

PATH2220 - Inflammation Module - Student Worksheet

Prof Jennet Harvey
Dr Ben Dessauvague

Learning Outcomes

By the end of the class, students will be able to:

- Learning Outcome 1: describe the inflammatory reaction including possible sequelae
- Learning Outcome 2: describe the typical presentation and progression of a patient with acute appendicitis and give an account of the way in which such patients are diagnosed and treated

Pre-reading

Revise three lectures on Inflammation

Inflammatory response: definition

Macroscopic and microscopic features

Cardinal signs of inflammation

Terminology used in inflammatory reactions

Classification of inflammatory reactions

Chemical mediators of inflammation

Sequelae, including complications of inflammation

Examples of common inflammatory diseases

Briefly read through worksheet to familiarize yourself with the objectives of this session

The worksheet will be printed out and provided for you in the tutorial.

Note:

- ❓ *Students who miss the in-class session, remember to use the tutor's notes as the guide to completing this worksheet together with other sources as indicated.*
- ❓ *Times in the worksheet are listed as suggestions for how long it should take to complete those sections.*

Tutor presentation: Introduction, case study and worksheet

15 minutes

Revision of Inflammation

Definition: The response of living tissues to injury

Description: Brings leukocytes and plasma proteins to site of tissue damage to eliminate harmful agent and initiate healing

Classified in different ways: often as **acute** or **chronic** which have different presentation, time course, cellular constituents and outcome

Purpose: Essential for survival, usually beneficial but can be detrimental (severe insult, inability to eradicate causative agent, misdirected against host as in autoimmune reactions)

Cardinal signs: redness, heat, swelling, pain, loss of function

The process:

Harmful stimulus – various types

Release of chemical mediators from injured cells

Activation of local host cells (WBCs, macrophages endothelial cells) with release of further chemical mediators

Local response: (vascular and cellular components) result in influx of circulating cells and plasma proteins to site of injury

Systemic (general) response

Outcome: Resolution and/or healing

Activity 1

15 minutes

Tutors notes

Lectures this week have described specific examples of inflammatory reactions in different sites.

Today's case: **Acute appendicitis**

Appendix - a blind ended pouch attached to the caecum, situated in right lower quadrant of abdomen.

Appendicitis –acute inflammation of the appendix. Typical local and systemic manifestations of an acute inflammatory reaction.

- Initial non-specific manifestations and vague central abdominal pain
- Pain later localized to McBurney's point
- Diagnosis can usually be made on clinical grounds but laboratory tests may be useful in some instances. In particular you may like to consider the following: full blood picture, C-reactive protein, ESR

Commence case study: 'Eliza'

Answer question 1.1

Case Study 'Eliza'

Eliza is a 17 year old fit and healthy high school student who wakes one Monday morning complaining of abdominal pain centred around her umbilicus. She doesn't want to eat breakfast, thinks she might vomit and definitely doesn't want to go to school.

Use the internet, the tutor's presentation, and/or the provided resources to find answers to the following question:

Q1.1. List Eliza's symptoms. What might be the cause of her symptoms?

Symptoms: nausea; umbilical pain; anorexia.

Ddx: gynaecological e.g. menstruation, endometriosis, pregnancy complications, ovary torsion, pelvic inflammation;

gastrointestinal e.g. diarrhoea, constipation, appendicitis, irritable bowel disease, bowel obstruction; renal e.g. UTI

Tutor discussion of answer

Activity 2

15 minutes

Case study 'Eliza'

Eliza is allowed to stay home from school, but does not feel immediately better, indeed, over the next few hours her stomach ache worsens and shifts slightly to become a severe sharp pain in the lower right side of her abdomen. She feels extremely nauseous and has one episode of diarrhoea. Her mother is able to get an appointment for her to be seen by the family doctor, who listens to her story and examines her. He observes the following:

- *a distressed young woman in obvious pain*
- *coated tongue*
- *fever - 38.5 degrees*
- *rapid pulse - 110 per minute*
- *abdominal tenderness maximal at McBurney's point*
- *abdominal rebound tenderness*

The general practitioner makes a diagnosis of acute appendicitis and phones a surgeon for an urgent assessment.

