Histology Exam 1 · Lectures 1–7

All cheat sheets

Cheat sheet: your lecture slides, checked against Junqueira. Histology Exam 1 · PDF of all lectures

Histology Exam 1 · Lecture 1

Microscopy

1 High-yield facts

Resolution
Smallest distance at which two points are still seen as separate; d = 0.61λ / NA. Shorter wavelength or higher NA gives finer resolution.

Limits
Eye ~0.2 mm; light microscope ~0.2 µm; TEM ~1–3 nm in tissue sections (theoretical far less).

Magnification
Total = objective × eyepiece (40× × 10× = 400×). Magnifying past the resolution limit is empty magnification: no new detail.

Immersion oil
Oil (n ≈ 1.515, like glass) between coverslip and 100× objective raises NA to ~1.4, so resolution improves.

Worked example
Green light λ 550 nm, NA 1.4: d = 0.61 × 550 / 1.4 ≈ 240 nm = 0.24 µm.

Units
1 mm = 1000 µm; 1 µm = 1000 nm. RBC ~7.5 µm; ribosome ~25 nm (TEM only).

Bright-field parts
Light source, condenser (with diaphragm), stage, objective, eyepiece; image from light absorbed by stained tissue.

Working routine
Find and focus with the low-power objective first; bring a high-power lens to the coverslip watching from the side, then focus by moving it away.

Electron microscopy
Electrons have a far shorter wavelength than light; lenses are electromagnetic coils; vacuum column; image seen on a screen or camera.

TEM contrast
Heavy metals (osmium, uranium, lead) scatter electrons: bound areas look dark (electron-dense), others pale (electron-lucent).

Fluorescence
Fluorochrome absorbs short-wavelength light and emits longer-wavelength light (Stokes shift); fluorescein green, rhodamine red, DAPI blue.

Modern solutions
Confocal and multiphoton optical sectioning, super-resolution (Nobel 2014), cryo-EM (Nobel 2017), digital whole-slide imaging.

Basophilia and acidophilia
Basic dyes (haematoxylin) bind acidic groups, e.g. nucleic acid phosphates; acidic dyes (eosin) bind basic proteins of cytoplasm and collagen.

2 Cheat sheet

Basic shows the must-knows, Intermediate everything on your slides, Advanced adds textbook detail (marked +).

Light microscopes

TYPE	PRINCIPLE	BEST FOR
Bright-field	transmitted light absorbed by stained section	routine stained (H&E) sections
Phase contrast	converts differences in refractive index into light and dark	living, unstained cells (cell culture)
Dark-field	only light scattered by the specimen enters the objective	bright objects on black: spirochaetes, crystals
Polarising	polariser + analyser; birefringent structures shine	collagen, skeletal muscle A band, crystals, amyloid (Congo red)
Fluorescence	UV/blue excitation; longer-wavelength emission seen	fluorochrome-labelled antibodies, DNA dyes
Confocal (laser scanning)	pinhole rejects out-of-focus light; point scanning	optical sections and 3D reconstruction of thick tissue

Electron microscopes

TYPE	IMAGE FORMED FROM	SPECIMEN	SHOWS
Transmission (TEM)	electrons passing through the section	ultrathin section 40–90 nm, heavy-metal stained	ultrastructure: organelles, ribosomes, membranes
Scanning (SEM)	secondary electrons from the surface	whole specimen coated with gold/metal	3D surface of cells and tissues
Freeze-fracture	metal replica of fractured frozen tissue	cleaved along lipid bilayer	inner membrane faces (P and E), intramembrane proteins
Cryo-EM	electrons through frozen sample	molecules in vitreous ice, unstained	near-atomic protein structure (Nobel 2017)

Resolution: what decides it

FACTOR	EFFECT	NOTE
Wavelength (λ)	shorter λ gives finer d	blue/UV better than red; electrons best
Numerical aperture (NA = n sin α)	higher NA gives finer d	dry objective ≤0.95; oil ~1.4
Refractive index (n) of medium	oil raises n	air 1.0, water 1.33, oil 1.515
Magnification	does not change d	beyond ~1000× NA is empty magnification

Scale: what each instrument can see

OBJECT	SIZE	SEEN WITH
Red blood cell	~7.5 µm	LM
Bacterium	~1–2 µm	LM
Mitochondrion	~0.5–1 µm wide	LM (barely, special stains); detail by TEM
Cell membrane	~7.5–10 nm	TEM
Ribosome	~25 nm	TEM

Modern and super-resolution methods

METHOD	HOW IT BEATS THE LIMIT OR ADDS	RESOLUTION / USE
Super-resolution in general	breaks the 0.2 µm diffraction limit	Nobel Prize Chemistry 2014 (Betzig, Hell, Moerner)
Whole-slide scanning (digital pathology)	entire slide digitised at high power	virtual microscopy, telepathology, AI analysis
Cryo-EM	frozen-hydrated molecules, image averaging	near-atomic structure; Nobel 2017 (Dubochet, Frank, Henderson)

Common fluorochromes

LABEL	BINDS / USED FOR	EMISSION COLOUR
Fluorescein (FITC)	conjugated to antibodies	green
Rhodamine / Texas red	conjugated to antibodies	red
DAPI / Hoechst	DNA (nuclei)	blue

Other imaging and labelling techniques

TECHNIQUE	PRINCIPLE	SHOWS
Autoradiography	radioactive precursor (e.g. ^{3}H-thymidine) incorporated; emulsion develops silver grains	where and when molecules are synthesised
Immunohistochemistry (indirect)	unlabelled primary, then labelled secondary antibody against it	same, with signal amplification

3 Traps: the correct facts for common wrong answers

✓ A 10 µm structure that appears 5 mm long in a photomicrograph is magnified about ×500.

✓ A 40x objective with a 10x eyepiece gives 400x total magnification.

✓ A basophilic component stains with haematoxylin because it is rich in acidic groups, such as nucleic acid phosphates.

✓ A cell 25 µm across measures 0.025 mm.

✓ A confocal microscope uses a pinhole to reject light from outside the focal plane.

✓ A fluorochrome emits light of a longer wavelength than the light that excites it.

✓ A new slide is first found and focused with a low-power objective.

✓ Autoradiography shows, by silver grains, where a radioactive precursor was taken up.

✓ By $d = 0.61\lambda / NA$, light-microscope resolution depends on the wavelength of the light and the numerical aperture.

✓ Cryo-electron microscopy images molecules frozen in vitreous ice, unstained.

✓ Dark structures in a transmission electron micrograph scattered many electrons because they bound more heavy metal.

✓ Fluorescein-labelled antibodies in the fluorescence microscope emit green light.

✓ Freeze-fracture electron microscopy shows the inner faces of a membrane, split along its lipid bilayer.

✓ Immersion oil raises the numerical aperture and resolution of the 100x objective.

✓ In dark-field microscopy, the specimen appears bright on a black background.

✓ In indirect immunohistochemistry, the visible label is carried by a secondary antibody directed against the primary antibody.

✓ In microscopy, resolution is the smallest distance at which two points are still seen as separate.

✓ Light of a shorter wavelength improves the resolution of a light microscope.

✓ Living, unstained cells are best seen with phase contrast microscopy.

✓ Magnifying beyond what the resolution supports adds no detail.

✓ Polarised light microscopy shows birefringent structures, such as collagen and crystals.

✓ Ribosomes, about 25 nm across, can be seen only with the transmission electron microscope.

✓ Super-resolution microscopy resolves detail finer than the 0.2 µm limit of light microscopy.

✓ The best resolution of a light microscope with visible light is about 0.2 µm.

Histology Exam 1 · Lecture 2

Histological technique

1 High-yield facts

Routine sequence
Fixation → dehydration → clearing → embedding (infiltration) → sectioning → mounting → staining → coverslipping.

Fixation
Stops autolysis and bacterial decay, preserves structure; formalin (buffered 4% formaldehyde) cross-links proteins via methylene bridges.

EM fixation
Glutaraldehyde (protein cross-links) then osmium tetroxide (fixes and stains lipid membranes); embed in epoxy resin.

Dehydration and clearing
Graded alcohols (70% → 100%) remove water; xylene mixes with both alcohol and paraffin, so wax can enter.

Embedding
Paraffin (~56–60 °C) or resin infiltrates the tissue and gives it a firm consistency for thin sectioning.

Section thickness
Paraffin 3–10 µm (microtome); semithin resin ~1 µm (toluidine blue); ultrathin 40–90 nm (ultramicrotome, glass/diamond knife).

Frozen sections
Cryostat; no alcohol or xylene, so lipids and enzymes survive; minutes-long intraoperative diagnosis.

Processing losses
Paraffin processing dissolves lipids (empty adipocytes); water-soluble glycogen can wash out.

H&E
Haematoxylin (basic, with mordant) stains acidic structures blue-purple: nuclei, rER-rich cytoplasm. Eosin (acidic) stains basic proteins pink: cytoplasm, collagen.

Histochemistry
Chemical reaction in the section localises a substance: PAS (glycogen, basement membrane, mucins), Feulgen (DNA), Perls (ferric iron), enzyme reactions.

Immunohistochemistry
Labelled antibody shows where an antigen (protein) lies; direct or indirect (labelled secondary antibody amplifies signal).

In situ hybridisation
Labelled DNA/RNA probe binds a complementary sequence in the section (FISH if fluorescent).

Decalcification
Bone and calcified tissue are softened with acid or EDTA before cutting on the microtome.

Tissue context
Four basic tissues: epithelial, connective, muscle, nervous; all derive from ectoderm, mesoderm and endoderm by differentiation.

2 Cheat sheet

Basic shows the must-knows, Intermediate everything on your slides, Advanced adds textbook detail (marked +).

Steps of paraffin processing

STEP	AGENT	PURPOSE
1 Fixation	10% neutral buffered formalin	prevent autolysis, preserve structure
(Decalcification, if bone)	acids (formic, nitric) or EDTA	remove calcium so tissue can be cut
2 Dehydration	graded alcohols (ethanol 70→100%)	remove water
3 Clearing	xylene (or toluene)	replace alcohol; miscible with paraffin; tissue turns translucent
4 Infiltration and embedding	molten paraffin wax, set in a block	firm support for sectioning
5 Sectioning	rotary microtome, steel knife	sections 3–10 µm
6 Mounting	float on warm water, pick up on glass slide	flat section on slide
7 Dewaxing and rehydration	xylene, then descending alcohols to water	allow water-based dyes in
8 Staining	e.g. H&E	contrast for structures
9 Dehydrate, clear, coverslip	alcohol, xylene, resin mountant	permanent slide

Light vs electron microscopy preparation

STAGE	LIGHT MICROSCOPY	TEM
Fixative	buffered formalin	glutaraldehyde, then osmium tetroxide
Block size	~1–2 cm across, a few mm thick	~1 mm^3
Embedding medium	paraffin	epoxy resin (Epon, Araldite)
Instrument	microtome	ultramicrotome
Knife	steel	glass or diamond
Thickness	3–10 µm	40–90 nm (semithin survey 0.5–1 µm)
Support	glass slide	copper grid
Stain / contrast	dyes (H&E)	heavy metals: uranyl acetate, lead citrate

Fixatives

FIXATIVE	ACTION	USE
Formaldehyde (formalin)	cross-links proteins	routine LM, IHC
Glutaraldehyde	stronger cross-links (two aldehyde groups)	EM primary fixation
Osmium tetroxide	binds unsaturated lipids; adds electron density	EM secondary fixation; stains myelin black

Routine and special stains

STAIN	SHOWS	COLOUR
Haematoxylin	nuclei, rER, acidic matrix (basophilic)	blue-purple
Eosin	cytoplasm, collagen, RBCs (acidophilic)	pink-red
Masson's trichrome	collagen / muscle and cytoplasm / nuclei	blue or green / red / black
Orcein, Verhoeff, resorcin-fuchsin	elastic fibres	brown / black / purple
Silver impregnation (Gomori)	reticular fibres (type III collagen), nerve fibres	black (argyrophilic)
Toluidine blue	semithin sections; mast-cell granules metachromatic	blue; granules purple-red
Alcian blue	acidic mucins, sulfated GAGs	blue
Oil Red O, Sudan black	neutral lipid (frozen sections)	red / black
Congo red	amyloid	red; apple-green birefringence in polarised light

Histochemical reactions

REACTION	DETECTS	NOTE
PAS (periodic acid-Schiff)	glycogen, neutral mucins, basement membrane, glycoproteins	magenta
PAS + diastase	confirms glycogen	diastase (amylase) digests glycogen; loss of stain = glycogen
Feulgen	DNA	magenta; quantitative; RNA unstained
Perls' Prussian blue	ferric iron (haemosiderin)	blue
Enzyme histochemistry	phosphatases, dehydrogenases, peroxidase	frozen sections of unfixed or lightly fixed tissue; coloured or dense product at the site

Dye binding terms

TERM	MEANING	EXAMPLES
Basophilic	binds basic dye; rich in acidic groups	nuclei (DNA phosphate), plasma-cell cytoplasm (rRNA of rER), cartilage matrix
Acidophilic (eosinophilic)	binds acidic dye; rich in basic proteins	cytoplasm, mitochondria, collagen, RBCs
Metachromasia	dye changes colour on binding dense polyanions	mast-cell heparin with toluidine blue (purple-red)

Molecular localisation methods

METHOD	PROBE	DETECTS
Direct immunohistochemistry	labelled primary antibody	antigen
Indirect immunohistochemistry	unlabelled primary + labelled secondary anti-antibody	antigen, amplified signal
In situ hybridisation / FISH	labelled complementary nucleic acid	specific DNA or mRNA

Artefacts

ARTEFACT	CAUSE
Parallel scratches across the section	nick in the knife edge
Folds, wrinkles	poor flotation or mounting
Shrinkage spaces (cell retraction)	fixation and dehydration
Empty adipocytes, empty spaces	lipid dissolved in processing

3 Mnemonics

Fix, Dehydrate, Clear, Embed, Cut, Stain: order of routine paraffin processing

4 Traps: the correct facts for common wrong answers

- ✓ A less specialised cell becomes more specialised by differentiation.
- ✓ A rapid diagnosis during an operation is made on a frozen section cut on a cryostat.
- ✓ Alcian blue stains acidic mucins and sulfated glycosaminoglycans blue.
- ✓ Amyloid stained with Congo red shows apple-green birefringence in polarised light.
- ✓ Before bone is cut on a microtome, it is usually decalcified with acid or EDTA.
- ✓ Before paraffin embedding, tissue is dehydrated in graded alcohols.
- ✓ Contrast in transmission electron microscopy is given by uranyl acetate and lead citrate.
- ✓ Differentiated embryonic cells derive from ectoderm, mesoderm and endoderm.
- ✓ Elastic fibres are shown selectively with orcein or Verhoeff's stain.
- ✓ Embryonic tissue is a developmental stage, not one of the four primary tissue types.
- ✓ Enzymes such as alkaline phosphatase are demonstrated on frozen sections of unfixed or lightly fixed tissue.
- ✓ Eosin stains cytoplasm and collagen pink.
- ✓ Formalin fixes tissue chiefly by cross-linking proteins.
- ✓ Glycogen may be washed out of a routine paraffin section because it is soluble in water.
- ✓ Haematoxylin stains nuclei because nuclei are basophilic.
- ✓ Immunohistochemistry shows where a particular protein lies, using a labelled antibody.
- ✓ In Masson's trichrome, collagen stains blue or green.
- ✓ In routine paraffin processing, clearing in xylene follows dehydration in graded alcohols.
- ✓ In situ hybridisation locates a particular DNA or RNA sequence with a labelled probe.
- ✓ Neutral lipid in a frozen section is shown with Oil Red O.
- ✓ PAS-positive glycogen is confirmed by first treating the section with diastase.
- ✓ Paraffin processing dissolves lipids, so they are shown on frozen sections.
- ✓ Paraffin sections for routine light microscopy are about 3-10 µm thick.

