Inflammation

First Lab.
The cardinal signs of inflammation are rubor (redness), calor (heat), tumor (swelling), dolor (pain), and loss of function. Seen here is skin with erythema, compared to the more normal skin at the far right.

The arm at the bottom is swollen (edematous) and reddened (erythematous) compared to the arm at the top. Click to determine which areas are painful to touch.
Acute inflammation is marked by an increase in inflammatory cells. Perhaps the simplest indicator of acute inflammation is an increase in the white blood cell count in the peripheral blood, here marked by an increase in segmented neutrophils (PMN's).
Seen here is vasodilation with exudation that has led to an outpouring of fluid with fibrin into the alveolar spaces, along with PMN's. The series of events in the process of inflammation are:

1. **Vasodilation**: resulting in redness and heat.
2. **Vascular permeability**
3. **Exudation**: fluid, proteins, red blood cells, and white blood cells escape from the intravascular space as a result of increased osmotic pressure extravascularly and increased hydrostatic pressure intravascularly.
4. **Vascular stasis**: slowing of the blood in the bloodstream with vasodilation and fluid exudation to allow chemical mediators and inflammatory cells to collect and respond to the stimulus.
The diagram shown here illustrates the process of exudation, aided by endothelial cell contraction and vasodilation, which typically is most pronounced in venules.

Chemical mediators producing endothelial contraction include: histamine, leukotrienes, bradykinin, platelet activating factor, and the C3a and C5a components from complement activation. Mediators of this process over a longer term include tumor necrosis factor and interleukin-1. Chemical mediators that promote vasodilation include: histamine, prostaglandins, and nitric oxide.
PMN's that are marginated along the dilated venule wall (arrow) are squeezing through the basement membrane (the process of diapedesis) and spilling out into extravascular space.
Here is an example of the **fibrin mesh in fluid with PMN's** that has formed in the area of **acute inflammation**. It is this fluid collection that produces the "tumor" or swelling aspect of acute inflammation.
This tissue **gram stain of an acute pneumonia** demonstrates gram positive cocci that have been eaten by the numerous PMN's exuded into the alveolar space. Opsonins such as IgG and C3b facilitate the attachment of PMN's to offending agents such as bacteria so that the PMN's can phagocytose them.
The **vasculitis** shown here demonstrates the destruction that can accompany the acute inflammatory process and the interplay with the coagulation mechanism. The **arterial wall** is undergoing necrosis, and there is thrombus formation in the lumen.
At higher magnification, vasculitis with arterial wall necrosis is seen. Note the fragmented remains of neutrophilic nuclei (karyorrhexis). Acute inflammation is a non-selective process that can lead to tissue destruction.
inflammatory reactions are not neatly categorized by cell type. A variety of inflammatory cell types may be present, though one may predominate.

Seen here are mainly neutrophils, but there are also plasma cells, lymphocytes, and macrophages. Macrophages can phagocytose other cells as well as cellular debris. One macrophage here has "pigged out" by consuming a neutrophil, a red blood cell, and a nuclear fragment.
Here is simple edema, or fluid collection within tissues. This is "pitting" edema because, on physical examination, you can press your finger into the skin and soft tissue and leave a depression.
This example of a fluid collection, a **friction blister** of the skin, is an almost trivial example of edema.
This example of **edema** with inflammation is not trivial at all: there is marked laryngeal edema such that the airway is narrowed. This is life-threatening. Thus, fluid collections can be serious depending upon their location.
Here is an example of **fluid collection into a body cavity**, or an **effusion**. This is a right pleural effusion (in a baby). Note the clear, pale yellow appearance of the fluid. **This is a serous effusion.**
Extravascular fluid collections can be classified as follows:

**Exudate**: extravascular fluid collection that is rich in protein and/or cells. **Fluid appears grossly cloudy**.

**Transudate**: extravascular fluid collection that is basically an ultrafiltrate of plasma with little protein and few or no cells. **Fluid appears grossly clear**.

**Effusions** into body cavities can be further described as follows:

**Serous**: a transudate with mainly edema fluid and few cells.

**Serosanguinuous**: an effusion with red blood cells.

**Fibrinous** (serofibrinous): fibrin strands are derived from a protein-rich exudate.

**Purulent**: numerous PMN's are present. Also called "empyema" in the pleural space.
This radiograph demonstrates fluid in the left pleural cavity. This pleural effusion could result from a transudate (serous effusion) or from hemorrhage (hemothorax), or serous fluid tinged with blood (serosanguinous effusion). This effusion could be chylous (which is quite rare). A purulent exudate at this location may be termed empyema. An **air-fluid level** is seen in the stomach below the dome of the left diaphragmatic leaf.
Here is an example of bilateral pleural effusions. Note that the fluid appears reddish, because there has been hemorrhage into the effusion. This is a serosanguinous effusion.
The **milky white** fluid shown here in the peritoneal cavity represents a **chyloous ascites**. This is an uncommon fluid accumulation that can be due to blockage of lymphatic drainage, in this case by a malignant lymphoma involving the mesentery and retroperitoneum.
Collection of fluid in a space is a transudate. If this fluid is protein-rich or has many cells then it becomes an exudate.

