Must-knows

Four basic tissues Epithelial, connective, muscle and nervous tissue. Histology = tissues and how they build organs; 'histo' = tissue or web.

Origin from all three germ layers Epithelia arise from ectoderm, mesoderm and endoderm (e.g. epidermis, endothelium, gut lining).

Defining features Tightly packed polyhedral cells with little extracellular matrix, polarised (apical, lateral, basal domains), resting on a basement membrane. Avascular: fed by diffusion from capillaries in the lamina propria.

Functions Covering, lining, protection (epidermis, urothelium), absorption (intestine), secretion (stomach, glands), sensation, transport (cilia), contractility (myoepithelial cells).

Naming rule Number of layers (simple / stratified) + shape of the cells of the most superficial layer (squamous, cuboidal, columnar). Stratified squamous is further split by keratinisation.

Pseudostratified is simple Every cell rests on the basement membrane but not every cell reaches the lumen; nuclei lie at several levels so it looks layered. Short basal cells are stem cells.

Basement membrane Basal lamina (epithelial product: type IV collagen, laminin) plus reticular lamina (connective tissue product: type III collagen). Selective barrier; controls polarity, proliferation and differentiation.

Apical specialisations Microvilli (actin core, absorption), stereocilia (long microvilli, epididymis), cilia (9+2 axoneme on basal bodies, motile), glycocalyx (carbohydrate coat).

Goblet cell Unicellular exocrine gland secreting mucin (heavily glycosylated protein): PAS-positive, pale in H&E; apical mucin mass pushes the nucleus to the basal pole.

Stratified squamous: keratinised vs not Non-keratinised: living nucleated surface cells on moist surfaces (mouth, oesophagus, vagina, cornea). Keratinised: dead anucleate keratin-filled surface cells (epidermis).

Transitional epithelium (urothelium) Lines renal calyces, pelvis, ureter, bladder, proximal urethra. Relaxed 4–5 layers with dome-shaped (umbrella) surface cells, some binucleate; stretched 2–3 layers, flat surface cells.

Gland development Surface epithelium proliferates into the connective tissue. Exocrine: connection persists as a duct. Endocrine: connection is lost, product enters capillaries.

Modes of secretion Merocrine = exocytosis, no cytoplasm lost (most common). Apocrine = product plus apical cytoplasm (mammary lipid). Holocrine = whole cell breaks down (sebaceous).

Renewal Epithelia renew continuously by mitosis of basal / stem cells; holocrine glands replace lost cells from peripheral basal cells.

TYPES Classification of covering epithelia

Simple squamous Layers and cell shape one layer, flat cells, flat nuclei bulging into lumen Where endothelium (vessels, heart), mesothelium (pleura, peritoneum, pericardium), lung alveoli, parietal layer of Bowman's capsule, thin limb of loop of Henle, corneal endothelium, inner and middle ear Function exchange (gases, fluid), filtration, lubrication, low friction Note 'Pavement' epithelium; squamous = fish-scale-like

Simple cuboidal Layers and cell shape one layer, cells as tall as wide, round central nucleus Where kidney tubules, thyroid follicles, small exocrine ducts, ovary surface Function secretion, absorption, barrier

Simple columnar Layers and cell shape one layer, tall cells, oval nuclei near the basal pole Where stomach surface and gastric pits, small intestine and colon (with goblet cells), gallbladder (microvilli, no goblet cells); ciliated form in uterine tube Function absorption, secretion, protection

Pseudostratified columnar Layers and cell shape one layer, all cells on basement membrane, nuclei at several levels Where trachea and bronchi (ciliated, with goblet cells = respiratory epithelium), nasal cavity; epididymis and ductus deferens (stereocilia) Function secretion, moving mucus by cilia, protection

Stratified squamous non-keratinised Layers and cell shape many layers, cuboidal basal to flat nucleated living surface cells Where oral cavity, oesophagus, vagina, ectocervix, anal canal, corneal epithelium, inner lips Function protection on moist surfaces, some secretion

Stratified squamous keratinised Layers and cell shape many layers, surface cells dead, anucleate, filled with keratin Where epidermis of skin Function protection against abrasion, water loss, microbes

Stratified cuboidal Layers and cell shape two (or more) layers of cuboidal cells Where ducts of sweat glands, developing ovarian follicles Function protection, secretion Note Listed on slide 16 but not shown

Stratified columnar Layers and cell shape several layers, superficial cells columnar Where conjunctiva, large excretory ducts, parts of male urethra Function protection, secretion Note Rare

Transitional (urothelium) Layers and cell shape relaxed 4–5 layers (basal cuboidal, intermediate polygonal, dome-shaped umbrella surface cells); stretched 2–3 layers, flat surface cells Where renal calyces and pelvis, ureter, bladder, proximal urethra Function protection, distension, barrier to urine

CELLS Cell shapes

Squamous Proportions width greater than height Nucleus flat, elongated Example endothelium, alveoli

Cuboidal Proportions height ≈ width ≈ depth Nucleus round, central Example thyroid follicle, kidney tubule

Columnar Proportions height greater than width Nucleus oval, near basal pole Example intestine, stomach

SURFACE Apical surface specialisations

Microvilli Core / composition actin filaments anchored in terminal web Size and motility ≈1 µm long, 0.08 µm wide; non-motile; brush (striated) border Where enterocytes, proximal convoluted tubule Note Increase absorptive surface ~20–30×

Stereocilia Core / composition actin filaments (very long microvilli, not cilia) Size and motility long, non-motile; branched in epididymis Where epididymis, ductus deferens; sensory hair cells of inner ear

Cilia Core / composition axoneme of 9 peripheral doublets + central pair (9+2) of microtubules, dynein arms; arise from basal bodies Size and motility 5–10 µm long, 0.2 µm wide; motile, beat in one direction Where respiratory tract, uterine tube Note Row of basal bodies = dark apical line in LM

SURFACE Apical surface specialisations (cont.)

