Osmoregulation

Ionic and osmotic balance

- in multicellular organisms the interstitial fluid is the internal environment
- osmoregulatory organs maintain this environment isovolumic, isotonic, isoionic, isohydric, etc.
- further task of the osmoregulatory organs: removal of poisonous end products of metabolism (NH_3 from proteins) in the form of urea

- through plasma membrane different ionic composition, but equal osmotic pressure
- through epithelium fluids are different in both respects
- obligate and regulated osmotic exchange
- obligate exchange depends on physical factors, regulated exchange compensates for changes

Obligate osmotic exchange

- occurs through the skin, respiratory epithelium and other epithelia in contact with environment
- influencing factors:
  - gradient: determines direction of exchange
  - surface: small animal – relatively larger surface, faster exchange, e.g. dehydration
  - permeability: transcellular and paracellular exchange
  - eating, metabolism, excretes: metabolic water is very important for desert animals, but also for marine ones
  - respiration: function of nose – condense water during exhalation – dripping nose in winter
- human body contains 60% water on average, differences between male-female, young-old
- distributed in different compartments
- intracellularly 2/3, extracellularly 1/3
- of the extracellular water: 3/4 interstitially, 1/4 in blood plasma
- barriers and transport rules

Human kidney

- osmoregulatory organs always contain transport epithelium (skin, gill, kidney, gut) : polarized - apical (luminal, mucosal) and basal (serosal) surfaces are different
- capacity of the transport epithelium is increased by its special structure: tubular organization
- functioning of the mammalian kidney is well known – though it does not represent all types of vertebrate kidneys
- 0.5% of body weight, 20-25% of cardiac output
- cortex, medulla, renal pyramid, renal pelvis, ureter, urinary bladder, urethra
- volume of urine is 1 l daily, slightly acidic (pH 6), composition, volume changes with the food and the requirements of the water homeostasis - beer, Amidazophen, etc.

The nephron

5/24

- functional unit of human kidney is the nephron
- afferent and efferent arterioles, in between glomerulus; Bowman capsule, proximal tubule, loop of Henle, distal tubule, collecting duct
- most of the nephrons (85%) are cortical, the rest are juxtamedullary (15%) nephrons
- steps in the formation of urine:
  - ultrafiltration
  - reabsorption
  - secretion
- the kidney is very important in pH regulation
- the kidney removes ammonia formed during the decomposition of proteins

Ultrafiltration

6/24

- in the kidney 15-25% of water and solutes is filtrated, 180 l daily – proteins and blood cells remain
- filtration depends on:
  - hydrostatic pressure between the capillaries and the lumen of the Bowman capsule: 55-15 = 40 mmHg
  - colloid osmotic pressure of the blood: 30 mmHg – effective filtration pressure 40-30 = 10 mmHg
  - permeability of the filter: fenestrated capillaries, basal membrane (collagen + negative glycoproteins), podocytes (filtration slits between pedicels)
- voluminous blood supply due to the relatively low resistance – afferent arteriole is thick and short – high pressure in the glomerulus
- regulation of the blood flow: basal miogenic tone, paracrine effect of juxtaglomerular apparatus, sympathetic effect (afferent arteriole, glomerulus, podocyte)

Clearance

- clearance of a substance is the volume of plasma that is completely cleaned from the given substance in the kidney in one minute

$$CP = VU \quad \text{that is} \quad C = \frac{VU}{P}$$

C – clearance, P – concentration in plasma,
V – volume of urine in 1 minute, U – concentration in urine

- clearance of a substance that is neither reabsorbed nor secreted (e.g. inulin) equals the glomerulus filtration rate : GFR
- clearance of a substance that is not only filtrated, but completely secreted as well (e.g. PAH) equals the renal plasma flow : RPF
- knowing the hematocrit, renal blood flow (RBF) can be calculated

Tubular reabsorption I.

- 180 l primary filtrate is produced every day, but only 1 l is excreted, of 1800 g filtrated NaCl only 10 g remains in the urine
- role played by the subsequent sections of the tubules:
  - proximal tubule
    - 70% of Na^+ is reabsorbed by active transport, Cl^- and water follow passively, obligate reabsorption
    - on the apical membrane of epithelial cells microvilli
    - virtually all filtrated glucose and amino acids are reabsorbed using Na^+ dependent symporter
    - tubular maximum exists for glucose: below 1.8 mg/ml complete reabsorption (normal value: 1.0 mg/ml), above 3.0 mg/ml linear increase – sugar in urine in diabetes

Tubular reabsorption II.

- descending part of Henle's loop
  - no microvilli, few mitochondria – no active transport
  - low permeability for NaCl and urea, high for water
- thin ascending part of Henle's loop
  - no microvilli, few mitochondria – no active transport
  - low permeability for water, high for NaCl
- thick ascending part of Henle's loop
  - active reabsorption of Na^+
  - low water permeability
- distal tubule
  - active reabsorption of Na^+, and passive reabsorption of water
  - K^+, H^+ and NH_3 transport as needed – see later (pH regulation)
  - transport is regulated by hormones – facultative reabsorption
- collecting duct
  - active reabsorption of Na^+ at the cortical part, high urea permeability in the internal medullary part
  - regulated water permeability (ADH)

Tubular secretion

- several substances are secreted from the plasma to the tubule in the nephron – best examined: different electrolytes (K^+, H^+, NH_3) organic acids and bases
- active transport – recognizes substances conjugated with glucuronic acid in the liver
- K^+ is reabsorbed in the proximal tubule and Henle's loop (Na/2Cl/K transporter)
- excess K^+ is exchanged for Na^+ in the distal tubule
- secretion of H^+ and NH_3 serves pH regulation

pH regulation

- normal pH 7.4 – 7.35 acidosis, 7.45 alkalosis
- normal functioning is possible between 7.0-7.8
- respiratory alkalosis and acidosis: caused by hyper-, or hypoventilation
- metabolic alkalosis – e.g. vomiting
- metabolic acidosis – anaerobic energy production

