Model Questions and Answers

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What are stem cells? What do you mean by the term ‘stem cell niche’?

Stem cells are a group of cells in our bodies, with capacity to **self-renew** and **differentiate** to various types of cells, thus to construct tissues and organs. They are the earliest type of cell in a cell lineage. There are many types of stem cells, differing in their degree of differentiation and ability of self-renewing. Gametes cells (eggs or sperms) are stem cells they will develop to a whole body with various tissues after fertilizing.

- **Embryonic stem cells** derived from the part of a human embryo or foetus are stem cells also with full potential of differentiation. Embryonic stem cells are **pluripotent stem cells** derived from the **inner cell mass** of the **blastocyst**, an early-stage embryo.

- **Adult stem cells** are **partially differentiated** cells found among specialized (differentiated) cells in a tissue or organ.

- **Embryonic germ (EG) cells** are derived cells from **primordial germline cells (PGCs)** in early development. EG cells share many of the characteristics of human ES cells, but differ in significant ways. Human EG cells are derived from the primordial germ cells, which occur in a specific part of the embryo/foetus called the gonadal ridge, and which normally develop into mature gametes (eggs and sperm).

- **Cancer stem cells (CSCs)** are a small subpopulation of self-renewing malignant and oncogenic cells that drive tumor initiation and progression.

- **Induced pluripotent stem cells** (IPSCs) are a type of **pluripotent** stem cells **artificially derived** from a **non-pluripotent cell**, typically an adult somatic cell, by inducing a "**forced**" expression of specific genes.

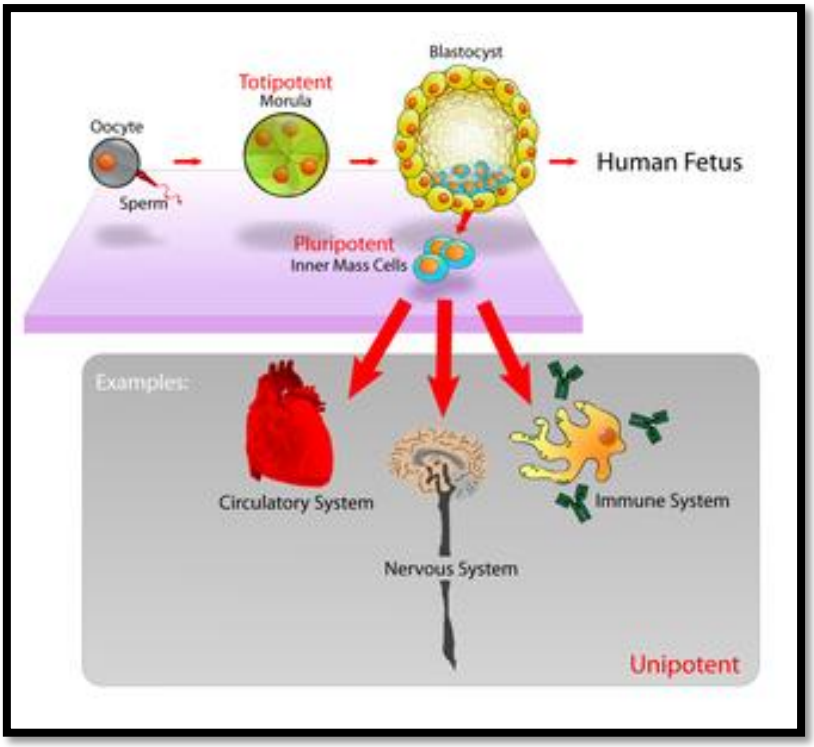

Fig. Pluripotent embryonic stem cells originate as inner cell mass (ICM) cells within a blastocyst. These stem cells can become any tissue in the body, excluding a placenta. Only cells from an earlier stage of the embryo, known as the morula are totipotent, able to become all tissues in the body and the extraembryonic placenta.

Stem cell niche:

The stem cell niche provides a specific **microenvironment** within a tissue in which direct **cell–cell interactions** and **molecular signals** either maintain stem cells in the undifferentiated state or promote their differentiation. Therefore, the niche should not be considered simply a physical location for stem cells, rather as the place where extrinsic signals interact and integrate to influence stem sell behaviour. These stimuli include cell-to-cell and cell matrix interactions and signals (molecules) that activate and/or repress genes and transcription programs. As a direct consequence of this interaction, stem cells are maintained in a dormant state, induced to self-renewal or commit to a more differentiated state.