Glycocalyx Core / composition carbohydrate chains of membrane glycoproteins and glycolipids Size and motility thin coat on apical membrane Where all cells, prominent on enterocytes Note Holds digestive enzymes, protects

Primary cilium Core / composition 9+0 axoneme Size and motility single, non-motile; sensory Where most cells, e.g. kidney tubule

Flagellum Core / composition 9+2 axoneme, longer Size and motility single, motile Where sperm only in humans

CELLS Cell domains and junctions

Apical domain What it is free surface facing the lumen Function absorption, secretion, specialisations

Lateral domain What it is surfaces facing neighbouring cells Function cell-cell junctions

Basal domain What it is surface on the basement membrane Function anchorage, receptors, ion transport (basal folds)

Tight junction (zonula occludens) What it is most apical; claudins, occludin seal the membranes Function blocks paracellular passage; separates apical and lateral membranes Note With zonula adherens + desmosome = junctional complex ('terminal bar' in LM)

Adherens junction (zonula adherens) What it is cadherins linked to actin Function adhesion

Desmosome (macula adherens) What it is cadherins linked to keratin intermediate filaments Function strong spot adhesion; 'spines' of stratum spinosum

Gap junction What it is connexons (connexins) forming channels Function passage of ions and small molecules between cells

Hemidesmosome What it is integrins linked to intermediate filaments Function binds the cell to the basal lamina

Focal adhesion What it is integrins linked to actin filaments Function binds the cell to the extracellular matrix (basal lamina)

SURFACE Basement membrane

Basal lamina Made of / by type IV collagen, laminin, nidogen, perlecan; made by epithelial cells Note 20–100 nm; seen by EM (lamina lucida + lamina densa)

Reticular lamina Made of / by type III collagen (reticular fibres); made by connective tissue cells Note together with basal lamina = basement membrane, PAS-positive in LM

Functions Made of / by selective filter, scaffold for regeneration Note controls polarity, proliferation, differentiation

Thick example Made of / by Descemet's membrane of corneal endothelium Note glassy pink layer between endothelium and stroma

SURFACE Epidermis layers (keratinised stratified squamous), deep to superficial

Stratum basale Cells one layer of cuboidal to low columnar cells on basement membrane Key feature mitosis (stem cells) Note Junqueira: stratum basale = stratum germinativum (slide 44 says germinativum = basale + spinosum)

Stratum spinosum Cells several layers of polygonal cells Key feature desmosomes give 'spiny' (prickle) look Note Basale + spinosum = Malpighian layer; also present in non-keratinised epithelium

Stratum granulosum Cells 3–5 layers of flattened cells Key feature keratohyalin granules

Stratum lucidum Cells thin layer of flat eosinophilic cells Key feature only in thick skin (palms, soles); eleidin, pale/bright

Stratum corneum Cells many layers of dead anucleate flat cells Key feature filled with keratin

SURFACE Germ layer origin

Ectoderm (outer) Epithelia derived epidermis, corneal epithelium, oral and nasal epithelium, distal anal canal

Mesoderm (middle) Epithelia derived endothelium, mesothelium, kidney tubules, reproductive tract

Endoderm (inner) Epithelia derived lining of gut and respiratory tract, liver, pancreas, thyroid

TYPES Gland classification

Ducts Type Exocrine Feature duct to surface or lumen Example sweat, sebaceous, salivary

Ducts Type Endocrine Feature ductless, secretes hormones into blood Example thyroid, adrenal, pituitary

Ducts Type Mixed Feature exocrine and endocrine parts Example pancreas, liver, gonads Note Slide 53 lists pancreas as endocrine only

Cell number Type Unicellular Feature single secretory cell Example goblet cell

Cell number Type Multicellular Feature many cells, secretory portion + duct Example sweat, salivary glands Note Slide 53 says pituitary and adrenal are multicellular exocrine glands; textbook: they are endocrine

Duct Type Simple Feature unbranched duct Example sweat gland

Duct Type Compound Feature branched duct Example salivary glands, pancreas

Secretory portion Type Tubular Feature tube of about duct diameter (simple, coiled or branched) Example intestinal crypts; sweat gland (coiled); gastric glands (branched)

Secretory portion Type Acinar (alveolar) Feature rounded sac-like end piece Example sebaceous gland (branched acinar), exocrine pancreas (compound acinar)

Secretory portion Type Tubuloacinar Feature both tubules and acini Example submandibular gland

Product Type Serous Feature watery, protein-rich; round basal nucleus, basophilic cytoplasm Example parotid, pancreatic acini

Product Type Mucous Feature viscous mucin; pale cells, flat basal nucleus Example sublingual, goblet cells

Product Type Mixed (seromucous) Feature both serous and mucous cells; serous demilunes capping mucous tubules Example submandibular, sublingual

MORE Modes of secretion

Merocrine (eccrine) How product leaves exocytosis of vesicles at apical surface Cell fate intact, keeps secreting Example most glands: eccrine sweat, salivary, pancreas Note Most common

Apocrine How product leaves product released with part of apical cytoplasm Cell fate apical region reforms Example lipid of mammary gland Note 'Apocrine' sweat glands actually secrete mostly by merocrine release (Ross)

Holocrine How product leaves whole cell fills with product and breaks down Cell fate dies; replaced by mitosis of peripheral basal cells Example sebaceous gland

Mnemonics

Mnemonic Come Let's Get Sun Burned = Epidermis superficial to deep: corneum, lucidum, granulosum, spinosum, basale

Mnemonic Mero = merely exocytosis, Apo = apex, Holo = whole = Merocrine loses nothing, apocrine loses apical cytoplasm, holocrine loses the whole cell

Must-knows

Three components Cells + extracellular matrix (ground substance and fibres). Matrix dominates; cells are scattered in it.

Origin: mesenchyme All connective tissues arise from embryonic mesenchyme (mostly mesoderm). Fibroblasts, chondroblasts, osteoblasts, adipocytes and haematopoietic stem cells descend from it.

Functions Support and binding, nutrition of avascular epithelia by diffusion through ground substance, defence (immune cells), protection, fat storage, repair.

Loose vs dense Loose: many cells, much ground substance, thin loosely woven fibres. Dense: few cells, little ground substance, thick collagen bundles; regular (one direction) or irregular (many directions).

Resident vs wandering cells Resident (fixed): fibroblasts, myofibroblasts, macrophages, adipocytes, mast cells, mesenchymal cells. Wandering (from blood): lymphocytes, plasma cells, neutrophils, eosinophils, basophils, monocytes.

