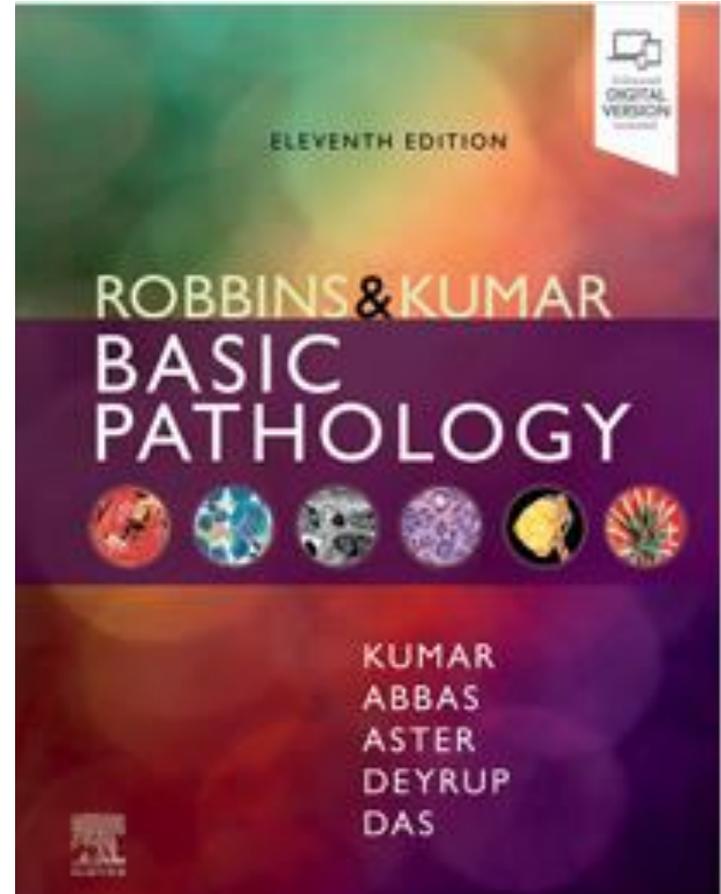


A close-up, shallow depth-of-field photograph of a microscope. The objective lens is in sharp focus, pointing down at a glass slide on the stage. The background is a soft, out-of-focus mix of blue and white light.

Introduction to Pathology

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Main Reference in
our course is



Pathology



The field of pathology is dedicated to understanding the causes of disease and the changes in cells, tissues and organs that are associated with development of disease.



Thus, pathology provides the scientific foundation for the practice of medicine.



There are two important terms that students will encounter throughout their study of pathology and medicine:



1- **Etiology:** is the origin of a disease, including the underlying causes and modifying factors. Notably, many common diseases, such as hypertension, diabetes, and cancer, are caused by a combination of inherited genetic susceptibility and various environmental triggers.



2- **Pathogenesis:** refers to the steps in the development of disease, from the initial etiologic trigger to the cellular and molecular changes that give rise to the specific functional and structural abnormalities which characterize any particular disease.



To render diagnoses and guide therapy in clinical practice, pathologists identify changes in the gross or/and microscopic appearance (morphology) of cells and tissues and in their constituents (e.g., genes and proteins), as well as biochemical alterations in body fluids (such as blood and urine).



Defining these alterations in diseased tissues aids in diagnosis as well as in predicting outcomes and optimal therapies.

