland by looking up the site of anastomosis between the superior and inferior thyroid arteries

d. Adrenal gland
    I. Superior suprarenal artery(cortex)
    II. Middle suprarenal artery(cortex)
    III. Inferior suprarenal artery

In histology, most types of tissues are stained by haematoxylin (**basophilic**) and eosin (**acidophilic**) but there are some issues related to staining:

1. The stained tissue could be strongly basophilic or acidophilic OR weakly basophilic or acidophilic depending on the processing of tissue and the differences of the staining reaction itself.
2. Some tissues don't stain by haematoxylin and eosin so we call them clear cells. We can find them in the stomach, thyroid (**parafollicular cells**, which are also known as C cells because they secrete calcitonin).

Relationship between the histological appearances and the function of the cell:

1. Protein producing cells have extensive RER and a well developed Golgi apparatus so they must be basophilic although they have mitochondria which are acidophilic but the basophilic stain is more dominant. Note that cells that are less active are not as basophilic as active cells. The stain appears due to the shrinkage of Golgi apparatus and less RER and vice versa.
2. Lipid/steroid producing cells need SER and mitochondria which are acidophilic to produce corticosteroids, aldosterone, and cortisol. Therefore, the whole cell appears acidophilic because it has small amounts of RER and Golgi. Note that many vacuoles (fake spaces) appear in lipid producing cells due to adding a lipid solvent (such as xylene or alcohol) so if you want to see the lipids you have to avoid using any lipid solvent in the processing and you have to use a special stain specific to lipids.

Immunohistochemistry

- Immunohistochemistry is used with cells that cannot stained by haematoxylin and eosin.

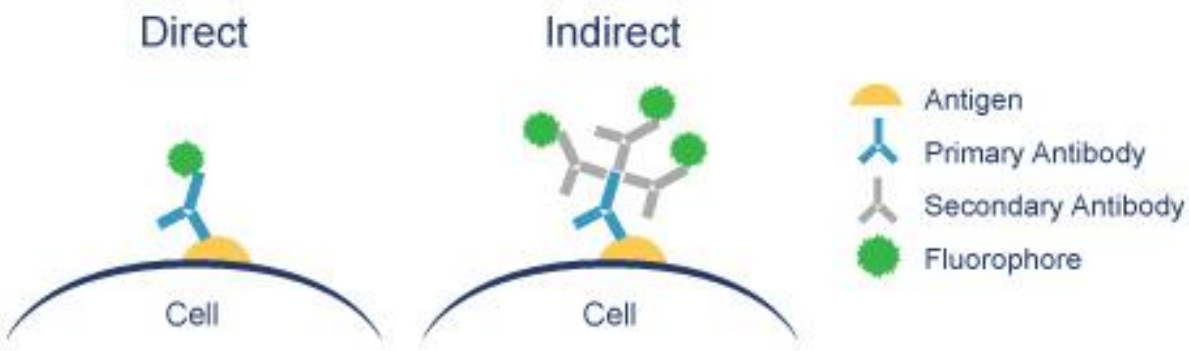
- It is the process that involves detecting antigens (e.g. proteins) in cells of a tissue section by exploiting the principle of antibodies binding specifically to antigens in biological tissues.

- A protein is injected into an animal which will develop antibodies against it. Then, these antibodies are taken and used to discover the location of a certain protein due to the fact that these antibodies are specific to this protein.

- Antibodies are classified into 2 types:
    a. Polyclonal: a heterogeneous mix of antibodies that recognizes several epitopes
    b. Monoclonal: shows specificity for a single epitope (more accurate)

- Visualizing an antibody-antigen interaction can be accomplished by tagging the antibody by fluorophore.

- Immunohistochemistry can be conducted in 2 methods:
    1. Direct method usually involves one step which includes the use of directly labeled antibodies to detect antigens of interest within the tissue. While this method is straightforward and less time-consuming, it is usually less sensitive and lacks the ability to amplify weak signals. As a result, it is not as widely used as other methods.
    2. Indirect method utilizes an unlabelled primary antibody to detect the antigen of interest in the tissue. A secondary labeled antibody is then used to bind to the primary antibody. This method is useful as it amplifies relatively weak antigen signals in tissue as many secondary antibodies can bind to different antigenic sites of the primary antibody. There is also a greater choice of labeled secondary antibodies and these can obviously be used with many different primary antibodies (species-dependent). This method is 100% accurate.



Islets of Langerhans

- Islets of Langerhans are regions in the pancreas that contain its endocrine cells.
- They were discovered by Paul Langerhans when he was working with has professor Rudolf Virchow on his research that focused on wound healing in the absence of the pancreas, so he used 2 sets of dogs. The pancreas was removed from the first group (pancreatectomized), but not the second group (control group) which was normal.
- Langerhans noticed something else about this experiment, he noticed that flies gather around the urine of the pancreatectomized group of dogs only, so he took the feces to test it and to look for the chemotactic factor that attracted the flies. He found out that **sugar** was the chemotactic factor.
- After that Langerhans described the pancreas and stated that it has special regions that are not connected to ducts. He assumed that they release their secretion to the circulation, so he called these regions islets (islands) that are surrounded by an ocean of exocrine cells. He also added a note saying that their secretion prevents the passage of glucose to the urine.
- The scientists later discovered a hormone that is released by islets of Langerhans which was Insulin.
- The islets of Langerhans were histologically appeared:
  1. Variable in size and shape (isolated)
  2. Distributed all over the pancreas
  3. Surrounded by a delicate capsule of connective tissue
  4. Having a profuse blood supply
  5. Paler than the exocrine part

- Note that the exocrine part of the pancreas is similar to the parotid gland.
- Note that the number of islets in the pancreas varies from 1 to 1.5 million and their number relatively increases from the head to the tail of the pancreas.
- Nowadays, the islets of Langerhans are viewed differently. Although microscopes can't be used to differentiate between the different types of cells in the islets of Langerhans, high power electron microscopes can help identify some differences between cells.
- Immunohistochemistry is the best method used to differentiate between different types of cells. For example, antibodies against insulin can be given so that all insulin producing cells are stained.
- Types of cells in the islets of Langerhans:
  a. Alpha cells produce glucagon and are found at the peripheral aspect of the islet. (20% of the total number of islet cells)
  b. Beta cells produce insulin and occupy the center of the islet (≈70% of the total number of islet cells)
  c. Delta cells produce somatostatin which inhibits the nearby alpha and beta cells (<10% of the total number of islet cells)
  d. PP cells produce pancreatic polypeptide which increases the activity of chief cells in the stomach (main action in digestion system). It also has a paracrine action which decreases the secretion of bicarbonate in the pancreas itself.

     Note that there are other types of cells which can be detected by giving antibodies against the abovementioned 4 types. When antibodies against the 4 mentioned types of cells are used, an unstained region of cells appears because it contains different types of undiscovered islet cells.

Shout out to Ahmad Hiary, Ahmad Hamadeen, Abdulrahman Santarsi, Abdulkarem Hiary, Ashraf Debi, Ayman Zirikly, Ibrahem Mobaiden (don), Mohammad Imam, Rami Ershed, and Omar Janabi

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