Tutorials in Biomedical Sciences

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Focus of subject teaching
• lectures
• seminars
• classes
• laboratory work
Sets degree course contents
Provides academic facilities
• lecture theatres
• libraries
• computing centre
Sets and marks exams
Awards degrees
So what do colleges do?

- colleges admit undergraduates
- each college houses 250-450 undergraduates
- differ in location, age and size
- colleges provide accommodation, food, library and computer facilities and financial support
- social hub: arts and sports
- they are responsible for tutorial teaching
What is a tutorial?

It is

• teaching provided by the college
• a weekly meeting with your tutor and one or two other students
• an opportunity to discuss a subject with someone who is an expert in the topic

It is not

• a lecture
• an oral examination of your knowledge
Preparing for a tutorial

• students are set some work
  – an essay, a set of notes, a problem sheet
• the work relates to material being covered at the time in lectures, practicals
• the tutor provides some suggested reading
• students use the lecture and the reading to inform themselves about the subject
• students complete the work
Preparing for a tutorial

• students should read all of the material suggested by the tutor, and probably more
• they should make notes
  – summarising the key points
  – identifying common ground between the lecture and the texts
  – highlighting the inconsistencies
• no two textbooks are the same
• some information will be common to all, but
  – the emphasis will be different
  – in some books some information may not be covered at all
• students need to identify what is really important and try to understand why other facts have been ignored in some books
At the tutorial

- the tutorial is *not* a question and answer session
- it is more like a debate, although students don't need to be experienced in debating
- it relies on an exchange of ideas between students and tutor
- students need to be ready to present and defend their opinions, listen to others and accept constructive criticism
What will happen?

• the tutor will assume that students have prepared for the meeting and have a sound grasp of the basics of the subject
• without that basis, the tutorial will fail
• at the start they will typically be asked questions that check this and identify any problems that they have encountered
• this is the opportunity to clarify anything that they found confusing or contradictory
Building on knowledge

• the tutor will then ask questions that build on (rather than confirm) your knowledge
• these make students think about the 'big picture'
  – HOW?
    • how was the information found out?
  – WHY?
    • why do things work the way they do?
  – SO WHAT?
    • what is the significance of the information?
  – WHAT'S MISSING?
    • what don't we know/understand - and why?
Gastric acid secretion

Functions of the stomach
- The stomach continues the process of digestion initiated by mastication, saliva. To this end, it
  - secretes HCl, pepsinogen, mucus, HCO₃⁻, intrinsic factor (IF)
  - mixes by muscular contraction
  - releases humoral factors
    - gastrin, somatostatin, histamine

Parietal cells
- In an unstimulated cell, there are large numbers of hydrogen ions in the cytoplasm.

Mechanism of acid secretion
- pH of intracellular fluid is around 7.4.
- Hydrogen ions are released into the paracellular space through paracellular channels.
- Acid secreted by parietal cells
  - Hydrogen ions diffuse down the electrochemical gradient into the tubular lumen.
  - Secreted hydrogen ions form gastric acid.

Regulation of ATPase insertion
- ATPases are inserted into the brush border membrane of parietal cells.
- ATPase activity is inhibited by proton-lowering agents.

 Ionic composition of gastric juice
- In an unstimulated cell, the luminal surface of the parietal cells
  - mucous, alkaline HCO₃⁻
  - CO₂, bicarbonate
  - water, electrolytes

Gastric epithelium
- Characterized by glands which increase the surface area, glandular compartments which evolve into tubules. Cells present include
  - parietal cells with the base and neck secreting HCl and intrinsic factor (vitamin B₁₂), adenylate kinase (ATPase) in the neck.
  - chief cells at the base and neck secreting pepsinogen.

Common mediator hypothesis
- ATPase activity is inhibited by proton-lowering agents.
- Secretin mediates action of HCl and water with bicarbonate production.
- Secretin mediates action of HCl and water with bicarbonate production.

Somatostatin
- D cells release somatostatin, which inhibits adenylyl cyclase, reduces gastric acid secretion.
- Inhibits histamine release.
- Stimulates somatostatin release.

Mucous cells
- Located between the stomach lining and the surface epithelium of the stomach.
Parietal cells

In an unstimulated cell, there are large numbers of tubulovesicles in the subapical cytoplasm.

Tubulovesicles contain $\text{H}^+, \text{K}^+$ ATPase. Stimulation of acid secretion triggers tubulovesicle insertion.