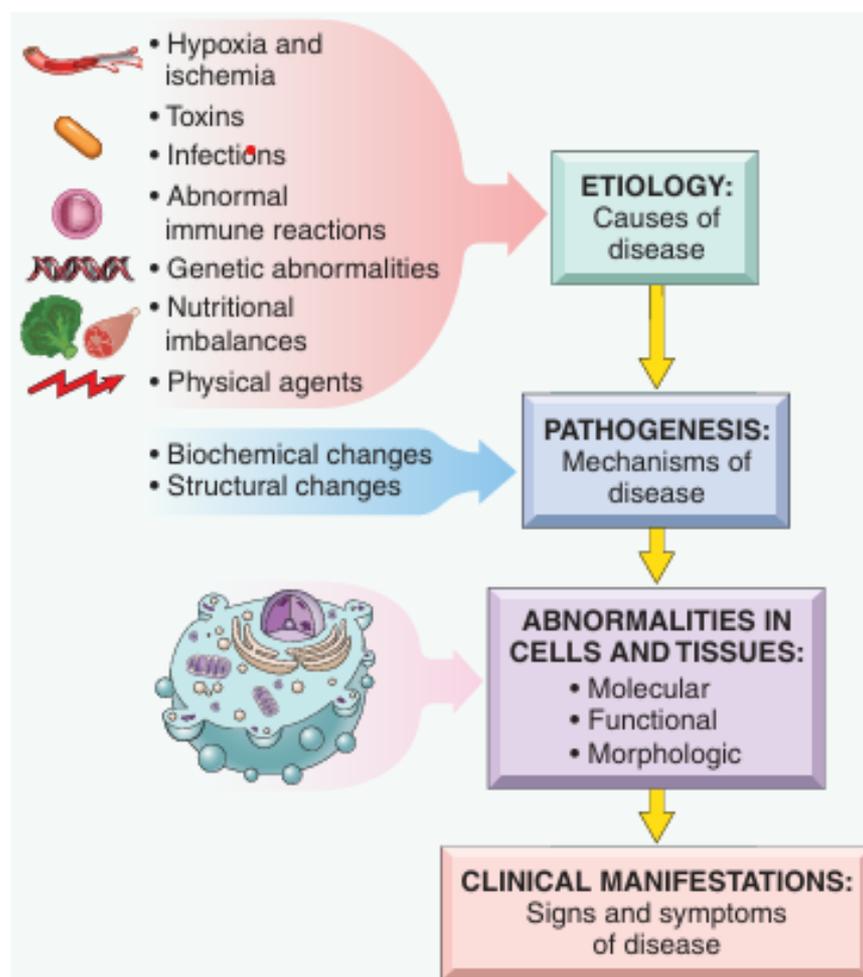


FIG. 1.1 Steps in the development of disease. Only some of the major etiologies are shown.

Morphology is structural alteration of cell and tissue as a result of the pathogenesis:

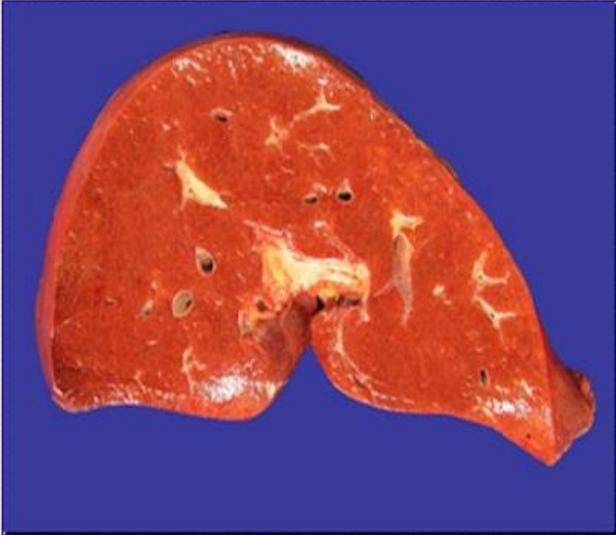
+ **Gross** : naked eye

+ **Microscopic**

+Pathologists also use a variety of molecular, and other techniques to define the biochemical, structural, and functional changes that occur in cells, tissues, and organs in response to injury.