Conserved components of the niche are:

1. **Stromal support cells**, including cell-cell adhesion molecules and secreted soluble factors, which are found in close proximity to stem cells.
2. **Extracellular matrix (ECM) proteins** that act as a stem cell "anchor" and constitute a mechanical scaffolding unit to transmit stem cell signaling.
3. **Blood vessels** that carry nutritional support and systemic signals to the niche from other organs and also participate in the recruitment of circulating stem cells from and to the niche.
4. **Neural inputs** that favour the mobilization of stem cells out of their niches and integrate signals from different organ systems. Neuronal cues appear to be particularly important in hematopoietic stem cells trafficking.

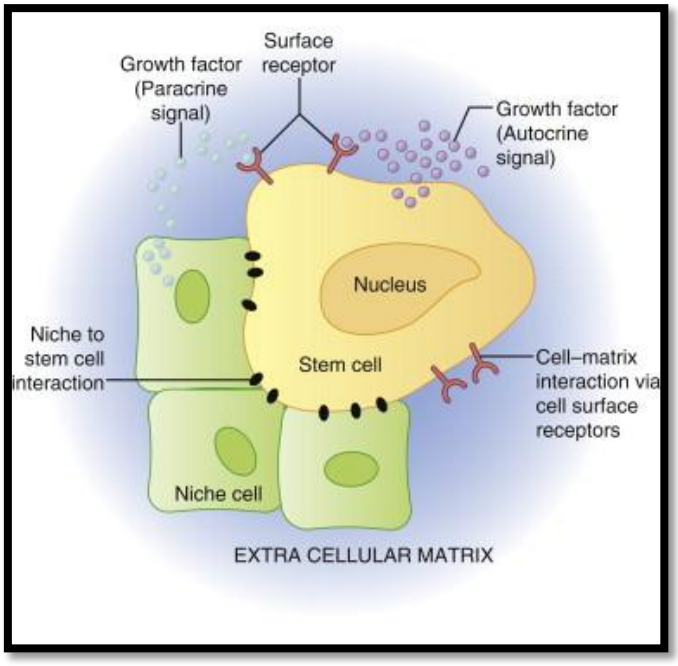

Fig.: The stem cells found in a niche interact with the niche cells and the extracellular matrix. The stem cell can receive signals from both components via direct interactions (cell to cell or cell to matrix). Stem cells can also receive signals such as growth factors that are secreted from themselves (**autocrine**) or from the niche cells (**paracrine**). These signals bind to cell surface receptors and trigger the stem cell to stay undifferentiated.

Write a short on the Hypothalamo-Hypophyseal-Gonadal Axis or Hypothalamic-Pituitary-Gonadal Axis.

The HPG axis is the hormone system that controls the release of sex hormones. In both genders, the system is activated by **GnRH**, which is released regularly in short bursts from the **hypothalamus**. **GnRH** then stimulates the release of **FSH** and **LH** from the **anterior pituitary**.

In men, **LH** stimulates certain cells in the testes (i.e., **Leydig cells**) to release **testosterone**. **FSH** and **testosterone** are key regulators of another set of testicular cells (i.e., **Sertoli cells**), which support and nourish the sperm cells during their maturation. The HPG axis in men is regulated through a variety of factors. For example, **testosterone** is part of a **negative feedback mechanism** that **inhibits GnRH** release by the hypothalamus and **LH** release by the pituitary. In addition, the **Sertoli cells** secrete a substance called **inhibin**, which **prevents FSH release** from the pituitary. Finally, the **Leydig cells** and, to a lesser extent, the **Sertoli cells** produce a substance called **activin**, which **stimulates FSH secretion** and thus has the opposite effects of inhibin.