Fibroblast Commonest cell; synthesises collagen, elastin, GAGs, proteoglycans and glycoproteins. Active form: large, pale oval nucleus, basophilic cytoplasm; resting fibrocyte: smaller, dark slim nucleus.

Macrophages and mast cells Macrophages come from blood monocytes; phagocytic, antigen-presenting. Mast cells: granules of histamine and heparin, metachromatic; release on IgE cross-linking (immediate hypersensitivity).

Ground substance Hydrated, viscous gel of GAGs, proteoglycans and multiadhesive glycoproteins; lubricant and barrier to microorganisms; fine granular in TEM, lost in routine sections.

Tissue fluid and oedema Plasma-like fluid filtered from capillaries by hydrostatic pressure, returned by colloid osmotic pressure and lymphatics. Excess in loose CT ground substance = oedema.

Collagen hierarchy Tropocollagen (3 alpha chains, triple helix, 300 nm) -> fibril (64-67 nm cross-banding) -> fibre -> bundle. Type I is the commonest (~90% of body collagen).

Elastic and reticular fibres Elastic: elastin core + fibrillin microfibrils, thin branching network; orcein / resorcin-fuchsin. Reticular: type III collagen, argyrophilic (silver, black) and PAS-positive, made by fibroblasts (by reticular cells in lymphoid organs and marrow).

White vs brown fat White: unilocular, one droplet, peripheral flattened nucleus (signet ring), energy store. Brown: multilocular, central round nucleus, many mitochondria with UCP1 (thermogenin) -> heat.

Why fat looks empty Alcohols and xylene of paraffin processing dissolve lipid; frozen section + Sudan or osmium shows it.

Embryonic connective tissue Mesenchyme: stellate cells, abundant viscous ground substance, almost no fibres. Mucous tissue (Wharton's jelly of umbilical cord): rich in hyaluronan, few fibres.

CELLS Cells of connective tissue proper

Fibroblast Origin / resident or wandering mesenchyme; resident How it looks elongated, pale oval nucleus with nucleolus; basophilic cytoplasm with RER and Golgi Function makes fibres and ground substance

Fibrocyte Origin / resident or wandering inactive fibroblast; resident How it looks smaller, spindle-shaped, dark slim nucleus, little cytoplasm Function maintenance; reactivates in repair

Myofibroblast Origin / resident or wandering fibroblast; resident How it looks fibroblast with actin bundles and smooth muscle actin Function wound contraction

Macrophage Origin / resident or wandering blood monocyte; resident (histiocyte) How it looks irregular surface with processes, indented nucleus, many lysosomes Function phagocytosis, antigen presentation, cytokines Note Fuse into foreign-body giant cells.

Mast cell Origin / resident or wandering bone-marrow progenitor; resident How it looks large oval, central nucleus hidden by many basophilic metachromatic granules; near small vessels Function releases histamine, heparin, leukotrienes, ECF-A Note IgE receptors (FcεRI) on surface; degranulation = exocytosis.

Adipocyte Origin / resident or wandering mesenchyme; resident How it looks white: one droplet, peripheral nucleus; brown: many droplets, central nucleus Function fat storage, insulation, heat (brown), leptin

Undifferentiated mesenchymal cell Origin / resident or wandering mesenchyme; resident How it looks small, stellate, near vessels (pericytes) Function stem cell for new CT cells in adults

Plasma cell Origin / resident or wandering B lymphocyte; wandering How it looks oval, eccentric nucleus with clock-face chromatin, basophilic cytoplasm, pale Golgi halo Function secretes antibodies Note Russell bodies = stored immunoglobulin.

Reticular cell Origin / resident or wandering specialised fibroblast; resident How it looks stellate, processes along fibres Function makes reticular (type III) fibres of lymphoid organs, marrow

Pigment cell (melanocyte) Origin / resident or wandering neural crest; resident How it looks branched, brown-black melanin granules Function melanin from tyrosine by tyrosinase; skin, choroid of eye

Lymphocyte Origin / resident or wandering blood; wandering How it looks small, round dark nucleus, thin rim of cytoplasm Function immune responses

Neutrophil Origin / resident or wandering blood; wandering How it looks multilobed nucleus, faint granules Function phagocytosis of bacteria (acute inflammation)

Eosinophil Origin / resident or wandering blood; wandering How it looks bilobed nucleus, large orange-red granules Function parasites, allergy

Basophil Origin / resident or wandering blood; wandering How it looks lobed nucleus hidden by large dark blue granules Function histamine release, like mast cell

Monocyte Origin / resident or wandering blood; wandering How it looks large, kidney-shaped nucleus, grey-blue cytoplasm Function becomes macrophage in tissue

CELLS Fibres of the extracellular matrix

Collagen Made of type I collagen (tropocollagen triple helix) Light / EM look thick, unbranched, wavy bundles; EM: fibrils with 64-67 nm banding Stain eosin pink; blue with Mallory/trichrome Property / where great tensile strength, little stretch; tendon, dermis, bone

Reticular Made of type III collagen, heavily glycosylated Light / EM look thin, branched delicate network Stain silver (black, argyrophilic), PAS+ Property / where supporting stroma of lymph nodes, spleen, marrow, liver, basement membranes

Elastic Made of elastin core + fibrillin microfibrils Light / EM look thin, straight, branching, form networks or fenestrated sheets Stain orcein, resorcin-fuchsin, Verhoeff Property / where stretch and recoil; arteries, lung, elastic ligaments Note Fibrillin defect = Marfan syndrome.

MATRIX Collagen types (main ones)

I Form thick fibrils, fibres Where skin (dermis), bone, tendon, ligaments, dentin, fibrocartilage Note ~90% of body collagen.

II Form thin fibrils Where hyaline and elastic cartilage, vitreous body

MATRIX Collagen types (main ones) (cont.)