Morphology, Gross (Naked eye)

Normal

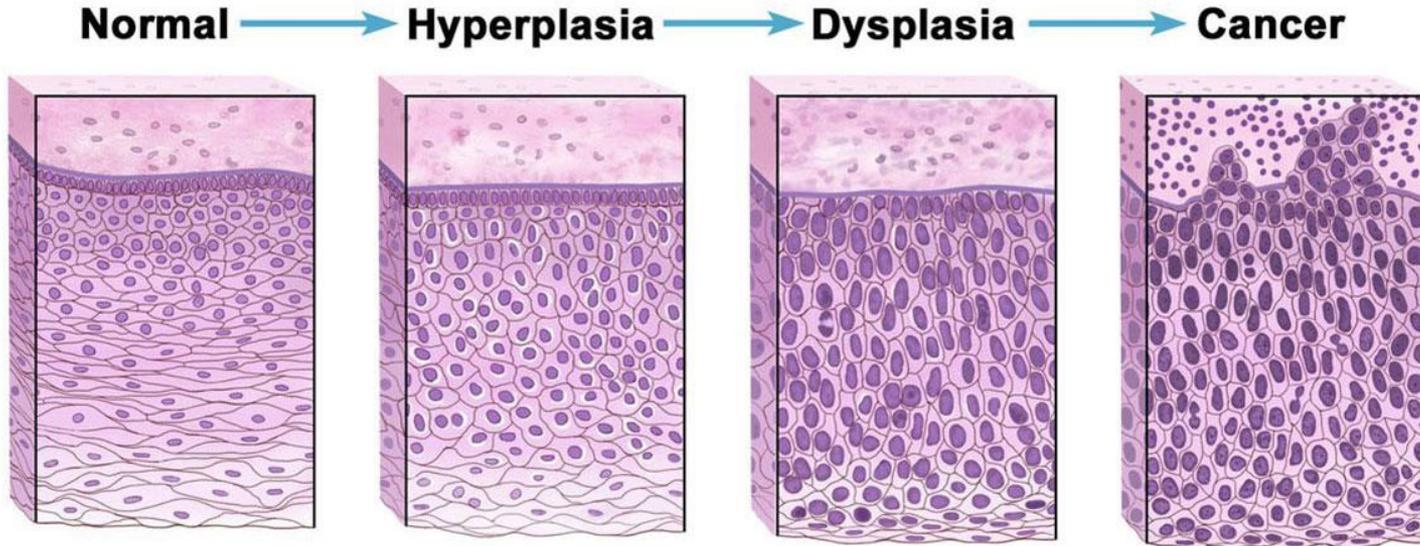


Cirrhosis



Nodules

Morphology, microscopic





**So, what do
pathologist
do?**

The Sample .. What do we get?

Biopsy, like :

