2401 Sample

Saturday, 18 June 2016
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Unit I – Cellular Foundations of Medical Science

Lecture 1: The Basics of Cell Structure and Function

Lecture Summary

- Methods for light and electron microscopy by histologists; Four basic tissue types; Overview of structure of human cells

Learning Outcomes

1.1 Define the histological terms described

Histology, study of the body cells and tissues + how tissues are organised into organs **Pathology**, study of diseased tissue

1.2 Summarise the basic steps of tissue preparation

FESS
Fix Embed Section Stain
=preserve, stiffen, resolution, contrast

The basic steps of tissue preparation are as follows:

1. Specimen Acquisition – fresh tissue is acquired in this step
2. **Fixation** – preserves structure
   Easier handling, prevent degradation, other internal factors: autolysis (attack by own enzymes), osmotic alterations (sudden movement of soluble ions), and ischemia (blood loss, thus O_2 & nutrients).
3. **Dehydration** – removes water
4. **Embedding** – stiffen to cut
5. **Section** – improves resolution, completed using microtome and sharp glass
6. Stain – produces contrast

Haematoxylin = blue/ nucleus; Eosin = pink-purple/ cytoplasm;
Masson's Trichrome Stain = red/ muscle and keratin, blue-green/ collagen and bone, pink/ cytoplasm, black/ cell nuclei

1.3 Explain the differences between a light and electron microscope image

	Light	**Electron**
Resolving Power	0.2 μm	3 nm
Maximum Magnification (eye)	2,000x	500,000x
Section Thickness	1 μm – 100 μm (5 μm)	0.025 μm

Typical magnification: 6,000x few cells, 12,000x one cell, 22,000x cell + organelles, 200,000x organelles

The resolving power, i.e. the ability to distinguish between two points of space in a microscope, differs for light and electron microscopes at 0.2 μm and 3 nm, respectively. The maximum magnification in regards to the human eye goes up to 2,000x for light versus 500,000x for electron (250-fold increase). Thicker sections are less resolved. Light usually have 1 μm – 100 μm sections but typically 5 μm; whereas, electron deals with 0.025 μm sections (200-fold smaller).

1.4 Know the classification parameters for the 4 basic tissue types

Tissue is an orderly arrangement and distinctive pattern of cells that co-operatively performs a function.

Based on Morphology (i.e. appearance)

1. **Epithelial** – free surface, continuous lining, repairs & renews, closely apposed cells junctions, single or multiple layers, basement membrane, underlying CT *Simple/ Stratified; Squamous/ Cuboidal/ Columnar*	2. **Connective** – support tissue, morphologically diverse, ground substance, fibroblast, fibres (elastin, collagen, etc.) *Loose/ Dense; Regular (tendon)/ Irregular (dermis)*

Based on Function

3. **Muscular** – muscle cell fibres, elongated, orientated, arranged in bundles Smooth/ Striated; Skeletal/ Cardiac	4. **Nervous** – PNS: nerve/ ganglia; CNS; white/ grey = cell bodies, axons, dendrites

1.5 Describe the plasma membrane

Lipid-bilayer structure surrounding cell, 9 nm wide, selectively permeable, dynamic/ fluid boundary, lipids & proteins, pumps, channels, receptors → TEM shows proteins/ hydrophilic heads, hydrophobic tails, and the intracellular space, *aka*. Rail tracks
Includes, cisternae (flat sheets of membrane e.g. ER), and cristae (folds of membrane e.g. mitochondria)

1.6 Explain how and why cells are compartmentalised

CELLULAR COMPARTMENTALISATION + acquiring/expenditure of energy occur → to maintain order (Entropy).
[Molecular chaos – cytoplasm crowded by organelles, inclusions small insoluble particles calcium crystals glycogen lipid droplet, and cytosol, water salt organic molecule soluble protein cytoskeletal protein filaments]

- Ensures correctness of molecule placement and timing
- Different compartments separated but functions co-operatively
- Cells contain large amounts of membrane to create compartments

Lecture 2: Nucleus and Cytoplasmic Organelles

Lecture Summary

- Structure of the nucleus and nuclear components, and of membranous and non-membranous organelles
- Relation of structure to physiological function in human cells