III Form reticular fibres Where skin, lung, blood vessels, lymphoid organs, smooth muscle

IV Form sheet-like network Where basal lamina

V Form fibril-forming, with type I Where with type I; placenta

VI Form beaded microfibrils Where muscle and most interstitial tissue

VII Form anchoring fibrils Where dermal-epidermal junction; binds basal lamina to dermal collagen

IX, XI Form fibril-associated / fibril-forming with II Where cartilage, with type II

X Form network Where hypertrophic cartilage of growth plate

XII, XIV Form fibril-associated Where with type I

XVII Form transmembrane Where hemidesmosomes of skin epithelium

MATRIX Components of ground substance

Glycosaminoglycans (GAGs) Nature long unbranched polysaccharides of repeating disaccharides, strongly negative, bind water Examples / role hyaluronan (not sulfated, no core protein), chondroitin, dermatan, heparan, keratan sulfate

Proteoglycans Nature core protein + sulfated GAGs Examples / role aggrecan (cartilage), decorin, syndecan, perlecan; give gel and turgor

Multiadhesive glycoproteins Nature proteins with binding sites for cells (integrins) and matrix Examples / role fibronectin, laminin; anchor cells to matrix

Tissue fluid Nature plasma-like filtrate with fewer proteins Examples / role carries nutrients and wastes; excess = oedema

TYPES Classification of connective tissues

Embryonic CT Ground substance viscous gel, few fibres Members mesenchyme; mucous (gelatinous) tissue

Connective tissue proper Ground substance semi-liquid gel Members loose (areolar); dense regular; dense irregular Note Slide 5 puts adipose and reticular in loose CT and elastic in dense; slide 36 lists them separately; Junqueira treats adipose and reticular as specialised CT.

Specialised: adipose, reticular, elastic Ground substance gel Members white (unilocular) and brown (multilocular) fat; reticular tissue; elastic tissue

Cartilage Ground substance firm, rubbery Members hyaline, elastic, fibrocartilage

Bone Ground substance calcified, very hard Members woven (immature), lamellar (mature): compact and spongy

Blood and lymph Ground substance liquid (plasma) Members blood cells and platelets in plasma

TYPES Types of connective tissue proper and related tissues

Mesenchyme Structure stellate cells joined by processes, abundant ground substance, almost no fibres Where embryo Function gives rise to all CT

Mucous (gelatinous) tissue Structure fibroblasts in hyaluronan-rich jelly, sparse type I and III fibres Where umbilical cord (Wharton's jelly), pulp of young teeth Function cushions cord vessels Note Slide 36 splits immature and mature gelatinous tissue.

Loose (areolar) Structure many cells of all types, much ground substance, thin collagen + elastic fibres in all directions Where lamina propria, papillary dermis, hypodermis, around vessels, mesentery Function binding, diffusion, defence, oedema site

Dense irregular Structure thick collagen bundles interwoven in many planes, few fibroblasts Where reticular dermis, organ capsules, submucosa of gut Function resists stretch from many directions

Dense regular Structure parallel collagen bundles with rows of flattened fibroblast (tenocyte) nuclei Where tendons, ligaments, aponeuroses, cornea stroma Function resists pull in one direction

Elastic tissue Structure thick parallel elastic fibres with some collagen Where ligamenta flava, suspensory ligament of penis, wall of large arteries Function stretch and recoil

Reticular tissue Structure reticular cells and type III fibre meshwork; free cells in spaces Where lymph nodes, spleen, bone marrow, liver sinusoids Function supporting stroma for free cells

White adipose Structure unilocular cells in lobules separated by CT septa, rich capillaries Where subcutaneous, visceral (omentum, mesentery), buttocks, thighs, breast Function energy store, insulation, padding, endocrine

Brown adipose Structure multilocular cells, very vascular, sympathetic nerves Where newborn: interscapular, neck; adult: supraclavicular, paravertebral, mediastinal, para-aortic, suprarenal Function non-shivering heat

TYPES White vs brown adipose tissue

Lipid droplets White (yellow, unilocular) one large droplet fills the cell Brown (multilocular) many small droplets

Nucleus White (yellow, unilocular) flattened, peripheral (signet ring) Brown (multilocular) round, central

Cell size White (yellow, unilocular) large, 50-150 µm Brown (multilocular) smaller, polygonal

Mitochondria White (yellow, unilocular) few Brown (multilocular) very many, with UCP1 (thermogenin)

Colour cause White (yellow, unilocular) yellow from dietary carotenoids Brown (multilocular) brown from cytochromes of mitochondria and rich blood supply

Function White (yellow, unilocular) energy store, insulation, padding, leptin secretion Brown (multilocular) heat production (uncoupled oxidation)

Nerve control White (yellow, unilocular) sympathetic: noradrenaline triggers lipolysis Brown (multilocular) sympathetic: noradrenaline activates UCP1 heat production

Distribution White (yellow, unilocular) most fat in adults: subcutaneous, visceral; in newborns too (e.g. buttocks) Brown (multilocular) newborns (~2-5% of body weight); adults: supraclavicular, paravertebral, mediastinal

H&E look White (yellow, unilocular) empty polygonal spaces with thin pink rims Brown (multilocular) pale, foamy (vacuolated) cytoplasm, many capillaries

METHOD Stains and how CT elements look

Collagen fibres Method H&E Result pink (eosinophilic)

Reticular fibres Method silver impregnation; PAS Result black; magenta

Elastic fibres Method orcein, resorcin-fuchsin, Verhoeff Result brown-red; dark purple; black

Mast cell granules Method toluidine blue Result purple-red (metachromasia, from heparin)

Fat Method frozen section + Sudan or osmium tetroxide Result orange-red or black droplets

Ground substance Method PAS / alcian blue (lost in routine paraffin) Result pink-magenta / blue

Mnemonics

Mnemonic Type 1: bONE; Type 2: carTWOlage; Type 3: reTHREEcular (reticular fibres, vessels); Type 4: floor (basement membrane) = Main collagen types and where they are

Must-knows

Three cartilage types — Hyaline, elastic and fibrocartilage; told apart by the kind and amount of fibres in the matrix. Hyaline is the commonest and forms most of the fetal skeleton.

Cartilage is avascular — No vessels, nerves or lymphatics; chondrocytes are fed by diffusion from perichondrial capillaries (or synovial fluid). Low metabolic rate, so it heals poorly.

Perichondrium — Dense connective tissue sheath: outer fibrous layer (collagen I, fibroblasts), inner chondrogenic layer (chondroblast precursors). Absent from articular cartilage and fibrocartilage.

Chondrocytes and isogenous groups — Chondroblasts trapped in matrix become chondrocytes, one per lacuna; mitosis yields isogenous groups. Superficial cells flattened parallel to the surface, deep cells larger and rounder.