- Bone marrow biopsy
- Cardiac biopsy
- Core biopsy
- Endometrial biopsy, D&C
- Endoscopic biopsy
- Bronchoscopic biopsy
- Excisional and incisional biopsy
- Lymph node biopsy
- CT guided Needle biopsy
- Punch biopsy
- Shave biopsy...etc

```
graph TD; A[Resections, like :  
Hysterectomy,  
colectomy... etc] --> B[Fluid and Cytology: Pleural  
effusion , bone marrow  
aspirate, CSF...etc]; B --> C[Blood film];
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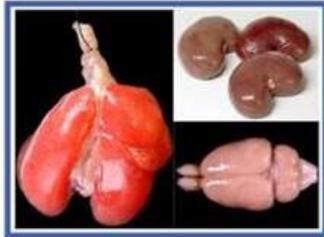
Resections, like :
Hysterectomy,
colectomy... etc

Fluid and Cytology: Pleural
effusion , bone marrow
aspirate, CSF...etc

Blood film

Grossing





Fixing



TP1020 Automatic Tissue Processor



Processing



EG1160 Paraffin Embedding Center



Embedding



RM2235 Rotary Microtome



VT1000S Vibrating-blade Microtome



Cutting

Leica CM 1900 Cryostat



Staining



Leica AutoStainer XL

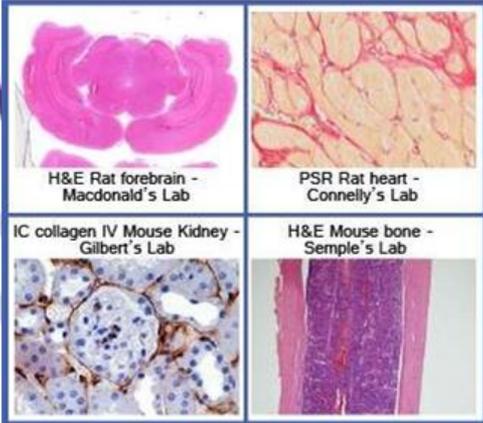


Microscopy



Olympus IMT-2 Microscope

Specimen journey in pathology lab



H&E Rat forebrain - Macdonald's Lab

PSR Rat heart - Connelly's Lab

IC collagen IV Mouse Kidney - Gilbert's Lab

H&E Mouse bone - Semple's Lab



Diagnosis



+ **General pathology:**

basic concepts that are shared among various disease in multiple organs/systems (Ex: Inflammation, cell injury and neoplasia)

+ **Systematic Pathology:**

discuss pathology of diseases of a specific organs/systems