✓ Parallel, evenly spaced scratches across a whole paraffin section are caused by a nick in the microtome knife edge.

Histology Exam 1 · Lecture 3

Epithelial tissue and glands

1 High-yield facts

Four basic tissues
Epithelial, connective, muscle and nervous tissue. Histology = tissues and how they build organs; 'histo' = tissue or web. slide 2, 3

Origin from all three germ layers
Epithelia arise from ectoderm, mesoderm and endoderm (e.g. epidermis, endothelium, gut lining). slide 5

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. slide 7, 11, 20, 30

Functions
Covering, lining, protection (epidermis, urothelium), absorption (intestine), secretion (stomach, glands), sensation, transport (cilia), contractility (myoepithelial cells). slide 8, 9

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. slide 16, 18, 41

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. slide 16, 36, 37

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. slide 10

Apical specialisations
Microvilli (actin core, absorption), stereocilia (long microvilli, epididymis), cilia (9+2 axoneme on basal bodies, motile), glycocalyx (carbohydrate coat). slide 12, 13, 14, 15

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. slide 34, 35, 53

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). slide 40, 43

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. slide 48, 49, 50

Gland development
Surface epithelium proliferates into the connective tissue. Exocrine: connection persists as a duct. Endocrine: connection is lost, product enters capillaries. slide 53, 54, 55, 56

Modes of secretion
Merocrine = exocytosis, no cytoplasm lost (most common). Apocrine = product plus apical cytoplasm (mammary lipid). Holocrine = whole cell breaks down (sebaceous). slide 58, 60, 62

Renewal
Epithelia renew continuously by mitosis of basal / stem cells; holocrine glands replace lost cells from peripheral basal cells. slide 39, 60, 61

2 Cheat sheet

Basic shows the must-knows, Intermediate everything on your slides, Advanced adds textbook detail (marked +).

Classification of covering epithelia

TYPE	LAYERS AND CELL SHAPE	WHERE	FUNCTION
Simple squamous *'Pavement' epithelium; squamous = fish-scale-like*	one layer, flat cells, flat nuclei bulging into lumen	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	exchange (gases, fluid), filtration, lubrication, low friction
Simple cuboidal	one layer, cells as tall as wide, round central nucleus	kidney tubules, thyroid follicles, small exocrine ducts, ovary surface	secretion, absorption, barrier
Simple columnar	one layer, tall cells, oval nuclei near the basal pole	stomach surface and gastric pits, small intestine and colon (with goblet cells), gallbladder (microvilli, no goblet cells); ciliated form in uterine tube	absorption, secretion, protection
Pseudostratified columnar	one layer, all cells on basement membrane, nuclei at several levels	trachea and bronchi (ciliated, with goblet cells = respiratory epithelium), nasal cavity; epididymis and ductus deferens (stereocilia)	secretion, moving mucus by cilia, protection
Stratified squamous non-keratinised	many layers, cuboidal basal to flat nucleated living surface cells	oral cavity, oesophagus, vagina, ectocervix, anal canal, corneal epithelium, inner lips	protection on moist surfaces, some secretion
Stratified squamous keratinised	many layers, surface cells dead, anucleate, filled with keratin	epidermis of skin	protection against abrasion, water loss, microbes
Stratified cuboidal *Listed on slide 16 but not shown*	two (or more) layers of cuboidal cells	ducts of sweat glands, developing ovarian follicles	protection, secretion
Stratified columnar *Rare*	several layers, superficial cells columnar	conjunctiva, large excretory ducts, parts of male urethra	protection, secretion
Transitional (urothelium)	relaxed 4–5 layers (basal cuboidal, intermediate polygonal, dome-shaped umbrella surface cells); stretched 2–3 layers, flat surface cells	renal calyces and pelvis, ureter, bladder, proximal urethra	protection, distension, barrier to urine

Cell shapes

SHAPE	PROPORTIONS	NUCLEUS	EXAMPLE
Squamous	width greater than height	flat, elongated	endothelium, alveoli
Cuboidal	height ≈ width ≈ depth	round, central	thyroid follicle, kidney tubule
Columnar	height greater than width	oval, near basal pole	intestine, stomach

Apical surface specialisations

STRUCTURE	CORE / COMPOSITION	SIZE AND MOTILITY	WHERE
Microvilli *Increase absorptive surface ~20–30×*	actin filaments anchored in terminal web	≈1 µm long, 0.08 µm wide; non-motile; brush (striated) border	enterocytes, proximal convoluted tubule
Stereocilia	actin filaments (very long microvilli, not cilia)	long, non-motile; branched in epididymis	epididymis, ductus deferens; sensory hair cells of inner ear
Cilia *Row of basal bodies = dark apical line in LM*	axoneme of 9 peripheral doublets + central pair (9+2) of microtubules, dynein arms; arise from basal bodies	5–10 µm long, 0.2 µm wide; motile, beat in one direction	respiratory tract, uterine tube
Glycocalyx *Holds digestive enzymes, protects*	carbohydrate chains of membrane glycoproteins and glycolipids	thin coat on apical membrane	all cells, prominent on enterocytes

Cell domains and junctions

ITEM	WHAT IT IS	FUNCTION
Apical domain	free surface facing the lumen	absorption, secretion, specialisations
Lateral domain	surfaces facing neighbouring cells	cell–cell junctions
Basal domain	surface on the basement membrane	anchorage, receptors, ion transport (basal folds)
Tight junction (zonula occludens) *With zonula adherens + desmosome = junctional complex ('terminal bar' in LM)*	most apical; claudins, occludin seal the membranes	blocks paracellular passage; separates apical and lateral membranes
Desmosome (macula adherens)	cadherins linked to keratin intermediate filaments	strong spot adhesion; 'spines' of stratum spinosum
Gap junction	connexons (connexins) forming channels	passage of ions and small molecules between cells

Basement membrane

PART	MADE OF / BY	NOTE
Basal lamina	type IV collagen, laminin, nidogen, perlecan; made by epithelial cells	20–100 nm; seen by EM (lamina lucida + lamina densa)
Functions	selective filter, scaffold for regeneration	controls polarity, proliferation, differentiation

Epidermis layers (keratinised stratified squamous), deep to superficial

LAYER	CELLS	KEY FEATURE
Stratum basale *Junqueira: stratum basale = stratum germinativum (slide 44 says germinativum = basale + spinosum)*	one layer of cuboidal to low columnar cells on basement membrane	mitosis (stem cells)
Stratum spinosum *Basale + spinosum = Malpighian layer; also present in non-keratinised epithelium*	several layers of polygonal cells	desmosomes give 'spiny' (prickle) look
Stratum granulosum	3–5 layers of flattened cells	keratohyalin granules
Stratum lucidum	thin layer of flat eosinophilic cells	only in thick skin (palms, soles); eleidin, pale/bright
Stratum corneum	many layers of dead anucleate flat cells	filled with keratin

Germ layer origin

GERM LAYER	EPITHELIA DERIVED
Ectoderm (outer)	epidermis, corneal epithelium, oral and nasal epithelium, distal anal canal
Mesoderm (middle)	endothelium, mesothelium, kidney tubules, reproductive tract
Endoderm (inner)	lining of gut and respiratory tract, liver, pancreas, thyroid

Gland classification

BASIS	TYPE	FEATURE	EXAMPLE
Ducts	Exocrine	duct to surface or lumen	sweat, sebaceous, salivary
Ducts	Endocrine	ductless, secretes hormones into blood	thyroid, adrenal, pituitary
Cell number	Unicellular	single secretory cell	goblet cell
Cell number *Slide 53 says pituitary and adrenal are multicellular exocrine glands; textbook: they are endocrine*	Multicellular	many cells, secretory portion + duct	sweat, salivary glands
Duct	Simple	unbranched duct	sweat gland
Duct	Compound	branched duct	salivary glands, pancreas
Secretory portion	Tubular	tube of about duct diameter (simple, coiled or branched)	intestinal crypts; sweat gland (coiled); gastric glands (branched)
Secretory portion	Acinar (alveolar)	rounded sac-like end piece	sebaceous gland (branched acinar), exocrine pancreas (compound acinar)
Secretory portion	Tubuloacinar	both tubules and acini	submandibular gland

Modes of secretion

MODE	HOW PRODUCT LEAVES	CELL FATE	EXAMPLE
Merocrine (eccrine) *Most common*	exocytosis of vesicles at apical surface	intact, keeps secreting	most glands: eccrine sweat, salivary, pancreas
Apocrine *'Apocrine' sweat glands actually secrete mostly by merocrine release (Ross)*	product released with part of apical cytoplasm	apical region reforms	lipid of mammary gland
Holocrine	whole cell fills with product and breaks down	dies; replaced by mitosis of peripheral basal cells	sebaceous gland

3 Mnemonics

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

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

4 Slide by slide

Slide 2 **What histology is**

- Study of tissues and their arrangement into organs
- 'Histo' = tissue or web

Slide 3 **Four tissue types**

- Epithelial, connective, muscle, nervous

Slide 5 **Germ layers**

- Ectoderm, mesoderm, endoderm
- Epithelia come from all three

Slide 6 **Overview of epithelia**

- Simple squamous lines alveoli
- Pseudostratified ciliated columnar: nuclei at several levels
- Transitional: dome-shaped surface cells

Slide 7 **Cell shapes and junctions**

- Squamous, cuboidal, columnar cells
- Tight junctions seal cells near the apex; gap junctions link them

Slide 9 **Functions of epithelium**

- Covering, lining, protection (skin, urothelium)
- Absorption (intestine), secretion (stomach), sensation

Slide 10 **Basement membrane**

- Selective barrier to particles and macromolecules
- Influences cell shape, polarity and paracellular permeability

Slide 11 **Cell surface domains**

- Apical faces lumen; lateral faces neighbours; basal faces basement membrane

Slide 12 **Apical domain**

- Free surface facing the lumen
- Microvilli, cilia, glycocalyx

Slide 13 **Microvilli**

- Brush border of enterocytes
- Enlarge the absorptive surface

Slide 14 **Stereocilia**

- Long non-motile microvilli of the epididymis

Slide 15 **Cilia (EM)**

- Basal bodies at the base of each cilium
- 9+2 axoneme; microvilli are shorter with actin cores

Slide 16 **Classification**

- Simple: squamous, cuboidal, columnar, pseudostratified
- Stratified: squamous (keratinised / not), cuboidal, columnar

Slide 17 **Cell shapes**

- Squamous flat; cuboidal boxy; columnar tall

Slide 18 **Simple, stratified, squamous**

- Simple = one layer; stratified = two or more
- Squamous = wider than high

Slide 19 **Cuboidal and columnar**

- Cuboidal: height ≈ width
- Columnar: height exceeds width

Slide 20 **Simple epithelia**

- Squamous, cuboidal, ciliated columnar on basement membrane
- Lamina propria with capillaries deep to it

Slide 21 **Simple squamous epithelium**

- Flat irregular cells, 'pavement' epithelium
- Thin: passive transport of gases and fluid

Slide 22 **Simple squamous: sites and functions**

- Endothelium (vessels, heart) and mesothelium (serosae)
- Alveoli, loop of Henle, parietal Bowman's capsule, ear
- Exchange, filtration, lubrication

Slide 23 **Simple squamous in section**

- Recognised by thin flat nuclei bulging into the lumen

Slide 24 **Mesothelium, silver nitrate**

- Surface view; silver outlines the cell borders

Slide 25 **Corneal endothelium**

- Simple squamous on posterior cornea
- Rests on thick Descemet's membrane

Slide 26 **Capillary endothelium**

- Very flat cells, elongated nuclei; walls look like thin pink lines

Slide 27 **Parietal layer of Bowman's capsule**

- Simple squamous lining of the renal corpuscle (H&E)

Slide 28 **Simple cuboidal epithelium**

- Round central nucleus
- Kidney tubules, thyroid follicles, gland ducts, ovary surface

Slide 29 **Simple cuboidal: functions**

- Secretion, absorption, surface barrier

Slide 30 **Simple cuboidal diagram**

- Cells tightly joined laterally, mosaic in surface view
- Capillaries in lamina propria