Answer Questions 1.2-1.4

Q1.2. Which signs/symptoms are most helpful in localizing the inflammatory process to the appendix?

Maximal pain at McBurney's point; rebound tenderness; fever.

Q.1.3. What systemic (i.e. 'general', whole body) manifestations of inflammation are exhibited in this patient?

Fever; tachycardia; distress; dehydration.

Q1.4. What mechanisms underlie these changes?

Chemical mediators released in inflammation act both locally and systematically, e.g. prostaglandin, the cytokines TNF and IL-1, and kinin.

Tutor discussion of answers

Activity 3

15 minutes

Proceed to answer Questions 2.1-2.3 using internet, tutors notes and provided resources

Q2.1. What is the appendix and what is its function?

It is a blind-ended tube connected to the cecum.

Function: vestigial organ that may now serve as a haven for good bacteria when illness flushes them from the rest of the intestines as is the case in diarrhoea.

2.2 Label the organs on this image, including the appendix.

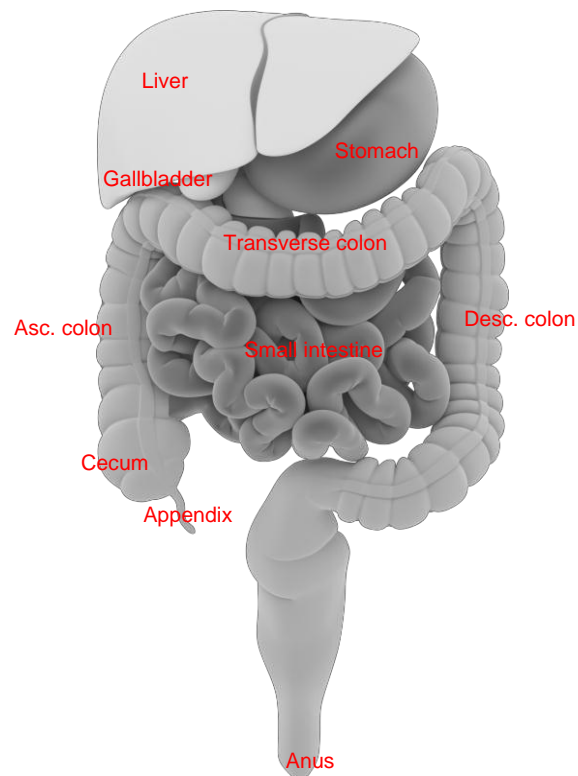


Image obtained from the creative commons scientific image library at www.somersault1824.com

Q.2.3 What is McBurney's point? Indicate where it is located on this image:



In the right iliac fossa, where pain and tenderness is most commonly seen in the abdomen.

Photo credit: Rico Heil, published on commons.wikimedia.org and licensed under the GNU Free

Tutor discussion of answers**Activity 4**

15 minutes

Case study 'Eliza'

The Surgeon makes similar clinical observations and arranges for Eliza to be admitted immediately to the local hospital. He requests the following blood tests - full blood count, ESR and CRP. The results show a raised white cell count of $15.0 \times 10^9/L$, mainly neutrophils, raised ESR of 15mm/hour and raised CRP - 6mg/L.

Use the internet, the tutor's presentation and/or the provided resources to find answers to the following questions 3.1-3.5.

Q.3.1. What are the main parameters reported in a full blood count?

Number of blood cells including red, white, and platelets; MCV, Hb concentration, MCHC

Concentrations of proteins & minerals.

Q.3.2. What is the normal range for white blood cells? What is the significance of Eliza's white cell count?

4 to $10 \times 10^9/L$ is normal range for WBC

Eliza's raised count with neutrophilia indicates an acute inflammatory reaction.

Q.3.3. What does CRP measure? What is its physiological function? Why would it be used in this case?

The concentration of C-reactive protein, which activates a component of innate immunity called the complement cascade.

It's a marker for acute inflammation in the body. If CRP is very high, there is a high suggestion of perforation as a high CRP means there is an high incidence of opsonisation of microorganisms in order to assist in their destruction.

Q.3.4 What does ESR measure? Why would it be used in this case?