Anatomical pathology

- +Cytopathology
- +Dermatopathology
- +Forensic pathology
- +Histopathology
- +Neuropathology
- +Pulmonary pathology
- +Renal pathology
- +Surgical pathology
- + GYN and Breast pathology

Clinical pathology

- +Hematopathology
- +Immunopathology
- +Radiation pathology

Molecular pathology

**anatomy,
physiology,
biochemistry,
pharmacology,
microbiology,
..etc**

Pathology

**medicine ,
surgery,
orthopedic,
gyne-obs,
pediatrics,
ENT,
Psychiatry,
Radiology**



OVERVIEW OF CELLULAR RESPONSES

OVERVIEW OF CELLULAR RESPONSES TO STRESS AND NOXIOUS STIMULI

Cells actively interact with their environment, constantly adjusting their structure and function to accommodate changing demands and extracellular stresses in order to maintain a steady state, a process called **homeostasis**.

As cells encounter physiologic stresses or injurious stimuli, they can undergo **adaptation**, achieving a new steady state and preserving viability and function.

If the adaptive capability is exceeded or if the external stress is inherently harmful, **cell injury** occurs.

Within certain limits, injury is reversible, and homeostasis is restored; however, if the stress is severe or persistent, it results in irreversible injury and death of the affected cells.

CAUSES OF CELL INJURY

- Hypoxia and ischemia. Hypoxia refers to oxygen deficiency, and ischemia means reduced blood supply. These are among the most common causes of cell injury.