Slide 31 **Thyroid follicle**

- Simple cuboidal follicle cells next to capillary endothelium

Slide 32 **Simple columnar epithelium**

- Tall cells, polarised elongated nuclei
- Intestine, stomach and gastric glands, gallbladder

Slide 33 **Simple (ciliated) columnar**

- Terminal bars = apical junctional complexes
- Ciliated form lines the uterine tube

Slide 34 **Goblet cell**

- Modified columnar cell secreting mucin
- PAS-positive; apical mucin compresses neighbours, nucleus basal

Slide 35 **Goblet cells in section**

- Pale in H&E (mucin washed out)
- Nucleus at the basal pole

Slide 36 **Stratified vs pseudostratified**

- Stratified: only basal layer on basement membrane
- Pseudostratified: all cells on it; basal cells are stem cells

Slide 37 **Pseudostratified: functions**

- Secretion, absorption, lubrication, transport, protection
- Cilia move mucus and particles

Slide 38 **Respiratory epithelium**

- Pseudostratified ciliated columnar with goblet cells (trachea)
- Basal bodies form a dark apical line

Slide 39 **Stratified squamous epithelium**

- Cuboidal basal layer to flat surface
- Basal cells divide; surface loss tolerated (abrasion)
- Nuclei become pyknotic superficially

Slide 40 **Non-keratinised stratified squamous**

- Living nucleated surface cells
- Cornea, mouth, oesophagus, anal canal, cervix, vagina

Slide 41 **Stratified squamous in section**

- Named after superficial cell shape
- Cuboidal/columnar basal cells to flat surface cells

Slide 42 **Non-keratinised example**

- Nucleated surface cells, no anucleate keratin layer (oesophagus, vagina)

Slide 43 **Keratinised stratified squamous**

- Dry, dead, anucleate surface cells
- Epidermis; protection

Slide 44 **Strata: basale and spinosum**

- Basale: dividing cells on basement membrane
- Spinosum: cells joined by desmosomes (prickle layer)

Slide 45 **Strata: granulosum, lucidum, corneum**

- Granulosum: keratohyalin granules
- Lucidum: palms and soles only
- Corneum: dead horny cells

Slide 46 **Epidermis layers (micrograph)**

- Basale, spinosum, granulosum, lucidum, corneum

Slide 47 **Non-keratinised layers**

- Basal layer, stratum spinosum, flat nucleated surface cells

Slide 48 **Transitional epithelium**

- Built to stretch; between stratified cuboidal and squamous
- Relaxed: 4–5 layers, polygonal intermediate cells, large rounded surface cells

Slide 49 **Transitional: stretched, sites**

- Stretched: 2–3 layers, flat surface cells
- Calyces, renal pelvis, ureter, bladder, proximal urethra

Slide 50 **Umbrella cells**

- Dome-shaped surface cells identify urothelium

Slide 51 **Stratified columnar epithelium**

- Conjunctiva, large excretory ducts, parts of male urethra
- Secretion, absorption, protection

Slide 52 **Stratified columnar in section**

- Two or more layers, columnar surface cells (large duct)

Slide 53 **Glandular epithelium**

- Endocrine: ductless, hormones to blood; exocrine: ducts
- Unicellular (goblet) vs multicellular

Slide 54 **Gland formation**

- Surface epithelium proliferates into connective tissue
- Exocrine keeps duct; endocrine loses it, joins capillaries

Slide 55 **Exocrine vs endocrine**

- Exocrine: secretory portion + duct
- Endocrine: duct cells disappear, secretion to blood vessels

Slide 56 **Gland shapes**

- Unbranched duct = simple; branched = compound
- Tubular, alveolar (acinar) or tubuloalveolar secretory portion

Slide 57 **Exocrine glands by structure**

- Simple vs compound
- Tubular vs acinar (sac-like)

Slide 58 **Merocrine gland**

- Exocytosis at apical surface
- Most common mode

Slide 59 **Merocrine example**

- Sweat gland; cell stays intact

Slide 60 **Holocrine gland**

- Whole cell breaks down into secretion
- Sebaceous gland

Slide 61 **Sebaceous gland (section)**

- Peripheral small dividing cells; central lipid-filled pale cells
- Lost cells replaced by basal mitosis

Slide 62 **Apocrine gland**

- Product released with apical cytoplasm
- Mammary gland lipid

5 Traps: the correct facts for common wrong answers

✓ Gross anatomy, not histology, studies the dissection of body regions.

✓ Histology is the study of tissues and how they are arranged to build organs.

✓ Pathology, not histology, studies diseases of organs.

✓ The Greek root 'histo-' means tissue or web.

✓ Nervous tissue is the fourth basic tissue, alongside epithelial, connective and muscle tissue.

✓ Epithelia develop from all three germ layers.

✓ The middle germ layer of the three-layered embryo is the mesoderm.

✓ Alveolar air spaces are lined by simple squamous epithelium.

✓ Dome-shaped, sometimes binucleate superficial cells identify transitional epithelium (urothelium).

✓ Nuclei at several heights with every cell on the basement membrane identify pseudostratified columnar epithelium.

✓ Polarised epithelial cells are sealed together near their apex by tight junctions.

✓ Gastric surface and glandular epithelium mainly serves secretion.

✓ The epidermis and the urothelium are protective epithelia.

✓ The epidermis of the skin is mainly protective.

✓ The simple squamous alveolar epithelium allows gas diffusion.

✓ The urothelium of the bladder is mainly protective.

✓ Cilia grow from basal bodies in the apical cytoplasm.

✓ The basement membrane contains no vessels and acts as a selective barrier.

✓ The basement membrane influences epithelial polarity, proliferation and differentiation.

✓ The basement membrane is not contractile; it acts as a selective barrier.

✓ Tight junctions are formed between the membranes of neighbouring epithelial cells.

✓ The lateral domain of an epithelial cell surface faces the neighbouring epithelial cells of the sheet.

✓ Compared with a smooth apical surface, enterocyte microvilli chiefly give the cell a much larger area of membrane for absorption.

✓ The glycocalyx on the apical surface of an absorptive intestinal cell is a carbohydrate coat formed by the sugar chains of membrane molecules.

Histology Exam 1 · Lecture 4

Connective tissue proper

1 High-yield facts

Three components
Cells + extracellular matrix (ground substance and fibres). Matrix dominates; cells are scattered in it. slide 2, 7, 26

Origin: mesenchyme
All connective tissues arise from embryonic mesenchyme (mostly mesoderm). Fibroblasts, chondroblasts, osteoblasts, adipocytes and haematopoietic stem cells descend from it. slide 3, 9

Functions
Support and binding, nutrition of avascular epithelia by diffusion through ground substance, defence (immune cells), protection, fat storage, repair. slide 4

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). slide 5, 6, 41

Resident vs wandering cells
Resident (fixed): fibroblasts, myofibroblasts, macrophages, adipocytes, mast cells, mesenchymal cells. Wandering (from blood): lymphocytes, plasma cells, neutrophils, eosinophils, basophils, monocytes. slide 7, 8, 25

Fibroblast
Commonest cell; synthesises collagen, elastin, GAGs, proteoglycans and glycoproteins. Active form: large, pale oval nucleus, basophilic cytoplasm; resting fibrocyte: smaller, dark slim nucleus. slide 10

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). slide 11, 18, 19, 20

Ground substance
Hydrated, viscous gel of GAGs, proteoglycans and multiadhesive glycoproteins; lubricant and barrier to microorganisms; fine granular in TEM, lost in routine sections. slide 27

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. slide 28

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). slide 30, 31, 32

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). slide 34, 35, 53

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. slide 12, 13, 15, 16, 50

Why fat looks empty
Alcohols and xylene of paraffin processing dissolve lipid; frozen section + Sudan or osmium shows it. slide 14, 17

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. slide 36, 38, 40

2 Cheat sheet

Basic shows the must-knows, Intermediate everything on your slides, Advanced adds textbook detail (marked +).

Cells of connective tissue proper

CELL	ORIGIN / RESIDENT OR WANDERING	HOW IT LOOKS	FUNCTION
Fibroblast	mesenchyme; resident	elongated, pale oval nucleus with nucleolus; basophilic cytoplasm with RER and Golgi	makes fibres and ground substance
Fibrocyte	inactive fibroblast; resident	smaller, spindle-shaped, dark slim nucleus, little cytoplasm	maintenance; reactivates in repair
Myofibroblast	fibroblast; resident	fibroblast with actin bundles and smooth muscle actin	wound contraction
Macrophage *Fuse into foreign-body giant cells.*	blood monocyte; resident (histiocyte)	irregular surface with processes, indented nucleus, many lysosomes	phagocytosis, antigen presentation, cytokines
Mast cell *IgE receptors (FcεRI) on surface; degranulation = exocytosis.*	bone-marrow progenitor; resident	large oval, central nucleus hidden by many basophilic metachromatic granules; near small vessels	releases histamine, heparin, leukotrienes, ECF-A
Adipocyte	mesenchyme; resident	white: one droplet, peripheral nucleus; brown: many droplets, central nucleus	fat storage, insulation, heat (brown), leptin
Undifferentiated mesenchymal cell	mesenchyme; resident	small, stellate, near vessels (pericytes)	stem cell for new CT cells in adults
Plasma cell *Russell bodies = stored immunoglobulin.*	B lymphocyte; wandering	oval, eccentric nucleus with clock-face chromatin, basophilic cytoplasm, pale Golgi halo	secretes antibodies
Reticular cell	specialised fibroblast; resident	stellate, processes along fibres	makes reticular (type III) fibres of lymphoid organs, marrow
Pigment cell (melanocyte)	neural crest; resident	branched, brown-black melanin granules	melanin from tyrosine by tyrosinase; skin, choroid of eye
Lymphocyte	blood; wandering	small, round dark nucleus, thin rim of cytoplasm	immune responses
Neutrophil	blood; wandering	multilobed nucleus, faint granules	phagocytosis of bacteria (acute inflammation)
Eosinophil	blood; wandering	bilobed nucleus, large orange-red granules	parasites, allergy
Basophil	blood; wandering	lobed nucleus hidden by large dark blue granules	histamine release, like mast cell
Monocyte	blood; wandering	large, kidney-shaped nucleus, grey-blue cytoplasm	becomes macrophage in tissue

Fibres of the extracellular matrix

FIBRE	MADE OF	LIGHT / EM LOOK	STAIN	PROPERTY / WHERE
Collagen	type I collagen (tropocollagen triple helix)	thick, unbranched, wavy bundles; EM: fibrils with 64-67 nm banding	eosin pink; blue with Mallory/trichrome	great tensile strength, little stretch; tendon, dermis, bone
Reticular	type III collagen, heavily glycosylated	thin, branched delicate network	silver (black, argyrophilic), PAS+	supporting stroma of lymph nodes, spleen, marrow, liver, basement membranes
Elastic *Fibrillin defect = Marfan syndrome.*	elastin core + fibrillin microfibrils	thin, straight, branching, form networks or fenestrated sheets	orcein, resorcin-fuchsin, Verhoeff	stretch and recoil; arteries, lung, elastic ligaments

Collagen types (main ones)

TYPE	FORM	WHERE
I *~90% of body collagen.*	thick fibrils, fibres	skin (dermis), bone, tendon, ligaments, dentin, fibrocartilage
II	thin fibrils	hyaline and elastic cartilage, vitreous body
III	reticular fibres	skin, lung, blood vessels, lymphoid organs, smooth muscle
IV	sheet-like network	basal lamina
V	fibril-forming, with type I	with type I; placenta
VII	anchoring fibrils	dermal-epidermal junction; binds basal lamina to dermal collagen

Components of ground substance

COMPONENT	NATURE	EXAMPLES / ROLE
Glycosaminoglycans (GAGs)	long unbranched polysaccharides of repeating disaccharides, strongly negative, bind water	hyaluronan (not sulfated, no core protein), chondroitin, dermatan, heparan, keratan sulfate
Proteoglycans	core protein + sulfated GAGs	aggrecan (cartilage), decorin, syndecan, perlecan; give gel and turgor
Multiadhesive glycoproteins	proteins with binding sites for cells (integrins) and matrix	fibronectin, laminin; anchor cells to matrix
Tissue fluid	plasma-like filtrate with fewer proteins	carries nutrients and wastes; excess = oedema

Classification of connective tissues

GROUP	GROUND SUBSTANCE	MEMBERS
Embryonic CT	viscous gel, few fibres	mesenchyme; mucous (gelatinous) tissue
Connective tissue proper *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.*	semi-liquid gel	loose (areolar); dense regular; dense irregular
Specialised: adipose, reticular, elastic	gel	white (unilocular) and brown (multilocular) fat; reticular tissue; elastic tissue
Cartilage	firm, rubbery	hyaline, elastic, fibrocartilage
Bone	calcified, very hard	woven (immature), lamellar (mature): compact and spongy
Blood and lymph	liquid (plasma)	blood cells and platelets in plasma

Types of connective tissue proper and related tissues

TISSUE	STRUCTURE	WHERE	FUNCTION
Mesenchyme	stellate cells joined by processes, abundant ground substance, almost no fibres	embryo	gives rise to all CT
Mucous (gelatinous) tissue *Slide 36 splits immature and mature gelatinous tissue.*	fibroblasts in hyaluronan-rich jelly, sparse type I and III fibres	umbilical cord (Wharton's jelly), pulp of young teeth	cushions cord vessels
Loose (areolar)	many cells of all types, much ground substance, thin collagen + elastic fibres in all directions	lamina propria, papillary dermis, hypodermis, around vessels, mesentery	binding, diffusion, defence, oedema site
Dense irregular	thick collagen bundles interwoven in many planes, few fibroblasts	reticular dermis, organ capsules, submucosa of gut	resists stretch from many directions
Dense regular	parallel collagen bundles with rows of flattened fibroblast (tenocyte) nuclei	tendons, ligaments, aponeuroses, cornea stroma	resists pull in one direction
Elastic tissue	thick parallel elastic fibres with some collagen	ligamenta flava, suspensory ligament of penis, wall of large arteries	stretch and recoil
Reticular tissue	reticular cells and type III fibre meshwork; free cells in spaces	lymph nodes, spleen, bone marrow, liver sinusoids	supporting stroma for free cells
White adipose	unilocular cells in lobules separated by CT septa, rich capillaries	subcutaneous, visceral (omentum, mesentery), buttocks, thighs, breast	energy store, insulation, padding, endocrine
Brown adipose	multilocular cells, very vascular, sympathetic nerves	newborn: interscapular, neck; adult: supraclavicular, paravertebral, mediastinal, para-aortic, suprarenal	non-shivering heat