In women, during the menstrual cycle, **LH** and **FSH** stimulate the ovarian follicle that contains the maturing egg to produce **estradiol**. After ovulation has occurred, **LH** also **promotes production** of **progesterone and estradiol** by the **corpus luteum**. Both hormones participate in a **negative feedback mechanism** through most of the menstrual cycle, **suppressing GnRH** release from the **hypothalamus** and **LH** release from the **pituitary**. Shortly before ovulation, however, a **positive feedback mechanism** is activated by which **estradiol** actually **enhances LH** release from the **pituitary**. The resulting **surge in LH levels** ultimately **leads to ovulation**, the **formation of the corpus luteum**, and progesterone release. Progesterone exerts a negative feedback on LH and FSH release, causing **LH** levels to **decline** again. In addition to those mechanisms, **FSH** release from the pituitary is regulated by **inhibin**, a substance produced by certain cells in the ovarian follicle.

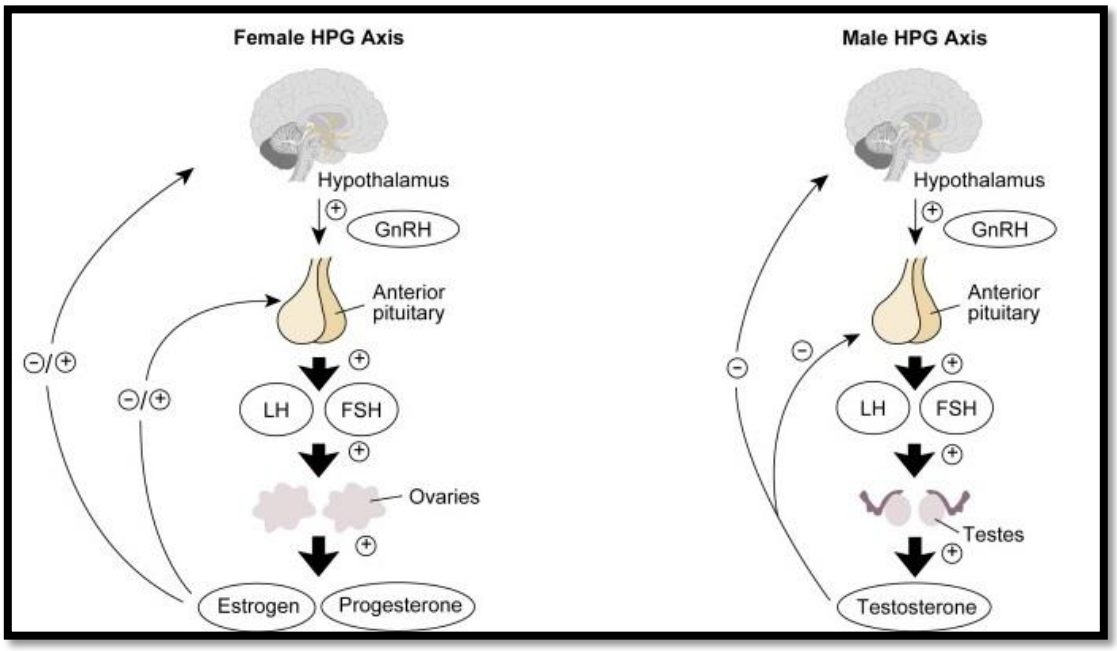

Fig.: Schematic representation of the female and male HPG axes. For each system, the hypothalamus secretes releasing hormones (GnRH) that act on the pituitary gland. In response to those stimuli, the pituitary gland releases gonadotropins (i.e., LH and FSH). LH and FSH in women stimulate the ovaries to produce estrogens and progesterone. Depending on the phase of the menstrual cycle, those hormones act back on the hypothalamus and pituitary gland in either a stimulatory or inhibitory manner. In men, LH stimulates the testes to release testosterone, which feeds back on the hypothalamus and pituitary.

What are neurohormones?

A neurohormone refers to any of the hormones produced and released by specialized neurons called **neuroendocrine** cells. Neurohormones are secreted by these cells into the bloodstream for systemic effect. Some of them though act as **neurotransmitters** as well. As a neurotransmitter, they serve as a signal molecule from one neuron to another. Thus, some of them are not just for endocrine signaling (where they act as hormones) but also for **autocrine** or **paracrine** signaling.

