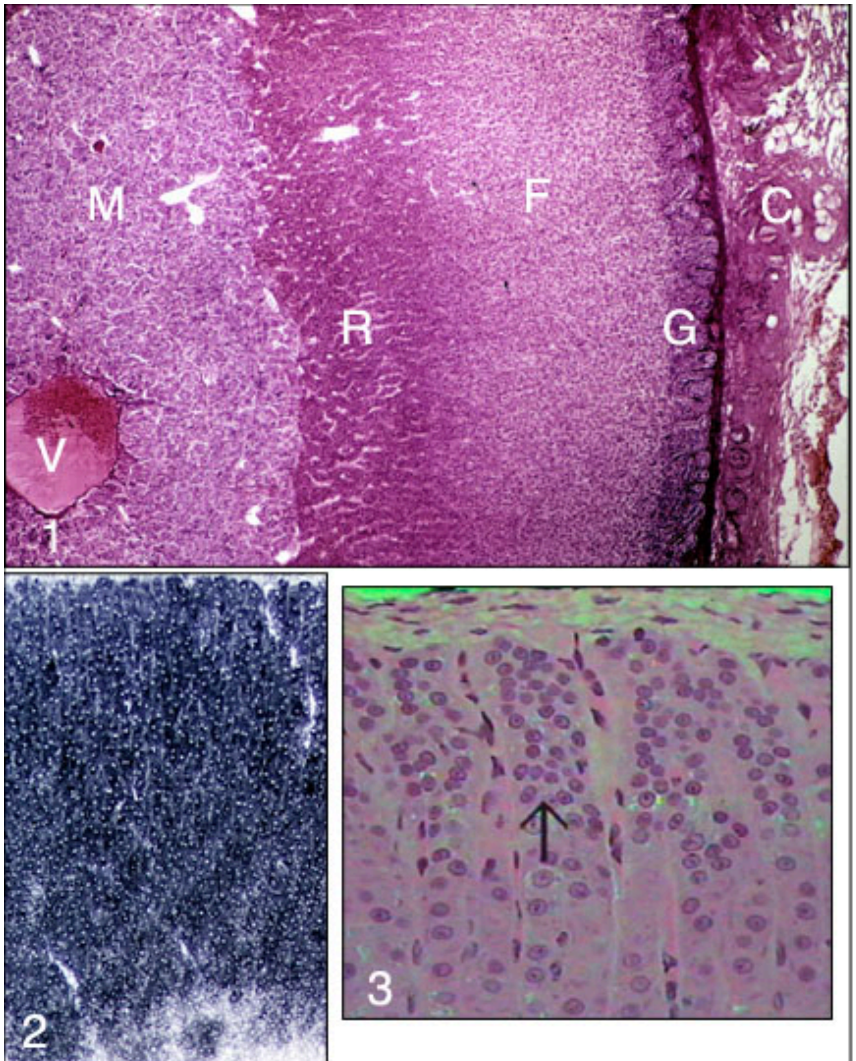
Adrenal



1. Adrenal Gland. The capsule (C), zona glomerulosa (G), zona fasciculata (F), zona retiularis (R), medulla (M) and a large medullary vein (V) are shown.
2. Zona fasciculata stained with osmium to demonstrate lipid which appears black.
3. The capsule and zona glomerulosa lie abobe the arrow; zona fasciculata lies below the arrow.

The adrenal glands in humans are a pair of flattened, triangular structures with a combined weight of 14 to 16 gm. One adrenal gland is situated at the upper pole of each kidney. The adrenal gland is a complex organ consisting of a cortex and medulla, each differing in structure, function, and embryonic origin.

Adrenal Cortex

A thick capsule of dense irregular connective tissue that contains scattered elastic fibers surrounds each adrenal gland. The capsule contains a rich plexus of blood vessels - mainly small arteries - and numerous nerve fibers. Some blood vessels and nerves enter the substance of the gland in the trabeculae that extend inward from the capsule and then leave the trabeculae to enter the cortex.

The parenchyma of the adrenal cortex consists of continuous cords of secretory cells that extend from the capsule to the medulla, separated by blood sinusoids. The cortex is subdivided into three layers according to the arrangement of the cells within the cords. These cortical layers consist of an outer zona glomerulosa (10%), a middle zona fasciculata (75%), and an inner zona reticularis (15%). The cytologic changes from one zone to the next are gradual.