White vs brown adipose tissue

FEATURE	WHITE (YELLOW, UNILOCULAR)	BROWN (MULTILOCULAR)
Lipid droplets	one large droplet fills the cell	many small droplets
Nucleus	flattened, peripheral (signet ring)	round, central
Cell size	large, 50-150 µm	smaller, polygonal
Mitochondria	few	very many, with UCP1 (thermogenin)
Colour cause	yellow from dietary carotenoids	brown from cytochromes of mitochondria and rich blood supply
Function	energy store, insulation, padding, leptin secretion	heat production (uncoupled oxidation)
Distribution	most fat in adults: subcutaneous, visceral; in newborns too (e.g. buttocks)	newborns (~2-5% of body weight); adults: supraclavicular, paravertebral, mediastinal
H&E look	empty polygonal spaces with thin pink rims	pale, foamy (vacuolated) cytoplasm, many capillaries

Stains and how CT elements look

ELEMENT	METHOD	RESULT
Collagen fibres	H&E	pink (eosinophilic)
Reticular fibres	silver impregnation; PAS	black; magenta
Elastic fibres	orcein, resorcin-fuchsin, Verhoeff	brown-red; dark purple; black
Mast cell granules	toluidine blue	purple-red (metachromasia, from heparin)
Fat	frozen section + Sudan or osmium tetroxide	orange-red or black droplets

3 Mnemonics

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

4 Slide by slide

Slide 1 **Connective tissue holds you together**
- CT includes CT proper, cartilage, bone, blood and fat

Slide 2 **Most abundant tissue**
- Most widespread and varied basic tissue, widest range of functions
- Cells scattered in abundant matrix

Slide 3 **Embryonic origin**
- All CT from mesenchyme
- Descendants: fibroblast, chondroblast, osteoblast, haematopoietic stem cell (blood cells, macrophages)

Slide 4 **Functions**
- Nutritional, defence, protective, supporting, regenerative
- Avascular epithelia fed by diffusion through ground substance

Slide 5 **Four types of CT**
- CT proper (loose: areolar, adipose, reticular; dense: regular, irregular, elastic)
- Cartilage, bone, blood

Slide 6 **Components of CT**
- CT proper invests epithelium, muscle, nerve
- Loose vs dense by fibre content and arrangement
- Specialised: adipose, bone, cartilage, blood

Slide 7 **Structure**
- Resident cells: fibroblasts, myofibroblasts, macrophages, adipocytes, mast cells, mesenchymal cells
- Wandering cells: lymphocytes, plasma cells, granulocytes, monocytes
- Matrix: fibres + ground substance (GAGs, proteoglycans, glycoproteins, tissue fluid)

Slide 8 **CT cells overview**
- Drawing of fibroblasts, macrophage, mast cell, fat cell, leukocytes in loose CT

Slide 9 **Undifferentiated mesenchymal cells**
- Source of new CT cells in adults

Slide 10 **Fibroblast**
- Fibroblast = active, fibrocyte = smaller resting form
- Myofibroblast: fibroblast + smooth muscle features, wound contraction

Slide 11 **Macrophage**
- From monocytes; processes for phagocytosis

Slide 12 **Adipose cells**
- Unilocular (white) vs multilocular (brown)

Slide 13 **Unilocular adipocyte**
- One droplet pushes nucleus to the rim

Slide 14 **White fat, H&E**
- Empty polygonal spaces; lipid dissolved in processing

Slide 15 **Multilocular adipocyte**
- Many vacuoles (droplets) and many mitochondria

Slide 16 **Brown fat, H&E**
- Central round nucleus, foamy cytoplasm, many capillaries
- Heat from mitochondria with thermogenin

Slide 17 **Fat stained for lipid**

- Frozen section + Sudan keeps lipid, orange-red

Slide 18 **Mast cells, LM**

- Toluidine blue metachromasia
- Granules: histamine, heparin

Slide 19 **Mast cells, EM**

- TEM: many dense membrane-bound granules
- SEM: degranulation at surface

Slide 20 **Mast cells in spread**

- Large granular cells beside small vessels

Slide 21 **Plasma cells**

- Eccentric clock-face nucleus, basophilic cytoplasm, Golgi halo

Slide 22 **Plasma cells (cont.)**

- Micrograph: plasma cells (P) with eccentric round nucleus, clock-face chromatin and abundant basophilic cytoplasm

Slide 23 **Pigment cells**

- Branched melanocytes with melanin (skin, choroid)
- Melanin from tyrosine via tyrosinase

Slide 24 **Reticular cells**

- Modified fibroblasts making reticular fibres of lymphoid organs

Slide 25 **Influent elements from blood**

- Neutrophils, eosinophils, basophils, lymphocytes, monocytes enter CT

Slide 26 **Extracellular matrix**

- Ground substance + fibres (collagen, reticular, elastic)

Slide 27 **Ground substance**

- Viscous gel: lubricant and barrier
- Fine granular in TEM
- GAGs, proteoglycans, glycoproteins

Slide 28 **Tissue fluid and oedema**

- Plasma-like fluid driven out of capillaries by hydrostatic pressure
- Excess in loose CT = oedema

Slide 30 **Collagen structure**

- Molecule -> microfibril/fibril -> fibre
- Fibrils cross-banded in EM

Slide 31 **Collagen fibre formation**

- Tropocollagen -> fibrils -> fibres -> bundles
- Gap and overlap regions give banding

Slide 32 **Types of collagen**

- I: skin, bone, tendon; II: cartilage, vitreous; III: reticular; IV: basement membrane
- VII: anchoring fibrils of dermal-epidermal junction; X: hypertrophic cartilage

Slide 33 **Collagen fibres**

- Thick, unbranched bundles; high tensile strength
- Tendon fibroblast nuclei in rows

Slide 34 **Reticular fibres**

- Thin branched type III fibres, black with silver

Slide 35 **Elastic fibres**

- Thin, branching network; elastin + fibrillin
- Orcein or resorcin-fuchsin

Slide 36 **Division of CT: CT proper**

- Semi-liquid gel ground substance
- Mesenchyme, gelatinous, loose, dense regular/irregular, reticular, adipose (white, brown)

Slide 37 **Division of CT: cartilage, bone, blood**

- Cartilage (hardened matrix): hyaline, elastic, fibro
- Bone (very hard): woven, lamellar (spongy, compact)
- Blood and lymph: liquid

Slide 38 **Mesenchymal CT**

- Stellate cells in viscous ground substance, almost no fibres

Slide 39 **Mesenchyme (micrograph)**

- Mesenchymal cells with oval nuclei, several in mitosis (arrows), in abundant pale ground substance; C = capillaries

Slide 40 **Gelatinous tissue**

- Wharton's jelly of umbilical cord = mucous CT
- Fibroblasts in jelly-like matrix

Slide 41 **Loose vs dense CT**

- Dense: more fibres, fewer cells, less ground substance

Slide 42 **Loose CT**

- Thin collagen and elastic fibres, many cell types, much ground substance

Slide 43 **Loose CT spread**

- Thick pink collagen + thin dark branching elastic fibres
- Lamina propria, around vessels

Slide 44 **Loose CT (micrograph)**

- Spread: thick wavy pink collagen bundles, thin dark branching elastic fibres, scattered fibroblast nuclei and granular mast cells

Slide 45 **Dense regular CT**

- Tendon: parallel collagen bundles, rows of fibroblast nuclei

Slide 46 **Dense regular CT (micrograph)**

- Tendon, H&E, longitudinal: parallel wavy collagen bundles with rows of flattened, elongated fibroblast nuclei between them

Slide 47 **Dense regular CT, H&E**

- Resists pull in one direction

Slide 48 **Dense irregular CT**

- Collagen bundles cut in many planes, dermis

Slide 49 **Skin block diagram**

- Epidermis, dense irregular dermis, loose CT hypodermis with fat, muscle
- Dense irregular resists stretch from many directions

Slide 50 **Types of adipose tissue**

- Yellow/white unilocular vs brown multilocular
- Yellow colour from carotenoids

Slide 51 **White adipose tissue**

- CT septa divide fat into lobules
- Each cell: one triglyceride droplet

Slide 52 **Fat map of the body**

- White: subcutaneous, visceral, thighs, buttocks
- Brown: supraclavicular, paravertebral, mediastinal, para-aortic, suprarenal

Slide 53 **Reticular tissue**

- Silver-stained black type III fibre network in lymphoid organs
- Made by reticular cells

5 Traps: the correct facts for common wrong answers

✓ Neuroglia is nervous tissue, not connective tissue.

✓ Smooth muscle is muscle tissue, not connective tissue.

✓ The epidermis is epithelium, not connective tissue.

✓ All connective tissues have cells scattered within abundant extracellular matrix.

✓ Connective tissue is the most abundant and varied basic tissue.

✓ Fibroblasts, chondroblasts and osteoblasts all differentiate from mesenchymal cells.

✓ Macrophages in inflamed connective tissue arise from blood monocytes.

✓ Nutrients reach the cells of an avascular surface epithelium by diffusing through the ground substance of the connective tissue.

✓ Adipose tissue is classed as loose connective tissue.

✓ Areolar tissue is loose connective tissue.

✓ Areolar, adipose and reticular tissues are loose connective tissue.

✓ Chondrocytes in lacunae are found in cartilage, not in areolar connective tissue.

✓ Reticular tissue is loose connective tissue.

✓ Bone and cartilage are classed with the specialised connective tissues rather than with connective tissue proper.

✓ Loose connective tissue has more cells and ground substance, with fewer fibres, than dense connective tissue.

✓ Connective tissue consists of cells, ground substance and protein fibres.

✓ A connective tissue cell packed with granules hiding its nucleus is a mast cell.

✓ A single lipid droplet with a peripheral crescent nucleus marks a white fat cell.

✓ Neutrophils and lymphocytes migrate into connective tissue from the blood.

✓ In adults, new connective tissue cells originate from mesenchymal cells.

✓ Fibroblasts make the fibres and ground substance of connective tissue.

✓ Myofibroblasts in a healing wound contract, drawing the wound edges together.

✓ The fibroblast has a long, pale, oval nucleus lying along collagen fibres.

✓ The myofibroblast of a healing wound resembles a smooth muscle cell in containing bundles of contractile actin filaments.

Histology Exam 1 · Lecture 5

Cartilage and bone

1 High-yield facts

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. slide 2, 9

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. slide 6

Perichondrium
Dense connective tissue sheath: outer fibrous layer (collagen I, fibroblasts), inner chondrogenic layer (chondroblast precursors). Absent from articular cartilage and fibrocartilage. slide 8, 11, 13, 16

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. slide 10, 11, 12, 19

Hyaline matrix zones
Capsular (pericellular) matrix richest in sulfated GAGs and most basophilic; territorial matrix around each group; interterritorial matrix between groups stains paler. slide 4, 10, 11

Cartilage growth
Interstitial: mitosis of chondrocytes inside the matrix (young cartilage, epiphyseal plates). Appositional: chondroblasts from the inner perichondrium add matrix on the surface. slide 10, 11

Bone = cells + mineralised matrix
Cells: osteoprogenitors, osteoblasts, osteocytes, osteoclasts. Matrix: type I collagen (organic) with hydroxyapatite Ca10(PO4)6(OH)2 laid along and between the fibrils. slide 30, 31, 50

Osteoblast lineage
Osteoprogenitor -> osteoblast (secretes osteoid toward the bone surface) -> osteocyte in a lacuna, or flattened bone lining cell. slide 33, 34, 35

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. slide 32, 35, 36, 51

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. slide 37, 39

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. slide 29

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. slide 45, 46, 47, 48, 49

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. slide 27, 41

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. slide 51

2 Cheat sheet

Basic shows the must-knows, Intermediate everything on your slides, Advanced adds textbook detail (marked +).