- buffers: CO_2/HCO_3^-, plasma proteins, phosphate
- respiration: changing respiratory rate
- kidney:
  - proximal tubule, Henle's loop: Na^+/H^+ exchanger, distal tubule, collecting duct: HCO_3^- uptake, H^+ secretion through A-cells
  - in distal tubule and collecting duct: HCO_3^- secretion, H^+ uptake through B-cells

Hyperosmotic urine

- birds and mammals can produce hyperosmotic urine - water reabsorption in the collecting duct due to osmotic pressure differences
- generation of osmotic pressure difference is helped by the counter-current principle
- Na+ transport in the ascending part of the Henle's loop – do not enter the descending part, but attracts water leading to the same result
- in addition, urea present in high concentration because of the reabsorption of water, can only leave the tubule in the internal medulla
- osmotic pressure increases from the cortex to the medulla
- blood supply to the tubules (vasa recta) is running in parallel to the Henle's loop, does not decrease the osmotic gradient

Regulation of the kidney

13/24

- granular cells in the juxtaglomerular apparatus produce renin in response to a decrease in blood pressure or NaCl delivery to the distal tubule
- renin cuts off angiotensin I (10 amino acids) from angiotensinogen (glycoprotein)
- converting enzyme (mostly in the lung) cuts off 2 amino acids from angiotensin I – angiotensin II
- angiotensin II enhances aldosterone secretion in the adrenal gland, increases blood pressure through vasoconstriction and increases ADH production
- aldosterone increase Na+ reabsorption through 3 different ways: facilitation of the pump, ATP production, increased apical Na+ permeability
- ADH producing cells detect blood pressure and osmolality and are sensitive to alcohol
- atrial natriuretic peptide (ANP) – released in the atria when venous pressure increases - inhibits renin, aldosterone, ADH production

Digestion

15/24

Alimentary canal in vertebrates

- in unicellular and primitive multicellular organisms intracellular digestion
- in more developed multicellular organisms – extracellular digestion
- topologically external to the body
- entrance and exit are protected by sphincters and other devices
- ingested material is subjected to various mechanical, chemical and bacterial effects
- tubular organization allows for functional specialization (i.e. acidic and alkaline environment)
- parts of the alimentary canal: headgut, foregut, midgut, hindgut

16/24

Headgut - Foregut

- headgut
  - food enters here – structures related to feeding and swallowing: mouth-parts, buccal (oral) cavity, pharynx, bills, teeth, tongue, salivary glands, additional structures to direct the flow of ingested materials and inspired water or air
- foregut
  - in most species: esophagus and stomach
  - esophagus carries food from headgut to stomach
  - digestion starts in the stomach
  - in most vertebrates: pepsinogen and HCl
  - monogastric stomach in omnivorous and carnivorous vertebrates
  - invaginations with gastric pits with gland cells

Midgut I.

- in vertebrates it consists of the small intestine (duodenum, jejunum, ileum), it is separated from the stomach by the pylorus
- shorter in carnivores, longer in herbivores – dynamic changes
- duodenum: production of mucus and fluids + receives secretions from liver and pancreas – neutralization of stomach acid and digestion
- jejunum: secretion of fluids, digestion, absorption
- ileum: mainly absorption, some secretion
- small intestine is characterized by a large-surface epithelium: gross cylindrical surface would be 0.4 m^2, but circular folds, intestinal villi, brush border - 200-300 m^2

Midgut II.

- circular folds slow down the progress of food – more time for digestion
- each villus (approx. 1 mm long) sits in a circular depression (crypt of Lieberkühn)
  - inside: network of arterioles, capillaries and venules
  - in the middle: central lacteal (lymph vessel)
- longitudinal smooth muscle fibers – their contraction empties the lymph vessels
- epithelium is made up of enterocytes (lifespan 3-6 days) proliferating at the bottom of the crypts (chemotherapy!) and bearing brush border (~1 μ long, 0.1 μ wide, 200,000/mm^2); tight junctions, desmosomes
- on the microvilli (brush border) glycocalyx: hydrolases (glycoproteins) and luminal transporters, inside actin filaments – in the basolateral membrane Na-K-pumps and different transporters
- among the enterocytes sporadic goblet cells (mucus)

Hindgut

- stores remnants of digested food – absorption of inorganic ions, water
- fermentation in plant-eaters (cecum or colon), absorption of volatile organic acids
- in vertebrates it consists of the final portion of small intestine and of the large intestine (colon)
- hindgut terminates in the rectum
- defecation and urination are under behavioral control
- the alimentary canal in vertebrates have many differences, but similarities as well

Motility of alimentary canal I.

- motility is the ability of the alimentary canal to contract
- its roles:
  - propulsion of food from intake to excretion
  - grinding and kneading the food to mix it with digestive juices and to convert it to a soluble form
  - stirring the gut contents to ensure the continuous renewal of material in contact with the epithelium

Motility of alimentary canal II.

- layers of the alimentary canal in vertebrates: serosa, longitudinal and circular muscle, submucosa, muscularis mucosa, lamina propria, epithelium
- there are two basic forms of motility: peristalsis (longitudinal and circular muscles) and segmentation (circular muscles)
- sphincters: upper and lower esophageal, cardia (functional), pylorus, ileocecal valve (between the small and large intestine), internal and external anal

Motility of alimentary canal III.