Zona glomerulosa forms a narrow band just beneath the capsule. The columnar cells are arranged into ovoid groups or arcades and have centrally placed spherical nuclei. In electron micrographs, the cells show a well-developed smooth endoplasmic reticulum and numerous mitochondria that are evenly distributed throughout the cytoplasm. Occasional lipid droplets and scattered profiles of granular endoplasmic reticulum also are present.

Zona fasciculata forms the widest zone of the cortex and consists of long cords that usually are one or two cells thick. The cords run parallel to one another, separated by sinusoids that are lined by an attenuated endothelium. The cells of zona fasciculata are larger than those of the other two zones and have a polyhedral shape, and their spherical nuclei are centrally placed; binucleate cells are common. The cytoplasm contains numerous rounded mitochondria with tubular cristae, abundant smooth endoplasmic reticulum, and well-developed granular endoplasmic reticulum. Many lipid droplets also are present and contain neutral fat, fatty acids, and fatty acyl esters of cholesterol; these represent stored precursors for the synthesis of the steroid hormones secreted by the zona fasciculata. Short microvilli often are present on the plasmalemma adjacent to sinusoids.

Zona reticularis forms the innermost zone and is made up of a network of irregular, anastomosing cords that also are separated by sinusoids. In general, the cells of this zone resemble those of zona fasciculata except that they are smaller, the cytoplasm contains fewer fat droplets, the nuclei stain more deeply, and lipofuscin granules are prominent. Light and dark forms of the cells have been described, but their significance is not known.

The adrenal cortex synthesizes and secretes in excess of twenty-four steroid hormones, which generally can be placed in three broad categories: mineralocorticoids that control water and electrolyte balance, glucocorticoids that affect carbohydrate metabolism, and sex steroids (androgens). All are derived from cholesterol. Enzymes for the synthesis of these steroid hormones are located mainly in the smooth endoplasmic reticulum and mitochondria of the adrenal cortical cells. The pathway involves transfer of precursor molecules and intermediate products back and forth between these two organelles. Adjacent lipid droplets provide the substrates needed for the biosynthetic processes. The mineralocorticoids, primarily aldosterone, are secreted by zona glomerulosa. Aldosterone plays a major role in the regulation of extracellular fluid and blood volumes as well as maintaining potassium balance. It acts on the distal and collecting tubules of the kidney to increase the rate of sodium chloride and water reabsorption from the glomerular filtrate and, at the same time, to increase potassium secretion. It also lowers the concentration of sodium chloride in the secretions of sweat and salivary glands and intestinal mucosa. Aldosterone secretion is controlled primarily by the renin-angiotensin system, which is sensitive to changes in blood pressure and to the concentration of sodium chloride and potassium in the blood plasma and extracellular fluid. It has been suggested that the juxtaglomerular apparatus of the kidney receives signals created by decreased arterial renal blood pressure (which reduces the degree of stretch on the juxtaglomerular cells) and/or by a decrease in the amount of sodium chloride and potassium detected by the macula densa. In response to this signal, juxtaglomerular cells release renin, which acts enzymatically on a circulating protein called angiotensinogen changing it to angiotensin I. A converting enzyme produced primarily by endothelial cells within the lung converts angiotensin I to angiotensin II. The latter stimulates the zona glomerulosa to secrete aldosterone. Angiotensin II also is a vasoconstrictor and acts directly to increases blood pressure. In addition, angiotensin II acts on the renal proximal tubule to promote sodium chloride and water reabsorption and proton (H^+) secretion.

Adrenocorticotrophic hormone (ACTH) elaborated by basophils (corticotrophs) in the anterior pituitary has only a limited role in the control of secretion by the zona glomerulosa. However, it has a permissive effect and small amounts of ACTH are needed for aldosterone secretion to occur in response to renin-angiotensin system activity. Aldosterone is metabolized by the liver and has a half-life of about 20 minutes.