Hyaline matrix zones — Capsular (pericellular) matrix richest in sulfated GAGs and most basophilic; territorial matrix around each group; interterritorial matrix between groups stains paler.

Cartilage growth — Interstitial: mitosis of chondrocytes inside the matrix (young cartilage, epiphyseal plates). Appositional: chondroblasts from the inner perichondrium add matrix on the surface.

Bone = cells + mineralised matrix — Cells: osteoprogenitors, osteoblasts, osteocytes, osteoclasts. Matrix: type I collagen (organic) with hydroxyapatite $Ca_{10}(PO_4)_6(OH)_2$ laid along and between the fibrils.

Osteoblast lineage — Osteoprogenitor -> osteoblast (secretes osteoid toward the bone surface) -> osteocyte in a lacuna, or flattened bone lining cell.

Osteocyte network — One osteocyte per lacuna; processes in canaliculi joined by gap junctions pass nutrients and signals; fluid flow in the lacunocanalicular system lets them sense load.

Osteoclast — Huge (up to ~100 um), up to ~50 nuclei, acidophilic; fused monocyte-macrophage cells. Resorbs bone in Howship lacunae via a ruffled border sealed off by a clear zone.

Woven vs lamellar bone — Woven (primary): irregular collagen, many osteocytes, less mineral; first in development and repair, persists at sutures, tooth sockets, tendon insertions. Lamellar (secondary) forms adult compact and spongy bone.

Osteon (Haversian system) — Structural unit of compact bone: 4-20 concentric lamellae around a central canal, bounded by a cement line; collagen changes direction in neighbouring lamellae. Volkmann canals link central canals crosswise.

Periosteum and endosteum — Periosteum: outer fibrous + inner osteogenic layer, anchored by Sharpey fibres, absent at articular surfaces. Endosteum: thin single cell layer lining marrow cavity, trabeculae and canals.

Bone biomechanics — Collagen gives tensile strength and flexibility, mineral gives hardness and stiffness. Shaft is stiffest along its long axis; trabeculae follow lines of stress.

TYPES Cartilage types

Hyaline | Matrix fibres fine type II collagen fibrils, masked by ground substance | Perichondrium yes (not on articular surfaces) | Where articular surfaces, costal, nasal, larynx (thyroid, cricoid, most of arytenoid), trachea, bronchi, epiphyseal plates, fetal skeleton | Key features glassy, homogeneous, basophilic; isogenous groups; calcifies with age | Note (slide 9 says 'bundles' of type II collagen; Junqueira: fine fibrils, not bundles)

Elastic | Matrix fibres dense elastic fibre network + type II collagen | Perichondrium yes | Where auricle, wall of external acoustic meatus, auditory tube, epiglottis, corniculate and cuneiform cartilages, vocal process of arytenoid | Key features yellowish fresh; flexible support; elastic fibres shown by orcein (brown) or resorcin-fuchsin; does not calcify

Fibrocartilage | Matrix fibres thick type I collagen bundles + some type II | Perichondrium no | Where intervertebral disc (anulus fibrosus), pubic symphysis, menisci, articular discs (temporomandibular, sternoclavicular), some tendon and ligament insertions | Key features small chondrocytes single or in rows between bundles; mostly acidophilic; withstands compression and tension

CELLS Cartilage cells and matrix regions

Perichondrium, fibrous layer | Description outer dense connective tissue, type I collagen, fibroblasts | Note carries the capillaries that feed the cartilage

Perichondrium, chondrogenic layer | Description inner cellular layer of chondroprogenitor cells | Note source of appositional growth

Chondroblast | Description matrix-secreting cell at the surface, not yet in a lacuna | Note becomes a chondrocyte once enclosed

Chondrocyte | Description cell in a lacuna; flattened superficially, large and round deep | Note shrinks from the lacunar wall in paraffin sections

Isogenous group | Description cluster of chondrocytes from one parent cell | Note sign of interstitial growth

Chondron | Description chondrocyte or isogenous group + its pericellular matrix | Note functional unit

Capsular (pericellular) matrix | Description thin rim lining each lacuna; richest in sulfated GAGs; type VI collagen | Note stains most intensely

Territorial matrix | Description basophilic matrix around each isogenous group | Note high sulfated GAG content

Interterritorial matrix | Description matrix between groups; fewer proteoglycans, type II collagen | Note stains paler | Note (slide 10 says type III collagen; Junqueira: type II)

MATRIX Hyaline matrix molecules

Type II collagen | Role fine fibrils, ~40% of dry weight; resist tension

Aggrecan | Role proteoglycan with chondroitin and keratan sulfate; binds water, resists compression; makes matrix basophilic

Hyaluronan | Role long GAG backbone; aggrecan attached by link proteins into huge aggregates

Chondronectin | Role adhesive glycoprotein binding cells to collagen and GAGs

Water | Role 60-80% of fresh weight; diffusion route and shock absorption

MATRIX Hyaline matrix molecules (cont.)

Minor collagens (VI, IX, X, XI) — Role: VI pericellular; IX and XI regulate fibrils; X in hypertrophic zone

CELLS Bone cells

Osteoprogenitor cell — Origin: mesenchymal stem cells. Look: flattened, spindle-shaped, pale oval nucleus, scant cytoplasm. Where: inner periosteum, endosteum. Function: divides; differentiates into osteoblasts

Osteoblast — Origin: osteoprogenitor cell. Look: cuboidal to columnar, basophilic (much RER), in a single layer. Where: bone surfaces where bone forms. Function: secretes osteoid (type I collagen, proteoglycans, osteocalcin) toward the bone; starts mineralisation (alkaline phosphatase, matrix vesicles)

Osteocyte — Origin: osteoblast enclosed in matrix. Look: less RER, smaller Golgi, condensed chromatin; many processes. Where: one per lacuna; processes in canaliculi. Function: maintains matrix; senses load; gap junctions with neighbours. Note: (slide 38 is titled 'Osteoclast' but shows an osteocyte in its lacuna)

Bone lining cell — Origin: inactive osteoblast. Look: flat, thin. Where: quiescent bone surfaces (part of endosteum). Function: maintains surface; can reactivate