- swallowing
  - complex reflex: tongue presses the food to the palate, soft palate closes the nasal cavity, food is propelled into the pharynx, mechanoreceptors induce the reflex, swallowing is unstoppable
- reflux
  - cardia is leaking, acidic chyme reenters the esophagus – can lead to inflammation, cancer
- regurgitation
  - in ruminants – chyme reenters the buccal cavity without vomiting
- vomiting
  - complex reflex, helped by the respiratory muscles – reverse peristalsis, inspirational muscles contract – negative pressure in the chest, abdominal muscles contract – chyme enters the esophagus
  - chyme returns to the stomach during retching
  - during vomiting expiratory muscles contract, upper esophageal sphincter relaxes
- defecation
  - is a complex process: posture, contraction of abdominal wall, sphincters
  - internal sphincter autonomic, external voluntary regulation

Regulation of the intestines

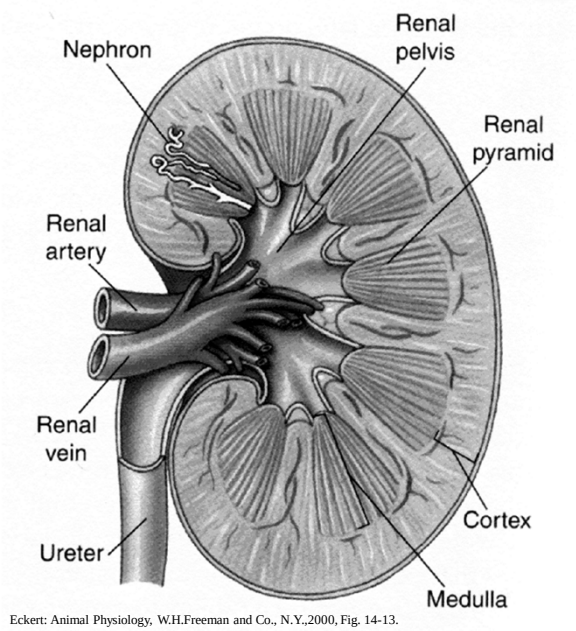
- **intrinsic control: contraction is myogenic in the alimentary canal – smooth muscle is capable of inducing electrical activity**

- **extrinsic control:**
  - **enteric nervous system - myenteric (Auerbach's) and submucosal (Meissner's) neuronal networks**
  - **central nervous system**
    - **parasympathetic innervation (preganglionic):**
      - acting mostly on interneurons of the enteric nervous system – excitatory effect
    - **sympathetic innervation (postganglionic):**
      - vasoconstriction, pre-, and postsynaptic inhibition, sphincters
  - **local peptide hormones**
    - **gastrin family: gastrin and CCK (cholecystokinin)**
    - **secretin family – secretin and GIP (glucose-dependent insulinotropic peptide)**
    - **produced by unicellular glands detecting the composition and pH of the chyme directly – neuronal regulation in some of them**

Gastrointestinal hormones

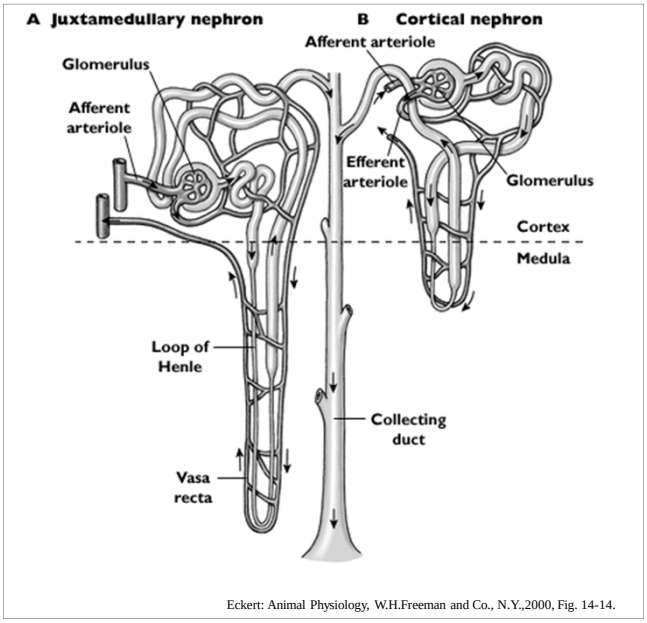
cell	hormone	stimulus	stomach	bile	pancreas
G	gastrin	peptides, amino acids in the stomach	HCl production, motility up		
CCK	cholecystokinin	lipids, proteins in the small intestine	motility, emptying inhibited	emptying the gall bladder	increased enzyme production
S	secretin	acid in the small intestine	emptying inhibited		increased HCO_3^- secretion
GIP	glucose-dependent insulinotropic peptide	carbohydrates in the small intestine	HCl production emptying inhibited		glucose dependent insulin secretion

Structure of mammalian kidney



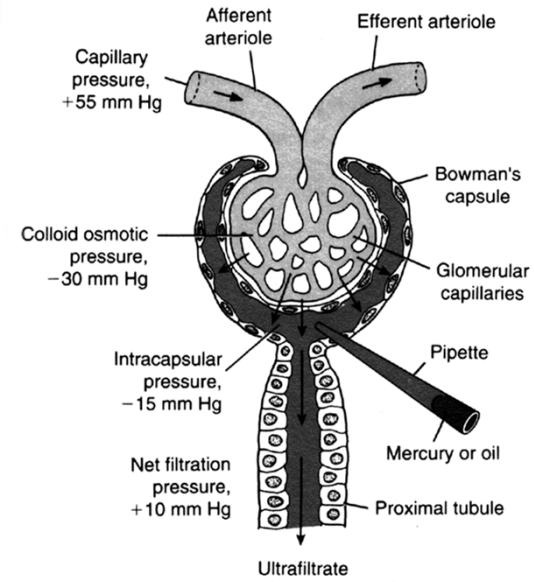
Eckert: Animal Physiology, W.H.Freeman and Co., N.Y.,2000, Fig. 14-13.

Structure of a nephron



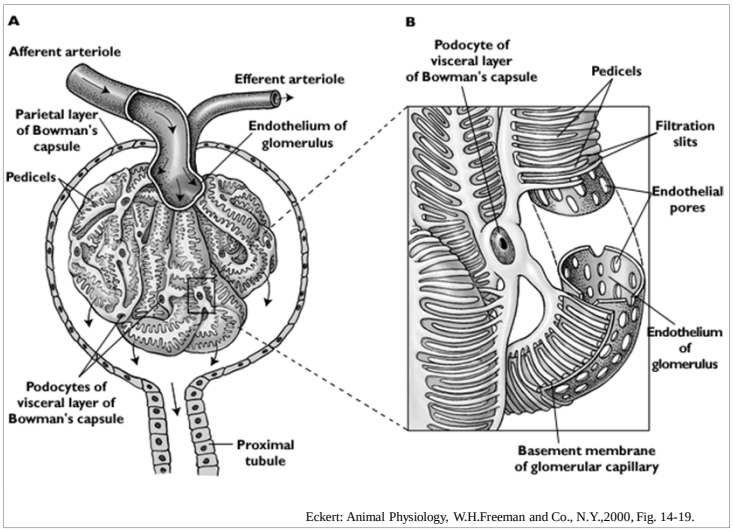
Eckert: Animal Physiology, W.H.Freeman and Co., N.Y.,2000, Fig. 14-14.