Cartilage types

TYPE	MATRIX FIBRES	PERICHONDRIUM	WHERE	KEY FEATURES
Hyaline *(slide 9 says 'bundles' of type II collagen; Junqueira: fine fibrils, not bundles)*	fine type II collagen fibrils, masked by ground substance	yes (not on articular surfaces)	articular surfaces, costal, nasal, larynx (thyroid, cricoid, most of arytenoid), trachea, bronchi, epiphyseal plates, fetal skeleton	glassy, homogeneous, basophilic; isogenous groups; calcifies with age
Elastic	dense elastic fibre network + type II collagen	yes	auricle, wall of external acoustic meatus, auditory tube, epiglottis, corniculate and cuneiform cartilages, vocal process of arytenoid	yellowish fresh; flexible support; elastic fibres shown by orcein (brown) or resorcin-fuchsin; does not calcify
Fibrocartilage	thick type I collagen bundles + some type II	no	intervertebral disc (anulus fibrosus), pubic symphysis, menisci, articular discs (temporomandibular, sternoclavicular), some tendon and ligament insertions	small chondrocytes single or in rows between bundles; mostly acidophilic; withstands compression and tension

Cartilage cells and matrix regions

COMPONENT	DESCRIPTION	NOTE
Perichondrium, fibrous layer	outer dense connective tissue, type I collagen, fibroblasts	carries the capillaries that feed the cartilage
Perichondrium, chondrogenic layer	inner cellular layer of chondroprogenitor cells	source of appositional growth
Chondroblast	matrix-secreting cell at the surface, not yet in a lacuna	becomes a chondrocyte once enclosed
Chondrocyte	cell in a lacuna; flattened superficially, large and round deep	shrinks from the lacunar wall in paraffin sections
Isogenous group	cluster of chondrocytes from one parent cell	sign of interstitial growth
Chondron	chondrocyte or isogenous group + its pericellular matrix	functional unit
Capsular (pericellular) matrix	thin rim lining each lacuna; richest in sulfated GAGs; type VI collagen	stains most intensely
Territorial matrix	basophilic matrix around each isogenous group	high sulfated GAG content
Interterritorial matrix *(slide 10 says type III collagen; Junqueira: type II)*	matrix between groups; fewer proteoglycans, type II collagen	stains paler

Hyaline matrix molecules

MOLECULE	ROLE
Type II collagen	fine fibrils, ~40% of dry weight; resist tension
Aggrecan	proteoglycan with chondroitin and keratan sulfate; binds water, resists compression; makes matrix basophilic

Bone cells

CELL	ORIGIN	LOOK	WHERE	FUNCTION
Osteoprogenitor cell	mesenchymal stem cells	flattened, spindle-shaped, pale oval nucleus, scant cytoplasm	inner periosteum, endosteum	divides; differentiates into osteoblasts
Osteoblast	osteoprogenitor cell	cuboidal to columnar, basophilic (much RER), in a single layer	bone surfaces where bone forms	secretes osteoid (type I collagen, proteoglycans, osteocalcin) toward the bone; starts mineralisation (alkaline phosphatase, matrix vesicles)
Osteocyte *(slide 38 is titled 'Osteoclast' but shows an osteocyte in its lacuna)*	osteoblast enclosed in matrix	less RER, smaller Golgi, condensed chromatin; many processes	one per lacuna; processes in canaliculi	maintains matrix; senses load; gap junctions with neighbours
Bone lining cell	inactive osteoblast	flat, thin	quiescent bone surfaces (part of endosteum)	maintains surface; can reactivate
Osteoclast	fusion of monocyte-macrophage precursors (haematopoietic)	giant (up to ~100 um), up to ~50 nuclei, acidophilic	Howship lacunae on bone surfaces	resorbs bone: H+ pumps dissolve mineral, cathepsin K and MMPs digest collagen

Bone matrix composition

PART	COMPONENTS	GIVES BONE
Organic (osteoid)	~90% type I collagen; proteoglycans; glycoproteins osteocalcin, osteonectin, osteopontin, bone sialoprotein	tensile strength, flexibility
Inorganic *(slide 31 gives inorganic 67%, Ca 39%, phosphate 17%, carbonate 9.8%; Junqueira: inorganic ~50% of dry matrix weight)*	hydroxyapatite Ca10(PO4)6(OH)2 along and between collagen fibrils; also carbonate, citrate, Mg, Na, K	hardness, stiffness

Bone tissue types

TYPE	STRUCTURE	WHERE
Woven (primary)	irregular collagen, many osteocytes, lower mineral (less dense on X-ray)	embryo, fracture repair; adult sutures, tooth sockets, tendon insertions
Lamellar (secondary)	collagen in parallel sheets (lamellae, 3-7 um)	all adult compact and spongy bone
Compact (cortical)	dense, osteons + circumferential and interstitial lamellae	shafts of long bones, outer and inner tables of flat bones
Spongy (cancellous)	network of trabeculae with marrow spaces; usually no osteons; fed from marrow	epiphyses, metaphyses, diploe, vertebral bodies

Structures of compact bone

STRUCTURE	DESCRIPTION
Osteon (Haversian system)	4-20 concentric lamellae around a central canal, parallel to the long axis
Concentric lamellae	collagen parallel within a lamella, at a different angle in the next
Central (Haversian) canal	lengthwise canal with vessels, nerves, loose connective tissue; lined by endosteum
Perforating (Volkmann) canal	crosswise canal joining central canals and the surfaces; not ringed by lamellae
Lacunae	spaces holding osteocytes; in compact and spongy bone
Canaliculi	fine channels running radially between lacunae and to the central canal
Cement line	outer boundary of each osteon; mineralised matrix with few collagen fibres
Interstitial lamellae	angular remnants of older osteons partly resorbed in remodelling
Outer circumferential lamellae	around the whole shaft, deep to the periosteum
Inner circumferential lamellae	around the shaft at the endosteal surface, facing the medullary cavity

Coverings and marrow

STRUCTURE	MAKE-UP	NOTE
Periosteum, fibrous layer	outer dense connective tissue, type I collagen, fibroblasts	covers bone except articular surfaces
Periosteum, osteogenic layer	inner cellular layer, osteoprogenitor cells	bone growth in width and fracture repair
Sharpey (perforating) fibres	type I collagen bundles from periosteum into outer circumferential lamellae	anchor periosteum, tendons, ligaments
Endosteum	thin, mostly one layer of osteoprogenitor and lining cells	lines marrow cavity, trabeculae, central and perforating canals
Red marrow	haematopoietic cells on a stroma of reticular cells and fibres	high activity; spongy bone of flat bones, vertebrae, epiphyses
Yellow marrow	mostly adipocytes	low activity; adult diaphyses; can revert to red marrow

Bones by shape and parts of a long bone

TERM	MEANING	EXAMPLE OR NOTE
Long bone	longer in one dimension; shaft and two ends	tibia, femur, metacarpals
Short bone	length about equal to width	carpals, tarsals
Flat bone	thin plate: two compact tables + diploe	skull vault, sternum, scapula
Irregular bone	complex shape	vertebrae
Epiphysis	end of a long bone; spongy bone with red marrow, thin compact shell	covered by articular hyaline cartilage
Metaphysis	flared zone between diaphysis and epiphysis, next to the growth plate	mostly spongy bone
Diaphysis	shaft: thick compact bone around the medullary cavity	nutrient artery enters via nutrient foramen
Epiphyseal plate / line	hyaline growth cartilage; replaced by a line of bone after closure	site of lengthwise growth

3 Mnemonics

Osteoblasts Build, osteoClasts Chew (Carve): blasts form bone, clasts resorb it

4 Slide by slide

Slide 2 **Cartilage tissue (3 types)**

- Hyaline: commonest, glassy, fetal skeleton, joint surfaces
- Elastic: flexible (auricle, epiglottis)
- Fibrocartilage: resists compression (disc, menisci)

Slide 3 **Three cartilage types compared**

- Hyaline with perichondrium
- Elastic: fibres in gel-like ground substance
- Fibro: chondrocytes among collagen bundles

Slide 4 **Chondron drawing**

- Isogenous group + capsular (pericellular) matrix = chondron
- Each cell sits in a lacuna

Slide 5 **Functions of cartilage**

- Skeletal support with some flexibility
- Smooth articular surfaces; bears mechanical stress
- Template for endochondral bone

Slide 6 **Properties of cartilage**

- Resists compression and tension
- Low metabolic rate; keeps growing
- Avascular: fed by diffusion, so heals poorly

Slide 7 **Cartilage structure**

- Extracellular matrix (most of the volume) + cells

Slide 8 **The perichondrium**

- Outer fibrous layer, inner chondrogenic layer
- Chondrocytes flattened superficially, rounder deep

Slide 9 **Types by fibre content**

- Hyaline: fine type II fibrils
- Elastic: elastic fibres + type II
- Fibrous: thick type I bundles

Slide 10 **Hyaline cartilage**

- Chondrocytes in lacunae; isogenous groups from one cell
- Territorial matrix around each group, interterritorial between
- Matrix collagen is type II (slide says type III interterritorially)

Slide 11 **Hyaline cartilage drawing**

- Perichondrial fibroblast -> chondroblast -> chondrocyte
- Territorial vs interterritorial matrix

Slide 12 **Hyaline cartilage, H&E**

- Perichondrium on both faces
- Large central chondrocytes, shrunken from lacunar wall

Slide 13 **Hyaline cartilage, isogenous groups**

- Darker territorial matrix around groups
- Flattened cells at the periphery

Slide 14 **Elastic cartilage**

- Elastic fibres + type II collagen + proteoglycans; yellowish
- Auricle, external acoustic meatus, auditory tube, epiglottis, small laryngeal cartilages

Slide 15 **Elastic cartilage, H&E**

- Perichondrium on both faces
- Large chondrocytes in lacunae

Slide 16 **Elastic cartilage features**

- Elastin network marks it; has perichondrium
- Lacunae, isogenous groups; flexible support
- Stains: orcein, resorcin-fuchsin

Slide 17 **Elastic cartilage, auricle**

- Elastic fibres stained in the matrix
- Chondrocytes in lacunae

Slide 18 **Elastic cartilage, orcein**

- Elastic fibres dark brown

Slide 19 **Hyaline (articular) cartilage**

- Superficial chondrocytes flattened, parallel to surface
- Deep cells larger, in lacunae

Slide 20 **Fibrocartilage, intervertebral disc**

- Chondrocytes in lacunae among collagen fibres
- No perichondrium

Slide 21 **Fibrocartilage, H&E**

- Chondrocytes in rows between parallel collagen bundles

Slide 22 **Intervertebral disc**

- Anulus fibrosus: concentric fibrocartilage layers, bundles crossing at angles
- Nucleus pulposus: gel core

Slide 23 **Fibrocartilage, trichrome**

- Collagen bundles coloured by trichrome
- Small isogenous groups in long rows

Slide 24 **Fibrocartilage, low power**

- Thick pale acidophilic bundles
- Sparse small chondrocytes

Slide 25 **Fibrocartilage, H&E detail**

- Rounded cells in lacunae with basophilic rim
- Distinguishes it from dense regular connective tissue

Slide 27 **Periosteum and endosteum**

- Periosteum: outer fibrous + inner cellular layer
- Endosteum lines the marrow cavity

Slide 28 **Medullary cavity**

- Marrow in medullary cavity and spongy bone spaces
- Stroma of reticular cells and fibres
- Red = active haematopoiesis; yellow = fat

Slide 29 **Two types of bone tissue**

- Woven: embryo; adult sutures
- Lamellar: spongy and compact

Slide 30 **Bone histology**

- Cells: osteoblasts, osteocytes, osteoclasts
- Mineralised matrix: hydroxyapatite

Slide 31 **Chemical analysis of bone**

- Organic part mostly type I collagen
- Inorganic: calcium, phosphate, carbonate + traces of Na, Mg, K

Slide 32 **Bone matrix, ground section**

- Dark lacunae with radiating canaliculi

Slide 33 **Osteoblast lineage**

- Osteoprogenitor (spindle) -> osteoblast -> osteocyte

Slide 34 **Osteoblasts**

- Cuboidal, basophilic, eccentric nucleus
- Layer on the bone surface, secreting toward it

Slide 35 **Osteocyte, EM**

- Nucleus, sparse RER, mitochondria
- Thin unmineralised collagenous rim inside the mineralised lacunar wall

Slide 36 **Osteocyte lacunae, ground section**

- Spider-like lacunae with canaliculi
- Inner canaliculi open into the central canal

Slide 37 **Osteoclasts, SEM**

- Large cells spread on bone and trabecular surfaces

Slide 38 **Osteocyte in lacuna, SEM**

- Slide titled 'Osteoclast' but shows an osteocyte in a lacuna amid collagen
- One osteocyte per lacuna

Slide 39 **Osteoclast, H&E**

- Giant multinucleated acidophilic cell
- Sits in a Howship lacuna on the bone surface

Slide 40 **Classification of bones by shape**

- Long, short, flat, irregular
- Plus pneumatic and sesamoid in textbooks

Slide 41 **Long bone**

- Epiphyses, metaphyses, diaphysis, epiphyseal line
- Periosteum with Sharpey fibres; endosteum; nutrient artery
- Spongy bone in the ends, compact in the shaft

Slide 42 **Bone types by histology**

- Cancellous (spongy) and compact (cortical)

Slide 43 **Spongy bone in the skull**

- Diploe between compact tables
- Trabeculae

Slide 44 **Flat skull bone**

- Compact-spongy-compact sandwich

Slide 45 **Compact and spongy bone**

- Osteons with central canals; circumferential and interstitial lamellae
- Perforating canals and fibres; endosteum on trabeculae

Slide 46 **Lamellar systems drawing**

- Outer and inner circumferential lamellae
- Osteons and interstitial lamellae

Slide 47 **Osteon, ground section**

- Rings of lamellae around a central canal
- Lacunae between the rings

Slide 48 **Bone lamellae**

- Haversian canal, lamellae, lacunae, cement line
- Osteocyte processes in canaliculi

Slide 49 **Haversian and Volkmann canals**

- Volkmann canals join central canals crosswise
- Osteons run parallel to the long axis

Slide 50 **What is bone matrix**

- Mineralised extracellular framework of bone

Slide 51 **Biomechanics**

- Collagen + hydroxyapatite: tough and stiff
- Stiffer and tougher along the long axis; trabeculae follow stress
- Osteocytes sense fluid shear stress

5 Traps: the correct facts for common wrong answers

✓ The articular cartilage on the head of the femur is hyaline cartilage.

✓ Articular surfaces are covered by hyaline cartilage.

✓ Cells in lacunae scattered in a glassy matrix indicate hyaline cartilage.

✓ Costal cartilages are made of hyaline cartilage.

✓ Fibrocartilage forms the menisci of the knee and some tendon attachments to bone.

✓ Fibrocartilage suits intervertebral discs and menisci because it withstands both compression and strong pulling forces.

✓ Hyaline cartilage is named after glass because its fresh matrix is homogeneous and translucent.

✓ Hyaline cartilage is the most abundant cartilage and forms most of the fetal temporary skeleton.

✓ Intervertebral discs contain fibrocartilage.

✓ The anulus fibrosus and the pubic symphysis are made of fibrocartilage.

✓ The epiglottis is made of elastic cartilage.

✓ The C-shaped rings of the trachea are made of hyaline cartilage.

✓ The fibrocartilage matrix looks mostly pink in H&E because it is dominated by thick bundles of type I collagen.