Learning Outcomes

2.1 Know the structure of the nucleus, chromatin and nucleolus

Nucleus of *non-dividing interphase cells* contain **chromatin**, DNA + HISTONES

- Euchromatin = DNA wraps around histones forming nucleosomes (extended, active, pale)
- Heterochromatin = multiple nucleosomes wrap to form a 30 nm chromatin fibre (condensed, inactive, dark)
  - Close to periphery, fibres bundle together to form chromosomes

Nucleus of *metaphase cells* (mitosis) has visible **chromosomes**

2.2 Compare and contrast the structure to the physiological function of the cell; know the structure of the membranous and non-membranous organelles; apply your knowledge of structure to the function of the organelle

	Structure	*Function*
Nucleolus	No membrane ~2 μm diameter, spherical, 1+ in nucleus (usually undistinguishable from chromatin)	Site of rRNA synthesis; Ribosomal assembly; rRNA DNA contained;
Nuclear pore	70 nm pore with thin diaphragm where nuclear envelope membranes merge	
Centrioles	Close to nucleus; Paired cylinders of 9 microtubule triplets	MTOC microtubule organising centre; Control microtubule number, polarity, direction and orientation; Organisation during interphase, cell cycle;
Cytoskeleton	(internal framework of filaments and tubules)	Structural support; Intracellular movement of organelles/ metabolites; Extracellular transport;
Microtubules	Tubulin protein; Hollow cylinders; 22 nm diameter, 5 nm thick walls; Dynamic instability (continually forming & disassembling, $t_{1/2}$ = minutes);	Intracellular transport; Cell shape; Cilia movement; Chromosome arrangement;
Microfilaments	Actin; Flexible; Helical array; 6 nm diameter;	Microvilli structure; Extension of cell processes;
Intermediate filaments	8 nm diameter; Heterogenous;	Mechanical strength and resistance to extracellular forces;
Mitochondria	Outer membrane/ Intermembrane space/ Inner membrane (cristae, elementary particles) Matrix (enzymes, Ca^{2+})	ATP generation via oxidative phosphorylation, citric acid cycle, b-oxidation of fatty acids; Initiate apoptosis via release of cytochrome c
rER	Cisternae + ribosomes	Protein synthesis for secretion; Chemical modifications; Membrane lipid synthesis;
sER	Cisternae, (anastomosing tubules with many enzymes) Glycogen, (inclusions)	Lipid, glycogen, steroid metabolism; Synthesise and secrete steroids; Isolates Ca^{2+}; Detoxification e.g. hepatocytes; Membrane formation;
Golgi apparatus	Crescent shape of stacked, flattened membrane bound cisternae with small vesicles budding off	Post-translational modification; Sorting and packaging proteins;
Secretory vesicles	Membrane bound	Contain protein to be exocytosed; Lysosome biogenesis;
Endosomes	Membrane bound Formed during endocytosis, via Golgi	Internalization of extracellular material; Recycling of membranes; Lysosome biogenesis;
Lysosomes	Membrane bound Formed from Golgi and Endosomes	Digestive enzymes (proteases, nucleases, lipases), hence common in macrophages and neutrophils

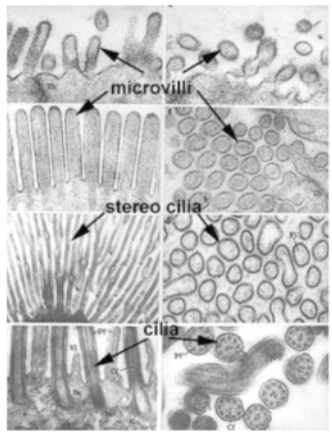
Lecture 5: Cell Membrane Specializations

Lecture Summary

- Interaction of the cell surface with the external environment
- Attachment and communication between cells, how and why?