Glomerular filtration



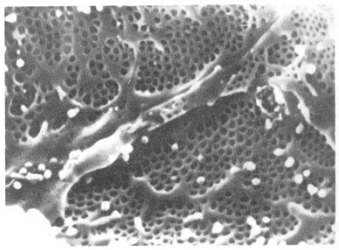
Eckert: Animal Physiology, W.H.Freeman and Co., N.Y.,2000, Fig. 14-18

Podocytes of the capsule



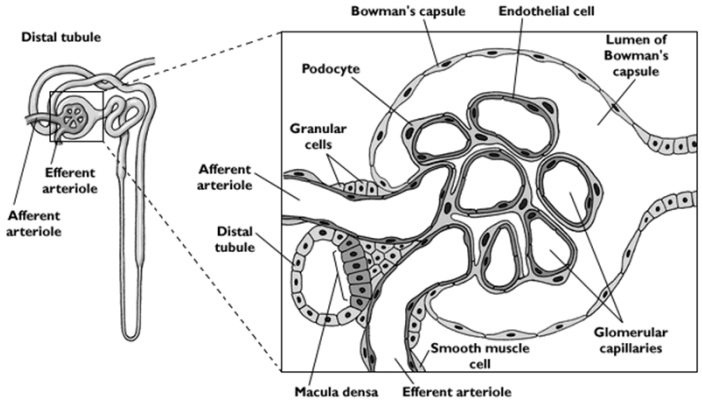
Eckert: Animal Physiology, W.H.Freeman and Co., N.Y.,2000, Fig. 14-19.

Podocytes of the capsule - EM



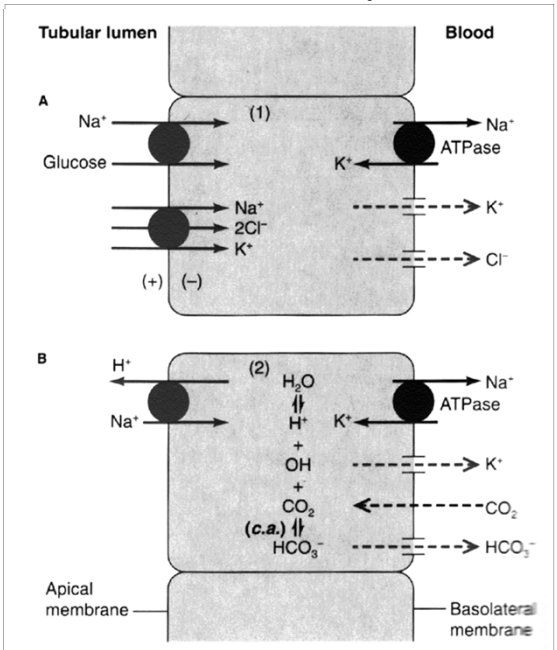
Berne and Levy, Mosby Year Book Inc, 1993, Fig. 41-7

Juxtaglomerular apparatus



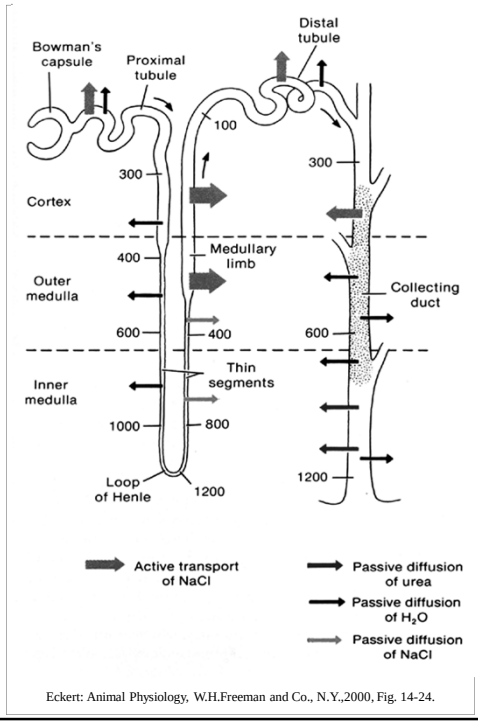
Eckert: Animal Physiology, W.H.Freeman and Co., N.Y.,2000, Fig. 14-20.

Na^+ reabsorption



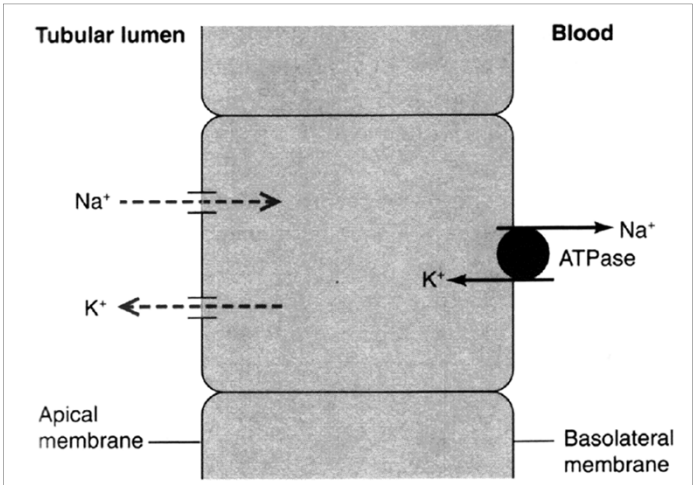
Eckert: Animal Physiology, W.H.Freeman and Co., N.Y.,2000, Fig. 14-25.