The most common cause of hypoxia is ischemia resulting from blockage of an artery, but it can also result from inadequate oxygenation of the blood, as in diseases of the lung, or from reduction in the oxygen-carrying capacity of the blood, as with anemia of any cause.

- Toxins.

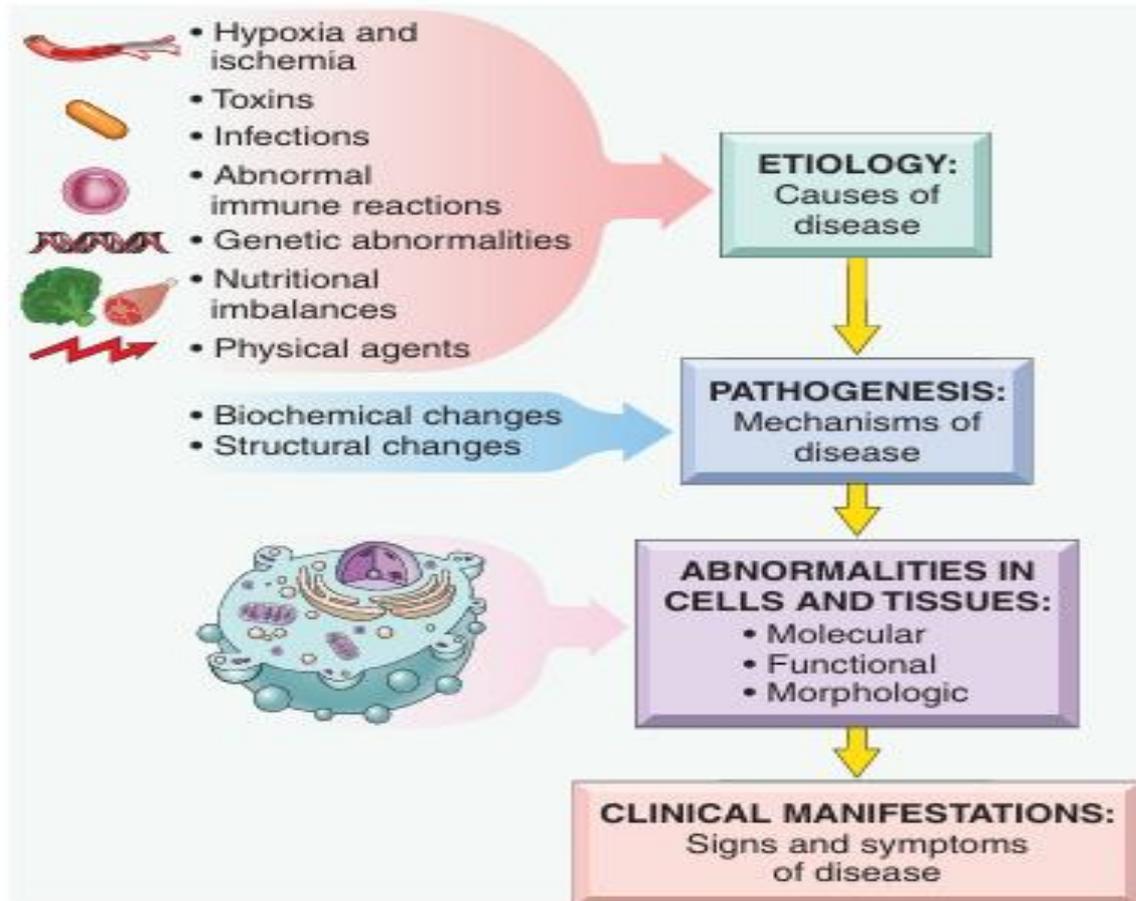
- Infectious agents.

- Immunologic reactions.

- Genetic abnormalities.

- Nutritional imbalances.

- Physical agents.



Steps in the development of disease. Only some of the major etiologies are shown.

SEQUENCE OF EVENTS IN CELL INJURY AND CELL DEATH

- Reversible Cell Injury
- Irreversible Cell Injury
- Other processes that affect cells and tissues, the deposition of abnormal substances and cell aging.

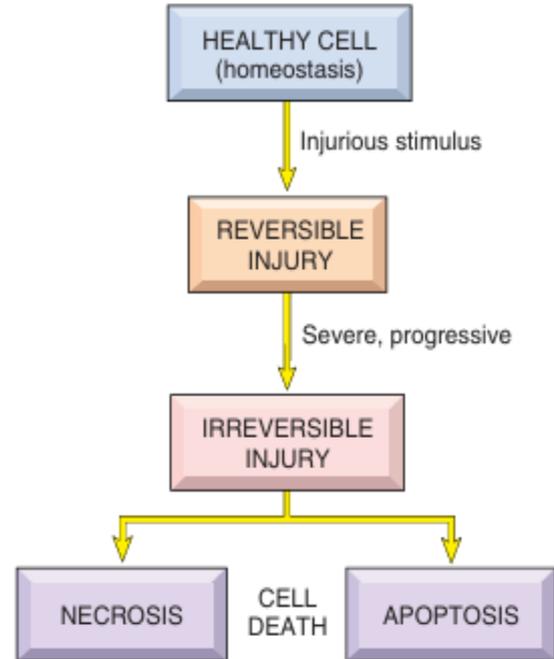


FIG. 1.2 Sequence of reversible cell injury and cell death.

Reversible Cell Injury

- Reversible cell injury is defined as a derangement of function and morphology that cells can recover from if the damaging stimulus is removed.

Morphology

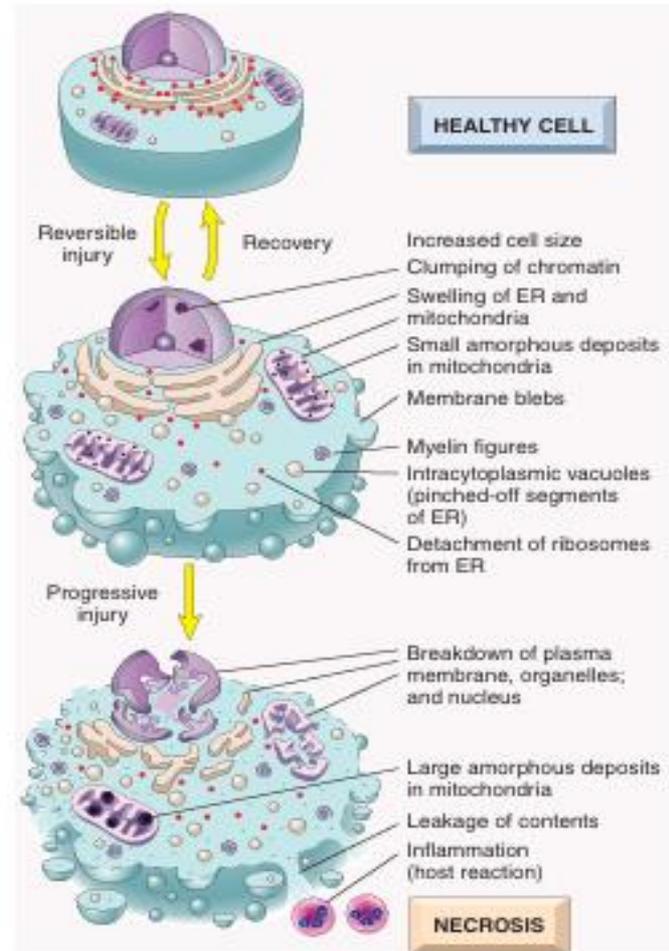
- The two most consistent morphologic correlates of reversible cell injury are cellular swelling and fatty change.
- **Cellular swelling** is commonly seen when cells are injured by hypoxia, toxins, and other causes. This pattern of nonlethal injury is sometimes called hydropic change or vacuolar degeneration.