Learning Outcomes

5.1 Know the types of specialisations on the apical, lateral, and basal plasma membranes; relating structure and location to function



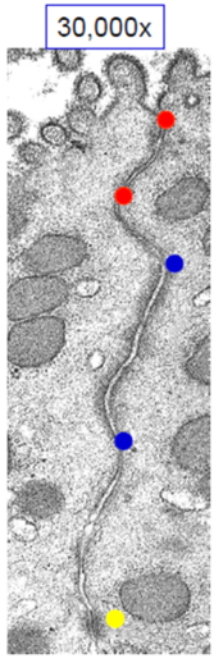
Cell membrane specialisations

Apical (facing a lumen/ free space required): microvilli, cilia, sterocilia

Villi are NOT an apical plasma membrane (PM) specialisation – folds of mucosa (epithelium + lamina propria/ CT)

- **Microvilli** – (i.e. brush border) 1-3 μm long, cytoplasmic protrusions, covered by PM, actin filament core, villi protein cap, ↑ free SA = ↑ absorption capacity
- **Cilia** – 2-10 μm long, axoneme core (= a cylinder of microtubules MTs formed into 9 doublets surrounding a central pair 9+2 arrangement, and dynein motor protein arms project out from the MTs), regular synchronous sweeping motion
  - Tubulin (MT), dynein arms (motor via temp. x-bridges) and nexin (passive elastic recoil) project out of MT doublets [assembled by centrioles + basal bodies]
- **Sterocilia** – 25-120 μm long immotile microvilli, twice diameter, actin filament core, located in epididymis and cochlear, passive movement due to fluid flow

[Special: Flagella: 50 μm long, propeller-like motion]



Lateral (facing other cells of the same type):

The junctional complex, or the terminal bar, is located at the apical pole of the lateral PM.

Occluding Junction

1. (0) **Zonula Occludens** = tight junctions, diffusion barrier

Adhesion: draws neighbouring cell PMs close together via cell adhesion molecules (CAMs)
Transmembrane proteins: Occludin and Claudin reinforce the site → electron dense region
Permeability: Selective movement of ions through the intercellular space (e.g. blood-brain barriers in capillaries of the brain) i.e. barrier
Linkage: into actin filaments of the cytoskeleton in the cytoplasm

Anchoring Junctions

2. (0) **Zonula adherens** = lateral adhesion between cells/ anchor via cytoskeleton

Reinforce: against mechanical stress
Adhesion: prevent lateral disruption by stabilizing the epithelial cells
Transmembrane protein: E-Cadherin, span uniform 15 nm spaces, Ca^{2+} dependent
Anchorage: cytoplasm actin filaments anchors

3. (0) **Macula adherens** (desmosomes) = spot adhesion/ anchor via cytoskeleton

Spot Adhesion: strong spot attachment site between cells, important in maintain integrity of epidermis
Transmembrane protein: Cardherin Zipper, Ca^{2+} dependent = electron dense line, 30 nm intercellular
Anchorage: sites for intermediate filaments

[Special: Located between epithelial cells and cardiac/ smooth muscle cells]

Communicating Junction

4. **Gap junctions** (nexus) = communication sites

Communication: Metabolic, ionic and electrical communication – type of voltage-gated channel
Transmembrane protein: 6 connexin proteins create circular channel, conformational changes open/ close channel (cylindrical channel 10 nm long, 3 nm diameter; 1.5 nm diameter aqueous pore; 2 nm intercellular space → not very electron dense)

Lateral interdigitations → lateral surface folds i.e. plicae of PM forming interdigitating border;
(1) ↑ Lateral PM SA for fluid and electrolyte transport
(2) Helps maintain cell's connections; form tissue

Lecture 6: The Four Basic Tissue Types

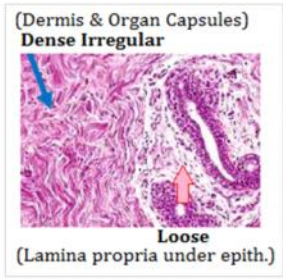
Lecture Summary

- Embryology of the 4 basic tissue types; Connective tissue in detail; Examples of specialised connective tissue discussed

Learning Outcomes

6.1 Define the embryology terms presented in this lecture

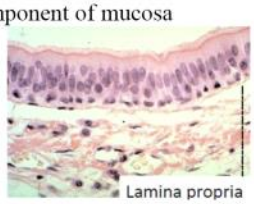
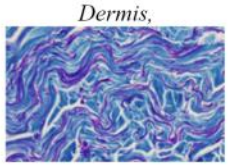
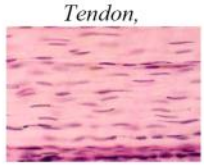
- **Tissue** – An orderly arrangement and distinctive pattern of cells which co-operatively perform a particular function
  - Structural = epithelial, connective; Functional = muscular, neural;
- **Connective Tissue** (CT) –cells and extracellular materials that provide the support and connecting framework for all the other tissue of the body