Neurohormones include **releasing hormones**, **neurohypophysial hormones, adrenomedullary hormones** as well as **enteric neurohormones**. Releasing hormones and neurohypophysial hormones are hormones produced by the neuroendocrine cells in the hypothalamus. The releasing hormones, as opposed to neurohypophysial hormones, are released from the axon terminals that extend to the median eminence and reach to act on the anterior pituitary. Examples of **releasing** hormones are **thyrotropin-releasing hormone, corticotropin-releasing hormone, growth hormone-releasing hormone, gonadotropin-releasing hormone**, etc. The neurohypophysial hormones are hormones produced by the neuroendocrine cells in the hypothalamus with axon terminals extending to the neurohypophysis. These hormones are stored inside the Herring bodies in the axon terminals and are secreted into the circulation to reach and act on target cells. Examples of **neurohypophysial** hormones are **oxytocin** and **vasopressin**.

Adrenomedullary neurohormones are **catecholamines** secreted from the adrenal medulla by the neuroendocrine cells, **chromaffin cells**. Examples of adrenomedullary hormones are **epinephrine, norepinephrine** and **dopamine**.

Enteric neurohormones are neurohormones produced and released by **enterochromaffin-like cells** in the **gastric glands** of the **stomach lining**. These cells release **histamine**.

Write a short note on the structure of nephron.

Nephrons are both the structural and functional units of the kidneys. Each human kidney contains about 1,200,000 nephrons.

Each nephron is a long, coiled tube and consists of:

- a **renal corpuscle**, which is the initial filtering component, and
- a **renal tubule** that processes and carries away the filtered fluid.

1. **Renal corpuscle or Malpighian corpuscle**

The Malpighian corpuscle is formed of two parts:

(a) **Bowman's Capsule**- The blind end of nephron is like a double-walled cup. It is called Bowman's Capsule. Its outer layer is formed of flattened epithelial cells and inner layer of specialised **podocyte cells**.

(b) **Glomerulus**- The cavity of the cup encloses a bunch of capillaries, the **glomerulus**. It is formed by the capillaries of **afferent** and **efferent arterioles**. The **afferent arteriole** brings blood into the glomerulus and **efferent arteriole** collects blood from here. The Bowman's Capsule alon with its glomerulus is called **Malpighian corpuscle**. It lies in the cortex part of kidney.

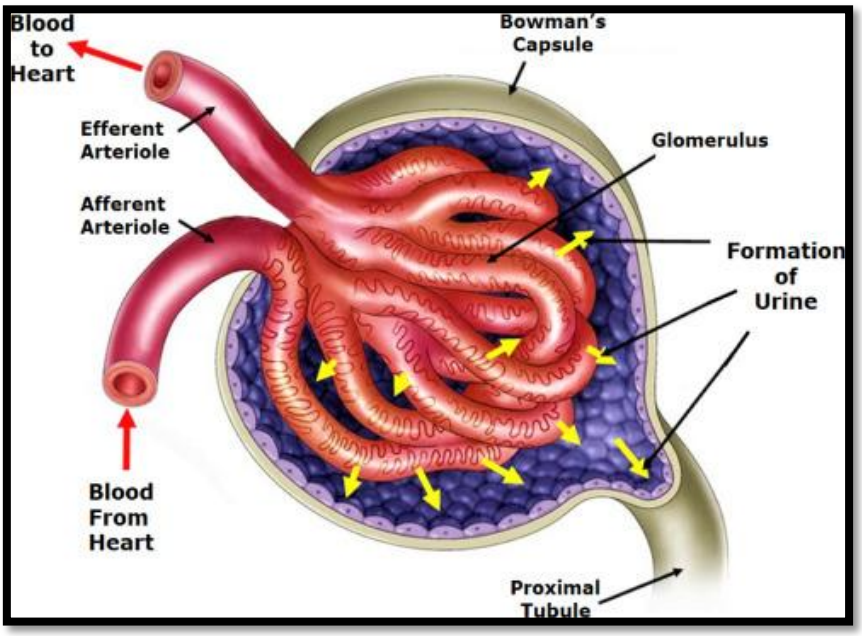

Fig.: Renal corpuscle consists of the Bowman's capsule and the glomerulus.