Processes of reabsorption



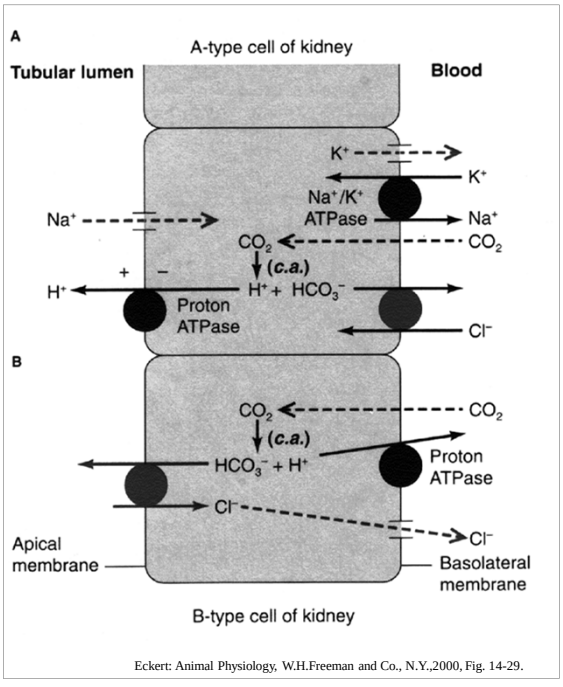
Eckert: Animal Physiology, W.H.Freeman and Co., N.Y.,2000, Fig. 14-24.

Mechanism of K^+ secretion



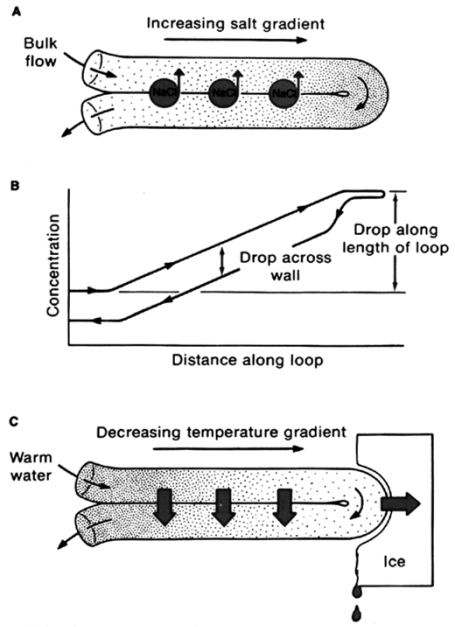
Eckert: Animal Physiology, W.H.Freeman and Co., N.Y.,2000, Fig. 14-28.

pH regulation



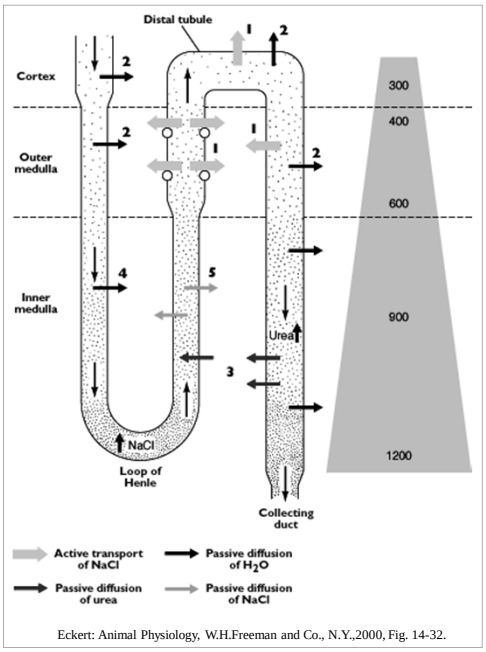
Eckert: Animal Physiology, W.H.Freeman and Co., N.Y.,2000, Fig. 14-29.

Counter-current principle



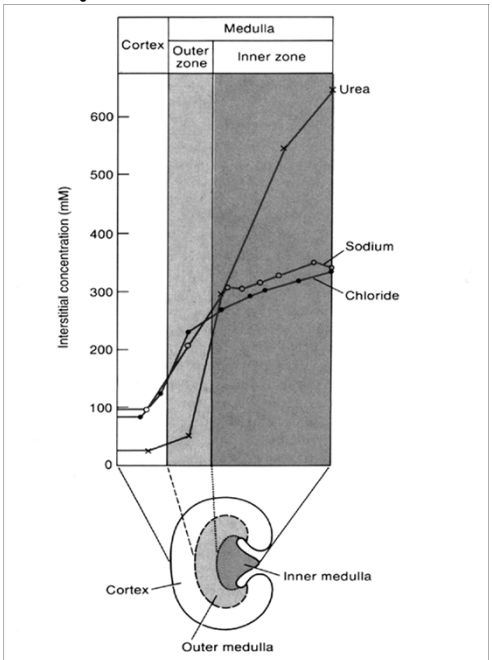
Eckert: Animal Physiology, W.H.Freeman and Co., N.Y.,2000, SL. 14-2.

Mechanism of urine concentration



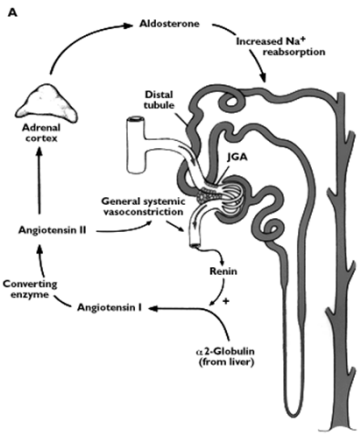
Eckert: Animal Physiology, W.H.Freeman and Co., N.Y.,2000, Fig. 14-32.

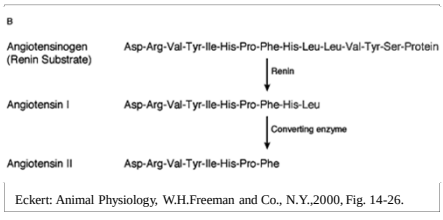
Osmotic pressure in the kidney



Eckert: Animal Physiology, W.H.Freeman and Co., N.Y.,2000, Fig. 14-32.