ESR = erythrocyte sedimentation rate. Measures the rate at which RBCs sediment in one hour. Non-specific marker for inflammation; in inflammation, ESR is decreased due to the presence of WBCs, fibrinogen, and chemical mediators forming aggregates with the RBCs and leading to faster sedimentation.

Q.3.5 What other test may be useful in the diagnosis of acute appendicitis in some circumstances?
[Hint: what other results are presented in the Digital Slide Box for this case?]

Ultrasound of the abdomen.

Tutor discussion of answers

Activity 5

15 minutes

Tutor notes

Appendicitis does not usually spontaneously resolve and rarely progresses to chronic inflammation

Significant and potentially life threatening sequelae if untreated

Specimen should ALWAYS be sent to pathology laboratory for examination

Appendiceal specimens in the laboratory

(Role of pathologist in examination of appendix)

Macroscopic (gross) examination

- Specimen and patient identification
- Description of gross external findings (need to know 'normal')
- Size, colour, (weight – some specimens only)
- Specimen dissection and further observation
- ? pus or exudates
- ? other (eg obstruction due to faecolith)
- Any focal lesions eg tumour – describe characteristics

Case study Eliza

The Surgeon confirms the diagnosis of acute appendicitis and Eliza proceeds to theatre late in the evening. At operation the Surgeon inserts a laparoscope into the abdominal cavity and performs an appendicectomy (removal of the appendix). The removed appendix looks swollen and reddish with white patches, and the surface is dull rather than shiny. The surgeon places the specimen into a jar of formalin and sends it to the Pathology Laboratory together with a completed request form.

- Use the internet, the tutor's presentation and **watch the appendix dissection video** on LMS to see how the Pathologist prepares the sample for embedding into wax.
- Then, review the pathology reports and images for two specimens of Acute Appendicitis available on display in our museum (PELC) and available online as listed under the Week Two heading '**Acute Appendicitis Specimens in the Pathology Education and Learning Centre**':

Image 1 <http://edupalm.meddent.uwa.edu.au/museum/search.php?specimen=87>

Image 2 <http://edupalm.meddent.uwa.edu.au/museum/search.php?specimen=585>

Answer Questions 4.1-4.7

Q.4.1. Is appendicectomy the usual treatment for acute appendicitis?

Yes, as appendicitis does not resolve spontaneously.

Q.4.2. What are the possible complications of acute appendicitis

PERFORATION which can lead to: ruptured appendix -> spread infection throughout abdomen [=PERITONITIS]; or [ABSCCESS] formation -> may form [LIVER ABSCCESS] due to portal system.

BLOCKAGE/OBSTRUCTION of the intestine.

SEPSIS whereby infecting bacteria enter the bloodstream [SEPTICAEMIA]

GANGRENE whereby necrosis occurs ["FULL-THICKNESS NECROSIS GANGRENE"]

Q.4.3. Why is it important for the pathologist to check the details of the pathology request form with those on the specimen container?

To ensure it is the correct specimen for the correct patient, and thus guarantee the correct diagnosis.

Q.4.4. What macroscopic features characterise a normal appendix?

Significantly smaller; smooth, shiny external surface (peritoneal coating); thin wall.

Lumen has no pus.

Pink in colour; no white patches (i.e. exudates)

Q.4.5. What macroscopic features characterise an appendix with acute appendicitis? (Refer to Image 1)

Entire organ swollen; approx. triples in size.

Thickened walls.

White patches present on serosal surface; suppurative exudate; dull, rough surface.

Mucosa haemorrhaged, ulcerated; pus in lumen.

Q.4.6. The appearance displayed in Image 2 is not typical of acute appendicitis. Explain in what way and why this may be.

Very thickened walls; external surfaces haemorrhagic.

A lot of fibrosis.

More gelatinous appearance.

--> Because inflammation has become CHRONIC, hence there are less neutrophils (exudate) and more macrophages, leading to organisation and FIBROSIS.

Q.4.7. Once the sample has been cut and placed into the cassette, where does it go next?

Specimen processed in laboratory and the paraffin blocks are then cut with a microtome, mounted onto glass slides, stained with haematoxylin & eosin stain, and examined by pathologist under microscope.