✓ The pink band with fibroblast-like nuclei at the edge of a tracheal cartilage ring is the perichondrium.

✓ A chondron is a chondrocyte or isogenous group together with the matrix immediately around it.

✓ Hyaline cartilage matrix is basophilic because it is rich in sulfated glycosaminoglycans.

✓ In H&E-stained hyaline cartilage, the deep purple-blue colour of the matrix immediately around each chondrocyte comes from a high concentration of acidic sulfated glycosaminoglycans.

✓ The capsular (pericellular) matrix lining each lacuna is richest in sulfated glycosaminoglycans and stains most intensely.

✓ Articular cartilage covers bone surfaces where they move against each other.

✓ Bone, not cartilage, is the body's main reserve of calcium salts.

✓ Cartilage heals poorly because it has no blood vessels.

✓ Cartilage is avascular with a low metabolic rate.

✓ Cartilage is slow to heal because it is avascular.

✓ The capillaries supplying tracheal-ring chondrocytes lie in the perichondrium around the cartilage.

Histology Exam 1 · Lecture 6

Blood and haemopoiesis

1 High-yield facts

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. slide 2, 3

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

Centrifuged blood
Plasma ~55%, packed erythrocytes ~45% (haematocrit), buffy coat <1% (leukocytes + platelets) between them. slide 6, 7

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. slide 12, 14, 17

Haemoglobin
HbA = 2 α + 2 β globin chains, each with a haem whose Fe2+ binds one O2: up to 4 O2 per molecule, reversibly. slide 17, 18

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. slide 15

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. slide 21, 22, 23, 24

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. slide 26, 29, 31

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. slide 33, 35, 36

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. slide 37, 40, 41, 42, 43

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). slide 44, 45

Diapedesis
Leukocytes leave postcapillary venules by squeezing between endothelial cells (selectin rolling → integrin adhesion → transmigration); they use blood only for transport. slide 36, 57

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. slide 49, 56, 58, 61

2 Cheat sheet

Basic shows the must-knows, Intermediate everything on your slides, Advanced adds textbook detail (marked +).

Composition of blood

COMPONENT	AMOUNT	NOTE
Plasma	~55% of blood volume	water ~92%, proteins ~7%, other solutes ~1% (by weight)
Erythrocytes (haematocrit)	~45% of volume; ~4–6 million/μL	women ~3.9–5.5, men ~4.1–6.0 million/μL
Buffy coat	<1% of volume	leukocytes + platelets
Leukocytes	4 500–11 000/μL	granulocytes (neutrophil, eosinophil, basophil) and agranulocytes (lymphocyte, monocyte)
Platelets	150 000–400 000/μL	fragments, not cells

Plasma proteins

PROTEIN	MADE BY	FUNCTION
Albumin (most abundant)	liver	main source of colloid osmotic (oncotic) pressure; carrier of hormones, drugs, fatty acids
α and β globulins	liver	carriers of iron (transferrin), haemoglobin (haptoglobin), lipids; add to oncotic pressure
γ globulins (immunoglobulins)	plasma cells	antibodies; the one major plasma protein not made by liver
Fibrinogen (smallest share of the main groups, ~4–7%)	liver	converted to fibrin threads of the clot
Prothrombin and other clotting factors	liver	coagulation cascade (thrombin forms fibrin)
Lipoproteins	liver	transport of triglycerides and cholesterol

Leukocytes

CELL	DIAMETER	% OF LEUKOCYTES	NUCLEUS	CYTOPLASM / GRANULES	LIFE	MAIN ROLE
Neutrophil (granulocyte) *slide 21 gives 60–79% and slide 23 1–5 lobes*	12–15 µm	50–70%	3–5 lobes; drumstick (Barr body) in women; band = unsegmented young form	pale lilac-pink specific granules (lysozyme, lactoferrin, collagenase, alkaline phosphatase) + azurophilic lysosomes	blood ~6–7 h, tissue 1–4 days	phagocytosis of bacteria; H_2O_2 and other oxidants
Eosinophil (granulocyte)	12–15 µm	1–4%	bilobed	large orange-red specific granules with crystalloid core (major basic protein, eosinophil peroxidase, histaminase)	1–2 weeks	kills helminths; phagocytoses antigen–antibody complexes; rises in allergy, falls with corticosteroids
Basophil (granulocyte) *slide 31 says heparan sulfate; Junqueira gives heparin*	12–15 µm	0.5–1% (rarest)	bi- or irregularly lobed, hidden by granules	coarse dark blue-purple granules: heparin, histamine, leukotrienes (SRS-A)	several months	vasodilation and allergy (IgE receptors); supplements mast cells
Lymphocyte (agranulocyte)	small 6–8 µm, large up to 18 µm	20–30%	round, dense, heterochromatic, nearly fills cell	thin rim of pale blue cytoplasm (free ribosomes), few azurophilic granules	days to years	specific immunity
Monocyte (agranulocyte) *slide 35 gives 12–100 h in blood*	12–20 µm (largest)	3–8%	oval, indented or kidney-shaped, eccentric, finer paler chromatin	grey-blue, fine azurophilic granules (lysosomes), often vacuolated	blood 1–3 days, then months as macrophage	becomes macrophage; removes debris and microbes with lysosomal enzymes; antigen presentation
— B lymphocyte	small	~15–20% of lymphocytes	as lymphocyte	surface immunoglobulin	memory cells years	matures in marrow; becomes antibody-secreting plasma cell (humoral immunity)
— T lymphocyte	small	~75–80% of lymphocytes (most)	as lymphocyte	T-cell receptor	memory cells years	matures in thymus; helper (CD4), cytotoxic (CD8), regulatory (slide 41: 'suppressor') and memory cells; cell-mediated immunity

CELL	DIAMETER	% OF LEUKOCYTES	NUCLEUS	CYTOPLASM / GRANULES	LIFE	MAIN ROLE
— NK cell	larger	~5–10% of lymphocytes	as lymphocyte	large granular lymphocyte (perforin, granzymes)	—	kills virus-infected and tumour cells without prior sensitisation

Erythrocyte membrane skeleton

COMPONENT	POSITION / LINK	ROLE
Spectrin	network on cytoplasmic (inner) face of membrane	flexibility and biconcave shape; lets cell deform through capillaries
Actin (short filaments) + tropomyosin	junctional complexes joining spectrin tetramers	nodes of the network
Ankyrin	binds spectrin to band 3	anchors network to membrane
Band 3	transmembrane protein	Cl^-/HCO_3^- exchanger; ankyrin anchor
Protein 4.1	binds spectrin–actin junctions to glycophorin C	second anchor

Platelet zones and granules

PART	CONTENTS	ROLE
Hyalomere (peripheral, pale blue)	marginal bundle of microtubules, actin, myosin	keeps disc shape; contraction for clot retraction
Granulomere (central, purple)	α, δ, λ granules, mitochondria, glycogen	secretion and energy
α granules (largest, most numerous)	fibrinogen, PDGF, platelet factor 4, von Willebrand factor, other clotting factors	clotting, vessel repair
δ (dense) granules	serotonin, ADP, ATP, Ca^{2+}	vasoconstriction, platelet recruitment
λ granules	lysosomal enzymes	clot removal
Open canalicular system	invaginations of plasma membrane	rapid release of granule contents

Haemostasis by platelets (in order)

STEP	WHAT HAPPENS
1 Primary aggregation	platelets adhere to exposed collagen (via vWF) and form a plug
2 Secondary aggregation	released adhesive glycoproteins and ADP recruit more platelets; plug enlarges
3 Coagulation *slide 47 ties coagulation to fibrinogen + vWF; vWF acts mainly in adhesion*	clotting cascade: prothrombin → thrombin; fibrinogen → fibrin mesh trapping cells
4 Clot retraction	platelet actin and myosin contract; clot shrinks
5 Clot removal	plasminogen → plasmin (activators from endothelium) digests fibrin

Bone marrow

ITEM	FEATURE
Red marrow	haemopoietic; all marrow at birth; in adults in flat bones (skull, ribs, sternum, pelvis), vertebrae and proximal epiphyses of femur and humerus
Yellow marrow	mostly adipocytes; replaces red marrow with age; reverts to red after severe bleeding or hypoxia
Stroma	reticular cells + reticular fibres (type III collagen), macrophages
Parenchyma	haemopoietic cords between sinusoids
Sinusoids *slide 53 says continuous endothelium; Junqueira: discontinuous*	discontinuous endothelium; new cells cross the wall to enter blood
Matrix	collagen I and III, fibronectin, laminin, proteoglycans; hemonectin binds blood cells to matrix
Functions	blood cell production; destruction of old RBCs; iron storage in macrophages (haemoglobin breakdown)
Megakaryocyte position	lies on sinusoid wall, pushes proplatelets into lumen
Section look	empty round spaces = adipocytes (fat dissolved); islands of haemopoietic cells; giant megakaryocytes

Haemopoietic lineages

LINEAGE	PROGENITOR	STAGES	PRODUCT
Erythropoiesis	common myeloid → MEP (CFU-E)	proerythroblast → basophilic → polychromatophilic → orthochromatophilic erythroblast → reticulocyte	erythrocyte
Granulopoiesis	common myeloid → GMP (CFU-G)	myeloblast → promyelocyte → myelocyte → metamyelocyte → band → segmented	neutrophil, eosinophil, basophil
Monocytopoiesis *slide 61 derives monocytes from the myeloblast; textbooks: monoblast*	common myeloid → GMP (CFU-M)	monoblast → promonocyte → monocyte	monocyte → macrophage, osteoclast, myeloid dendritic cell
Thrombopoiesis	common myeloid → MEP (CFU-Meg)	megakaryoblast → promegakaryocyte → megakaryocyte (endomitosis, polyploid)	platelets (cytoplasm fragments)
Mast cell line	common myeloid	precursors leave marrow, mature in connective tissue	mast cell
Lymphopoiesis *slide 56 lists the blasts as 'stem cells'; they are committed precursors*	common lymphoid	lymphoblast → prolymphocyte → lymphocyte; T precursors mature in thymus	B, T, NK cells; B → plasma cell

Maturation stages: red and granulocyte series

STAGE	NUCLEUS	CYTOPLASM
Proerythroblast	large, nucleoli, fine chromatin	basophilic (ribosomes)
Basophilic erythroblast	smaller, condensing	strongly basophilic
Polychromatophilic erythroblast	condensed, checkerboard	grey-lilac (Hb + ribosomes)
Orthochromatophilic erythroblast (normoblast)	small, pyknotic; extruded at this stage	pink (Hb)
Reticulocyte	none	pink, residual ribosomes; ~1 day more in marrow/blood
Myeloblast	large, nucleoli	basophilic, no granules
Promyelocyte	round, nucleoli	azurophilic (primary) granules appear
Myelocyte	round to slightly flattened	specific granules appear; lineage (N, E, B) now recognisable; last stage that divides
Metamyelocyte	kidney-shaped indentation	specific granules
Band (stab) cell	curved, unsegmented band	specific granules; up to a few % in blood
Segmented granulocyte	lobed	mature

3 Mnemonics

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

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

4 Slide by slide

Slide 2 **General characteristics**
- Viscous red fluid in a closed circulation
- pH 7.35–7.45, ~38 °C

Slide 3 **Blood as connective tissue**
- Cells in a liquid matrix (plasma)
- Fibres (fibrin) appear only in clotting
- Transport medium of the body

Slide 4 **Blood volume**
- ~7–8% of body weight
- men 5–6 L, women 4–5 L

Slide 5 **Functions of blood**
- Transport of gases, nutrients, wastes, hormones
- pH, osmotic and heat regulation
- Defence and clotting

Slide 6 **Centrifuged blood**
- Plasma ~55%, red cells ~45%
- Buffy coat <1%: leukocytes + platelets

Slide 7 **Composition of blood**
- Plasma: water ~92%, proteins ~7%
- Formed elements and their counts
- Differential: neutrophils most, basophils fewest

Slide 8 **Plasma and formed elements (diagram)**
- Albumin the largest protein fraction
- Platelets 150 000–400 000/µL

Slide 9 **Plasma proteins**
- Albumin: oncotic pressure, made in liver
- α/β globulins carriers; γ globulins = antibodies from plasma cells
- Fibrinogen, prothrombin, lipoproteins from liver

Slide 10 **Formed elements**
- Erythrocytes, leukocytes, platelets
- Granulocytes: neutrophil, eosinophil, basophil
- Agranulocytes: lymphocyte, monocyte

Slide 11 **Formed elements table**
- Size, count, share, maturation time, lifespan of each element
- RBC 120 days; neutrophil commonest, lymphocyte second, basophil rarest

Slide 12 **Erythrocytes**

- Biconcave ~7.5 µm disc, no nucleus or organelles
- Hb, carbonic anhydrase
- Spectrin on inner membrane face gives flexibility

Slide 13 **Erythrocyte membrane skeleton**

- Spectrin–actin network with tropomyosin
- Ankyrin to band 3; protein 4.1 to glycophorin C

Slide 14 **Structure suits gas transport**

- Biconcave shape: large surface area
- ~97% of dry mass Hb
- Anaerobic ATP: carried O2 not consumed

Slide 15 **Reticulocytes**

- Immature RBC ~1% (slide: 1–2%), slightly larger
- Residual ribosomal RNA
- Rise when RBC output rises

Slide 16 **Blood smear**

- Drop spread thin with a second slide edge
- Romanowsky-type stain (Wright, Giemsa)

Slide 17 **Erythrocyte function**

- Respiratory gas transport
- Hb binds O2 reversibly; 4 O2 per molecule

Slide 18 **Haemoglobin**

- 2 α + 2 β globin chains
- Each with a haem; its iron binds one O2

Slide 20 **Leukocyte classes**

- Granular: neutrophil, eosinophil, basophil
- Non-granular: lymphocyte, monocyte

Slide 21 **Granular leukocytes compared**

- Neutrophil 50–70%, multilobed, fine pale granules
- Eosinophil 1–4%, bilobed, pink-red granules
- Basophil 0.5–1%, S-shaped nucleus, dark blue granules