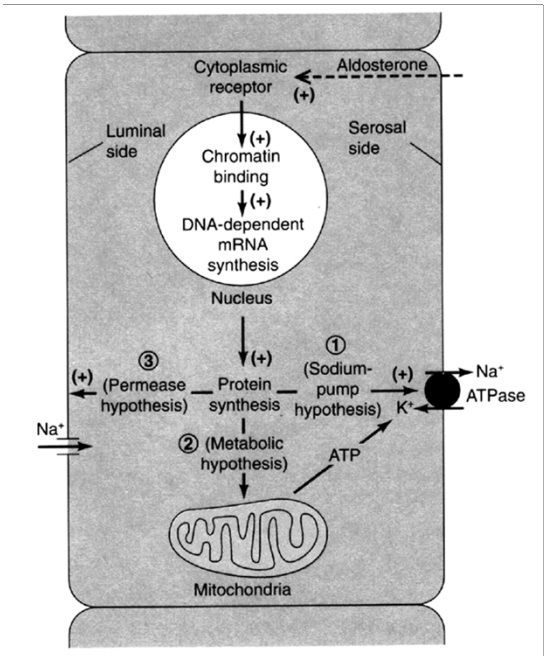
Renin-angiotensin system





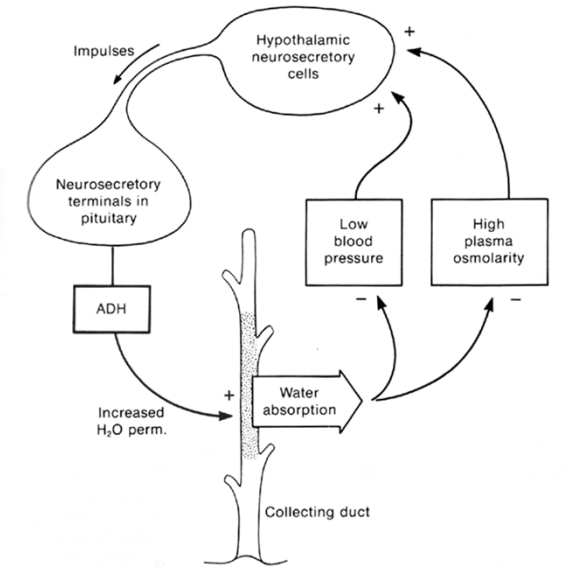
Eckert: Animal Physiology, W.H.Freeman and Co., N.Y.,2000, Fig. 14-26.

Actions of aldosterone



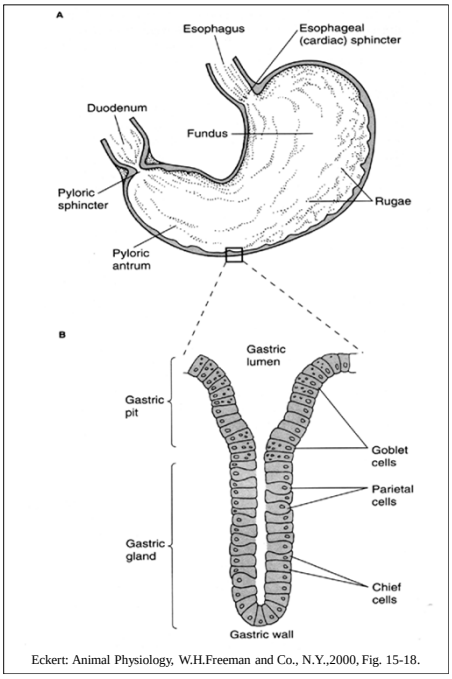
Eckert: Animal Physiology, W.H.Freeman and Co., N.Y.,2000, Fig. 14-27.

Regulation of ADH secretion



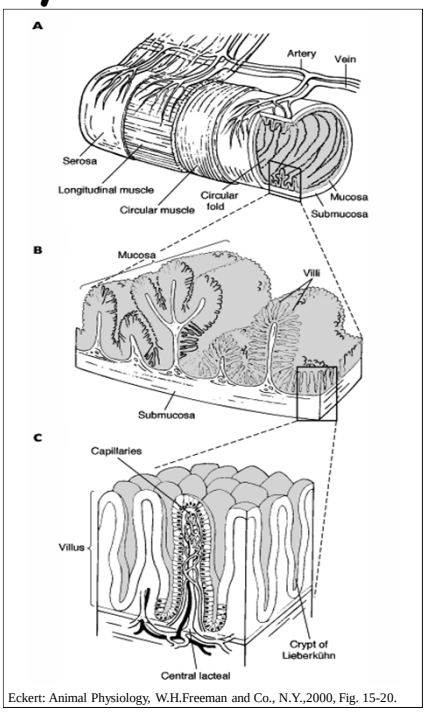
Eckert: Animal Physiology, W.H.Freeman and Co., N.Y.,2000, Fig. 14-35.

Monogastric stomach



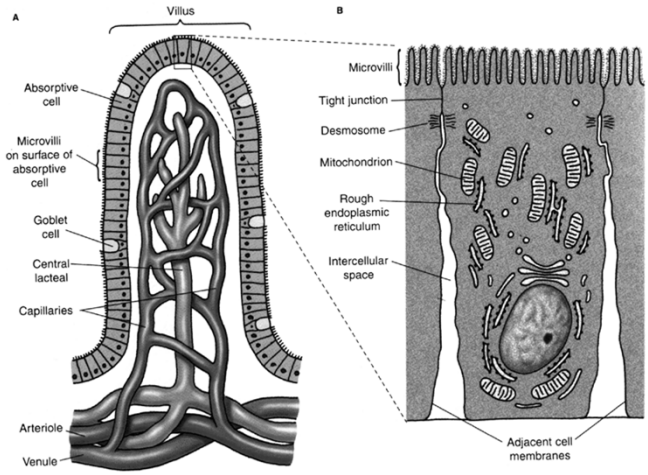
Eckert: Animal Physiology, W.H.Freeman and Co., N.Y.,2000, Fig. 15-18.