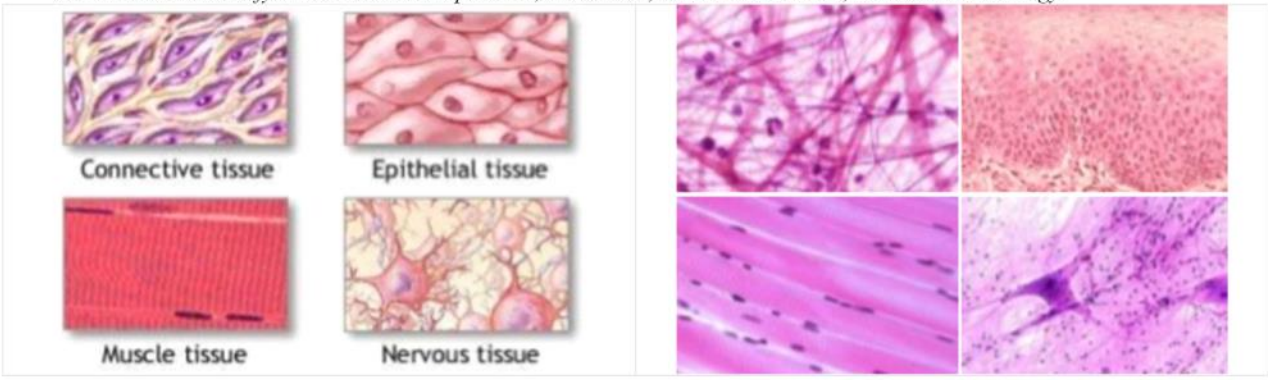
6.2 Know the tissue derivatives of the three germ layers

Refer to Practical 3, "All tissue derived from 3 primary germ cell layers: **ectoderm** (=skin/ glands), **endoderm** (=gut, respiratory, liver, pancreas, etc.), and **mesoderm** (=endothelium/ mesothelium glands)"

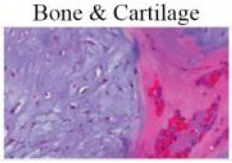
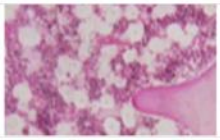
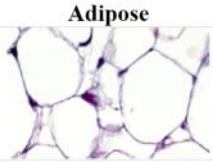
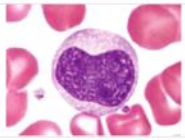
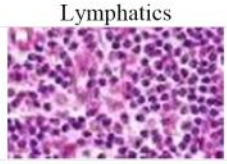
6.3 Define and classify the connective tissues

Proper			**Specialised**
Loose, -Highly cellular (fibroblasts, immune cells) -Few fibres (collagen ±elastin) -Numerous small BVs -Fluid-filled spaces present in the tissue due to excessive accumulation of fluid = oedema	**Dense**		
	Irregular, - Few cells (fibroblasts, immune cells) -Many fibres (all types), <u>random orientation</u> - Less fluid	**Regular**, - Few cells (fibroblasts) - Many fibres <u>in parallel</u> (collagen) - less fluid	
Lamina Propria, Loose CT under an epithelium, Commonly described in respir. & GIT CT component of mucosa  	*Dermis*,  *Submucosa*, (loose OR dense irregular CT) supports mucosa, contains BV and nerve plexi	*Tendon*, 	*Adipose, Blood, Bone, Cartilage, Lymphatic*
→includes areolar, reticular, adipose tissue →most common, holds organs in place and attaches epithelial tissue to underlying	→large portion of dermis, GIT submucosa, organ capsules, periosteum, perichondrium	→provides connection between different tissues →no elastic and reticular fibres = completely absent →tendons, ligaments	