Osteoclast — Origin: fusion of monocyte-macrophage precursors (haematopoietic). Look: giant (up to ~100 um), up to ~50 nuclei, acidophilic. Where: Howship lacunae on bone surfaces. Function: resorbs bone: H+ pumps dissolve mineral, cathepsin K and MMPs digest collagen

MATRIX Bone matrix composition

Organic (osteoid) — Components: ~90% type I collagen; proteoglycans; glycoproteins osteocalcin, osteonectin, osteopontin, bone sialoprotein. Gives bone: tensile strength, flexibility

Inorganic — Components: hydroxyapatite $Ca_{10}(PO_4)_6(OH)_2$ along and between collagen fibrils; also carbonate, citrate, Mg, Na, K. Gives bone: hardness, stiffness. Note: (slide 31 gives inorganic 67%, Ca 39%, phosphate 17%, carbonate 9.8%; Junqueira: inorganic ~50% of dry matrix weight)

Hydration shell — Components: water and ions around the crystals. Gives bone: ion exchange with body fluids

TYPES Bone tissue types

Woven (primary) — Structure: irregular collagen, many osteocytes, lower mineral (less dense on X-ray). Where: embryo, fracture repair; adult sutures, tooth sockets, tendon insertions

Lamellar (secondary) — Structure: collagen in parallel sheets (lamellae, 3-7 um). Where: all adult compact and spongy bone

Compact (cortical) — Structure: dense, osteons + circumferential and interstitial lamellae. Where: shafts of long bones, outer and inner tables of flat bones

Spongy (cancellous) — Structure: network of trabeculae with marrow spaces; usually no osteons; fed from marrow. Where: epiphyses, metaphyses, diploe, vertebral bodies

MORE Structures of compact bone

Osteon (Haversian system) — Description: 4-20 concentric lamellae around a central canal, parallel to the long axis

Concentric lamellae — Description: collagen parallel within a lamella, at a different angle in the next

Central (Haversian) canal — Description: lengthwise canal with vessels, nerves, loose connective tissue; lined by endosteum

Perforating (Volkmann) canal — Description: crosswise canal joining central canals and the surfaces; not ringed by lamellae

Lacunae — Description: spaces holding osteocytes; in compact and spongy bone

Canaliculi — Description: fine channels running radially between lacunae and to the central canal

Cement line — Description: outer boundary of each osteon; mineralised matrix with few collagen fibres

Interstitial lamellae — Description: angular remnants of older osteons partly resorbed in remodelling

Outer circumferential lamellae — Description: around the whole shaft, deep to the periosteum

Inner circumferential lamellae — Description: around the shaft at the endosteal surface, facing the medullary cavity

MORE Coverings and marrow

Periosteum, fibrous layer — Make-up: outer dense connective tissue, type I collagen, fibroblasts. Note: covers bone except articular surfaces

Periosteum, osteogenic layer — Make-up: inner cellular layer, osteoprogenitor cells. Note: bone growth in width and fracture repair

Sharpey (perforating) fibres — Make-up: type I collagen bundles from periosteum into outer circumferential lamellae. Note: anchor periosteum, tendons, ligaments

Endosteum — Make-up: thin, mostly one layer of osteoprogenitor and lining cells. Note: lines marrow cavity, trabeculae, central and perforating canals

Red marrow — Make-up: haematopoietic cells on a stroma of reticular cells and fibres. Note: high activity; spongy bone of flat bones, vertebrae, epiphyses

Yellow marrow — Make-up: mostly adipocytes. Note: low activity; adult diaphyses; can revert to red marrow

MORE Bones by shape and parts of a long bone

Long bone — Meaning: longer in one dimension; shaft and two ends. Example or note: tibia, femur, metacarpals

Short bone — Meaning: length about equal to width. Example or note: carpals, tarsals

Flat bone — Meaning: thin plate: two compact tables + diploe. Example or note: skull vault, sternum, scapula

Irregular bone — Meaning: complex shape. Example or note: vertebrae

Pneumatic bone — Meaning: contains air sinuses. Example or note: maxilla, frontal, sphenoid, ethmoid. Note: (slide 40 lists 'sinuses' among irregular bones)

Sesamoid bone — Meaning: develops in a tendon. Example or note: patella

Epiphysis — Meaning: end of a long bone; spongy bone with red marrow, thin compact shell. Example or note: covered by articular hyaline cartilage

Metaphysis — Meaning: flared zone between diaphysis and epiphysis, next to the growth plate. Example or note: mostly spongy bone

Diaphysis — Meaning: shaft: thick compact bone around the medullary cavity. Example or note: nutrient artery enters via nutrient foramen

Epiphyseal plate / line — Meaning: hyaline growth cartilage; replaced by a line of bone after closure. Example or note: site of lengthwise growth

Mnemonics

Mnemonic — Osteoblasts Build, osteoClasts Chew (Carve) = blasts form bone, clasts resorb it

Must-knows

Blood is a connective tissue — Cells (formed elements) suspended in a fluid matrix, plasma. Its fibres, fibrin threads, appear only when blood clots. pH 7.35–7.45; about 38 °C.

Volume — About 5 L in an adult (men 5–6 L, women 4–5 L), roughly 7–8% of body weight.

Centrifuged blood — Plasma ~55%, packed erythrocytes ~45% (haematocrit), buffy coat <1% (leukocytes + platelets) between them.

Erythrocyte — Biconcave disc ~7.5 µm, no nucleus or organelles; ~97% of dry content haemoglobin, plus carbonic anhydrase. ATP from anaerobic glycolysis, so it uses none of the O2 it carries. Lives ~120 days.

Haemoglobin — HbA = 2 α + 2 β globin chains, each with a haem whose Fe2+ binds one O2: up to 4 O2 per molecule, reversibly.

Reticulocyte — Newest red cell, ~1% of circulating RBCs, slightly larger, keeps residual ribosomes (shown by brilliant cresyl blue). A raised count means faster marrow output.

Neutrophil — Commonest leukocyte (50–70%), 12–15 µm, 3–5 nuclear lobes; pale specific granules + azurophilic granules. Phagocytoses bacteria; blood half-life ~6–7 h, 1–4 days in tissue, then apoptosis.

Eosinophil and basophil — Eosinophil: bilobed nucleus, orange-red granules; fights helminths, phagocytoses antigen-antibody complexes, falls with corticosteroids. Basophil: rarest (<1%), dark granules with heparin + histamine, mast-cell-like.