Anatomy of the small intestine



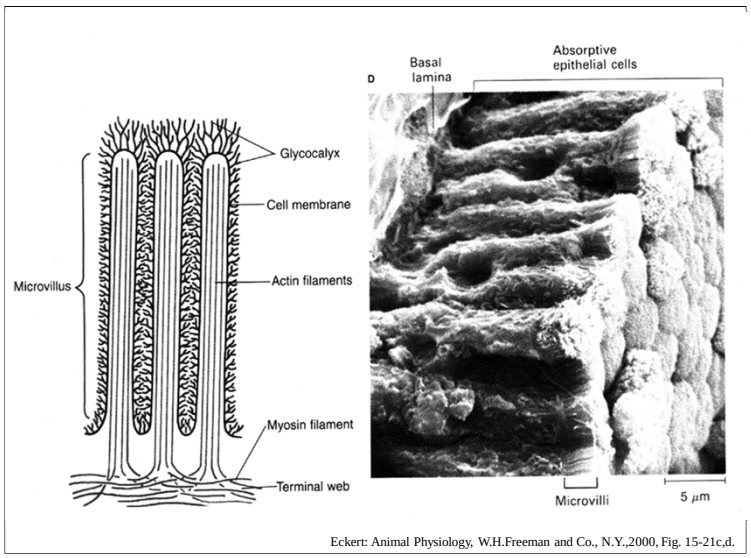
Eckert: Animal Physiology, W.H.Freeman and Co., N.Y.,2000, Fig. 15-20.

Structure of a villus



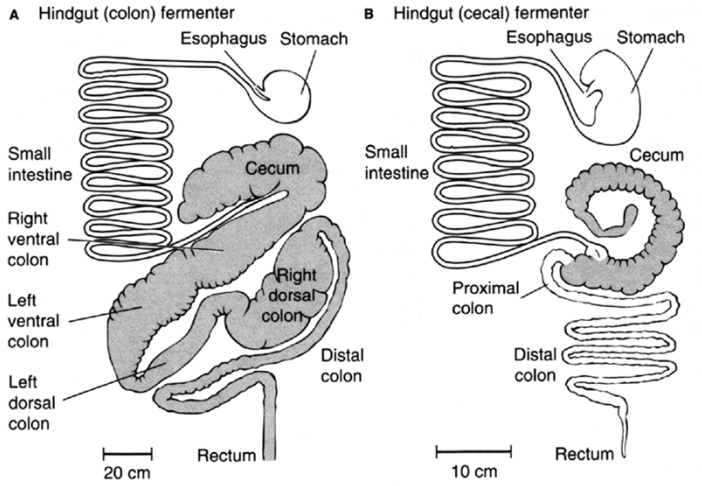
Eckert: Animal Physiology, W.H.Freeman and Co., N.Y.,2000, Fig. 15-21a,b.

Brush border



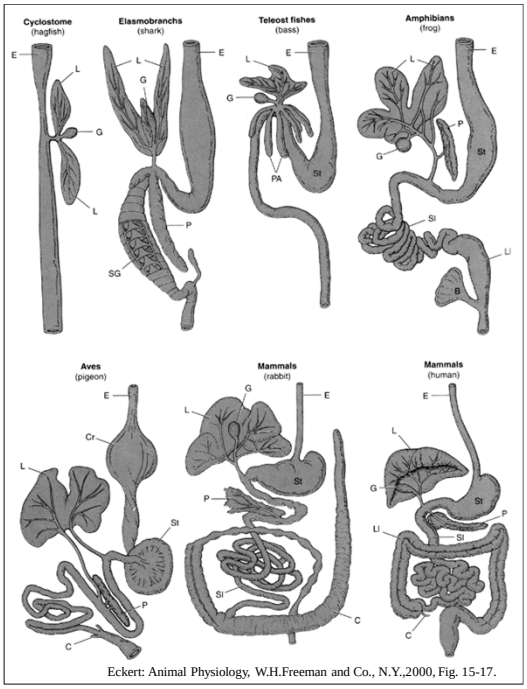
Eckert: Animal Physiology, W.H.Freeman and Co., N.Y.,2000, Fig. 15-21c,d.

Colon and cecal fermenters



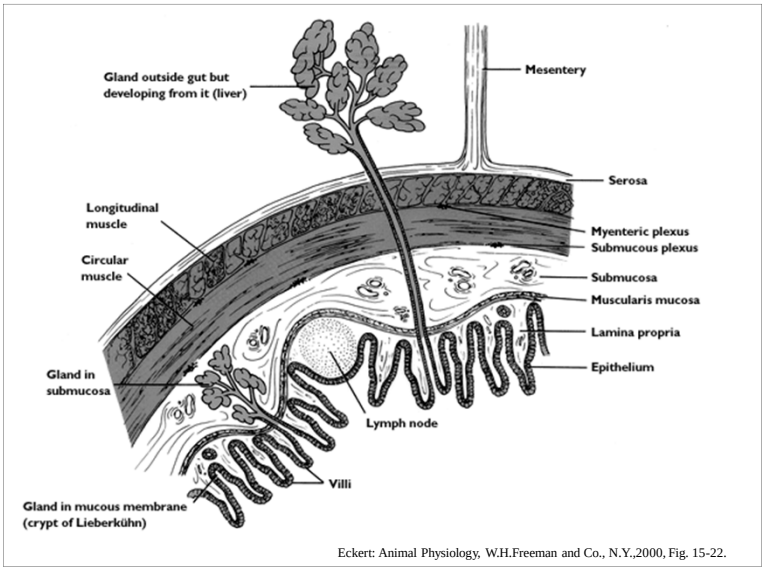
Eckert: Animal Physiology, W.H.Freeman and Co., N.Y.,2000, Fig. 15-22.