Stimulated parietal cells possess deep invaginations of apical membrane.
Mechanism of acid secretion

- pH of lumen can be as low as 1 (10^6-fold gradient)
- Intracellular carbonic anhydrase catalyses hydration of CO₂ to yield H⁺ and HCO₃⁻
- H⁺,K⁺-ATPase pumps H⁺ ions into the lumen in exchange for K⁺
- K⁺ recycles out of the cell through apical K⁺ channels
- HCO₃⁻ exits across basolateral membrane to interstitial fluid, then blood, on Cl⁻-HCO₃⁻ exchange
- Cl⁻ ions diffuse through apical channels to join H⁺ ions in the lumen.
- Water follows by osmosis.

Net result: secretion of HCl, alkalisation of blood ('alkaline tide')
Regulation of ATPase insertion

Tubulovesicle insertion is initiated by cytoskeletal rearrangement induced by kinase activation by:
- **ACh** *(neurocrine)* from vagus: binds M₃ muscarinic receptors, triggers IP₃ cascade
- **gastrin** *(endocrine)*: released from G cells in response to stimulation of GRP-containing nerves by vagus or protein digestion products in lumen. Binds CCK₉ receptors, triggers IP₃ cascade ['Gastrinoma' in pancreas - Zollinger-Ellison syndrome]
- **histamine** *(paracrine)*: released from enterochromaffin-like cells. Binds H₂ receptors, activates adenylyl cyclase cascade

H₂ receptors antagonised by **ranitidine** ('Zantac')
The basic understanding

• From the lecture and their own study, students would be expected to be able to answer some basic questions
  – what does the stomach do?
  – how is the structure of the stomach specialised to fulfill its functions?
  – what is the composition of gastric juice, and how can it vary?
  – what is the mechanism by which the stomach secretes acid?
  – what regulates stomach secretion?
  – how can stomach secretion become excessive and what are the ways in which secretion can be reduced?
  – how does the stomach protect itself against damage from acid and from enzymes that digest proteins?
Points to make them *think*

- lots of hormones exert effects through Ca$^{2+}$
- the ATPase doesn't work unless it is in the luminal membrane
- vagotomy is a really good way to stop acid secretion
- CO$_2$ hydration is at equilibrium
Lots of hormones exert effects through \( \text{Ca}^{2+} \)

(a) Acetylcholine: salivary gland cells

(b) Noradrenaline: liver cells

(c) Histamine: endothelial cells
Points to make them *think*

- lots of hormones exert effects through $\text{Ca}^{2+}$
- the ATPase doesn't work unless it is in the luminal membrane
- vagotomy is a really good way to stop acid secretion
- $\text{CO}_2$ hydration is at equilibrium
The ATPase doesn't work unless it is in the luminal membrane

- vesicle is arranged so that ATPase is 'inside out'
- although ATP is freely available in the cytoplasm, $K^+$ cannot recycle
- low $K^+$ availability within the vesicle 'brakes' the activity of the ATPase
Points to make them *think*

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- $\text{CO}_2$ hydration is at equilibrium
Vagotomy is a really good way to stop acid secretion.
Points to make them think

- lots of hormones exert effects through Ca\(^{2+}\)
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- vagotomy is a really good way to stop acid secretion
- CO\(_2\) hydration is at equilibrium
CO₂ hydration is at equilibrium
Why interview?

• the interview is an 'audition for a tutorial place'
• explore their interests and motivation for the subject
• establish what insight they have about the subject and studying it at Oxford
• examine how they think
  – how they handle information
    • how? why? so what? what’s missing/wrong?
Misconceptions

• there are trick questions
• it's a test of knowledge
• everyone gets the same questions
• wrong answers are always a bad thing
• you will know how it's gone
• one bad interview and it's all over
• it's an ordeal
Types of question

• 'warm-up' questions
• questions based on your statement
  – reading
  – projects
  – experience
  – interests
• questions based on schoolwork
• current affairs
• tutorial-style questions
  – passages to read/graphs to interpret
% lysis

[NaCl] (mM)

Human
Cow

0 20 40 60 80 100 120 140 160

0 20 40 60 80 100

% lysis

[NaCl] (mM)
$\text{NH}_3 \quad \text{fast} \quad \text{NH}_3 + H^+ \rightarrow \text{NH}_4^+$

$\text{NH}_4^+ \quad \text{slow} \quad \text{NH}_3 + H^+ \rightarrow \text{NH}_4^+$