Glucocorticoids (cortisol, cortisone, and corticosterone) are secreted by cells of the zona fasciculata and zona reticularis. These steroid hormones act mainly on the metabolism of fats, proteins, and carbohydrates, resulting in an increase in blood glucose and amino acid levels and in the movement of lipid into and out of fat cells. Cortisol also suppresses the inflammatory response and some allergic reactions by inhibiting the enzyme phospholipase A2. Cortisol is metabolized by the liver and has a half-life of about 70 minutes.

Adrenal androgens, dehydroepiandrosterone and androstenedione, also are secreted by cells of the zona fasciculata and zona reticularis, although cells of the reticularis are said to be the more active in androgen secretion. Androgens are anabolic steroids leading to increased muscle mass and bone growth. In women adrenal androgens contribute to the development of secondary sexual characteristics such as growth of axillary and pubic hair, and sebaceous gland hypertrophy at puberty.

Abnormally high levels of adrenal androgens may have masculinizing effects on women and in boys induce precocious puberty.

The adrenal cortex is the primary source of circulating androgens in women whereas in men testicular androgens are of greater importance and are produced in much greater amounts.

Secretion by zona fasciculata and zona reticularis is controlled by adrenocorticotrophic hormone (ACTH), a polypeptide hormone secreted by corticotrophs in the anterior pituitary. Adrenocorticotrophic hormone stimulates the synthesis and release of steroids, increases blood flow through the cortex, and promotes growth of the two inner zones of the adrenal cortex. The adrenal cortex is essential for life.

Adrenal Medulla

The adrenal medulla is composed of large round or polyhedral cells arranged in clumps or short cords. These are the chromaffin cells, so named because they show numerous brown granules when treated with chromium salts (the chromaffin reaction). A framework of reticular fibers supports the parenchyma, and this stroma contains numerous capillaries, veins, and nerve fibers. Sympathetic ganglion cells are present also and may occur singly or in small groups. Chromaffin cells secrete catecholamines. By special histochemical means, two types of chromaffin cells have been identified, one containing epinephrine and the other norepinephrine.

Ultrastructurally, chromaffin cells are characterized by numerous electron-dense granules, 100 to 300 nm in diameter, that are limited by a membrane. The granules from cells that secrete norepinephrine have intensely stained electron-dense cores, whereas cells that elaborate epinephrine have homogeneous, less dense secretory granules. Both cell types show profiles of granular endoplasmic reticulum, scattered mitochondria, and well-developed Golgi complexes that lie close to the nucleus.

Although not essential for life, hormones of the adrenal medulla help individuals meet stressful situations. Epinephrine increases cardiac output, causes bronchial dilation, elevates blood glucose, and increases the basal metabolic rate. Norepinephrine acts primarily to elevate and maintain blood pressure by causing vasoconstriction in the peripheral segments of the arterial system. Secretion of both hormones is controlled by the sympathetic nervous system. Epinephrine and norepinephrine are metabolized by the liver and have a half-life of about 2 to 3 minutes.

Blood Supply

The rich plexus of small arteries in the capsule of the adrenal provides cortical arterioles that enter the parenchyma of the adrenal to empty into the vast network of cortical sinusoids that separates the cords of epithelial cells making up the cortex. The attenuated endothelium of the sinusoids has numerous fenestrations and is supported only by a thin basal lamina and a delicate network of reticular fibers. The sinusoids pass through all three layers of the cortex and near the corticomedullary junction begin to merge to form large collecting veins. These drain toward the central medulla and finally collect into a single, large suprarenal vein that drains the entire adrenal gland. The cortex has no separate venous drainage. Some small arteries enter the cortex in the trabeculae and provide a direct arterial supply to the medulla. Hence, the medulla receives blood from cortical sinusoids and medullary arteries. The capillaries that surround the medullary cords also are lined by a thin, fenestrated endothelium.

In addition to their systemic effects, adrenocorticosteroids (especially glucocorticoids) affect the adrenal medulla, and the steroid-rich blood from the cortex influences the secretion of epinephrine or norepinephrine by the chromaffin cells. Cortisol induces an enzyme (phenylethanolamine-N-methyl transferase) in the adrenal medullary cells that converts norepinephrine to epinephrine. Thus, epinephrine is the major catecholamine secreted and accounts for between 70%-80% of the medullary secretion.