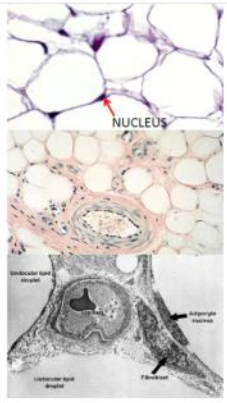
6.4 Be able to classify a tissue as either epithelial, connective, neural or muscular, based on its histology



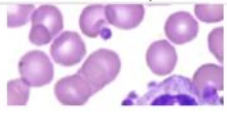
Specialised connective tissues

Bone & Cartilage	Marrow	**Adipose**	**Blood**	Lymphatics
				

Adipose

White adipose	Found in loose CT & adult bone marrow Functions: energy homeostasis, endocrine secretions, insulation & cushioning of vital organs • >100 µm diameter; round cells; flattened peripheral nucleus; thin rim of cytoplasm around lipid; produce leptin & angiotensinogen; rich BV supply, mast cells & nerves • e.g. epicardium, hypodermis, parathyroid gland • With limited energy storage as carbohydrate + proteins, energy reserves stored in lipid droplets (triglycerides) in adipocytes o Meal→pancreas releases insulin→adipocytes surface receptors→fatty acids & glycerol released → muscle & cardiac tissue/ liver → glycogenolysis & gluconeogenesis (+glucose) • Endocrine function, release of leptin into capillaries → hypothalamus→ counteracts Neuropeptide Y (feeding stimulant) + others→ inhibits appetite = satiety [obese, high leptin but desensitisation]	
Brown adipose	Found in newborns Functions: generate body heat	

Blood – fluid CT; cell 45:55 plasma; ~6L/ average adult; transports O_2 CO_2 hormones humoral agents and cells; maintains homeostasis by acting as a buffer, coagulator and thermoregulator;

Plasma	91% water; 8% albumins, globulins, fibrinogens (proteins); 1% Na^+, HCO_3^- (electrolytes), urea, creatinine (nitrogens), glucose, lipids aa (nutrients), O_2 CO_2 N (gases), hormones and enzymes;				
Erythrocytes	7-8 µm diameter; anucleate, lacks organelles; biconcave disc; 120 days; phagocytosed by macrophages in spleen, bone marrow and liver;				
Leukocytes	Neutrophils (most common)	Multilobed	Cytoplasmic granules varying size, contains cytokines, anti-microbials enzymes	Phagocytosis, deployed within minutes	 10-12 µm
	Eosinophil	Bilobed	Cytoplasmic granules eosinophillic, abundant lysosomes	Allergic reactions, parasite infections, chronic inflammation	 10-12 µm
	Basophil (least common)	Granule obscured	Cytoplas ic granules large, abundant lysosomes, contains heparine, histamine, leukotriens, interleukins	Similar to mast cells, bind IgE→release vasoactive agents→ vascular distrubances of hypersensitivity and anaphylaxis	 10-12 µm
	Lymphocyte	Large, slight indent	hin rimmed cytoplasm surrounds nucleus	Functionally classified, T-mediates, B- antibodies, NK kills	 6-8 µm (6-16 µm)
	Monocytes (largest)	Large, slight indent	Many organelles	Antigen-presenting cells, transforms into tissue macrophage after 3 days	 18 µm
Platelets	Thrombocytes: small, membrane-bounded cytoplasmic fragments; anucleate; derived from megakaryocytes in bone marrow. • Cell membrane has a glycocalys, cytoskeletal components, mitochondria, peroxisomes, glycogen, granules – coagulation factors, fibrinogen, serotonin… • Vasoconstriction, vessel repair, blood coagulation, platelet aggregation				

Lecture 17: Prokaryotic Structure – Specific Features

Lecture Summary

- Key structural features of bacterial cell envelope; effect of environmental conditions on cell properties and relationship to limits of bacterial life; distinctive and common bacterial molecules, relevance to pattern recognition receptors and immune surveillance (PG, LPS, flagellin); distinctive and essential bacterial molecules, relevance as drug targets (PG, ribosome); visible bacterial structures, relevance to immune evasion, diagnostics and vaccination;