Monocyte — Largest leukocyte (12–20 µm), indented/kidney-shaped nucleus, grey-blue cytoplasm. Leaves blood after 1–3 days and becomes a macrophage (mononuclear phagocyte system, incl. osteoclasts); does not return.

Lymphocytes — Small 6–8 µm, round dark nucleus, thin blue rim. B cells mature in marrow → plasma cells (humoral immunity); T cells mature in thymus (cellular immunity, most blood lymphocytes); NK cells kill infected/tumour cells without prior sensitisation.

Platelets — Anucleate fragments of megakaryocyte cytoplasm, 2–4 µm, 150 000–400 000/µL, ~10 days. Peripheral hyalomere (marginal microtubule bundle) + central granulomere (granules, mitochondria, glycogen).

Diapedesis — Leukocytes leave postcapillary venules by squeezing between endothelial cells (selectin rolling → integrin adhesion → transmigration); they use blood only for transport.

Haemopoietic hierarchy — Pluripotent stem cell → common myeloid progenitor (erythrocytes, platelets, granulocytes, monocytes, mast cells) or common lymphoid progenitor (B, T, NK). Red marrow is the adult site.

Growth factors — Erythropoietin (kidney) drives erythropoiesis; thrombopoietin (liver) megakaryocytes; G-CSF, GM-CSF, M-CSF and interleukins drive the white series. Erythrocyte maturation ~1 week; granulocyte ~11 days.

MORE Composition of blood

Plasma — Amount ~55% of blood volume — Note water ~92%, proteins ~7%, other solutes ~1% (by weight)

Erythrocytes (haematocrit) — Amount ~45% of volume; ~4–6 million/µL — Note women ~3.9–5.5, men ~4.1–6.0 million/µL

Buffy coat — Amount <1% of volume — Note leukocytes + platelets

Leukocytes — Amount 4 500–11 000/µL — Note granulocytes (neutrophil, eosinophil, basophil) and agranulocytes (lymphocyte, monocyte)

Platelets — Amount 150 000–400 000/µL — Note fragments, not cells

Serum — Amount plasma minus clotting factors — Note fluid left after a clot forms

MORE Plasma proteins

Albumin (most abundant) — Made by liver — Function main source of colloid osmotic (oncotic) pressure; carrier of hormones, drugs, fatty acids

α and β globulins — Made by liver — Function carriers of iron (transferrin), haemoglobin (haptoglobin), lipids; add to oncotic pressure

γ globulins (immunoglobulins) — Made by plasma cells — Function antibodies; the one major plasma protein not made by liver

Fibrinogen (smallest share of the main groups, ~4–7%) — Made by liver — Function converted to fibrin threads of the clot

Prothrombin and other clotting factors — Made by liver — Function coagulation cascade (thrombin forms fibrin)

Lipoproteins — Made by liver — Function transport of triglycerides and cholesterol

Complement proteins — Made by liver — Function innate defence, inflammation, lysis of microbes

CELLS Leukocytes

Neutrophil (granulocyte) — Diameter 12–15 µm — % of leukocytes 50–70% — Nucleus 3–5 lobes; drumstick (Barr body) in women; band = unsegmented young form — Cytoplasm / granules pale lilac-pink specific granules (lysozyme, lactoferrin, collagenase, alkaline phosphatase) + azurophilic lysosomes — Life blood ~6–7 h, tissue 1–4 days — Main role phagocytosis of bacteria; H2O2 and other oxidants — Note slide 21 gives 60–79% and slide 23 1–5 lobes

Eosinophil (granulocyte) — Diameter 12–15 µm — % of leukocytes 1–4% — Nucleus bilobed — Cytoplasm / granules large orange-red specific granules with crystalloid core (major basic protein, eosinophil peroxidase, histaminase) — Life 1–2 weeks — Main role kills helminths; phagocytoses antigen-antibody complexes; rises in allergy, falls with corticosteroids

Basophil (granulocyte) — Diameter 12–15 µm — % of leukocytes 0.5–1% (rarest) — Nucleus bi- or irregularly lobed, hidden by granules — Cytoplasm / granules coarse dark blue-purple granules: heparin, histamine, leukotrienes (SRS-A) — Life several months — Main role vasodilation and allergy (IgE receptors); supplements mast cells — Note slide 31 says heparan sulfate; Junqueira gives heparin

Lymphocyte (agranulocyte) — Diameter small 6–8 µm, large up to 18 µm — % of leukocytes 20–30% — Nucleus round, dense, heterochromatic, nearly fills cell — Cytoplasm / granules thin rim of pale blue cytoplasm (free ribosomes), few azurophilic granules — Life days to years — Main role specific immunity

Monocyte (agranulocyte) — Diameter 12–20 µm (largest) — % of leukocytes 3–8% — Nucleus oval, indented or kidney-shaped, eccentric, finer paler chromatin — Cytoplasm / granules grey-blue, fine azurophilic granules (lysosomes), often vacuolated — Life blood 1–3 days, then months as macrophage — Main role becomes macrophage; removes debris and microbes with lysosomal enzymes; antigen presentation — Note slide 35 gives 12–100 h in blood

— B lymphocyte — Diameter small — % of leukocytes ~15–20% of lymphocytes — Nucleus as lymphocyte — Cytoplasm / granules surface immunoglobulin — Life memory cells years — Main role matures in marrow; becomes antibody-secreting plasma cell (humoral immunity)

— T lymphocyte — Diameter small — % of leukocytes ~75–80% of lymphocytes (most) — Nucleus as lymphocyte — Cytoplasm / granules T-cell receptor — Life memory cells years — Main role matures in thymus; helper (CD4), cytotoxic (CD8), regulatory (slide 41: 'suppressor') and memory cells; cell-mediated immunity

— NK cell — Diameter larger — % of leukocytes ~5–10% of lymphocytes — Nucleus as lymphocyte — Cytoplasm / granules large granular lymphocyte (perforin, granzymes) — Life — — Main role kills virus-infected and tumour cells without prior sensitisation

CELLS Erythrocyte membrane skeleton (cont.)