Slide 22 **Neutrophil (micrograph)**

- Segmented mature nucleus
- Neutral-staining specific granules

Slide 23 **Neutrophil structure**

- 12–15 µm, 3–5 lobes; drumstick = inactive X in women
- Specific granules: alkaline phosphatase, collagenase, lactoferrin, lysozyme
- Azurophilic granules = lysosomes

Slide 24 **Neutrophil life and function**

- Blood half-life ~6–7 h; tissue 1–4 days, then apoptosis
- Phagocyte; H2O2; lysozyme digests bacterial wall

Slide 25 **Neutrophil in a smear**

- ~2× RBC diameter, 3–5 lobes joined by strands
- Pale pink-lilac fine granules

Slide 26 **Eosinophils**

- Bilobed nucleus, many specific granules
- Kill parasites; phagocytose immune complexes; rise in allergy
- Corticosteroids lower their count

Slide 27 **Eosinophil in a smear**

- Two-lobed nucleus
- Large uniform orange-red granules

Slide 28 **Basophil (micrograph)**

- Lobed nucleus obscured by granules
- Coarse basophilic granules

Slide 29 **Basophils**

- Rare in smears
- Granules: heparin and histamine; vasodilation
- Function overlaps mast cells

Slide 30 **Basophil in a smear**

- Neutrophil-sized; nucleus hidden by dark blue-purple granules
- 0.5–1% of leukocytes

Slide 31 **Basophil granule contents**

- Heparin (sulfated GAG)
- Histamine, leukotrienes (SRS-A): dilate small vessels

Slide 32 **Agranulocytes (micrographs)**

- Lymphocyte: round dark nucleus
- Monocyte: indented nucleus, grey-blue cytoplasm

Slide 33 **Lymphocyte vs monocyte**

- Lymphocyte 20–30%, round nucleus, B and T cells
- Monocyte 3–8%, indented oval nucleus, largest leukocyte

Slide 34 **Monocyte (micrograph)**

- Kidney-shaped nucleus, finer chromatin
- Low N:C ratio, vacuoles common

Slide 35 **Monocytes**

- 12–20 µm, eccentric kidney-shaped nucleus, paler than lymphocyte
- Grey-blue cytoplasm, azurophilic granules
- Short stay in blood, then macrophages; no return

Slide 36 **Monocyte function**

- Work in tissues as macrophages
- Clear necrotic debris and microbes with lysosomal enzymes

Slide 37 **Lymphocytes**

- Small 6–8 µm, large up to 18 µm
- Dense nucleus, thin blue ribosome-rich rim
- B mature in marrow, T in thymus

Slide 38 **Small lymphocyte in a smear**

- RBC-sized, nucleus nearly fills cell
- Pale blue rim from free ribosomes

Slide 39 **Lymphocyte (EM)**

- Heterochromatin-rich round nucleus
- Thin cytoplasm, short microvilli

Slide 40 **Types of lymphocytes**

- T, B and NK cells
- B cells: humoral immunity

Slide 41 **B and T cells**

- B → plasma cells → antibodies
- T cells most blood lymphocytes: helper, regulatory, cytotoxic
- Memory cells give lasting immunity

Slide 42 **T lymphocytes**

- Cell-mediated immunity

Slide 43 **NK cells**

- Large granular lymphocytes
- Kill tumour and virus-infected cells without sensitisation

Slide 44 **Platelets**

- Anucleate megakaryocyte fragments, 2–4 μm, ~10 days
- Hyalomere (microtubule bundle) and granulomere

Slide 45 **Platelet ultrastructure**

- α, δ (dense) and λ (lysosome) granules
- Open canalicular and dense tubular systems, mitochondria, glycogen

Slide 46 **Platelets in a smear**

- Small purple fragments between RBCs, often clumped
- Purple granulomere, pale rim

Slide 47 **Platelet function**

- Primary then secondary aggregation
- Coagulation, clot retraction (actin–myosin)
- Clot removal by plasmin

Slide 49 **Bone marrow**

- Main adult site of haemopoiesis
- Output matches demand; rises several-fold fast

Slide 50 **Red and yellow marrow**

- Red: haemopoietic; all marrow at birth
- Yellow: adipocytes; reverts to red after bleeding or hypoxia

Slide 51 **Marrow section**

- Empty round spaces = dissolved adipocyte fat
- Islands of haemopoietic cells

Slide 52 **Red marrow structure**

- Stroma: reticular cells and fibres, macrophages
- Parenchyma: haemopoietic cords + sinusoids

Slide 53 **Marrow matrix**

- Collagen I and III, fibronectin, laminin, proteoglycans
- Hemonectin binds blood cells to matrix
- Sinusoid endothelium discontinuous (slide: continuous)

Slide 54 **Red marrow (micrograph)**

- Megakaryocytes: giant cells, lobulated nucleus
- New cells enter blood through sinusoid walls

Slide 55 **Functions of red marrow**

- Blood cell production
- RBC destruction; iron stored in macrophages

Slide 56 **Production of blood cells**

- Proerythroblast → RBC; myeloblast → granulocytes
- Lymphoblast → lymphocytes; monoblast → monocytes
- Megakaryoblast → platelets

Slide 57 **Diapedesis**

- Leukocytes cross intact venule walls
- Squeeze between endothelial cells

Slide 58 **Haemopoietic tree**

- Stem cell → common myeloid and common lymphoid progenitors
- Stage sequences of each lineage
- Band cell = unsegmented young neutrophil

Slide 59 **Erythropoiesis**

- Proerythroblast → basophilic → polychromatophilic → orthochromatophilic erythroblast → reticulocyte
- Nucleus extruded from orthochromatophilic erythroblast

Slide 60 **Granulocyte differentiation**

- Myeloblast → promyelocyte → myelocyte → metamyelocyte → band → segmented
- Lineage fixed at myelocyte (specific granules)

Slide 61 **Simplified haemopoietic tree**

- Myeloid: RBC, platelets, granulocytes, monocytes, mast cells
- Lymphoid: B, T, NK; B → plasma cell
- Monocytes come from monoblast (slide: myeloblast)

Slide 62 **Megakaryocyte**

- Endomitosis → polyploid lobulated nucleus
- Sits on sinusoid wall, releases platelets into lumen

5 Traps: the correct facts for common wrong answers

✓ Circulating blood is slightly warmer than core body temperature, at about 38 degrees C.

✓ The normal pH of arterial blood is 7.35-7.45.

- ✓ The fibres of blood become visible as fibrin threads only when blood clots.
- ✓ An adult man has about 5-6 litres of blood.
- ✓ Blood makes up about 7-8% of adult body weight.
- ✓ Antibodies are secreted by plasma cells derived from B lymphocytes.
- ✓ Centrifuged blood is about 55% plasma, 45% erythrocytes and less than 1% buffy coat.
- ✓ The buffy coat of centrifuged blood contains leukocytes and platelets.
- ✓ Albumin holds water in the blood vessels by oncotic pressure.
- ✓ Albumin is produced by the liver.
- ✓ By weight, the chief constituent of blood plasma is water, at about 90%.
- ✓ Fibrinogen, at about 4%, is the smallest of the three main plasma protein groups.
- ✓ Plasma occupies about 55% of the volume of centrifuged blood.
- ✓ Proteins make up about 7% of blood plasma by weight.
- ✓ The normal adult red cell count is about 4.2-6.2 million per microlitre.
- ✓ The total leukocyte count of a healthy adult is about 4,000-11,000 per microlitre (4-11 x 10^9 per litre).
- ✓ Albumin is the most abundant plasma protein, about 58% of the total.
- ✓ Plasma is about 92% water by weight.
- ✓ The normal platelet count is about 150,000 to 400,000 per cubic millimetre.
- ✓ Albumin is the plasma protein chiefly responsible for oncotic pressure.
- ✓ Albumin, fibrinogen and most other plasma proteins are synthesised by the hepatocytes of the liver.
- ✓ Alpha and beta globulins carry iron, haemoglobin and lipids in the plasma.
- ✓ Immunoglobulins are produced by plasma cells, not by the liver.
- ✓ Prothrombin and fibrinogen are both made in the liver and needed for clot formation.

Histology Exam 1 · Lecture 7

Muscle tissue

1 High-yield facts

Three muscle types
Skeletal (striated, voluntary), cardiac (striated, involuntary), smooth (no striations, involuntary). Striation = sarcomeres of neighbouring myofibrils lying in register. slide 2, 3

Muscle vocabulary
Sarcolemma = cell membrane; sarcoplasm = cytoplasm; sarcoplasmic reticulum (SR) = smooth ER storing Ca2+; a skeletal 'fibre' = one whole multinucleated cell. slide 4, 9

Origin and development
Mostly mesoderm. Skeletal fibre = syncytium from fusion of many myoblasts into a myotube (central nuclear chain), whose nuclei then move to the periphery. slide 4, 6

Satellite cells
Quiescent mononuclear myogenic stem cells between sarcolemma and external lamina; on injury they proliferate and fuse to repair or form fibres. slide 6

Sarcomere
Z disc to Z disc, ~2.5 um at rest = one A band + half of each flanking I band. The contractile unit of striated muscle. slide 12, 14

Sliding filament model
Filaments keep their length; thin filaments slide toward the M line. Sarcomere, I band and H zone shorten; A band constant. slide 19, 22

Triad vs diad
Skeletal: triad = T tubule + 2 terminal cisternae, at each A-I junction (2 per sarcomere). Cardiac: diad = T tubule + 1 cistern, at the Z line. slide 21, 35

Ca2+ controls contraction
ACh at the motor end plate -> action potential along sarcolemma and T tubules -> SR releases Ca2+ -> Ca2+ binds troponin C -> tropomyosin shifts, uncovering the myosin-binding sites on actin -> cross-bridge cycling. slide 23

Intercalated discs
Step-like dark transverse lines at cardiac cell ends, at the level of a Z line. Transverse part: fasciae adherentes + desmosomes; lateral part: gap junctions (functional syncytium). slide 26, 33, 34

Purkinje fibres
Modified cardiomyocytes in the subendocardial layer: larger, pale, glycogen-rich, sparse peripheral myofibrils; conduct faster than ordinary myocardium. slide 37, 39

Smooth muscle contractile apparatus
No myofibrils or sarcomeres; actin and myosin form an oblique lattice anchored to dense bodies (cytoplasmic) and dense plaques (sarcolemmal), linked by intermediate filaments. slide 42, 44

2 Cheat sheet

Basic shows the must-knows, Intermediate everything on your slides, Advanced adds textbook detail (marked +).

Skeletal vs cardiac vs smooth muscle

FEATURE	SKELETAL	CARDIAC	SMOOTH
Cell shape	long unbranched cylinder	short, branched, joined end to end	spindle (fusiform), tapering ends
Size	10-100 um wide, up to many cm long	~15 um wide, 85-100 um long	5-10 um wide, 20 um (small vessels) to 500 um (pregnant uterus)
Nuclei	many, flattened, peripheral, deep to sarcolemma	1 (or 2), central, oval	1, central, elongated (cigar); corkscrew when contracted
Striations	yes	yes	no
Myofibrils / sarcomeres	yes	yes	no; oblique lattice on dense bodies
Cell junctions	none between fibres	intercalated discs (fascia adherens, desmosome, gap junction)	gap junctions
T tubules / SR	triads at A-I junction; extensive SR	diads at Z line; wider T tubules, less SR	no T tubules; caveolae; sparse SR
Control	voluntary (somatic motor nerve)	involuntary, intrinsic pacemaker + autonomic	involuntary: autonomic, hormones, stretch
Contraction	strong, quick, discontinuous	strong, quick, rhythmic, continuous	weak, slow, sustained; fatigue-resistant
Connective tissue	epi-, peri-, endomysium	endomysium rich in capillaries	external lamina + reticular fibres

Organisation of skeletal muscle

LEVEL	WHAT IT IS	WRAPPING / CONTENTS	NOTE
Whole muscle	many fascicles	epimysium (dense CT)	continues into tendon; deep fascia superficial to it
Fascicle	bundle of fibres	perimysium	larger arteries, veins, nerves run here
Muscle fibre	one multinucleated cell	endomysium (reticular fibres, capillaries, nerve twigs) + external lamina	nuclei between fibres = fibroblasts, endothelium
Myofibril	chain of sarcomeres, ~1-2 um wide	wrapped by SR network	dots in TS; mitochondria in rows between
Myofilament	thick (myosin) and thin (actin)	-	thick ~15 nm x 1.6 um; thin ~8 nm x 1.0 um

Bands and lines of the sarcomere

BAND / LINE	CONTAINS	APPEARANCE	IN CONTRACTION
Z disc (line)	alpha-actinin; anchors thin filaments, titin	thin dark line bisecting I band	Z discs move closer
I band	thin filaments only	light; isotropic in polarised light	narrows; almost gone at full contraction
A band	thick filaments (+ overlapping thin)	dark; anisotropic (birefringent)	constant length (= thick filament)
H zone	thick filaments only (no thin-filament overlap); its centre is the bare zone, without myosin heads	paler zone in middle of A band	narrows; disappears at full contraction
M line	myomesin, creatine kinase cross-linking thick filaments	thin dark line bisecting H zone	stays central
Overlap zone (TS)	each thick among 6 thin (hexagon); each thin among 3 thick	rosettes in EM	widens
Sarcomere *(slide 12 writes it as Z + I/2 + A/2 + H + M + H + A/2 + I/2 + Z, i.e. H and M are inside the A band)*	Z to Z: A band + 2 half I bands	~2.5 um resting	shortens