Learning Outcomes

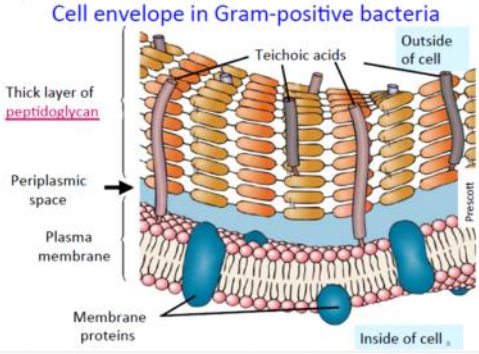
17.1 Be able to describe the typical structure of Gram-negative and Gram-positive cell envelopes. Know the key functions of the cell wall, and the plasma and outer membranes; Be able to give examples of phenotypically variable properties (environmentally influenced expression) and their ramifications;

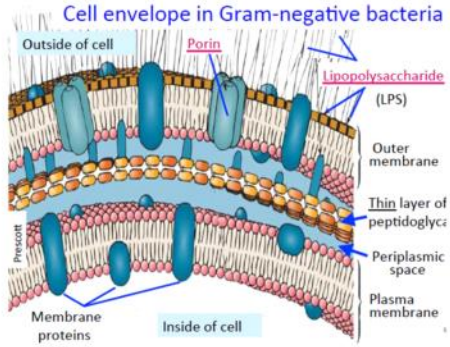
Replication, transcription and translation are conserved in intracellular processes:

- General presence of nucleoid, RNA polymerase, ribosome, does not provide a sound basis for discriminating good from bad bacteria (too conserved)
- However, the long evolutionary separation of the bacteria (and to a lesser extent archaea) means sequence variation in these conserved structures is useful in classification

Different shapes and staining behaviours reflect the **Cell Envelope** = membrane + wall

- Membrane = lipid bilayer // Wall = rigidity (thick layer of peptidoglycan)
  - Prokaryotic structural significance; different morphologies have different SA/ Vol. ratio
    - Coccus: low SA/ V ratio, survival
    - Rod: medium ratio, compromise
    - Filament: high, nutrient uptake
- Function: protective barrier against environment, separates ordered cytoplasm from chaotic exterior
- Differences in gram-negative and gram-positive (differences in staining; composition)





Cell envelope in **Gram-Positive** bacteria [PURPLE]

- Thick peptidoglycan outside cell (rigidity/ structure)
- Attached to PM by number of molecules, particularly Teichoic acids

Cell envelope in **Gram-Negative** bacteria [PINK]

- PM is common to both types
- Thinner peptidoglycan layer and no Teichnoic acids
- Second, outer membrane ("gate-keeper"); distinctive composition; asymmetric whereby outer is LPS → lipopolysaccharide, inner is phospholipid

Plasma membrane structure

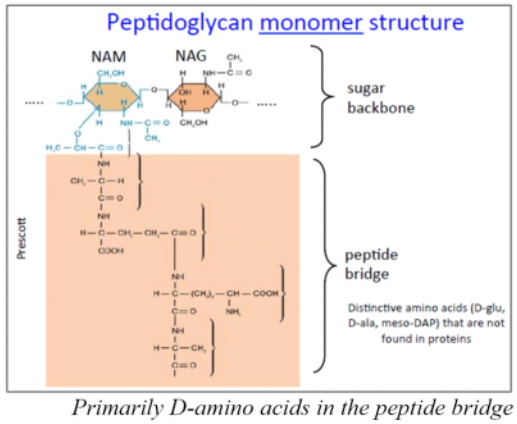
- Phospholipid bilayer; integral membrane proteins (embedded or attached); glycolipid, glycoprotein (+ carbohydrates);
- Functions
  - Selective permeability: nutrient influx, waste efflux; critical selectivity no cytoplasm out or toxins in
  - Metabolic processes: e.g. ETC, resp., lipid biosynthesis occurs within the membrane
  - Site of environmental signal transduction: membrane receptors switch on regulatory proteins → activate transcription
- Clinical and other significance
  - Many antimicrobials disrupt membrane structure → leakage of cytoplasm → cell death
    - **Synthetic**: detergents (*e.g. SDS*), antiseptics (*e.g. Benzalkonium*)
    - **Antibiotics**: polymyxin, lantibiotics [probiotic stains of *lactobaccilus* activate against positive grams, specific targets in the PM → peptidoglycan precursors]
    - **Innate immune system**: defensins, cathelicidins [body produces, particularly in mucous membranes]
- Temperature extremes → maintaining membrane humidity e.g. cannot solidify or gel (low temp vs. high temp grower)
  - @minimum temp→ gelling, transport processes so slow that growth cannot occur; max→collapse of PM, thermal lyses