Spectrin Position / link network on cytoplasmic (inner) face of membrane Role flexibility and biconcave shape; lets cell deform through capillaries

Actin (short filaments) + tropomyosin Position / link junctional complexes joining spectrin tetramers Role nodes of the network

Ankyrin Position / link binds spectrin to band 3 Role anchors network to membrane

Band 3 Position / link transmembrane protein Role Cl−/HCO3− exchanger; ankyrin anchor

Protein 4.1 Position / link binds spectrin–actin junctions to glycophorin C Role second anchor

Protein 4.2 Position / link with ankyrin at band 3 Role stabilises the ankyrin link

Glycophorins Position / link transmembrane glycoproteins Role carry sialic acid (negative surface charge); glycophorin C anchors protein 4.1

Defects (spectrin, ankyrin) Position / link — Role hereditary spherocytosis: spherical, fragile cells removed by spleen

CELLS Platelet zones and granules

Hyalomere (peripheral, pale blue) Contents marginal bundle of microtubules, actin, myosin Role keeps disc shape; contraction for clot retraction

Granulomere (central, purple) Contents α, δ, λ granules, mitochondria, glycogen Role secretion and energy

α granules (largest, most numerous) Contents fibrinogen, PDGF, platelet factor 4, von Willebrand factor, other clotting factors Role clotting, vessel repair

δ (dense) granules Contents serotonin, ADP, ATP, Ca2+ Role vasoconstriction, platelet recruitment

λ granules Contents lysosomal enzymes Role clot removal

Open canalicular system Contents invaginations of plasma membrane Role rapid release of granule contents

Dense tubular system Contents smooth ER remnant Role stores Ca2+

Glycocalyx (surface coat) Contents glycoproteins, receptors (e.g. GPIb for vWF) Role adhesion to exposed collagen

CELLS Haemostasis by platelets (in order)

1 Primary aggregation What happens platelets adhere to exposed collagen (via vWF) and form a plug

2 Secondary aggregation What happens released adhesive glycoproteins and ADP recruit more platelets; plug enlarges

3 Coagulation What happens clotting cascade: prothrombin → thrombin; fibrinogen → fibrin mesh trapping cells Note slide 47 ties coagulation to fibrinogen + vWF; vWF acts mainly in adhesion

4 Clot retraction What happens platelet actin and myosin contract; clot shrinks

5 Clot removal What happens plasminogen → plasmin (activators from endothelium) digests fibrin

MORE Bone marrow

Red marrow Feature haemopoietic; all marrow at birth; in adults in flat bones (skull, ribs, sternum, pelvis), vertebrae and proximal epiphyses of femur and humerus

Yellow marrow Feature mostly adipocytes; replaces red marrow with age; reverts to red after severe bleeding or hypoxia

Stroma Feature reticular cells + reticular fibres (type III collagen), macrophages

Parenchyma Feature haemopoietic cords between sinusoids

Sinusoids Feature discontinuous endothelium; new cells cross the wall to enter blood Note slide 53 says continuous endothelium; Junqueira: discontinuous

Matrix Feature collagen I and III, fibronectin, laminin, proteoglycans; hemonectin binds blood cells to matrix

Functions Feature blood cell production; destruction of old RBCs; iron storage in macrophages (haemoglobin breakdown)

Megakaryocyte position Feature lies on sinusoid wall, pushes proplatelets into lumen

Section look Feature empty round spaces = adipocytes (fat dissolved); islands of haemopoietic cells; giant megakaryocytes

Prenatal sites Feature yolk sac → liver (+ spleen) → bone marrow

MORE Haemopoietic lineages

Erythropoiesis Progenitor common myeloid → MEP (CFU-E) Stages proerythroblast → basophilic → polychromatophilic → orthochromatophilic erythroblast → reticulocyte Product erythrocyte

Granulopoiesis Progenitor common myeloid → GMP (CFU-G) Stages myeloblast → promyelocyte → myelocyte → metamyelocyte → band → segmented Product neutrophil, eosinophil, basophil

Monocytopoiesis Progenitor common myeloid → GMP (CFU-M) Stages monoblast → promonocyte → monocyte Product monocyte → macrophage, osteoclast, myeloid dendritic cell Note slide 61 derives monocytes from the myeloblast; textbooks: monoblast

Thrombopoiesis Progenitor common myeloid → MEP (CFU-Meg) Stages megakaryoblast → promegakaryocyte → megakaryocyte (endomitosis, polyploid) Product platelets (cytoplasm fragments)

Mast cell line Progenitor common myeloid Stages precursors leave marrow, mature in connective tissue Product mast cell

Lymphopoiesis Progenitor common lymphoid Stages lymphoblast → prolymphocyte → lymphocyte; T precursors mature in thymus Product B, T, NK cells; B → plasma cell Note slide 56 lists the blasts as 'stem cells'; they are committed precursors

CELLS Maturation stages: red and granulocyte series

Proerythroblast Nucleus large, nucleoli, fine chromatin Cytoplasm basophilic (ribosomes)

Basophilic erythroblast Nucleus smaller, condensing Cytoplasm strongly basophilic

Polychromatophilic erythroblast Nucleus condensed, checkerboard Cytoplasm grey-lilac (Hb + ribosomes)

Orthochromatophilic erythroblast (normoblast) Nucleus small, pyknotic; extruded at this stage Cytoplasm pink (Hb)

Reticulocyte Nucleus none Cytoplasm pink, residual ribosomes; ~1 day more in marrow/blood

Myeloblast Nucleus large, nucleoli Cytoplasm basophilic, no granules

Promyelocyte Nucleus round, nucleoli Cytoplasm azurophilic (primary) granules appear

Myelocyte Nucleus round to slightly flattened Cytoplasm specific granules appear; lineage (N, E, B) now recognisable; last stage that divides

Metamyelocyte Nucleus kidney-shaped indentation Cytoplasm specific granules

Band (stab) cell Nucleus curved, unsegmented band Cytoplasm specific granules; up to a few % in blood

Segmented granulocyte Nucleus lobed Cytoplasm mature

Mnemonics

Mnemonic Never Let Monkeys Eat Bananas = Leukocytes from commonest to rarest: neutrophil, lymphocyte, monocyte, eosinophil, basophil

Mnemonic 60, 30, 6, 3, 1 = Approximate differential count (%) in the same order