- **Fatty change** is manifested by the appearance of lipid vacuoles in the cytoplasm. It is principally encountered in organs that are involved in lipid metabolism, such as the liver

Cellular swelling

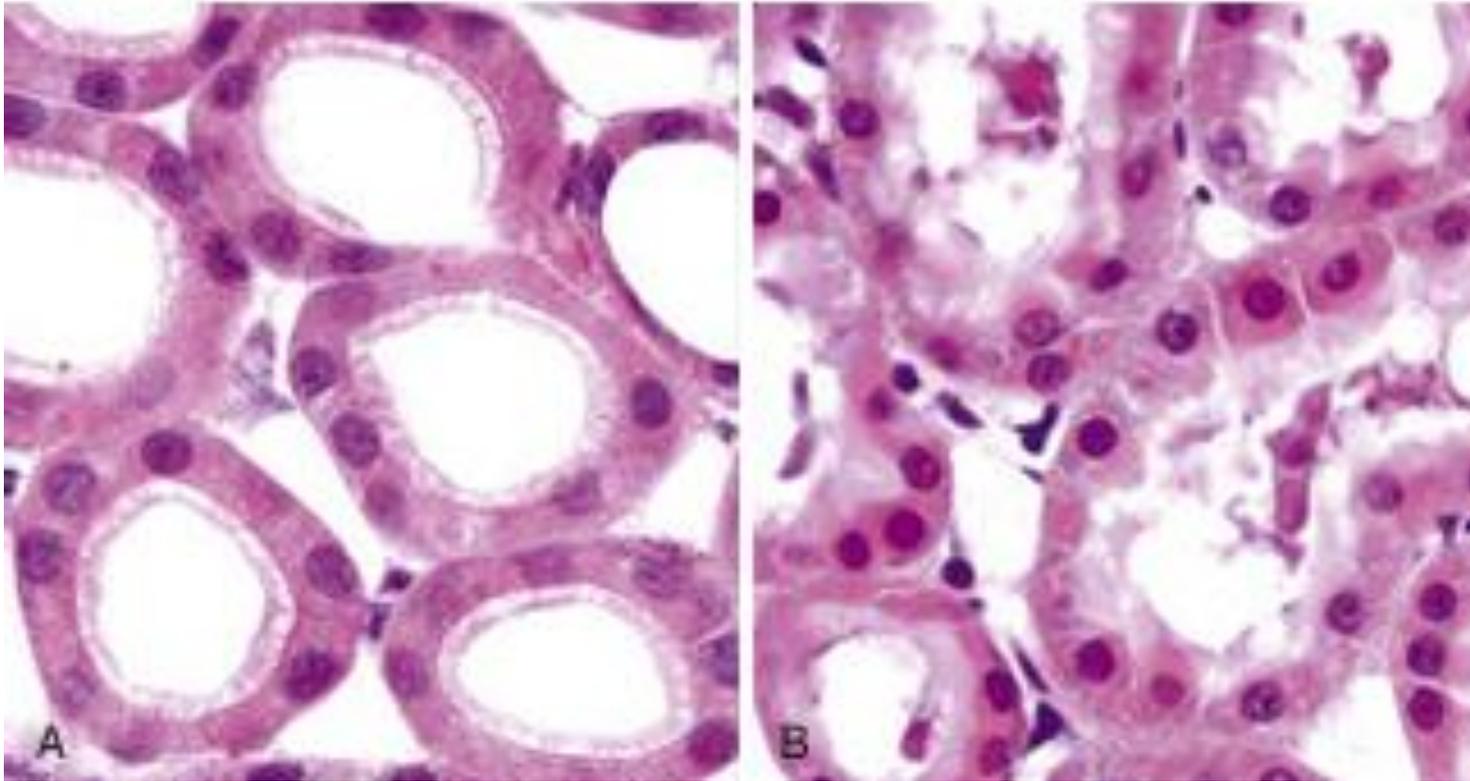
- It may be difficult to appreciate with the light microscope (since fluid from cells is extracted during tissue processing) but is often apparent grossly when the whole organ is examined.
- When many cells in an organ are affected, there can be pallor (due to compression of capillaries), increased turgor, and increased organ weight.
- Microscopic examination may reveal small, clear vacuoles within the cytoplasm; these represent distended and pinched-off segments of the endoplasmic reticulum (ER).

Cellular swelling

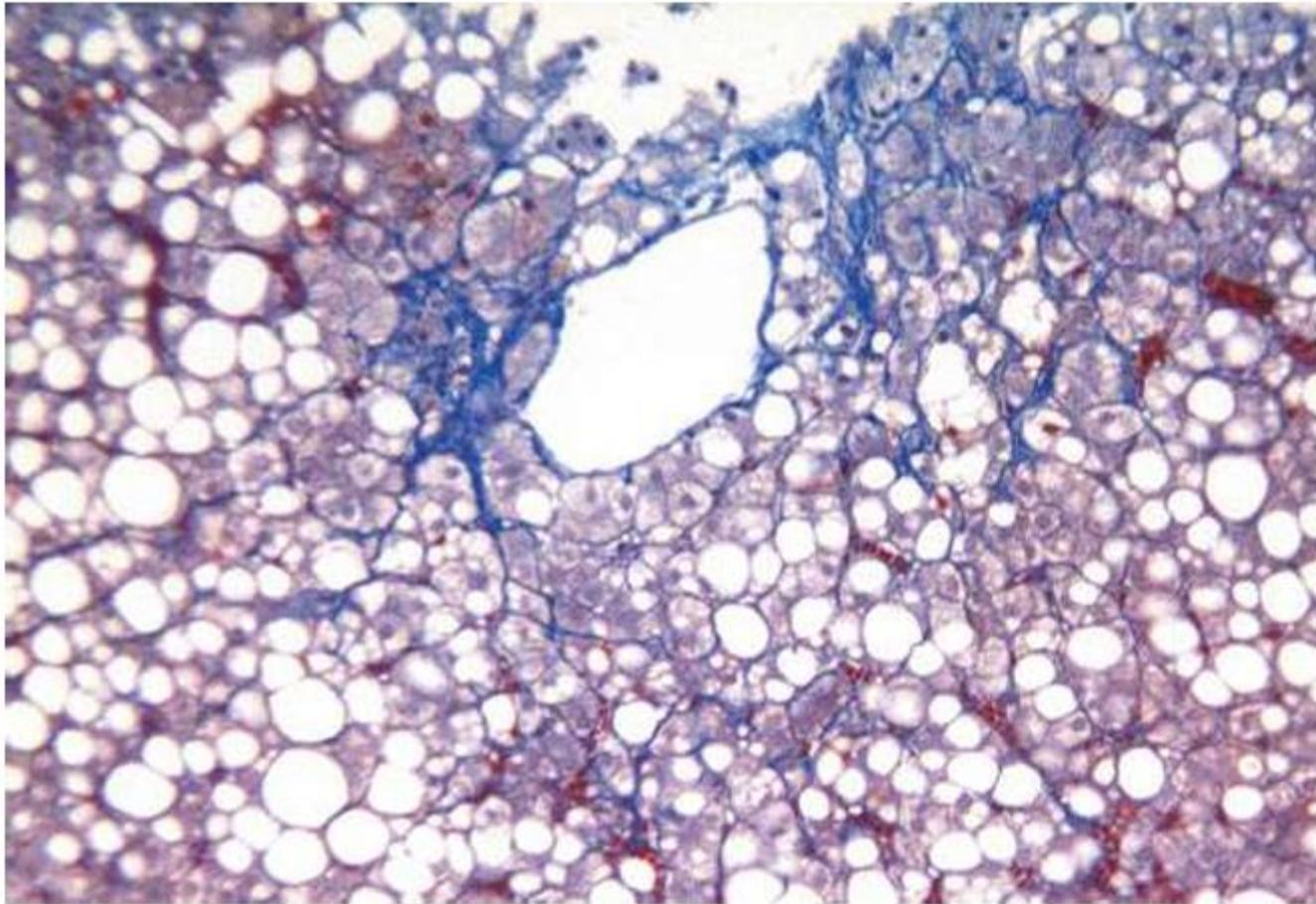
- The cytoplasm of injured cells also may become **redder** (eosinophilic, meaning stained red by the dye eosin in the hematoxylin and eosin [H&E] stain)
- Other intracellular changes associated with cell injury, which are best seen by electron microscopy include:
 - (1) plasma membrane alterations such as blebbing, blunting, or distortion of microvilli, and loosening of intercellular attachments
 - (2) mitochondrial changes such as swelling and the appearance of phospholipid-rich amorphous densities
 - (3) dilation of the ER with detachment of ribosomes and dissociation of polysomes
 - (4) nuclear alterations, with clumping of chromatin. The cytoplasm may contain so-called **myelin** figures, collections of phospholipids resembling myelin sheaths that are derived from damaged cellular membranes.



Reversible cell injury and necrosis. The principal cellular alterations that characterize reversible cell injury and necrosis are illustrated. If an injurious stimulus is not removed, reversible injury culminates in necrosis.



Morphologic changes in reversible cell injury. (A) Normal kidney tubules with viable epithelial cells. (B) Early (reversible) ischemic injury showing surface blebs, increased eosinophilia of cytoplasm, and swelling of occasional cells.



Fatty liver disease associated with chronic alcohol use. A mix of small and large fat droplets (seen as clear vacuoles) is prominent.

“Point of no return”

Persistent or excessive injury causes injured cells to pass the nebulous “point of no return” and undergo cell death, typically by the process of necrosis.

Although there are no definitive morphologic or biochemical correlates of irreversible injury, it is consistently characterized by three phenomena:

- The inability to restore mitochondrial function (oxidative phosphorylation and adenosine triphosphate [ATP] generation) even after resolution of the original injury.
- Altered structure and loss of function of the plasma membrane and intracellular membranes.
- The loss of structural integrity of DNA and chromatin. As discussed in more detail later.