- Optimum temp. close to max → narrow difference between optimal and protein denaturation/ collapsing
  - Membrane structure determines growth limits of Bacteria
  - Specialised for different temps = different lipid composition = different growth temperatures

- All domains, limited variation
  - Archea → ether linked PM
  - All **Bacteria → ester-linked** phospholipids in PM
    - Vary in PM lipids varying in chain length, and in degree of saturation between saturation
    - Thermophiles tend to have more rigid (saturated) and psychrophiles more flexible (unsaturated) phospholipids
  - Eukarya → ester-linked
  - Fungi → **distinctive sterols** in PM (may be targeted by anti-fungals)

Bacterial cell wall contains peptidoglycan [but not all – some lack cell wall, etc.]

- Cell wall definition
  - Gram + (thick peptidoglycan + teichoic acids)
  - Gram – (thin peptidoglycan + outer membrane LPS)
- Peptidoglycan (PG): unique; structural polymer of sugars and amino acids
  - PG backbone made of repeating di-saccharide unit, N-acetylglucosamine (NAG) + N-acetylmuramic acid (NAM); cross-linked by peptide bridges (figure→)
- Functions
  - Osmotic protection, salty cytoplasm → high pressure, membrane alone cannot resist; enzymes of innate immunity target PG (*e.g. lysozyme = lysis/ death*);
  - Many antibiotics target PG biosynthesis (*e.g. penicillin, cephalosporins, vanomycin*);
  - Many Eukaryote pattern recognition receptors target PG and initiate signalling pathways to inform bacterial presence (*e.g. Vibrio-Squid mutualism; Tracheal cytotoxin in whooping cough*);



Primarily D-amino acids in the peptide bridge Number not found in proteins; very distinctive (But just a singal)

- Rigid envelope layer: variably present in all domains but domain-sepcifiec
  - Only bacteria have PG →combination of surface exposure & chemical conservation makes PG a useful signalling molecule & drug target
    - Thickness varies: Firmicutes (gram+) thicker; Proteobacteria and bacteroidetes (gram-) thin layer
    - Some do not have PG (*e.g. Planctomycetes, Chlamydia*)
  - Only Arachaea have pseudomurein (PG-like molecule)
  - Eukarya is diverse in types of cell envelope *(e.g. plants=lignocellulose; fungi=chitin; animal=no cell wall)*

17.2 Recognise the significance and applications of the distinctive structures of peptidoglycan; LPS (conserved Lipid A and variable O-antigen); Be able to give examples of genetically variable bacterial properties (feature present but structure varies between species) and their applications;

Outer membrane structure (Gram Neg **only**)

- Outer of the two layer – **Lipopolysaccharide (LPS)**
  - Lipid A core = truly unique and distinctive to gram negative cell wall
  - First O unit core/ LPS Core = sugar chains
  - O-antigen = repeating sugar chains
  - Proteins *e.g. Porins*
- Outer membrane (OM) function
  - **Border control**: Protective barrier against toxins (*e.g. antibiotics, bile*) and entry port (*e.g. soluble nutrients*)
  - **Phase variation** (O-antigen is highly variable): LPS Presence of many sugars define bacterial surface properties: hydrophilic, negative charge → capable of changing this sugar structure, change surface coding e.g. immune system target can cause change in the antigen
  - **Lipid A component** target for pattern recognition receptors (TLR4) usually triggers inflammatory response, endotoxin → systemic toxic effects in gram neg. infections

- Glycocalyx, capsule, slime layer → extra-cellular polysaccharide secreted to lie around surface (fundamentally the same)
  - Glycocalyx = layer of polyssacharides secreted by bacteria outside envelope
    - Used in attachment – especially biofilms formation *(e.g. dental plaque)*
    - Protection against dessication and other stresses
    - Help bacteria to evade immune system – difficult for phagocytes to recognise bacteria
  - Capsule = not necessarily attached, difficult to remove, well-organised glycocalyx
  - Slime layer = more diffuse glycocalyx, can be removed by washing cells

→ Variable expression of outer membrane and glycocalyx
  - [rapid change protein expression, how much glycocalyx, what type of antigen, etc.]