The large amount of fibrin in such fluid can form a fibrinous exudate on body cavity surfaces. Here, the pericardial cavity has been opened to reveal a fibrinous pericarditis with strands of **Stringy pale fibrin** between visceral and parietal pericardium.
Microscopically, the fibrinous exudate is seen to consist of pink strands of fibrin jutting from the pericardial surface at the upper left. Below this, there are a few scattered inflammatory cells.
This yellow-green exudate on the surface of an inflamed, hyperemic (erythematous) bowel mucosa consists of many neutrophils along with fibrin and amorphous debris from dying cells.
Here is a purulent exudate in which the exuded fluid also contains a large number of acute inflammatory cells. Thus, the yellowish fluid in this opened pericardial cavity is a **purulent exudate**.
A purulent exudate is seen beneath the meninges in the brain of this patient with acute meningitis from *Streptococcus pneumoniae* infection. The exudate obscures the sulci.
The abdominal cavity is opened at autopsy here to reveal an extensive purulent peritonitis that resulted from rupture of the colon.

A thick yellow exudate coats the peritoneal surfaces. A paracentesis yielded fluid with the properties of an exudate: high protein content with many cells (mostly PMN's).
The PMN's seen here are in alveoli, indicative of an acute bronchopneumonia of the lung. The PMN's form an exudate in the alveoli. This patient had a "productive" cough because large amounts of purulent sputum were produced. The source, the neutrophilic alveolar exudate, is seen here.
This radiograph demonstrates patchy infiltrates consistent with a bronchopneumonia from a bacterial infection. Typical organisms include *Streptococcus pneumoniae*, *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Hemophilus influenzae*, *Klebsiella pneumoniae*, among others.
The **neutrophils** are seen infiltrating the mucosa and submucosa of the gallbladder in this patient with acute cholecystitis and right upper quadrant abdominal pain with tenderness on palpation.
At medium power magnification, numerous neutrophils fill the alveoli in this case of acute bronchopneumonia in a patient with a high fever. *Pseudomonas aeruginosa* was cultured from sputum. Note the **dilated capillaries** in the alveolar walls from vasodilation with the acute inflammatory process.
The white arrows mark areas of abscess formation in the upper lobe of this lung. The liquefactive necrosis of an abscess is apparent, because the purulent contents are draining out to leave a cavity. On a chest radiograph, the liquefied central contents of an abscess can appear as an "air-fluid level".
Much smaller abscesses are seen here. These could be termed "microabscesses" due to their small size. Abscesses can come in a variety of sizes. Perhaps the most common abscess is the pimple on the face of a teenager.
An abscess is a localized collection of PMN's. Here is a microabscess in the myocardium. The irregular dark purple center is a collection of bacteria that are the cause for this abscess.
This abscessing bronchopneumonia has numerous areas of raised, lighter tan appearance which are the areas containing the extensive neutrophilic infiltrates.
Microscopically, the extensive neutrophilic exudate of an acute abscessing pneumonia is seen here. Normal tissues are destroyed in the region of the abscess.
Here is another more focal abscess in the lung. The alveoli in that area have been destroyed.
One consequence of acute inflammation is ulceration. This occurs on epithelial surfaces. Here the gastric mucosa has been lost, or ulcerated. A larger ulcer and several adjacent smaller ones with surrounding erythema appear at the left of center.
This is a larger ulceration. The cause for the ulceration in this case was an underlying neoplasm.
Below the vocal cords in this larynx are **large ulcerations**. Such subglottic ulcers are produced with prolonged endotracheal intubation in which the cuff of the endotracheal tube fits too tight. Thus, ulcerations can be produce by mechanical forces. In fact, so-called "pressure ulcers" or "decubitus ulcers" can form on skin over bony prominences in persons who are bedridden for an extended time.
An esophageal acute ulcer is shown here in which the squamous mucosa has been lost. In the ulcer base are **inflammatory cells and fibrin**.
This patient had diabetes mellitus for many years. This disease leads to marked atherosclerosis with arterial narrowing.

When peripheral arteries to the legs are involved, then ischemia of soft tissues and bone occurs. Even minor trauma leads to ulceration that heals poorly and often becomes secondarily infected. A transmetatarsal amputation has already been performed in this patient because of the severity of peripheral vascular disease.
Chronic inflammation is more difficult to understand, because it is so variable.