Proteins of the striated contractile apparatus

PROTEIN	LOCATION	ROLE
Actin (G -> F)	thin filament: 2 F-actin strands in a helix	has myosin-binding sites
Tropomyosin	in grooves of F-actin helix	covers myosin-binding sites at rest
Troponin (TnT, TnC, TnI)	on tropomyosin, thin filament	TnT binds tropomyosin, TnC binds Ca2+, TnI inhibits actin-myosin binding
Myosin II	thick filament (~200-500 molecules, bipolar)	2 heavy + 4 light chains; head = actin-binding site + ATPase; hinge lets head pivot
Light / heavy meromyosin	trypsin fragments of myosin	LMM = rod (tail); HMM = heads + short rod
Titin	Z disc to M line, along thick filament	elastic spring; centres thick filament; passive elasticity
Nebulin	along thin filament from Z disc	sets thin filament length
Alpha-actinin	Z disc (and smooth muscle dense bodies)	anchors thin filaments

Excitation-contraction coupling in skeletal muscle

STEP	EVENT	STRUCTURE
1	ACh released from axon terminal (blocked by botulinum toxin)	neuromuscular junction (motor end plate)
2	ACh binds receptors -> sarcolemma depolarises; acetylcholinesterase ends signal	junctional folds of sarcolemma
3	action potential spreads into the fibre	sarcolemma -> T tubules
5	Ca2+ binds troponin C; tropomyosin shifts, exposing the myosin-binding sites on actin	thin filament
6	myosin heads bind actin, power stroke pulls thin filament toward M line; ATP detaches head	cross-bridges
7	relaxation: ATP-dependent Ca2+ pump returns Ca2+ to SR	SR membrane

Skeletal muscle fibre types

TYPE	LOOK	METABOLISM / SPEED	USE
Type I (slow oxidative, red)	small, dark red: much myoglobin, many mitochondria, rich capillaries	aerobic, slow twitch	fatigue-resistant, posture, endurance
Type IIb/IIx (fast glycolytic, white)	large, pale: little myoglobin, few mitochondria, much glycogen	anaerobic glycolysis, fast twitch	short bursts of force, fatigue quickly
Mixed muscles *(slide 25 shows only white (fast) vs red (slow); textbook has three types)*	most human muscles contain all types	proportions differ by muscle	fibre type set by its motor nerve

Cardiac muscle specialisations

STRUCTURE	WHERE	FEATURE	FUNCTION
Fascia adherens	transverse part of intercalated disc	anchors actin of terminal sarcomere	transmits pull cell to cell
Desmosome (macula adherens)	transverse part of intercalated disc	anchors intermediate filaments	keeps cells from pulling apart
Gap junction	lateral part of intercalated disc	ionic channels	spreads excitation: functional syncytium
Diad	at Z line	T tubule + one SR cistern	Ca2+ release
Mitochondria	between myofibrils	~40% of cytoplasm	continuous aerobic ATP supply
SA node	wall of right atrium	small modified cardiomyocytes	pacemaker
AV node -> AV bundle (His) -> bundle branches	atrial septum / interventricular septum	modified cardiomyocytes	conduct impulse to ventricles
Purkinje fibres	subendocardial layer of ventricles	large, pale, glycogen-rich, peripheral myofibrils, sometimes 2 nuclei	fast conduction to ventricular myocardium
Heart wall layers	endocardium, myocardium, epicardium	myocardium thickest	cardiac muscle in myocardium

Smooth muscle cell structure

STRUCTURE	FEATURE	FUNCTION
Dense bodies	cytoplasmic; contain alpha-actinin (like Z discs)	anchor thin filaments
Dense plaques	dense bodies attached to inner face of sarcolemma	transmit force to cell membrane
Thin and thick filaments	oblique crisscross lattice; thick filaments side-polar	contraction; cell shortens and bulges, nucleus corkscrews
Intermediate filaments	desmin (vimentin in vascular SM) linking dense bodies	spread pull across the whole cell
Caveolae	flask-shaped invaginations of sarcolemma	Ca2+ entry (T tubule equivalent)
Gap junctions	between neighbouring cells	coordinated contraction (visceral / single-unit)
External (basal) lamina	around each cell + reticular fibres	binds cells into a working unit
Organelles	mitochondria, Golgi, RER at the two poles of the nucleus	energy; secretion of collagen, elastin, proteoglycans
Arrangement	middle of one cell next to tapering ends of neighbours; in vessels circular or low helix	narrows lumen / propels contents

Identifying muscle in sections

TISSUE	LONGITUDINAL SECTION	TRANSVERSE SECTION	CLUE
Skeletal	long parallel fibres, cross-striations, many flattened peripheral nuclei	large polygonal profiles of even size, peripheral nuclei, none central	myofibrils as fine dots in TS
Cardiac	branching fibres, central nuclei, step-like intercalated discs	irregular profiles of varied size, single central nucleus in pale area; many capillaries	pale perinuclear zone
Smooth	overlapping spindles, elongated central nuclei, wavy when contracted	small round profiles, only some with a nucleus; little CT	no striations
Purkinje fibres	broad pale fibres deep to endocardium	large pale cells, central nucleus, myofibrils at periphery	glycogen-rich

3 Mnemonics

H zone, I band shrink; A stays: In contraction H and I narrow, A band constant ("HI shrink, A is Always the same")

dArk = Anisotropic; lIght = Isotropic: A band dark and anisotropic, I band light and isotropic

Epi-Peri-Endo: Wrappings from surface to single fibre: epimysium, perimysium, endomysium

4 Slide by slide

Slide 2 **Three muscle types compared**

- Skeletal: striated, voluntary, strong quick discontinuous; long cell, peripheral nuclei
- Cardiac: striated, involuntary, continuous; short branched cells, central nuclei
- Smooth: not striated, involuntary, slow; small spindles

Slide 3 **Types of muscle cells**

- Skeletal in limbs, cardiac in heart (branching), smooth in intestinal wall

Slide 4 **Common features of all muscle tissue**

- Mesodermal origin; contractile elements parallel to cell axis
- Loose CT between cells; specialised SR; sarcolemma

Slide 5 **Skeletal muscle, LM longitudinal**

- Flattened peripheral nuclei, cross-striations
- Endomysium between fibres

Slide 6 **Development of skeletal muscle**

- Myoblasts fuse into myotubes, which differentiate into fibres
- Satellite cells persist alongside fibres

Slide 7 **Organisation of skeletal muscle**

- Epimysium around muscle, perimysium around fascicle, endomysium around fibre
- Vessels and nerves run in perimysium

Slide 8 **Muscular architecture**

- Myofibrils, sarcoplasm, mitochondria between myofibrils
- SR network, terminal cisternae, T tubules, triads

Slide 9 **Skeletal muscle fibre**

- Nuclei near periphery; striations in LM

Slide 10 **Skeletal muscle micrographs**

- LS: peripheral nuclei, cross-striations
- TS: polygonal fibres, peripheral nuclei, CT between

Slide 11 **Hierarchy of skeletal muscle**

- Muscle > fascicle > fibre > myofibril > myofilament
- TS: I band thin only, H zone thick only, overlap hexagons
- G-actin -> F-actin; myosin -> light (rod) + heavy (head) meromyosin

Slide 12 **Sarcomere in EM**

- Sarcomere = A band + half of each flanking I band
- Z bisects I; M bisects H; I light, A dark

Slide 13 **Striation of myofibres**

- LM: cross-striations
- EM: Z line, A band, I band, H band, M band

Slide 14 **Sarcomere and myofilaments**

- Thick = myosin, thin = actin, titin from Z to M
- Filament arrangement produces the banding; present in skeletal and cardiac

Slide 15 **Filament lattice**

- Thin filaments anchored at Z
- Overlap TS: thick in hexagon, each thin among 3 thick

Slide 16 **A band and filament cross sections**

- Nebulin along thin, titin Z to thick filament
- Thick filament bipolar with bare central zone near M line

Slide 17 **Components of the sarcomere**

- Thick filaments joined at M line; titin as spring to Z
- Myosin molecule: tail, hinge, head that pivots

Slide 18 **Structure of actin and myosin**

- Thin: two F-actin strands, tropomyosin in groove, troponin
- Myosin: 2 heavy chains (coiled rod), hinge, 2 heads with light chains; heads = cross-bridges

Slide 19 **Sliding filaments**

- Sarcomere shortens, filaments keep length
- I and H narrow, A constant

Slide 20 **Skeletal fibre in 3D**

- Peripheral nucleus, myofibrils, SR, T tubules, triads, mitochondria

Slide 21 **Triad**

- T tubule flanked by two terminal cisternae
- At A-I junction, two per sarcomere

Slide 22 **Relaxed vs contracted sarcomere**

- Full contraction: I band almost gone, H zone gone
- Z discs reach thick filament ends; A band unchanged

Slide 23 **Excitation-contraction infographic**

- ACh at synapse (botulism blocks release); T tubules carry signal
- SR releases Ca2+, which binds troponin; myosin pulls actin using ATP
- ATP also pumps Ca2+ back into SR

Slide 24 **Skeletal muscle TS**

- Large polygonal fibres, flattened peripheral nuclei, thin endomysium
- Myofibrils as stippling; no central nucleus

Slide 25 **Skeletal fibre types**

- White (fast) pale vs red (slow) dark fibres

Slide 26 **Cardiac muscle**

- Central nucleus, branching, striations
- Intercalated discs as dark step-like transverse lines

Slide 27 **Heart wall**

- Endocardium, myocardium (thickest), epicardium

Slide 28 **Muscle types, renders**

- Skeletal long fibres, cardiac branching with discs, smooth spindles
- Cardiac TS: central nuclei, many capillaries

Slide 29 **Cardiac and smooth, renders**

- Smooth spindles with elongated central nuclei
- Cardiac and smooth TS: central nuclei, capillaries between

Slide 30 **Cardiac muscle (repeat)**

- Central nuclei, intercalated discs, striations

Slide 31 **Cardiac muscle in 3D**

- Branching fibres, intercalated discs, central nucleus
- T tubules, SR, abundant mitochondria

Slide 32 **Cardiac muscle LM**

- Oval central nuclei, discs as dark lines across fibres
- Cardiomyocyte nuclei larger and paler than fibroblast nuclei

Slide 33 **Cardiac muscle structure**

- Discs contain desmosomes and gap junctions
- T tubules at Z disc, SR, many mitochondria

Slide 34 **Intercalated disc**

- LM: dark step-like lines (iron haematoxylin)
- EM: interdigitating; fascia adherens and desmosome in transverse part

Slide 35 **Triad vs diad**

- Skeletal: triad around myofibrils
- Cardiac: T tubule at Z disc with one SR cistern (diad), larger T tubules, less SR

Slide 36 **Cardiac muscle TS**

- Irregular profiles, single central nucleus, some without
- Myofibrils radiating around nucleus; many capillaries

Slide 37 **Purkinje fibres**

- Specialised conducting cells in subendocardial CT
- Large, pale, glycogen-rich, myofibrils peripheral

Slide 38 **Conducting system**

- Gap junctions integrate cells
- SA node -> AV node -> AV bundle -> bundle branches -> Purkinje fibres

Slide 39 **Purkinje fibre micrograph**

- Broad pale-centred cells in loose CT deep to endocardium
- Sometimes binucleate

Slide 40 **Smooth muscle**

- Spindle cell, one central elongated nucleus
- TS: profiles of different sizes, nuclei only in some

Slide 41 **Isolated smooth muscle cell**

- Fusiform, tapering ends, rod-shaped central nucleus

Slide 42 **Actin and myosin in smooth muscle**

- Thin filaments oblique, anchored to dense bodies and dense plaques
- Side-polar thick filaments; caveolae, gap junctions

Slide 43 **Smooth muscle EM**

- Cells separated by external lamina
- Few organelles, cytoplasm full of filaments

Slide 44 **Smooth muscle contraction**

- Intermediate filaments link dense bodies
- Contracted cell shortens and bulges; nucleus corkscrew

Slide 45 **Vascular smooth muscle, SEM**

- Cells wrap circumferentially round vessel
- Contraction shortens cells, which bulge

Slide 46 **Comparison LS and TS**

- Skeletal: striated, peripheral nuclei, polygonal TS
- Cardiac: central nuclei, irregular TS
- Smooth: wavy elongated nuclei; small round TS profiles

5 Traps: the correct facts for common wrong answers

✓ A skeletal muscle fibre can reach a length of many centimetres.

✓ Aligned sarcomeres make skeletal and cardiac muscle striated.

✓ Cardiac muscle cells are about 100 µm long.

✓ Cardiac muscle gives strong, quick, rhythmic, continuous involuntary contractions.

✓ Cardiac muscle is striated yet contracts involuntarily.

✓ Skeletal muscle fibres are long multinucleated cells with nuclei at the edge.

✓ Skeletal muscle gives strong, quick, intermittent voluntary contractions.

✓ Smooth muscle gives weak, slow, involuntary contractions.

✓ Smooth muscle has no sarcomeres, so it shows no cross striations.

✓ Smooth muscle of the arterial wall is involuntary and not striated.

✓ Smooth muscle of the gut wall is involuntary and not striated.

✓ Striations, cylindrical cells and multiple nuclei are seen only in skeletal muscle.

✓ The largest smooth muscle cells, in the pregnant uterus, reach only about 0.5 mm.

✓ The muscle layers of the small intestine are smooth muscle.

✓ Cross striations are seen only in skeletal and cardiac muscle, not in smooth muscle.

✓ In every muscle type the contractile filaments run along the length of the cell, obliquely in smooth muscle, so contraction shortens the cell.

✓ Most muscle tissue in the body develops from mesoderm.

✓ The cell membrane of a muscle fibre is the sarcolemma.

✓ The cytoplasm of a muscle cell is called the sarcoplasm.

✓ In a longitudinal section of skeletal muscle, the nuclei are flattened and elongated at the edge of the fibre, just deep to the sarcolemma.

✓ Small dark nuclei between skeletal muscle fibres belong mostly to fibroblasts and capillary endothelial cells of the endomysium.

✓ A myotube has a central chain of nuclei with myofibrils around them.

✓ A skeletal muscle fibre arises by fusion of many myoblasts into a myotube.

✓ Damaged skeletal muscle is repaired mainly by satellite cells that proliferate and fuse into new fibres.