- Cell surface polysaccharides – most cells have glycosylated surface molecules; varies in attachment
  - Bacterial polysaccharides attached (capsule) or loosely associated (slime layer)
    - G–ve → LPS attached to lipid A core; unique
    - O-antigen (long carbohydrate chain) highly variable structurally in types of sugars in chain and branching order; often a basis of Serotyping schemes for epidemiology; target for vaccines
  - Eukarya have surface polysaccharides, no LPS; fungi form capsules
    - Higher eukarya have LPS target for bacterial surveillance (TLR4 receptor), and stimulated adaptive response (e,g. igG) by the highly immunogenic O-antigen side chain

17.3 Recognise the significance and applications of surface adornments such as capsule, pili, flagella and fimbriase; Be able to describe the significance of endospores for sterilisation and diagnostics

- Fimbriae: thin (~5 nm diameter), numerous (~1000/ cell); attachment to surfaces
- Pili: thicker (~10 nm diameter) less numerous (few/ cell); transferring DNA i.e. sex; often encoded by conjugative plasmids, self-transmissible between bacterial cells;
- Flagella: most motile bacteria, presence/ absence of flagella, & distribution pattern around cell useful for identification
  - Structure – filament (Self-assembled subunits of flagellin protein, hollow filament allows transport of flagellin units, cytoplasm→growing tips), hook, PG, Basal body (motor), PM
  - Function – helical corkscrew filament propels bacterium forward, proton gradient = energy source, +allow chemo taxis towards nutrients or away from toxins, -need protein to build, cost of energy, highly immunogenic (H antigen), target of pattern recognition receptors (TLR5)

- Endospores (within)
  - Some G+ve bacteria *(e.g. Bacillus, Clostridium)* [NOT G-ve]
  - Endospores survive under stressful conditions; extremely tough e.g. heat, dessication, radiation, disinfectants
  - Metabolically inactive but can geminate to yield new vegetative cells
  - Clinical significance: spore-forming bacteria difficult to kill via standard procedures → autoclaving required; many clinically-important bacteria are spore-formes (*e.g. Bacillus anthracis* → *anthrax*)

Summary

- Cell morphology: diagnostic value in specific situation, not generally useful
- Nucleoid: site of replication and transcription, flexible gene expression patterns (resulting from operons – organisation, and regulons – co-ordinated by transcription factors) mean relationship with humans depond on context
- Ribosomes: protein factory sufficiently different from eukarya to be antibiotic target – *e.g. stretomcyin*
- PM: selective barrier, target for antibacterial agents that are synthetic (disinfectant), biological (lantibiotic) and immunological (defensin)
- Cell wall PG: osmotic protection, structural scaffold, PG = diagnostic bacterial molecule – target of receptors and drugs
- Outer membrane: protection and 'communication, O and H antigens modulate bacterial cell signal, LPS is a diagnostic bacterial molecule and TLR4 receptor target, H antigen is diagnostic of flagellin and TLR5 receptor target, widely used for serotyping schemes and as vaccine targets

Cell envelope is essential to bacteria – but is also a drug target for biocides. It is **surface-exposed**, a target for the immune system. The fundamental cell envelope differences between **G+VE** (one membrane + thick PG) and **G-VE** (two membranes, thin PG) is informative for higher level classification.
Diversity in the cell envelope is **diagnostically useful** but requires caution as it adapts to the environment by varying: **cell shape** (determined by rigid peptidoglycan layer), **membrane fluidity** (determined by fatty acids and sterol composition), **membrane permeability** (determined by membrane proteins) and **attached structures**. Bacterial surface diversity aims to change immune evasion, motility, permeability and fimbriae.
The combination of its surface exposure and chemical conservation makes PG useful for **eukaryotic detection** (via PG receptors) and target bacteria (e.g. lysozymes). Lipid A, surface polysaccharides, flagellin, etc. also used for detection.