2. **Secretory Part of Uriniferous tube-** The remaining part of the nephron after the Bowman's capsule is called the secretory part. It is lined with ciliated epithelium. It is differentiated into the following parts:
    (a) Proximal convoluted tubule (PCT)- It lies next to Bowman's capsule and is greatly twisted. It is a wide tube lined with a layer of columnar epithelial cells having brush border.
    (b) Loop of Henle- Henle's loop is U-shaped. It lies in the medulla and is formed of a **descending limb** and an **ascending limb.**
    (c) Distal convoluted tubule (DCT)- It is also a twisted tube and lies in renal cortex. Its short terminal part is called collecting tubule. It opens into a collecting duct. It is lined by columnar cells with microvilli on the free surface. The cells contain numerous mitochondria.

3. **Collecting ducts-** These are larger ducts each receiving the collecting tubules of several nephrons. These pass into the renal medulla and join with each other forming larger **ducts of Bellini**. These ducts run through the renal pyramids and open into **calyces** which lead into the pelvis. The urine formed in the nephrons is conducted by collecting ducts to ducts of Bellini and calyces and then into the pelvis. From here it is carried by ureter into the urinary bladder from where it is passed out.

4. **Blood vessels of kidneys**- A renal artery brings blood to each kidney. It divides into afferent arterioles. An **afferent arteriole** forms glomerulus in the cavity of Bowman's Capsule. The capillaries of glomerulus then join to form an **efferent arteriole**. The efferent arteriole leaves the Bowman's Capsule and forms a network of **peritubular capillaries** around the remaining renal tubule.

    Cortical nephrons (the majority of nephrons) start high in the cortex and have a short loop of Henle which does not penetrate deeply into the medulla.
    Juxtamedullary nephrons start low in the cortex near the medulla and have a long loop of Henle which penetrates deeply into the renal medulla, only they have their loop of Henle surrounded by the vasa recta. These long loops of Henle and their associated vasa recta create a hyperosmolar gradient that allows for the generation of concentrated urine. The juxtamedullary nephrons comprise only about one-fifth of total nephrons in the human kidney.

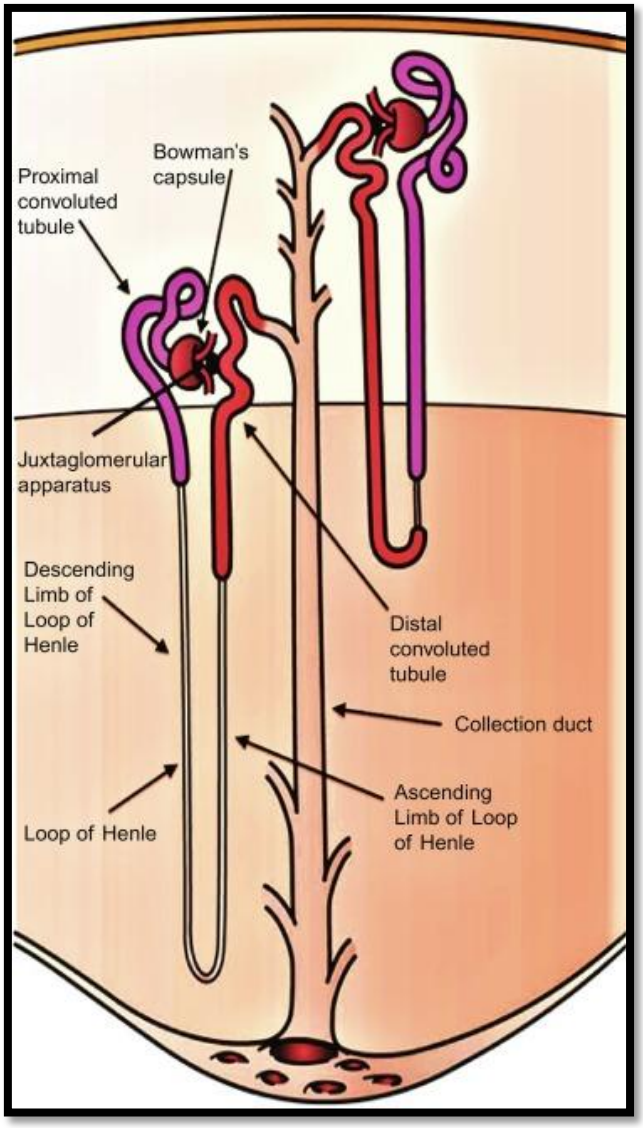

Fig.: Structure of two types of nephrons—juxtamedullary nephron (left) and cortical nephron (right)