Digestive systems in vertebrates



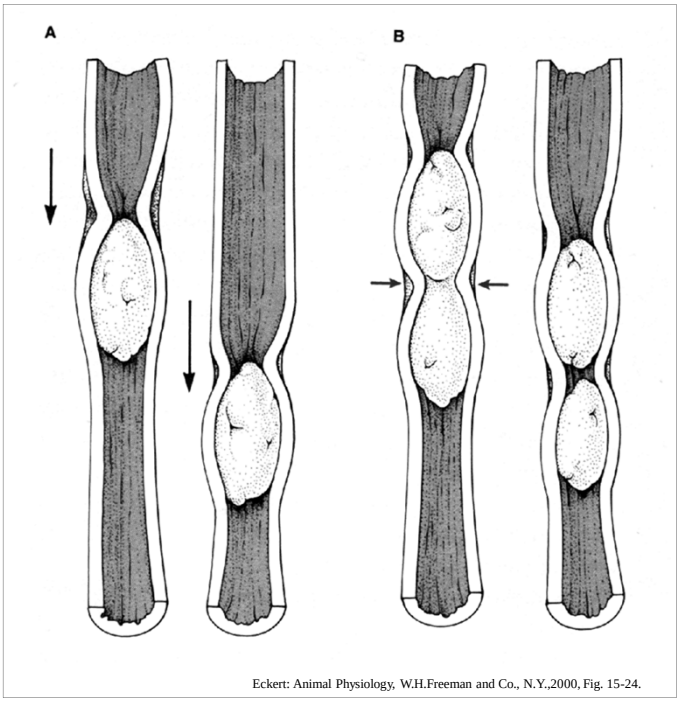
Eckert: Animal Physiology, W.H.Freeman and Co., N.Y.,2000, Fig. 15-17.

Cross-section of the intestine



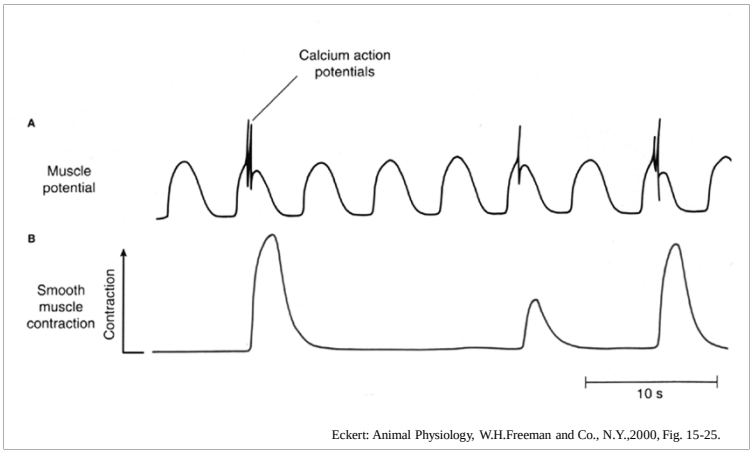
Eckert: Animal Physiology, W.H.Freeman and Co., N.Y.,2000, Fig. 15-22.

Motility of the intestine



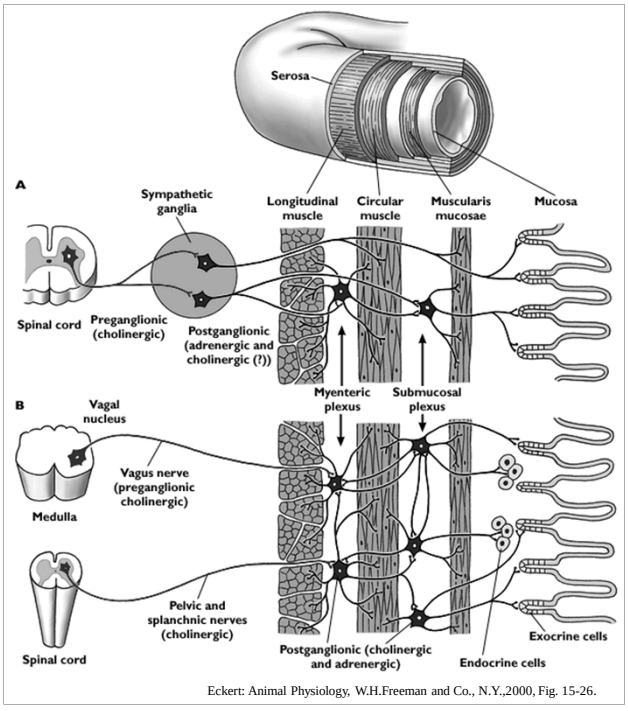
Eckert: Animal Physiology, W.H.Freeman and Co., N.Y.,2000, Fig. 15-24.

Basic membrane potential rhythm



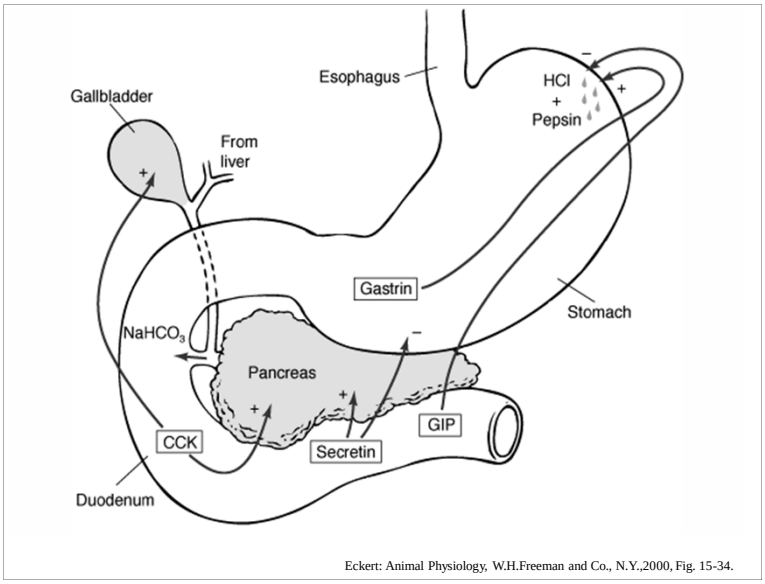
Eckert: Animal Physiology, W.H.Freeman and Co., N.Y.,2000, Fig. 15-25.

Autonomic innervation



Eckert: Animal Physiology, W.H.Freeman and Co., N.Y.,2000, Fig. 15-26.

Gastrointestinal hormones



Eckert: Animal Physiology, W.H.Freeman and Co., N.Y.,2000, Fig. 15-34.