Seen here is chronic endometritis with **lymphocytes** as well as **plasma cells** in the endometrial stroma. In general, the inflammatory infiltrate of chronic inflammation consists mainly of mononuclear cells ("round cells"): **lymphocytes**, **plasma cells**, and **macrophages**.
Here is **chronic cervicitis**.
Prolonged acute inflammation or repeated bouts of acute inflammation may lead to the appearance of more mononuclear cells, and chronic inflammation. In this case the inflammation is severe enough to produce mucosal damage with hemorrhage.
Chronic inflammation can go on for a long time: weeks to months to years. Seen here in the **synovium** from the joint of a patient with rheumatoid arthritis are collections of dark blue lymphocytes.
Certain etiologic agents such as viruses are more likely to lead to chronic inflammation, as seen here in the lung of a patient with influenza A. Note also that the inflammatory infiltrates of chronic inflammation are more likely to be interstitial (within tissues) rather than exudative (above surfaces or in spaces) like acute inflammation.
Microscopically, this abscess has a mixture of inflammatory cells, but the wall of the abscess is "organizing" with ingrowth of capillaries (filled with red blood cells) and fibroblasts.

As organization continues there is resolution with decreasing size of the abscess, until only a scar remains. If the body's defensive systems cannot contain the agent causing the abscess, then the process may continue and even spread.
Healing of inflammation often involves ingrowth of capillaries and fibroblasts. This forms granulation tissue. Here, an acute myocardial infarction is seen healing. There are numerous capillaries, and collagen is being laid down to form a scar.
The wall of an abscess that is organizing has **granulation tissue**.

The **purulent exudate** with some hemorrhage is seen at the right in the abscess center.
At high magnification, granulation tissue has **capillaries**, **fibroblasts**, and a variable amount of **inflammatory** cells (mostly **mononuclear**, but with the possibility of some **PMN**'s still being present).
The end result of inflammation can be **scarring**. Here, the alveolar walls are thickened and filled with **pink collagen** following an autoimmune disease lasting for decades.
Resolution of inflammatory processes in body cavities may result in the formation of **adhesions**.

Thin bands of collagenous connective tissue, as seen here between the **right lung** and the **chest wall** at autopsy. Adhesions, if extensive can restrict motion or cause retraction to an abnormal position of internal organs.
This is a healing biopsy site on the skin seen a week following the excision. The skin surface has re-epithelialized, and below this is granulation tissue with small capillaries and fibroblasts forming collagen. After a month, just a small collagenous scar will remain.
The focal nature of granulomatous inflammation is demonstrated in this microscopic section of lung in which there are scattered granulomas in the parenchyma. This is why the chest radiograph with tuberculosis or other granulomatous diseases is often described as "reticulonodular". A biopsy could miss such lesions from sampling error, too.
Here are two pulmonary granulomas. Granulomatous inflammation typically consists of mixtures of cells including epithelioid macrophages, giant cells, lymphocytes, plasma cells, and fibroblasts. There may even be some neutrophils.
Granulomatous inflammation occurs in response to some agents which persist for a long time and require a more orchestrated immune response to fight them.

The granuloma seen here demonstrates the typical rounded and focal nature of this type of inflammation. A couple of spherules of *Coccidioides immitis* are present in the giant cell in the center.
Giant cells are a "committee" of epithelioid macrophages. Seen here are two **Langhans type giant cells** in which the nuclei are lined up around the periphery of the cell. Additional pink epithelioid macrophages compose most of the rest of the granuloma.
These are *epithelioid cells* around the center of a granuloma. They get their name from the fact that they have lots of pink cytoplasm similar to squamous epithelial cells. Their nuclei tend to be long and stringy.
This is a caseating granuloma. Epithelioid cells surround a central area of **necrosis** that appears irregular, amorphous, and pink. Grossly, areas of caseation appear cheese-like.
Here is a **foreign body type giant cell** at the upper left of center adjacent to a segment of vegetable material aspirated into the lung. Such foreign body giant cells have nuclei scattered haphazardly about the cell.
Two foreign body giant cells are seen just to the right of center where there is a bluish strand of suture material from a previous operation.
Seen under polarized light are numerous bright white crystals of talc in a patient who was an intravenous drug user. The injected drug was diluted with the talc. Such foreign material can produce a granulomatous reaction.
Sometimes the inflammatory reaction is mainly one of scarring, as seen here with a *silicotic nodule* of the lung. The inhaled silica persists indefinitely and produces an inflammatory reaction that is marked by prominent fibrosis. Dense pink collagen is seen in the center of the nodule.
The next Lab. Is Neoplasia