Tutor discussion of answers

Activity 6

20 minutes

Tutor notes

Microscopic examination of appendix

Description of histological finding (need to know normal histology)

General architecture

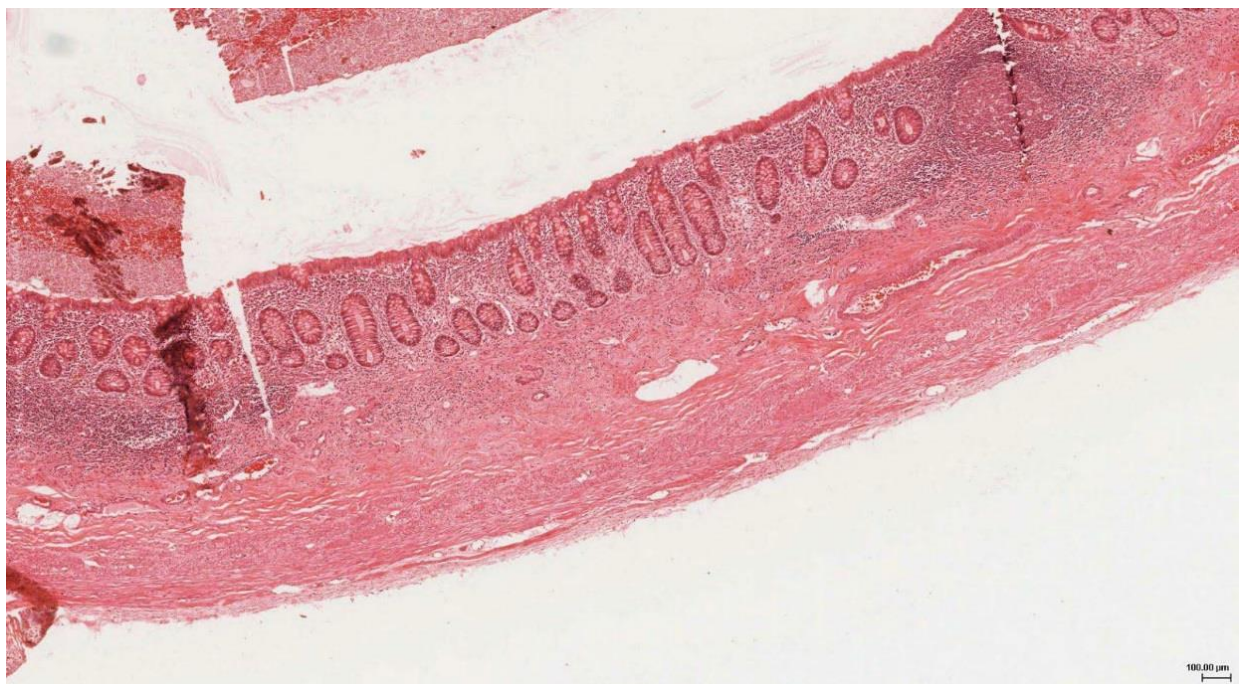
Presence of inflammatory infiltrates – location and description

? abscess ? perforation ? peritonitis ? other pathology including parasites

(If tumour present need to characterize histological type, determine whether benign or malignant, comment of cytological features and extent of spread)

- **Open the Digital Slide Box (DSB) and navigate to Week 2, Case 1.** A snapshot of normal appendix microscopy has been provided below (use the DSB if you would like to zoom in for greater detail or view this snapshot in the context of the whole slide).
- Also look at the images of Acute Appendicitis listed under the heading '**Acute Appendicitis Microscopy**' (after the DSB link above) in the Week Two module in the PATH2220 LMS site.

Then answer Questions 5.1-5.3



Q.5.1. What type of epithelium lines the normal appendix? Where else would you expect similar epithelium?

Large bowel-type glandular epithelium, mainly simple columnar, absorptive enterocytes, mucin-producing goblet cells. Appendix has crypts but no villi.

Q.5.2. What cells characterise an acute inflammatory process?

Neutrophils are predominant. Some macrophages present.

Q.5.3. What are the diagnostic features in the appendix with acute appendicitis?

Transmural neutrophils (major feature); vascular congestion; mucosal ulceration; fibrinopurulent exudate on serosal surface.
